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Sri Lankan Journal of Cardiology

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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.

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Heart Failure with Preserved Ejection Fraction - HFpEF

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Definition of heart failure

> The inability to provide adequate cardiac output to the body at rest or with exertion or to do so only in the setting of elevated cardiac filling pressure.
> *E.Braunwald*
> *(Modified by B. Borlaug and M. Redfield)*

Clinically: A syndrome characterized by breathlessness, fatigue, and oedema caused by an abnormality of the heart.

Physiologically: An inadequate cardiac output to meet metabolic demands or adequate cardiac output secondary to compensatory neurohormonal activation – generally manifest as increased left ventricular filling pressure.

Note: None of the definitions of heart failure incorporated the Ejection Fraction (EF).

The terms "diastolic" and "systolic" heart failure was abandoned for the following reasons:

Diastolic dysfunction occurs in
- healthy elderly people
- heart failure with systolic dysfunction and reduced EF

Systolic strain used to measure reduced systolic function may occur in patients with preserved or normal EF.

Definition of HFpEF

The following criteria are included in the definition

1. Symptoms and signs of heart failure
2. Preserved Ejection Fraction (EF ≥ 50%)
3. Elevated natriuretic peptide levels (B-type) >35pg/mL and/or N-terminal pro-BNP>125pg/mL in stable untreated patients
4. Structural heart disease (LVH and /or LA enlargement) or diastolic dysfunction

HFmrEF (heart failure with mid-range EF) "The Middle Child" – Heart failure meeting the above 4 criteria and with an EF of 40-49%.

History of HFpEF

The key papers were,

1. Congestive Heart Failure with Normal Systolic function – 1984 The American Journal of Cardiology – Anne Hamilton Dougherty et al

2. Intact Systolic Left Ventricular Function in Clinical Congestive Heart Failure – 1985 The American Journal of Cardiology – Robert Souffer, MD et al

Epidemiology and burden of HFpEF

HFpEF is a global pandemic affecting half the heart failure population. While the prevalence of HFrEF appears constant, that of HFpEF is increasing over time. Patients with HFpEF are more likely to be older and female and have a greater prevalence of cardiovascular risk factors (i.e.obesity, hypertension and diabetes), other cardiovascular co-morbidities (i.e. atrial fibrillation and valvular disease) and non-cardiovascular co-morbidities (i.e. anaemia, chronic pulmonary disease, chronic kidney disease, hypothyroidism, cancer and peptic ulcer disease) but a lower prevalence of ischaemic heart disease.

Quality of life was similarly impaired in both the HFpEF and HFrEF although proportion of patients with worse NYHA (III-IV) was significantly higher in HFrEF.

HFmrEF was comparable to HFpEF in most aspects except for a high prevalence of coronary artery disease.

	HFpEF	HFrEF
Non CV death	49	36
Coronary artery deaths	29	43
Other CV deaths	22	21

Review

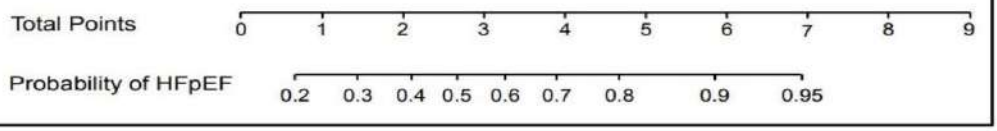
The two faces of Heart Failure	
HFrEF	**HFpEF**
• Patients present with signs and Symptoms consistent with heart failure and imaging reveals systolic dysfunction • Diagnosis is both sign/symptom based with supportive mechanistic data • Large body of evidence based on clinical trials • No evidence-based treatment	• Diagnosis has been more complex and the subject of debate • Relied on signs and symptoms without mechanistic support • Large differential diagnosis for primary symptom • No evidenced –based treatment

Diagnostic challenges of HFpEF

- Symptoms are often revealed with exercise
- Patients often initially present to GP's, pulmonologists and geriatricians
- Patients are often elderly with co-morbidities that may mask symptoms

H_2FPEF Scoring

	Clinical Variable	Values	Points
H_2	Heavy	Body mass index > 30 kg/m²	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial Fibrillation	Paroxysmal or Persistent	3
P	Pulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	Elder	Age > 60 years	1
F	Filling Pressure	Doppler Echocardiographic E/e' > 9	1
	H_2FPEF score		Sum (0-9)



Some differences between HFpEF scores

- Counting the "points" in the scoring process
  - *US score* – includes clinical characteristics
  - *European score* – based on echocardiogram and NT-pro BNP
- Presence of Atrial Fibrillation (AF)
  - *US score* – increases likelihood of HFpEF
  - *European score* – NT-proBNP must first be evaluated before determining if HFpEF is likely in the presence of AF

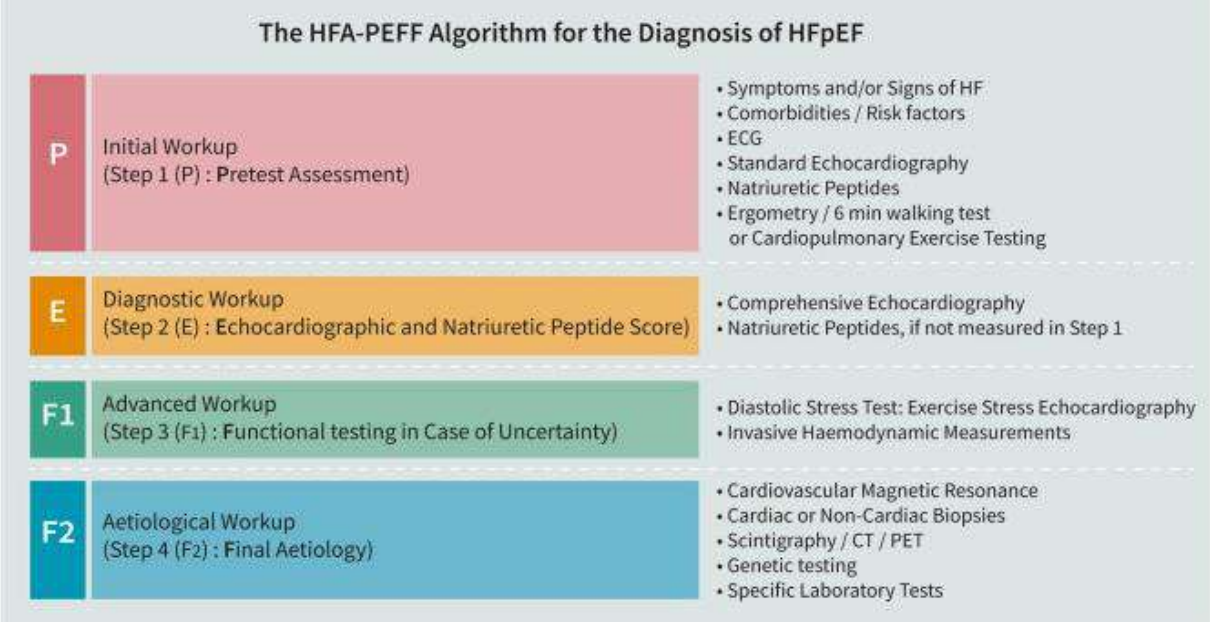
Scoring is a combination of domains

- ≥ 5 points – HFpEF
- < 1 point – unlikely
- 40% - gray zone

Assessment of BNP in AF and HFpEF Trials

- Cross-sectionally, 40% of patients with HFpEF have AF
- If one considers the whole life span of an HFpEF, approximately 67% of the patients will have AF
- Value for BNP cutoffs are usually higher in HFpEF trials including patients with AF
- Goal is to secure that the level that has been set is high enough to identify the patient with HFpEF in the presence of AF
- In several trials, the value for BNP has been doubled for patients with AF

Diagnosing HFpEF – a Stepwise approach



Diagnostic Workup – Step 2 (E step) Echocardiographic and natriuretic peptide score:

- NT-pro BNP – if not done in Step I – cut offs differ for AF
- Elevated natriuretic peptides support but normal levels do not exclude a diagnosis of HFpEF
- Comprehensive Echocardiography
  - *Function domain*
    e'(mitral annular early diastolic velocity) or E/e' (Estimated LV filling pressure – most feasible as well as reproducible)
  - *Structural domain*
    LA volume index
    LV mass index
    LV relative wall thickness
    Tricuspid regurgitation velocity
    LV global longitudinal systolic strain (GLS)

Natriuretic peptides

Major criterion: NT-proBNP >220pg/mL or BNP >80pg/mL [in sinus rhythm]

Major criterion: NT-proBNP >660pg/mL or BNP >240pg/mL [in atrial fibrillation]

Minor criterion: NT-proBNP 125-220pg/mL or BNP 35-80pg/mL [in sinus rhythm]

Minor criterion: NT-proBNP 375-660pg/mL or BNP 105-240pg/mL[in atrial fibrillation]

In Step 1(P) a single low cut-point was recommended to have a sensitive marker for cardiac abnormalities. In Step 2(E) a higher cut-off value is recommended to increase specificity. Cut-offs are also stratified in the presence of SR or AF.

Septal and lateral mitral annular peak early diastolic velocity (e')

<75 years - Major criterion septal e'<7cm/s or lateral e'<10cm/s

>75 years - Major criterion septal e'<5cm/s or lateral e'<7 cm/s

[e' – main determinant is LV relaxation. This reflects LV lengthening and is influenced by preload. LV Longitudinal e' declines with age.

Average septal-lateral E/e' ratio

Major criterion: average septal-lateral E/e' ratio ≥15

Minor criterion: average septal-lateral E/e' ratio 9-14

E/e'ratio – recorded by pulsed Doppler reflects the mPCWP.

E/e' index correlates with LV stiffness and fibrosis and is less age dependent than e'

It also has diagnostic value during exercise. It's influenced by severity of LVH not volume.

Tricuspid regurgitation peak velocity of Pulmonary arterial systolic pressure

Major criterion: TR peak velocity >2.8m/s

Major criterion: PASP >35mmHg

Elevated PASP and reduced RV function are important predictors of mortality in HFpEF.

A leftward shift of the ventricular septum impairs LV filling. TR peak velocity >2.8m/s is an indirect marker of LV diastolic dysfunction.

Left Ventricular Global Longitudinal Systolic Strain (GLS)

Minor criterion: GLS < 16%

LV peak GLS is measured using speckle-tracking echocardiography as the average of systolic strain obtained from all LV segments. Reduced GLS and LV early diastolic strain rate have both been identified in HFpEF. Impaired GLS predict – heart failure hospitalization and CV death. It correlates with invasive measurements of LV stiffness and with NP levels.

Left atrial volume index

Major criterion >34mL/m^2 [in sinus rhythm] – independently predicts death, heart failure, AF and ischaemic stroke

Major criterion >40mL/m^2 [in atrial fibrillation]

Minor criterion 29-34mL/m^2 [in sinus rhythm]

Minor criterion 34-40mL/m^2 [in atrial fibrillation]

Left atrial volume index (LAVI) – maximal volume of LA indexed to the body surface area (BSA) is an indirect correlate of LV filling pressures and an accurate marker of chronic LA remodeling. It correlates with other echocardiographic indices of LV diastolic function.

Left ventricular mass index and relative wall thickness

Major criterion: LVMI ≥149g/m2 in men or ≥122g/m2 in women and RWT>0.42

Minor criterion: LVMI≥115g/m2 in men or ≥95g/m2 in women or RWT>0.42 or LV end diastolic wall thickness ≥12mm

Left ventricular geometry is often classified using relative wall thickness (RWT) [LVPWx2/LVIDD] and using LVMI normalized to BSA or height.

4 patterns described are:-

(i) Normal
(ii) Concentric remodeling
(iii) Concentric hypertrophy
(iv) Eccentric hypertrophy.

In HFpEF both concentric remodeling and concentric LVH can be observed.

