Volume 4: Issue 2
June 2021

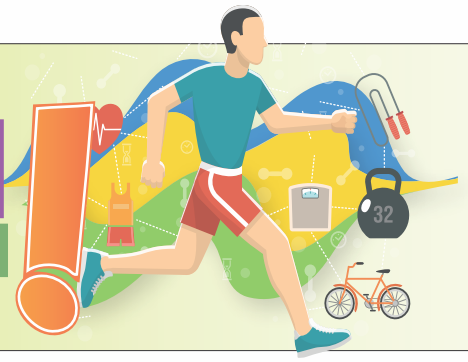
Sri Lankan Journal of Cardiology

An official publication of the
Sri Lanka College of Cardiology (SLCC)

ROLIP

Rosuvastatin 5,10 & 20 mg Tablet

FROM ACTION to PREVENTION



- Robust risk reduction in CVD
- Effectively rises HDL-C
- First Line treatment in primary prevention
- Recommended by 2019 ACC / AHA Guideline

Working Towards a Healthy Future...

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The scope of this journal will be broadly based in order to realize three objectives.

First and foremost, the objective is to publish high quality research which deals with problems which are of universal relevance but with greater focus on work targeting locally relevant problems.

Secondly, the journal will be a forum for cardiologists and other specialists to share their clinical experiences via case reports. Most cardiologists have cases worth reporting for their value in providing insights into pathophysiology, guiding selection of therapeutic pathways and shedding light on problem solving. The journal will encourage such case reports.

The third objective is for this publication to be a fruitful avenue of Continuing Medical Education (CME). The lack of time should not be a limiting factor to assimilate knowledge. The journal will utilize reviews, tutorials, journal scans and updates to provide a well-balanced CME course in Cardiology.

ISSN 2630-7596

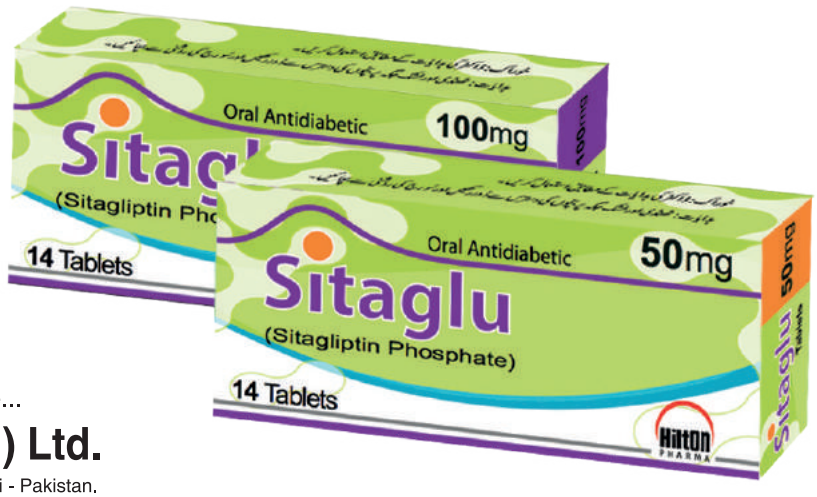
Sitaglu

Sitagliptin Phosphate

Tablet
50mg & 100mg

4 Goals one TREE Therapy

- Tolerability
- Reliability
- Efficacy
- Endorsements



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Cardiac Care-Triage-Priority and Protection (CTPP) Guidance for Cardiology Units in Sri Lanka where Potential COVID Patients Present with Cardiovascular Diseases

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2) causing coronavirus disease 2019 (COVID-19) has reached global pandemic levels. Patients with cardiovascular (CV) risk factors and established cardiovascular disease (CVD) have higher rates of adverse outcomes when infected with COVID-19. Here the authors suggest a Cardiac Care - Triage – Prioritization - Protection (CTPP) guidance to the cardiology specialty units to continue / function their services and procedures optimally during COVID pandemic. This guidance has identified 7 main cardiac care settings and out of them the ambulatory cardiac care setting is further divided into 7 sub-services provided in Sri Lanka. This document gives a quick reference guidance on initially how to triage, then how to prioritize the care depending on clinical needs of the patient, while exercising and maintaining optimum protection of care giver, care giving environment and patient to minimize transmission of SARS-CoV 2 virus during the pandemic.

This guidance identifies and clarifies the types of the cardiac services and procedures that are feasible / appropriate to carry out and the procedures that may be deferred based on the 3 epidemic impact states of COVID-19 spread in Sri Lanka subject to resource availability.

Cardiac Care Settings in Sri Lanka

For Sri Lanka, the following 7 cardiac care settings are identified for cardiovascular disease (CVD) patients presenting with potential COVID-19 positive status.

Following guidance is given to the Health Care Worker (HCW) for cardiology Care - Triage - Prioritization - Protect (CTPP) at these points of care (Table 1). Further guidance is given regarding **operational restrictions** in these settings according to **the level of COVID epidemic status in Sri Lanka** and **the level of protective measures** the HCW should adhere to in each setup.

Table 1 | Seven cardiac care settings identified in Sri Lanka.

A). Ambulatory Settings (Has 7 sub-services functioning as follows)

1) Specialist clinics, **2)** General clinics, **3)** 2D Echocardiography, **4**) Exercise ECG, **5)** Dobutamine Stress Echocardiography - DSE, **6)** 24-hour studies (Holter and ambulatory blood pressure), **7)** CT Coronary Angiography / MRI / Nuclear cardiac imaging services.

B) Ward Setting

C) Emergency Department (A&E/ED/ETU/PCU/OPD)

D) Intensive Care Unit (CCU/ICCU/MICU/SICU/ICU)

E) Catheterization Laboratory

F) Electrophysiology Laboratory

G) High risk aerosol generating procedures

- **Transesophageal Echocardiography (TOE)**
- **Continuous Positive Airway Pressure (CPAP)**
- **Orotracheal Intubation of patients and cardiac arrest situations**

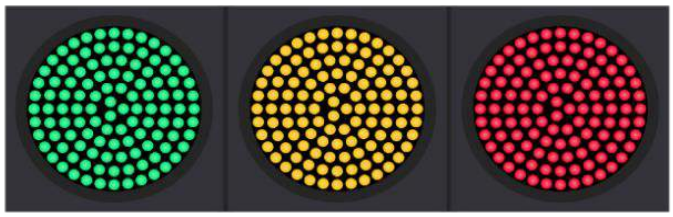
Abbreviations | CTCA: CT Coronary angiogram**, CCU**: Coronary Care Unit, **ICCU**: Intermediate Coronary Care Unit, **MICU** -Medical Intensive Care Units, **SICU** – Surgical Intensive Care Unit, **ICU** – Intensive Care Unit, **A&E** – Accident and Emergency, **ED** – Emergency Department, **ETU**- Emergency Treatment Unit, **PCU** – Preliminary Care Unit, **OPD** - Outpatient Patient Department

CARE RESTRICTIONS

"The degree of COVID-19 spread adversely affects the health care delivery forcing restrictions on usual cardiac care services"

Three levels of **anticipated impact of the epidemic on usual cardiac care services are identified. (Figure 1)**

Figure 1 | Anticipated impact of the epidemic on usual cardiac care services



A). Marginal impact colour coded -Green.

B). Moderate impact colour coded -Amber

C). Heavy impact colour coded -Red.

Four levels of spread of the epidemic within the community are also identified:

Pandemic Level 1 (P1) No community spread, colour coded **Green.**

Pandemic Level 2 (P2) Sporadic cases, colour coded **Green.**

Pandemic Level 3 (P3) Community spread beyond districts / provinces, colour coded **Amber.**

Pandemic Level 4 (P4) Severe community spread, colour coded **Red.**

Prioritization

Due to severe constrains on the resources, there is a need to reallocate the available resources taking in to account the clinical urgency of the procedures. The procedures are categorized into four groups according to varying levels of restrictions in terms of time frames to perform a specific procedure. Cardiac care teams led by the consultants should determine the clinical urgency of the procedure in each and individual case (Table 2).

1. **ROU**: All routine procedures carried out without any restriction – colour coded **Green**
2. **LPP < 3**: **L**ow **P**riority **P**rocedures that can be **performed or postponed up to 3 months** as decided by the consultant – colour coded **Amber**
3. **ELP > 3**: **Elective** Procedures that **can be postponed beyond 3 months** as decided by the consultant – colour coded **Amber**.
4. **EM & UR**: Only Emergency & Urgent procedures are performed – colour coded **Red**.

Table 2 | Impact and restriction levels on regular cardiac services and procedures based on the COVID-19 epidemic level in Sri Lanka.

		A	B	C
1	IMPACT ON REGULAR CARDIAC SERVICES	MARGINAL (None or minor restrictions)	MODERATE Major restrictions	HEAVY Inability to provide.
2	EPIDEMIC / COMMUNITY SPREAD LEVEL	Level 1-2 Spread No Community Spread - 1 Only Sporadic Cases - 2	Level 3 spread Community spread beyond districts/provinces. Covid Positive Patients can be logistically managed at Covid Dedicated centers.	Level 4 spread Severe community spread beyond districts/provinces. Influx of Covid Positive Patients to Non covid hospitals /Cardiac settings.
3	LEVEL OF RESTRICTIONS ON CARDIAC PROCEDURES	ROU All routine procedures carried out without any restrictions.	LPP3, ELP >3 LP3 – Low priority Procedures that can be performed or postponed up to 3 months. EL >3 – Elective procedures that can be postponed beyond 3 months.	EM, Ur Em – Emergency cases only (to perform at point of care or within 24 hours). Ur – Urgent procedures (to perform within 72 hours or as in patient).

(A) Ambulatory Cardiac Care Settings

It is advisable to provide an appropriate mask (N95/KN95/Surgical) to every outpatient and Health Care Worker (HCW) as a universal precaution at ambulatory cardiology settings (7 sub settings as explained above) in Sri Lanka to minimize transmission of COVID-19 infection (Figure 2&3). Each ambulatory setting should perform a common triage check list to assess patient's risk status (Table 3 & 4) and avoid overcrowding of potentially COVID-19 infectious patients inside and outside the cardiology ambulatory setting.

Figure 2 | Different levels of protection to HCW according to type of procedure and level of risk. [1]

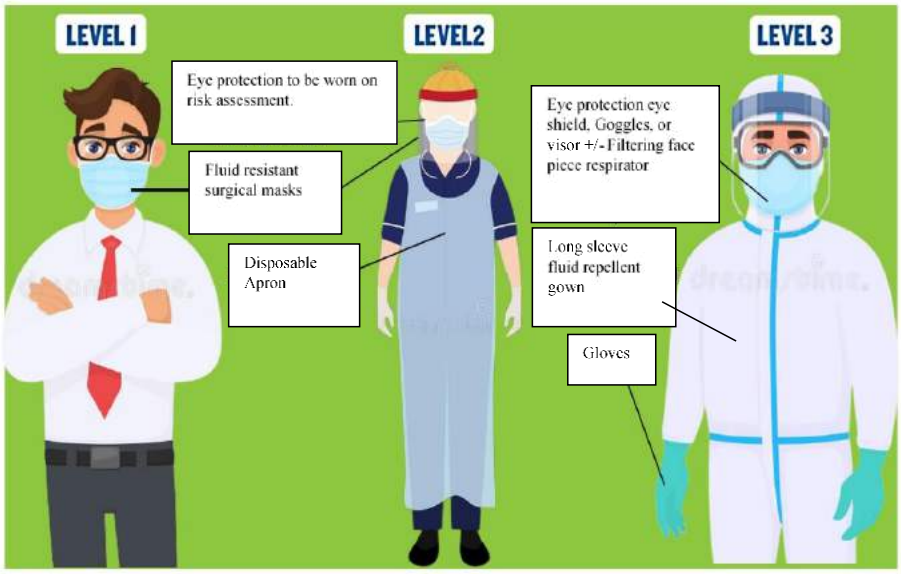


Table 3 | General recommendations for Health Care Worker (HCW) with adaption differentiated to local community level of risk and containment strategies. [1]

Monitor and record the health status, including body temperature and respiratory symptoms, of all health care personnel.
In case of any relevant symptom, HCW should be isolated immediately, withdrawn from patient care activities, and nasopharyngeal swab for rapid antigen test (RAT) or reverse transcription polymerase chain reaction (RT-PCR) should be performed.
Symptoms compatible with SARS-cov-2 infection include: [6,7] ✓ Fever (>37.2 C, may be intermittent or may not be present in some patients) ✓ Cough ✓ Shortness of breath ✓ Sore throat ✓ Anosmia and/or ageusia (loss of smell and/or taste) ✓ Muscle aches ✓ Nausea and /or vomiting. ✓ Diarrhoea ✓ Abdominal pain ✓ Headache ✓ Runny nose ✓ Fatigue
It is advisable that HCW **always** wear an appropriate mask (N95/KN95/Surgical) in hospital facilities (at least at epidemic / community spread level 3-4).
Use Level II or III protective masks (FFP2, FFP3 or N95) when assessing a probable/suspected case or managing a confirmed case. Emphasize hand hygiene; limit the numbers of staff providing patient care, implement personal protective equipment (PPE) optimization strategies.
Health Care Worker (HCW) should try to avoid transmission to their family members (hygiene measures, physical distancing, hand washing) particularly if they live with persons at risk (e.g. elderly, patients with multiple morbidities). In case of shortage of medical-grade masks, they could use home-made mask **at home**.
Limit how virus can enter the hospital to reduce the infection risk for both HCWs and patients: cancel elective outpatient visit, use telemedicine, when possible, limit hospital entrance points and number of care givers, well separated in-hospital pathways should be organized even when the risk is reduced to separate SARS-COV-2- positive patients from negative patients.
Observe social distancing rules inside the hospital.
Relevant precautions should be taken locally to limit COVID-19 exposure to HCWs with co morbidities and /or pregnancy.
It is strongly recommended that immunization for COVID-19 infection of the HCWs and his/her immediate members at risk.

Table 4 | Patient risk status [1,5]

Confirmed case	**A person with laboratory confirmation of SARS-CoV-2 infection, irrespective of clinical signs and symptoms.**
Probable case	A) A suspected case for whom testing for the SARS-Cov-2 virus is inconclusive, **OR** B) A suspected case for whom testing could not be performed for any reason
Suspected case	A) A patient with fever or at least one sign/symptom compatible with SARS-Cov-2 infection AND a history of travel to OR residence in a location reporting community transmission of COVID-19 during the 14 days prior to symptom onset. **OR** B) A patient with fever or at least one sign/symptom compatible with SARS-CoV-2 infection AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to symptom onset, **OR** C) A patient with severe acute respiratory disease AND requiring hospitalization AND in the absence of an alternative diagnosis that fully explains the clinical presentation.
Negative case	A) A person without COVID-19 symptoms who had contacts with a confirmed or probable COVID-19 case and has a negative SARS-CoV-2 test, **OR** B) A suspected case with two negative SARS-COV-2 tests, **OR** C) COVID-19 patient who recovered from COVID-19 infection who has two negative tests with an interval between the two tests of at least 48h

Definition of a Contact [1,5]

A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:

- Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes.
- Direct physical contact with a probable or confirmed case.
- Direct care of a patient with probable or confirmed SARS-CoV-2 infection without using proper personal protective equipment.

  OR

- Other situations as indicated by local risk assessments.

This will allow distinguishing of two types of patients.

a) **Probable/suspected case →** should/ideally be managed/reviewed in a dedicated ambulatory setting with HCW protection level II

b) **Not probable/suspected or negative case →** can be managed in a common ambulatory setting with HCW protection level I

In a busy clinic setting where only common ambulatory setting is available to see **non selective patients→** HCW protection Level II or III is recommended.

Patients should always wear appropriate masks at cardiac ambulatory settings (protection level 1) as a universal precaution to minimize community spread of Covid 19 infection (Table 5 and Figure 3).

Table 5 | SARS – CoV-2 related personal protection management. [1,5]

Protection level	Personal Protective Equipment (PPE)	Application setting / procedures
Level I	• Disposable surgical cap • Disposable surgical mask • Work uniform • Latex gloves	• Pre-examination triage, outpatient department (not suspected/non probable SARS-CoV-2 patients) • SARS-CoV-2 negative in-patient
Level II	• Disposable surgical cap • Medical grade protection mask (N95/FFP2) • Work uniform • Gown • Disposable surgical gloves • Goggles	• All suspected/probable or confirmed SARS-CoV-2 patients should wear a disposable surgical mask • Outpatient department (suspected/ probable or confirmed SARS-CoV-2 patients) • Isolation ward and ICU areas • Nasopharyngeal swab • Non-respiratory specimen examination of suspected/probable or conformed SARS-CoV-2 patients • Percutaneous invasive procedures (coronary angiography, PCI, EP procedures) in suspected/probable or confirmed SARS-CoV-2 patients • Cleaning of surgical or diagnostic instruments (TTE/TEE transducers, stethoscope) used in suspected/probable or confirmed SARS-CoV-2 patients
Level III	• Disposable surgical cap • Medical grade protection mask (FFP3) • Work uniform • Gown • Disposable surgical gloves • Full-face respiratory protective devices or powered air-purifying respirator, if available	• TEE in suspected/probable or confirmed SARS-CoV-2 patients • Aerosol generation procedures (AGP) during which the suspected /probable or confirmed SARS-CoV-2 patient may spray or splash respiratory secretions, body fluids or blood

Figure 3 | Different types of masks to be used according to type of procedure and level of risk. [1,5]

- Health Care worker (HCW) should know the correct technique on **donning** (putting on) and **doffing** (removing) the PPE as illustrated in following figures **(Figure 4 & 5).**

Figure 4 | Guidance on donning personal protective equipment (PPE) to manage COVID-19 patients [1]

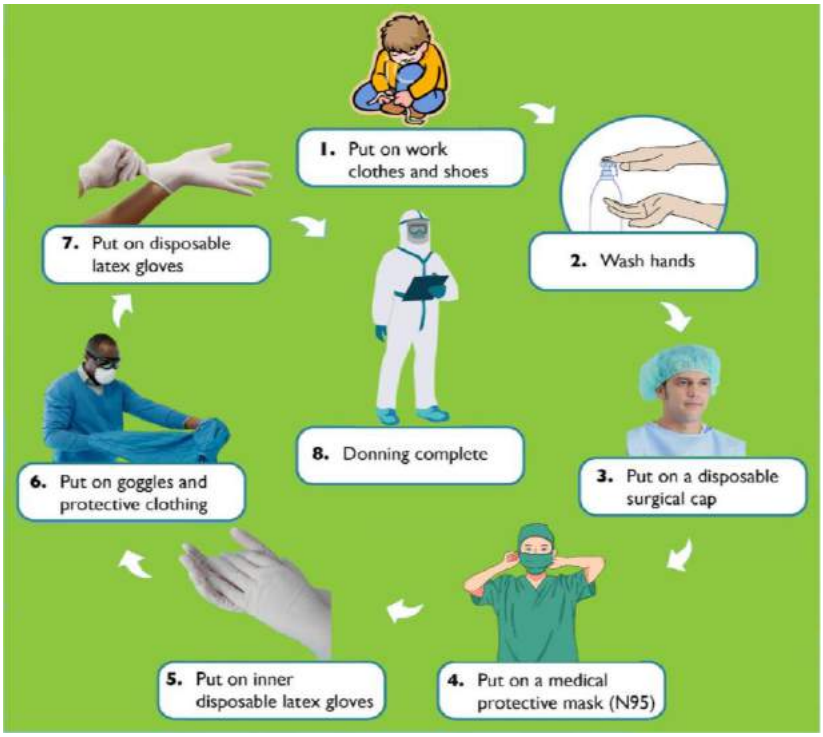
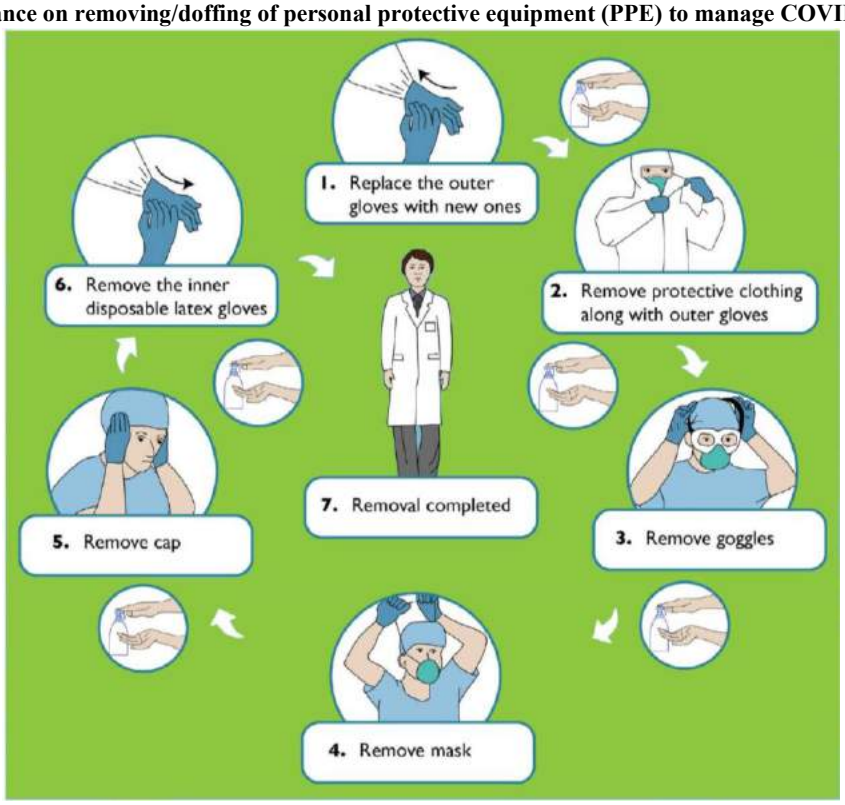


Figure 5 | Guidance on removing/doffing of personal protective equipment (PPE) to manage COVID-19 patients [1]



Ambulatory Cardiac Settings in Sri Lanka and its Triage, Prioritization and Protection (CTPP) Guidance in the Context of Covid 19 Pandemic.

Following are the seven (7) different ambulatory **C**ardiac care sub settings in Sri Lanka. Their services provided with suggested **T**riage, **P**rioritization and **P**rotection (**CTPP**) guidance for the HCW, and patients based on COVID-19 epidemic status of Sri Lanka are illustrated below (Please note that same colour codes are used as illustrated in Table 1). This highlights levels of restriction of services and procedures based on pandemic level 1 (P1) to pandemic level 4 (P4) with the key guidance message for each service.

Table 6 | CTPP guidance at different cardiac ambulatory settings

1:	**Ambulatory setting**	**HCW**	**Patient**
C	**Specialist Cardiology Clinic**	Cardiologist, CEP*, MO*, Nurse, HCA*	New/First visits
T	Triage	Number of consultations per clinic based on staff allocations and pandemic status	All patients should triage for risk evaluations as per table 4
Level of restriction/priority & protection			
P	Priority Based on pandemic level	P1	Perform all
		P2	Perform all and avoid crowding
		P3	Perform limited routine reviews and all urgent referrals
		P4	Stop all
P	Protection	Level II	Level I

2:	Cardiology setting	HCW	Patient
C	**General Cardiology Clinic**	MO*, Nurse, HCA*	Follow up/regular visits
T	Triage	Number of consultations per clinic based on staff allocations and pandemic status	All patients should triage for risk evaluations as per table 4
Level of restriction/priority & protection			
P	Priority Based on pandemic level	P1	Perform all
		P2	Perform all and avoid crowding
		P3	Perform limited routine reviews, facilitate drug dispatch for 1-2 months and perform all urgent reviews, avoid crowding
		P4	Stop all and drug dispatch for 1-2 months
P	Protection	Level II	Level I

3:	Cardiology setting	HCW	Patient
C	**2D echo list**	Cardiologist, MO*, Nurse, HCA*	New & Routine
T	Triage	Number of Echo tests per clinic based on staff allocations and pandemic status	All patients should be triaged for risk evaluations as per table 4
Level of restriction/priority & protection			
P	Priority Based on pandemic level	P1	Perform all
		P2	Perform all and avoid crowding
		P3	Perform limited routine 2D echoes as per staff and space allocations, perform all urgent 2D echoes, avoid crowding
		P4	Stop all routines and perform emergency calls only
P	Protection	Level II or III (if emergency)	Level I

5:	Cardiology setting	HCW	Patient
C	Exercise ECG	MO*, Nurse, Cardiographer	New & Routine
T	Triage	Number of Ex ECG tests based on staff allocations and pandemic status	All patients should triage for risk evaluations as per table 4
Level of restriction/priority & protection			
P	Priority Based on pandemic level	P1	Perform all
		P2	Perform all and avoid crowding
		P3	Stop all and plan an alternative low risk test (CTCA/CA)
		P4	Stop all and plan an alternative low risk test (CTCA/CA)
P	Protection	Level III (if emergency)	Level I

6:	Cardiology setting	HCW	Patient
C	24-hour ambulatory Holter/BP study	MO*, Nurse, Cardiographer	New & Routine
T	Triage	Number of tests based on staff allocations and pandemic status	All patients should triage for risk evaluations as per table 4
Level of restriction/priority & protection			
P	Priority Based on pandemic level	P1	Perform all
		P2	Perform all and avoid crowding
		P3	Stop all routines and perform only urgent calls
		P4	Stop all routines and perform only emergency calls
P	Protection	Level III (if emergency)	Level I

7	Cardiology setting	HCW	Patient
C	DSE/CTCA/MRI/Nuclear imaging	Cardiologist, MO*, Nurse, Cardiographer	New & Routine
T	Triage	Number of tests based on staff allocations and pandemic status	All patients should triage for risk evaluations as per table 4
Level of restriction/priority & protection			
P	Priority Based on pandemic level	P1	Perform all
		P2	Perform all and avoid crowding
		P3	Stop all routines and perform only urgent calls
		P4	Stop all routines and perform only emergency calls
P	Protection	Level III (if emergency)	Level I

*** MO-** ***Medical Officer,*** **NO –** ***Nursing Officer,*** **CEP –** ***Cardiac Electrophysiologist,*** **HCA –** ***Health Care Assistant***

Management of Chronic Coronary Syndromes (CCS) at Cardiac Ambulatory Settings During Covid-19 Pandemic

Uninterrupted continuation of medications in stable CCS patients is highly recommended during COVID-19 pandemic. Maintaining a digital patient database as initiated and facilitated by the Ministry of Health Sri Lanka is highly recommended during this COVID-19 pandemic to identify the patients' demographics, emergency contact details and to maintain updated drug prescriptions. In level 3 and 4 pandemic situations, routine clinic drugs of these patients are suggested to be sent by post to their respective living addresses to minimize crowding and cross contaminations at hospital clinic settings. Symptom follow-up of these CCS patients via tele-health is recommended if facilities permit. Methods such as telephone/video conversations and social media platform can be utilized for this purpose.

Revascularization of CCS patients must be postponed in low to intermediate risk patients. Postponing of non-invasive testing of CCS patients should be considered during COVID-19 pandemic.

CT angiography should be preferred to non-invasive functional testing during COVID-19 pandemic. Screening for SARS-CoV-2 infection should be considered before any cardiac surgery using nasopharyngeal swab and CT scan (chest) where indicated. Revascularization of high-risk CCS patients with high-risk symptoms AND/OR high-risk coronary anatomy AND/OR large area of ischaemia as assessed by Heart team may be considered during COVID-19 pandemic. PCI may be considered over CABG in selected patients during COVID-19 pandemic to shorten hospital stay and keep ICU beds available for patients with COVID-19. Identification of COVID-19 free hospitals may be considered as "Hubs" for cardiac surgery. Invasive management of CCS in SARS-CoV-2 positive patients should be deferred whenever possible until the patient has recovered.

CCS patients are highly vulnerable to have a complication if they contract SARS-CoV-2 infection and should be advised to avoid overcrowding and maintain adequate physical distancing. Further timely vaccination against SARS-CoV-2 infection should be encouraged for CCS patients.

(B) Ward Setting

It is advisable to provide an appropriate mask (N95/KN95/Surgical) to every inpatient and care giver in all cardiology wards. Newly admitted patients in a cardiology ward should be regarded as possibly infected by SARS-CoV-2. In these cases, the patient should undergo a swab test (RAT or PCR) at ETU/OPD on first contact or intermediate/ isolation ward setting before coming to the cardiology ward. If a patient comes without a swab test, a dedicated first contact area in the cardiology department to perform this test should be established before coming into the ward setup. If a patient is critically ill, direct admissions are allowed with HCW adhering to level II/III protection (Table 5). These patients need to be managed in a dedicated isolation area of the cardiology ward if tests are delayed without mixing with other patients. Isolation area in each Cardiology ward need to be identified and prepared well in advance as a surge plan. This should be led by a team comprising of Cardiologist, hospital director (administrative team) and approved by the infection control team (Virologist/Microbiologist). Confirmed cases should be transferred or managed with level II or III protection in a dedicated COVID treatment unit in the same hospital or in a COVID treatment centre ideally with individual isolation capacity or group isolation capacity.

The use of dedicated medical equipment without mixing with other patients (e.g., blood pressure [BP] cuffs, stethoscopes and thermometers) for confirmed / probable / suspected COVID-19 cases is strongly recommended. If not possible, equipment must undergo disinfection according to local instructions.

If the swab test is negative, but suspicion of SARS-CoV-2 infection is maintained, it is advisable to perform either a second swab test / endotracheal aspirate and/or a lung CT scan, depending on local capabilities. These patients should be maintained in a dedicated isolation area of the ward, ideally with a private room and bathroom.

Other cases should be managed with level I protection (Table 5), ideally in the "clean" area of the ward. If there are sufficient resources, there is a benefit in testing patients even without COVID-19 symptoms, in high COVID prevalence areas for all cardiac admissions considering the detrimental risk of transmission of SARS-CoV-2 infection to cardiac patients.

(C) Emergency Department

Cardio Pulmonary Resuscitation (CPR) is an aerosol generating procedure (AGD*)*. It is advisable to provide an appropriate mask (N95/KN95/Surgical) to every emergency department (ED) patient (Figure 1 & 2). The safety of HCW in the setting of ED and ICU is a major challenge and requires detailed and dedicated training on the appropriate use (donning & doffing) of PPE (Figure 4 & 5). COVID-19 triage should be performed, and dedicated areas should be identified to manage unsuspected from suspected/probable cases. Before performing cardiology consultations in the ED, it is advisable to carry out a quick telephone interview to assess whether patient has suspected COVID-19 symptoms or risk factors for COVID-19 (Table 3) or suspicious chest X ray/CT scan. If any suspicion is present and cardiology advice is urgent (without having the time frame to postpone it until the result of the swab test RAT/PCR), the patient should be assumed as potentially positive for SARS-CoV-2 infection and maximum personal protection/PPE measures must be taken (Level II protection). Level III protection is recommended in case of aerosol generation procedures, (Table 5). *Remember that CPR is an aerosol generating procedure (AGD)*. Other ED cases should be managed with level I protection (Table 5).

(D) Intensive Care Unit

It is advisable/ideal that every patient managed in CCU/ICCU are in isolation cubicles. If personal isolation cubicles are not available at CCU/ICCU, all patients in CCU/ICCU should undergo RAT and/or PCR and should be tested negative for COVID-19 in order to be managed in a mixed CCU/ICCU setup with Level I protection (Table 5).

If a patient admitted to cardiology ward/CCU/ICCU, is detected with positive SARS-CoV-2 infection, that patient will need triage to a dedicated COVID high dependency unit (HDU) or ICU setting depending on oxygen requirement and other organ failures. It is suggested to start supplemental oxygen if the peripheral oxygen saturation (SPO_2) is less than 94% on room air. [8] Oxygen supplementation using devices such as venturi masks, non-rebreather mask (NRBM) etc., can be done in an isolation room in the cardiology ward/CCU/ICCU with HCW adhering to level II/III protection until transfer to a dedicated COVID HDU/ICU.

When oxygen demand increases, high flow nasal cannula (HFNC) system or non-invasive ventilation with continuous positive airway pressure – CPAP or bilevel positive airway pressure – BiPAP should be used with level III protection since these are aerosol generating procedures. In worsening respiratory status, intubation and ventilation is recommended. Patients with non-invasive or invasive ventilation should be managed in a dedicated COVID ICU setting.

Not only for respiratory support, but also COVID-19 positive cardiac patients may need ICU care due to other organ failures like acute renal failure, liver failure and also due to septic shock.

Patients directly admitted to COVID dedicated HDUs and ICUs with COVID pneumonia are referred to cardiologists due to new development of acute coronary syndrome, myocarditis and heart failure. Clinical assessment of these patients, performing echocardiography etc should be done with level III protection.

Table 7 | Detailed inclusion and exclusion criteria for intensive care unit (ICU) admission

Inclusion criteria
• Requirement for **invasive ventilator support**. • Requirement for **hemodynamic support with vasoactive agents** (noradrenaline-equivalent dose > 0.1 μg/kg/min) **or mechanical support**. • Requirement for **renal replacement therapy**. If at least **1** criterion is fulfilled, check for exclusion criteria.
Exclusion criteria:
Patients' end of life decision preferences. Unwitnessed cardiac arrest, witnessed cardiac arrest not responsive to electrical therapy, recurrent cardiac arrest. Metastatic malignant disease. End-stage neurodegenerative disease. Severe and irreversible neurological event or condition. Chronic condition: ✓ Patients with NYHA class IV heart failure not eligible to left ventricle assist device or heart transplantation. ✓ GOLD group D COPD ✓ Cystic fibrosis or pulmonary fibrosis with baseline PaO_2 <55 mmHg ✓ Liver cirrhosis, Child-Pugh score >7 ✓ End-stage kidney disease on dialysis with refractory symptoms despite active medical management treatment. ✓ Severe dementia. ✓ Estimated survival <12 months. If not even one criterion is met and ICU beds are not available, check for additional exclusion criteria.
Additional exclusion criteria to be checked if no ICU beds are available:
✓ Severe trauma. ✓ Severe cerebral deficits after stroke. ✓ Moderate dementia. ✓ Estimated survival <24 months. ✓ Chronic condition: o Home oxygen therapy o Liver cirrhosis with refractory ascites or encephalopathy > stage I ✓ Age>80 years ✓ Age >70 years and at least one criterion: o Cirrhosis o Stage III chronic kidney disease KDIGO o NYHA class > II heart failure ✓ Patients aged >60 years with NYHA class III heart failure without acute treatable cardiac disease and/or LVEF <30% even if eligible to left ventricle assist device or heart transplantation. If neither of these criteria is fulfilled, consider withdrawing ICU support from patients who arrived earlier to save those with better prognosis.

Table 8 | Criteria for little or no likelihood of benefit with ICU treatment (occurrence of at least 1 criteria)

• Occurrence of two new significant organ failures which did not present on admission
• No improvement in respiratory or hemodynamic status
• Advanced multiple organ failure defined by an increase in SOFA score (≥ 25% compared to admission values after 10 days of treatment) associated with accumulated TISS ≥ 500

SOFA - *Sequential Organ Failure Assessment, TISS - therapeutic intervention scoring system*

(E) CATHETERIZATION LABORATORY

HCW should be well trained in proper techniques for donning and doffing PPE. Catheterization laboratory directors/consultant cardiologist in charge should ensure adequate availability, replacement, and training in the use of these equipment well in advance. All patients entering the catheterization laboratory should wear appropriate mask (N95/KN95/Surgical). In a center where multiple cardiac catheterization laboratories are available; one should be modified/designed to cater to emergency cardiac catheterization procedures of COVID positive or suspected cases. This modification should include a floor plan with 2 separate entrances for COVID positive/suspected and COVID negative cases to avoid cross infection among these two groups. Further a separate area for donning and doffing PPE is recommended in a dedicated COVID cardiac catheterization laboratory to protect the HCW and equipment from being contaminated.

Routine post procedure sterilisation techniques should be used, and fumigation is optional. Detailed summery given in the following table regarding 4 strategical categorisation of cardiac catheterization procedures and the suggested level of restrictions of these procedures based on pandemic level in Sri Lanka (Table 9). These procedures need to be triaged by the cardiologist /CEP as 'Emergency-Urgent-Selective-Routine' cases and their likelihood of performance/postponement time frames. Further guidance is given to the cardiologist to prioritise these procedures depending on the COVID epidemic level and staff adequacy as given in the bottom of the table as a rough guidance. If the cardiac catheterization lab is not functioning 24/7 due to lack of minimum number of interventional cardiologists (Currently 5 as per NICE guidelines) and/or lack of cardiac catheterization lab staff for 24/7 service, and/or without dedicated COVID treatment facility in the same center for post PCI care the patients should be transferred to a 24/7 functioning cardiac catheterization laboratory center with dedicated COVID-19 treatment/ICU facility (1).

Table 9 | Strategic categorization of cardiac procedures based on clinical indications & level of personal protection level advised for Health Care worker (HCW) in the context of COVID 19.

CLINICAL CONDITION	EMERGENCY (Do not postpone)	URGENT (Perform within days)[a]	LOWER PRIORITY (perform within <3 months)[a]	ELECTIVE (May be postponed >3 months)	PERSONAL PROTECT LEVEL
ISCHAEMIC HEART DISEASE	• STEMI • NSTE-ACS in very high risk and high-risk patients • Cardiogenic shock	• NSTE-ACS in intermediate risk patients • Unstable angina • Left main PCI • Last remaining vessel PCI • Decompensated ischaemic heart failure. • Angina pectoris class IV • CABG in patients with NSTE-ACS unsuitable for PCI	• Advanced CAD with angina class III or NYHA III symptoms • Staged PCI of non-culprit lesions in STEMI • Proximal LAD PCI	• CTO interventions • CCS with angina class II or NYHA II symptoms	Level II/III protection

VALVULAR HEART DISEASE	• BAV as bridge to TAVI / SAVR in highly selected decompensated patients • Surgery in aortic dissection or cardiovascular trauma • Valve repair / replacement for acute failing native or prosthetic valve causing shock. • PTMC as a bridge to MVR in highly selected acutely decompensated or pregnant patients with MVA < 1.0 cm^2	• TAVI in patients with decompensated aortic stenosis • Transcatheter mitral edge-to-edge repair in haemodynamically unstable patient with acute MR who are unsuitable for surgery. • Mitral valve surgery in haemodynamically unstable patient with acute ischaemic MR • MR and aortic regurgitation in patient with endocarditis • High risk of embolism in acute infective endocarditis • Surgery for left atrial myxoma	• TAVI / SAVR in severe aortic stenosis (AVA < 0.6 cm^2, mean transvalvular gradient >60 mmHg, symptoms with minimal exertion) • TAVI/ SAVR in symptomatic patient with low-flow low-gradient AS (AVA <1.0 CM^2,mean transvalvular gradient <40 mmHg, LVEF < 50%) • Mitral valve surgery or transcatheter mitral edge-to-edge repair in patients with MR and congestive HF who cannot be stabilized with medical therapy. • PTMC for MVA < 1.0 cm^2 with class 3 symptoms	• TAVI/SAVR for symptomatic severe aortic stenosis (AVA <1.0 cm^2, mean transvalvular gradient <40 mmHg) • TAVI / SAVR with symptomatic paradoxical low-gradient aortic stenosis (AVA <1.0 cm^2, mean transvalvular gradient <40 mmHg, LVEF > 50%) • Mitral valve surgery or surgery or transcatheter mitral edge-to-edge repair for secondary MR with stable HF • PTMC for MVA 1.0 -1.5 cm^2 with class 2-3 symptoms	Level II/III protection
ACUTE/ CHRONIC HEART FAILURE	• Mechanical circulatory support for cardiogenic shock (< 65 years)	• Urgent heart transplant	• LVAD	• Cardiac Resynchronisation	Level II/III protection
ARRHYTHMIC HEART DISEASE	• Refer table 10	• Refer table 10	• Refer table 10	• Refer table 10	Refer table 10
OTHER INTERVENTIONS	• Pericardiocentesis in cardiac tamponade		• Biopsies	• LAA occlusion in stable patient • PFO / ASD closure • Right heart cath • Alcohol ablation in hypertrophic cardiomyopathy • Invasive evaluation of dilated cardiomyopathy	Level II/III protection

LEVEL OF RESTRICTIONS ON CARDIAC PROCEDURES AS PER PANDEMIC LEVEL

Pandemic level 4	Pandemic level 3	Pandemic level 1-2
EM, Ur Em – Emergency cases only (to perform at point of care or within 24 hours). Ur – Urgent procedures (to perform within 72 hours or as in patient).	LPP3, ELP >3 LP3 – Low priority Procedures that can be performed or postponed up to 3 months. EL >3 – Elective procedures that can be postponed beyond 3 months.	ROU All routine procedures carried out without any restrictions.