	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg)	LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 #	NT-proBNP > 220 pg/ml or BNP > 80 pg/ml	NT-proBNP > 660 pg/ml or BNP > 240 pg/ml
Minor	Average E/e' 9 -14 or GLS < 16 %	LAVI 29-34 ml/m2 or LVMI > 115/95 g/m2 (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm	NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml	NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml

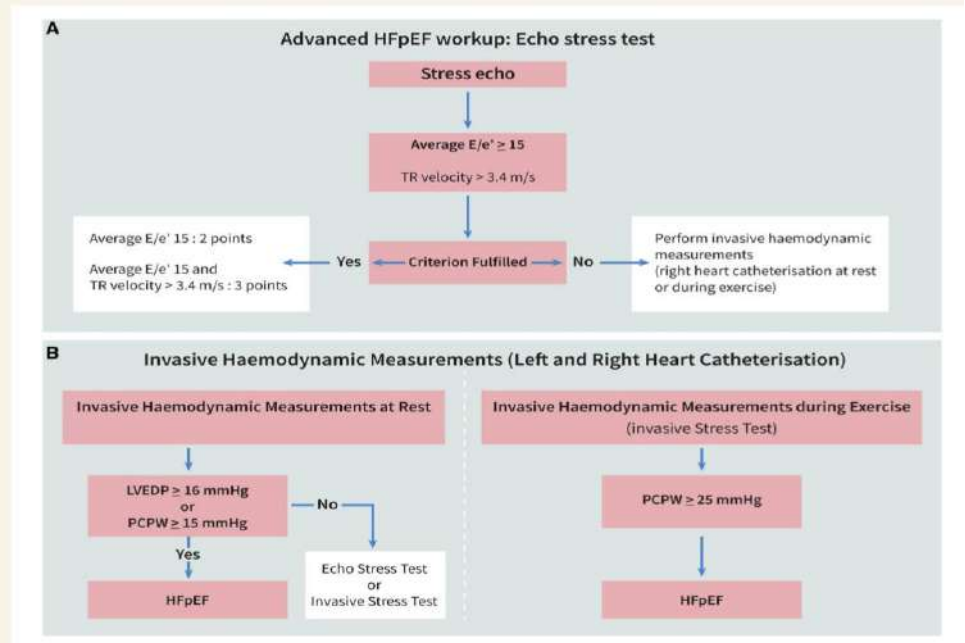
Major Criteria: 2 points	≥ 5 points: HFpEF
Minor Criteria: 1 point	2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements

Step 3 (F step) – Advanced Workup

Functional testing in Case of Uncertainty:

Symptoms compatible with HF can be confirmed to originate from the heart if haemodynamic abnormalities such as reduced stroke volume, reduced CO and elevated LV filling pressures are detected either at rest or during exercise.

In a typical elderly patient with multiple comorbidities, the presence or absence of isolated cardiac structural and/or functional abnormalities at rest does not always establish or exclude the diagnosis of HFpEF.



Step 3 (F): Functional tests in cases of diagnostic uncertainty. (A, upper panel) It shows the diastolic stress test workup with exercise echocardiography. If key haemodynamic abnormalities are identified, a definite heart failure with preserved ejection fraction diagnosis can be made. (B, lower panel) It shows the invasive haemodynamic measurements at rest (left) or during exercise (right) that may complement stress echocardiography and are recommended in cases with remaining diagnostic uncertainty.

Exercise stress echocardiography: the diastolic stress test

HFpEF shows the following during exercise –

(i) impaired early diastolic relaxation

(ii) inadequate increases in SV and CO on exercise

(iii) increased LV filling pressure

(iv) increased PASP

(v) impaired RV reserve

Invasive haemodynamic tests at rest and with exercise

Right heart catheterization (using a Swan-Ganz catheter) - if mPCWP is elevated in the presence of normal LV end diastolic volume index then usually LV end-diastolic distensibility is reduced. Resting mPCWP ≥ 15 confirms HFpEF.

Normal LVEDP or mPCWP levels at rest do not exclude HFpEF. In compensated HFpEF haemodynamic alterations may be detected only during exercise or when the patient deteriorates.

High resting mPCWP and a pathological increase in mPCWP during exercise predict poor outcomes from HFpEF. Normal (<12mmHg) mPCWP at rest but a steep increase (≥25mmHg) during exercise have a 2 fold increase in mortality.

Exercise mPCWP reclassifies patients with a normal mPCWP and stratifies risk.

mPCWP at rest	mPCWP during exercise	10 year mortality
<12mmHg	<25mmHg	6.6%
<12mmHg	High >25mmHg	28.2%
High ≥ 15mmHg	High >25mmHg	35.2%

If other investigations have been inconclusive, invasive measurement of mPCWP or LVEDP is considered as the clinical reference investigation.

This Step 4 (F2 step) – Aetiologic workup Final Aetiology

The aetiology of HFpEF is almost certainly heterogeneous.

Identification of specific HFpEF aetiologies will advance the field of targeted therapies.

Specific heart muscle diseases that may present with the HFpEF phenotype include

- Hypertrophic cardiomyopathies
- Myocarditis and chronic Inflammatory cardiomyopathies
- Autoimmune diseases
- Non infiltrative and infiltrative cardiomyopathies
- Idiopathic or acquired endomyocardial fibrosis
- Storage disease
- Genetic disorders including early stages of cardiomyopathies associated with muscular dystrophy
- Rare causes – toxicity from drugs and heavy metals, radiation and metabolic causes related to hormonal or nutritional disease.

The trigger may occur long before the onset of symptoms.
Eg. Radiation-induced HFpEF develops after 10-15 years.

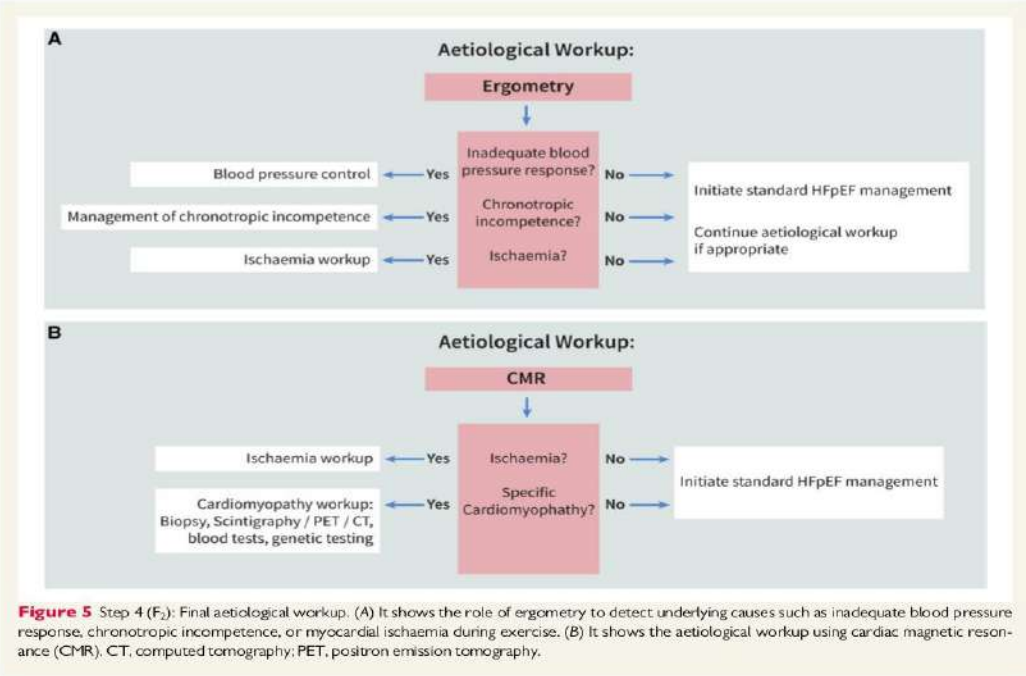


Figure 5 Step 4 (F_2): Final aetiological workup. (*A*) It shows the role of ergometry to detect underlying causes such as inadequate blood pressure response, chronotropic incompetence, or myocardial ischaemia during exercise. (*B*) It shows the aetiological workup using cardiac magnetic resonance (CMR). CT, computed tomography; PET, positron emission tomography.

Aetiological workup (Fig5) may include a *standard exercise test* that may identify myocardial ischaemia, abnormal blood pressure response to exercise, chronotrophic incompetence or supraventricular or ventricular arrhythmias.

Cardiac Magnetic Resonance (CMR) is a more sophisticated tool for an aetiological work up and is most accurate for determining,

- LA and LV volumes and mass
- Detects scar and myocardial ischaemia due to epicardial coronary disease of microvascular dysfunction
- Diffuse sub endocardial defects through stress perfusion imaging
- Regional and diffuse myocardial oedema (T2-imaging) and infiltration or fibrosis are quantified using LGE (late gadolinium enhancement)

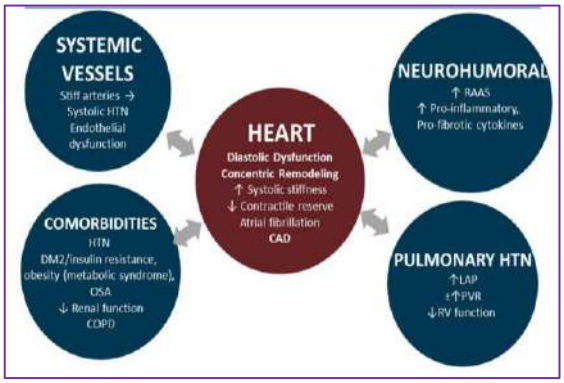
Right or Left ventricular myocardial biopsy

Tc-DPD scintigraphy to identify cardiac amyloidosis

PET-CT and specific *genetic laboratory tests* should be considered in selected cases

Note: Aetiologies that may mimic HFpEF eg. Constrictive pericarditis, primary valvular disease and high output failure should not be considered part of HFpEF.

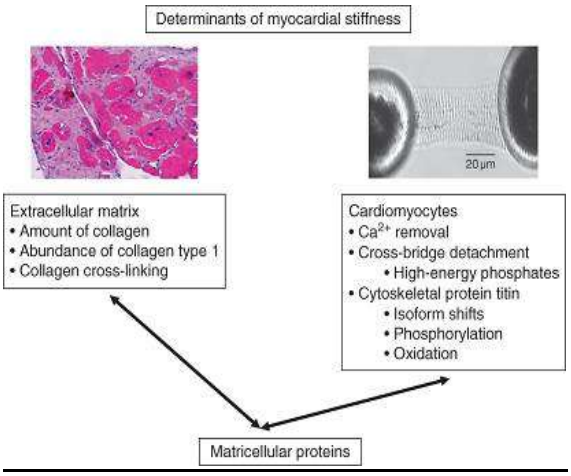
Pathophysiology of HFpEF



Diastolic left ventricular dysfunction

In the absence of endocardial or pericardial disease, diastolic LV dysfunction is regulated by two compartments within the myocardium – extracellular matrix and the cardiomyocytes. Matricellular proteins transmit stiffness change between the compartments.

Review



Delayed calcium uptake by the myocyte sarcoplasmic reticulum and delayed calcium efflux from the myocyte leads to altered relaxation and increased stiffness of the ventricle which in turn leads to impaired diastolic filling of the ventricle (LV).

Right ventricular (RV) sub endocardial systolic and diastolic dysfunction (detected by echocardiographic strain rate imaging) are common in patients with HFpEF. This is associated with the same fibrotic processes affecting the subendocardial layer of the LV.

An increase in LV chamber stiffness occurs secondary to any one, or any combination of the following mechanisms

- Rise in filling pressure
- Shift to a steeper ventricular pressure-volume curve
- Decrease in ventricular distensibility

Patients with diabetes and hypertension are at an increased risk for myocardial fibrosis.

Titin is a giant elastic protein expressed in cardiomyocytes in 2 main isoforms – stiffer spring (N2B) and more compliant spring (N2BA). Abnormalities in titin protein leads to increased passive stiffness of the myocardium.

Left ventricular relaxation is dependent on both cross-bridge detachment and sarcoplasmic reticular Ca++ reuptake. Nitric oxide (NO) signaling is involved as well. Cyclic guanosine monophosphate (cGMP) facilitates cross-bridge detachment. Lower cGMP is postulated to lead to impaired LV relaxation.

However LV diastolic dysfunction is not the sole contributor to the disease pathophysiology in HFpEF. Other mechanisms identified are,

- Resting and exercise-exacerbated systolic dysfunction
- Impaired ventricular-vascular coupling
- Abnormal exercise-induced and flow mediated vasodilation
- Chronotropic incompetence
- Pulmonary arterial hypertension

Systolic dysfunction

Ejection fraction is preserved in HFpEF. EF is more accurately regarded as a measure of ventricular-arterial coupling than contractility alone. Regional measures of systolic function assessed by Tissue Doppler imaging are impaired in HFpEF despite a normal EF. Longitudinal and radial systolic function has been shown to be depressed. A large population based study had shown that at both chamber levels myocardial contractility was subtly but significantly depressed in HFpEF compared with hypertensive and healthy controls. Importantly the extent of dysfunction was associated with increased mortality.

Ventricular-arterial coupling and vascular dysfunction

- Ventricular and vascular stiffening increase with ageing, hypertension and diabetes and is abnormally elevated in patients with HFpEF. Reduced aortic distensibility is strongly associated with impaired exercise capacity.

- Both arterial elastance (Ea) and end-systolic elastance (Ees) are elevated in tandem in HFpEF, explaining the labile blood pressure swings commonly seen in HFpEF. Any alteration in preload or afterload amplifies blood pressure changes creating a “high gain” system leading to greater blood pressure lability.

- Abnormal v-a coupling during exercise in HFpEF causes blunted increases in contractility and impaired reductions in arterial afterload both leading to exertional intolerance. Attenuation of systemic vasorelaxation with exercise promotes impaired delivery of blood flow to skeletal muscle. Impaired flow mediated vasodilatation (a biomarker of endothelial function) leads to effort intolerance during low-level exercise in HFpEF.

- Pulmonary hypertension is frequently observed. Among elderly patients with normal EF and high PAP, HFpEF may be the most common aetiology. PAP increases with ageing and correlates with systemic vascular stiffening. High pulmonary vascular resistance (PVR) develops in response to elevated left heart pressures and predicts increased mortality in HFpEF.

Chronotropic incompetence and cardio - vascular reserve dysfunction

During physical exertion, cardiac output increases due to enhancement of (i) venous return (ii) contractility (iii) heart rate and (iv) peripheral vasodilation.

Abnormalities in all these components have been seen in HFpEF.

Diastolic reserve with exercise: Normal diastolic reserve ensures that with exercise the ventricle fills to a larger preload volume within a shorter time with no increase in filling pressures. In HFpEF both diastolic reserve and diastolic function are impaired. Thus, despite marked elevation in filling pressures due to increased chamber stiffness and inadequate enhancement of early relaxation, there is a blunted increase in preload volume with exertion.

Systolic reserve with exercise; Impaired due to blunted increase in (i) EF (ii) contractility (iii) longitudinal systolic shortening velocities during exercise. Stroke volume responses during exercise is limited by (i) mild deficits in resting systolic function (ii) inability to reduce end-systolic volume and (iii) reduced increase in end diastolic volume.

The causes of systolic and diastolic reserve dysfunction in HFpEF remain unclear.

Chronotropic reserve: Depressed in HFpEF independent of rate slowing medication use.

Increase in plasma catecholamines with exercise is similar to healthy controls. Reduced baroceptor sensitivity and impaired heart rate recovery due to autonomic dysfunction may contribute to chronotropic incompetence.

Treatment of HFpEF

Clinical trials in HFpEF have produced largely neutral results to date and the management is mostly directed toward associated conditions e.g. hypertension and symptoms e.g. oedema.

Hypertension (systolic and diastolic) should be managed in accordance with published clinical guidelines.

Diuretic therapy should be used to relieve symptoms due to volume overload.

Results of clinical trials have demonstrated that therapies effective in HFrEF i.e. neurohumoral antagonists such as beta blockers, angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) as well as cardiac resynchronization (CRT) have failed to decrease morbidity and mortality in HFpEF. All the therapies mentioned also reverse the LV dilatation in HFrEF. As patients with HFpEF either have no or minimal LV dilatation it is not surprising the medications do not have a significant impact.

Management of associated conditions

Hypertension: The choice of a specific antihypertensive must be individualized in the presence of coexisting diseases e.g. diabetes and COPD. There may be class specific effects – in ancillary analysis of data from ALLHAT trial chlorthalidone reduced the incidence of new-onset HFpEF compared with amlodipine, lisinopril and doxazosin whereas both lisinopril and chlorthalidone were effective in reducing incidence of HFrEF. However these studies dealt with prevention rather than treatment. At present there is no compelling evidence that hypertension control improves signs or symptoms of heart failure in patients with HFpEF.

Atrial fibrillation: AF is identified at some point of time in two-thirds of patients with HFpEF and is associated with increased morbidity and mortality. AF is managed according to published clinical practice guidelines.

LV filling in HFpEF occurs mainly in late diastole and is more dependent on atrial contraction than in normal hearts. Thus restoration and maintenance of sinus rhythm are preferred when AF occurs in patients with HFpEF. Beta blockers and calcium channel blockers are the usual first-line agents (digoxin is very often used in patients with HFrEF). It is important to measure heart rate during moderate exercise and not to base heart rate control solely on values obtained in the resting state.

Anticoagulation to prevent systemic embolism is an important component in the management of AF regardless of whether rhythm control or rate control is chosen.

Myocardial ischaemia: In HFpEF can result from (i) epicardial CAD, (ii) high wall stress or (iii) microvascular dysfunction. Presence of CAD was an independent predictor of increased mortality along with greater deterioration of LV systolic function over time.

Patients with symptoms and signs of ischaemia are treated with standard therapy including beta blockers and calcium channel blockers. Nitrates by reducing preload can lead to hypotension in some patients. Patients with drug resistant ischaemic HFpEF may require PCI or CABG. Revascularization was associated with improved survival and less deterioration of EF. However prospective trial data are not available regarding the effects of revascularization in HFpEF.

Hyperlipidaemia: Antilipaemic therapy is recommended for primary and secondary prevention of cardiovascular disease. No randomized trials have been done to demonstrate that statins benefit patients with HFpEF. Statins are recommended in patients with HFpEF who have an indication for statin therapy.

Conditions to avoid: Management includes avoidance and treatment of common precipitants of heart failure exacerbation such as (i) tachycardia (ii) abrupt severe elevations in systemic blood pressure (iii) ischaemia and (iv) AF.

Caveats include avoidance of excessive preload reduction – a patient with LV diastolic dysfunction with a small, stiff LV chamber may be particularly susceptible to excessive preload reduction leading to under filling of the LV, a fall in cardiac output and hypotension. Thus diuretics or venodilators such as nitrates and dihydropyridine calcium channel blockers must be administered with caution. Over diuresis can result in prerenal azotemia.

Cardiac rehabilitation: During exercise in healthy individuals, diastolic function is enhanced so that LV input remains precisely matched to LV output. This is achieved in the normal LV by a rapid and marked decrease in intraventricular pressure during early diastole creating a greater LV suction effect with no increase in LA pressure. This mechanism is lost in patients with diastolic dysfunction which makes dyspnea with exertion their most common complaint. Supervised endurance /resistance exercise training is the only intervention shown to improve exercise capacity and quality of life in in HFpEF. Exercise capacity measured by peak VO2 was significantly increased by diet and exercise. HF specific quality of life (QOL) measured by KCCQ (Kansas City Cardiomyopathy Questionnaire) was increased mainly by diet.

Implantable haemodynamic monitoring: The wireless CardioMEMS pulmonary artery monitoring device was found to reduce HF-related hospitalizations at 6 months in the CHAMPION randomized single-blind trial in both HFpEF and HFrEF. However the efficacy of this device has not been established.

Investigational device-based therapy: An interatrial shunt device – an investigational device that creates an interatrial septostomy to decompress the LA pressure overload by causing a left to right shunt.

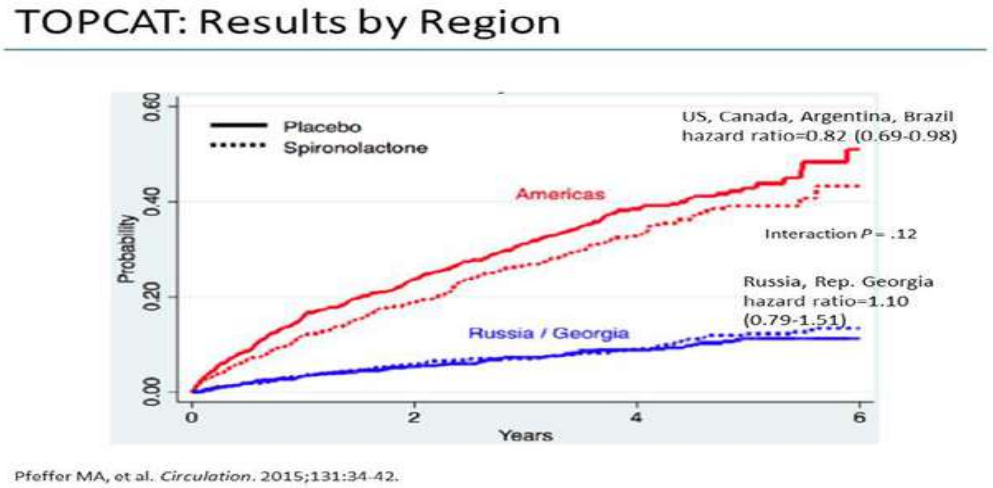
Specific medications:

Mineralocorticoid receptor antagonists (MRA): For patients with clear evidence of HFpEF and current or recent (within 60 days) elevated BNP ≥ 100pg/mL or N-T proBNP ≥ 360pg/mL who can be carefully monitored for changes in serum potassium and renal function (eGFR ≥ 30 mL/min/1.73m^2) treatment with MRA is recommended.

Evidence – TOPCAT trial where patients with symptomatic HF and LVEF ≥45% were randomized to receive either spironolactone or placebo. The primary outcome wasn't statistically significant apart from hospitalization being less frequent with spironolactone.

Subgroup analysis showed a significant reduction in the primary outcome with spironolactone among patients enrolled according to BNP but not among those enrolled on the basis of hospitalization for HF in the past year.

Subgroup analysis between regions showed a lower rate of primary outcome with spironolactone in the Americas (27.3 vs 31.8%) but not in those enrolled in Russia and Georgia (9.3 vs 8.4%). It was later found that many Russian participants did not take the study medication.



Pfeffer MA, et al. *Circulation*. 2015;131:34-42.

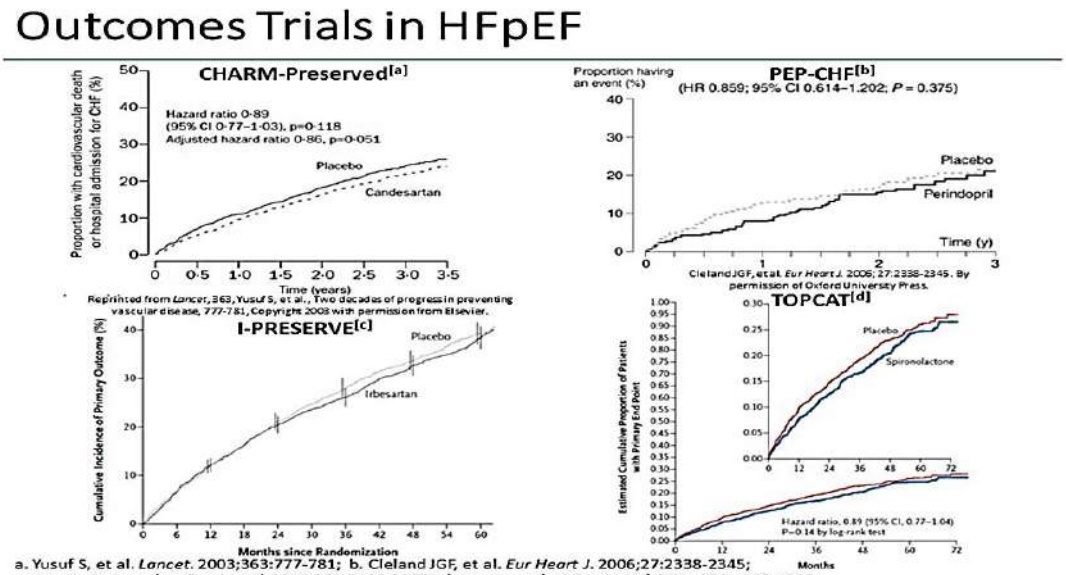
Other outcome trials;

1. PEP-CHF – 850 patients with diastolic dysfunction, age > 70 years and hypertension were randomized to an ACE inhibitor (perindopril) or placebo. There was no impact on the primary endpoint of all-cause mortality or unexpected hospitalization for HF.

2. CHARM-Preserved – 3023 patients with symptomatic HF and LVEF > 40% and controlled blood pressure were randomly assigned to either candasarten 25mg or placebo (mean EF – 54%).

CHARM-Preserved included more patients with mildly depressed EF (40-49%).

3. I-PRESERVE trial – 4126 patients with symptomatic HF, controlled blood pressure and LVEF ≥ 45% were randomly assigned to either irbesarten 300mg or placebo. Mean EF-59%. Mean follow up of 49.5 months – no significant difference in the primary endpoint of death from any cause or hospitalization for a cardiovascular cause.