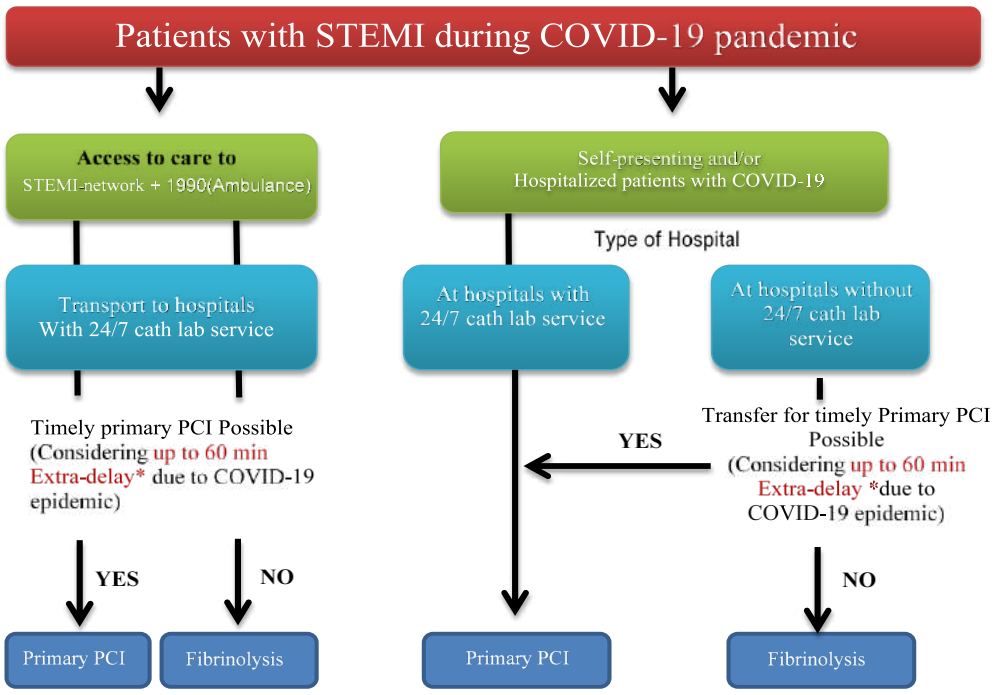
[a]Timing might be a affected by overwhelming demand on system in the setting of a COVID-19 outbreak, ASD = atrial septal defects; AVA=aortic valve area; CCS= chronic coronary syndromes; CTO=chronic total occlusions; STEMI = ST-segment elevation myocardial infarction. LAA=left atrial appendage; LAD= left anterior descending coronary artery; LVAD = left ventricle assist device; LVEF = left ventricle ejection fraction. NYHA = New York Heart Association; NSTE=ACS=non-ST=segment elevation acute coronary syndromes; PCI= percutaneous coronary intervention. PFO= patent foramen ovale; TAVI= transcatheter aortic valve interventions. PTMC = Percutaneous Trans-Mitral Commissurotomy

(1) ST-Segment Elevation Myocardial Infarction (STEMI)

The maximum delay from STEMI diagnosis to reperfusion of 120 minutes should remain the goal for reperfusion therapy under the following considerations: Primary PCI remains the reperfusion therapy of choice if feasible within this time frame and performed in facilities approved for the treatment of COVID-19 patients in a safe manner for healthcare providers and other patients. Primary PCI pathways may be delayed during the pandemic (up to 60 minutes - according to multiple experiences) due to delays in the delivery of care and the implementation of protective measures. **If the target time cannot be met and fibrinolysis is not contraindicated, fibrinolysis should then become first line therapy** (Figure 6).

As SARS-CoV-2 test results are not immediately available in STEMI patients; any STEMI patient should be considered potentially infected and operated under level III protection. All STEMI patients should undergo testing for SARS-CoV-2 as soon as possible following first medical contact irrespective of reperfusion strategy. Until the result of the test is known, all precautionary measures should be taken to avoid potential infection of other patients and HCW. Consider immediate complete revascularization if indicated and appropriate to avoid staged procedures and reduce hospital stay. All physicians involved in the management of patients with STEMI should be familiar with indications, contraindications and dosage of fibrinolysis and adhere to established administration protocols.

Figure 6 | STEMI presentations during COVID 19 pandemic – Management algorithm [1]



General recommendations:

- Only hospitals equipped to manage patients with COVID-19 should maintain 24/7 cath lab service Primary PCI.
- Any STEMI patient should be managed assuming positive COVID-19 Status.
- Perform fibrinolysis only if not contraindicated.
- * Time acceptable for a primary PCI is termed as **door to balloon (D2B)** time and is generally acceptable to perform **within 90 minutes (Ideally within 60 minutes)** from the **first medical contact (FMC).** But considering the limited logistics and resources during Covid pandemic an **extra delay up to 60 minutes (Total D2B up to 120 minutes)** may be allowed in PPCI decisions by the cardiac/cath lab teams.
- All primary or rescue PCI should perform by the most experienced operator on call with minimum required staff in a COVID-19 suspected or confirmed patient.

(2) NON-ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION – NSTEMI

Very high-risk non-ST-segment elevation (NSTE)-ACS should follow the ST-segment elevation myocardial infarction (STEMI) pathway and HCW protected accordingly. Others should undergo a nasopharyngeal swab for RAT preferably or point of care rapid PCR immediately after admission to ETU/A&E/ED/PCU (Figure 7).

If waiting for swab result, patients must be isolated in a dedicated and monitored ETU/A&E/ED/PCU area because of the prevalence of asymptomatic patients with SARS-CoV-2 infection, with the aim to reduce the risk of infection spreading within the hospital.

Even though the ESC 2020 guidance suggest to perform two negative RAT/PCR results within 48 hours, to perform a non-urgent coronary angiography / PCI in a catheterization laboratory reserved for COVID negative patients, it is practical to perform a RAT at point of care and perform the angiographic procedure with level II protection in a country like Sri Lanka.

Patients with NSTEMI and SARS-CoV-2 positive test

If an invasive approach is clinically indicated, the procedure should be performed in a dedicated COVID-19 catheterization laboratory if available. Elective intubation threshold should be lowered in patients with borderline respiratory status to avoid risk of emergency intubation need and high aerosol generation in the catheterization laboratory.

For this reason, use of powered air-purifying respirator (PAPR) systems, if available, may be reasonable (Figure 1&2).

In case of manual ventilation during CPR, a viral filter/HEPA filter may be placed between the tube and the bag valve mask to reduce the risk of aerosol dispersion.

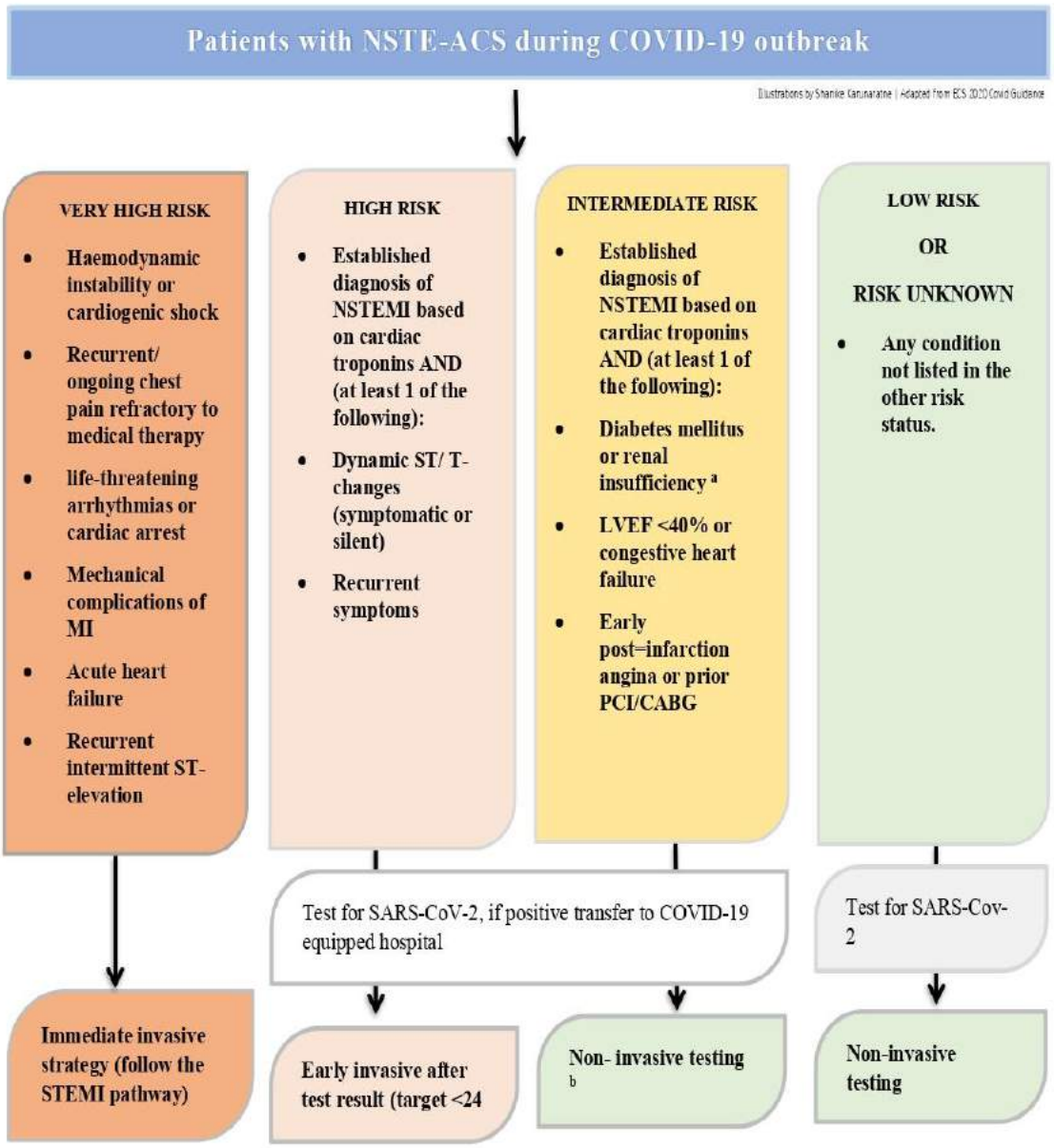
Because most catheterization laboratories are not designed for infection isolation with negative pressure, a terminal cleaning and sanitization should be performed after each procedure.

Of note, air exchange times of the catheterization laboratory should be checked (minimum 15 exchanges per hour, ideally 30 exchanges per hour).

Because patient transportation from the ward to the catheterization laboratory may carry the risk of in-hospital infection transmission, some procedures routinely performed in the catheterization laboratory (e.g., Swan-Ganz catheter placement, pericardiocentesis, and intra-aortic balloon pump insertion) should be considered for bedside performance.

The catheterization laboratory staff should be minimized and, in case of haemodynamic instability of the patient, should wear level II or level III PPE (Table 5). Any intubation, suction, or cardiopulmonary resuscitation (CPR) cause aerosol dispersion of respiratory secretions with increased likelihood of exposure to the staff.

Figure 7 | Recommendations for management of patients with NSTE-ACS in the context of COVID 19 outbreak [1]



LVEF= left ventricular ejection fraction; MI = myocardial infarction; NSTEMI=non-ST-segment-elevation MI.
a-estimated glomerular filtration rate <60mL/min/1.73m2.
b-Computed Tomography Coronary angiography (CTCA) should be favoured if equipment and expertise are available.
In low-risk patient, other non-invasive testing might be favoured in order to shorten hospital stay. It is suggested to perform left ventriculography during catheterization if echocardiography not performed before Cath lab admission.

(F) Electrophysiology Laboratory

Most of the electrophysiology (EP) activity are elective and thus is being markedly reduced or suspended in areas that have been severely affected by COVID-19 outbreak all over the world. Cardiac EP procedures for selected categories of patients are suggested to be performed based on the pandemic burden and clinical indication as follows (Table 10).

Table 10 | Strategic categorization of specific CEP procedures based on clinical indications & level of personal protection level advised for Health Care worker (HCW) in the context of COVID 19.

SPECIFIC CEP PROCEDURE	URGENT PROCEDURES (perform within days)	SEMI-URGENT PROCEDURES (Perform within weeks, within <3 months)	NON-URGENT/ELECTIVE PROCEDURES (Can be postponed beyond ≥ 3 months)	PERSONAL PROTECTION LEVEL
CATHETER ABLATION	• VT/VF ablation for electrical storm • AF or A flutter ablation for AF/A flutter causing tachycardiomyopathy or syncope • WPW syndrome with fast preexisted AF and or syncope and/or cardiac arrest	• VT ablation for medically refractory recurrent VT • AF/A flutter ablation for medically refractory AF/A flutter with repeated ER visits • Medically repeated ER visits	• PVC ablation • PSVT ablation • AF/A flutter ablation • EP testing	• Level II/III protection
CARDIAC IMPLANTABLE ELECTRONIC DEVICE	• Urgent PM implantion for symptomatic high-degree AV block or sinus node dysfunction with long a systolic pause • Urgent secondary prevention ICD implantation for cardiac arrest or VT • ICD/PM battery replacement for imminent or actual EOL in PM dependent for symptomatic malfunction • Lead extraction for infection	• ICD/PM Battery replacement for ERI • Primary prevention ICD in very-high risk of life-threatening ventricular arrhythmias	• Primary prevention ICD • CRT implantation • CIED upgrade • Lead extraction in patient without infection • Lead revision for asymptomatic malfunction	• Level II/III protection
CARDIOVERSION / OTHER EP PROCEDURES	• Highly symptomatic medically refractory new onset of AF/A flutter	• Symptomatic medically refractory AF/A Flutter	• LAA closure • ILR implantation • Tilt table testing • Ambulatory rhythm zonitoring	• Level II/III protection

LEVEL OF RESTRICTIONS ON HIGHLY SPECIFIC EP PROCEDURES AS PER PANDEMIC

Pandemic level 4	Pandemic level 3	Pandemic level 1-2
(EM , Ur) Em – Emergency cases only (to perform at point of care or within 24 hours). Ur – Urgent procedures (to perform within 72 hours or as in patient).	(SE , EL >3) SE – Semi Urgent Procedures that can be performed or postponed up to 3 months. EL >3 – Elective procedures that can be postponed beyond 3 months.	ROU All routine procedures carried out without any restrictions.

Protection of the HCP during cardiac electrophysiological procedures.

EP laboratories which are exclusively dedicated to patients potentially infected with SARS-CoV-2 are not readily available in most institutions. But these COVID dedicated EP labs should be identified whenever possible ideally in a center which has more than 1 Cath lab. All patients with clinical indication for an EP procedure should undergo a nasopharyngeal swab for RAT/PCR immediately after admission. In case of haemodynamic instability and possible COVID-19 case, the procedure should be performed at least with level II protective measures (Table 5).

In critical conditions such as syncope and complete atrioventricular (AV) block, patients should immediately be transferred to the EP laboratory (without RAT or PCR) and undergo pacemaker (PM) implantation at least under level II protection (Table 5). After the procedure, these patients should be transferred to a dedicated COVID-19 isolation area until performance and availability of SARS-CoV-2 infection results. If procedure could be delayed for 48 hours with two negative swab results within those 48 hours and absence of suspicious symptoms of COVID-19 infection, the planned procedure may be performed using standard protective tools.

Patients with SARS-CoV-2 positive test:

If patient is haemodynamically stable, ablation procedures should be deferred using intravenous (I V) antiarrhythmic drugs (AADs) as indicated by the underlying arrhythmia. The number of operators should be limited to the essential. Ideally, one nurse, one operator, one assistant at the console and one anaesthesiologist, when indicated.

(G) Transoesophageal Echocardiography, Continuous Positive Airway Pressure (CPAP) and Orotracheal Intubation

The major issue is that the viral load in the airway is probably extremely high and very contagious. This poses significant risks for HCW performing non-invasive ventilation by CPAP or invasive ventilation with orotracheal intubation. Accordingly, a high level of vigilance is necessary to prevent contracting the infection when managing patients using CPAP, when intubation is performed, or the transoesophageal echocardiogram (TEE) probe is inserted.

Patients undergoing TEE should be tested for SARS-CoV 2 status (RAT or PCR). If the procedure is not an emergency (Red) but urgent (Orange) and need to perform as an inward procedure; ESC guidance suggest two negative swab results within 48 hours and absence of suspicious symptoms of COVID-19 infection, to proceed with the planned procedure using standard protective tools. However, in a low resource setting, single negative RAT in an asymptomatic patient is reasonable to perform the procedure under level II/III protection. If emergency TOE procedure is indicated, rapid antigen test for SARS-CoV 2 and subsequent level II/III protection is advised.

In patients with positive SARS-CoV 2 test or unknown status:

A "point-of-care" focused ultrasound (POCUS) 2D echo examination may be performed at the bedside in SARS-CoV-2 positive patients to avoid TEE and the associated infection risk for HCW. In case of invasive ventilation and CPAP, a level III protection should be used, whereas for TEE a Level III protection is advised (Table 5).

Acknowledgements:
Dr Ruvan Ekanayaka, Senior Consultant Cardiologist
Dr W S Santharaj, Consultant Cardiologist
for reviewing the article.

References

1. *ESC Guidance for the Diagnosis and Management of CV Disease during the COVID-19 Pandemic (Last updated on 10 June 2020)*
2. *Interim guidelines for primary care physician's Sri Lanka - version 3 (Last updated on 15th April 2020).*
3. *Michael D. Christian, Laura Hawryluck, et al., Development of a triage protocol for critical care during an influenza pandemic. CMAJ November 21, 2006. 175 (11): 1377-1381.*
4. *Ibanez B, James S, Agewall S, et al., Group ESCSD. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018. 39(2): 119-177.*
5. *World Health Organization. Global surveillance for COVID-19 caused by human infection with COVID-19 virus: interim guidance, 20 March 2020. https://extranet.who.int/iris/restricted/handle/10665/331506 (2020; date last accessed).*
6. *Centre for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19) - symptoms of coronavirus. https://www.cdc.gov /coronavirus/2019-ncov/symptoms-testing/symptoms.html (March 20, 2020; date last accessed).*
7. *Guan WJ, Ni ZY, et al., for the China Medical Treatment Expert Group for C. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382(18):1708-1720.*
8. *Revised Clinical Practice Guidelines on Institutional Management of COVID-19 Patients in Sri Lanka, Ministry of Health (Issued on 25.05.2021)*

Research

Gender Differences in Presentations of ST Segment Elevation Myocardial Infarctions (STEMI) to the Accident and Emergency department in a Tertiary Care Hospital of Sri Lanka

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Abstract

Introduction: The clinical manifestation of ST segment elevation myocardial infarction (STEMI) varies and patients present frequently with symptoms other than chest pain. Myocardial infarction chest pain is typically described as tight and squeezing, like a weight on the chest. Females with STEMI present frequently with atypical symptoms. Early diagnosis and treatment of STEMI is crucial to reduce mortality and morbidity.

Methods: This prospective observational study was carried out from January 15, 2017 to July 15, 2018 (18 months) to identify the presenting symptoms of STEMI to the A&E department. Patients with previous myocardial infarction and ischaemic heart disease were excluded. STEMI patients (n=370) were enrolled in the study within 24 hours of admission. Data analysis was done using SPSS (version 21).

Results: There were 272 (73.5%) males with a mean age of 58.0 (+12.8) years and females 98 (26.5%), with a mean age of 64.4 (+10.8) years. Women with STEMI were significantly older than men (p<.0001). STEMI was more prevalent in men with no known risk factors (51.8 vs 32.7% p=.001) and in women with hypertension (18.4 vs 10.7% p=.05). The chest pain itself had no significance in gender whereas nausea was more prevalent among women (12.2 vs 5.1% p=.018) and diaphoresis among men (10.3 vs 2.0% p=.010). The symptoms of squeezing chest pain (19.1 vs 10.4% p=.029) and pain radiation (73.2 vs 61% p=.032) were more prevalent among women.

Conclusion: Women with STEMI were 6.4 years older than men on average. A striking gender difference in STEMI symptoms found that where diaphoresis was more common among men, nausea, pain radiation, and squeezing chest pain were more common among women. STEMI was more common among men with no known risk factors and among women with hypertension. Chest pain was the predominant presentation and there was no related difference between the two genders. This finding was not comparable with previous study findings.

Key Message: Previous studies showed women had more atypical features than men [6,7,8] and the mortality of women is higher than men [9,10,11,13], whereas our study showed no significant difference.

Most of the studies were retrospective studies with only a few studies [11] being prospective ones. This study was prospective, with interviews conducted within a 24 to 48-hour period by two investigators and all ECGs confirmed by a consultant to minimize bias.

History is one of the key features for the diagnosis of STEMI before obtaining an ECG. Men and women can present with typical/atypical chest pain symptoms, therefore making it more important to have good detailed history in everyone. Squeezing chest pain and nausea is highly suggestive of STEMI in women while chest pain with diaphoresis is highly suggestive of STEMI in men. It is important to ask about pain radiation in both genders. Further studies with chest pain presentation and outcomes with angiographic findings would provide more comprehensive data.

Key words: Presentation of STEMI, gender difference

Introduction

Myocardial ischaemia in a clinical setting can most often be identified from the patient's history and from the ECG. For the sake of immediate commencement of treatment strategies such as reperfusion therapy, it is the usual practice to designate myocardial infarction (MI) in patients with chest discomfort or other ischaemic symptoms who develop new ST-segment elevations in two contiguous leads or new bundle branch blocks with ischaemic repolarization patterns as an ST-elevation Myocardial Infarction (STEMI) [1]. Correct recognition of MI symptoms by the patient is vital in order to seek medical care promptly.

Possible ischaemic symptoms include various combinations of chest, upper extremity, mandibular or epigastric discomfort during exertion or at rest or an ischaemic equivalent such as dyspnoea or fatigue [2]. Often, the discomfort is diffused; not localized or positional, nor affected by movement of the region. However, these symptoms are not specific for myocardial ischaemia and can be observed in other conditions such as gastrointestinal, neurological, pulmonary, or musculoskeletal complaints. MI may occur with atypical symptoms such as palpitations or cardiac arrest or even without symptoms.

Correct symptom recognition is vital in order to promptly seek care for STEMI where fast reperfusion therapy is of utmost importance. Women and men with acute coronary syndromes have different clinical profiles, presentations and outcomes. Symptom presentation has been sparsely studied from a gender perspective. Cardiovascular disease is the leading cause of death amongst women, with acute coronary syndromes (ACS) representing a significant proportion [3]. Females have been found to be associated with atypical presentations in studies on mixed MI populations, but it is unclear whether this is also valid in STEMI [4]. It has been reported that in women presenting with ACS that underdiagnosis and consequent undertreatment often occur, leading to an increase in hospital and long-term mortality. Women are generally not aware of the cardiovascular risk and symptoms, which are often atypical and therefore wait longer to seek medical attention [4]. Females have been found to be subject to prehospital delays in several studies [4] possibly due to a higher risk of failure to recognize the symptoms as an evolving MI.

The aim of this study is to identify the gender differences in presentations of STEMI to the Accident and Emergency (A&E) department in a tertiary care centre in a Sri Lankan hospital.

Methods

A prospective observational study was conducted from January 15, 2017 to June 15, 2018 (18 months) at the A&E department and cardiology unit of Provincial General Hospital Kurunegala (PGHK), Sri Lanka. All patients presenting to the A&E department with ECG evidence of STEMI were included into the study. Patients with a previous history of myocardial infarction (STEMI, Non-ST elevating MI, Unstable angina), patients who underwent revascularization and unconscious patients were excluded. Data collection was done using an interviewer-administered questionnaire which was performed by two co-investigators who were qualified senior medical officers, to avoid bias.

These two medical officers were trained to interview the patients by the supervisor (specialist in internal medicine) of the study.

Patients with STEMI were diagnosed by using a history of chest pain and/or ST-elevations in ECG (ECG diagnosis - ST-segment elevation of ≥2mm in at least 2 contiguous precordial leads or ST-segment elevation of ≥1 mm in at least 2 inferior leads II, III, or aVF). Each ECG diagnosis of STEMI was confirmed by the supervisor. This questionnaire was pretested in the A&E department with ten patients, face validated with cardiologist and internist, and changes were done accordingly. It included gender, age, territory of STEMI, a detailed history of chest pain and associated symptoms, past medical history, medication history, and information about smoking and alcohol consumption. In addition, the questionnaire included blood pressure on admission and capillary blood sugar which were taken from patients' notes.

Pain assessment was done according to the following five qualitative categories:
[1] squeezing, [2] tightening, [3] burning, [4] pricking, and [5] pleuritic nature.

The site of the pain was categorized as,
[1] left side of the chest, [2] retrosternal, [3] right side of the chest, [4] epigastric, [5] right upper back, [6] left upper back, and [7] middle upper back.

Pain radiation was taken as to,
[1] jaw, [2] neck, [3] left upper limb, [4] right upper limb, and [5] upper back.

The associated factors were taken as,
[1] nausea/vomiting, [2] diaphoresis, [3] dizziness/syncope, [4] dyspnoea [5] palpitation, [6] diarrhoea, and [7] altered level of consciousness.
The duration of pain was considered as lasting for less than 20 minutes, one hour and more than one hour

Patients and public involvement

All patients presenting to the A&E department with ECG evidence of STEMI who consented were taken into the study. Ethical approval was taken from the Ethical review committee, provincial general hospital, Kurunegala. Patients' details were kept confidentially.

Statistical analysis

The data is expressed as mean ± SD. The statistical significance of differences between men and women was evaluated with the use of unpaired t-tests. Differences in prevalence were assessed with the use of chi-square tests. A *p* value of < .05 was considered statistically significant.

Logistic multivariable regression analyses were performed with specific symptoms as dependent variables and sex, age, pain radiation, and nature of pain as independent variables.

Results

The total study population consisted of 370 participants, 73.5% of which were men (n=272). The women in the study were older than the men (64.4+/-10.8 years vs 58+/-12.8 years, *p*=.001) [Table 1]. The overall mortality rate was 2.97% (male=6/272, 2.2%; female=5/98, 5.1% *p*=.147). Anterior STEMI and inferior STEMI were more prevalent without gender differences. STEMI is more prevalent in men with no risk factors (51.8% vs 32.7% *p*=.001) and women with hypertension (18.4 vs 10.7% *p*=.05). The presenting symptom of chest pain itself had no difference in both genders – all participants presented with chest pain. The associated symptom of nausea was more prevalent among women (12.2 vs 5.1% *p*=.018) and diaphoresis among men (10.3 vs 2.0% *p*=.01). There is a gender difference in the character of chest pain which is squeezing chest pain (19.1 vs 10.4% *p*=.029). Pain radiation (73.2 vs 61% *p*=.032) was more prevalent among women.

In men, pain radiating to the left upper limbs was more common (22.8 vs 10.2% *p*=.007) whereas pain radiating to the neck was more significant among women (17.34 vs 5.51% *p*=.000). There was no difference in tightening, burning, pricking, pleuritic type chest pain and duration among both genders. Additionally, there was no difference in the sites of pain such as retrosternal, shoulder, and arm pain. The retrosternal pain was most common while epigastric pain was uncommon in both genders without any difference.

In multivariable logistic regression models, nausea was more predictable in women [odds ratio of 2.57, a 95% confidence interval 1.15-5.77]. STEMI is more prevalent in hypertensive women [odds ratio of 1.885, a 95% confidence interval 0.99-3.57], along with pain radiation [odds ratio of 1.744, a 95% confident interval 1.05-2.9]. Squeezing chest pain was also predictable in women, [odds ratio 1.961, 95% confident interval 1.03-3.73].

STEMI was more prevalent in men who were not on aspirin who actually have double the chance of developing STEMI compared to women who are not on aspirin, [odds ratio 2.011, 95% confidence interval 1.038 – 3.895]. Further analysis revealed men without aspirin aged 46-55 years (*p*=.045), 56-65 years (*p*=.000), 66-75 years (*p*=.000) and above 75 years (*p*=.023) had highest chance of developing STEMI. Most of them were not on beta blockers, ACE inhibitors, or ARBs. A significant finding was that none of the women were smokers/ex-smokers or consumed alcohol. However, 14.3% and 17.3% of the men were smokers and ex-smokers respectively, with 31.1% of men consuming alcohol.

	Men	Women	*p* value
Socio-demographic variables			
Age mean (years)	58.04±12.8	64.42 ± 10.8	0.000
Height (cm)	163.67 ± 6.91	158.89 ± 7.96	0.000
Weight (kg)	63.56±10.02	59.04 ± 9.41	0.000
BMI (kg/m^2)	23.74 ± 3.66	23.40 ± 3.49	0.421
Clinical history			
Diabetes Mellites	40, 14.70 %	09, 9.18 %	0.367
Hypertension	29, 10.66 %	18, 18.36 %	0.050
No risks	141, 5%	32, 32.65 %	0.001
Associated symptoms			
Chest pain	266, 97.80 %	96, 97.95 %	0.466
Nausea	14, 5.14 %	12, 12.24 %	0.018
Dizziness	11, 4.04 %	2, 2.04 %	0.356
Palpitation	1, 0.4%	0, 0.00 %	0.548
Diaphoresis	28, 10.30%	2, 2.04 %	0.010
Dyspnoea	17, 6.25%	5, 5.10 %	0.680
Nature of Pain			
Squeezing	28 ,10.45%	18 ,19.15%	0.029
Tightening	164, 61.20%	53, 56.38%	0.413
Burning	51,19.02%	19, 20.21%	0.803
Pain Radiation			
Present	166, 61.03%	71, 73.2%	0.032
Duration of Pain			
<20min (short)	11,4.15%	2, 2.12%	0.367
20-60 (moderate)	27, 10.18%	6, 6.38%	0.273
>60 (long)	227, 85.66%	86, 91.49%	0.146
Site of Pain			
Left Side (Chest, Back)	75, 27.57 %	8, 8.16 %	0.567
Right Side (Chest, back)	8, 2.95 %	1, 1.02 %	0.290
Retrosternal	112, 41.17 %	45, 45.91 %	0.415
Epigastric	16, 5.88 %	9, 9.18 %	0.264
Other	44, 16.17 %	8, 8.16 %	0.050
Site of Radiation			
Jaw	6, 2.20 %	3, 3.06 %	0.637
Neck	15, 5.51 %	17, 17.34 %	0.000
Left upper limb	62, 22.80 %	10, 10.20 %	0.007
Right upper limb	11, 4.04 %	2, 2.04 %	0.356
Back	12, 4.41 %	8, 8.16 %	0.159
Other	4, 1.47 %	3, 3.06 %	0.322
ST Elevation			
Anterior	126,46.32%	49,50%	0.532
Inferior	129,47.42%	40,41%	0.260
Other	8,2.94%	2,2.04%	0.637

Discussion

Chest pain was the most common symptom of myocardial infarction where both genders presented with typical chest pain without atypical features. It is incomparable with previous studies where women had more atypical features than men [6,7,8] . In previous studies, there were more risk factors in women [16]. In this study, a significant percentage of women with hypertension suffered from STEMI which is similar to other studies [19]. Previous studies showed that the mortality of women is higher than men [9,10,11,13] , whereas our study showed no significant difference. Our study confirms the previous finding that women with STEMI tend to be older than men [18].

Less risk factors in our cohort of women such as diabetes mellitus and dyslipidemia may explain the less atypical features [15]. However, the mortality of women did not increase despite them being older than men. Comparatively, men without risk factors had a larger prevalence of STEMI than men with risk factors – a significant finding. Squeezing chest pain and associated nausea were more prevalent in women than men, a finding that is comparable with other studies. However, in other studies atypical chest pain, vomiting, and shortness of breath were common among women (in addition to nausea) [17]. Additionally, similarly to other studies, diaphoresis occurs more in men as well [17]. Chest pain radiation to the left upper limb is prevalent in men and pain radiation to the neck is prevalent in women.

Pain radiation, squeezing chest pain were predictable presentations in women. STEMI was more predictable in hypertensive women. Among both men and women, a larger number of men without aspirin developed STEMI and have double the chance of getting STEMI than women who are not on aspirin. It is highly significant among the men above the age of 46 years. A significant finding was that none of the women were smokers/ex-smokers or consumed alcohol. However, 1/3 of men were smokers and ex-smokers, with 1/3 of men consuming alcohol without a significant effect on STEMI.

Most of the studies were retrospective studies with only a few studies [11] being prospective studies. This study was prospective, with interviews conducted within a 24 to 48-hour period by two investigators and all ECGs confirmed by a consultant to minimize bias.

Conclusion

History is the key feature for the diagnosis of STEMI. Men and women can present with typical chest pain symptoms, therefore making it more important to have good history in everyone. Squeezing chest pain and nausea is highly suggestive of STEMI in women while chest pain with diaphoresis is highly suggestive of STEMI in men. It is important to ask about pain radiation in both genders. Aspirin is beneficial as primary prophylaxis in men above 46 years of age. Further studies with chest pain presentation and outcomes with angiographic findings would provide more comprehensive data.

Limitations

The study was done in a single center and the interviews were done by two medical officers. As there were no cardiac interventional facilities at the time of commencement of the study, we were unable to assess the actual angiographic findings.

Conflict of Interest

The authors declare that they have no conflict of interest of any type.

Author's Contributions

Jayasekera MMPT, the corresponding author was involved in the supervision of research proposal writing, data collection, the verification of the accuracy of data, funding, statistical analysis, and the preparation of the final document. Adikari AMSB has developed the research concept and done the proposal writing. Wijewardhana MGDD and Jayarathna BB aided with the data collection. Edirisinghe EMDT has done the statistical analysis.

Acknowledgement

We acknowledge all patients who participated the study, without them this will not be a reality.

References

1. *Thygesen, K., Alpert, J.S., Jaffe, A.S., Chaitman, B.R., Bax, J.J., Morrow, D.A., White, H.D., Mickley, H., Crea, F., Van de Werf, F. and Bucciarelli-Ducci, C., 2019. Fourth universal definition of myocardial infarction (2018). European heart journal, 40(3), pp.237-69.*
2. *SPOLEČNOST, Č.K., 2013. Third universal definition of myocardial infarction$. cor et vasa, 55, pp.e228-35.*
3. *Chieffo A, Buchanan GL, Mauri F, Mehilli J, Vaquerizo B, Moynagh A, Mehran R, Morice MC. ACS and STEMI treatment: gender-related issues. EuroIntervention. 2012 Aug;8 Suppl P P27-35. doi:10.4244/eijv8spa6. PMID: 22917787.*
4. *Hochman JS1, Tamis JE, Thompson TD, Weaver WD, White HD, Van de Werf F, Aylward P, Topol EJ, Califf RM : Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators.*
5. *Lawesson, Sofia & Isaksson, Rose-Marie & Thylén, Ingela & Ericsson, Maria & Hellström Ängerud, Karin & Swahn, Eva. (2018). Gender differences in symptom presentation of ST-elevation myocardial infarction – An observational multicenter survey study. International Journal of Cardiology. 264. 10.1016/j.ijcard.2018.03.084.*
6. *Meischke, H., Larsen, M.P. and Eisenberg, M.S., 1998. Gender differences in reported symptoms for acute myocardial infarction: impact on prehospital delay time interval. The American journal of emergency medicine, 16(4), pp.363-6.*
7. *Meischke, H., Eisenberg, M.S., Schaeffer, S.M., Damon, S.K., Larsen, M.P. and Henwood, D.K., 1995. Utilization of emergency medical services for symptoms of acute myocardial infarction. Heart & lung, 24(1), pp.11-8.*
8. *McSweeney, J.C. and Crane, P.B., 2000. Challenging the rules: women's prodromal and acute symptoms of myocardial infarction. Research in nursing & health, 23(2), pp.135-46.*
9. *Kudenchuk, P.J., Maynard, C., Martin, J.S., Wirkus, M., Weaver, W.D. and MITI Project Investigators, 1996. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (the Myocardial Infarction Triage and Intervention Registry). The American journal of cardiology, 78(1), pp.9-14.*
10. *Chandra, N.C., Ziegelstein, R.C., Rogers, W.J., Tiefenbrunn, A.J., Gore, J.M., French, W.J. and Rubison, M., 1998. Observations of the treatment of women in the United States with myocardial infarction: a report from the National Registry of Myocardial Infarction-I. Archives of internal medicine, 158(9), pp.981-8.*
11. *Yarzebski, J., Col, N., Pagley, P., Savageau, J., Gore, J. and Goldberg, R., 1996. Gender differences and factors associated with the receipt of thrombolytic therapy in patients with acute myocardial infarction: a community-wide perspective. American heart journal, 131(1), pp.43-50.*
12. *Kosuge, M., Kimura, K., Ishikawa, T., Ebina, T., Hibi, K., Tsukahara, K., Kanna, M., Iwahashi, N., Okuda, J., Nozawa, N. and Ozaki, H., 2006. Differences between men and women in terms of clinical features of ST-segment elevation acute myocardial infarction. Circulation journal, 70(3), pp.222-6.*
13. *Zhang, Z., Fang, J., Gillespie, C., Wang, G., Hong, Y. and Yoon, P.W., 2012. Age-specific gender differences in in-hospital mortality by type of acute myocardial infarction. The American journal of cardiology, 109(8), pp.1097-103.*
14. *Lawesson, S.S., Alfredsson, J., Fredrikson, M. and Swahn, E., 2012. Time trends in STEMI—improved treatment and outcome but still a gender gap: a prospective observational cohort study from the SWEDEHEART register. BMJ open, 2(2), p.e000726.*
15. *Heer, T., Schiele, R., Schneider, S., Gitt, A.K., Wienbergen, H., Gottwik, M., Gieseler, U., Voigtländer, T., Hauptmann, K.E., Wagner, S. and Senges, J., 2002. Gender differences in acute myocardial infarction in the era of reperfusion (the MITRA registry). The American journal of cardiology, 89(5), pp.511-7.*
16. *Lu, H.T., Nordin, R., Ahmad, W.A.W., Lee, C.Y., Zambahari, R., Ismail, O., Liew, H.B., Sim, K.H. and NCVD Investigators, 2014. Sex Differences in Acute Coronary Syndrome in a Multiethnic Asian Population: Results of the Malaysian National Cardiovascular Disease Database—Acute Coronary Syndrome (NCVD-ACS) Registry. Global heart, 9(4), pp.381-90.*
17. *Patel, H., Rosengren, A. and Ekman, I., 2004. Symptoms in acute coronary syndromes: does sex make a difference? American heart journal, 148(1), pp.27-33.*
18. *Goldberg, R.J., Goff, D., Cooper, L., Luepker, R., Zapka, J., Bittner, V., Osganian, S., Lessard, D., Cornell, C., Meshack, A. and Mann, C., 2000. Age and sex differences in presentation of symptoms among patients with acute coronary disease: the REACT trial. Coronary artery disease, 11(5), pp.399*
19. *Vakili BA, Kaplan RC, Brown DL. Sex-based differences in early mortality of patients undergoing primary angioplasty for first acute myocardial infarction.*
    Circulation 2001;104:3034 – 8.

Research

Characteristics of Patients with Ischemic Ventricular Septal Defects, Following Myocardial Infarction

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Abstract

Introduction: Acute Ventricular Septal Rupture (VSR) following Myocardial Infarction (MI) is one of the rare complications which carries a high morbidity and mortality.

Objective: The aim of the study was focused to elaborate the characteristics of post MI acquired Ventricular Septal Defects (VSD) patients and to follow them up to observe the outcome.

Methodology: A prospective, descriptive observational study was conducted in Teaching Hospital Kandy on a consecutive sample from August 2017 to July 2018. Patients who had acquired VSDs following acute MIs were evaluated by clinical, echocardiographic and coronary angiography and follow up was established.

Results: There were 22 patients in the study sample over a one-year period. The mean age of the sample was 70.09±10.45years and there were 59.10%(n=13) females. 95.45%, (n=21) had acute anterior ST Segment Elevation Myocardial Infarction (STEMI) and 4.55%, (n=1) had acute Inferior STEMI. Out of the sample, 63.64%, (n=14) had received medical thrombolysis. In patients who had anterior MI, 95.45% (n=21) of the VSDs were located at the apical septum. There was a 68.18%, (n=15) mortality observed in the study sample at the end of the 7th day following acquired VSDs. As the treatment options, 22.73%, (n=5) had surgical interventions and 4.55%, (n=1) had catheter-based interventions for the closure of the defect. Interestingly, all the survivals had apically located, functionally restricted VSDs by RV apex.