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Review

Ineffective drugs:

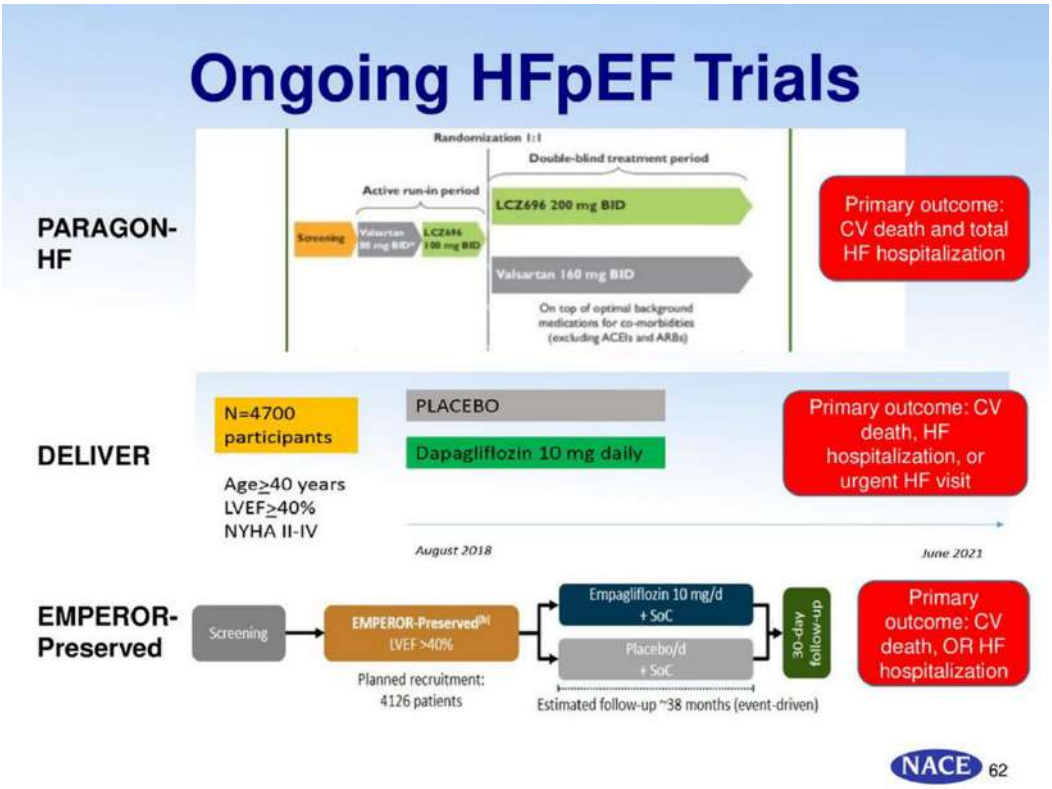
Nitrates: The NEAT-HFpEF (Nitrate's Effect on Activity Tolerance in Heart Failure with Preserved Ejection Fraction) trial with 110 patients randomly assigned to a 4 week regiment of escalating doses of isosorbide mononitrate (ISMN) or placebo, showed decreased activity level with increased doses of ISMN. There was no significant differences in six-minute walk distance, QOL scores or NT-proBNP levels between the treatment groups.

Sodium nitrite: A nitric oxide donor is currently under investigation

Phosphodiesterase-5-inhibitors: RELAX – a multicenter randomized double-blind placebo controlled study of sildenafil (titrated from 20mg to 60mg three times per day). 216 patients with HFpEF with LVEF>50% and elevated BNP or invasively measured PCWP were enrolled. At 24 weeks sildenafil had no effect on exercise capacity or clinical status. Another trial restricting enrollment to patient with HFpEF with pulmonary hypertension also showed no benefit.

Digoxin: Is not recommended except for atrial fibrillation with poorly controlled ventricular rate. The DIG ancillary trial evaluated the role of digoxin in patients with HF with LVEF >45%. At mean follow up digoxin had no effect on all-cause or cause specific mortality or cardiovascular hospitalization.

Vericiguat: A novel oral soluble guanylate cyclase stimulator in SOCRATES-Preserved showed no reduction in the primary endpoints of log-NT-proBNP and LA volume in HFpEF. In contrast the VICTORIA placebo controlled study presented at ACC 2020 for HFrEF over and above the best evidence based treatment showed the primary endpoint of death and heart failure hospitalization to be significantly reduced.



Angiotensin receptor-neprilysin inhibitor: In the PARAGON-HF trial, the effect of the angiotensin receptor-neprilysin inhibitor sacubitril/valsartan was evaluated compared with valsartan alone. 2730 patients ≥50 years, EF ≥ 45%, elevated natriuretic peptides and structural heart disease. Mean follow up was 27 months. In the main trial the primary endpoint of total HF hospitalizations and CV death just missed statistical significance.

The study investigated the relationship between NT-proBNP and outcomes in HFpEF patients and the effect of sacubitril/valsartan on NT-proBNP after 48 weeks.

Conclusion: This sub analysis of the PARAGON-HF trial showed that use of sacubtril/valsartan resulted in a 19% reduction of NT-proBNP levels compared to valsartan ($p<0.001$). Furthermore, baseline NT-proBNP levels were associated with outcome of HF hospitalization CV death in HFpEF patients.

SGLT2 Inhibitors: Sodium-glucose co-transporter 2 inhibitors exert a broad range of biological effects (including actions to inhibit cardiac inflammation and fibrosis, antagonize sodium retention and improve glomerular function) that can ameliorate the pathophysiological derangements of HFpEF.

They have been found in large-scale trials to reduce the risk for serious heart failure events in patients with type 2 diabetes, many of whom were retrospectively identified as having HFpEF. The aims of EMPEROR-Preserved and DELIVER trials will assess a wide range of biomarkers that reflect important pathophysiological mechanisms that may drive the evolution of HFpEF – a disorder for which there are currently few therapeutic options.

Conclusion

Heart failure with preserved ejection function (HFpEF) is a heterogenous disorder associated with co-morbidities and accounts for half of the heart failure population. It is associated with an alarmingly high morbidity and mortality.

The cardiac phenotype is broader than was previously thought. Diastolic dysfunction cannot entirely account for the disorder and abnormalities of systole are becoming more recognized.

Unfortunately, the majority of multi-center randomized clinical trials have failed to identify treatments with proven benefit in quality of life or outcomes, especially in the outpatient setting but there are promising potential therapies being tested.

Early diagnosis of heart failure is important to ensure prompt start of treatment, thus a higher index of suspicion is warranted.

There are still many gaps in understanding about the aetiology, pathophysiology and treatment of HFpEF with a clear need to improve both diagnosis and treatment—further research is a key component to improving the well-being and longevity of such patients.

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Research

Utilization of Clinical Criteria and Laboratory Investigations to Identify High Risk Children for Coronary Involvement in Kawasaki Disease Presenting to Lady Ridgeway Hospital, Colombo, Sri Lanka

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Abstract

Kawasaki disease is an acute medium and small vessel vasculitis, which has a predilection for coronary arteries. Coronary artery involvement can vary from mild ectasia occurring in nearly 40% to giant coronary artery aneurysms [(1)]. Hence, we sought to determine a correlation between selected clinical and laboratory criteria in order to predict high risk for coronary involvement in children with Kawasaki disease in order to optimize the initial management and follow up. Serial analysis of clinical, biochemical and echocardiographic parameters of 101 patients with diagnosed Kawasaki disease was carried out within the first 10 days of the illness and follow up was done paying special attention to coronary artery dilatation according to coronary artery standard deviation charts and visual assessment up to 12 weeks after the onset of the disease. This research was done for a 15 month period at the National Paediatric Cardiology unit, Colombo, Sri Lanka. Maximum recorded internal diameter of the coronaries was considered for the analysis during the follow up. Thereafter, analysis was also performed to identify coronary artery risk predictors with Pearson chi square test and odds ratio. Mean age of the patients were 44 months (±36.8 months), 62 (61.4%) were males. Out of the 101 patients, 42 (41.6%) had coronary involvement (Coronary artery diameter >2 SD adjusted to the body surface area/ visual dilatation to Coronary artery aneurysm formation. All children were treated with at least a single dose of intravenous immunoglobulin during the acute stage. Age between 7 months to 60 months, fever more than 102^0F, CRP more than 100 mg/L and increased coronary echogenicity within first 10 days of the illness showed significant association with coronary involvement. However, duration of fever, platelet count, AST (Aspartate aminotransferase), ALT (Alanine aminotransferase), Serum bilirubin and Serum sodium or ESR did not demonstrate statistically significant association with coronary dilatation or aneurysm formation in the Sri Lankan sample, although utilized in standard risk stratification scores. Also, diagnosis of complete Kawasaki disease, hypoalbuminemia and hyper echogenic coronaries were found to be important predictors of coronary aneurysms. In the Sri Lankan centre, Age between 7 months to 60 months, fever more than 102^0 F, CRP more than 100mg/dl, increased coronary echogenicity, hypoalbuminemia and diagnosis of complete Kawasaki disease during early stage of Kawasaki disease demonstrated high predictive utility for the development of coronary pathology.

Keywords: Kawasaki disease, Coronary artery involvement, Coronary aneurysms, Risk Prediction

Introduction

Kawasaki disease (KD) is a medium and small vessel vasculitis mainly seen in young children. There is no known aetiology for the disease. It is mainly recognized by clinical features including fever, cervical lymphadenopathy, erythema of the lips and oral mucosa, bilateral non-exudative conjunctivitis, rash and changes in the extremities. Hence Kawasaki disease is a clinical diagnosis after excluding other diseases, mainly sepsis [(2)].

The disease can be seen in a worldwide distribution including all races with Asians at highest risk [(3)]. Boys are affected more than girls by 1.5 - 1.7: 1; and about 76% of children are below the age of 5 years [(4, 5)].

The major complication of Kawasaki disease is coronary arteritis leading to long term morbidity and mortality [(6)].

During the acute phase, pancarditis including coronary arteritis can be seen. Coronary artery aneurysms or ectasia develop in nearly 15% to 25% of children with Kawasaki disease, who had not received timely treatment [(6)]. Some studies indicate that coronary involvement might be as common as 40% [(1)].

However, with intra venous immuno globulin (IVIG) therapy, persistent coronary artery aneurysms are considerably less common but still occur in 4% to 6% of patients, with 1% developing giant coronary artery aneurysms of absolute CA dimension of ≥8 mm [(7)] (1984 Japanese Ministry of Health criteria).

The difference may be due to the criteria utilized to identify coronary artery involvement. Main criteria utilized are Japanese Health ministry criteria and Z score criteria.

The Japanese Ministry of Health categorizes abnormal coronaries if the internal lumen diameter is more than 3 mm in children less than 5 years old or more than 4 mm in children more than 5 years old, or if the internal diameter of a segment measures more than 1.5 times that of an adjacent segment, or if the coronary lumen is irregular [8].

However, adjusted coronary artery measurements to body surface area in the new guidelines is more accurate than population based coronary dimensions which were used earlier [9,10]. Manlhiot *et al*, demonstrated that incidence of coronary abnormalities is greater when calculated using Z score criteria [11].

Cardiac imaging plays a pivotal role in the evaluation of all patients with prolonged fever with clinical features suggestive of Kawasaki disease. Echocardiography is the ideal imaging modality, because of its non-invasive nature and high sensitivity and specificity for the detection of pathological changes in proximal LMCA and RCA [6]. Early echocardiographic features of Kawasaki disease are, perivascular brightness, ectasia, and lack of tapering of the coronary arteries representing coronary arteritis. Other described echocardiographic findings during the acute stage of the illness described in literature are reduced left ventricular (LV) function, mild valvular regurgitation (most commonly mitral regurgitation) and pericardial effusion [6] .Hence, echocardiography is considered the gold standard for imaging in KD.

Children with large or giant coronary aneurysms are high risk candidates for coronary artery thrombosis or stenosis due to calcification leading to myocardial infarction [12].

Therefore, it is important to identify patients who are more at risk to develop coronary involvement during the initial stage of the illness with the view of rendering intense primary treatment along with close cardiology follow up. Recent studies have shown that repeat echocardiographic evaluation at 1 year is negative when the initial echocardiogram at 4-8 weeks was normal [13,14]. Therefore the follow up echocardiographic evaluation was scheduled at 12 weeks of illness, during this study.

High risk children are identified using scoring systems which were developed using clinical, laboratory and imaging criteria. Many studies proved that the duration of fever, was a powerful predictor of involvement of the coronary arteries, indicating the on-going vasculitis [15,16]. Harada *et al*, [17] developed a risk score to predict coronary involvement in children with Kawasaki disease. At some centers in Japan, the Harada score is used to decide on IVIG treatment. Specific treatment is given to children who fulfill 4 of the following criteria, assessed within 9 days of onset of illness: (1) white blood cell count >12000 /mm^3 (2) platelet count <350000 /mm^3 (3) CRP >3; (4) haematocrit <35%; (5) albumin <3.5 g/dL (6) age ≤12 months and (7) male sex. However patients with incomplete criteria are also assessed daily in view of taking the important management decision of immunoglobulin administration.

A retrospective study involving 105 children showed sensitivity of 90% and positive predictive value of 98% in identifying high risk patients to develop coronary aneurysms by using Harada score in US population which is on par with studies done in Japan.[18]

Other risk predicting criteria described in literature are, as tabulated below (Table 1).

Kobayashi criteria – Cut off for high risk >4	**Sano criteria – Cut off for high risk >2**	**Egami criteria – Cut off for high risk >3**
fever <4 days – 2*	CRP >7 mg/dl – 1*	Fever <4 days -1*
age <12 months – 1*	AST >200 IU/l – 1*	Age <6 months -1*
2CRP >10 mg/dl – 1*	Total bilirubin 0.7 mg/dl – 1*	CRP >8 mg/dl – 1*
Platelets <300/mm3 – 1*		Platelets 300/mm3 – 1*
AST >100IU/l – 2*		ALT >80 IU/l – 2*
Sodium 133mmol/l – 2*		
Neutrophils >80% - 2*		

Table 1: Other risk predicting criteria. * Last number indicates points awarded for each component

Research

In our study we sought to determine the predictive utility of selected clinical and laboratory criteria in view of identifying coronary pathology in Kawasaki disease referred to Cardiology Unit Lady Ridgeway Hospital, Colombo, Sri Lanka in view of optimizing initial management and follow up.