Conclusion: Though there is a high cardiac mortality observed in patients with acquired VSDs, some echocardiographic features were observed to be associated with better survival in some cases.

Key Words: Ischemic Ventricular Septal Rupture, Acquired Ventricular Septal Defects, Acute Myocardial Infarction, apically located VSD, functionally restricted VSD

Introduction

Acute perforation of the Interventricular Septum (IVS) is a rare complication of Myocardial Infarction (MI). Recent advances in diagnosis and invasive treatment modalities of this complication have changed it to a treatable condition though it has a poor prognosis.

Latham L et al provided an anatomical description of this lesion in 1845, but it was not until 1923, that an ante-mortem diagnosis was made [(1)]. By 1934, Sager had collected 18 cases of perforation, all of which were identified at postmortem examination [(2)].

Perforation of the myocardium following MI is secondary to massive muscle necrosis and mostly occurs within the first 2 weeks following the infarction [(3,4)].

Once perforation has occurred, it is usually tolerated poorly because it is almost always associated with a larger area of trans-septal infarction, with extension of the infarct onto free wall of the left ventricle. This is often accompanied with either an aneurysm of the left ventricle or left ventricular dysfunction.

However, large congenital defects behave differently to this as a result of the various postnatal adaptive processes. Interestingly, in adults with normal pulmonary vascular resistance, acute septal perforations are associated with larger left-to-right shunt [(5)] making them more symptomatic.

Surgical intervention or catheter-based interventions are indicated for majority of patients as the definitive treatment for this condition. The goal of any intervention is to improve the cardiac output and to achieve a hemodynamic stability. However, it has been recognized that the post infarction acquired VSD is one of the poor prognostic markers among all other post MI complications.

Due to the rarity of its presentation and the lack of data among our Sri Lankan population, the aim of this study was focused to elucidate the characteristics of patients with post MI acquired VSDs and to follow them up to observe the outcome.

Research

Methodology

Study design and setting

A prospective observational study was conducted in the Cardiology Unit, Teaching hospital Kandy on a consecutive sample of patients with acquired VSDs following acute MIs from August 2017 to July 2018. These patients were evaluated by clinical, echocardiographic and coronary angiographic findings and a follow up procedure was established.

Inclusion criteria

All the patients with ischemic VSDs following acute MI who presented during the study period were included.

Exclusion criteria

Patients who had already diagnosed congenital VSDs or any other structural heart diseases were excluded from the study.

Data collection process

Demographic and other clinical data was collected through interviewer administered questionnaire. Patient's serial echocardiograms were recorded from the point of diagnosis and followed up to post-operative period in surgically treated patients by a cardiologist.

Coronary angiograms were reported by an experienced cardiologist blinded to the diagnosis of specific echocardiographic features of the VSD of the respective patient.

Ethical clearance

Ethical clearance was obtained from the ethical review committee of Teaching hospital Kandy. Informed written consent was obtained from all participants to participate in the research.

Statistical analysis

Continuous variables were presented as mean with Standard Deviation (SD) and categorical variables as percentages. The Statistical Package for Social Sciences version 17 (SPSS) was used for all calculations and statistical analyses.

Results

There were 22 patients in the study sample over the 1-year period. The mean age of the sample was 70.09±10.45 years and there were 40.90% (n=9) of males. The demographic characteristics are shown in *Table 01*.

Table 01. Baseline characteristics of patients with acquired Ventricular Septal Defect.

Variable	Number
Age, (Mean ± SD)	70.09±10.45 years
Female: male ratio	13:9 (1.4: 1)
Hypertension	11 (50.00%)
Diabetes mellitus	9 (40.90%)
Dyslipidemia	5 (22.73%)
Location of infarction	
Anterior	21 (95.45%)
Inferior	1 (4.55%)
Diseased vessel	
Single Vessel	50.00%
Double Vessel	18.18%
Infarct related artery	
Left coronary artery	82.00%
Right coronary artery	9.00%
Time from MI to VSD diagnosis	
<24 hours	12 (54.55%)
>24 hours	10 (45.45%)
SD= Standard Deviation	

There were 95.45 %, (n=21) acute anterior ST Segment Elevation Myocardial Infarctions (STEMI) and 4.55%, (n=1) had acute Inferior STEMI. Out of the sample, 63.64 %, (n=14) had received medical thrombolysis. 54.55%, (n=12) of patients developed VSDs in the first 24 hours following MI with a mean duration of 2.85±6.58 days and rest of the patients had developed ventricular septal ruptures with a mean duration of 4.65±5.02 days following MI (*Table 02*). None of them had undergone primary PCI on admission. In the patients who had anterior MI, 95.45%, (n=21), the VSDs were located at the apical septum (*Figure-01*).

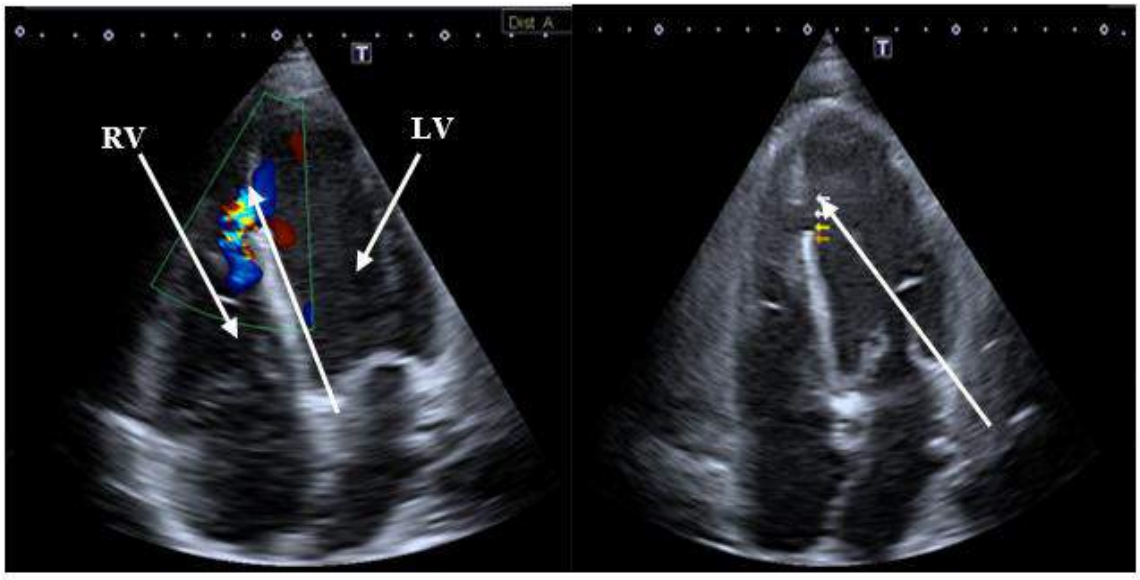

Figure 1: 2D Echocardiogram demonstrating VSD located at the apex with left to right shunt

The patient who had an inferior MI had a large VSD in the inferior septum (Figure 02).

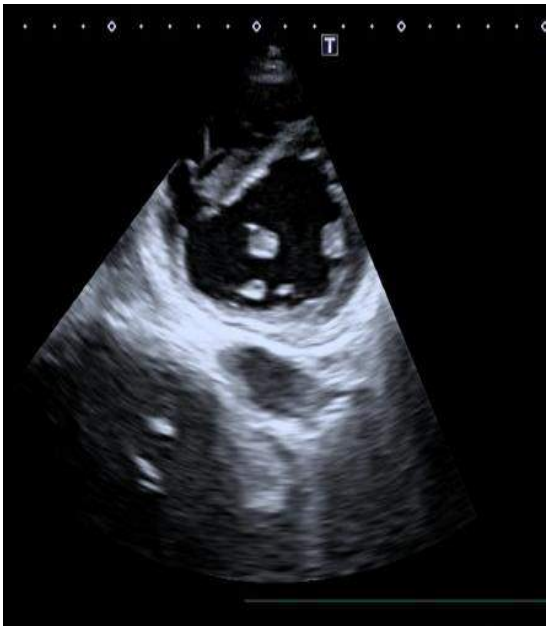

Figure2: Transthoracic 2D Echocardiogram demonstrating a large acquired VSD located at inferior septum

The characteristics of ischemic VSDs are summarized in *Table 02*.

VSD Characteristics	Percentage Mean±SD
Anatomic Location	
Anterior	95.45% (n=21)
Inferior	4.55% (n= 01)
Size, mm	7.40±2.32
Time from MI to VSD diagnosis (days)	4.65±5.02

MI= Myocardial Infarction, SD= Standard Deviation, VSD=Ventricular Septal Defect

Table 2: Ventricular Septal Defect Characteristics.

31.82% (n=7) and 36.36% (n=8) had complicated scenarios with Acute Kidney Injury (AKI) and cardiogenic shock respectively. In addition to that one patient had a ventricular free wall rupture with pericardial effusion (Table 03). None of them had any other complications such as acute Mitral Regurgitation (MR).

Research

Variable	Results n (%)
Acute Kidney Injury	31.82% (n=7)
Cardiogenic Shock	36.36% (n=8)
Ventricular free wall rupture	4.55% (n=1)
Heart Failure	81.81% (n=18)
Acute MR	9.10% (n=2)

In the sample, 45.45%, (n=10) had Single Vessel Disease (SVD) involving Left Anterior Descending (LAD) artery acute occlusions whereas 18.18%, (n=4) had double vessel involvement and only one had a significant left main stem involvement (Figure 03). There were no CTOs of any culprit arteries.

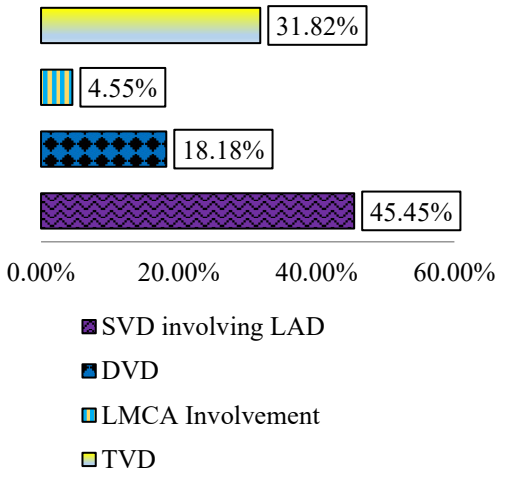

Figure 3: Vascular territorial involvement of the patients with acquired VSDs

There were 68.18%, (n=15) deaths observed in the study sample at the end of the 7th day following acquired VSDs. As the treatment options, 22.73%, (n=5) had surgical interventions and 4.55%, (n=1) had catheter-based interventions for the closure of the defect. Out of the surgically corrected patients, 80.00%, (n=4) survival was seen at the 90th day of follow-up. However, 13.64%, (n=3) survived without surgical or catheter-based interventions. Most interestingly, all survivors in this category had epically located, functionally restricted VSDs by RV apex and SVD involving LAD (Figure 04).

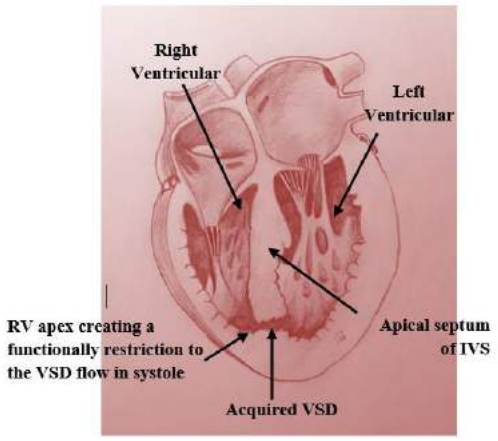

Figure 4: The most common location of the acquired VSD patients who survived without mechanical intervention

Discussion

Acquired VSD following Ventricular Septal Rupture (VSR) is accounted as one of the three major mechanical complications of acute MI, the other two being ventricular free wall rupture and acute mitral regurgitation. In the current era of primary PCI, the incidence of this complication has considerably reduced to less than 1% of cases but still is associated with a high cardiac morbidity and mortality [6]. Though the incidence is falling, both short-term and long-term prognosis following acute ischemic VSDs remains unsatisfactory.

In general, the post infarction VSDs appear 2-8 days after the infarction and often precipitate cardiogenic shock [1]. In our series, the average timing of the VSR was within 5 days following the MI.

There are three varieties observed in acquired ischemic VSDs.

The first, is a direct through and through simple defect, which opens through the IVS. Secondly, complex ruptures can occur which results in blood tracking through one point in the LV aspect of the septum and exiting into RV from a remote site to the entry point. This type of defects enlarges as a result of the pressure gradient between the left and right ventricle. Third, multiple defects occur in 5–11% of cases [7,8].

The hemodynamic instability occurs as a result of acute left-to-right shunt, with RV volume overload, acute rise of pulmonary arterial pressure and secondary volume overload of the left heart causing acute LV dysfunction.

Interestingly, the authors would like to highlight an important observance in this small observational study, which is, that all patients who survived without any mechanical interventions had apically located functionally restricted VSDs by the RV apex. This anatomical orientation might dilute the sudden hemodynamic stress that occurs in classical acquired VSDs and make them into a better tolerable state.

Angiographic data of our study, consistent with some previous study findings, indicates that acquired VSD patients are more likely to have acute total occlusions of the infarct related artery [9,10,11]. In our study, nearly 50% had acute total occlusion of LAD artery but interestingly, none had any chronic total occlusion or retrograde collaterals. This may suggest that the mechanism of ischemic VSR involves abrupt and severe ischemia, propagating to widespread myocardial necrosis in an otherwise well perfused myocardium.

Other important point to consider is that the mortality of post ischemic acquired VSDs remains high. Nearly half of these patients die within the first week and about 85% within 60 days [12,13]. Efforts with medical therapy to stabilize these patient's hemodynamics and other complications are often unsuccessful because many have rapid deterioration with early multi-organ dysfunction [14]. The patients who were managed medically without any mechanical treatment were found to have a 30-day mortality rate as high as 94% [15]. Similarly, in our study the 7th day mortality of such patients was 87.50%. As a treatment modality surgery has traditionally been encouraged as the favored treatment strategy. However, even in the surgical treatment arm, mortality rates can be high ranging from 23–81% [12,14,15]. In our series, the surgically treated ones showed an 80% survival rate by the day 90 follow up.

Though the surgery is successful, an incomplete closure or secondary defects can account for postoperative residual shunts. However, most of these shunts are physiologically well tolerated and spontaneous closure has also been reported [14]. Similarly, there were 2 patients who had post-surgical residual shunts in our study but all remained hemodynamically insignificant.

One interesting observation in the prognosis of these patients is that the mortality rates for all patients with acquired VSDs were analogous at one month and twelve months (74% and 78%) [7]. This indicates that if the patient survives following the initial admission, the long-term prognosis is relatively good.

There is some proof that the myocardium is too fragile for a safe repair immediately after an acute ischemic VSR. Therefore, a brief waiting period following the diagnosis is expected to generate a firmer scar around the infarcted tissues, thus facilitating surgical repair [16]. However, more recent studies, have reported an improved survival rate with rapid and aggressive intervention after this diagnosis [17,18].

Therefore, it is still debatable whether immediate aggressive surgical intervention or interval surgery is best to improve the survival of these patients.

Apart from the surgery, catheter-based intervention is also emerging as a potential treatment modality in post infarct VSDs. The accumulating evidence regarding the device closure suggests that percutaneous trans catheter closure of post infarction VSD achieves a reasonable outcome, with a low rate of major complications [19]. However, there is also a need for long term surveillance of patients to enable making firm decisions on the treatment modality which will improve patient prognosis.

Limitations

The study is limited in some aspects. First, the number of patients of the study sample was small. Therefore, further investigations including larger study samples are needed to confirm these findings. Second, a significant referral bias was present due to the single-center study design. However, our institute has a wide range of population drainage from various parts of the country as the unit is one of the main cardiology centers in Sri Lanka.

This study is further limited by the fairly short-term follow up period. Thus, a long-term follow up is needed to obtain the accurate prognostic data of these patients. Hence, a multicenter large-scale study comparing different treatment modalities is warranted in order to assess the prognosis and long-term treatment outcomes of these patients with ischemic VSR.

Research

Conclusions

Post-MI ischemic VSR still represents a notable challenge for both cardiologists and cardiac surgeons. There is a high cardiac mortality observed in patients with acquired VSDs. However, apically located and functionally restricted nature of the VSDs by the RV apex was observed to have a better survival even without mechanical or surgical intervention in this series of patients.

Acknowledgement

We would like to thank the staff of the Cardiology unit of Teaching hospital Kandy and Dr. Prashan Edirisinghe, Medical officer, Teaching hospital Kandy for providing the schematic diagram.

References

1. *Creighton B. Wright, M.D., and Johann L. Ehrenhaft, M.D.,Ventricular Septal Defect Following Myocardial Infarction Berkeley Brandt, 111, M.D., The Annals of Thoracic Surgery 1979; 27(6): 580-589.*
2. *Sager R. V.: Coronary thrombosis: perforation of the infarcted interventricular septum. Arch Intern Med 1934 (53):140,.*
3. *Cooley DA, Belmonte BA, Zeis LB, et al: Surgical repair of ruptured interventricular septum fol- 588 lowing acute myocardial infarction. Surgery 1957 (41):930.*
4. *Kitamura S, Mendez A, Kay JH: Ventricular septal defect following myocardial infarction: experience with surgical repair through a left ventriculotomy and review of literature. J Thorac Cardiovasc Surg 1971 (61):186*
5. *Selzer A, Gerbode F, Kerth WJ: Clinical, hemodynamic, and surgical considerations of rupture of the ventricular septum after myocardial infarction. Am Heart J 1969 (78):598.*
6. *Alok R, Kalpesh M, Manik C, Arool S, Kanaiyalal P., Perventricular device closure of post-myocardial infarction ventricular septal defect: Can it combine best of both worlds, Int J Case Rep Imag 2016;7(4):272–274*
7. *Brian S. Crenshaw, Christopher B. Granger, Yochai Birnbaum, Karen S. et al, Risk Factors, Angiographic Patterns, and Outcomes in Patients With Ventricular Septal Defect Complicating Acute Myocardial Infarction, Circulation. 2000;101:27-32*
8. *Kasim O, Sinan T, Aron F, Jose H, Jan D, Kerstin B, et al., Experiences with surgical treatment of ventricle septal defect as a post infarction complication, Journal of Cardiothoracic Surgery 2009, 4:3*
9. *Skehan JD, Carey C, Norrell MS, DeBelder M, Balcon R, Mills PG. Patterns of coronary artery disease in post-infarction ventricular septal rupture. Br Heart J. 1989;62:268 –272.*
10. *Cheriex EC, de Swart H, Dijkman LW, Havenith MG, Maessen JG, Engelen DJM, Wellens HJJ. Myocardial rupture after myocardial infarction is related to the perfusion status of the infarct-related artery. Am Heart J. 1995;129:644–650.*
11. *Topaz O, Mallon SM, Chahine RA, Sequeira RF, Myerburg RJ. Acute ventricular septal rupture: angiographic-morphologic features and clinical assessment. Chest. 1989;95:292–298.*
12. *Michael SF, Jason R. Post Myocardial Infarction Ventricular 55 Septal Defect. Front Lines of Thoracic Surgery. InTech; 2012*
13. *Daggett WM, Guyton RA, Mundth ED, et al. Surgery for post-myocardial infarct ventricular septal defect. Ann Surg 1977 Sep;186(3):260–71.*
14. *Xu XD, Liu SX, Liu X, et al. Percutaneous closure of postinfarct muscular ventricular septal defects: a multicenter study in China. J Cardiol 2014 Oct;64(4):285–9.*
15. *Nikolaos K, Stephen JD. Device Closure for Ventricular Septal Defect after Myocardial Infarction. Cardiology Interventions Today 2009; 43- 9.*
16. *Simon Maltais, Reda Ibrahim, Arsène-Joseph Basmadjian, Michel Carrier, Denis Bouchard, Raymond Cartier, et al., Postinfarction Ventricular Septal Defects: Towards a New Treatment Algorithm?, Ann Thorac Surg 2009; (87); 687-93*
17. *Landzberg MJ, Lock JE. Transcatheter management of ventricular septal rupture after myocardial infarction. Semin Thorac Cardiovasc Surg 1998;10:128 –32.*
18. *Pesonen E, Thilen U, Sandström S, et al. Transcatheter closure of post-infarction ventricular septal defect with the Amplatzer Septal Occluder device. Scand Cardiovasc J 2000; 34:446–8.*
19. *Ruoxi Zhang, Yong Sun, Meng Sun, Hui Zhang, Jingbo Hou, and Bo Yu, In-Hospital Outcomes and Long-Term Follow-Up after Percutaneous Transcatheter Closure of Postinfarction Ventricular Septal Defects, BioMed Research International, 2017*

Research

Analysis of the Utility of JCTO Score in Real Life Chronic Total Occlusion (CTO) PCI Revascularization in Sri Lanka- Insights from a Two-year Single centre, Single Operator Study

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Abstract

Chronic total occlusion revascularization by PCI offers new options for treating severe coronary artery disease in Sri Lanka, with ability to successfully treat complex coronary lesions. A single centre study of 75 CTO revascularizations in Sri Lanka suggests presence of lesions with longer angulated calcific lesions with higher JCTO Scores (>96% of JCTO=/>2, usually with additional lesions), in comparison to multinational registries. Despite this, a higher degree of success (>82.7%) with sometimes double CTOs + non-CTO lesion revascularizations can be achieved by contemporary techniques, in a single setting with very low serious complications (<1.3%). In order to identify truly impossible-to-revascularize lesions by PCI, a recalibration of the existing JCTO score or development of different scale for Sri Lankan patients may need to be considered.

Keywords: Chronic total occlusions, revascularization, PCI, JCTO score

Introduction

Chronic Total Occlusions (CTOs) are considered to be the most difficult subset of coronary artery disease encountered by cardiologists for revascularization by percutaneous coronary interventions (PCI). Prior to availability of skillsets and equipment for undertaking PCI on CTOs, majority of patients with these lesions were either sent for coronary artery bypass grafting (CABG) as the only option, or tried on medical therapy with varying degrees of success (or failures+/- crossing over to surgical treatment later).

The benefits of CTO revascularization have sometimes, due to technical difficulties, been overlooked or felt to be largely applicable to reduction of symptoms[(1)], but reduction in ischaemia driven complications such as life threatening arrhythmias or left ventricular dysfunction [(2)] is as important as the improved functional status of the patient post PCI, so that lifestyle changes can be facilitated to mitigate cardiac risk factors such as diabetes, hypertension and lack of physical exercises. Many studies have also suggested that successful CTO PCI is associated with reduced long-term cardiac mortality and need for coronary artery bypass graft surgery [(3, 7)].

Careful pre-procedural planning and patient evaluation by experienced CTO operators is mandatory to achieve success and prevent complications.

The patient selection is helped by a multitude of tests supplemented by careful review of clinical parameters such as symptoms, left ventricular function, renal function, previous surgeries/interventions and comorbidities. High-quality, simultaneous dual coronary angiography is the most useful tool to assess the strategy and level of difficulty of performing successful PCI in a CTO lesion. Anatomical complexity is the single most important factor that may determine the chances of success or failure of many lesions, followed by special training, availability of advanced imaging adjuncts and financial/cathlab constraints.

Various CTO risk evaluation scores have been devised and validated to assess the complexity of CTOs, including the widely used J-CTO score (Multicenter CTO Registry of Japan), PROGRESS-CTO score, RECHARGE (Registry of Crossboss and Hybrid Procedures in France, the Netherlands, Belgium and United Kingdom) CL-score (Clinical and Lesion related score), ORA score, Ellis et al score, the weighted angiographic scoring model (W-CTO score), CASTLE score, CT-RECTOR multicenter registry score and the Korean Multicenter CTO CT Registry Score. The J-CTO score has been validated in several settings outside Japan and followed up with one year of clinical validation[(5)]. However, the biggest drawback of these scores is the fact that their applicability needs to be validated on a given population in order to adapt their widespread use[(6)].

In the Sri Lankan setting, the utility of these scores have not been validated systematically. Neither are substantial numbers of CTO procedures being performed annually, despite there being large numbers of patients who can potentially benefit, primarily due to limited resources in terms of cathlab times and financial constraints. Therefore, we attempted to systematically evaluate CTO revascularization process of a single operator in a single setting in Sri Lanka to understand some of the complexities of the process in our population and whether the scoring system is fit for the purpose for identifying high risk CTOs.

Methodology

Inclusion criteria:

All patients undergoing a CTO revascularization procedure at Durdans hospital, Colombo under the author (PA) for 2 years were included for the study. All CTOs performed as single lesion or multiple lesions were included. The data for 100% of cases including initial angiograms for the full calendar years of 2018 and 2020 were available, and were analyzed by us.

Study method:

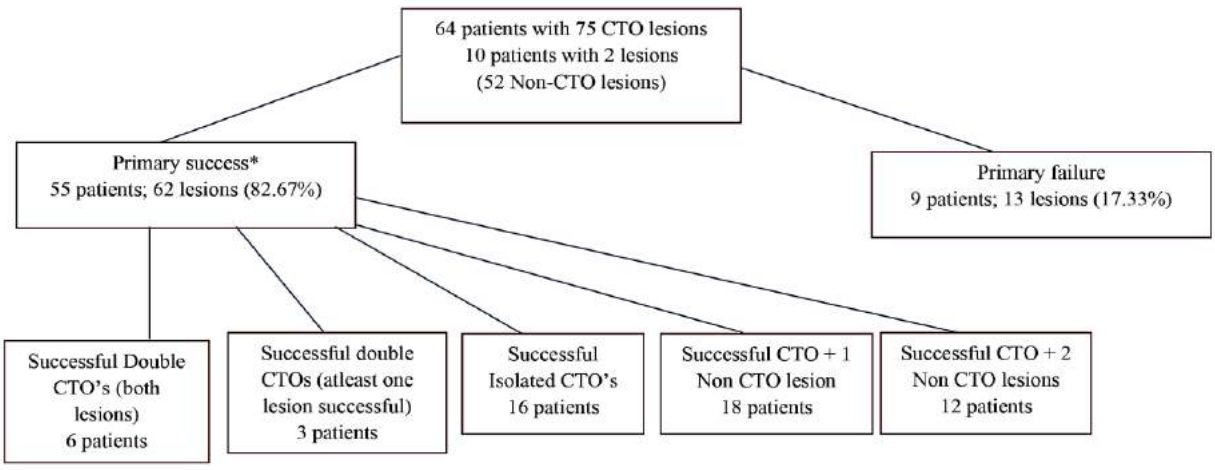
All eligible cases were selected from cathlab case reports and linked report systems and by retrospective evaluation of coronary cine-angiograms (initial and dual injection shots) obtained or imported into Phillips Allura Clarity or Phillips Azurion platforms.

Patient demographic data was obtained and tabulated. Each CTO lesion was separately assessed and approximate occlusion length and angles calculated using Phillips's software. JCTO score was calculated and outcomes were assessed according to definitions.

Definitions:

Coronary CTOs were defined as coronary lesions with thrombolysis in myocardial infarction (TIMI) grade 0 flow of at least 3 months duration. Estimation of the duration of occlusion was clinical, based on the first onset of angina, prior history of myocardial infarction in the target vessel territory, or comparison with a prior angiogram. Procedure success was defined as successful completion of PTCA by wire crossing, pre-dilating and implanting a well apposed stent and restoration of full flow in a CTO lesion. Partial success was defined as crossing the CTO lesion and being able to perform a minimum of a POBA with reestablishment of any grade of antegrade flow. All other outcomes were documented as failures. Immediate serious complications (death, stroke, coronary perforation, tamponade, cardiac arrest, need for in-hospital dialysis) Summary of cases and lesions included according to definitions are stated in flowchart 1.

Flowchart 1- Patient selection and evaluation.



Statistical analysis

Descriptive statistics were expressed as percentages and were tabulated. Where comparisons with external databases were made, Student's t-test & Pearson's Chi-square test was used to analyze for significance of difference. All statistical analyses were performed with GraphPad Prism (version 9.0) or SPSS software. A two-sided p-value of <0.05 was considered statistically significant.

Results

Descriptive statistical data

A total of 75 CTO lesions were attempted for revascularization in 64 patients in the time period stipulated. The mean age of the patients was 59.87 +/- 13.46 (61.27 +/- 13.98 & 56.2 +/- 12.58) years. There were 56 males (87.5%) and 8 (12.5%) females.

A total of 6 of 64 (9.37%) patients had a history of recent myocardial infarction and 5 of 64(7.81%) patients had a previous CABG. 20 of 64 (31.25%) had a single CTO lesion alone and another 21 of 64 (32.81%) had a single CTO with another non-CTO lesion revascularized and another 13 of 64 (20.31%) had a single CTO and 2 other non-CTO lesions revascularized in the same procedure.

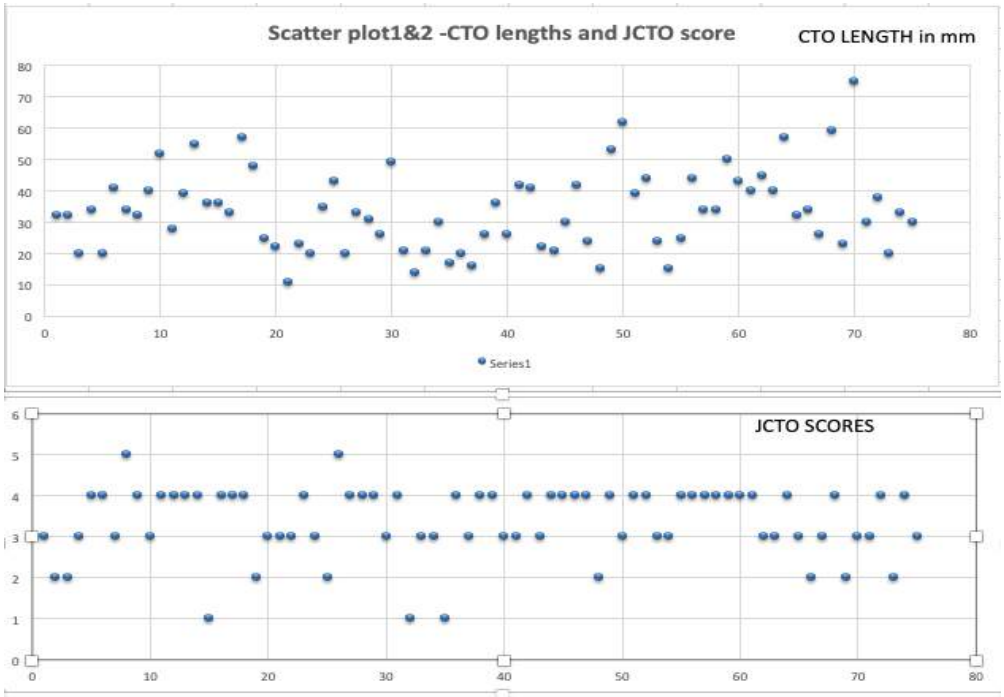
10 of 64 (15.62%) had double CTO lesions treated in the same procedure, of which 5 of 64 (7.81%) had a non-CTO lesion in addition to a double CTO for revascularization. For the completion of all the procedures a total of 138 drug eluting stents were placed in the 64 patients (2.16 per patient). Out of the lesions 8% were located in left main-Os LAD location and another 38%in the LAD territory, yielding a total of 46% of LMS or LAD CTO indication for revascularization (see Table 1).

Of the CTO lesions, re-do procedures for previously failed CTOs done elsewhere accounted for 5.33% of the cases. The average occlusion length of the CTO lesions in this series was 34.52 +/- 15.49 mm and 66 of the 75 (88%) of the lesions exceeded 20 mm in occlusion length. 56 of the 75 lesions (66%) had calcification and 70 of 75 (93.3%) lesions had angulation(s). The average JCTO score was 3.36 +/- 0.86. Only 3 of the 75 (4%) of the CTO lesions had a JCTO score <2 and 72 of the 75 (96%) had a JCTO score =/> 2. 2 of 75 (2.67%)lesions were CTOs in stents (re-stenotic/thrombosed) lesions. All others were native vessel CTOs and no graft CTOs were undertaken for revascularization (as expected in this lesion subset). The number of CTOs attempted per patient was 1.17.

The scatter plots 1 & 2 show CTO lesion lengths and JCTO scores encountered in this series.

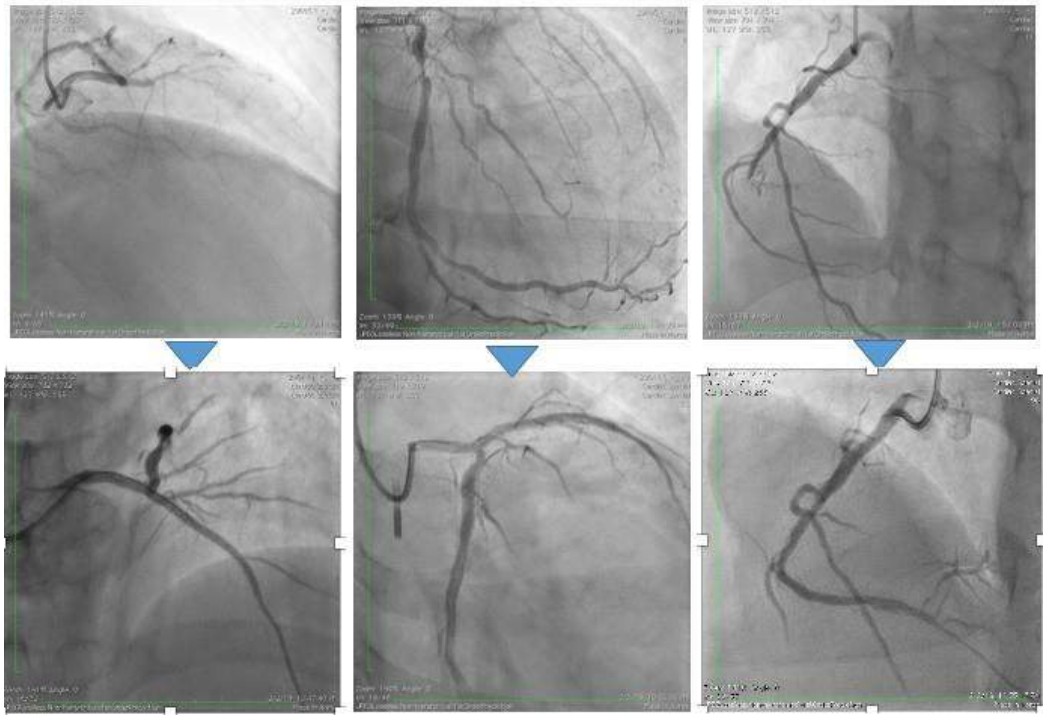
Table1	Successful CTO	Failed CTO	Total in our cohort
Baseline characteristics			
Age (Yrs)	59.23 +/- 12.89	62.36+/-11.83	**59.87 +/- 12.809**
Male	84.91%	100%	**87.50%**
Prior MI	5/6*100	1/6*100	**6/64*100= 9.38%**
Prior CABG	4/5	1/5	**5/64*100= 7.81%**
CTO located in			
LAD	35.48%	53.84%	**38.67%**
LCx	14.52%	15.38%	**14.67%**
RCA	40.32%	30.77%	**38.67%**
LMS	9.68%	-	**8.00%**
CTO length	32.52 +/- 12.61	38.76 +/- 12.66	**33.60 +/- 12.76**
Number of stents	127/138	11/138	**138**
JCTO	**3.31 +/- 0.82**	**3.62 +/- 1.04**	**3.36 +/- 0.86**

Research



An example of complex CTOs of a young patient with double CTO + non-CTO critical disease successfullyrevascularized by PCI in a single setting is shown in figure 1.

Figure 1-Double CTO+non-CTO PCI (3 lesions in one setting) in a 32year old with LVSD



Comparative Statistical data

We compared our data to the external dataset available with the Multinational Chronic Total Occlusion Registry [MNCTOR][6]. This comparison is summarized in Table 2.

The mean age of patients was numerically lower at 59.87 +/- 13.46 years in comparison to 61.48 +/- 10.61 but statistically non-significant (2 tailed unpaired t-Test $p<0.24$).

Mean CTO lesion length in our cohort of 33.6+/-12.76mm, was higher in comparison to 22.3+/-15.6mm in the MNCTO registry. This length difference is statistically highly significant (2 tailed unpaired t-Test p<0.0001).

The primary technical success rate in our cohort was 82.7% (62/75) and technical failure rate was 17.3% (13/75). In comparison, the MNCTO registry reported primary success rates of 62.3% and failure rate of 37.7%. Using a Chi-Square test, the two-tailed p value was calculated <0.0001 (highly statistically significant) for primary success and <0.0025 for all successes (very significant even after including success in the second attempt at failed cases in the MNCTOR vs single attempt in our cohort), in favor of higher success rates in our cohort.

The percentage of double CTO procedures performed in the same setting was 15.63% (10/64), in comparison to 3.40% (61/1791) in the MNCTO registry percentage. On average, 1.17 CTO lesions were attempted in our cohort vs 1.034 lesions per patient in MNCTOR.

The success-to-failure rates of revascularizing double CTOs in a single procedure were higher in our cohort (60%:40% vs 49% :51%) and statistically significant (two tail Chi-square test p value = 0.0278).

Of the CTO lesions 72 of 75 (96%) were of a JCTO score=>2.

The revascularization of the group of 64 patients needed 138 stents (100% drug eluting stents) with a mean of 2.15 stents per patient per procedure in an intent-to treat basis. This is in contrast to the MNCTO registry data of use of a mean of 1.6 stents per patient.

The occurrence of immediate peri-procedural complications was next reviewed. Target vessel perforation/residual severe coronary dissection during CTO recanalization was recorded in one the 75 lesions described (This was successfully sealed with balloon tamponade and use of a covered stent, without a significant clinical consequence), amounting to 1.3%. This was in sharp contrast to the combined 8.7% instances of target vessel perforation/residual severe coronary dissection reported in the MNCTO registry, statistically significantly different in favour of our cohort (Chi-square two-tailed p value = 0.0063). Perioperative MI/death/stroke/need for renal replacement therapy following CTO PCI was zero in our cohort.

To assess the utility of the JCTO score, we compared the scores for all cases of technical success vs failures. Table 1 illustrates the summary of JCTO scores. Analysis of those with JCTO<2 vs JCTO=>2scores in the two groups within our study surprisingly did not differ statistically (Chi square, two-sided p<0.45). However, when the cutoff was changed to JCTO<4 vs JCTO =>4, there was a statistically significant difference (Chi square, two-sided p<0.0479).

Table 2	Our cohort	MNCTO Registry	P value
Baseline characteristics			
Mean Age (Yrs)	59.87 +/- 13.46	61.48 +/-10.61	**<0.24 (NS)**
Mean CTO length	33.6 +/- 12.76	22.30 +/- 15.6mm	**<0.0001(HS)**
Primary success rate	82.7% (62/75)	62.3%	**<0.0001 (HS)**
Technical failure rate	17.3% (13/75)	37.7%	
% of Double CTO	15.63% (10/64)	3.40% (61/1791)	
Avg CTO lesions attempted/patient	1.17	1.034	
Success: Failure of Double CTO	60% : 40%	49% : 51%	**0.0278 (S)**
No of Stents / patient/ procedure	2.15	1.6	
Incidence of peri-procedural complications	1.3%	8.7%	**0.0063 (HS)**
Sri Lankan cohort **JCTO<4 vs ≥4**	**Success vs failure analysis**	-	**0.0479 (S)**

Research

Discussion

The study above illustrates that the typical patient in this cohort of patients in Sri Lanka undergoing CTO revascularization, is of similar age group to other patients in MNCTO registries, but appear to have much longer CTO occlusions, more double CTOs per patient and more lesions need to be revascularized with a higher number of stents in one setting. The CTO lesions in this cohort had a JCTO score of = >2 in almost all patients, indicating higher grades of difficulty for CTO PCI. Nearly half of all these cases involved LMS- Os LAD or LAD location.

On a positive note, despite the higher complexity of current day CTO procedures, both the efficacy and safety aspects were substantially better with higher immediate success rate and lower complication rates in our cohort of patients.

The reasons for this improved outcome may be multifactorial. Over the past decade, CTO revascularization techniques have evolved substantially and with extensive training, operator skills, the understanding of how to overcome these lesions are substantially better at present. Enhanced guidewire technology, trackable microcatheters /septal dilators, dedicated CTO balloons, intracoronary imaging and high resolution fluoro imaging systems all support the skills of present day CTO operators. Hence, more complex CTO lesions can be undertaken at present with success.

Therefore, in the present era, it is evident that current cutoff of 2 in the JCTO score, the once most validated scoring system that predicted ease of CTO crossability is no longer able to predict the chances of success or failure in our study. When the cut off of 4 of the JCTO score is used, there appears to be a statistically significant, better discrimination of CTOs that are likely to fail.

Based on these findings, we propose that our patient population will require a larger scale study to revalidate of the JCTO score with a view to reset the cutoff for complexity level (4 instead of 2?) or derivation of a different CTO scoring system for risk analysis in Sri Lankan patients undergoing CTO PCI. With growing number of CTO PCI cases in our database, we hope to conduct a larger scale study to assess these findings in due course.

References

1. *Brilakis E., Mashayekhi K., Tsuchikane E. et al. Guiding Principles for Chronic Total Occlusion Percutaneous Coronary Intervention A Global Expert Consensus Document. Circulation. July 2019: 140(5):420-433*
2. *Laroussi L. , Gaemperli O., Behnes M., Akin I., Lüscher T., Neumann F. et al. Percutaneous coronary intervention of chronic total occlusions in patients with low left ventricular ejection fraction. JACC Cardiovasc Interv. Nov 2017:10:2158–2170.*
3. *Mehran R., Claessen B., Godino C., Dangas G. et al. Long-Term Outcome of Percutaneous Coronary Intervention for Chronic Total Occlusions. JACC: Cardiovascular Interventions. Sep 2011: 9(4):952–61*
4. *Christopoulos, G, Wyman, RM, Alaswad, K, Karmpaliotis, D, Lombardi, W, Grantham, JA, Yeh, RW, Jaffer, FA, Cipher, DJ, Rangan, BV, et al. Clinical utility of the Japan-chronic total occlusion score in coronary chronic total occlusion interventions: results from a multicenter registry. Circ Cardiovasc Interv. Jul 2015: 8(7): e002171.*
5. *Nombela-Franco L., Urena M., Jerez-Valero M. et al. Validation of the J-Chronic Total Occlusion Score for Chronic Total Occlusion Percutaneous Coronary Intervention in an Independent Contemporary Cohort. Circulation: Cardiovascular Interventions Dec 2013: 6(6): 635-643*
6. *Barbara A. Danek, , Aris Karatasakis, , Dimitri Karmpaliotiset al . Impact of lesion age on outcomes of chronic total occlusion percutaneous coronary intervention: Insights from a contemporary US multicenter registry. Can J Cardiol. Dec 2016 ; 32(12): 1433–1439*
7. *Park TK, Lee SH, Choi KH et al. Late Survival Benefit of Percutaneous Coronary Intervention Compared With Medical Therapy in Patients With Coronary Chronic Total Occlusion: A 10-Year Follow-Up Study. J Am Heart Assoc. Mar 2021;10(6): e019022*

Review

Periprocedural Permanent Pacemaker Requirement in Transcatheter Aortic Valve Implantation (TAVI).

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Introduction

Transcatheter Aortic Valve Implantation (TAVI) is becoming increasingly popular in recent times globally. Conceptually it is an improvement on Balloon Aortic Valvuloplasty (BAV), which was first performed in 1985 for symptomatic severe aortic stenosis in patients with prohibitive surgical risks [(1)]. After the first human TAVI procedure was performed in 2002 in France [(2)] , the technique has advanced extensively and is expanding fast to include patient categories traditionally managed by surgical aortic valve replacement (SAVR) and aggressive medical management. Although initially licensed for symptomatic severe/critical aortic stenosis new data has elaborated its usefulness in moderate valve disease [(1)]. Hence TAVI numbers are expected to rise exponentially in the next decade in the majority of the cardiac centers globally.

Any major surgical procedure, especially cardiovascular, will have its own risks. TAVI's major complications traditionally has been vascular injury, major stroke, acute coronary ischaemia, cardiac trauma, regurgitation and permanent conduction tissue damage. As per registry data, the permanent conduction tissue damage requiring permanent pacemaker implantation (PPM) is the commonest complication and ranges from 14-17% in Europe+ United States. Combined meta-analysis of registry data[(3)] disclose this complication of TAVI as 13% in Belgium, 20% in Brazil and 16% in the UK (United Kingdom). Importantly PPM implantation did not affect overall or cardiovascular mortality in almost all the cohort studies[(2)]. But it was an important morbidity parameter including longer hospital stay and infection. An important factor also to note is that, even in SAVR the PPM rates are around 10-20% worldwide, which keeps both at an equipoise[(4).]

Why is conduction tissue affected frequently?

This association is multifactorial and multi-hit insult pathophysiology is the currently accepted theory for the aetiology.

The Atrio-Ventricular node (AV), His bundle, left bundle and fascicle are in close proximity to the aortic valve anatomically. The AVN lies in right atrium floor in an area called triangle of Koch, delineated by septal tricuspid valve and tendon of Todaro forming the apex and coronary sinus forming the base. His bundle crosses the atrio-ventricular fibrous rim and lies in close proximity to membranous intraventricular septum (IVS). It may lie towards the left endocardial surface or be buried within the septum. The LBB is a thick endocardial structure at the membranous-muscular IVS junction. In essence the core-conduction system is juxtaposed with the non-coronary cusp (NCC), Right Coronary Cusp (RCC) and Left Ventricular Outflow Tract (LVOT)[(4)]. Post-mortem studies have shed light into possible mechanisms of injury to specialized conduction tissue during TAVI. They are direct pressure and compression, haemorrhage - haematoma, ischaemia of tissue and transient inflammation [(2)] .

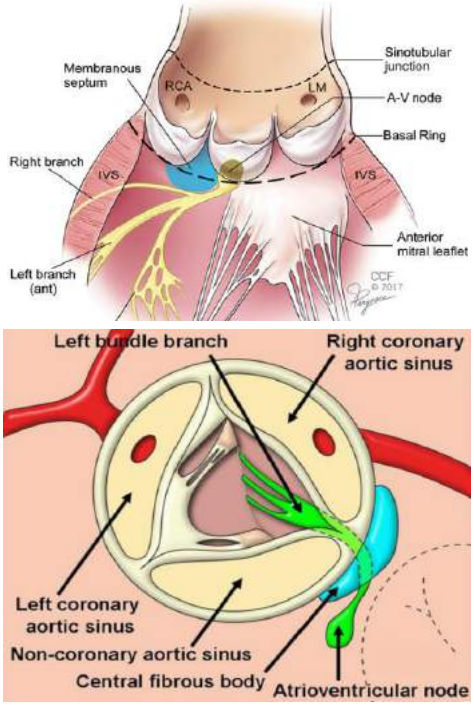

Figure 1: Anatomical relationships of aortic annulus to conduction system.

There has been an interesting study looking in to dormant conduction tissue disease pre-TAVR. Results show that calcific long-term aortic stenosis leads to concealed conduction tissue disease in approximately one third (33%) of patients which included high degree AV block (HAVB)[4]. This is further supported by the epidemiological data showing the TAVI patient population with advanced age and comorbidities having significant degenerative conduction tissue disease too.

Is the damage reversible?

The insult to conduction tissue leading to PPM can happen in two scenarios: Peri procedurally or delayed usually up to 7 days postoperative. When it comes to HAVB it is found that 8.7% of all pacemakers are decided peri-procedurally and 6.7% during the delayed time frame up to day 7 [5]. This shows the importance of ECG monitoring in the immediate post-operative period. Daily 12-lead ECG's, telemetry, and infrequently Holter and EP studies are the methods by which observation can be performed. As a general rule a patient without pre-existing conduction disease on surface ECG and with 48 hours stable rhythm without significant changes can be deemed not to need pacemaker implantation. Some researchers have challenged the need of pacemaker insertion showing pacemaker dependency data at 30 days and 6 months of TAVI and PPM implantation. PPM independency is defined as ventricular pacing frequency of less than 1% on day 30 pacing check. With regards to LBBB and HAVB the criteria were fulfilled in around 50% of patients on average. This significant proportion may be due to relief from mechanical strain as tissue inflammation settles down in the para-Hisian area. On the contrary even in the few occasions the pacing has occurred may have been lifesaving. On the other hand, there is no reliable way of identifying which patient would be dependent and who will not. Additionally, the actual indication for the PPM affects the pacing dependency. For example, new onset LBBB + first degree HB will have totally different natural course to HAVB/CHB.

Intraprocedural rapid pacing

Because of the need of extremely accurate valve placement, TAVI procedure utilizes rapid ventricular pacing for transient periods.

This is on an average at 160-200bpm and for a few seconds cardiac systolic contraction is suppressed. Both predilatation and valve implantation uses pacing. This is a very important step and needs to be reliable without loss of capture. Previously all the TAVI procedures utilized balloon tipped RV pacing with 5Fr catheter. Currently three main systems are utilized.

1) If patient has dual chamber pacing already, we put him to asynchronous pacing mode and achieve pacing through pacemaker generator.

2) A RV balloon tipped catheter is connected to pacing box through separate venous access.

3) Pacing the LV endocardium through LV stiff wire used to implant valve.

The third technique, which is relatively novel, minimizes the theoretical risk of RV pacing perforation and does not need additional venous access.

What factors have positive correlation with need of PPM?

This has been the key question of a majority of research in the field. Broadly the variables have been categorized in to four separate areas: clinical, anatomical, Trans catheter heart Valve (THV) device and THV technique related. Universally the most significant hazard ratios and reproducibility of results have been associated with Right Bundle Branch Block (RBBB)[8]. It has shown hazard ratios (HR) of 4-49 in various patient populations across the world. This is because RBB is relatively safe anatomically than the LBB and any pre-existing disease of RBB with procedural injury to LBB means diffuse conduction damage. Next has been the valve type (THV) used. Traditionally self-expanding valves have had worse outcomes than balloon dilated THV's.

Next most significant associations were found with regards to first degree heart block>240ms, aortic pressure mean gradient>50mmHg and depth of deployment >7mm in to LVOT. As an example, if you have RBBB+ >50 mmHg mean gradient + self-expanding THV you have 63 times higher risk of PPM than without any of them [5].

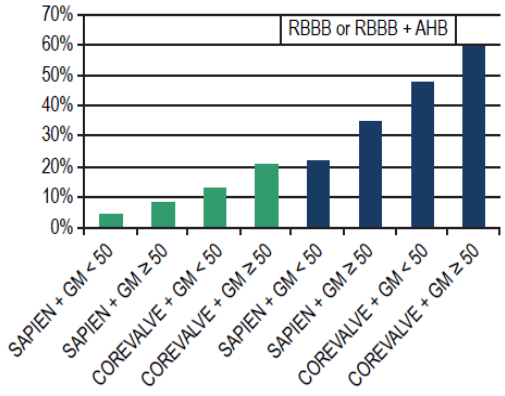

Figure 2: Risk of PPM implantation in Brazilian registry according to variables[2].

General consensus is that TAVI patients are categorized in to one of the following five categories after TAVI in order to best manage them peri-operatively [(5)],

1) Sinus rhythm (SR) at baseline, No RBBB and remains same post-procedure.
2) SR with RBBB at baseline and remains same post procedure.
3) RBBB/LBBB/IVCD (intra-ventricular conduction delay) >120ms, 1st Degree AVB at baseline and new ECG changes (worsening >20ms) post procedure.
4) New onset LBBB.
5) HAVB/CHB (Complete heart block peri-procedurally)

These categories have separate algo rhythms for follow up and decision making on PPM as well as when to remove temporary pacing wire safely. Generally, group one can be off temporary pacemaker (TPM) at the end of procedure, group 2 will keep TPM 24 hours/telemetry 24 hours, group 3 will definitely keep TPM 24 hours and proceed to telemetry for further 24 hours and then a decision will be taken on further action depending on progression/regression of ECG changes.

Group 4 will need to keep TPM 24 hours and have low threshold for worsening ECG changes. Group 5 will get intraprocedural PPM if persistent, if transient we can observe with TPM cover for 48 hours.

Despite these guidelines there is a huge inter-center variation. Hence, one has to pick the custom-tailored policies best suitable to the respective unit.

Summary

Periprocedural PPM in TAVI is a major concern. Number of centers including ours are working on developing an accurate risk prediction model. Careful analysis of pre-peri-post procedural 12 lead ECG is the cornerstone of management. Pre-procedure PPM prediction as well as score calculator if validated would be useful for the following reasons:

1) We can produce reasonably accurate percentage data for need of PPM, during consenting process customized to the patient in question.
2) Hospital stay in PPM group is significantly longer (1.5:1 ratio in studies)
3) For particular patients with high pre-test score, need to liaise with electrophysiologists and be prepared for early pacemaker plan.
4) Costing of overall procedure.
5) Deciding on the particular types of THV and techniques of implantation.
   (For example, avoiding pre and post dilatation and implantation depth).
6) Although TAVI is expected to improve LVEF in EF impaired patient group due to burned out aortic stenosis, significant RV pacing in PPM patients would not gain that advantage at one year according to latest research.

Factors considered:

1) Clinical and Electrocardiographic:

Age, gender, diabetes, ischaemic heart disease, ejection fraction, atrial fibrillation., hypertension. RBBB and duration, 1st degree AVB, LBBB and duration, fascicular, Left Anterior Fascicular Block (LAFB), Left Posterior Fascicular Block (LPFB).

2) Anatomical:

Membranous septum length, LVOT and valve calcium, calcium score in CT, bicuspid, valve area, perimeter, Coronary heights, RCC and NCC calcium, significant ostial coronary disease, AV pressure gradient.

3) Device:

THV type, THV size, balloon inflated or not, recapture/dislodgement.

4) Technique:

Implantation depth from annulus, pre-dilatation, post dilatation, balloon-annulus ratio.

References

1. *Auffret V, Puri R, Urena M. et al. Conduction Disturbances After Transcatheter Aortic Valve Replacement: Current Status and Future Perspectives. Circulation. 2017 Sep 12;136(11):1049-1069.*
2. *Alain G. Cribier; The Odyssey of TAVR from Concept to Clinical Reality. Tex Heart Inst J 1 April 2014; 41 (2): 125–130.*
3. *Permanent pacing after transcatheter aortic valve implantation. Incidence, Predictors and Evolution of Left Ventricular Function. Cláudio Monteiro,1 Andres Di Leoni Ferrari,1 Paulo Ricardo Avancini Caramori et al.*
4. *TAVI and Post Procedural Cardiac Conduction Abnormalities.Antonio Mangieri, Claudio Montalto, Matteo Pagnesi et al.*
5. *Arrhythmia burden in elderly patients with severe aortic stenosis as determined by continuous electrocardiographic recording. Urena M, S, Cheema AN, et al.Circulation: 2015; 131:469–77.*
6. *Management of Conduction Disturbances Associated WithTranscatheter Aortic Valve Replacement-JACC Scientific Expert Panel Josep Rodés-Cabau, Kenneth A. Ellenbogen,b Andrew D. Krahn.*
7. *The Electrocardiogram After Transcatheter Aortic Valve Replacement Determines the Risk for Post-Procedural High-Degree AV Block and the Need for Telemetry Monitoring. Stefan Toggweiler, Stefan Stortecky, Erik Holy.*

Tutorial

Novel Therapeutic Agent for Hyperlipidaemia: Inclisiran

From the editorial desk

1. What is inclisiran?

Inclisiran is a siRNA which blocks the expression of PCSK-9.

2. What is the action of inclisiran?

This molecule blocks the transcription of PCSK-9.

This leads to a reduction of PCSK-9 levels in hepatocytes which in turn causes the increased expression of LDL receptors on the hepatocyte membrane. Hence blood levels of LDL fall.

3. What is siRNA?

siRNA refers to short interfering RNA also called silencing RNA. It is a double stranded RNA.

When a siRNA enters a cell, it is processed into a single stranded RNA which gets incorporated into an RNA induced silencing complex (RISC).

The siRNA (in the RISC) can bind to the mRNA which we wish to silence (by finding a complementary RNA strand) and cut it so that it is now recognized as being abnormal and destroyed by the cell.

Hence the mRNA can no longer synthesize the molecules it is programmed to produce

4. What are the other drugs that reduce PCSK-9 levels?

The monoclonal antibodies against PCSK-9 are already in use. These are evolocumab and alirocumab.

5. What is the advantage of inclisiran?

While the PCSK-9 inhibitors now in use have to be administered monthly, inclisiran has to be given only once in six months.

6. Is inclisiran approved for clinical use?

It is approved by the USA FDA and is included in the UK, NICE guidelines.

6. When is inclisiran indicated?

When a patient on maximum tolerated doses of statins and ezetimibe does not achieve guideline recommended lipid levels PCSK-9 inhibitors must be considered.

7. What clinical trials are available?

Inclisiran has been tested in a series of clinical trials named ORION trials.

8. Do we have good evidence of clinical benefit?

No, we do not. The results of ORION4 are awaited in 2024 which will give us the data on cardiovascular outcomes.

One meta-analysis reported that inclisiran reduced major adverse cardiovascular events by 24%.

9. What are the side effects of inclisiran?

Adverse effects at the site of injection were reported in the trials.ie: pain, erythema, rash. There was no need to withdraw the drug due to local reactions.

10. To what levels does inclisiran reduce serum lipids?

In a meta-analysis the following reductions were seen:

LDL-C	by	51%
TC	by	37%
ApoB	by	41%
Non-HDL	by	45%

No muscle, liver or renal side effects were noted.

11. Do anti inclisiran antibodies form during treatment?

Approximately 5% develop such antibodies but safety and efficacy of continued administration are not compromised.

Journal scan

Rapid Journal Scan of scientific papers

From the editorial desk

Myopathy Associated with Statins and SGLT2 - A Review of Literature

Rahul Gupta et al.
Current Problem in Cardiology.2021 Apr;46(4):100765.

Drug-induced myopathy is a well-described clinical entity characterized by muscle damage leading to symptoms ranging from myalgias to rhabdomyolysis and acute kidney injury. Many pharmacotherapies are known to precipitate myopathic symptoms.
Recent case reports suggest a potential relationship between the use of sodium/glucose cotransport 2 (SGLT2) inhibitors and onset of myopathy. The pathogenesis of this has yet to be elucidated. The relevance of this association is augmented by the recent popularity of SGLT2 inhibitors as well as the tendency for them to be prescribed alongside statins. This study reviewed the literature on the incidence and mechanism of drug-induced myopathy in patients with type 2 diabetes mellitus who are taking SGLT2 inhibitors with and without the use of statins.

Can Radiation Dose Burden of CT Angiography be Reduced While Still Accurately Diagnosing Etiology of Acute Chest Pain?

Sherine M.Sharara et al.
Current Problem in Cardiology. 2021 Apr;46(4):100766

Multidetector-row computed tomography is often used as a first-line test in the diagnostic evaluation of cardiovascular diseases including aortic dissection, coronary artery disease and pulmonary embolism. This study evaluated the impact of reducing the tube potential from 120 KVp to 100 KVp in a selected group of patients presenting to the Emergency Room with acute chest pain. The primary end point was how the reduction of radiation dose affected image quality.

Methods: The current study was performed over a period of 2 years between July, 2016 and July, 2018. This study included patients who presented to the Emergency Room or to an outpatient clinic and were suspected to have a coronary, a pulmonary (pulmonary embolism), or an aortic (aortic dissection) etiology. Suspicion was determined by the medical provider based on clinical picture, ECG, and lab results when available. All patients were referred for computed tomography angiography (CTA) testing as part of their diagnostic evaluation. A total of 84 patients were involved in the study. Seventy patients underwent the low acquisition KVp technique (100 KVp - Group I). In the remaining 14 patients, the standard acquisition technique (120-140 KVp - Group II) was utilized. Results: This study showed the feasibility of using low energy CTA to significantly reduce the patient's radiation exposure without markedly affecting the image quality and diagnostic accuracy. Conclusion: The use of low energy CTA protocols in cases of acute chest pain revealed no major difference regarding the image quality with marked reduction of the radiation dose received by the patient.

Septic Cardiomyopathy: From Basics to Management Choices

Nidhruv Ravikumar et al.
current Problems in Cardiology 2021 Apr;46(4):100767.

Septic cardiomyopathy (SCM) is increasingly recognized as a potential complication of septic shock; it is understood to be a reversible left ventricular systolic dysfunction. The presence of SCM in septic shock, in previous studies, infer a poorer prognosis as it significantly increases the mortality rate of patients to 70%-90% and its incidence varies from 18% to 40% of septic shock patients. The pathogenesis is unclear, but believed to be a combination of bacterial toxins, cytokines, nitric oxide, and cardiac mitochondrial dysfunction, that depresses intrinsic cardiac contractility. The presence of SCM can be diagnosed in patients using a bedside transthoracic echocardiogram which typically shows left ventricular ejection fraction <45% and right ventricular dilatation.

For management, levosimendan provides a good hemodynamic response without increasing cardiac oxygen demand when compared to dobutamine, while more invasive techniques such as extracorporeal membrane oxygenation, and intra-aortic balloon pulsation are being explored as well as potential rescue strategies for patients with severe SCM.

Commercial Air Travel for Passengers with Cardiovascular Disease: Recommendations for Less Common Conditions, Considerations for Venous Thromboembolism, and General Guidance

Choong Hou Koh et al.
Current Problem in Cardiology. 2021 Apr;46(4):100782.

The accelerated growth of commercial flights has resulted in a huge upswing of air travelers over the last few decades, including passengers with a wide range of cardiovascular conditions.

Notwithstanding the ongoing COVID-19 pandemic that has set back the aviation industry for the next 1-2 years, air travel is expected to rebound fully by 2024. Guidelines and evidence-based recommendations for safe air travel in this group vary, and physicians often encounter situations where opinions and assessments on fitness for flights are sought. This article aims to provide an updated suite of recommendations for the aeromedical disposition of passenger with uncommon cardiovascular conditions, such as congenital heart diseases, inflammatory cardiac conditions (endocarditis/pericarditis/myocarditis), pulmonary hypertension, and venous thromboembolism.

Endomyocardiofibrosis: A Systematic Review

Cristhian Emmanuel Scatularo et al.
Current Problem in Cardiology. 2021 Apr;46(4):100784.)

Endomyocardiofibrosis was described first time in Uganda as an infrequent restrictive cardiomyopathy with a poor prognosis, characterized by fibrosis of the ventricular sub endocardium and severe restrictive physiology leading to difficult therapeutic management and frequently associated with hyper eosinophilic syndrome. Its higher prevalence in the tropics and its relationship in some cases with hyper eosinophilic endocarditis has led to the search for genetic, infectious, autoimmune and nutritional causes, but its etiology remains unclear.

It is a rare cardiomyopathy, difficult to diagnose and with a nonexistent effective treatment. Imaging methods such as echocardiography and cardiac magnetic resonance are essential for the initial diagnosis, although endomyocardial biopsy establishes the definitive diagnosis. Immunosuppressive treatment is only useful in the early stages of the disease and usually ineffective if installed late when signs of heart failure are present. Surgical treatment is generally palliative

Challenges of Combining Opioids and P2Y 12 Inhibitors in Acute Coronary Syndrome: Should the Future Be Opioid Free?

Catherine H Moore et al.
Current Problem in Cardiology. 2021 Apr;46(4):100781

Morphine has been long recognized as standard of care in the treatment of acute coronary syndrome (ACS) patients; however, its safety has recently been called into question due to a drug interaction with P2Y12 inhibitors. Opioids, given in combination with P2Y12 inhibitors, can reduce antiplatelet effects by slowing gastrointestinal motility and ultimately reducing drug absorption. While there are proposed benefits of opioids in ACS patients, conflicting data regarding clinical outcomes exist.

The majority of clinical data slightly favors opioid use in ST-elevation myocardial infarction over

non-ST-elevation myocardial infarction, although trends for increased myocardial infarction are present in both settings. Current practice should be aimed at discerning the need for routine opioid use in ACS. Alternative strategies may be needed to overcome these interactions; however, no robust data are currently available to support these treatment options. Future research should be aimed at non-opioid treatment options in ACS, as opioid use remains controversial in this population.

Prognostic Value of Left Ventricular Global Strain Analysis by Two-Dimensional Speckle-Tracking Echocardiography in Non-Hemodynamically Significant Intermediate Coronary Lesions

Manolo Rubio et al.
Current Problem in Cardiology. 2021 Apr;46(4):100787

Intermediate coronary lesions represent a major challenge for the invasive and noninvasive cardiologist. Left ventricular strain calculation by speckle tracking echocardiography has the capacity to analyze the motion of the cardiac tissue. This study aimed to evaluate its usefulness and prognostic significance in non-hemodynamically significant intermediate coronary lesions. We studied 247 patients who underwent a clinically indicated coronary angiogram. Each of the patients had a single non-revascularized non-hemodynamically significant intermediate severity coronary lesion (ISCL) with a fractional flow reserve greater than 0.80 The left ventricular global longitudinal strain (GLS) was calculated using speckle-tracking echocardiography with TomTec 2D Cardiac Performance Analysis (Unterschleissheim, Germany). An abnormal GLS was defined as less than 20%. The primary endpoints were revascularization of the target lesion, admissions for major adverse cardiac events (MACE), and cardiac-related mortality, all within 2 years. On multivariate logistic regression data analysis, we found that patients with an ISCL and abnormal GLS had an increased risk for admissions due to MACE (odds ratio [OR] 1.06, $P < 0.05$, confidence interval [CI] 95%, 1.005-1.120], and an increased risk of cardiac-related death (OR 1.12, $P < 0.05$, CI 95% 1.012-1.275). There was no difference in the need for target lesion revascularization among individuals with normal and abnormal GLS (1.00, P 0.88, CI 95% .950-1.061).

Left ventricular strain analysis by speckle-tracking echocardiography showed an independent prognostic value in patients with non-revascularized non-hemodynamically significant coronary lesions.

Outdoor light at night and risk of coronary heart disease among older adults: a prospective cohort study

Shengzhi Sun et al.
European Heart Journal (2021) 42, 822–830

We estimated the association between outdoor light at night at the residence and risk of coronary heart disease (CHD) within a prospective cohort of older adults in Hong Kong.

Over a median of 11 years of follow-up, we identified 3772 incident CHD hospitalizations and 1695 CHD deaths. Annual levels of outdoor light at night at participants' residential addresses were estimated using time-varying satellite data for a composite of persistent night-time illumination.

Conclusions:
Among older adults, outdoor light at night at the residence was associated with a higher risk of CHD hospitalizations and deaths. We caution against causal interpretation of these novel findings. Future studies with more detailed information on exposure, individual adaptive behaviors, and potential mediators are warranted to further examine the relationship between light at night and CHD risk.

Midlife blood pressure is associated with the severity of white matter hyperintensities: analysis of the UK Biobank cohort study

Karolina Agnieszka Wartolowska et al.
European Heart Journal (2021) 42, 750–757

White matter hyperintensities (WMH) progress with age and hypertension, but the key period of exposure to elevated blood pressure (BP), and the relative role of systolic BP (SBP) vs. diastolic BP (DBP), remains unclear. This study aims to determine the relationship between WMH and concurrent vs. past BP.

Conclusions:
WMH were strongly associated with concurrent and past elevated BP with the population burden of severe WMH greatest for SBP. However, before the age of 50, DBP was more strongly associated with WMH. Long-term prevention of WMH may require control of even mildly elevated midlife DBP

A leucopoietic-arterial axis underlying the link between ambient air pollution and cardiovascular disease in humans.

Shady Abohashem et al.
European Heart Journal (2021) 42, 761–772

Air pollution [i.e., particulate matter with diameter <2.5 μm (PM2.5)] is a risk factor for major adverse cardiovascular events (MACE). While PM2.5 promotes leucopoiesis and atherosclerotic inflammation in experimental models, it is unknown whether this occurs in humans. We tested in humans (i) whether PM2.5 associates with higher leucopoietic tissue activity and arterial inflammation (ArtI), (ii) whether these associations persist after accounting for the effects of potential confounders including socioeconomics, traffic noise, and risk factors, and (iii) whether these tissue effects mediate the association between air pollution and MACE.

Conclusions:
Higher air pollution exposure associates with heightened leucopoietic activity and ArtI and independently predicts MACE through a biological pathway that includes higher leucopoietic activity and ArtI in series.

Salt and cardiovascular disease: insufficient evidence to recommend low sodium intake

Martin O'Donnell et al.
European Heart Journal (2020) 41, 3363–3373

Several blood pressure guidelines recommend low sodium intake (<2.3 g/day, 100 mmol, 5.8 g/day of salt) for the entire population, on the premise that reductions in sodium intake, irrespective of the levels, will lower blood pressure, and, in turn, reduce cardiovascular disease occurrence.

These guidelines have been developed without effective interventions to achieve sustained low sodium intake in free-living individuals, without a feasible method to estimate sodium intake reliably in individuals, and without high-quality evidence that low sodium intake reduces cardiovascular events (compared with moderate intake). In this review, we examine whether the recommendation for low sodium intake, reached by current guideline panels, is supported by robust evidence. Our review provides a counterpoint to the current recommendation for low sodium intake and suggests that a specific low sodium intake target (e.g. <2.3 g/day) for individuals may be unfeasible, of uncertain effect on other dietary factors and of unproven effectiveness in reducing cardiovascular disease.

We contend that current evidence, despite methodological limitations, suggests that most of the world's population consume a moderate range of dietary sodium (2.3–4.6g/day; 1–2 teaspoons of salt) that is not associated with increased cardiovascular risk, and that the risk of cardiovascular disease increases when sodium intakes exceed 5 g/day. While current evidence has limitations, and there are differences of opinion in interpretation of existing evidence, it is reasonable, based upon observational studies, to suggest a population-level mean target of <5 g/day in populations with mean sodium intake of >5 g/day, while awaiting the results of large randomized controlled trials of sodium reduction on incidence of cardiovascular events and mortality.

Effect of alirocumab on cardiovascular outcomes after acute coronary syndromes according to age: an ODYSSEY OUTCOMES trial analysis

Peter R Sinnaeve et al.
European Heart Journal (2020) 41, 2248-2258.

Lowering low-density lipoprotein cholesterol (LDL-C) reduces cardiovascular risk irrespective of age, but the evidence is less strong for older patients.

This prespecified analysis from ODYSSEY OUTCOMES compared the effect of alirocumab vs. placebo in 18 924 patients with recent acute coronary syndrome (ACS) according to age.

Journal scan

Conclusion: In patients with recent ACS, alirocumab improves outcomes irrespective of age. Increasing absolute benefit but not harm with advancing age suggests that LDL-C lowering is an important preventive intervention for older patients after ACS.

Statin therapy increases lipoprotein(a) levels

Sotirios Tsimikas et al
European Heart Journal (2020) 41, 2275–2284.

This subject-level meta-analysis includes 5256 patients (1371 on placebo and 3885 on statin) from six randomized trials, three statin-vs.-placebo trials, and three statin-vs.-statin trials, with pre- and on-treatment (4–104 weeks) Lp(a) levels. Statins included atorvastatin 10 mg/day and 80 mg/day, pravastatin 40 mg/day, rosuvastatin 40 mg/day, and pitavastatin 2 mg/day.

Conclusions:
This meta-analysis reveals that statins significantly increase plasma Lp(a) levels. Elevations of Lp(a) post-statin therapy should be studied for effects on residual cardiovascular risk.

Profound reductions in first and total cardiovascular events with icosapent ethyl in the REDUCE-IT trial: why these results usher in a new era in dyslipidaemia therapeutics

William E Boden et al.
European Heart Journal (2020) 41, 2304-2312.

The aims of this clinical review are to: (i) highlight the importance of elevated baseline triglycerides (TG) in the setting of well-controlled low-density lipoprotein cholesterol (LDL-C) on statins as a major contributor to residual atherosclerotic cardiovascular disease (ASCVD) risk, particularly among patients with type 2 diabetes mellitus, metabolic syndrome, and obesity whose distinctive lipid phenotype cannot be optimally treated with LDL-C reduction therapy alone; (ii) describe the findings and clinical implications of the landmark REDUCE-IT trial in which ethyl eicosapentaenoic acid significantly improved ASCVD outcomes.

While many genetic studies have shown that elevated TG are an independent causal factor for ASCVD, prior placebo-controlled trials using niacin, fibrates, omega-3 fatty acids, and dietary supplement fish oil preparations have failed to demonstrate significant CV event reduction when added to statin therapy. In contrast, the REDUCE-IT trial in 8179 participants showed convincingly that the administration of 4 g daily of icosapent ethyl (an ethyl ester of eicosapentaenoic acid) in patients at high risk for ASCVD with increased levels of baseline TG [median value, 2.44 mmol/L (216.0 mg/dL)] but well-controlled LDL-C [median value, 1.94 mmol/L (75.0 mg/dL)] reduced significantly incident events across both the trial primary endpoint and multiple prespecified secondary endpoints, including cardiovascular death, as well as both subsequent and total primary endpoint and key secondary endpoint events. Icosapent ethyl unequivocally contributed to ASCVD event reduction over and above statin therapy. The REDUCE-IT trial results should alter our approach to managing a growing population of hypertriglyceridaemic patients whose lipid phenotype requires more intensive treatment beyond LDL-C lowering alone.

Cardiac procedural myocardial injury, infarction, and mortality in patients undergoing elective percutaneous coronary intervention: a pooled analysis of patient-level data

Johanne Silvain et al.
European Heart Journal (2021) 42, 323–334

The prognostic importance of cardiac procedural myocardial injury and myocardial infarction (MI) in chronic coronary syndrome (CCS) patients undergoing elective percutaneous coronary intervention (PCI) is still debated.

Methods and results: We analyzed individual data of 9081 patients undergoing elective PCI with normal pre-PCI baseline cardiac troponin (cTn) levels. Multivariate models evaluated the association between post-PCI elevations in cTn and 1-year mortality, while an interval analysis evaluated the impact of the size of the myocardial injury on mortality.

Procedural myocardial injury, as defined by the Fourth Universal Definition of MI (UDMI) [post-PCI cTn elevation ≥1 × 99th percentile upper reference limit (URL)], occurred in 52.8% of patients and was not associated with 1-year mortality. The association between post-PCI cTn elevation and 1-year mortality was significant starting ≥3 × 99th percentile URL. Major myocardial injury defined by post-PCI ≥5 × 99th percentile URL occurred in 18.2% of patients and was associated with a two-fold increase in the adjusted odds of 1-year mortality. In the subset of patients for whom periprocedural evidence of ischaemia was collected (n = 2316), type 4a MI defined by the Fourth UDMI occurred in 12.7% of patients and was strongly associated with 1-year mortality [adj OR 3.21, 95% CI (1.42-7.27), P = 0.005]. We also present our results according to the type of troponin used (hs-cTn or conventional troponin).

Conclusions:
Our analysis has demonstrated that in CCS patients with normal baseline cTn levels, the post-PCI cTn elevation of ≥5 × 99th percentile URL used to define type 4a MI is associated with 1-year mortality and could be used to detect 'major' procedural myocardial injury in the absence of procedural complications or evidence of new myocardial ischaemia.

Angiotensin-converting enzyme 2 (ACE2) levels in relation to risk factors for COVID-19 in two large cohorts of patients with atrial fibrillation

Lars Wallentin
European Heart Journal (2020) 41, 4037-4046

The global COVID-19 pandemic is caused by the SARS-CoV-2 virus entering human cells using angiotensin-converting enzyme 2 (ACE2) as a cell surface receptor. ACE2 is shed to the circulation, and a higher plasma level of soluble ACE2 (sACE2) might reflect a higher cellular expression of ACE2. The present study explored the associations between sACE2 and clinical factors, cardiovascular biomarkers, and genetic variability.

Plasma and DNA samples were obtained from two international cohorts of elderly patients with atrial fibrillation (n = 3999 and n = 1088). The sACE2 protein level was measured by the Olink Proteomics® Multiplex CVD II96 × 96 panel.

Levels of the biomarkers high-sensitive cardiac troponin T (hs-cTnT), N-terminal probrain natriuretic peptide (NT-proBNP), growth differentiation factor 15 (GDF-15), C-reactive protein, interleukin-6, D-dimer, and cystatin-C were determined by immunoassays. Genome-wide association studies were performed by Illumina chips. Higher levels of sACE2 were statistically significantly associated with male sex, cardiovascular disease, diabetes, and older age. The sACE2 level was most strongly associated with the levels of GDF-15, NT-proBNP, and hs-cTnT. When adjusting for these biomarkers, only male sex remained associated with sACE2. We found no statistically significant genetic regulation of the sACE2 level.

Male sex and clinical or biomarker indicators of biological ageing, cardiovascular disease, and diabetes are associated with higher sACE2 levels. The levels of GDF-15 and NT-proBNP, which are associated both with the sACE2 level and a higher risk for mortality and cardiovascular disease, might contribute to better identification of risk for severe COVID-19 infection.

A randomized controlled trial of dapagliflozin on left ventricular hypertrophy in people with type two diabetes: the DAPA-LVH trial

Alexander J M Brown
European Heart Journal (2020) 41, 3421-3432

We tested the hypothesis that dapagliflozin may regress left ventricular hypertrophy (LVH) in people with type 2 diabetes (T2D).

Conclusions:
Dapagliflozin treatment significantly reduced LVM in people with T2D and LVH. This reduction in LVM was accompanied by reductions in systolic BP, body weight, visceral and SCAT, insulin resistance, and hsCRP. The regression of LVM (Left Ventricular Mass) suggests dapagliflozin can initiate reverse remodeling and changes in left ventricular structure that may partly contribute to the cardio-protective effects of dapagliflozin.

Journal scan

Where have all the myocardial infarctions gone during lockdown? The answer is blowing in the less-polluted wind

Eugenio Picano
European Heart Journal (2020) 41, 2146–2147

Pollution drop-off for lockdown is likely to reduce acute cardiovascular admissions and acute environmental cardiovascular mortality, due to the falling concentration of fine particulate matter and nitrogen dioxide in the air

The COVID-19 crisis brought about a plummet of urban pollution due to lockdown of public offices, schools, and industries. The lockdown was started in China and Italy but later adopted in March 2020 by most countries worldwide as the most effective strategy for containment of virus diffusion. The improvement in air quality was the best possible result achieved for the worst possible reason.

A reduction in fine particulate matter (PM), nitrogen dioxide, and ozone in the air mean less acute hospital admissions for cardiovascular disease and possibly a lower cardiovascular mortality due to environmental causes in the long run. In China in the Wuhan region, the concentration of mean tropospheric nitrogen dioxide density (an index of pollution) fell from values > 500 lg/m3 to 10-fold lower values. In Europe 1 month after of lockdown, the concentration of nitrogen dioxide fell by 50% on average.

Three weeks after the starting of regional lockdown leading to economic slowdown and traffic restrictions, the concentration of fine PM (<2.5 microns) fell by 54% in South Korea capital Seoul, by 44% in the Chinese city of Wuhan and by 60% in the Indian capital of New Delhi. Los Angeles experienced its longest stretch of clean air on record meeting World Health Organization guidelines.

In general, cities with historical levels of higher levels of PM pollution witnessed the more substantial drops. The pollution decrease paradoxically could be expected to translate in a health benefit.

A 10 $\mu g/m^3$ increase in fine PM concentration on the same day is associated with an 11% increase in hospital admissions due to circulatory causes. All-cause cardiovascular mortality increases by 10% per 10 $\mu g/m^3$ elevation in long-term average fine PM exposure. It has been calculated that in Spain a mean overall reduction in fine particles levels of 1 $\mu g/m^3$ from 2007 to 2013 will postpone, for 100 000 population annually, all-cause deaths, for lung cancer, and for ischaemic heart disease.

In the lockdown days, we are on the downhill steep curve linking pollution and cardiovascular disease. The observed reduction in pollution markers might be mirrored by a parallel reduction in acute admissions in the short-term, and this is already being anecdotally reported 1 week after lockdown in several countries. The abatement of environmental pollution may also lead to a reduced disease burden in the long run, although this clearly depends on the duration of the pandemic and maintenance of containment measures.

The cardiac sympathetic co-transmitter neuropeptide Y is pro-arrhythmic following ST-elevation myocardial infarction despite beta-blockade

Manish Kalla et al.
European Heart Journal (2020) 41, 2168-2179

ST-elevation myocardial infarction is associated with high levels of cardiac sympathetic drive and release of the co-transmitter neuropeptide Y (NPY). We hypothesized that despite beta-blockade, NPY promotes arrhythmogenesis via ventricular myocyte receptors.

In 78 patients treated with primary percutaneous coronary intervention, sustained ventricular tachycardia (VT) or fibrillation (VF) occurred in 6 (7.7%) within 48 h. These patients had significantly ($P < 0.05$) higher venous NPY levels despite the absence of classical risk factors including late presentation, larger infarct size, and beta-blocker usage.