Method

Identification of Cohort

Demographic, clinical, laboratory and echocardiographic data were abstracted from the patients referred or admitted to National Paediatric cardiology unit at Lady Ridgeway Hospital for Children, Colombo Sri Lanka with diagnosed Kawasaki disease (both complete and incomplete Kawasaki disease) diagnosed according to American Heart Association scientific statement regarding Diagnosis, Treatment and Long Term Management of Kawasaki disease in 2017 and also children referred because of continued fever who demonstrated coronary artery dilatation on echocardiography from January 2018 to March 2019. Children with suspected Kawasaki disease without clinical criteria and negative echocardiography together with patients being already followed up for KD were excluded.

Detailed echocardiograms were performed with standard evaluation of left main coronary artery (LMCA), left anterior descending artery (LAD) and right coronary artery (RCA) using high frequency dedicated paediatric probe for better image quality by a Senior Registrar in Paediatric Cardiology or a Consultant Paediatric Cardiologist. Second opinion was taken if there were any doubts. Internal coronary artery diameters were standardized according to the body surface area combined with visual assessment. Coronary artery involvement was determined at the commencement and followed up as far as 12 weeks. Maximum coronary artery diameter was taken during the study period to determine the coronary involvement. Coronary artery aneurysms were identified from echo-cardiographic images and categorized according to the Japanese Health Ministry Criteria.

Risk Predictors

Identified clinical and laboratory criteria, performed within the first 10 days of the illness, were documented. Standard laboratory values used in the national centre were used to categorise laboratory values.

Analysis

Demographic, clinical, laboratory and echocardiographic characteristics were summarized using frequencies and percentages. Coronary involvement was assessed by using Z scores/ standard deviations (SD) plotted against Body Surface Area (BSA) and internal diameter of LMCA (Left Main Coronary artery), RCA (Right Coronary Artery), LAD (Left Descending Artery). A score of more than 2 standard deviations (SD), visual coronary artery dilatation or presence of aneurysms were taken as positive coronary involvement. Then, the coronary involvement was analyzed together with clinical and laboratory criteria, which were documented during the first 10 days of the illness, using Pearson chi square test and odds ratios. Significance of results was determined using the statistical significance level of 5%.

Ethical considerations

Ethical clearance was obtained from the ethical review committees of Sri Lanka College of Paediatricians and Lady Ridgeway Hospital, Colombo, Sri Lanka. Permission to conduct the study was obtained from the Lady Ridgeway Hospital, Colombo, Sri Lanka.

Participation was voluntary after obtaining informed written consent from the guardian / patient. Utmost privacy was maintained during the data collection and storage.

Management of patients with KD was done according to the accepted guideline under particular paediatricians' care and echo-cardiographic follow up arranged by Department of Cardiology at Lady Ridgeway Hospital. Management decisions were not influenced by the research project.

Results

A total of 101 patients with Kawasaki disease (KD) referred to the Cardiology Department of Lady Ridgeway hospital were recruited and formed the cohort of this study. 53 patients (52.5%) were diagnosed as complete KD, 47 (46.5%) as incomplete KD and 1 (1%) belonged to the category with prolonged fever with coronary involvement in echocardiogram. Patients with coronary involvement (cases) comprised of 42 (41.6%) children and patients without coronary involvement (controls) comprised of 59 (58.4%) children.

The cohort showed 1.6: 1, male: female ratio which is in par with international statistics. Age distribution showed commonest incidence in the 7 months to 60 months age category which is showed in Figure 1. Ethnic distribution of the sample is demonstrated in Figure 2.

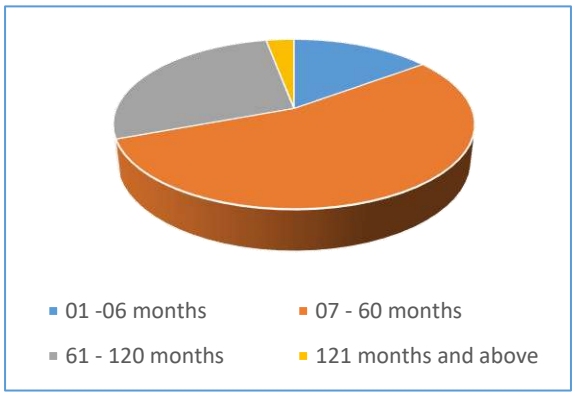

Figure 1: Age distribution of the studied sample

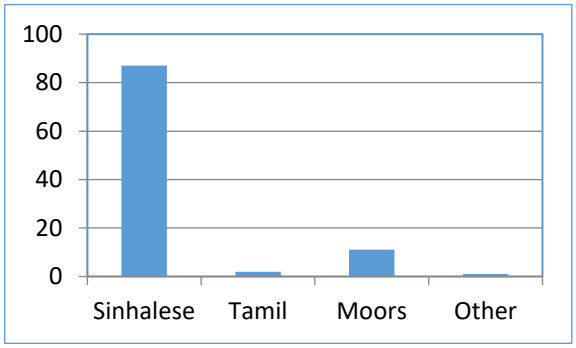

Figure 2: Ethnic distribution of the sample

BCG site inflammation was only seen in 4 (4%) patients with KD.

When comparing the group with the coronary arteries involved with non-involved group, age category of 7 months to 60 months showed a p value of 0.0, fever more than 102^0 F showed a p value of 0.027 and CRP more than 100 mg/L showed a p value of 0.046 leading to a statistically significant positive correlation with coronary involvement. (Table 1).

Also, coronary hyper echogenicity gave an odd ratio of 29 (95% Confidence interval 3.63 - 22.13) significantly predicting coronary involvement in patients with KD.

Coronary aneurysms were seen in 12 (11.8%) patients in the cohort and their distribution is as follows (Table 2 and Figure 3).

With regard to the coronary aneurysm development, diagnosis of complete KD, hypoalbuminemia (serum albumin <34g/L) and hyper echogenic coronaries were positively correlated with p values of 0.047, 0.011 and 0.008 respectively. (Table 3, 4, 5) Analysis of bivariate association is shown in Table 6.

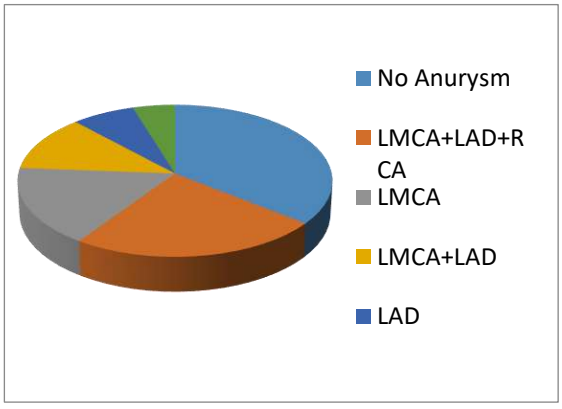

Figure 3: Distribution of coronary aneurysms

Table 1: Analysis bivariate of associations by Pearson Chi squared test of different factors for coronary involvement

	Risk factor	Test Stat. (Chi Square)	Degree of freedom (df)	*p* value
1	Sex	3.059	1	0.080
2	Age category (age 7 - 60 months)	13.785	3	0.003*
3	Ethnicity	7.242	3	0.065
4	Diagnosis	1.960	3	0.375
5	Fever duration	5.831	2	0.054
6	Fever degree (more than 102^0 F)	4.876	1	0.027*
7	BCG flare	0.121	1	0.554
8	WBC	0.820	2	0.664
9	Neutrophils	2.345	1	0.126
10	Platelets	3.746	2	0.154
11	PCV	5.580	1	0.180
12	CRP - High/Low	0.524	1	0.469
13	CRP2 (more than 100mg/L)	7.994	3	0.046*
14	ESR - High/Low	0.231	1	0.631
15	ESR2	0.911	2	0.634
16	AST	0.322	1	0.571
17	ALT	0.360	1	0.849
18	Albumin	1.783	1	0.182
19	Bilirubin	3.699	2	0.157
20	Na^+	1.267	1	0.260

*Statistically significant association

Table 2: Distribution of coronary aneurysms according to the coronary artery

Aneurysm location	Number	%
No Aneurysm	15	35.71
LMCA+LAD+RCA	10	23.81
LMCA	7	16.67
LMCA+LAD	5	11.90
LAD	3	7.14
RCA	2	4.76
Total	**42**	**100.00**

Table 3: Coronary aneurysm development according to the KD diagnosis

		Echo - Aneurysms		
		Absent	Present	Total
Diagnosis	Complete Kawasaki	15	10	25
	Incomplete Kawasaki	15	2	17
Total		30	12	42

Table 4: Coronary aneurysm development according to serum Albumin level

		Echo - Aneurysms		Total
		Absent	Present	
Lab - Albumin	Low	12	10	22
	Normal	18	2	20
Total		30	12	42

Table 5: Coronary aneurysm development according to increased echogenicity

		Echo - Aneurysms		Total
		Absent	Present	
Echo - Increased echogenicity	No	23	4	27
	Yes	7	8	15
Total		30	12	42

Table 6: Analysis bivariate of associations by Pearson Chi squared test of different factors for coronary artery aneurysms

	Risk factor	Test Stat. (Chi Square)	Degree of freedom (df)	*p* value
1	Sex	0.105	1	0.746
2	Age category	2.310	2	0.315
3	Ethnicity	4.353	3	0.226
4	Diagnosis	3.953	1	0.047
5	Fever duration	2.386	2	0.303
6	Fever degree	0.356	1	0.551
7	BCG flare	0.840	1	0.505
8	WBC	2.816	2	0.245
9	Neutrophils	0.356	1	0.551
10	Platelets	0.788	1	0.375
11	PCV	2.270	1	0.132
12	CRP -High/Low	0.840	1	0.359
13	CRP2	1.148	1	0.765
14	ESR -High/Low	0.204	1	0.651
15	ESR2	9.750	2	0.153
16	AST	0.187	1	0.666
17	ALT	0.010	1	0.921
18	Albumin	6.453	1	0.011*
19	Bilirubin	2.270	2	0.321
20	Na+	0.622	1	0.430
21	Echo - Increased echogenicity	7.010	1	0.008*

*Statistically significant association

However, duration of fever, neutrophil percentage, platelet count, haematocrit, ESR, AST/ ALT, serum sodium or bilirubin did not show a statistically significant correlation with coronary involvement in the studied cohort.

Discussion

Kawasaki disease is an acute vasculitis of unknown origin commonly occurring in children less than 5 years of age [19] and the development of coronary artery aneurysms associated with high morbidity and mortality during adulthood [20].

Treatment of KD requires the timely initiation of intravenous immunoglobulin, which prevents coronary complications. However, long-term prognosis depends on initial coronary involvement. Therefore, detecting or suspecting coronary involvement in the initial stage of the disease will prevent devastating consequences. It is very important and practical if we can utilize routinely performed laboratory investigations or clinical parameters to predict coronary involvement in KD, which will be cost effective. During our study it was evident that the sex and age distribution of KD in Sri Lanka was in par with international studies [21]. Although, BCG vaccination at birth is routinely practiced in Sri Lanka only 4% of patients demonstrated BCG induration/ inflammation with the acute illness and there is no statistically significant correlation between coronary artery involvement.

Coronary artery abnormalities in the acute phase of the illness range from dilatation to aneurysm formation, initially at proximal segments and extending to distal segments. In the international studies, sites of aneurysm formation in the order of frequency was proximal LAD and proximal RCA followed by LMCA [19]. On the contrary, our study revealed coronary aneurysms were more in LMCA.

There are several risk scoring systems developed to predict the coronary involvement. Most of the risk assessment scores use Age, duration of fever, CRP, AST, ALT and platelet count. But there are no uniform criteria. This is probably due to geographical or genetic variation of the affected population. In our study we established significant positive correlation with degree of fever, high CRP and age range of 7 months to 60 months, which is the commonest affected age.

Degree of fever was not included in any of the commonly used risk predictive scores. Hence, this is a new finding in predicting the coronary involvement. Probable pathophysiology of the association between high fever and the high inflammatory markers is severe inflammation leading to cytokine mediated coronary dilatation.

With regards to the aneurysm formation, hypoalbuminaemia had a significant positive correlation. However, hypoalbuminaemia is used as a diagnostic criterion in atypical KD diagnosis. On the other hand, our research indicates high prevalence of aneurysms in the complete KD category. Another statistically significant coronary aneurysm predictor is increased coronary echogenicity. This fact indicates the importance of doing a baseline echocardiogram at the initial stage of the illness although coronary changes occur during the 2nd week of the illness.

However, the duration of fever, neutrophil percentage, platelet count, haematocrit, ESR, AST/ ALT, serum sodium or bilirubin did not show statistically significant correlation with coronary involvement in this study.

In conclusion, high fever $>102^0$ F and CRP >100mg/L in patients with KD between 7 months to 60 months needs close follow up and intensive initial management as they tend to develop coronary dilatations. Also, among patients with coronary involvement, category of complete KD with hypoalbuminaemia, and coronary hyperechogenicity in echocardiogram predict coronary aneurysm formation.