Conclusions:
The co-transmitter NPY is released during sympathetic stimulation and acts as a novel arrhythmic trigger. Drugs inhibiting the Y receptor work synergistically with beta-blockade as a new anti-arrhythmic therapy.

Clinical application of the 4th Universal Definition of Myocardial Infarction

Tau S Hartikainen
European Heart Journal (2020) 41, 2209–2216

The recently released 4th version of the Universal Definition of Myocardial Infarction (UDMI) introduces an increased emphasis on the entities of acute and chronic myocardial injury. We applied the 4th UDMI retrospectively in patients presenting to the emergency department with symptoms potentially indicating myocardial infarction (MI) to investigate its effect on diagnosis and prognosis.

Conclusion
By accentuating the categories of acute and chronic myocardial injury the 4th UDMI succeeds to identify patients with higher risk for cardiovascular events and poorer outcome and thus seems to improve risk assessment in patients with suspected MI. Application of established diagnostic algorithms remains safe when using the 4th UDMI.

Multicenter, randomized comparison of two-stent and provisional stenting techniques in patients with complex coronary bifurcation lesions: the DEFINITION II trial

Jun-Jie Zhang et al.
European Heart Journal (2020) 41, 2523-2536

The present study aimed to assess the benefits of two-stent techniques for patients with DEFINITION criteria-defined complex coronary bifurcation lesions.

Conclusions:
For DEFINITION criteria-defined complex coronary bifurcation lesions, the systematic two-stent approach was associated with a significant improvement in clinical outcomes compared with the provisional stenting approach. Further study is urgently warranted to identify the mechanisms contributing to the increased rate of type V MI after provisional stenting.

Mortality after drug-eluting stents vs. coronary artery bypass grafting for left main coronary artery disease: a meta-analysis of randomized controlled trials

Yousif Ahmad et al
European Heart Journal (2020) 41, 3228–3235

The optimal method of revascularization for patients with left main coronary artery disease (LMCAD) is controversial. Coronary artery bypass graft surgery (CABG) has traditionally been considered the gold standard therapy, and recent randomized trials comparing CABG with percutaneous coronary intervention (PCI) with drug-eluting stents (DES) have reported conflicting outcomes. We, therefore, performed a systematic review and updated meta-analysis comparing CABG to PCI with DES for the treatment of LMCAD.

Conclusions:
The totality of randomized clinical trial evidence demonstrated similar long-term mortality after PCI with DES compared with CABG in patients with LMCAD. Nor were there significant differences in cardiac death, stroke, or MI between PCI and CABG. Unplanned revascularization procedures were less common after CABG compared with PCI. These findings may inform clinical decision-making between cardiologists, surgeons, and patients with LMCAD.

Coexistence and outcome of coronary artery disease in Takotsubo syndrome

L Christian Napp et al.
European Heart Journal (2020) 41, 3255–3268

Takotsubo syndrome (TTS) is an acute heart failure syndrome, which shares many features with acute coronary syndrome (ACS). Although TTS was initially described with angiographically normal coronary arteries, smaller studies recently indicated a potential coexistence of coronary artery disease (CAD) in TTS patients. This study aimed to determine the coexistence, features, and prognostic role of CAD in a large cohort of patients with TTS.

Conclusions:
Coronary artery disease frequently coexists in TTS patients, presents with the whole spectrum of coronary pathology including acute coronary occlusion, and is associated with adverse outcome.

Rheumatic heart disease and COVID-19 Critical considerations for patients, providers, and health systems dealing with rheumatic heart disease during and post-pandemic

L Christian Napp et al.
European Heart Journal (2020) 41, 4085–4086

Rheumatic heart disease (RHD) affects >39 million persons around the world, with the highest prevalence in low-resource populations with constrained health systems.

The World Heart Federation lists RHD as a risk factor for severe COVID disease "unique to low-income countries". Although the magnitude of the direct risk is not known, this risk is likely to be higher in those living with more severe forms of valvular heart disease and highest among patients with pulmonary hypertension and those with heart failure, requiring medication to improve cardiac function. Individual risk of death may be further augmented by resource constraints in low- and middle-income countries (LMICs) where most patients with RHD live, and where there is the least capacity to respond.

We recommend that patients continue to take all prescribed cardiac medications, including those classified as angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), due to a lack of data supporting COVID specific risk of these therapies. In addition, patients with prosthetic heart valves on warfarin and requiring regular international normalized ratio (INR) checks will find this time particularly challenging to access regular review, where clinics and even hospitals are curtailing normal services. In contrast to the direct risk of COVID-19 to people living with RHD, which is largely unknown, there are known indirect risks of the COVID-19 pandemic to people living with RHD, largely driven by the global disruption in healthcare systems and supply chains.

RHD patients are sensitive to receiving regular and timely care—and disruptions to service access increases risk of progression and adverse outcomes.

Time-to-treatment initiation of colchicine and cardiovascular outcomes after myocardial infarction in the Colchicine Cardiovascular Outcomes Trial (COLCOT)

Nadia Bouabdallaoui
European Heart Journal (2020) 41, 4092-4099

The COLchicine Cardiovascular Outcomes Trial (COLCOT) demonstrated the benefits of targeting inflammation after myocardial infarction (MI). We aimed to determine whether time-to-treatment initiation (TTI) influences the beneficial impact of colchicine. In COLCOT, patients were randomly assigned to receive colchicine or placebo within 30 days post-MI. Time-to-treatment initiation was defined as the length of time between the index MI and the initiation of study medication. The primary efficacy endpoint was a composite of cardiovascular death, resuscitated cardiac arrest, MI, stroke, or urgent hospitalization for angina requiring coronary revascularization. The relationship between endpoints and various TTI (<3, 4-7 and >8 days) was examined using multivariable Cox regression models. Amongst the 4661 patients included in this analysis, there were 1193, 720, and 2748 patients, respectively, in the three TTI strata. After a median follow-up of 22.7 months, there was a significant reduction in the incidence of the primary endpoint for patients in whom colchicine was initiated < Day 3 compared with placebo [hazard ratios (HR) = 0.52, 95% confidence intervals (CI) 0.32-0.84], in contrast to patients in whom colchicine was initiated between Days 4 and 7 (HR = 0.96, 95% CI 0.53-1.75) or > Day 8 (HR = 0.82, 95% CI 0.61-1.11). The beneficial effects of early initiation of colchicine were also demonstrated for urgent hospitalization for angina requiring revascularization (HR = 0.35), all coronary revascularization (HR = 0.63), and the composite of cardiovascular death, resuscitated cardiac arrest, MI, or stroke (HR = 0.55, all P < 0.05).

Conclusions: Patients benefit from early, in-hospital initiation of colchicine after MI.

Complete revascularization reduces cardiovascular death in patients with ST-segment elevation myocardial infarction and multivessel disease: systematic review and meta-analysis of randomized clinical trials.

Rita Pavasini et al
European Heart Journal (2020) 41, 4103-4110.

The aim of this work was to investigate the prognostic impact of revascularization of non-culprit lesions in patients with ST-segment elevation myocardial infarction (STEMI) and multivessel disease by performing a meta-analysis of available randomized clinical trials (RCTs).

Data from six RCTs comparing complete vs. culprit-only revascularization in STEMI patients with multivessel disease were analyzed with random effect generic inverse variance method meta-analysis. The endpoints were expressed as hazard ratio (HR) with 95% confidence interval (CI). The primary outcome was cardiovascular death. Main secondary outcomes of interest were all-cause death, myocardial infarction (MI), and repeated coronary revascularization.

Conclusions: In a selected study population of STEMI patients with multivessel disease, a complete revascularization strategy is associated with a reduction in cardiovascular death. This reduction is concomitant with that of MI and the need of repeated revascularization.

Effect of alirocumab on major adverse cardiovascular events according to renal function in patients with a recent acute coronary syndrome: prespecified analysis from the ODYSSEY OUTCOMES randomized clinical trial

José Tuñón et al.
European Heart Journal (2020) 41, 4114-4123.

Statins reduce cardiovascular risk in patients with acute coronary syndrome (ACS) and normal-to-moderately impaired renal function. It is not known whether proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors provide similar benefit across a range of renal function.

We determined whether effects of the PCSK9 inhibitor alirocumab to reduce cardiovascular events and death after ACS are influenced by renal function.

ODYSSEY OUTCOMES compared alirocumab with placebo in patients with recent ACS and dyslipidaemia despite intensive statin treatment. Estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m2 was exclusionary. In 18 918 patients, baseline eGFR was 82.8 ± 17.6 mL/min/1.73 m2, and low-density lipoprotein cholesterol (LDL-C) was 92 ± 31 mg/dL. At 36 months, alirocumab decreased LDL-C by 48.5% vs. placebo but did not affect eGFR (P = 0.65). Overall, alirocumab reduced risk of the primary outcome (coronary heart disease death, non-fatal myocardial infarction, ischaemic stroke, or unstable angina requiring hospitalization) with fewer deaths. There was no interaction between continuous eGFR and treatment on the primary outcome or death (P = 0.14 and 0.59, respectively). Alirocumab reduced primary outcomes in patients with eGFR ≥90 mL/min/1.73 m2 (n = 7470; hazard ratio 0.784, 95% confidence interval 0.670–0.919; P = 0.003) and 60 to <90 (n = 9326; 0.833, 0.731–0.949; P = 0.006), but not in those with eGFR < 60 (n = 2122; 0.974, 0.805–1.178; P = 0.784). Adverse events other than local injection-site reactions were similar in both groups across all categories of eGFR.

Conclusions: In patients with recent ACS, alirocumab was associated with fewer cardiovascular events and deaths across the range of renal function studied, with larger relative risk reductions in those with eGFR > 60 mL/min/1.73 m2.

Journal scan

Effects of clopidogrel vs. prasugrel vs. ticagrelor on endothelial function, inflammatory parameters, and platelet function in patients with acute coronary syndrome undergoing coronary artery stenting: a randomized, blinded, parallel study

Boris Schnorbus et al
European Heart Journal (2020) 41, 3144–3152 .

In a randomized, parallel, blinded study, we investigate the impact of clopidogrel, prasugrel, or ticagrelor on peripheral endothelial function in patients undergoing stenting for an acute coronary syndrome.

Methods and results

The primary endpoint of the study was the change in endothelium-dependent flow-mediated dilation (FMD) following stenting. A total of 90 patients (age 62 ± 9 years, 81 males, 22 diabetics, 49 non-ST elevation myocardial infarctions) were enrolled. There were no significant differences among groups in any clinical parameter.

Acutely before stenting, all three drugs improved FMD without differences between groups (P = 0.73). Stenting blunted FMD in the clopidogrel and ticagrelor group (both P < 0.01), but not in the prasugrel group. During follow-up, prasugrel was superior to clopidogrel [mean difference 2.13, 95% confidence interval (CI) 0.68–3.58; P = 0.0047] and ticagrelor (mean difference 1.57, 95% CI 0.31–2.83; P = 0.0155), but this difference was limited to patients who received the study therapy 2 h before stenting. Ticagrelor was not significantly superior to clopidogrel (mean difference 0.55, 95% CI −0.73 to 1.82; P = 0.39). No significant differences were seen among groups for low-flow-mediated dilation. Plasma interleukin (IL)-6 (P = 0.02 and P = 0.01, respectively) and platelet aggregation reactivity in response to adenosine diphosphate (P = 0.002 and P = 0.035) were lower in the prasugrel compared to clopidogrel and ticagrelor group.

Conclusions:

As compared to ticagrelor and clopidogrel, therapy with prasugrel in patients undergoing stenting for an acute coronary syndrome is associated with improved endothelial function, stronger platelet inhibition, and reduced IL-6 levels, all of which may have prognostic implications. This effect was lost in patients who received the study medication immediately after stenting.

Notwithstanding the clear and consistent clinical results in favour of prasugrel in the ISAR-REACT 5 trial, the mechanism underlying it could not easily be elucidated, Reversibility of the $P2Y_{12}$. receptor antagonism by ticagrelor might render the stability of platelet inhibition more vulnerable to short term patient non-adherence, especially with a drug given twice daily, On the other hand, the patient adherence is more likely to be compromised for a drug associated with more side effects, as in the case of ticagrelor. Dyspnoea, dizziness, syncope, elevation of creatinine, elevation of uric acid and consequent exacerbation of gout are unique side effects of ticagrelor. These reasons may explain part of the difference in efficacy between prasugrel and ticagrelor shown in the ISAR-REACT 5 trial"In this regard, the study of Schnorbus and colleagues suggests additional plausible mechanisms related to the differential response of vascular function and inflammation to prasugrel and ticagrelor. Although cardiologists who care for patients with CS usually do not wait for the full elucidation of the mechanisms underlying differences in drug efficacy before adopting the results of large randomized trial findings of mechanistic studies such as this shnorbus and colleagues may well facilitate changes in practice.

Low-grade endotoxaemia enhances artery thrombus growth via Toll-like receptor 4: implication for myocardial infarction

Roberto Carnevale
European Heart Journal (2020) 41, 3156-3165.

Low-grade endotoxaemia is detectable in human circulation but its role in thrombosis is still unclear.

Methods and results: We measured serum lipopolysaccharide (LPS) concentration, soluble P-selectin (sP-selectin), a marker of platelet activation, and zonulin, a marker of gut permeability, in peripheral circulation, coronary thrombi, and intracoronary blood of patients with ST-elevation myocardial infarction (STEMI, n = 50) and stable angina (SA) (n = 50), respectively, and in controls (n = 50). Experimental study was carried out in mice to assess if *Escherichia coli*-LPS (E. coli-LPS) possess thrombotic property. Coronary thrombi from STEMI showed higher concentrations of LPS, sP-selectin vs. intracoronary blood of SA and peripheral blood of controls ($P < 0.001$). Zonulin was higher in STEMI compared to the other two groups [4.57 (3.34-5.22); 2.56 (0.41-4.36); 1.95 (1.22-2.65) ng/mL; $P < 0.001$] and correlated with LPS ($Rs = 0.585$; $P < 0.001$). Escherichia coli DNA was positive in 34% of STEMI vs. 12% of SA and 4% of controls ($P < 0.001$). In a subgroup of 12 STEMI, immunohistochemical analysis of coronary thrombi showed positivity for leucocyte Toll-like receptor 4 (TLR4), cathepsin G, and LPS from E. coli in 100%, 80%, and 25% of samples, respectively. E. coli-LPS injected in mice to reach LPS concentrations like those detected in coronary thrombi was associated with enhanced artery thrombosis and platelet activation, an effect blunted by TLR4 inhibitor co-administration. In vitro study demonstrated that LPS from E. coli enhanced platelet aggregation via TLR4-mediated leucocyte cathepsin G activation.

Conclusions:

ST-elevation myocardial infarction patients disclose an enhanced gut permeability that results in LPS translocation in human circulation and eventually thrombus growth at site of artery lesion via leucocyte-platelet interaction.

Time to rename the middle child of heart failure: heart failure with mildly reduced ejection fraction

Carolyn S P Lam et al
European Heart Journal (2020) 41, 2353-2355.

The 'middle child' of heart failure (HF) [patients with left ventricular ejection fraction (EF) in the 40–50% range] was christened HF with mid-range EF in 2014, in recognition of the large gap in treatment evidence in this neglected subgroup of HF, with prior clinical trial evidence limited to those patients with EF of 40% or lower, and recent attention being showered upon those with EF of 50% or greater. While the EF 40–50% group was recognized as a 'grey area' in prior European Society of Cardiology Heart Failure Guidelines, the name 'heart failure with mid-range EF' and acronym 'HFmrEF' was adopted in the 2016 guidelines, with the intention of bringing attention to this group of patients and addressing the evidence gap.

Beyond nomenclature, the recent trial evidence also calls to question the cutoffs with which we define "mildly reduced" EF. As a continuous variable with a normal distribution within the population, the threshold value to define "normal" versus "reduced" EF is arbitrary. Guidelines from the American Society of Echocardiography and European Society of Echocardiography define a normal EF as >55%. Indeed, Framingham Heart Study participants with EF 50-55% were at greater risk of HF and death compared to those with EF>55%. Notably, the "normal" distribution of EF rises with age and is higher in women than men in the general population, since EF is a fraction which increases as the heart remodels and left ventricular end-diastolic volume (denominator) shrinks out of proportion to the stroke volume (numerator). Using a common EF cutoff of, say, 50% to define "normal" would therefore include elderly women who actually have relatively reduced EF for their age and sex. Such sex differences may explain the observation in the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial, where women appeared to benefit across the EF spectrum beyond 55%, but men only at EF lower than ~55%. 5 Further supporting this concept, in combined PARAGON-HF and PARADIGM-HF data, treatment effect splines across the entire EF spectrum showed

efficacy of sacubitril/valsartan in the EF 40-50% range, with the upper 95% confidence interval boundary of the rate ratio for sacubitril.

Given the totality of the evidence, we propose renaming "heart failure with mid-range ejection fraction" as “heart failure with mildly reduced ejection fraction” and considering sex-based cutoffs in the definition. The implications of this new nomenclature are threefold: (i) attempts should be made to obtain as precise a measurement of EF as possible in patients with heart failure, especially in those whose EF measurements are borderline, to avoid misclassification; (2) patients with a mildly reduced EF should be given the benefit of the doubt and considered for treatment with established therapies in HF with more severely reduced EF; (3) future clinical trials for heart failure with reduced EF may consider enrolling patients with EF up to the normal range.

A putative placebo analysis of the effects of sacubitril/valsartan in heart failure across the full range of ejection fraction

Muthiah Vaduganathan
. European Heart Journal (2020) 41, 2356-2362.

The PARADIGM-HF and PARAGON-HF trials tested sacubitril/valsartan against active controls given renin–angiotensin system inhibitors (RASi) are ethically mandated in heart failure (HF) with reduced ejection fraction and are used in the vast majority of patients with HF with preserved ejection fraction. To estimate the effects of sacubitril/valsartan had it been tested against a placebo control, we made indirect comparisons of the effects of sacubitril/valsartan with putative placebos in HF across the full range of left ventricular ejection fraction (LVEF).

Treatment benefits of sacubitril/valsartan vs. putative placebo varied non-linearly with LVEF with attenuation of effects observed at LVEF above 60%. When analyzing data from PARADIGM-HF and CHARM-Alternative, the estimated risk reduction of sacubitril/valsartan vs. putative placebo was 48% (95% CI 35–58%); $P < 0.001$. When analyzing data from PARAGON-HF and CHARM-Preserved (with LVEF ≥ 45%), the estimated risk reduction of sacubitril/valsartan vs. putative placebo was 29% (95% CI 7–46%); $P = 0.013$.

Across the full range of LVEF, consistent effects were observed for time-to-first endpoints: first primary endpoint (RR 0.72, 95% CI 0.64–0.82), first HF hospitalization (RR 0.67, 95% CI 0.58–0.78), cardiovascular death (RR 0.76, 95% CI 0.64–0.89), and all-cause death (RR 0.83, 95% CI 0.71–0.96); all $P < 0.02$.

Conclusions:
This putative placebo analysis reinforces the treatment benefits of sacubitril/valsartan on risk of adverse cardiovascular events across the full range of LVEF, with most pronounced effects observed at a LVEF up to 60%.

Effects of dapagliflozin in DAPA-HF according to background heart failure therapy

Kieran F Docherty
European Heart Journal (2020) 41, 2379–2392.

In the DAPA-HF trial, the SGLT2 inhibitor dapagliflozin reduced the risk of worsening heart failure (HF) and death in patients with HF and reduced ejection fraction. We examined whether this benefit was consistent in relation to background HF therapy.

In this post hoc analysis, we examined the effect of study treatment in the following yes/no subgroups: diuretic, digoxin, mineralocorticoid receptor antagonist (MRA), sacubitril/valsartan, ivabradine, implanted cardioverter-defibrillating (ICD) device, and cardiac resynchronization therapy.

We also examined the effect of study drug according to angiotensin-converting enzyme inhibitor/angiotensin receptor blocker dose, beta-blocker (BB) dose, and MRA (≥50% and <50% of target dose).

Conclusions: The benefit of dapagliflozin was consistent regardless of background therapy for HF.

Progression of ultrasound plaque attenuation and low echogenicity associates with major adverse cardiovascular events

Daisuke Shishikura et al
European Heart Journal (2020) 41, 2965–2973

Intravascular ultrasound (IVUS) imaging can visualize vulnerable plaque features including attenuation (AP) and echolucency (ELP). While IVUS-derived vulnerable plaque features associate with microvascular obstruction during percutaneous coronary intervention, the relationship between these plaque features and clinical outcomes has not been established. This analysis aimed to evaluate the association of AP/ELP with cardiovascular events.

Conclusions: Attenuation/ELP progression was associated with a higher prevalence of cardiovascular events, supporting a potential role for the identification of high-risk vulnerable plaques in patients with coronary artery disease.

Cardiovascular outcomes, bleeding risk, and achieved blood pressure in patients on long-term anticoagulation with the thrombin antagonist dabigatran or warfarin: data from the RE-LY trial

Michael Böhm
European Heart Journal (2020) 41, 2848–2859

A J-shaped association of cardiovascular events to achieved systolic (SBP) and diastolic (DBP) blood pressure was shown in high-risk patients. This association on oral anticoagulation is unknown. This analysis from RELY assessed the risks of death, stroke or systemic emboli, and bleeding according to mean achieved SBP and DBP in atrial fibrillation on oral anticoagulation.

Conclusions:
Low achieved SBP associates with increased risk of death, Systemic embolic event (SEE), and bleeding in patients with atrial fibrillation on oral anticoagulation. Major bleeding events did not occur at higher BP. Low BP might identify high-risk patients not only for death but also for high bleeding risks.

Rhythm control for patients with atrial fibrillation complicated with heart failure in the contemporary era of catheter ablation: a stratified pooled analysis of randomized data

Shaojie Chen
European Heart Journal (2020) 41, 2863-2873

The optimal treatment for patients with atrial fibrillation (AF) and heart failure (HF) has been a subject of debate for years. We aimed to evaluate the efficacy and safety of rhythm control strategy in patients with AF complicated with HF regarding hard clinical endpoints.

Conclusion: Catheter ablation as rhythm control strategy substantially improves survival rate, reduces re-hospitalization, increases the maintenance rate of sinus rhythm, contributes to preserve cardiac function, and improves quality of life for AF patients complicated with HF.

An autoantibody profile detects Brugada syndrome and identifies abnormally expressed myocardial proteins

Diptendu Chatterjee et al
European Heart Journal (2020) 41, 2878–2890

Brugada syndrome (BrS) is characterized by a unique electrocardiogram (ECG) pattern and life-threatening arrhythmias. However, the Type 1 Brugada ECG pattern is often transient, and a genetic cause is only identified in <25% of patients. We sought to identify an additional biomarker for this rare condition. As myocardial inflammation may be present in BrS, we evaluated whether myocardial autoantibodies can be detected in these patients.

Conclusions:
A biomarker profile of autoantibodies against four cardiac proteins, namely α-cardiac actin, α-skeletal actin, keratin, and connexin-43, can be identified from sera of BrS patients and is highly sensitive and specific, irrespective of genetic cause for BrS. The four involved proteins, along with the SCN5A-encoded Nav1.5 alpha subunit are expressed abnormally in the myocardium of patients with BrS.

Journal scan

Left atrial appendage occlusion with the Amplatzer™ Amulet™ device: full results of the prospective global observational study

David Hildick-Smith
European Heart Journal (2020) 41, 2894–2901.

To evaluate the safety and efficacy of left atrial appendage occlusion (LAAO) with the Amplatzer™ Amulet™ occluder.

Conclusions: Following LAAO with the Amplatzer Amulet device, the ischaemic stroke rate was reduced by 67% compared to the predicted risk. Closure was complete in 98.4% of cases and DRT (Device related thrombus) seen in only 1.6%.

Febuxostat and atrial fibrillation

Masanari Kuwabara
European Heart Journal (2020) 41, 2916–2917.

Recently there has been concern that febuxostat may be associated with increased cardiovascular risk than allopurinol, leading to a black-box warning by the Federal Drug Administration. Consistent with these concerns, Singh and Cleveland have recently reported that febuxostat also increased the risk for atrial fibrillation (AF) in a population-based cohort study of individuals greater than 65 years old, using Medicare data. The study evaluated individuals initiating allopurinol or febuxostat therapy and compared the incidence of AF with the prior year before starting treatment, controlling for comorbidities using the Charlson-Romero index and propensity matched Cox regression analysis.

The CARES (Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Gout and Cardiovascular Morbidities) trial, showed that all-cause mortality and cardiovascular mortality were higher with febuxostat than with allopurinol, but the difference started after 48 months and 85% of deaths occurred while subjects were off of therapy when serum uric acid can rapidly return to baseline levels. Other studies, such as the randomized control study of FREED, did not show any significant difference in AF incidence between febuxostat and non-febuxostat group.

Ticagrelor alone vs. ticagrelor plus aspirin following percutaneous coronary intervention in patients with non-ST-segment elevation acute coronary syndromes: TWILIGHT-ACS

Usman Baber et al.
European Heart Journal (2020) 41, 3533-3545.

The aim of this study was to determine the effect of ticagrelor monotherapy on clinically relevant bleeding and major ischaemic events in relation to clinical presentation with and without non-ST elevation acute coronary syndromes (NSTE-ACS) among patients undergoing percutaneous coronary intervention (PCI) with drug-eluting stents (DES).

Methods and results: We conducted a pre-specified subgroup analysis of The Ticagrelor with Aspirin or Alone in High Risk Patients After Coronary Intervention (TWILIGHT) trial, which enrolled 9006 patients with high-risk features undergoing PCI with DES. After 3 months of dual antiplatelet therapy (DAPT) with ticagrelor plus aspirin, 7119 adherent and event-free patients were randomized in a double-blind manner to ticagrelor plus placebo versus ticagrelor plus aspirin for 12 months.

Conclusions: Among patients with or without NSTE-ACS who have completed an initial 3-month course of DAPT following PCI with DES, ticagrelor monotherapy reduced clinically meaningful bleeding events without increasing ischaemic risk as compared with ticagrelor plus aspirin. The benefits of ticagrelor monotherapy with respect to bleeding events were more pronounced in patients with NSTE-ACS.

Differential immunological signature at the culprit site distinguishes acute coronary syndrome with intact from acute coronary syndrome with ruptured fibrous cap: results from the prospective translational OPTICO-ACS study

David M Leistner
European Heart Journal (2020) 41, 3549–3560.

Acute coronary syndromes with intact fibrous cap (IFC-ACS), i.e. caused by coronary plaque erosion, account for approximately one-third of ACS. However, the underlying pathophysiological mechanisms as compared with ACS caused by plaque rupture (RFC-ACS) remain largely undefined. The prospective translational OPTICO-ACS study program investigates for the first time the microenvironment of ACS-causing culprit lesions (CL) with intact fibrous cap by molecular high-resolution intracoronary imaging and simultaneous local immunological phenotyping.

The CL of 170 consecutive ACS patients were investigated by optical coherence tomography (OCT) and simultaneous immunophenotyping by flow cytometric analysis as well as by effector molecule concentration measurements across the culprit lesion gradient (ratio local/systemic levels). Within the study cohort, IFC caused 24.6% of ACS while RFC-ACS caused 75.4% as determined and validated by two independent OCT core laboratories.

The IFC-CL were characterized by lower lipid content, less calcification, a thicker overlying fibrous cap, and largely localized near a coronary bifurcation as compared with RFC-CL. The microenvironment of IFC-ACS lesions demonstrated selective enrichment in both $CD4^+$ and $CD8^+$ T-lymphocytes (+8.1% and +11.2%, respectively, both $P < 0.05$) as compared with RFC-ACS lesions. T-cell-associated extracellular circulating microvesicles (MV) were more pronounced in IFC-ACS lesions and a significantly higher amount of $CD8^+$ T-lymphocytes was detectable in thrombi aspirated from IFC-culprit sites. Furthermore, IFC-ACS lesions showed increased levels of the T-cell effector molecules granzyme A (+22.4%), perforin (+58.8%), and granulysin (+75.4%) as compared with RFC plaques ($P < 0.005$).

Endothelial cells subjected to culture in disturbed laminar flow conditions, i.e. to simulate coronary flow near a bifurcation, demonstrated an enhanced adhesion of CD8+T cells. Finally, both CD8+T cells and their cytotoxic effector molecules caused endothelial cell death, a key potential pathophysiological mechanism in IFC-ACS.

Conclusions
The OPTICO-ACS study emphasizes a novel mechanism in the pathogenesis of IFC-ACS, favoring participation of the adaptive immune system, particularly CD4+ and CD8+ T-cells and their effector molecules. The different immune signatures identified in this study advance the understanding of coronary plaque progression and may provide a basis for future development of personalized therapeutic approaches to ACS with IFC.

Is vaping better than smoking cigarettes?

Thomas Münzel
European Heart Journal (2020) 41, 2612–2614.

Electronic (e)-cigarette vapour, which contains substantially less toxins than tobacco smoke, has been marketed as a 'healthy' alternative to traditional cigarettes and is reported to be an effective method of smoking cessation.

Is e-cigarette vaping as dangerous as tobacco smoking?

Certainly not.
Most investigators agree that the significant health concern coming from reports by the Center for Disease Control (CDC), the Food and Drug Administration (FDA), and the State Health Departments related to severe pulmonary disease and deaths among e-cigarette users are likely the consequence of the addition of vitamin E acetate, most notably as tetrahydrocannabinol contained in e-cigarettes or vaping products.

Switching from tobacco smoking to e-cigarettes good for our vessels?

Definitely.

Actually, there are several studies demonstrating an improvement in endothelial function in response to switching from tobacco to e-cigarettes.

What information are we missing so far for e-cigarettes?

There is considerable lack of clarity as to the overall population health consequences of e-cigarette use. As mentioned, a majority of available studies provide evidence that e-cigarette vaping is less detrimental than cigarette tobacco smoking. However, the number of long-term studies and the number of mechanistic insights is still limited.

Even if we are aware that e-cigarettes are less toxic than tobacco products, we are also aware of their potential to generate nicotine addicts, which should be enough to trigger stricter regulations of these products. There is no doubt, however, that smoking cessation is and will remain the most powerful approach to prevent smoking-induced cardiovascular and respiratory disease.

Genetic variability in the absorption of dietary sterols affects the risk of coronary artery disease

Anna Helgadottir
European Heart Journal (2020) 41, 2618–2628.

Aims
To explore whether variability in dietary cholesterol and phytosterol absorption impacts the risk of coronary artery disease (CAD) using as instruments sequence variants in the *ABCG5/8* genes, key regulators of intestinal absorption of dietary sterols.

Conclusions:
Genetic variation in cholesterol absorption affects levels of circulating non-HDL cholesterol and risk of CAD. Our results indicate that both dietary cholesterol and phytosterols contribute directly to atherogenesis.

The associations of major foods and fibre with risks of ischaemic and haemorrhagic stroke: a prospective study of 418 329 participants in the EPIC cohort across nine European countries

Tammy Y N Tong
European Heart Journal (2020) 41, 2632–2640.

Aim: To investigate the associations between major foods and dietary fibre with subtypes of stroke in a large prospective cohort.

Conclusions: Risk of ischaemic stroke was inversely associated with consumption of fruit and vegetables, dietary fibre, and dairy foods, while risk of haemorrhagic stroke was positively associated with egg consumption. The apparent differences in the associations highlight the importance of examining ischaemic and haemorrhagic stroke subtypes separately.

Effect of bariatric surgery on long-term cardiovascular outcomes: a nationwide nested cohort study

Osama Moussa
European Heart Journal (2020) 41, 2660–2667.

Aims
This study aims to evaluate the long-term effect of bariatric surgery on cardiovascular outcomes of patients with obesity.

Conclusions:
The results of this large, nationwide cohort study support the association of bariatric surgery with lower long-term risk of major cardiovascular events and incident heart failure in patients with obesity.

NHS England-funded CT fractional flow reserve in the era of the ISCHEMIA trial

Hazhee Rasoul
https://doi.org/10.7861/clinmed.2020-0691
Clin Med March 2021

Background: The National Institute for Health and Care Excellence (NICE) 2016 guidelines (CG95) recommend patients with new stable chest pain be investigated with computed tomography coronary angiography (CTCA).

An updated guideline (MTG32) recommended using CT fractional flow reserve (CTFFR) as a gatekeeper to invasive coronary angiography (ICA) for patients with coronary stenosis on CTCA. Subsequently, NHS England negotiated a UK-wide contract with Heart Flow, the provider of CTFFR. We describe our experience with CTFFR and consider the impact of the recent ISCHEMIA trial on these guidelines.

Results: One-hundred and twenty-five of 140 patients completed CTFFR analysis. Eighty-one patients had CTCA stenosis >50%. Thirty-six had positive CTFFR; 29 underwent ICA with 22 (75.9%) revascularized. Forty-five had negative CTFFR; 14 underwent ICA and four (28.6%) were revascularized. The average cost of investigation per patient (PP) was £971.95. Had these patients undergone ICA directly with no functional test after CTCA, the average cost would be £932.51 PP.

Conclusions: Our revascularization rates suggest that CTFFR can potentially be a gatekeeper to ICA but does not necessarily yield cost savings.

Association of β-blocker use with survival and pulmonary function in patients with chronic obstructive pulmonary and cardiovascular disease: a systematic review and meta-analysis

Yan-Li Yang et al.
European Heart Journal (2020) 41 ,4415–4422

The aim of this study was to clarify the effect of β-blockers (BBs) on respiratory function and survival in patients with chronic obstructive pulmonary disease with cardiovascular disease (CVD), as well as the difference between the effects of cardio selective and non-cardio selective BBs.

Conclusions:
The use of BBs in patients with chronic obstructive pulmonary disease is not only safe but also reduces their all-cause and in-hospital mortality. Cardio selective BBs may even reduce chronic obstructive pulmonary disease exacerbations. In addition, cardio selective BBs do not affect the action of bronchodilators. Importantly, BBs reduce the heart rate acceleration caused by bronchodilators. BBs should be prescribed freely when indicated in patients with chronic obstructive pulmonary disease and heart disease.

Metoprolol exerts a non-class effect against ischaemia–reperfusion injury by abrogating exacerbated inflammation

Agustín Clemente-Moragón et al.
European Heart Journal (2020) 41 , 4425–4440

Clinical guidelines recommend early intravenous β-blockers during ongoing myocardial infarction; however, it is unknown whether all β-blockers exert a similar cardioprotective effect. We experimentally compared three clinically approved intravenous β-blockers.

Conclusions:

Metoprolol exerts a disruptive action on neutrophil dynamics during exacerbated inflammation, resulting in an infarct-limiting effect not observed with atenolol or propranolol. The differential effect of β-blockers may be related to distinct conformational changes in the β1 adrenergic receptor upon metoprolol binding. If these data are confirmed in a clinical trial, metoprolol should become the intravenous β-blocker of choice for patients with ongoing infarction.

Note: Study done on mice.

Empagliflozin and health-related quality of life outcomes in patients with heart failure with reduced ejection fraction: the EMPEROR-Reduced trial

Javed Butler et al.
European Heart Journal (2020) 42 , 1203-1212

In this secondary analysis of the EMPEROR-Reduced trial, we sought to evaluate whether the benefits of empagliflozin varied by baseline health status and how empagliflozin impacted patient-reported outcomes in patients with heart failure with reduced ejection fraction.

Conclusions:
Empagliflozin improved cardiovascular death or heart failure hospitalization risk across the range of baseline health status. Empagliflozin improved health status across various domains, and this benefit was sustained during long-term follow-up.

Journal scan

Effects of dapagliflozin on mortality in patients with chronic kidney disease: a pre-specified analysis from the DAPA-CKD randomized controlled trial

Hiddo J L Heerspink et al.
European Heart Journal (2020) 42 , 1216–1227

Mortality rates from chronic kidney disease (CKD) have increased in the last decade. In this pre-specified analysis of the DAPA-CKD trial, we determined the effects of dapagliflozin on cardiovascular and non-cardiovascular causes of death.

Conclusions:
In patients with CKD, dapagliflozin prolonged survival irrespective of baseline patient characteristics. The benefits were driven largely by reductions in non-cardiovascular death.

Ventricular arrhythmia burden during the coronavirus disease 2019 (COVID-19) pandemic

Catherine J O'Shea et al.
European Heart Journal (2020) 42 , 520–528

Our objective was to determine the ventricular arrhythmia burden in implantable cardioverter-defibrillator (ICD) patients during COVID-19.

Methods and results:

In this multicentre, observational, cohort study over a 100-day period during the COVID-19 pandemic in the USA, we assessed ventricular arrhythmias in ICD patients from 20 centres in 13 states, via remote monitoring. Comparison was via a 100-day control period (late 2019) and seasonal control period (early 2019). The primary outcome was the impact of COVID-19 on ventricular arrhythmia burden. The secondary outcome was correlation with COVID-19 incidence. During the COVID-19 period, 5963 ICD patients underwent remote monitoring, with 16 942 episodes of treated ventricular arrhythmias (2.8 events per 100 patient-days). Ventricular arrhythmia burden progressively declined during COVID-19 ($P < 0.001$). The proportion of patients with ventricular arrhythmias amongst the high COVID-19 incidence states was significantly reduced compared with those in low incidence states [odds ratio 0.61, 95% confidence interval $P < 0.001$].

Comparing patients remotely monitored during both COVID-19 and control periods ($n = 2458$), significantly fewer ventricular arrhythmias occurred during COVID-19. This difference persisted when comparing the 1719 patients monitored during both the COVID-19 and seasonal control periods.

Conclusions:
During COVID-19, there was a 32% reduction in ventricular arrhythmias needing device therapies, coinciding with measures of social isolation. There was a 39% reduction in the proportion of patients with ventricular arrhythmias in states with higher COVID-19 incidence. These findings highlight the potential role of real-life stressors in ventricular arrhythmia burden in individuals with ICDs.

When less is more: dual antiplatelet therapy in elective percutaneous coronary intervention

Giovanna Liuzzo et al.
European Heart Journal (2021), 42, 965–966

Key Points

- ALPHEUS is a company-funded, multi centre, randomized, open-label trial including a total of 1910 stable chronic coronary syndrome (CCS) patients undergoing elective percutaneous coronary intervention (PCI) with at least one high-risk feature. Once the coronary anatomy was known, eligible patients were randomly assigned (1:1) to either ticagrelor (180 mg loading dose, 90 mg twice daily thereafter for 30 days) or clopidogrel (300–600 mg loading dose, 75 mg daily thereafter for 30 days) to investigate whether more effective and faster platelet inhibition by ticagrelor could reduce periprocedural atherothrombotic complications in this setting. Cardiac troponin levels were measured at baseline, 6 and 24 h after PCI or at discharge, and peak levels were used for outcome assessment. Clinical outcomes were evaluated at 48h and 30 days.

- At 48 h, the primary outcome, a composite of PCI-related type 4 (a or b) myocardial infarction (MI) or major myocardial injury (according to the third universal definition of MI) occurred in 334 (35%) of 941 patients in the ticagrelor group and 341 (36%) of 942 patients in the clopidogrel group [odds ratio (OR) 0.97; 95% confidence interval (CI) 0.80–1.17; $P = 0.75$).

- At 48 h, the primary safety outcome, major bleeding according to the Bleeding Academic Research Consortium (BARC 3 or 5), did not differ between the two groups. However, minor bleeding events were more frequently observed with ticagrelor than clopidogrel at 30 days [105 (11%) of 941 patients in the ticagrelor group vs. 71 (8%) of 942 patients in the clopidogrel group; OR 1.54; 95% CI 1.12–2.11; $P = 0.0070$]. None of the secondary clinical outcomes differed between groups at 30-day follow-up.

The neutrophil-lymphocyte ratio and incident atherosclerotic events: analyses from five contemporary randomized trials

Nicholas H Adamstein
European Heart Journal (2021), 42, 896-903.

The neutrophil-lymphocyte ratio (NLR) is a readily available inflammatory biomarker that may associate with atherosclerosis and predict cardiovascular (CV) events. The aims of this study are to determine whether the NLR predicts incident major adverse cardiovascular events (MACE) and is modified by anti-inflammatory therapy.

Conclusions: The NLR, an easily obtained inflammatory biomarker, independently predicts CV risk and all-cause mortality, and is reduced by interleukin-1β blockade with canakinumab.