Thus clinical parameters and commonly performed, widely available laboratory investigations can be effectively used to optimize the initial management and follow up of KD in a cost-effective way in Sri Lanka.

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Disclosures
None.

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Research

Observation of on-admission full blood count parameters among STEMI patients who received medical thrombolysis

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Abstract

Background : In the current understanding, the pathophysiology of atherosclerosis is considered to be inflammatory in origin.

Objectives: The principal objectives of the study were to observe the behavior of on admission Full Blood Count (FBC) parameters to early cardiac mortality, morbidity and ST segment resolution among ST Segment Elevation Myocardial Infarction (STEMI) patients who had medical thrombolysis.

Methods: A descriptive cross-sectional study was conducted at cardiology unit in Teaching Hospital Kandy over a period of one year from November 2016 by obtaining a convenient sample. All the eligible patients with STEMI admitted to the coronary care units were recruited for the study. Patients with preceding evidence of inflammatory or infective scenario, patients who were presented after 12 hours of initial symptoms and patients who subjected for primary angioplasties were excluded from the study. On admission blood samples were obtained and subjected for cell count analysis by a single automated FBC analyzer. Hematological parameters of White Blood Cell (WBC) count, Neutrophil/Lymphocyte Ratio (NLR), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Platelet/Lymphocyte Ratio (PLR) were derived for each individual patient.

Results: There were 350 patients in the study sample. Out of the acute STEMI patients, there were 74.00% (n=259) of males. The mean age of the study sample was 61.27±11.64 years. There was a 27.71% (n=97) mortality observed within the first month among STEMI patients who underwent medical thrombolysis. There was a significantly higher value of NLR (0.89±0.21 vs 0.79±0.25, p=0.00), PLR (225.56±98.23 vs 192.63±82.56, p=0.00), PDW (16.89±0.34vs15.96±0.52, p=0.00) observed among this group compared to their survival counterparts. There were 37.11% (n=36) and 62.89% (n=61) had Streptokinase (STK) and Recombinant Tissue Plasminogen Activator (RTPA) as their thrombolytic agents respectively. The group treated with STK had 55.63% (n=79) of satisfactory ST segment resolution (STR≥70%) i.e. resolution of ST segment by 70% or more from its baseline at the end of one hour of post thrombolysis. Similarly, the patients who had RTPA as the thrombolytic agent had 60.10% (n=125) satisfactory ST segment resolution (STR≥70%). Among the patients with incomplete STR had a significant higher value of NLR (0.75±0.15vs0.68±0.22, p=0.00) compared to the group with satisfactory ST segment resolution, irrespective of the thrombolytic agent.

Conclusion: We observed a higher value of NLR, PLR and PDW among STEMI patients who had death within 30 days following myocardial infarction. Addition to that a higher NLR also observed among who had inadequate STR following thrombolysis. Therefore, further large-scale prospective studies are recommended for the evaluation of the precise role of these FBC parameters and their effect on the long term cardiovascular prognosis.

Key words: ST elevation myocardial infarction (STEMI), Neutrophil/Lymphocyte Ratio (NLR), ST segment resolution, cardiovascular mortality and morbidity.

Introduction

The pathology of atherosclerosis is considered as a complex phenomenon involving both acute and chronic inflammatory process over a prolonged period[(1)]. However, the understanding of the precise mechanism of this process is still evolving as a result of the new gaining of knowledge regarding its underlining cellular mechanisms.

According to the current understanding, the traditional vascular risk factors such as hypertension, diabetes, dyslipidemia, age, gender and hereditary factors all contribute to the progression of atherosclerosis. Nevertheless, more interestingly, it is found that the inflammatory cells and various cytochemicals also play a vital role in this process [(2,3,4)] extending the knowledge of cellular involvement in atherosclerosis [(2)].

As the widening of the understanding of the process of atherosclerosis as a manifestation of generalized vascular inflammation [(5)], many thoughts were focused to explore novel risk factors to identify the etiology and progression of coronary artery disease (CAD), addition to the traditional vascular risk factors.

Several clinical studies have already shown some of the cellular biomarkers are able to estimate the development of future ischemic events and adverse cardiac outcome following Acute Coronary Syndromes (ACS) [(6)].

Full Blood Count (FBC) is one of a routinely performed investigations at the time of hospital admission in any patient with ACS and a number of evidences had been observed by different population studies highlighting the validity of this

initial hematological response in patients with ACS and its correlation to adverse cardiovascular outcomes [3].

Therefore, the place of initial hematological response has become one of an emerging research interest in recent era of clinical cardiology to evaluate as a widely available, cost effective prognostication tool in patients with ACS.

Objectives

The main objective of the study was to observe the variabilities of the variation of FBC parameters of STEMI patients who had early death, repeat hospitalization and inadequate ST segment resolution following medical thrombolysis.

Methodology

Study design and setting

A descriptive cross-sectional study was conducted at cardiology unit of Teaching Hospital Kandy over a period of one year from November 2016. On admission FBC parameters of eligible patients were evaluated and regular follow up was established.

Inclusion criteria

All consecutive patients with STEMI who had medical thrombolysis admitted to coronary care units at Teaching Hospital Kandy were recruited for the study. The patients who presented within 12 hours of onset of symptoms were included. STEMIs were diagnosed on the occurrence of classic symptoms of angina within 12 hours and detection of ST-segment elevation in two contiguous leads, which was defined by the guidelines of the American College of Cardiology and the European Society of Cardiology [7].

Exclusion criteria

Patients with following clinical conditions were excluded from the study. Those included; patient having clinical evidence of ongoing active infection, systemic inflammatory disease, known hematological disease, end-stage liver and kidney diseases, known systemic autoimmune disease, known malignancy, presence of left bundle branch block and paced ventricular rhythm on the presenting ECG. Patients who presented after 12 hours of initial symptoms and patients who underwent primary angioplasties were also excluded from the study.

A convenient sample of 350 patients was obtained by including all the consecutive, eligible patients over a period of one year from November 2016 to October 2017, who presented to cardiology units at Teaching Hospital Kandy with a diagnosis of STEMI.

Full blood count analysis

On admission blood samples were obtained and subjected for cell count analysis by a single automated FBC analyzer. Hematological parameters of White Blood Cell (WBC) count, Neutrophil/Lymphocyte Ratio (NLR), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Platelet/Lymphocyte Ratio (PLR) were formulated for each individual.

Electrocardiographic analysis

12 lead Electrocardiogram (ECG) was obtained at the time of admission in a standered rate of 25 mm/sec speed, and a gain of 10 mV. STEMI was determined by the occurrence of ST segment elevation of 0.2 mV in male and 0.15mV in female measured at the J point in leads V2-V3 or 0.1 mV on at least two contiguous leads of the remaining leads [8]. The first post thrombolytic ECG was obtained one hour after finishing the full dose of thrombolytic.

ST segment resolution (STR) was assessed by two individual examiners. The percentage difference between the sums of the ST-segment elevation on the ECGs performed on admission and after one hour of thrombolysis was considered for the calculation of STR [9,10,11]. Complete STR was defined as the finding of a resolution of ≥ 70% and incomplete STR was defined as having a resolution of < 70% [11].

Follow up of the subjects

All the patients were followed up at 30 days by the medical and research team during their first follow up clinic visit. The patients who did not appear in the respective clinics were contacted over the phone and the essential clinical details were obtained as well as subsequent clinic visit were arranged in coming 2 weeks' time. The data on death, details of hospital admissions during the first 30 days and available hospital records were studied for the patients who were admitted into a different institutions.

Statistical analysis

The SPSS statistical package (version 17) for windows, Chicago IL, USA was used to store and analyse the data.

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During the analysis, the continuous variables were presented as mean with standard deviation (SD) and categorical variables as percentages. Independent sample t test was used to compare quantitative data, between the groups. A p-value of 0.05 was used as the level of statistical significance. Multivariate logistic regression analysis was used to evaluate the independent variable among the above defined hematological parameters in-relation to cardiac mortality within the first month following STEMI.

Ethical clearance

Ethics approval was obtained from the Ethical and Research Committee of the Teaching Hospital Kandy. Informed written consent was obtained from all participants before obtain the information.

Results

Demographic data

There were 350 patients in the study sample. Out of the acute STEMI patients, there were 74.00% (n=259) of males. The mean age of the study sample was 61.27± 11.64 years. Baseline characteristics and co-morbidities of the study sample is demonstrated in Table 01.

Variable	Results n (%)
Age (mean ± SD)	61.27±11.64 years
Gender	
Male	259 (74.00%)
Female	091 (26.00%)
Co-morbidities	
Diabetes	73 (20.86%)
Hypertension	45 (12.86%)
Dyslipidemia	82 (23.43%)

Table 01: Baseline characteristics of the study sample

Hematological response and the all-cause mortality within the first month

There were 27.71% (n=97) deaths within the first month of STEMI following medical thrombolysis. Out of them, 37.11% (n=36) had Streptokinase (STK) and 62.89% (n=61) had Recombinant Tissue Plasminogen Activator (RTPA) as their thrombolytic agent. Among the death patients, there was a significantly higher value of NLR, PLR and PDW noted compared to their survival counterparts irrespective of the thrombolytic agent (Table 02).

Table 02: Comparison of the Haematological parameters of thrombolyzed STEMI patients who encountered death versus their survival counterparts. A separate analysis is shown for STK and RTPA treated groups for the comparison.

	Treated with STK			Treated with RTPA		
Parameters	**Death Patients (n=36)**	**Survivors (n=106)**	**P Value (P<0.05)**	**Death Patients (n=61)**	**Survivors (n=147)**	**P Value (P<0.05)**
	Mean ± SD	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**	
WBC	15.63±2.56	14.23±1.52	0.00	14.89±3.65	13.96±3.83	0.01
NLR	0.89±0.21	0.79±0.25	0.00	0.82±0.13	0.75±0.30	0.00
MC	7.56±2.89	7.11±1.59	0.02	7.56±3.02	7.03±2.58	0.00
WBC/MPV	1.78±0.42	1.75±0.41	0.06	1.45±0.75	1.44±0.41	0.53
Hb	13.69±1.85	14.86±1.36	0.85	14.96±1.53	15.25±1.02	0.79
RDW	13.66±1.55	14.02±0.98	0.31	13.85±1.56	14.73±1.51	0.46
RDW/PLT	0.05±0.04	0.06±0.02	0.22	0.06±0.03	0.07±0.01	0.88
MPV	8.63±1.22	8.03±0.64	0.01	8.78±0.96	7.99±0.85	0.02
PDW	16.89±0.34	15.96±0.52	0.00	16.99±0.63	15.42±0.36	0.00
PLR	225.56±98.23	192.63±82.56	0.00	217.86±92.22	186.35±78.56	0.00

STR= ST segment Resolution, WBC= Total White Blood cell count ($\times 10^9$/µL), NLR= Neutrophil-to-lymphocyte ratio, MC= Monocyte Count ($\times 10^9$/µL), WBC/MPV= Total white blood cell count to Mean Platelet Volume ratio, Hb= hemoglobin level (g/dL), RDW= Red blood cell distribution width (%), RDW/PLT= Red blood cell distribution width to Platelet count ratio, MPV= Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR= Platelet to lymphocyte ratio

Multivariate logistic regression analysis revealed that a high NLR was the independent predictor over the above hematological parameters in-relation to mortality within the first month following STEMI (Table 03).

Table 03: Multivariate Logistic Regression analysis of the FBC parameters in relation to death within first month following STEMI.

Variables	B	SE	Wald	P	OR	95% CI
WBC	-0.087	0.223	0.154	0.695	0.916	0.592-1.419
NLR	0.065	0.067	0.945	0.008	1.068	0.936-1.218
MC	0.137	0.080	2.924	0.087	1.146	0.980-1.341
WBC/MPV	0.449	1.909	0.055	0.814	1.566	0.037-66.019
Hb	-0.024	0.026	0.889	0.346	0.976	0.928-1.026
RDW	-0.049	0.092	0.287	0.592	0.952	0.796-1.139
RDW/PLT	-5.152	7.901	0.425	0.514	0.006	0.000-3.077
MPV	-0.085	0.331	0.066	0.797	0.918	0.480-1.758
PDW	0.008	0.034	0.060	0.807	1.008	0.944-1.077
PLR	0.000	0.003	0.024	0.877	0.999	0.993-1.006

CI= confidence interval, NLR= Neutrophil-to-lymphocyte ratio, OR= Odds Ratio.
WBC= Total White Blood cell count ($\times 10^9$/µL), NLR= Neutrophil-to-lymphocyte ratio, MC= Monocyte Count ($\times 10^9$/µL), WBC/MPV= Total white blood cell count to Mean Platelet Volume ratio, Hb= hemoglobin level (g/dL), RDW= Red blood cell distribution width (%), RDW/PLT= Red blood cell distribution width to Platelet count ratio, MPV= Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR= Platelet to lymphocyte ratio

Hematological response and the cardiac morbidity within the first month

The patients who were re-admitted within the first month to manage post MI angina, post myocardial infarction non-STEMIs, re-infarction, MI in another territory or ischemic left ventricular failure accounted for the cardiac morbidity. There were 11.06% (n=28) and 8.69% (n=22) re-admissions were noted in the STK and RTPA treated groups respectively. The group which had a significant cardiac morbidity, found to have a higher value of NLR, MPV, PLR and PDW irrespective of the thrombolytic agent Table 04. The medical records were studied to obtain the data of the patients who were admitted to other institutions for the management of ACS within this period.

Table 04: Comparison of the haematological parameters of thrombolyzed STEMI patients who had repeat hospitalisation with an ischemic complication versus their uneventful counterpart. A separate analysis is shown for STK and RTPA treated groups for the comparison.

	Treated with STK			Treated with RTPA		
Parameters	**Morbidity (n=28)**	**Un-eventful Recovery (n=78)**	**P Value (P<0.05)**	**Morbidity (n=22)**	**Un-eventful Recovery (n=125)**	**P Value (P<0.05)**
	Mean ± SD	*Mean ± SD*		*Mean ± SD*	*Mean ± SD*	
WBC	15.02±3.85	14.11±3.70	0.62	14.52±1.33	13.82±1.08	0.48
NLR	0.82±0.42	0.78±0.35	0.00	0.85±0.31	0.73±0.20	0.00
MC	6.55±4.52	7.34±3.21	0.36	7.13±4.12	7.26±4.54	0.35
WBC/MPV	1.58±0.67	1.43±0.54	0.48	1.34±0.42	1.32±0.12	0.39
Hb	13.31±1.48	13.96±0.82	0.75	14.12±0.34	14.85±1.56	0.79
RDW	12.15±1.05	13.05±1.16	0.22	13.34±1.02	13.86±1.13	0.37
RDW/PLT	0.05±0.04	0.05±0.03	0.16	0.06±0.03	0.07±0.01	0.62
MPV	9.35±1.05	8.76±0.89	0.00	8.11±0.96	7.35±1.43	0.00
PDW	17.86±0.32	16.44±0.48	0.00	17.36±0.85	17.15±0.52	0.00
PLR	196.42±85.16	185.18±92.68	0.01	206.12±98.63	186.99±86.52	0.00

STR= ST segment Resolution, WBC= Total White Blood cell count ($\times 10^9$/µL), NLR= Neutrophil-to-lymphocyte ratio, MC= Monocyte Count ($\times 10^9$/µL), WBC/MPV= Total white blood cell count to Mean Platelet Volume ratio, Hb= hemoglobin level (g/dL), RDW= Red blood cell distribution width (%), RDW/PLT= Red blood cell distribution width to Platelet count ratio, MPV= Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR= Platelet to lymphocyte ratio

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Multivariate logistic regression analysis revealed that a high NLR is the independent predictor of the significant cardiac morbidity within 30 days of STEMI (Table 05).

Table 05: Multivariate Logistic Regression analysis of the FBC parameters in relation to cardiac morbidity within first month following STEMI.

Variables	B	SE	Wald	P	OR	95% CI
WBC	0.336	0.268	1.574	0.210	1.399	0.828-2.365
NLR	0.150	0.106	2.025	0.002	1.162	0.945-1.430
MC	0.273	0.116	5.544	0.119	1.314	1.047-1.650
WBC/MPV	-3.329	2.236	2.216	0.137	0.036	0.000-2.867
Hb	-0.031	0.027	1.297	0.255	0.969	0.919-1.023
RDW	0.133	0.123	1.179	0.278	1.142	0.898-1.453
RDW/PLT	-6.616	11.010	0.361	0.548	0.001	0.000-3.152
MPV	-0.517	0.386	1.789	0.181	0.596	0.280-1.272
PDW	-0.002	0.036	0.002	0.964	0.998	0.931-1.071
PLR	-0.003	0.005	0.485	0.486	0.997	0.988-1.006

CI= confidence interval, NLR= Neutrophil-to-lymphocyte ratio, OR= Odds Ratio.
WBC= Total White Blood cell count ($\times 10^9$/µL), NLR= Neutrophil-to-lymphocyte ratio, MC= Monocyte Count ($\times 10^9$/µL), WBC/MPV= Total white blood cell count to Mean Platelet Volume ratio, Hb= hemoglobin level (g/dL), RDW= Red blood cell distribution width (%), RDW/PLT= Red blood cell distribution width to Platelet count ratio, MPV= Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR= Platelet to lymphocyte ratio

Hematological response and the ST segment resolution in STEMI patients after one hour of thrombolysis.

The group treated with STK had 55.63% (n=79) of satisfactory ST segment resolution (STR≥70%). Similarly, the patients who had RTPA as the thrombolytic agent had 60.10% (n=125) satisfactory ST segment resolution (STR≥70%) after one hour of thrombolysis.

A statistically significant higher number of WBC, NLR, PDW noted among the patients who had incomplete STR (SRT <70%) compared to the group with complete STR, irrespective of thrombolytic agent.

Table 06: Comparison of the haematological parameters of satisfactory STR group versus the group who had non-STR in in medically thrombolyzed STEMI patients.

	Treated with STK			**Treated with RTPA and TNK**		
Parameters	**STR≥70% (n=79)**	**STR<70% (n=63)**	**P Value (P<0.05)**	**STR≥70% (n=125)**	**STR<70% (n=83)**	**P Value (P<0.05)**
	Mean ± SD	*Mean ± SD*		*Mean ± SD*	*Mean ± SD*	
WBC	13.56±3.22	14.28±3.25	0.00	14.03±2.89	14.98±3.02	0.01
NLR	0.68±0.22	0.75±0.15	0.00	0.77±0.20	0.82±0.12	0.00
MC	7.15±2.63	7.64±3.33	0.51	7.00±4.85	8.42±1.84	0.72
WBC/MPV	1.52±0.47	1.44±0.41	0.78	1.52±0.34	1.84±0.43	0.07
Hb	14.56±1.02	13.15±1.22	0.82	14.82±2.48	13.89±1.75	0.86
RDW	13.25±1.96	13.73±1.65	0.33	14.86±1.12	14.62±1.22	0.34
RDW/PLT	0.05±0.02	0.06±0.02	0.75	0.07±0.03	0.08±0.02	0.26
MPV	8.11±1.02	8.56±0.62	0.36	7.94±1.32	8.89±0.92	0.09
PDW	16.44±0.24	17.95±0.32	0.01	16.13±0.56	17.25±0.41	0.00
PLR	198.56±62.22	198.52±84.78	0.86	185.63±75.29	195.75±65.28	0.54

STR= ST segment Resolution, WBC= Total White Blood cell coun ($\times 10^9$/µL), NLR= Neutrophil-to-lymphocyte ratio, MC= Monocyte Count ($\times 10^9$/µL), WBC/MPV= Total white blood cell count to Mean Platelet Volume ratio, Hb= hemoglobin level (g/dL), RDW= Red blood cell distribution width (%), RDW/PLT= Red blood cell distribution width to Platelet count ratio, MPV= Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR= Platelet to lymphocyte ratio

Discussion

As a result of the continuous expansion of our understanding of the pathophysiology of ischemic heart disease, there is a constant drive to identify novel risk markers that may allow for a more accurate risk stratification, with highly intensive and more focused treatment with an intention to improve the overall prognosis. Furthermore, identification of these novel risk factors that are also causative in the disease processes may reveal new insights that may direct for the discoveries of novel treatment strategies. However, the popularity of such a marker will depend over the accuracy as well as the cost-effectiveness in the long run.

In many ways, atherosclerosis is a chronic inflammatory condition, and this issue is confirmed by recent investigations, which have focused on its pathophysiology[12]. In addition several latest studies have addressed the role of hematological cellular parameters in vascular inflammation and its relationship to triggering of acute coronary events[13]. Certain evidences have been put forward from different sub-populations over the recent past indicating, that the initial hematological response and its' correlation on cardiovascular mortality and morbidity in patients with ACS [14]. One interesting study showed that Neutrophil-to-lymphocyte ratio (NLR) in acute MI setting indicates worse in-hospital outcomes which are independent of the Global Registry of Acute Coronary Events (GRACE) risk score [3]. More interestingly, our study also found that STEMI patients who suffered death during the first month following the event had a significantly higher NLR compared to their survival counterpart. Similarly, they also had a higher value of PDW and PLR compared to survivors irrespective of the thrombolytic agent. In addition higher NLR, MPV and PDW were also found in patients who had cardiovascular morbidity within the first month compared to patients who had an uneventful recovery during the same period. These findings highlight the association and the potential capacity of these on-admission FBC data to help predict the cardiovascular outcome in STEMI patients.

Varastech HR et al [15] had shown that on admission Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and White Blood Cell Count following STEMI might be valuable in the prediction of impaired ST segment resolution in STEMI patients treated with STK.

Similarly, our data also indicates that patients who had <70% STR had significantly higher NLR, WBC and PDW indicating a link of these initial FBC parameters to early risk predication and cardiovascular prognosis in STEMI patients.

Another interesting study showed that the correlation of higher value of on admission WBC count and MPV are independent predictors of impaired micro-vascular perfusion following primary Percutaneous Coronary Interventions (PCI) [16] in STEMI patients. Likewise, there are several studies that confirm the association of on-admission FBC parameters to the adverse cardiovascular outcomes in STEMI patients, which are also highlighted in our study.

In the developing world where primary PCI is not extensively available, medical thrombolysis is still the first line treatment strategy for STEMI patients. Hence, the requirement of a more sensitive risk stratification tool is largely relevant for the identification of high-risk individuals for an early revascularization strategy among these medically managed patients. If such a parameter can be derived from the routine investigations performed in the acute setting such as FBC, it will be very cost *effective* as a prognostication tool among these patients. It also can be used to select patients who require an early revascularization strategy among medically managed patients in very resource limited setting.

Conclusion

It has been observed a higher value of NLR, PLR and PDW among acute STEMI patients who had early adverse cardiovascular outcomes. Therefore, we would like to highlight the requirement of large-scale prospective trials in future in relation to patients' characteristics to illuminate the precise role of these FBC parameters and their role in the cardiovascular prognosis following ACS.

Limitations

The study was conducted in one of the major cardiology center in Sri Lanka. However, expanding the study into multicenter level can achieve a greater representative value of the whole population. In this study, we have analyzed the follow-up data in the context of one month only, but extending the follow up beyond this may elicit an additional insight on the long term outcomes.

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Perspectives In Medicine

Patient Safety: Gaps in Training and Learning from Induced Errors

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"I hear and I forget. I see and I remember. I do and I understand." – Confucius

Vignette

This is an actual incident that took place more than 40 years ago. I have taken it as an example to address patient safety issues that we need to address when carrying out procedures on patients. In mid-1970s, House Officers (HOs) in the Cardiology Unit (currently Institute of Cardiology, NHSL) of Sri Lanka, were tasked to carry out right heart catheterization in the catheter lab in addition to multitude of other duties. It was done under fluoroscopic guidance whilst the patient's cardiac rhythm being monitored. The catheter was introduced in the groin via a 'cut-down' of the right long saphenous vein done under local anaesthesia. After observing and assisting experienced colleagues carrying out the procedure, it took only a few weeks for HOs to perform this task confidently, on their own. On a middle aged man with a secondum ASD, a right heart study was initiated by a HO. He had already done more than a dozen cardiac catheterizations but he took more than the usual duration to enter the 'long saphenous vein' which appeared pink and fibrotic, rather unusual in appearance. As the catheter advanced, to his dismay, the technician found that the catheter tip was leading to the neck and not the heart as expected and he urged to call for assistance. His superior who was just outside the catheter lab quickly came in and took charge of the situation. Whilst grabbing the catheter he quipped *"Hey, you have entered the femoral artery and you are half-way up the carotid artery!"* Fortunately, the femoral artery had gone into spasm, gripping the catheter tight, and preventing any bleeding. The catheter was immediately withdrawn and pressure was applied directly on the site of incision using a gauze pack.

Within minutes, a cardiothoracic surgeon was contacted and the patient was sent to the Cardiothoracic Unit which was a few minutes away, while the HO maintained direct pressure over the artery.

As the patient arrived, the cardiothoracic surgeon had just finished an operation and stepped out of the theatre to see the patient. He said that the limb was not ischaemic but he would immediately repair the artery to establish the circulation. This was done. Patient was lucky to walk home in few days!

Discussion

The WHO defines patient safety as the prevention of errors and adverse effects in patients associated with health care [(1)]. Medical negligence encompasses acts of omission, in addition to medical errors. In December 1999, the United States Institute of Medicine reported that medical errors cause up to 98,000 deaths and more than 1 million injuries each year in the United States alone [(2)]. Data from well-resourced countries show considerable mortality and morbidity resulting from medical errors. Though data are not available, in Sri Lanka there are reasons to believe that this is a common occurrence with worse cases being highlighted as deaths due to medical errors in Coroner's reports, hospital inquiries, mortality and morbidity meetings, and inquiries into maternal deaths. As medical errors similar to what is given in the above vignette are likely to be occurring in Sri Lanka, it is taken as the focus of discussion to highlight some important educational philosophies underpinning the approaches in prevention of medical errors.