A randomized trial supports the recommendation to continue treatment with ACEi or ARBs during hospitalization for COVID-19

Massimo Volpe et al,
European Heart Journal (2021), 42, 1061–1062

Key points

The BRACE CORONA (Angiotensin Receptor Blockers and Angiotensin-converting Enzyme Inhibitors and Adverse Outcomes in Patients With COVID19) trial is a multicenter, registry-based, open-label, randomized clinical trial (RCT) with blinded end-point assessment of patients hospitalized with coronavirus 2019 disease (COVID-19) who were on treatment with angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARBs) prior to hospital admission. Patients taking >3 antihypertensive agents, those taking sacubitril/valsartan for heart failure (HF), and those hospitalized for HF within the last 12 months were not eligible. The aim was to determine whether discontinuation of ACEi/ARBs compared with continuation affected the number of days alive and out of the hospital through 30 days. Secondary outcomes included death, cardiovascular death, and COVID-19 progression.

The study included 659 patients (334 in the discontinuation group and 325 in the continuation group) with a median age of 55 years (15% >70 years), a median time from symptom onset to hospital admission of 6 days, and an oxygen saturation <94% of room air at baseline in 27% of patients. Clinical severity at hospital admission was considered mild in 57% and moderate in 43% of cases. All the enrolled subjects completed the 30-day follow-up.

The discontinuation of ACEi or ARBs did not affect the number of days alive and out of the hospital [22 days in the discontinuation group vs. 23 days in the continuation group; mean ratio 0.95, 95% confidence interval (CI) 0.90–1.01]. There was no difference in death rate [2.7% vs. 2.8% in the discontinuation and continuation groups, respectively; odds ratio (OR) 0.97, 95% CI 0.38–2.52], cardiovascular death (0.6% vs. 0.3%; OR 1.95, 95% CI 0.19–42.12), or COVID-19 progression (38.3% vs. 32.3%; OR 1.30, 95% CI 0.95–1.80).

Moreover, the incidence of respiratory failure requiring invasive mechanical ventilation (9.6% in the discontinuation group vs. 7.7% in the continuation group), shock requiring vasopressors (8.4% vs. 7.1%,), acute myocardial infarction (7.5% vs. 4.6%; RR 1.62, 95% CI 0.88–3.09), new or worsening HF (4.2% vs. 4.9%), and acute kidney failure requiring haemodialysis (3.3% vs. 2.8%) was not significantly different between the discontinuation and continuation groups.

Short dual antiplatelet therapy followed by P2Y12 inhibitor monotherapy vs. prolonged dual antiplatelet therapy after percutaneous coronary intervention with second-generation drug-eluting stents: a systematic review and meta-analysis of randomized clinical trials

Daniele Giacoppo
European Heart Journal (2021), 42, 308–319.

After percutaneous coronary intervention (PCI) with second-generation drug-eluting stent (DES), whether short dual antiplatelet therapy (DAPT) followed by single antiplatelet therapy (SAPT) with a P2Y12 receptor inhibitor confers benefits compared with prolonged DAPT is unclear.

Conclusions:
After second-generation DES implantation, 1–3 months of DAPT followed by P2Y12 inhibitor SAPT is associated with lower major bleeding and similar stent thrombosis, all-cause death, myocardial infarction, and stroke compared with prolonged DAPT. Whether P2Y12 inhibitor SAPT is preferable to aspirin SAPT needs further investigation.

Discussion
The main results of this meta-analysis can be summarized as follows:

1. One to 3 months of DAPT followed by P2Y12 inhibitor SAPT reduces major bleeding compared with prolonged DAPT;

2. This advantage does not occur at the cost of an increase in stent thrombosis and major endpoints including all-cause death, myocardial infarction, and stroke;

3. High heterogeneity exists among trials with respect to the endpoint of major bleeding and conservative summary estimate 95% CI adjustment reveals that more data are needed;

4. Whether short-term DAPT followed by $P2Y_{12}$ inhibitor SAPT is associated with different clinical outcomes compared with short-term DAPT followed by aspirin SAPT requires further evaluation.

Case Report

Infective Endocarditis with Mitral Leaflet Abscess due to *Elizabethkingia meningoseptica* Infection- A Rare Opportunistic Infection in a CKD Patient on Chronic Hemodialysis.

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Abstract

Elizabethkingia meningoseptica is a gram-negative aerobic bacillus and a very rare cause of infective endocarditis in immunocompromised patients. A 59-year-old male with a past history of bio prosthetic tissue aortic valve replacement, long standing diabetes and end stage kidney failure with recent arterio-venous [AV] fistula creation and regular twice a week haemo-dialysis presented with fever of one week's duration. Blood tests revealed neutrophil leukocytosis and raised inflammatory markers. His blood cultures were repeatedly positive for gram negative rods which were, on re-evaluation identified as *Elizabethkingia meningoseptica*. Cardiac imaging with trans esophageal echocardiogram [TOE] revealed an anterior mitral valve leaflet abscess. Follow up TOE assessments demonstrated objective worsening of abscess with involvement of the bioprosthetic aortic valve rim and tricuspid valve annulus despite being on recommended IV antibiotics. The patient refused re-do surgery and thus was medically managed with extended course of intravenous [IV] vancomycin and oral cotrimoxazole which was subsequently changed to IV piperacillin, tazobactam and oral cotrimoxazole while continuing regular hemodialysis. A repeat blood culture done at 6 weeks became positive again for the same organism necessitating the extension of duration of IV antibiotics to a total of 12 weeks. After nearly three months of in- hospital IV antibiotic treatment the patient self-discharged against medical advice while refusing further treatment and expired at home subsequently due to sepsis. Infective endocarditis caused by *Elizabethkingia meningoseptica* is very rare and reportedly carries a poor outcome. To the best of our knowledge this is the first reported case of intra-cardiac abscess formation due to this organism.

Key words: *Elizabethkingia meningoseptica*, mitral leaflet abscess, Infective endocarditis

Introduction

Infective endocarditis (IE) can occur due to a wide spectrum of organisms and in different clinical situations. Its presentation, severity and subsequent outcome can be highly variable and is influenced by many parameters. The pathogen causing IE will be important in outcome and host parameters play a role as well. *Streptococcus viridans* and *Staphylococcus aureus* are well known to cause IE in native and non-native valves. However, in immunocompromised patients, uncommon organisms are known to cause IE [(4)] . We report a patient with mitral leaflet abscess formation due to *Elizabethkingia meningoseptica* [(6)] , a very rare cause of infective endocarditis. To the best of our knowledge intra cardiac valve leaflet abscess formation has not been reported previously in endocarditis due to this organism.

Case presentation:

A 59-year-old male with a past history of bioprosthetic tissue aortic valve replacement presented with fever of one week's duration. He had long standing diabetes mellitus and was in end stage chronic kidney disease (CKD) on regular hemodialysis. He recently underwent creation of an AV fistula two months prior to his recent presentation. Clinical examination including general, cardiac and systemic was normal. He had no classic peripheral stigmata of IE.

His blood tests showed neutrophil leukocytosis of 19 x 10^3 /dl, a raised CRP of 160mg/L and ESR of 95 mm/1st hour on admission. His urine culture was sterile and sputum cultures showed normal flora. Chest X-ray was normal. He was negative for HIV, Hepatitis B and C. His serum creatinine was 6.5mg/dl. Ultrasound scans of the abdomen and the AV fistula site were negative for abscess formations. His blood culture was positive for gram negative rods which were later identified as *Elizabethkingia meningoseptica* sensitive to vancomycin, ciprofloxacin and trimethoprim-sulfamethoxazole. Initial trans-thoracic echocardiography and a transesophageal echo cardiography (TOE) soon after admission were negative for any evidence of vegetations. His colonoscopy visualizing up to distal ileum demonstrated an isolated diverticulum without evidence of diverticulitis. He was treated with renal doses of IV meropenem, levofloxacin and oral cotrimoxazole for 14 days but his blood cultures remained positive for the same organism and was referred to us for repeat TOE.

TOE and real time three dimensional trans esophageal echocardiogram [RT 3D TOE] at two weeks, demonstrated a bulging mass with hypoechoic center in the anterior mitral leaflet suspicious of an abscess in the A3 segment measuring 14mm x 11mm with mild mitral regurgitation [Figure 1]. His bioprosthetic tissue aortic valve was functioning well and did not show any evidence of endocarditis.

Case Report

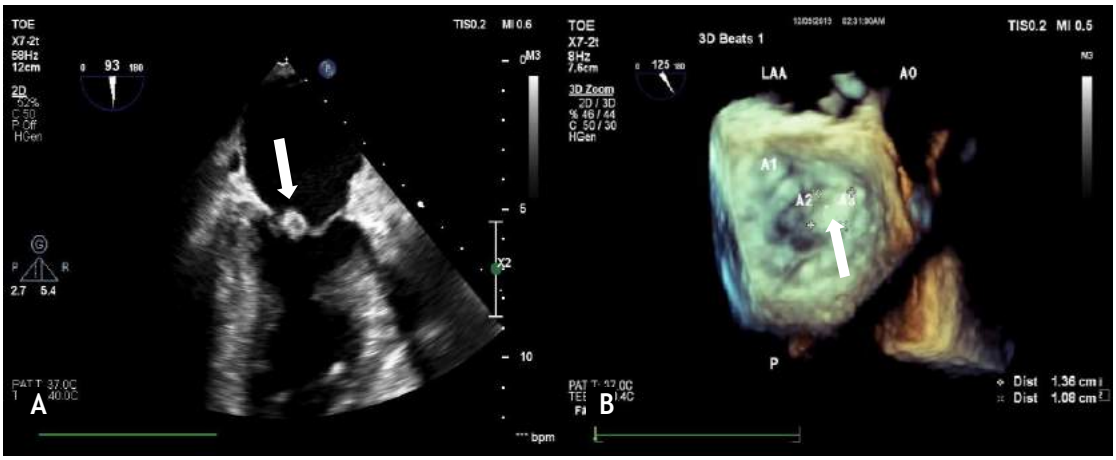

Figure 1. A. Trans esophageal echocardiogram [TOE] images showing a mass attached to the anterior mitral valve leaflet (arrow) with hypoechoic center suggestive of a mitral leaflet abscess. B. Real time three dimensional trans esophageal echocardiogram [RT 3D TOE] view of mitral valve viewed from LA side showing a 1.3cm x 1cm anterior mitral valve leaflet bulge (arrow) corresponding to the abscess.

A cardiothoracic surgical consultation was done regarding redo surgery with mitral valve replacement. However, medical management was decided due to the high risk of re-do surgery given his dialysis dependent, end stage CKD and rare blood group of AB+. Patient also refused redo cardiothoracic surgery. He was started on IV piperacillin and tazobactam along with oral cotrimoxazole according to the antibiotic sensitivity pattern. Hemodialysis was continued twice a week.

A repeat TOE done two weeks later demonstrated the mitral leaflet abscess to have enlarged to 18 x 13mm in size [Figure 2] and extending into tricuspid valve (TV) annulus and bioprosthetic tissue AV rim.

Patient was referred again to the heart team to discuss management options but the patient remained unwilling for redo surgery. It was decided to continue IV piperacillin, tazobactam and oral cotrimoxazole for a total of 8 weeks. His blood cultures were initially sterile at 5 weeks on this regimen but became positive again at 6th week for the same organism. A repeat TOE showed further extension of the abscess into TV annulus and bioprosthetic AV rim but his prosthetic AV did not show any involvement. Antibiotics were continued for an extended period of 12 weeks. The patient refused any further medical management and self-discharged against medical advice and expired at home due to complications of sepsis.

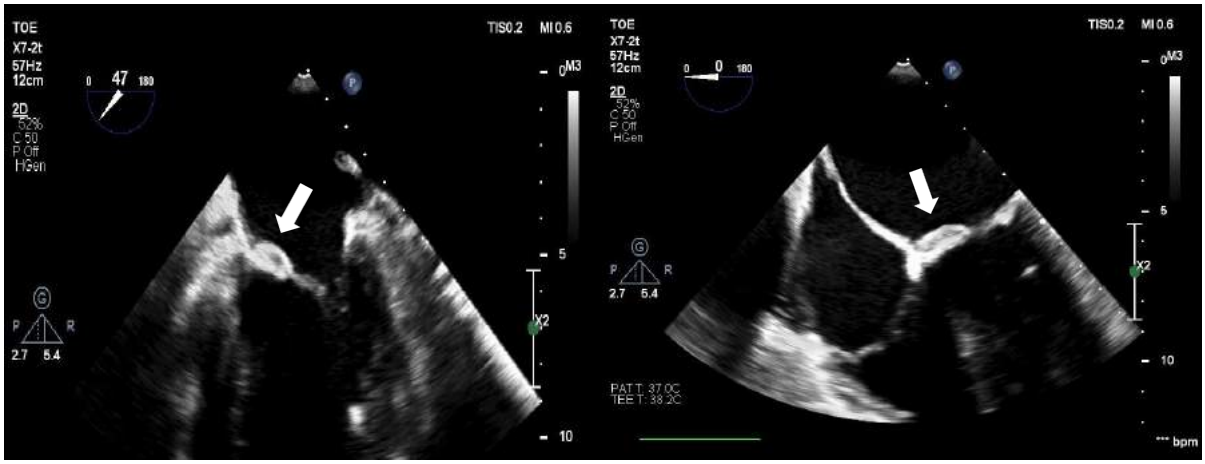

Figure 2: Trans esophageal echocardiogram [TOE] images showing subsequent enlargement of anterior mitral valve leaflet abscess left image at 2 weeks and right image at 6 weeks.

Discussion

Elizabethkingia meningoseptica [1] isolated by the American bacteriologist Elizabeth O King and previously known as *Cryseobacterium* or *Flavobacterium* is a non-fermenting, non-motile gram-negative aerobic bacillus. It is found in water systems, wet surfaces and antiseptic solutions from which contamination can give rise to nosocomial infections in susceptible patients. Contaminated intravascular devices and implanted devices such as prosthetic valves have been reported as a nidus of the infections. *Elizabethkingia* infection is primarily an opportunistic pathogen known to cause meningitis in premature infants but is also reported to cause pneumonia, meningitis and keratitis in immune compromised adults. It is rarely known to cause infective endocarditis.

Intra-cardiac abscesses are a known complication of infective endocarditis. Mitral leaflet abscess formation is a rare complication mainly described in acute infective endocarditis with *Staphylococcus aureus* and *Streptococcus pyogenes*. Although *Elizabethkingia meningoseptica* is known to cause abscesses in the lung with pneumonia to the best of our knowledge this is the first report of it causing an abscess in the mitral valve leaflet.

This patient had a bio-prosthetic tissue aortic valve implanted 2 years ago for tight aortic stenosis. He had only mild mitral regurgitation at the time of surgery without any significant mitral leaflet abnormality. Thus, his endocarditis appears to have started in the native mitral valve despite him having a bio-prosthetic tissue AV.

Despite being a gram-negative bacillus *Elizabethkingia meningoseptica* is resistant to most antibiotics used to treat gram negative bacilli e.g., aminoglycosides, beta lactams and carbapenem but sensitive to most of the antibiotics used to treat gram positive cocci e.g., vancomycin, ciprofloxacin, rifampicin, and cotrimoxazole (trimethoprim-sulfamethoxazole) [2] . Rifampicin has been used as a part of combination therapy along with vancomycin to eliminate meningitis in neonates but there is no clear guidance to treat *Elizabethkingia* infections [3] . Thus, treatment was initiated based on antibiotic sensitivity. Our patient's culture sensitivity test revealed the organism's sensitivity to vancomycin, rifampicin and cotrimoxazole.

He was initially treated with IV vancomycin and cotrimoxazole but due to deteriorating renal functions the treatment was changed to IV piperacillin-tazobactum with oral cotrimoxazole and continued up to 12 weeks.

Our patient is likely to have acquired the infection through contamination during haemodialysis. All his intra- vascular catheters were changed and sent for culture but none were positive for any organisms. His AV fistula site was inspected periodically for signs of infection and scanned repeatedly for evidence of abscess formation but all were negative. Cleaning and sterilization procedures were carried out in the haemodialysis unit and no other patients were reported with the same infection.

Patient's blood cultures were repeatedly positive for the organism while on IV antibiotic therapy and this could possibly be due to the growing abscess within the mitral leaflet and the surrounding tissue where antibiotic penetration is poor, leading to breakthrough infection and septicemia. This further highlights the need for early surgical management in treating mitral leaflet abscesses as even an extended duration of antibiotic therapy could not achieve the eradication of the organism as in this patient who was unwilling to undergo re do surgery.

Additionally, *Elizabethkingia meningoseptica* [5] could be an emerging virulent pathogen leading to nosocomial infections. It can result in septicemia, infective endocarditis with abscess formation and have devastating outcomes especially in immunocompromised hosts e.g., CKD.

Acknowledgement:

We wish to thank Dr. Geethika Patabandige Consultant microbiologist at NHSL and Dr. A L M Nazar Consultant nephrologist at NHSL and their teams of doctors for their invaluable advice in the management of this patient.

References

1. *Jiun-Nong Lin et al: Comparison of clinical manifestations, antimicrobial susceptibility patterns and mutations of fluoroquinolone target genes between Elizabethkingia meningoseptica and Elizabethkingia anopheles isolated in Thaiwan: Journal of clinical medicine 2018,7:538*
2. *K. Bomb et al: Endocarditis due to Chryseobacterium meningoseptica: Indian J of Med Micro. (2007)25 (2):161-2*
3. *Namita Jaggi, Vyoma Singh: Successful control of Elizabethkingia meningoseptica outbreak in a neuro-surgical intensive care unit of a tertiary care center in India, Int J infect control 2018, v 14: i2*
4. *Y Nulens E, et al Recurrent bacteraemia by Chryseobacterium indologenes in an oncology patient with a totally implanted intravascular device. Clin microbiol Infect 2001; 7(7): 391-393. DOI: https://doi.org/10.1046/j.1198-743x.2001.00273.x*
5. *Ratnamani MS, Rao R. Elizabethkingia meningoseptica: Emerging nosocomial pathogen in bedside hemodialysis patients. Indian J Crit Care Med 2013; 17:304-7.*
6. *Elizabethkingia meningoseptica. https://en.wikipedia.org/wiki/Elizabethkingia_meningoseptica. Accessed on 29.5.2021*

Case Report

Stent Fracture - A Rare Cause of Stent Thrombosis resulting in Anterior ST Elevation Myocardial Infarction (STEMI)

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Abstract

Stent thrombosis (ST) remains one of the most dreaded and deadly consequence of the coronary stent deployment. Although stent thrombosis is less following the introduction of new generations of Drug Eluting Stents (DES), specific patient related factors, target lesion and procedure related factors play a role in the pathogenesis of SF. Stent fracture (SF) has been identified as one of the less common cause of STEMI resulting in major adverse cardiovascular events. SFs usually cause restenosis which are asymptomatic or minimally symptomatic. We present an unusual case of a 64-year-old lady coming with anterior STEMI following stent thrombosis secondary to stent fracture.

Key words – Stent thrombosis (ST), Stent fracture (SF), Drug Eluting Stents (DES)

Case History

Our patient, a 64-year-old lady, diagnosed with diabetes, hypertension and dyslipidaemia presented late to National hospital of Sri Lanka (NHSL) with late anterior STEMI with ischaemic time of 18 hours. She was taken for primary Percutaneous Coronary intervention (PCI). Her coronary angiogram revealed a critical left anterior descending artery (LAD) lesion. Lesion was predilated with 2x15mm compliant balloon at 10 atm and lesion was stented with Promus Element 3x20mm drug eluting stent (DES) and stent deployed at high pressure, 14 atm.

Echocardiography revealed an ejection fraction (EF) of 45% and she was discharged on day 2 on aspirin, clopidogrel, high intensity statin, bisoprolol, enalapril, furosemide and oral hypoglycaemic agents.

2 weeks later she presented to NHSL with ischaemic type chest pain and was found to have an anterior STEMI and was thrombolysed with tenectaplase at emergency treatment unit (ETU) due to unavailability of a vacant slot in catheter laboratory. Post tenectaplase resolution was poor and patient went into left ventricular failure with persistent chest pain and autonomic symptoms. Patient was subsequently taken into catheter lab for rescue PCI.

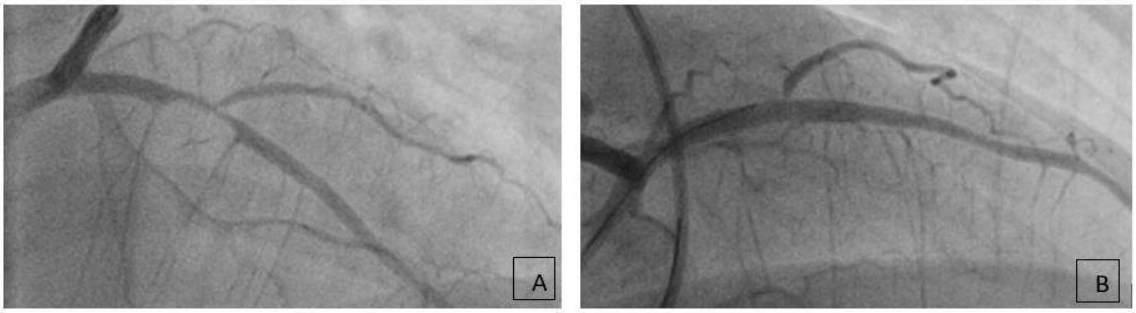

Figure 1 – Critical LAD lesion (A); LAD following PCI with Promus Element DES (B)

Post dilatation of the DES done with 3x8mm Non-compliant (NC) balloon at 14 to 20 atm. Proximal optimization technique (POT) was done at diagonal branch ostium at 18 atm. Post procedure, well apposed stent and TIMI 3 flow in LAD and diagonal branch was achieved (**Figure-1**). Patient's post PCI period was uneventful.

Coronary angiogram revealed stent thrombosis of the previously inserted proximal LAD DES. Stent thrombosis was wired and crossed with a Sion blue guidewire. The thrombus was predilated with 2x15mm compliant balloon at 20 atm and 3x8mm NC balloon at 20 atm. Increased thrombus burden was noted within the previous LAD DES despite establishment of the distal LAD flow.

Case Report

Therefore, intracoronary abcicimab and adenosine were given.

Thrombus aspiration was done. Careful examination of the angiogram with cine images revealed mild contrast extravasation into vessel wall and stent strut discontinuation in the middle part of the DES at the D1 ostium (**Figure-2**) before and after contrast injection.

The patient had a temporary pacemaker (TPM) inserted and was managed conservatively after withholding betablockers. Post procedure rhythm abnormalities were attributed to ischaemia, reperfusion and medication.

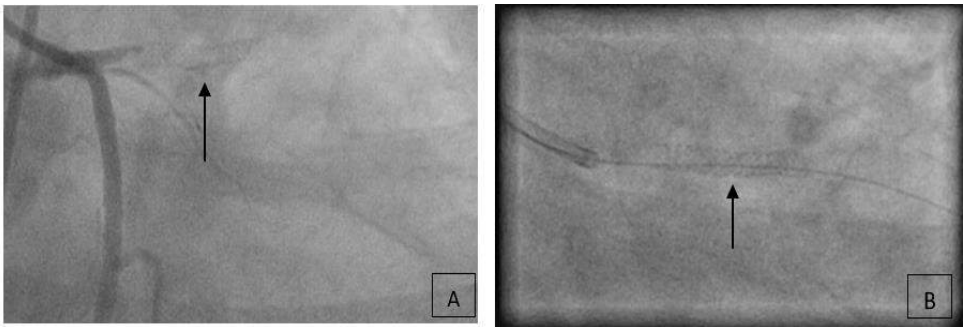

Figure 2: (A). Stent thrombosis with contrast extravasation in the mid portion of the stent (B). Stent fracture in the middle part of the LAD stent

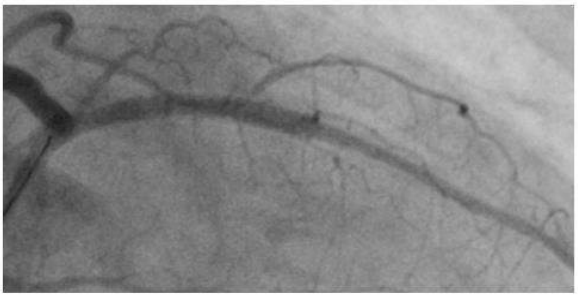

Figure 3: LAD after PCI across the fractured DES

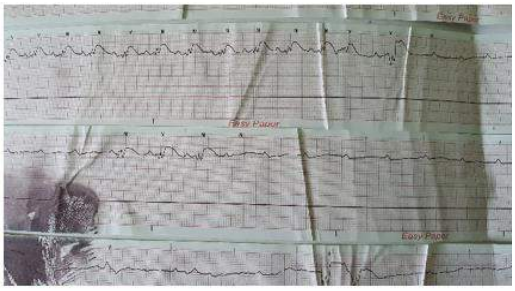

Figure 4: Ventricular stand still rhythm

Thus, type 2/3 Stent fracture with Type 1 coronary perforation was diagnosed. The proximal LAD was stented with Xience Prime 3x23mm DES across the fractured Promus Element 3x20 DES and stent deployed at 16 atm. DES post dilated with 3x8mm NC balloon at 14 to 20 atm. Post procedure well apposed stent and TIMI 3 flow in LAD achieved (**Figure-3**).

Patient compliance to medication was good before the STEMI. Post PCI, patient was given aspirin, prasugrel, atorvastatin, bisoprolol, enalapril, spironolactone, furosemide and basal bolus insulin regime. On day 1 post procedure patient developed recurrent bradycardic cardiac arrest and was resuscitated successfully.

By day 3 patient was asymptomatic, clinically stable and TPM independent. Echocardiogram revealed an EF of 40% with hypokinetic LAD territory with preserved muscle mass. By day 7 patient was discharged with above medications, oral hypoglycemics and insulin. In one month, we reviewed the patient at the clinic and she was found to be asymptomatic with good compliance to medications.

Discussion

Stent Fracture (SF) has been defined as complete or partial separation of stent segments observed by plain fluoroscopy without contrast injection or IVUS. The incidence of stent fracture ranges between 0.8 and 19%.

Fluoroscopic classification of SF is graded with regard to the number of the fractured struts seen during angiography [1,2]: single strut fracture as type I; 2 strut fractures as type II; 2 strut fractures with deformation as type III; fracture with transection but no gap as type IV; and fracture with a gap within as type V.

The incidence of SF in the BMS is inconsiderable [3,4]. Amongst the various types of the DES, the sirolimus Stent (SES) is the main culprit [3,5,6]. Chakravarty *et al.* [7] and Chhatriwalla *et al.* [8] found that more than 95% of their SF cases had occurred in the Cypher stent, and Lee *et al.* reported a stent fracture prevalence of 1.9%, all in the Cypher stents [5]. The interaction between stent and vessel geometry is considered the most important factor in causing SF, so stent flexibility influences the vessel geometry and is directly related to fracture resistance. The least flexible DES (Cypher) was the most susceptible to SF.[9] Another large consecutive series of everolimus-eluting stents demonstrated stent fracture in 2.9% of lesions [10]. Flexibility and fracture resistance has been addressed in the design of new generation of stents. Platinum chromium everolimus-eluting stent (PROMUS Element) with "a modified scaffold design" creates a more flexible and fracture resistant stent [11, 12].

Longer stents are more vulnerable to fractures [6, 8,13]. Overlapping stents by enhancing "axial stiffness" possibly increases the risk of SF [5,14]. Increased rate of restenosis along with fractures were reported in overlapped stents. Excessive pressure during stent deployment, balloon post dilation and resultant damage to the stent strut has also increased the possible risk of stent fractures. The stent and balloon diameter, number of the implanted stents, residual post-stenting stenosis, smaller minimal lumen diameter and greater acute gain and late loss are some other predictors. [15] Park et al. demonstrated higher maximal inflation pressure in the SF group (13.42 ± 3.86 atm) and significant relation between the number of the implanted stents and SF [15]. Kim et al. showed a higher incidence rate of SF in lesions with smaller minimal lumen diameters before the procedure (0.38 ± 0.55) and larger acute gain (2.28 ± 0.39) [16]

The higher rate of SF is in the RCA due to its tortuosity, sharp angularity and increased hinge movements which increases metal fatigue during a cardiac cycle [3,6,15]. Plaque calcification, osteal and bifurcations lesions also increase the risk of stent fracture.

Stent fracture is usually associated with binary restenosis (commonly), thrombosis, aneurysm, embolization, ischemic events, and target lesion revascularization (TLR) and could thereby increase morbidity and mortality [3].

Stent thrombosis, albeit apparently uncommon [5], has also been proposed as a complication of SF. Thrombosis caused by SF can be seen at any time, and was reported as a risk factor for late stent thrombosis. Chhatriwalla et al. reported a 6% incidence rate of STEMI and 42% of NSTEMI in their SF population [8]. Kuramitsu *et al.* also reported an increased risk of TLR and MI caused by SF following everolimus- eluting stent implantation and that the stent thrombosis was also more common in the SF group than in the non-SF group [10].

In our case, type 2/3 SF was diagnosed and we assume excessive post dilatation of the DES and POT performed at high pressures with NC balloon could have been the cause of the SF.

Fluoroscopy with or without contrast injection, cine images and stent boost can be used to diagnose SF. IVUS and multi slice CT are the other superior modalities which can used for the diagnosis of SF [17,18,19] .

Many SF causes ISR which are benign and usually asymptomatic, accompanied by a negligible incidence rate of cardiac events and, therefore, only the continuation of antiplatelet therapy was advocated [20]. Lee *et al.* proposed [20] the continuation of antiplatelet therapy regardless of ischemic symptoms and suggested intervention for the following patients: a) symptomatic or asymptomatic ISR with > 70% stenosis and b) symptomatic ISR with 50-70% stenosis, which shows positive results in physiological stress test with or without IVUS.
Balloon-only, BMS, and DES have all been applied for the treatment of SF but use of DES, seems to be more reasonable.

Conclusions

Stent fracture is one of the complications of coronary stenting regardless of the stent type. Many patient related, DES related and procedural technique related factors contribute towards stent fracture. It can cause stent thrombosis at any time following a PCI and lead to major adverse cardiovascular events.

However, many cases of stent fracture are undiagnosed as they are asymptomatic or cause minimal symptoms mostly due to in-stent restenosis (ISR). Various new imaging modalities such IVUS and multi slice CT scans are available now to diagnose stent fracture. Treatment is mostly reserved for patients who are symptomatic or presenting with acute events.

References

1. *Nakazawa G, Finn AV, Vorpahl M, et al. Incidence and predictors of drug-eluting stent fracture in human coronary artery a pathologic analysis. J Am Coll Cardiol 2009; 54(21): 1924-31.*
2. *Jaff M, Dake M, Pompa J, Ansel G, Yoder T. Standardized evaluation and reporting of stent fractures in clinical trials of noncoronary devices. Catheter Cardiovasc Interv 2007; 70(3): 460-2.*
3. *Canan T, Lee MS. Drug-eluting stent fracture: incidence, contributing factors, and clinical implications. Catheter Cardiovasc Interv 2010; 75(2): 237-45.*
4. *Kwon SU, Doh JH, Namgung J, Lee SY. Stent strut fractureinduced restenosis in the right coronary artery: detection by MDCT. Heart 2008; 94(2): 221.*
5. *Lee MS, Jurewitz D, Aragon J, Forrester J, Makkar RR, Kar S. Stent fracture associated with drug-eluting stents: clinical characteristics and implications. Catheter Cardiovasc Interv 2007; 69(3): 387-94.*
6. *Ino Y, Toyoda Y, Tanaka A, et al. Predictors and prognosis of stent fracture after sirolimus-eluting stent implantation. Circ J 2009; 73(11): 2036-41.*
7. *Chakravarty T, White AJ, Buch M, et al. Meta-analysis of incidence, clinical characteristics and implications of stent fracture. Am J Cardiol 2010; 106(8): 1075-80.*
8. *Chhatriwalla AK, Cam A, Unzek S, et al. Drug-eluting stent fracture and acute coronary syndrome. Cardiovasc Revasc Med 2009; 10(3): 166-71.*
9. *Ormiston JA, Webber B, Webster MW. Stent longitudinal integrity bench insights into a clinical problem. JACC Cardiovasc Interv 2011; 4(12): 1310-7.*
10. *Kuramitsu S, Iwabuchi M, Haraguchi T, et al. Incidence and clinical impact of stent fracture after everolimus-eluting stent implantation. Circ Cardiovasc Interv 2012; 5(5): 663*
11. *Stone GW, Teirstein PS, Meredith IT, et al. A prospective, randomized evaluation of a novel everolimus-eluting coronary stent: the PLATINUM (a Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of Up to Two de Novo Coronary Artery Lesions) trial. J Am Coll Cardiol 2011; 57(16): 1700-8.*
12. *Stone GW, Teirstein PS, Meredith IT, et al. Two-year results of the PLATINUM randomized trial comparing PLATINUM chromium promus element and cobalt chromium PROMUS/XIENCE V everolimus-eluting stents in de novo coronary artery lesions. J Am Coll Cardiol 2012; 59(13s1): E323-3.*
13. *Doi H, Maehara A, Mintz GS, et al. Classification and potential mechanisms of intravascular ultrasound patterns of stent fracture. Am J Cardiol 2009; 103(6): 818-23.*
14. *Lousinha A, Fiarresga A, Cardona L, et al. Stent fracture: case report and literature review. Rev Port Cardiol 2011; 30(2): 213-21.*
15. *Park KW, Park JJ, Chae IH, et al. Clinical characteristics of coronary drug-eluting stent fracture: insights from a two-center des registry. J Korean Med Sci 2011; 26(1): 53-8.*
16. *Kim HS, Kim YH, Lee SW, et al. Incidence and predictors of drugeluting stent fractures in long coronary disease. Int J Cardiol 2009; 133(3): 354-8.*
17. *Hecht HS, Polena S, Jelnin V, et al. Stent gap by 64-detector computed tomographic angiography relationship to in-stent restenosis, fracture, and overlap failure. J Am Coll Cardiol 2009; 54(21): 1949-59.*
18. *Choe H, Hur G, Doh JH, et al. A case of very late stent thrombosis facilitated by drug eluting stent fracture: comparative images before and after stent fracture detected by 64-multidetector computed tomography. Int J Cardiol 2009; 133(3): e125-8.*
19. *Pang JH, Kim D, Beohar N, Meyers SN, Lloyd-Jones D, Yaghmai V. Detection of stent fractures: a comparison of 64-slice CT, conventional cine-angiography, and intravascular ultrasonography. Acad Radiol 2009; 16(4): 412-7.*
20. *Lee SE, Jeong MH, Kim IS, et al. Clinical outcomes and optimal treatment for stent fracture after drug-eluting stent implantation. J Cardiol 2009; 53(3): 422-8.*

Case Report

Inconspicuous yet Sinister Cause of Angina in a Young Male -Apical Hypertrophic Cardiomyopathy (ApHCM)

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Abstract

Hypertrophic cardiomyopathy (HCM) with or without outflow obstruction is an important diagnosis to consider in young adults with exertional symptoms and a normal angiogram. In the differential diagnosis of these patients ApHCM should also be entertained. Our patient presented in his first hospital admission with ongoing classical angina and characteristic ECHO and ECG features. ECG had giant anterolateral dagger type T inversions fulfilling LVH criteria and ECHO showed apical predominant hypertrophy. Angiogram revealed no obstructive lesion and showed no evidence of spasm. The pain and the moderate troponin elevation are explained by type 2 myocardial infarction with oxygen demand mismatch due to bulk of the hypertrophied muscle. The contrast ECHO and the CMRI performed later confirmed pure apical type of ApHCM. Detailed history assessment, holter monitoring and risk assessment score showed he had low risk of sudden death, so patient was managed without ICD but with first line pharmacological medication and anticoagulation for paroxysms of atrial fibrillation. He will be closely followed up with family screening in the inherited cardiomyopathy clinic.

Key words: Apical hypertrophic cardiomyopathy, ApHCM, angina,

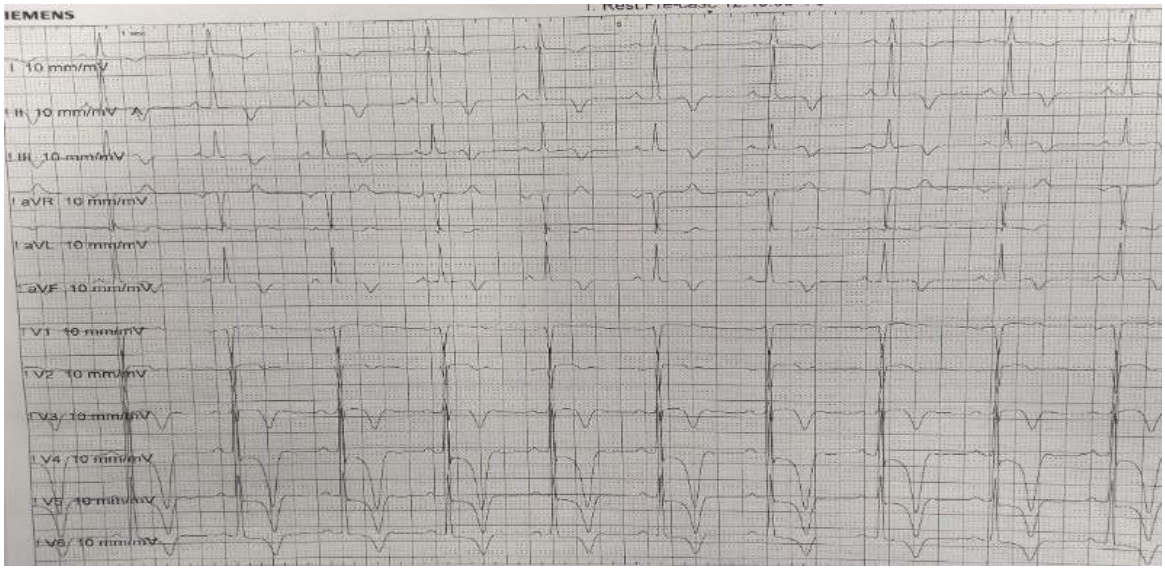
Introduction

It is infrequent for a young person devoid of any standard atherosclerotic risk factors to present with ischemic chest pain. Specially so when symptoms are repetitive and related to exertion and coronary angiography shows normal coronaries. If cardiac biomarkers are also elevated this case scenario creates a diagnostic dilemma and results in classifying the patient as a myocardial infarction with non-obstructive coronary arteries (MINOCA). Along with a whole spectrum of possibilities such as aortic valve lesions, vasospasm, embolic, microvascular angina etc, hypertrophic cardiomyopathy is a very important consideration, especially it's elusive apical variant (ApHCM) [(1)].

Case report

41-year-old eastern European gentleman was rushed into emergency care by paramedics for acute onset classical angina after a gym workout. This was his first such presentation. He had no past medical history of any significance. There was ongoing chest pain and his presenting ECG was grossly abnormal.

Figure 1: Presenting ECG showing giant T inversions (Dagger T's) with down sloping ST segments. Most prominent in V3-V5 but also noted in inferolateral leads. It also fulfils Sokolov-Lyon Voltage criteria for LVH.



Case Report

We proceeded to radial angiography which proved to be normal. Administration of intracoronary nitrates (IC GTN) did not result in an anti spastic response. First troponin was reported as 110 (reference range<19) which meant, the patient was having some form of an acute myocardial insult.

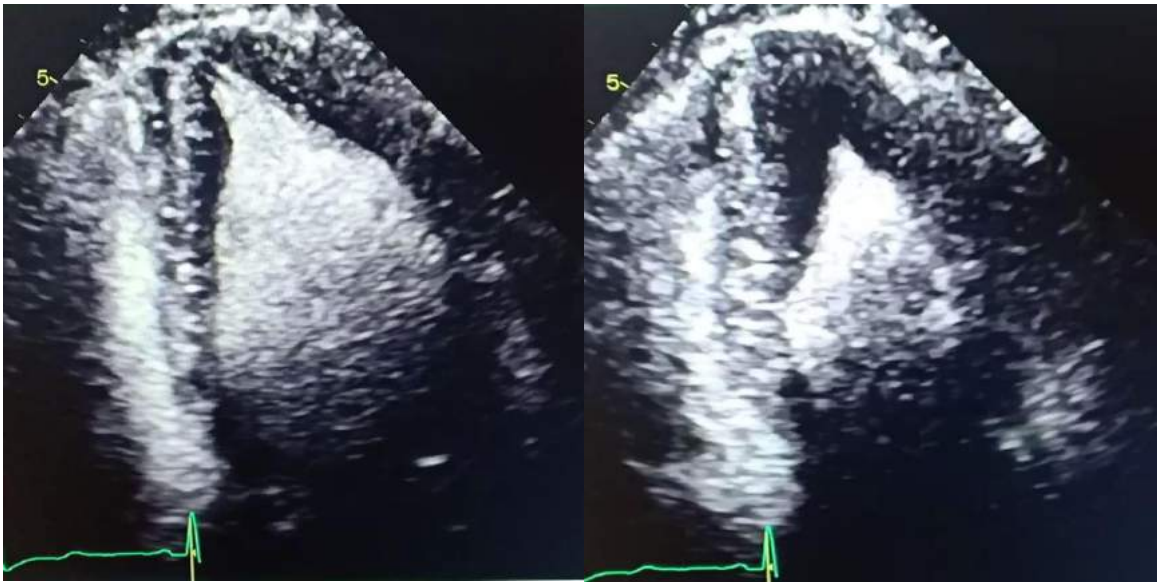
Due to the ECG showing deep asymmetrical anterior T inversions with LV strain criteria we performed a bedside transthoracic echocardiogram (TTE) which showed mild LVH which was concentric with LVEF of >65% without any regional hypokinesia. There was no evidence of pulmonary embolism, pericarditis or valvular lesions. The apical views were not clear but appeared thicker than the rest of the myocardium. Therefore, the possibility of ApHCM as the diagnosis was considered.
We were able to successfully alleviate the angina with beta blockers, isosorbide mononitrates and stat dose of intravenous morphine in addition to the aspirin and statin loading. Pulse rate was 80bpm, sinus rhythm and blood pressure 110/74mmHg. On detailed history taking it was noted that he has had occasional angina on exertion for the last 6 months and infrequent runs of palpitations not associated with dizzy spells. There was no personal or family history of syncope or sudden cardiac death. To delineate and visualize the apical anatomy better, we performed a contrast ECHO assessment, which confirmed our probable diagnosis with certainty by showing the classic "Ace of spades" sign where apical cavity obliteration is noted from mid-systole.

There was no outflow obstruction (LVOTO) or standard features of hypertrophic obstructive cardiomyopathy such as asymmetrical septal hypertrophy, systolic anterior motion of the mitral valve and mitral regurgitation. Left atrium was normal in size. Posterior wall was 11mm and apex was 21mm in thickness.

Regarding investigations, repeat troponin was: 130 (showing evidence of Type 2 myocardial infarction), WBC: $11.8X10^3$, hemoglobin: 132 g/l, d-dimer: normal, serum electrolytes: normal, eGFR: 76 and CRP: 8.

We also performed several other investigations as an outpatient to delineate the risk of sudden cardiac death. CMRI confirmed the features of apical hypertrophic cardiomyopathy - "pure" variant where changes were limited to apex. However, there was no evidence of late gadolinium enhancement suggestive of subendocardial scars, fibrosis and also no evidence of aneurysm or thrombus formation was detected. 48-hour holter showed paroxysms of atrial fibrillation (lasting for more than 5-minutes with rates varying from 130-170bpm, and associated with few polymorphic couplets, triplets and one salvo but overall burden was <5% with no NSVT/VT episodes).

Figure 2: Contrast ECHO in systolic phases showing "Ace of spades" sign of ApHCM.



Genetic studies confirmed heterozygous MYBPC3 sarcomere protein mutation. He was assessed afterwards at the specialized inherited cardiomyopathy clinic and he was informed of the disease nature, prognosis and the low likelihood of sudden cardiac arrest (<2% annual sudden death risk) and hence that ICD (Implantable cardioverter-defibrillator) is generally not indicated.

Common modes of presentation are ischaemic chest pain with clear coronaries, palpitations, exertional dyspnoea, syncope, positive family screening and thromboembolic events.

About 54% are symptomatic and sudden cardiac death as first mode of presentation is very rare [5].

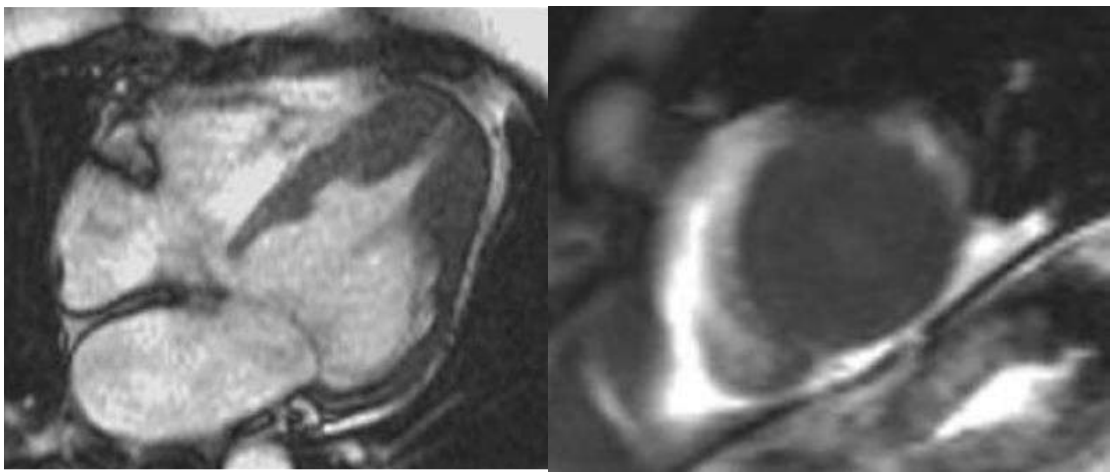


Figure 3: CMRI showing ApHCM without basal hypertrophy, minimal scarring and short axis showing cavity obliteration.

He was additionally put on apixaban in view of the paroxysmal atrial fibrillation and beta blockers were optimized to give good control over symptoms.

Discussion:

The entity was initially described in Japan [2] where 25% of their hypertrophic cardiomyopathy variants were classified as the apical variety. But in western populations the prevalence is much less and the quoted values are around 2% of all HCM patients. Importantly western patients have more sinister outcomes whereas in the patients of eastern origin it is known to be benign. 25% of western population develop significant complications which includes, heart failure, refractory angina, apical scar-fibrosis, associated VT/VF rhythms, atrial fibrillation, apical aneurysms and associated thromboembolic events as TIA-Stroke and pulmonary hypertension [3]. Male to female ratio is 2:1 and mean age of presentation is 41+/- 15 years [4]. ApHCM is an uncommon variant of HCM for which detectable sarcomere protein mutation is much less, compared to the other variants. The commonest gene mutation associated with HCM is MYBPC3 [1] , which is autosomal dominant and was also detected in this patient.

Regarding baseline investigations the ECG is considered paramount. The anterolateral dagger like deep giant T inversions with voltage criteria and strain pattern is unmistakable. Giant T waves (>10mm deep) are seen in 47% of patients but a lesser degree of asymmetrical T inversion and voltage criteria are noted in the majority of the patients. Usually, the thickness of apical myocardium does not correlate well with T wave magnitude. In holter monitoring NSVT is detected in 18% of patients while atrial fibrillation is identified in 12%. [4]

The TTE has a tendency to miss apical hypertrophy due to multiple reasons. Some studies have shown that ApHCM was missed in standard TTE in 40% of cases and retrospectively diagnosed through CMRI [6] .

Traditionally it has been described that ApHCM has three subtypes namely pure apical, mixed (distal dominant), and evolving juvenile phase.

Pure apical is the rarer form and has overall better prognosis but higher chance of apical aneurysm formation although absolute risk is low [7]. General ECHO criteria are distal predominant hypertrophy where apical wall thickness is >15mm and apex: posterior wall ratio is >1.5.

In classic ApHCM cases one can identify mid systolic apical obliteration called, "Ace of spades" sign which is best identified in contrast Echocardiography [8]. Strain imaging is also useful in identifying low global longitudinal strain in apical areas, but this is not frequently observed.

CMRI is useful not only to confirm the overall diagnosis but to ascertain structural complications as scar formation, aneurysms and exclude differential diagnoses. Late gadolinium enhancement can show apical subendocardial scars (similar to ischaemic aetiologies), and intramural fibrosis which are driving substrates for the origin of ventricular tachyarrhythmias [9]. It also excludes differential diagnoses of apical hypertrophy appearance of ECHO namely apical tumours, thrombus, non-compaction and endomyocardial fibrosis [3].

Management is multi-disciplinary from the outset. The medical geneticist, inherited cardiomyopathy specialist, interventional cardiologist and electrophysiologist are all involved. Although the genetic variant carries much less chance of poor outcomes, we still assess each patient with risk scores- which include maximum wall thickness, LVOT gradient, left atrium size index, history of syncope, family history and non-sustained VT (NSVT).

The management of each patient is a customized decision with input from the patient too.

Genetic testing of family lineage is important and involves pre-testing and counselling.

General symptom management involves beta blockers as first line therapy (for angina as well as fibrillation), non-dihydropyridine calcium channel blockers as second line, anticoagulation as needed (depending on LV thrombus, aneurysm, AF).

Radiofrequency ablation of VT is not standard practice as the anatomical location is non favorable and yields high recurrence rates. Same is true of myomectomy.

The scoring tools used for HOCM are applied to ApHCM to decide on ICD therapy as there is no validated specific tool. The general belief is that ICD as a treatment modality for ApHCM is underutilized.

References

1. *Gruner C, Care M, Siminovitch K, Moravsky G, Wigle ED, Woo A, Rakowski H. Sarcomere protein gene mutations in patients with apical hypertrophic cardiomyopathy. Circ Cardiovasc.Genet 2011;4(3):288-95.*
2. *Sakamoto T, Tei C, Murayama M, Ichiyasu H, Hada Y. Giant T wave inversion as a manifestation of asymmetrical apical hypertrophy (AAH) of the left ventricle. Echocardiographic and ultrasono-cardiotomographic study. Jpn Heart J.1976;17(5):611-29.*
3. *Moon J, Shim CY, Ha JW, Cho IJ, Kang MK, Yang WI, et al. Clinical and echocardiographic predictors of outcomes in patients with apical hypertrophic cardiomyopathy. Am J Cardiol.2011;108(11):1614-9.*
4. *Eriksson MJ, Sonnenberg B, Woo A, Rakowski P, Parker TG, Wigle ED, Rakowski H, Douglas Wigle E, Rakowski H, Toronto F. Long-term outcome in patients with apical hypertrophic cardiomyopathy. J Am Coll Cardiol. 2002; 39:638–645.*
5. *Choi EY, Rim SJ, Ha JW, Kim YJ, Lee SC, Kang DH, Park SW, Song JK, Sohn DW, Chung N. Phenotypic spectrum and clinical characteristics of apical hypertrophic cardiomyopathy: multicentre echo-Doppler study. Cardiology 2008; 110: 53-61.*
6. *Pons-Llado G, Carreras F, Borras X, Palmer J, Llauger J, Bayes De Luna A. Comparison of morphologic assessment of hypertrophic cardiomyopathy by magnetic resonance versus echocardiographic imaging. Am J Cardiol. 1997; 79:1651–1656.*
7. *Chen CC, Lei MH, Hsu YC, Chung SL, Sung YJ. Apical hypertrophic cardiomyopathy correlations between echocardiographic parameters, angiographic left ventricular morphology, and clinical outcomes. Clin Cardiol. 2011; 34:233–238.*
8. *Yamaguchi H, Ishimura T, Nishiyama S, Nagasaki F, Nakanishi S, Takatsu F, Nishijo T, Umeda T, Machii K. Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): ventriculographic and echocardiographic features in 30 patients. Am J Cardiol. 1979; 44:401–412.*
9. *Kim KH, Kim HK, Hwang IC, Lee SP, Park EA, Lee W, et al. Myocardial scarring on cardiovascular magnetic resonance in asymptomatic or minimally symptomatic patients with "pure" apical hypertrophic cardiomyopathy. J Cardiovasc Magn Reson 2012; 14:52.*

Case Report

A Rare Organism Causing Infective Endocarditis (IE)

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Abstract

Infective endocarditis (IE) is a serious and potentially life-threatening condition. Here we present a case of IE caused by *Pseudomonas putida* in a 54-year-old ornamental fish farmer. He presented with intermittent fever with chills, loss of appetite and loss of weight for three months. He had no history of any medical illness. Following three weeks of antibiotics, the symptoms improved. It is postulated that the acquisition of the organism was related to his occupation as *Pseudomonas putida* is abundant in soil and water.

Keywords: infective endocarditis, native valve endocarditis, IE, *Pseudomonas putida,* ornamental fish farming

Introduction

IE is an acute or sub-acute infection of the endocardium. Micro-organisms involved are mainly gram-positive cocci such as *Streptococci* (55%) and *Staphylococci* (35%) and miscellaneous organisms (10%) e.g., HACEK organisms (*Haemophilus, Actinomyces, Cardiobacterium, Ekinella* and *Kingella*). Rarely, it occurs due to fungal pathogens. It can be broadly classified as native or prosthetic valve endocarditis. The diagnosis of IE is based on modified Duke's criteria. Major modified Duke criteria include positive blood cultures and presence of vegetations on echocardiography. The incidence of IE is 5-10 per 100,000 population annually and mortality remains high as 1 per 100,000 from 1970 to 2000 [(1)]. We report a case of sub-acute, native valve IE caused by *Pseudomonas putida*, which was well associated with the occupation of the patient.

Case report

A 54-year-old previously healthy, ornamental fish farmer from Anuradhapura, Sri Lanka, presented with a three month's history of intermittent chills, loss of appetite and loss of weight. He had very infrequent fever episodes which were very mild. He did not have any other symptoms or features suggestive of an immune suppressive condition, contact or past history of tuberculosis. Also, he did not have a history of rheumatic valvular heart disease. He had not received any intravenous (IV) drugs.

On examination, he was underweight and had mild pallor. He did not have peripheral stigmata of infective endocarditis. Cardiovascular system examination revealed a pansystolic murmur at the apex. Other systems examination was normal. Three blood cultures were positive for growth of *P. putida* and transthoracic echocardiogram showed vegetations in both the mitral valve leaflets with severe mitral regurgitation. Transesophageal echocardiogram confirmed the above findings and showed mitral annular abscesses. Erythrocyte sedimentation rate was 100 mm/ 1st hour, C-reactive protein 74.1 mg/dl and total white cell count was 12,100 mm [(3)] with 76% neutrophils. Urine full report showed 20 to 30 red blood cells without pus cells, casts or protein. His liver and renal function tests were within the normal range. Human immunodeficiency virus (HIV) 1 and 2 antibodies, venereal disease research laboratory (VDRL) test and hepatitis B surface antigen were negative. The diagnosis of IE was confirmed by presence of two major and two minor Duke's criteria.

He was treated with IV imepenum 1g/ 8 hourly and gentamycin 5 mg/kg following antibiotic sensitivity tests with continuous monitoring of renal functions. Three weeks after antibiotics, his clinical condition improved with normalized appetite and absence of fever. Repeat blood cultures were negative. The echocardiogram now showed healed vegetations with persistent severe mitral regurgitation. ESR dropped to 42 mm/hour. The patient was referred to a cardiothoracic surgeon for mitral valve replacement as a routine procedure.

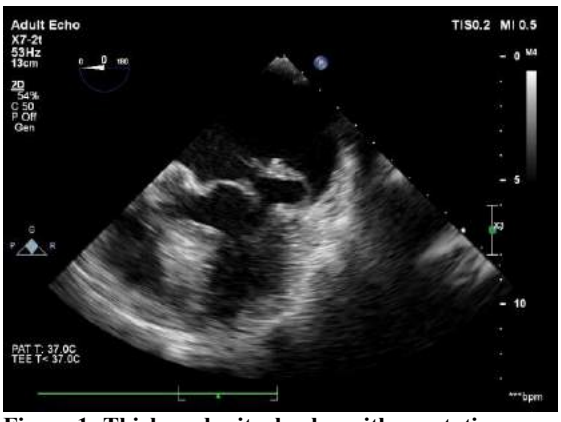

Figure 1: Thickened mitral valve with vegetations

Case Report

Discussion

Infections caused by *P. putida* are comparatively rare and are usually restricted to immunocompromised patients or patients with invasive medical devices in place. It is a flagellated, gram-negative rod and a member of the fluorescent group of pseudomonads, which is found throughout the natural environment. Our patient is an ornamental fish farmer and his occupation may have led to the extensive exposure to the bacterium which resulted in the bacteremia and subsequent endocarditis. The ornamental fish farming is a developing industry worldwide and Pseudomonas spp. is found frequently in fresh water of the fish tanks associated with normal bacterial flora, frequently acting as an opportunistic pathogen to fish living in 'at-risk' environment such as poor water quality and overcrowding [(2)] . Thus, colonizing freshwater by the *P.putida* in ornamental fish tanks could occur due to the zoonotic potential of this bacterium.

P. putida is a group of opportunistic pathogens that primarily cause nosocomial infections and was previously thought to be of low pathogenicity.

Nowadays, due to emergence of multidrug-resistant and carbapenem-resistant *P. putida*, it causes difficult-to-treat nosocomial infections in seriously ill patients. Our patient was successfully treated with IV imepenum 1 g 8 hourly and gentamycin 5 mg/kg.

In earlier reports, *P. putida* showed high sensitivity to various antibiotics and Fass et al. reported 100% susceptibility to ciprofloxacin and tobramycin and 87% to imipenem and piperacillin/tazobactam [(3)] .

P. putida isolates were commonly reported to have a low level of virulence with little clinical significance compared to the well-known *P. aeruginosa* isolates [(4)] .

The ornamental fish farmer described in our case report had a good clinical and prognostic outcome. This could be due to receiving appropriate antibiotics, but further studies with more cases is required to verify this relationship.

Conclusion

P. putida could be identified in freshwater of ornamental fish tanks and can cause serious life threating conditions such as IE. In this case described, attention is drawn to an uncommon clinical presentation of IE in an adult Sri Lankan male. Heightened awareness on dangers of ornamental fish farming should be undertaken to reduce the incidence of IE, in developing countries such as Sri Lanka.

Usefulness of prescribing prophylactic antibiotic or use of personal protective equipment while handling fish tanks are highlighted by this case.

Conflicts of Interest

None.

Reference

1. *Murtaza M & Kamarudin M. Infective endocarditis diagnosis antimicrobial therapy and management. Int J Gen Med pharm 2013; 2: 75-84*
2. *Walczak N, Puk K, Guz L. Bacterial flora associated with diseased freshwater ornamental fish. J Vet Res 2017; 61:445.*
3. *Fass RJ, Barnishan J, Solomon MC, Ayers LW. In vitro activities of quinolones, beta-lactams, tobramycin, and trimethoprim-sulfamethoxazole against nonfermentative gram-negative bacilli. Antimicrob Agents Chem. 1996; 40:1412-8.*
4. *Blazevic DJ, Koepcke MH, Matsen JM. Incidence and identification of Pseudomonas fluorescens and Pseudomonas putida in the clinical laboratory. Appl. Microbiol. 1973; 25:107-10.*

Case Report

Transcatheter Device Closure of Ruptured Sinus of Valsalva in a Patient with Severe Aortic Regurgitation (AR), with Post Procedure Reduction of AR

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Abstract

Sinus of Valsalva aneurysms occur due to the weakness of the elastic lamina at the junction of aortic media and annulus fibrosis and is a rare cardiac defect. Aortic regurgitation is commonly associated with ruptured sinus of Valsalva (RSOV). Mechanism of AR in RSOV can be due to associated structural defects such as bicuspid aortic valve or lack of supporting tissue due to associated VSD or can be due to hemodynamic effect caused by RSOV. Reduction of AR after surgical repair of RSOV without any additional procedures is well known, and it is considered to be due to the reversal of the hemodynamic effect caused by RSOV. However, as presence of AR is used as an exclusion criterion for device closure, reduction of AR after device closure was not reported previously. We report a case of a 43-year-old female with RSOV with severe AR complicated with congestive hepatopathy, congestive cardiac failure and acute cardio renal syndrome who underwent transcatheter device closure as a life saving measure with a plan of surgically correcting AR later, due to an unexpected delay in performing the surgery. After the procedure, symptomatic improvement and also improvement of aortic regurgitation to a degree that surgical repair was not necessary was noted. This case highlights the possibility of using transcatheter device closure as a life saving measure of RSOV even in the presence of severe AR when surgery is not feasible and when hemodynamic effect of RSOV is considered the main mechanism for AR.

Key Words: Rupture of sinus of valsalva, aortic regurgitation, device closure

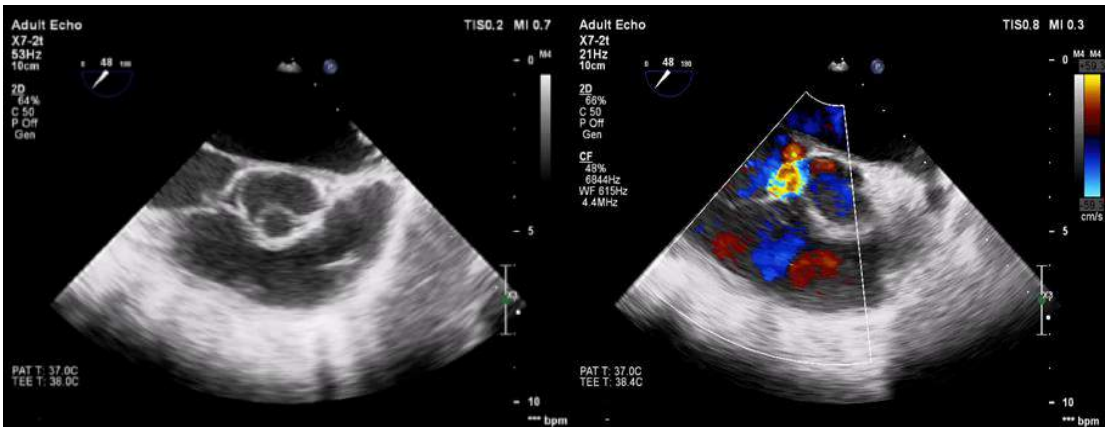
Introduction

Ruptured Sinus of Valsalva (RSOV) can be commonly associated with aortic regurgitation (AR) due to the associated structural defects or hemodynamic effects. Main methods of treatment of RSOV are surgical repair and transcatheter device closure. Surgical repair is the preferred method in patients with concomitant moderate to severe AR. Reduction of AR due to the reversal of hemodynamic effect of RSOV after surgical repair of RSOV is well known. As presence of concomitant AR is used as an exclusion criterion for device closure, reduction of AR after device closure was not reported previously. We report a case of RSOV complicated with severe AR corrected with transcatheter device closure as a life saving measure which led to reduction of AR to a degree that further surgical repair was not required.

Case report

43-year-old previously healthy lady presented with progressively worsening dyspnea, orthopnea, and paroxysmal nocturnal dyspnea of one week. Examination revealed, bilateral ankle oedema, elevated jugular venous pressure, and bilateral fine crepitations in lung bases with continuous murmur in left parasternal edge. Her blood pressure was 90/60 mm Hg and heart rate was 110 bpm. Her ECG showed sinus tachycardia. Liver transaminases and serum creatinine was elevated. Transthoracic and transesophageal echocardiogram revealed ruptured sinus of Valsalva (RSOV) with severe aortic regurgitation (AR) (Figure 1,2).

Figure 1: Ruptured sinus of Valsalva



Case Report

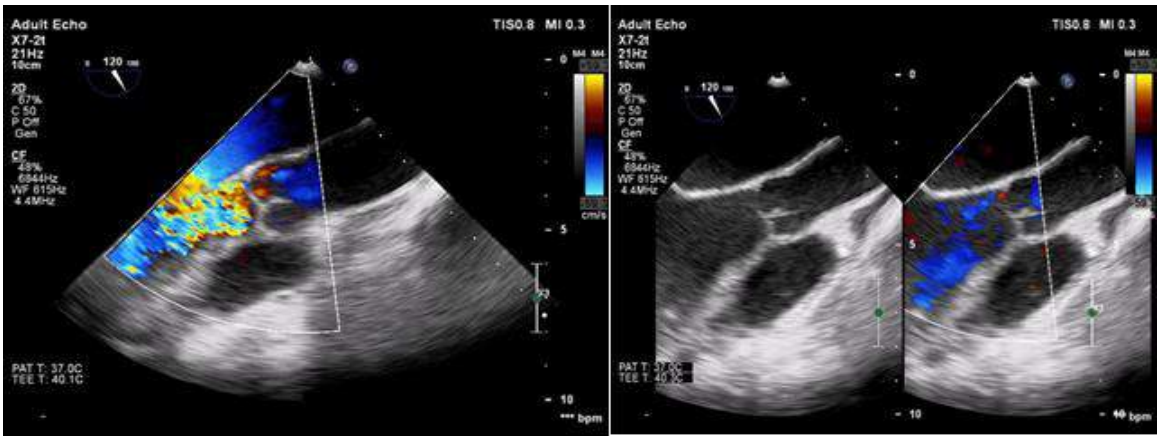


Figure 2: Severe AR

RSOV with severe AR complicated with congestive hepatopathy, congestive cardiac failure and acute cardio renal syndrome was diagnosed. Patient was referred for urgent surgery. However, as surgery was getting delayed, device closure was requested by the surgical team as a life saving measure with the plan of surgically correcting the AR later. Transcatheter closure of RSOV was done using an Amplatzer 14/12mm PDA device. Following transcatheter device closure patient improved symptomatically. Post procedure echo showed well sealed RSOV with trivial residual AR. Post procedure, the marked improvement of the aortic regurgitation to a degree that surgical repair was not necessary was noted (Figure3).

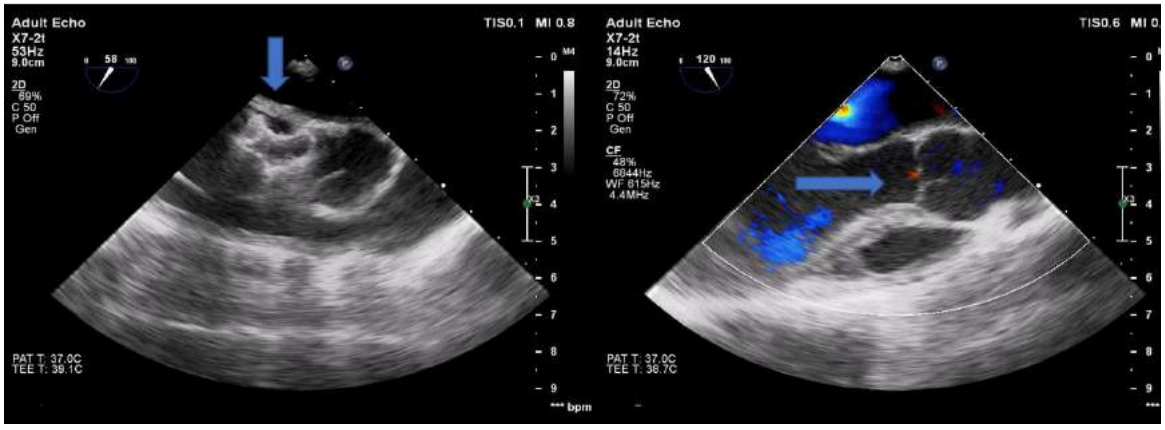
Discussion

Sinus of Valsalva aneurysm is a rare cardiac defect which occurs due to the weakness of the elastic lamina at the junction of aortic media and annulus fibrosis. It could be congenital or acquired and occurs in 0.09% of general population[1]. Rupture of sinus of Valsalva typically occurs at 20-40 years of age and acute rupture can cause hemodynamic instability as in our patient.

25-45% of patients with ruptured sinus of Valsalva can have aortic valve defects and aortic insufficiency. [2] Associated bicuspid aortic valve, lack of supporting tissue due to a sub arterial VSD can lead to anatomical prolapse of aortic cusps and predispose to aortic regurgitation. In addition, hemodynamic effect of RSOV can cause a low pressure zone via venturi effect and can distort aortic valve closure characteristics causing aortic regurgitation [3]

In our patient, improvement of AR to a degree which no longer necessitated aortic valve repair following closure of RSOV indicate that the most probable mechanism of AR was the venturi effect of RSOV.

Available treatment options for RSOV includes surgical repair and transcatheter device closure. Transcatheter device closure is a safe and feasible option if there are no associated lesions which required surgical repair. Moderate to severe AR is considered a contraindication for trans catheter device closure.[4] Only 17% of patients had preprocedural mild AR and none had preprocedural severe AR thus far in transcatheter device closure case series .[4]



Reduction of AR after surgical repair of RSOV without any additional procedures is well known , and it is considered to be due to the reversal of the hemodynamic effect caused by RSOV.[5] However, as the presence of AR is used as exclusion criteria for device closure, reduction of AR after device closure as in our patient has not been reported previously .

Conclusion:

This case highlights the possibility of using transcatheter device closure as a life saving measure of RSOV even in the presence of severe AR when surgery is not feasible and when hemodynamic effects of RSOV are considered the main causative mechanism for AR.

Reference

1. *Weinreich M, Yu P, Trost B. Sinus of Valsalva Aneurysms: Review of the Literature and an Update on Management. Clin Cardiol. 2015 Mar 1;38(3):185.*
2. *Feldman DN, Roman MJ. Aneurysms of the Sinuses of Valsalva. Cardiology. 2006 Aug;106(2):73–81.*
3. *Nascimbene A, Joggerst S, Reddy KJ, Cervera RD, Ott DA, Wilson JM, et al. Aortic valve regurgitation that resolved: After a ruptured coronary sinus aneurysm was patched. Texas Hear Inst J. 2013;40(4):489–92.*
4. *Kuriakose EM, Bhatla P, McElhinney DB. Comparison of reported outcomes with percutaneous versus surgical closure of ruptured sinus of valsalva aneurysm. Am J Cardiol. 2015 Feb 1;115(3):392–8.*
5. *Maruo A, Higami T, Obo H, Shida T. Ruptured sinus of Valsalva aneurysm associated with aortic regurgitation caused by hemodynamic effect solely. Eur J Cardio-thoracic Surg. 2003 Aug 1;24(2):318–9.*

Case Report

Synchronous Occurrence of a Left Atrial Myxoma and a Colorectal Cancer which were Successfully Managed with a Combined Surgery

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Abstract

Synchronous occurrence of two different tumours, with one of them involving the heart is rarely reported in literature and it is a challenge for the treating physician. For the patient to survive, those tumors, particularly if the tumor involving the heart causes valve outflow tract obstruction, require aggressive surgical treatment of multiple sites. We present a case of a 63-year-old gentleman who had a colorectal adenocarcinoma, with near obstruction of the lumen of the intestine and also a synchronous occurrence of an asymptomatic left atrial myxoma that nearly obstructed the mitral valve outflow tract. The patient underwent successful resection of both the cardiac mass and colorectal cancer simultaneously under the same general anesthetic procedure as a combined surgery.

Key words: Synchronous occurrence, colorectal cancer, LA myxoma, combined surgery

Introduction

Cardiac tumors may be primary or metastatic. Primary cardiac neoplasms are rare with an incidence of 0.02% in an autopsy series [1,2]. Most of them are benign and approximately 40% of primary cardiac tumors are atrial myxomas commonly affecting the left atrium [1,2]. Metastatic cardiac tumors are 20 to 40 times higher in incidence than primary cardiac neoplasms and are usually seen with disseminated malignancies [3]. Isolated cardiac metastasis is very rare and metastasis to left atrium is rarer than to the right atrium [4,5].

The synchronous occurrence of a cardiac tumor and a colorectal cancer is extremely rare. When a patient presents with an intra cardiac mass and a colorectal cancer, the physician should consider two differential diagnoses. It could be either an intra cardiac metastasis of the colorectal cancer or unrelated primary tumor of the heart. Both instances are rarely reported in literature and the synchronous presentation of a primary cardiac tumor and a colorectal carcinoma is even rarer. According to our knowledge there are only two cases of synchronous occurrence of cardiac tumor and colorectal cancer reported in literature.

In the first reported case, the resection of bowel malignancy was performed two weeks after the cardiac surgery[6]. The second reported case, urgent right hemicolectomy was performed because the patient presented with sub-acute intestinal obstruction. The atrial myxoma was identified incidentally during imaging done for the staging of the colorectal cancer[7]. Subsequently atrial myxoma was removed at a second surgery.

We believe that this is the first reported case of simultaneous resection of both the atrial myxoma and the colorectal cancer performed under a single anesthetic procedure.

Case report

A 63-year-old gentleman, with no notable medical history presented with 3 months history of constipation, per rectal bleeding, tenesmus and loss of appetite with loss of weight. Physical examination was unremarkable apart from a mid-diastolic murmur on cardiac examination. A colonoscopy was performed, and a large growth was found involving the rectum and sigmoid colon. The tumour was nearly obstructing the lumen of the intestine. Biopsy was taken from the recto- sigmoid growth and the histopathology examination revealed a moderately differentiated adeno carcinoma. The contrast enhanced CT scan of abdomen and pelvis was performed for the staging which showed upper rectal and recto sigmoid carcinoma with trans-serosal spread and perirectal lymph nodes – (T3N1M0).

Because of the cardiac murmur, transthoracic echocardiography was performed, which showed a large (4cmx5cm) intracardiac mass attached to inter-atrial septum in the left atrium, obstructing the mitral valve. Cardiac MRI was performed to further evaluate the cardiac mass before surgery. The cardiac MRI revealed a 4.3cm x5cm x 5cm size, T1 intermediate and T2 high signal intensity, pedunculated heterogeneously enhancing rounded lesion attached to the antero-septal wall of left atrium.

Cardiac MRI appearance and the location of the mass were more in favor of an atrial myxoma rather than a metastasis of the known rectal adenocarcinoma.

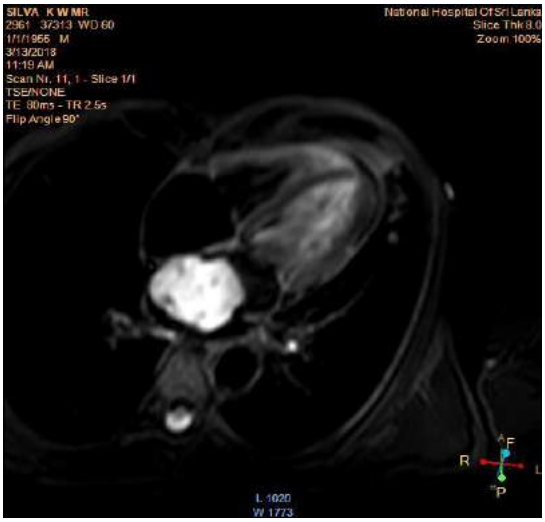

Figure 1: Cardiac MRI – Left atrial mass attach to inter-atrial septum

The patient was asymptomatic in respect to the cardiac mass but developed constipation and abdominal discomfort due to the subacute intestinal obstruction caused by the rectal carcinoma, warranting early surgery. Even though the cardiac mass was asymptomatic, it was nearly obstructing the orifice of the mitral valve. Therefore, we decided to proceed with combined surgery with resection of the cardiac mass followed by abdomino-perineal resection of the recto sigmoid adenocarcinoma under a single anesthetic procedure

The patient first underwent a successful resection of the cardiac mass without complications. Recto sigmoid resection was performed following the cardiac mass resection under the same general anaesthetic procedure.

The lower rectal tumor infiltrating in to prostate gland and serosa of the bladder was identified intra operatively and was also successfully resected.

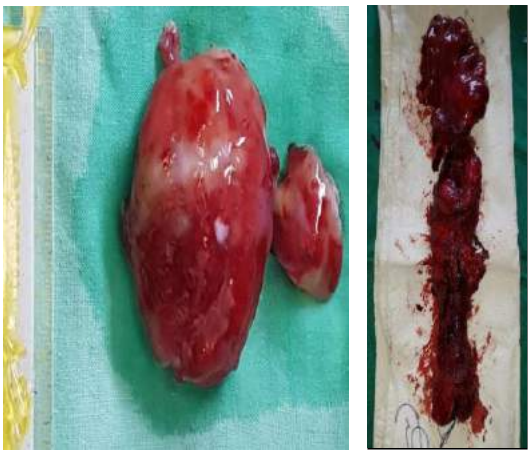

Figure 2: Left atrial mass and colorectal cancer after resection

Microscopic examination of the 60 × 50× 30 mm polypoidal atrial mass showed a myxoid lesion composed of thin cords and nests of cells. Cells were stellate with spindle shaped nuclei containing moderate eosinophilic cytoplasm with an indistinct cell border. The background contained myxoid material and areas of fresh hemorrhages and degeneration. There was no evidence of necrosis, nuclear pleomorphism or increased mitotic activity. Tumour cells showed cytoplasmic positivity with the S100 stain and both nuclear and cytoplasmic positivity with Calretinine. These findings are consistent with a benign cardiac myxoma.

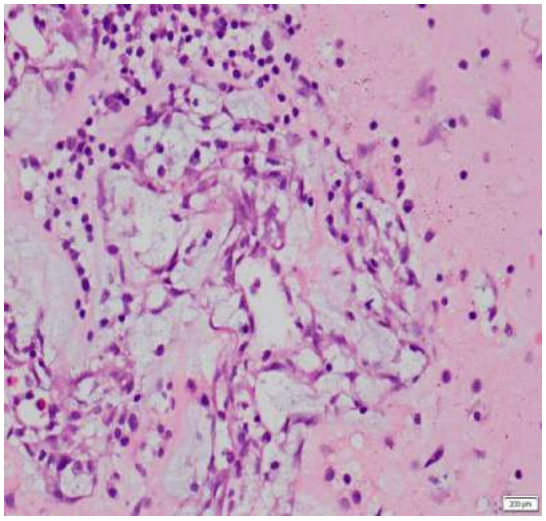

Figure 3: H& E of Atrial mass - Stellate cells with spindle nuclei containing moderate eosinophilic cytoplasm with indistinct cell borders with background myxoid material.

Case Report

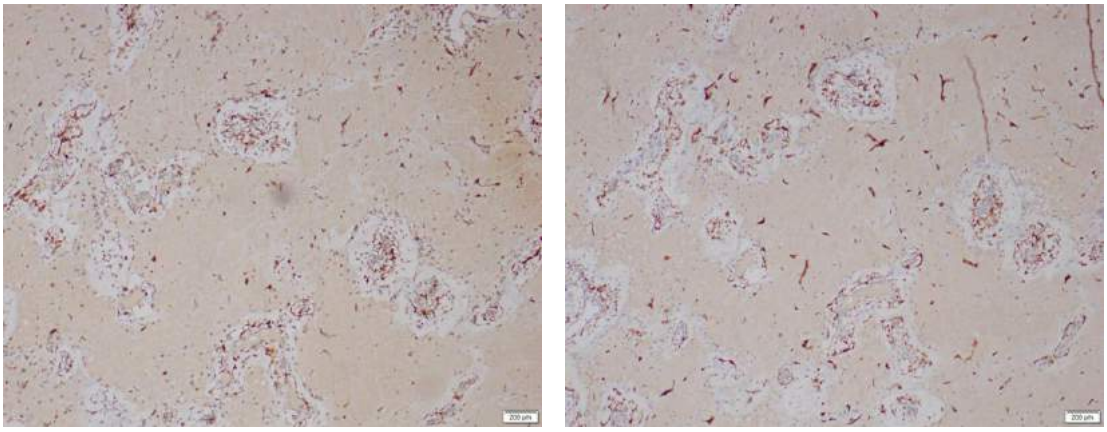

Figure 4: Atrial mass S100 stain – Cytoplasmic positivity and with Calretinine – nuclear and cytoplasmic positivity.

The 225mm length and 65mm in diameter abdomino-perineal resection specimen containing sigmoid colon, rectum and anal canal revealed a 58 x 50 mm size moderately differentiated adenocarcinoma invading the muscularis propria and infiltrating into the perirectal fat. The proximal, distal and circumferential resection margins were free of tumour. One out of ten lymph nodes contained tumour deposits. Staging of the tumor yielded a modified Dukes' classification of C and pathological tumour of pT4a.

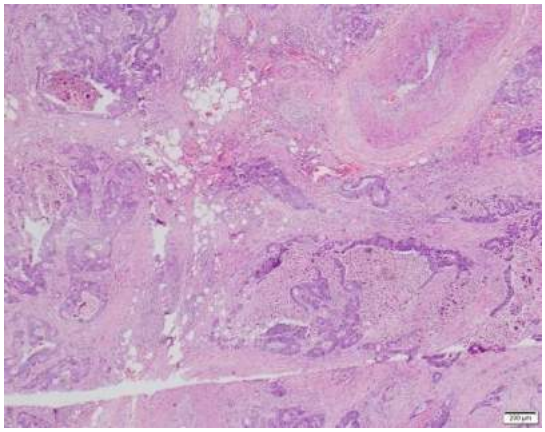

Figure 5: Moderately differentiated adenocarcinoma composed of irregular, complex and fused glandular structures and trabeculae infiltrate in to fibrous stroma with necrosis.

The patient recovered well and was subsequently discharged from the hospital without any major complications. Patient was independent with full functional capacity on the follow up clinic visit without clinical features of recurrence of either of the tumours. Furthermore, follow up echocardiography and colonoscopy confirmed the non-recurrence of both tumours.

Discussion

Even though atrial myxomas are rare, a large left atrial myxoma can prolapse into the mitral valve creating an intermittent obstruction. In a case series of atrial myxoma 44% of the patients presented with signs and symptoms of obstructive valvular disease [6,8]. Acute or sub-acute intestinal obstruction is a known presentation of colorectal carcinomas particularly if it is in an advanced stage [6,9]. However synchronous occurrence of an atrial myxoma and a colorectal carcinoma is rare, especially in which both the tumors were nearly obstructive.

According to the reported cases [6,7] in the literature, the usual presentation is bowel symptoms due to the colorectal cancer and the cardiac mass is diagnosed incidentally or while investigating the cause for the cardiac murmur. There are several possible explanations for acute or sub-acute intestinal obstruction in a patient with a cardiac mass. Cardiac metastasis of bowel malignancies and two different unrelated tumors such as cardiac myxoma and colorectal cancer are the possibilities which were reported in literature. There is also a reported case of synchronous occurrence of left atrial myxoma and small intestinal myxoma in a patient who presented with small bowel obstruction [11]. Other possible explanation is intestinal obstruction due to bowel ischaemia from tumor embolization of left side cardiac myxoma in to the mesenteric arteries. Therefore, careful evaluation is of utmost importance in the management of those patients.

The echocardiography remains the key diagnostic tool in the diagnosis of cardiac myxoma [12]. But the differentiation of cardiac myxoma and cardiac metastasis might be difficult with echocardiography alone [4].

Magnetic resonance imaging (MRI) is effective in the evaluation, because it can accurately define the pericardium, the myocardial walls, and the cardiac chambers [4]. In view of the management, the accurate diagnosis of the two conditions are important because the surgical resection remains the mainstay of treatment for cardiac myxomas while chemotherapy is a treatment option for intra cardiac metastatic tumours. Therefore, in patients with colorectal cancer with a cardiac mass, we recommend further diagnostic evaluation such as an MRI, in addition to echocardiography for the evaluation of the cardiac mass.

A complex presentation of synchronous tumors should prompt the surgeon to treat the most immediate life-threatening problem first [6,7]. Usually, the resection of colorectal cancer is considered secondary to the cardiac emergency if there is no intestinal obstruction [6]. According to the literature, the gap can be a few weeks post operative between the two surgeries [6]. Resection of the colorectal cancer should be performed first as an emergency in patients who present with intestinal obstruction and resection of the cardiac myxoma can be considered later as the second surgery [7] . In patients, such as ours, who presented with intestinal obstruction due to colorectal cancer and also had a cardiac myxoma which was obstructing the valve outflow tract warranted early surgery for both conditions. The resection of both the cardiac and the colorectal tumor can be performed under the same anesthetic procedure as a combined surgery. In the reported three cases, including ours, demonstrated that in all three, the combined surgery was performed successfully.

Even though there is no established association between colorectal cancer and cardiac myxomas; to our knowledge this is the third reported case in literature.

Furthermore, synchronous cardiac myxomas with other neoplasms have also been reported in the literature [7, 10] .

Therefore, this case report highlights the need of extensive research and reporting to evaluate whether there is any association between cardiac myxoma and other neoplasms; especially colorectal cancer.

Furthermore, these cases points to the possibility of the need of screening for extra-cardiac tumors for patients who present with cardiac myxomas.

Conclusion

To our knowledge, this is the third reported case in the medical literature of a synchronous occurrence of an atrial myxoma and a colorectal cancer. Therefore, this raises the need of further evaluation and reporting to identify the correlation of these two conditions, if any. Although the cardiac myxoma is generally considered the most life-threatening and is resected first, bowel resection should be performed under the same anesthesia if the intestinal mass is creating an obstruction. This is the first reported case in literature of simultaneous resection of atrial myxoma and colorectal cancer performed under the same anesthesia as a combined surgery.

References

1. *Reynen K (1996) Frequency of primary tumors of the heart. Am J Cardiol 77:107, This study incorporated the results of 22 large necropsy series, in order to provide reliable data on the frequency of the various primary cardiac tumours..CrossRefPubMedWeb of ScienceGoogle Scholar*
2. *Maraj S, Pressman GS, Figueredo VM. Primary Cardiac Tumours. Int J Cardiol. 2009; 133: 152–156.*
3. *Lam KY,Dickens P,Chan AC (1993) Tumors of the heart. A 20-year experience with a review of 12,485 consecutive autopsies. Arch Pathol Lab Med 117:1027–1031, This study analysed data from over 12 000 necropsies to provide accurate data on the incidence of primary and secondary cardiac tumours..PubMedWeb of ScienceGoogle Scholar*
4. *Choi PW, Kim CN, Chang SH, Chang WI, Kim CY, Choi HM. Cardiac metastasis from colorectal cancer: A case report. World J Gastroenterol. 2009; 15: 2675-2678.*
5. *Pizzicannella J, Ricci V, Gorla R, Spinapolice E, Esposito A. Isolated cardiac metastasis from colorectal cancer in a 35-year-old man. Case Rep Med. 2012; 2012: 751761.*
6. *Ismael N. Nuño, MD, FACS, FACC, Tyler Y. Kang, MS IV, Hector Arroyo, MD, and Vaughn A. Starnes, MD Synchronous Cardiac Myxoma and Colorectal Cancer- A Case Report, Tex Heart Inst J. 2001; 28(3): 215–217.*
7. *Kar A, Sudarsanam A, Papaspyros S, Prasad S. Sub-Acute Bowel Obstruction Preventing Sudden Cardiac Death: A Case of Synchronous but Unrelated Left Atrial Myxoma and Colorectal Adenocarcinoma. Clin Surg. 2016; 1: 1075.*
8. *McAllister HA. Primary tumors and cysts of the heart and pericardium. Curr Probl Cardiol 1979;4(2):1-51.*

9. *LaMont JT, Isselbacher KJ. Diseases of the small and large intestine. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harrison's principles of internal medicine. Vol 2. 13th ed. New York: McGraw-Hill; 1994. p. 1417-31.*
10. *Hong-cheng L, Xiao-feng C, Yu-ming Y, Ge-ning J. Synchronous left atrial myxoma and adenosquamous lung carcinoma. Chin Med J. 2013; 126: 2992-2993*
11. *Wang Y, Sharkey FE. Myxoma of the small bowel in a 47-year-old woman with a left atrial myxoma. Arch Pathol Lab Med. 2003; 127: 481-484.*
12. *Pepi M, Evangelista A, Nihoyannopoulos P et al. on behalf of the European Association of Echocardiography Recommendations for echocardiography use in the diagnosis and management of cardiac sources of embolism 2010;11:461-476.*

Case Report

Use of IVUS and FFR to Enhance the Accuracy of Decision Making in High-Risk PCI: A Case Report

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Abstract

Coronary angiogram is limited in its ability to differentiate calcium from thrombus. Assessing functional significance of lesions and assessing plaque morphology can help to minimize or negate the misdiagnosis of calcium as a thrombus and also misjudgment of the severity of lesions. Intravascular Ultrasound (IVUS) is a superior modality to assess large diameter vessels like LMCA due to its high tissue penetration depth and better correlation with physiological significance of LMCA lesions. IVUS can further help to identify the lesion morphology, determining the need for lesion preparation and post stent optimization. However, IVUS can poorly correlate with physiological significance in non LMCA lesions. Fractional flow reserve (FFR) is a reliable and reproducible method to assess functional significance of coronary lesions. We present a case of a 50-year-old male whose coronary angiography showed a filling defect in distal left main suggestive of a thrombus and tight lesions in RCA, LAD, LCX. However further assessment with IVUS and FFR helped to differentiate the filling defect of LMCA as mild circumferential calcium and both RCA LCX lesions were not physiologically significant, which led to the deferment of the stenting. IVUS further helped to determine the need of LAD lesion preparation in the form of calcium modification by non-compliant ballooning and post stent optimization by identifying unopposed struts. This case highlights the importance of integrating FFR and IVUS assessment for high-risk complex PCI procedures to enhance the accuracy of decision making.

Keywords: FFR, IVUS, LMCA-thrombus, Differentiating calcium

Introduction

Intravascular imaging in the form of Intravascular Ultrasound (IVUS) is superior to coronary angiogram in differentiating calcium, assessing intraluminal coronary structure, accurately assessing lesion severity and morphology, determining the need of lesion preparation, precise stent sizing, identifying optimal landing zones, and post stent optimization. Fractional flow reserve (FFR) is superior to coronary angiogram in assessing functional significance of coronary lesions. Integration of IVUS and FFR to angiography, help to enhance the accuracy of decision making in high-risk percutaneous coronary intervention (PCI). However, both methods are underutilized even in the developed countries.

Case report

50-year-old male with history of hypertension and dyslipidemia presented with anteroseptal ST elevation myocardial infarction (STEMI). Transthoracic echocardiogram showed ejection fraction of 60% and anteroseptal ischemia. Coronary angiography showed: a filling defect suggestive of a thrombus in left main coronary artery (LMCA), tight lesion in ostial to proximal left anterior descending artery (LAD),60% lesion in proximal left circumflex (LCX) and a tight lesion in right coronary artery (RCA). (Figure 1) Patient was given 6 weeks of antiplatelet therapy with aspirin and clopidogrel. However, the repeat coronary angiogram after anticoagulation showed the same results.

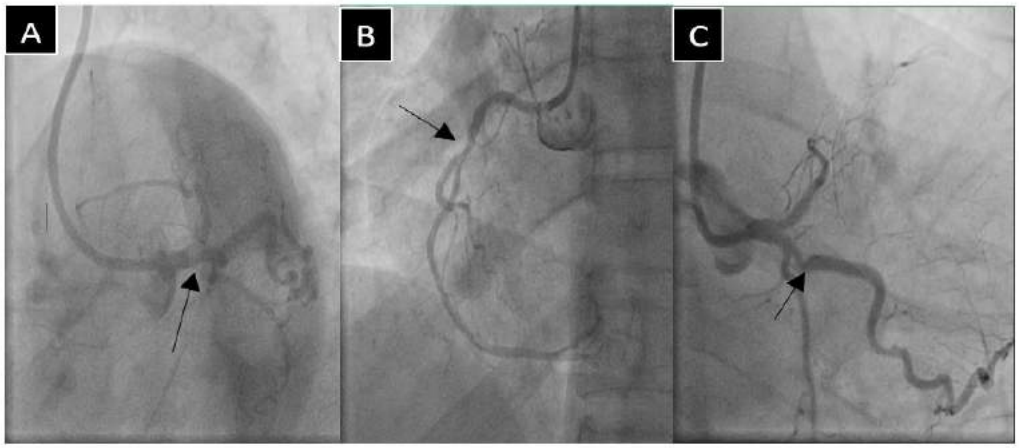

Figure 1 :A-LMCA filling defect suggestive of thrombus, B- Proximal RCA 60% lesion, C- Proximal LCX 60% lesion

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Intravascular ultrasound sonography (IVUS) pullback was performed from LAD to LMCA and LCX to LMCA after wiring LAD and predilating proximal to mid LAD with 2.0 mm normal pressure balloon. IVUS showed heavy non circumferential calcification in proximal, mid LAD and mild non circumferential calcification in distal LMCA without any thrombus (Figure 2). In the LAD tightest segment, minimum lumen area was 2.21 mm^2. (Figure 2). In the LCX tightest segment minimum lumen area was 3.23mm^2 and plaque burden was 65%. However, subsequent FFR assessment of LCX lesion revealed FFR of 0.86 and stenting was deferred.

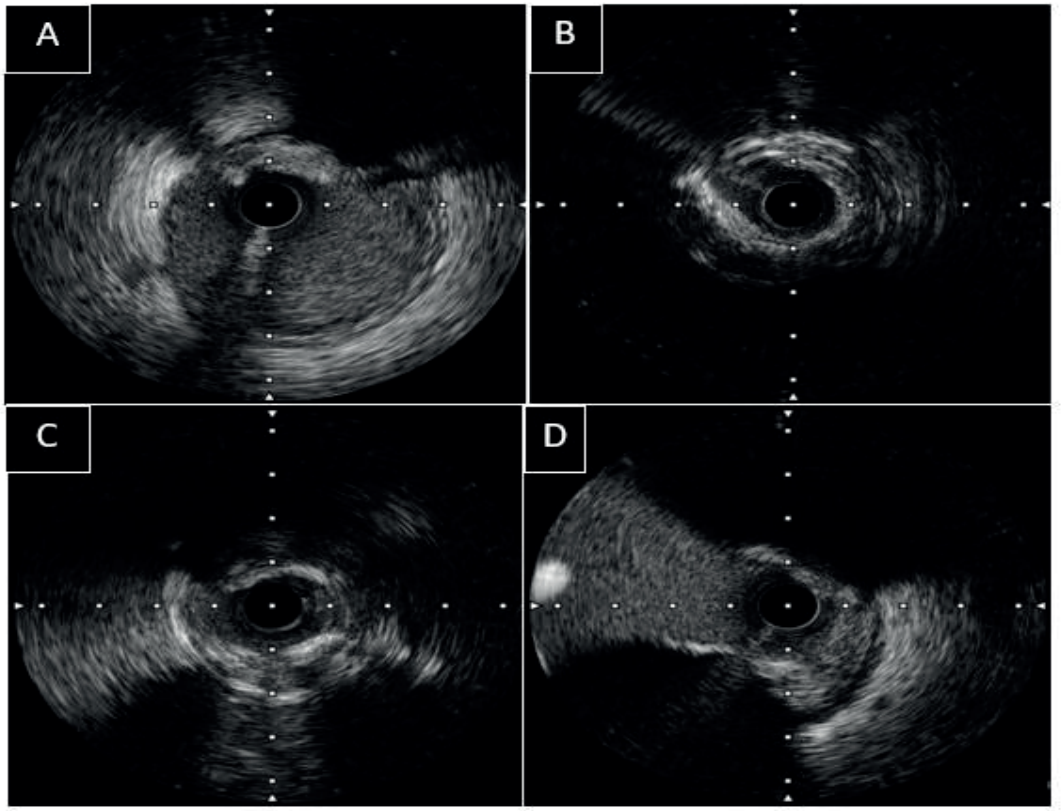

Figure 2 : (IVUS images) (A)-Present LM showing fibrocalcific plaque with adventitial calcium and wire artifact, (B)-LAD to LM showing attenuated plaque with thick fibrous cap, (C)- LAD tightest lesion showing attenuated fibrous plaque with non-circumferential calcium, (D)-LAD Ostium with significant fibro fatty plaque.

LAD was wired again with a buddy guidewire and predilated with a 3.0 mm non-compliant balloon for modification of calcium. A dissection flap in near ostial LAD was noted. Ostium to mid LAD was stented with 3.0 X 48 mm DES and post dilated with 3.0 X 15 mm non-compliant balloon. Post procedure IVUS was performed, showing inadequate strut apposition. The stent was again post dilated and calcium modification done with 3.5 mm non-compliant balloon. Post procedure IVUS images showed a well apposed stent struts. (Figure 3) Post procedure angiography revealed excellent results.

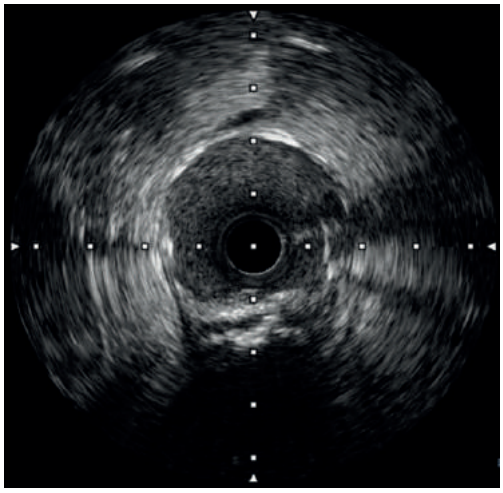

Figure 3: Post stenting well deployed stent

Even though the angiography revealed 70-80% stenosis in proximal RCA, FFR assessment of RCA lesion revealed FFR of 0.91 and again proximal RCA stenting was deferred. (Figure 4)

Figure 4: (A)- FFR of LCX, (B)- FFR of RCA

Discussion

Intravascular Imaging (IVI) is helpful in visualizing intraluminal coronary structure and accurately assessing lesion severity, lesion morphology, vessel dimensions for optimal stent sizing and achieve optimal stent expansions compared to coronary angiography. Intravascular ultrasound (IVUS) and the Optical Coherent tomography (OCT) are the main intravascular imaging methods used. These methods are especially helpful in planning PCI in high-risk subsets such as left main coronary lesions, bifurcation lesions and calcified lesions. [1] Despite the growing evidence of improved outcome with IVI, these modalities remain underutilized even in the developed world [2]

Compared to OCT, IVUS has higher tissue penetration depth and is preferred over OCT for complete visualization of LMCA and other large vessel walls. [3] In LMCA lesions, IVUS assessment has a better correlation with physiological significance. [4] Severe proximal LAD and LCX disease may impact physiological FFR assessments of LMCA stenosis and in these cases IVUS is preferred to FFR. In LMCA disease IVUS guided revascularization is associated with significant reduction in major adverse cardiac events (MACE)[5]. We used IVUS pullback from both LAD and LCX to LMCA for better visualization of our patient's LMCA lesion and FFR was not done to LMCA as proximal LAD lesion can impact FFR values of LMCA.

Heavy non circumferential calcification in proximal, mid LAD and mild non circumferential calcification in distal LMCA without any thrombus was identified by IVUS in our patient.

Previously identified LMCA filling defect suggestive of thrombus on coronary angiography was diagnosed as mild non circumferential calcification by IVUS in our patient and stenting was deferred. Coronary angiography is limited in its ability to accurately differentiate thrombus from intravascular calcium and can lead to misdiagnosing of calcium as thrombus. [6]. IVUS can detect the arc and length of the calcium and is a superior modality to asses intravascular calcium better than coronary angiogram. [7]. Even though OCT is superior to IVUS in assessing thrombus, because of the unavailability of OCT in the Sri Lankan setting it was not used.

IVUS is better than angiography in precise stent sizing, determining the optimal landing zones, determining the need for lesion preparation and post stent optimization. [8] In our patient, pre stent plaque assessment via IVUS helped to prepare the lesion by calcium modification in the form of non-compliant ballooning. Post stent IVUS assessment helped to identify the unopposed stent struts and further calcium modification was carried out by high pressure ballooning which optimized the stent expansion.

A coronary angiogram is limited in its ability for assessing functional significance of a coronary lesion. [9].

Other than the lumen narrowing which can be assessed by the coronary angiogram, multiple factors such as, lesion length, collateral flow, and health of the downstream myocardial bed supplied contribute to the functional significance of coronary lesions. FFR is a reproducible and reliable method to assess the functional significance of a coronary lesion. [10].

FFR guided strategy to defer or perform PCI is safe, cost effective and reduces long term major adverse cardiac events according to multiple trials such as FAME, FAME-2, DEFFERAL. FLOWER MI. In our patient angiography revealed 60-70% lesion in proximal RCA, but FFR of RCA was >0.8 which led us to defer the revascularization of RCA.

Even though intravascular imaging provides extensive anatomical details of coronary lesions, it is inferior to invasive physiology when assessing functional significance of coronary lesions.
Other than LMCA lesions, IVUS defined plaque morphology poorly correlates with FFR [11]. Even though IVUS showed significant plaque burden (65%) in left circumflex artery we deferred revascularization as FFR was >0.8 in our patient.

Conclusion:

This case demonstrates that integrating and combination of IVUS and FFR with angiography can enhance the accuracy of decision making in high-risk complex PCI procedures by accurately assessing calcium, plaque morphology, severity, and physiological significance of lesions and pre and post stent optimization.

List of abbreviations

FFR-Fractional flow reserve
IVI- Intravascular Imaging
IVUS-Intravascular Ultrasound
LMCA-left main coronary artery
LAD-left anterior descending artery
LCX-Left circumflex artery
MACE-Major adverse cardiac events
OCT-Optical coherence tomography
PCI-Percutaneous coronary intervention
RCA-Right coronary Artery
STEMI-ST elevation myocardial infarction

Reference

1. *Kim JS, Hong MK, Ko YG, Choi D, Yoon JH, Choi SH, et al. Impact of intravascular ultrasound guidance on long-term clinical outcomes in patients treated with drug-eluting stent for bifurcation lesions: Data from a Korean multicenter bifurcation registry. Am Heart J. 2011 Jan;161(1):180–7.*
2. *Elgendy IY, Ha LD, Elbadawi A, Ogunbayo GO, Olorunfemi O, Mahmoud AN, et al. Temporal Trends in Inpatient Use of Intravascular Imaging Among Patients Undergoing Percutaneous Coronary Intervention in the United States. Vol. 11, JACC: Cardiovascular Interventions. Elsevier Inc.; 2018. p. 913–5.*
3. *Ono M, Kawashima H, Hara H, Gao C, Wang R, Kogame N, et al. Advances in IVUS/OCT and Future Clinical Perspective of Novel Hybrid Catheter System in Coronary Imaging. Front Cardiovasc Med. 2020 Jul 31;7:119.*
4. *Jasti V, Ivan E, Yalamanchili V, Wongpraparut N, Leesar MA. Correlations between fractional flow reserve and intravascular ultrasound in patients with an ambiguous left main coronary artery stenosis. Circulation. 2004 Nov 2;110(18):2831–6.*
5. *De La Torre Hernandez JM, Baz Alonso JA, Gómez Hospital JA, Alfonso Manterola F, Garcia Camarero T, Gimeno De Carlos F, et al. Clinical impact of intravascular ultrasound guidance in drug-eluting stent implantation for unprotected left main coronary disease: Pooled analysis at the patient-level of 4 registries. JACC Cardiovasc Interv. 2014;7(3):244–54.*
6. *Duissaillant GR, Mintz GS, Pichard AD, Kent KM, Satler LF, Popma JJ, et al. Intravascular ultrasound identification of calcified intraluminal lesions misdiagnosed as thrombi by coronary angiography. Am Heart J. 1996;132(3):687–9.*
7. *Wang X, Matsumura M, Mintz GS, Lee T, Zhang W, Cao Y, et al. In Vivo Calcium Detection by Comparing Optical Coherence Tomography, Intravascular Ultrasound, and Angiography. JACC Cardiovasc Imaging. 2017 Aug 1;10(8):869–79.*
8. *Shlofmitz E, Ali ZA, Maehara A, Mintz GS, Shlofmitz R, Jeremias A. Intravascular Imaging-Guided Percutaneous Coronary Intervention: A Universal Approach for Optimization of Stent Implantation. Circ Cardiovasc Interv. 2020;(December):397–406.*
9. *Tonino PAL, Fearon WF, De Bruyne B, Oldroyd KG, Leesar MA, Ver Lee PN, et al. Angiographic Versus Functional Severity of Coronary Artery Stenoses in the FAME Study. Fractional Flow Reserve Versus Angiography in Multivessel Evaluation. J Am Coll Cardiol. 2010 Jun 22;55(25):2816–21.*
10. *Pijls NHJ, Van Gelder B, Van Der Voort P, Peels K, Bracke FALE, Bonnier HJRM, et al. Fractional flow reserve: A useful index to evaluate the influence of an epicardial coronary stenosis on myocardial blood flow. Circulation. 1995 Dec 1;92(11):3183–93.*
11. *Waksman R, Legutko J, Singh J, Orlando Q, Marso S, Schloss T, et al. FIRST: Fractional flow reserve and intravascular ultrasound relationship study. J Am Coll Cardiol. 2013;61(9):917–23.*

Case Report

The Value of Intra Vascular Ultrasound (IVUS) Guided Imaging in Assessing the Significance of Left Main stenosis and Deciding on the Stenting Strategy and Stent Optimization

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Abstract

Coronary artery bypass surgery (CABG) has been the traditional revascularization procedure for patients with unprotected left main coronary artery (LMCA) disease. Even though PCI techniques have evolved rapidly, LMCA PCI remains a challenging procedure. Stent thrombosis may be caused by stent under expansion and is often a fatal complication. [1-4] Intravascular ultrasound (IVUS) is an adjunct imaging modality that can provide valuable information including quantification of lesion and luminal dimensions. [5] .It aids the operator's stent selection pre-PCI and provides information on stent apposition and coverage post-PCI. [6-7] This case report shows the impact of IVUS imaging in left main revascularization strategies (CABG Vs.PCI), selecting an ideal stenting technique and stent optimization.

Key words: IVUS, LMCA, stent optimization

Introduction

Left main coronary artery (LMCA) disease is associated with high morbidity and mortality owing to the large area of compromised myocardium. Therefore, coronary artery bypass grafting has been the standard revascularization approach. However, remarkable advancements in stent devices, technical refinement and adjunctive medical therapy have led to improved PCI outcomes for unprotected LMCA disease. Especially, with the widespread use of drug-eluting stents, PCI for LMCA lesions have become technically more feasible and achieves favorable long-term clinical outcomes.

Existing clinical practice guidelines continue to advocate CABG surgery as the singular class I indication for myocardial revascularization. However, more recent RCTs and registry studies in Left Main Coronary arterial disease (LM CAD) support PCI as a reasonable alternative in select patients with less complex LM anatomy. Currently, in the US guidelines, PCI has a class IIa recommendation ("is reasonable") in select patients with isolated LM stenosis involving the ostium or shaft and without coexisting multi vessel disease and where the risk of surgical bypass is high. [8]

PCI has a class IIb recommendation ("may be reasonable") also in patients with LM stenosis involving the distal bifurcation or with less complex coexisting multi vessel disease as defined by a low or intermediate SYNTAX score (≤33) and have an elevated surgical risk.

During PCI, IVUS can be used to: select stent size, identify optimal proximal and distal stent edge landing zones, select stent length using motorized transducer pull back to measure the distance between the proximal and distal landing zones and to determine whether to cover the aorto-ostial junction when stenting an LMCA or proximal RCA lesion. The ability of IVUS to visualize the vessel size permits upsizing a stent to maximize final stent dimensions with no apparent disadvantage; true vessel size is larger than lumen dimensions because of accumulated plaque and positive remodeling. Conversely, an aggressive stent-sizing strategy should be avoided in lesions with IVUS detected negative remodeling because of the risk of perforation

Case presentation

A 63-year-old male who had a past history of hypertension for many years and a significant history of smoking, presented to us with a NYHA class 3 dyspnea of three months' duration. However, there were no significant findings on examination. Basic investigations including full blood count, electrocardiogram and chest radiograph, all were unremarkable. Echocardiography showed preserved left ventricular systolic function with grade one diastolic dysfunction and evidence of hypertensive heart disease. He was further evaluated with treadmill stress study, which was found to be positive in stage one.

Case Report

Subsequently a coronary angiogram was performed, which revealed significant LAD ostial, mild LCx and RI ostial disease with moderate RCA and hemodynamically controversial LMCA ostial disease. (Figure 1). Considering these findings, we were in a quandary in deciding and recommending the best revascularization strategy for this patient. Thus, we decided to proceed with intra vascular ultra sound (IVUS) imaging to find out the significance of left main, LCx as well as RI ostial lesions.

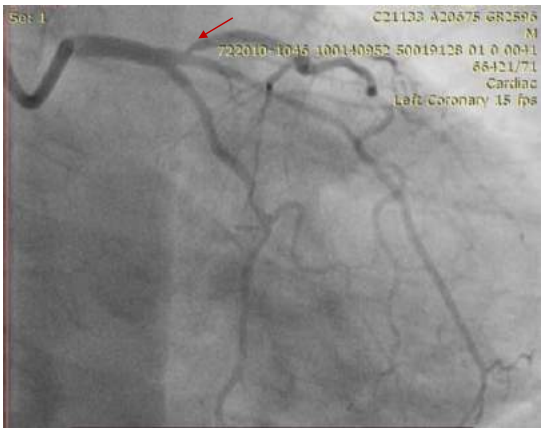

Figure 1: Angiographic appearance of LAD ostial lesion

After obtaining written consent from the patient, the IVUS was carried out. Through the right femoral arterial access LMCA was engaged with XB 3 guiding catheter and LAD lesion was crossed with 0.014" Sion blue guide wire. An intra-vascular ultrasound catheter "Boston Scientific OptiCross 18" was passed over the LAD guide wire and automatic fullback mode was activated to assess plaque characteristics, volume and intra vascular dimensions.

There was a significant plaque burden noted at the LAD ostium with minimal luminal area of 2.8 mm^2. Calculated plaque volume was 75%. No significant plaque burden was noted at RI or LCx ostium. However, there was an unraveled plaque noted at the LMCA ostium with minimal luminal area of 7.03mm^2. Calculated plaque volume was 51%. (Figure 2) After careful analysis of all these findings and detailed discussion of the risk-benefit of both revascularization strategies (CABG Vs PCI) the decision was taken to proceed with a single stent strategy from LMCA ostium to proximal LAD.

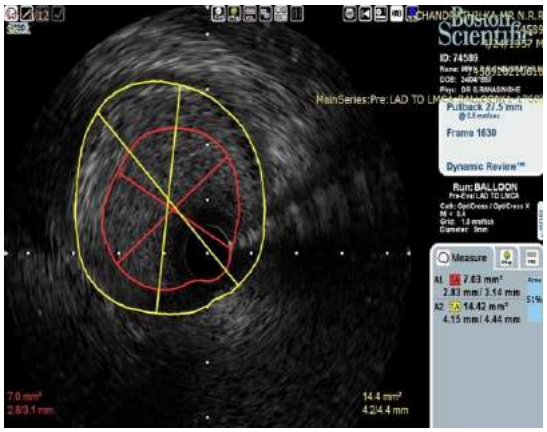

Figure 2: IVUS guided LMCA ostial assessment

Both LCx and RI vessels were engaged with sion and rinato guide wires. LAD and LMCA ostial lesions were pre dilated with 2 x 10 mm Sprinter and 2.75 x 8 mm NC Quantum balloons at 10- 14 atm respectively. LMCA ostium to LAD was stented with a 3.5 mm x 33mm Xience Prime DES The stent was deployed at 10 atm. Stented area of the LAD and LMCA was also post dilated with 3.5 x 12 mm NC Quantum balloon and 4.5 x 8 mm NC Sprinter balloon at 14 – 18 atm respectively. LMCA ostial flaring was carried out with a 4.5 x 8 mm NC Sprinter balloon at 22atm.

Post procedure IVUS run showed significant narrowing of LCx ostium due to plaque shifting. However, considering the wider angle of the carina, it was decided to carry out provisional stenting to LCx by T and protrusion (TAP) method.

After recrossing of the guide wire LCx ostium pre dilatation was done with 2 x 10 mm Sprinter balloon at 10 atm followed by TAP to LCx with 2.75 x 28 mm Xience prime DES at 8 atm. Post dilatation was done with 2.75 x 8mm NC Quantum balloon at 14-18 atm. Simultaneous kissing balloon inflation performed at 12 atm by placing 3 x 9mm NC Quantum balloon at LAD ostium and 2.75 x 8 mm NC Quantum balloon at LCx ostium. Post procedure angiography (Figure 3) and automatic IVUS pull back images revealed well apposed and good placement of the stents. (Figure 4)

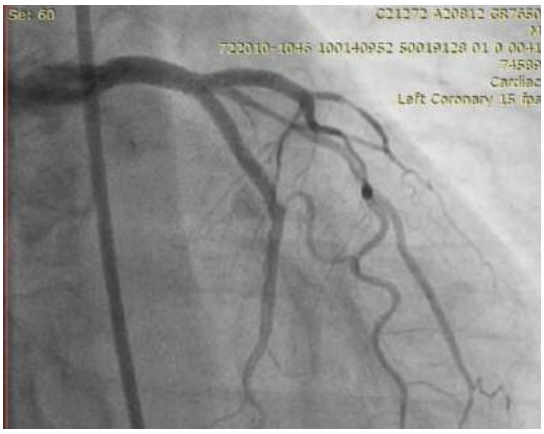

Figure 3: Post procedure angiographic result

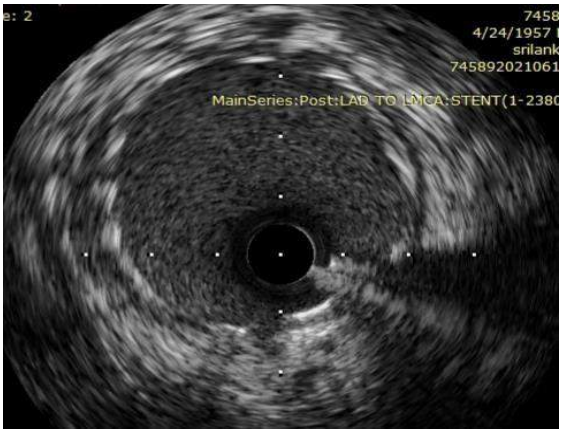

Figure 4: Post PCI IVUS assessment of LMCA ostium

Discussion

In this clinical scenario initially, we faced a dilemma when selecting the best revascularization option i.e., CABG vs PCI.

In the conventional angiograms, apart from severe LAD ostial disease, non-significant hemodynamic changes were noted (a ventricularized pressure wave pattern without a significant pressure dampening) to suggest LMCA ostial involvement. Therefore, we decided to use IVUS to assess the significance of LMCA, LCx and RI ostial disease.

First IVUS run showed significant LAD and LMCA ostial disease. Therefore, we proceeded with a single stent strategy to LMCA-LAD. However, there was a plaque shifting and a significant LCx ostial narrowing was noted in post procedure IVUS assessment. Thus, considering anatomical factors a TAP to LCx was performed.

IVUS was extremely helpful in this case to assess plaque characteristics, in quantification of plaque burden, selecting appropriate stent sizes, deciding suitable stent strategy as well as post stent optimization.

An under expanded stent is a known risk factor for stent thrombosis, an often-fatal event if it occurs in the unprotected LMCA**.** In this scenario revascularization strategy, stenting technique and stent optimization all were guided by intra vascular ultrasound. Several randomized controlled trials (RCTs) and observational studies examining intracoronary imaging during and after stent implantation have demonstrated that IVUS-guided stent implantation was associated with the reduction of major adverse cardiac events and target vessel revascularization in patients with complex coronary lesions, including lengthy lesions, severe calcification, bifurcation lesions, chronic total occlusions and unprotected left main disease. [9-12] It currently has a class 2A recommendation in international guidelines. [13-14]

Conclusion

IVUS guidance was associated with an independent and significant outcome benefit when performing unprotected LMCA PCI. Potential mediators of this benefit include, the ability to use larger and more appropriately sized stents, perhaps translating into lower risk of subsequent stent thrombosis. Our IVUS assessment findings indicate a possible hazard when performing unprotected LMCA PCI without IVUS guidance.

References

1. *Choi SY, Witzenbichler B, Maehara A, Lansky AJ, Guagliumi G, Brodie B, Kellett MA, Dressler O, Parise H, Mehran R, Dangas GD, Mintz GS, Stone GW. Intravascular ultrasound findings of early stent thrombosis after primary percutaneous intervention in acute myocardial infarction: a harmonizing outcomes with revascularization and stents in acute myocardial infarction (HORIZONS-AMI) substudy.Circ Cardiovasc Interv. 2011; 4:239–247. doi: 10.1161/CIRCINTERVENTIONS.110.959791.*
2. *xCheneau E, Leborgne L, Mintz GS, Kotani J, Pichard AD, Satler LF, Canos D, Castagna M, Weissman NJ, Waksman R. Predictors of subacute stent thrombosis: results of a systematic intravascular ultrasound study.Circulation. 2003; 108:43–47. doi: 10.1161/01.CIR.0000078636.71728.40.*

3. *Fujii K, Carlier SG, Mintz GS, Yang YM, Moussa I, Weisz G, Dangas G, Mehran R, Lansky AJ, Kreps EM, Collins M, Stone GW, Moses JW, Leon MB. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus- eluting stent implantation: an intravascular ultrasound study.J Am Coll Cardiol. 2005; 45:995–998. doi: 10.1016/j.jacc.2004.12.066.*
4. *De Labriolle A, Bonello L, Lemesle G, Steinberg DH, Roy P, Xue Z, Kaneshige K, Suddath WO, Satler LF, Kent KM, Pichard AD, Lindsay J, Waksman R. Clinical presentation and outcome of patients hospitalized for symptomatic in-stent restenosis treated by percutaneous coronary intervention: comparison between drug-eluting stents and bare-metal stents.Arch Cardiovasc Dis. 2009; 102:209–217. doi: 10.1016/j.acvd.2009.01.004.*
5. *Mäkikallio T, Holm NR, Lindsay M, Spence MS, Erglis A, Menown IB, Trovik T, Eskola M, Romppanen H, Kellerth T, Ravkilde J, Jensen LO, Kalinauskas G, Linder RBA,Pentikainen M, Hervold A, Banning A, Zaman A, Cotton J, Eriksen E, Margus S, Sørensen HT, Nielsen PH, Niemelä M, Kervinen K, Lassen JF, Maeng M, Oldroyd K, Berg G, Walsh SJ, Hanratty CG, Kumsars I, Stradins P, Steigen TK, Fröbert O, Graham ANJ, Endresen PC, Corbascio M, Kajander O, Trivedi U, Hartikainen J, Anttila V, Hildick-Smith D, Thuesen L, Christiansen EH; NOBLE Study Investigators. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial.Lancet. 2016; 388:2743–2752. doi: 10.1016/S0140-6736(16)32052-9.*
6. *Nissen SE, Yock P. Intravascular ultrasound: novel pathophysiological insights and current clinical applications.Circulation. 2001; 103:604–616. doi: 10.1161/01.CIR.103.4.604.*
7. *Witzenbichler B, Maehara A, Weisz G, Neumann FJ, Rinaldi MJ, Metzger DC, Henry TD, Cox DA, Duffy PL, Brodie BR, Stuckey TD, Mazzaferri EL, Xu K, Parise H, Mehran R, Mintz GS, Stone GW. Relationship between intravascular ultrasound guidance and clinical outcomes after drug-eluting stents: the assessment of dual antiplatelet therapy with drug-eluting stents (ADAPT-DES) study.Circulation. 2014; 129:463–470. doi: 10.1161/ CIRCULATIONAHA. 113.003942.*
8. *Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN, Lange RA, Mauri L, Mehran R, Moussa ID, Mukherjee D, Nallamothu BK, Ting HH. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation. 2011; 124:2574–2609.*
9. *Fitzgerald PJ, Oshima A, Hayase M, Metz JA, Bailey SR, Baim DS, Cleman MW, Deutsch E, Diver DJ, Leon MB, Moses JW, Oesterle SN, Overlie PA, Pepine CJ, Safian RD, Shani J, Simonton CA, Smalling RW, Teirstein PS, Zidar JP, Yeung AC, Kuntz RE, Yock PG. Final results of the Can Routine Ultrasound Influence Stent Expansion (CRUISE) Study.Circulation. 2000; 102:523–530. doi: 10.1161/01.CIR.102.5.523.*
10. *Hong SJ, Kim BK, Shin DH, Nam CM, Kim JS, Ko YG, Choi D, Kang TS, Kang WC, Her AY, Kim YH, Kim Y, Hur SH, Hong BK, Kwon H, Jang Y, Hong MK; IVUS-XPL Investigators. Effect of Intravascular Ultrasound-Guided vs Angiography-Guided Everolimus-Eluting Stent Implantation: The IVUS-XPL randomized clinical trial.JAMA. 2015; 314:2155–2163. doi: 10.1001/jama.2015.15454.*
11. *Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, Yun SC, Lee CW, Hong MK, Lee JH, Park SW; MAIN-COMPARE Investigators. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. Circ Cardiovasc Interv. 2009; 2:167–177. doi: 10.1161/ CIRCINTERVENTIONS. 108.799494.*
12. *Zhang YJ, Pang S, Chen XY, Bourantas CV, Pan DR, Dong SJ, Wu W, Ren XM, Zhu H, Shi SY, Iqbal J, Gogas BD, Xu B, Chen SL. Comparison of intravascular ultrasound guided versus angiography guided drug eluting stent implantation: a systematic review and meta-analysis.BMC Cardiovasc Disord. 2015; 15:153. doi: 10.1186/s12872-015- 0144-8.*
13. *Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN, Lange RA, Mauri L, Mehran R, Moussa ID, Mukherjee D, Nallamothu BK, Ting HH. 2011 ACCF/AHA/SCAI Guideline for percutaneous coronary intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions.Circulation. 2011; 124:2574–2609. doi: 10.1161/CIR.0b013e31823a5596.*
14. *Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI).Eur Heart J. 2014; 35:2541–2619. doi: 10.1093/eurheartj/ehu278.*

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