The incident narrated above is a serious medical error. Although seriousness to the patient was minimized by timely intervention, the worse outcomes could have been death from haemorrhage, gangrene, septicaemia or at least the loss of a lower limb.

The 'Swiss cheese model' shows how a fault in one layer of a system of care is usually not enough to cause serious harm [3].

Adverse events are usually seen when a number of faults occur in most of the sequential layers of care (for example, fatigued workers or workers with inadequate experience or faulty equipment) momentarily line up to permit a "trajectory" of accident opportunity (indicated by the arrow A in the Figure 1).

However, as in this case where the technician quickly detected that the catheter was not properly placed, further serious damage to the patient can be prevented, if the error is detected early and appropriate remedial action is taken (similar to the situation indicated by the arrow B in the Figure 1). In this case, the more experienced Cardiologist was outside the catheter lab, and was able to immediately come in and take charge of the situation.

The patient was then quickly taken to the Cardiothoracic Unit where a cardiothoracic surgeon could repair the damage early and prevent serious harm to the patient.

Could this medical error have been prevented?

Healthcare workers are not infallible. We need to understand that every one of us will make mistakes at some time and that the causes of errors are multifactorial and may involve latent factors not immediately obvious at the time the error was made. Therefore, I would like to discuss as to how this error could have been prevented and how such occurrences can be minimized by exposure to simulated medical errors.

- **Calling for help early**

A 'venous cut-down' is a simple surgical procedure. In this patient, the dissection took longer than usual and longer manipulation of tissues in itself may have caused spasm of the veins and arteries at the site of dissection, making identification of structures more difficult. Often HOs and even some postgraduate trainees are reluctant to 'call for help' early. Often they struggle and try to complete a procedure when they find it difficult, because they think it is 'not good' to show that they are finding it difficult to cope.

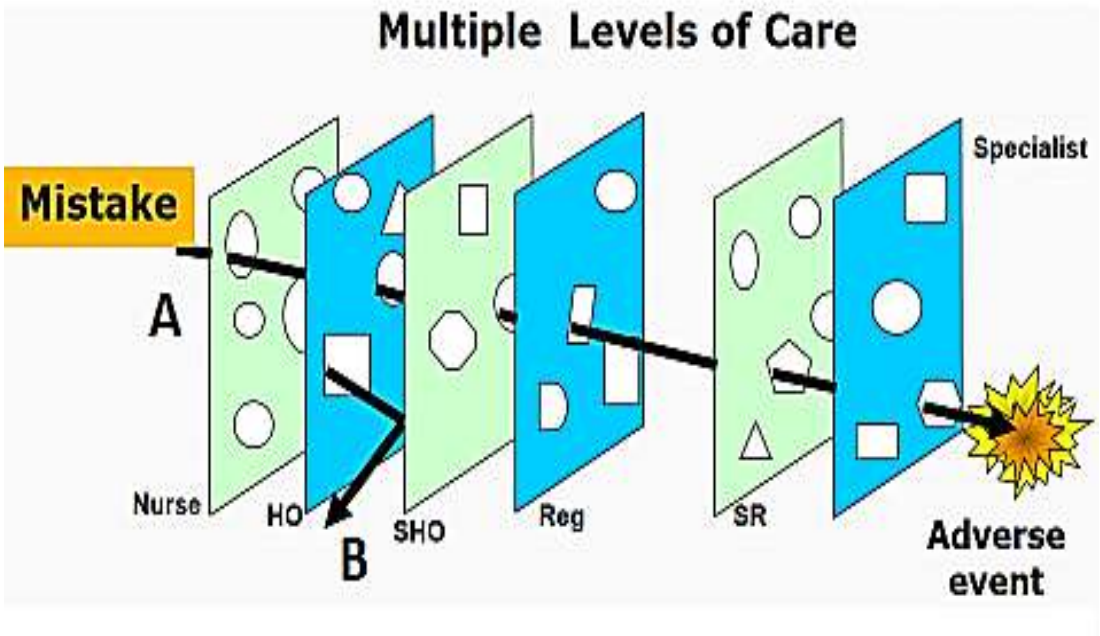

Figure 1: Swiss cheese model ***(Adapted from Ref 3)***

They ultimately end up by calling for help too late, when the condition has deteriorated or a serious complication has arisen [4, 5]. In this case, when the procedure became difficult, especially when there was doubt as to the identification of structures concerned, early advice and help should have been sought from an experienced colleague. The same procedure can be of varying levels of difficulty in different patients, as evident in this case. It is questionable as to whether the HO was equipped to handle such variations.

- **Level of competency**

Competency of trainees should be assessed by formatively using multiple assessment tools like multi-source feedback (360º assessment), Mini-CEX, OSCEs, DOPS etc.[6] If trainees do not demonstrate adequate level of skills, they should be given feedback about their performance and further training until they achieve the required level of competence. Such an approach was not in existence 40 years ago when this incident happened and it is hard to judge whether the HO was competent to perform the procedure.

- **Fatigue**

Did the HO lose focus and concentration due to fatigue? HOs have been known to cause serious medical errors when they worked frequent 24 hours shifts, than when they worked shorter on call shifts [7].

- **Level of supervision**

If there was direct supervision, his supervisor could have appropriately advised the HO when he found the *'long saphenous vein to be pink and fibrotic and rather unusual in appearance'*. However, a study on operative supervision in emergency setting within Australian hospitals though appearing potentially inadequate, suggested that unsupervised surgery did not result in worse post-operative outcomes [8].

Teaching and Learning Patient Safety

The following are known to increase the chances of medical errors :-

1. Situations associated with an increased risk of error such as inexperience, time pressure, inadequate checking, poor procedure and inadequate information.
2. Individual factors such as limited memory capacity, fatigue, stress, hunger, illness, language or cultural barriers and hazardous attitudes [9].

- **Conventional approach**

Standard training programmes such as didactic lectures to prevent patient harm have not been effective enough to reduce the incidence of medical errors [10]. Despite introduction verification of check lists before procedures, displaying posters and reinforcing a supportive culture; simple check lists were not adhered to by more than 30% nurses during medication administration [11]. This highlights insufficient impact of conventional training programs and practices in reducing medical errors. Hence, as an alternative an approach that is somewhat new and rarely used is discussed, below.

- **Approach to learning by experiencing errors**

Failures, especially self-experienced ones leave powerful and long lasting impressions. Errors can be important tools for achieving learning as shown in Flowchart 1[12].

In this approach, ***the goal is achieved by shifting focus from understanding and trying to avoid errors*** (which is the conventional approach to teach patient safety) ***to experiencing*** (induced errors) and recovering from errors [13].

As given in the flow-chart below, it is done in three stages – *first, inducing errors; then, identifying errors; and finally, responding to errors*. In the vignette given, one can imagine how the HO concerned would have 'walked through' the three steps given in this approach. Obviously, one should not wait for such things to happen in the real world to learn using this approach. On the other hand, such scenarios can be used proactively for simulation, in training workshops.

1) Inducing errors	***Selection of errors:*** Reproduce common errors	***Acting errors:*** Simulate errors closely	***Inducing errors in learners***: Make learners themselves to experience errors	
2) Identifying an error	***Gradual presentation:*** Expose to obvious errors committed by others	***Different usage of error identification:*** For training or assessment	**Adding complexity and challenge:** Make error detection more realistic by adding noise or other distractions	***Platforms:*** Make simulations in low or high technology means
3) Responding to the error by taking actions to counter and recover from the error	**Gradual demands:** Once an error is detected correct recovery action needs to be presented to learner. Later increase the level of complexity.	***Different usage of error recovery:*** For training or assessment	***Frequency:*** Trainees should be exposed at different times and in random to errors as surprise.	

Responding to and learning from medical errors involves a cognitive pathway similar to the model published by David Kolb [14]. This is a learning cycle where a person progresses through four stages (Figure 2): having a concrete experience *(inducing an error)* followed by observation of and reflection on that experience *(identifying the error)* which leads to the formation of abstract conceptualization or analysis *(responding to the error)* and generalizations or conclusions which are then used to test hypothesis by active experimentation *(taking action to recover from the error)* in future situations, resulting in new experiences. This concept is called experiential learning and the learner is expected to gain more experience as repetitive exposure to the task occurs; finally taking him to the level of 'mastery'.

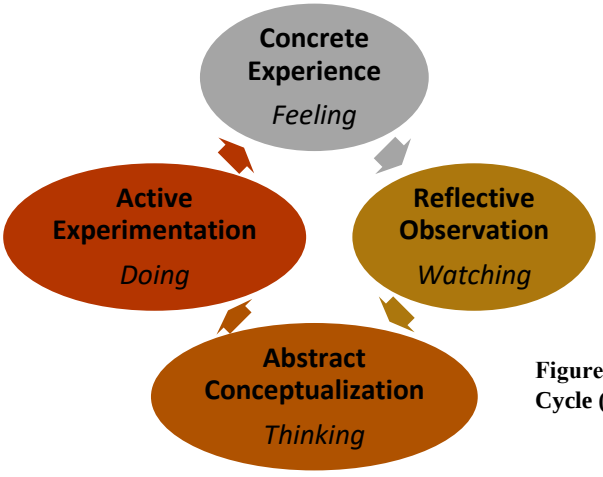

Figure 2: Kolb's Learning Cycle (Ref 14)

Conclusions

Although 'open venous cut downs' are rarely done in current Cardiology practice, a vast number of percutaneous cardiac catheterizations are done for diagnostic and therapeutic purposes. This vignette and the discussion is presented to raise awareness of medical errors in general, and not particularly with reference to cardiac catheterization. The importance of patient safety, factors which need to be considered to promote patient safety, and how to respond to errors as well as learning from errors, are highlighted.

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Updates

Extracts from guidelines

From the Editorial desk

'Ten Commandments' of the 2019 ESC Guidelines for Pulmonary Embolism

1. In the patient presenting with haemodynamic instability, perform bedside transthoracic echocardiography as an immediate step to differentiate suspected high-risk PE from other acute life-threatening situations.

2. If you suspect acute PE, institute anticoagulation therapy as soon as possible, while the diagnostic workup is ongoing, unless the patient is bleeding or has absolute contraindications.

3. Use recommended, validated diagnostic algorithms for PE, including standardized assessment of (pre-test) clinical probability and D-dimer testing.

4. If the CTPA report suggests single sub segmental PE, discuss the findings again with the radiologist and/or seek a second opinion to avoid misdiagnosis.

5. In a patient without haemodynamic instability, confirmation of PE must be followed by further risk assessment involving clinical findings and comorbidity along with evaluation of the size and/or function of the RV, and with laboratory biomarkers if appropriate.

6. As soon as you diagnose (or strongly suspect) high-risk PE, select the best reperfusion option (systemic thrombolysis, surgical embolectomy, or catheter-directed treatment), considering the resources and expertise available at your hospital. For patients with intermediate–high-risk PE, reperfusion is not a first-line treatment, but you should prospectively plan the management strategy with your team to have a contingency plan ready if the situation deteriorates

7. Prefer anticoagulation with a NOAC over the LMWH–VKA regimen unless the patient has contra-indication(s) to NOACs.

8. Always remember that, with the exception of acute PE provoked by a strong transient/reversible risk factor, there is a lifelong risk of VTE recurrence after the first episode of PE. Consequently, re-examine the patient after the first 3–6 months of anticoagulation, weigh the benefits vs. risks of continuing treatment, and decide on the extension and dose of anticoagulant therapy, also considering the patient's preference. Remember to recommend regular follow-up examinations.

9. If you suspect PE in a pregnant patient, utilize formal diagnostic pathways and algorithms, including CTPA or ventilation–perfusion lung scan if needed, which can be used safely during pregnancy.

10. After acute PE, patients should not be lost to follow-up. Apart from checking for possible signs of VTE recurrence, cancer, or bleeding complications of anticoagulation, ask the patient if there is persisting or new-onset dyspnoea or functional limitation. If yes, implement a staged diagnostic workup to exclude CTEPH or chronic thromboembolic disease, and to detect/treat comorbidity or 'simple' deconditioning. Follow-up imaging is not routinely recommended in an asymptomatic patient, but it may be considered in patients with risk factors for the development of CTEPH.

Tutorial

Tips for use of Loop Diuretics in Acute Decompensated Heart Failure

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Background

The natural history of heart failure is characterized by episodes of acute decompensation with remissions and relapses [(1)]. Majority of the heart failure episodes are associated with congestion and normal levels of blood pressure [(2)]. These patients get relieved of the congestion by the use of loop diuretics even though these drugs are not associated with any survival benefit.

Guideline directed medical management based on trials over the past 2 decades has established the use of vasodilators, beta-blockers and mineralocorticoid receptor antagonists as the key drugs in heart failure management. Though routinely used in Acute Decompensated Heart Failure (ADHF), how best to use the diuretics, how to assess diuretic responsiveness as well as resistance remained grey zones until recently in our knowledge. The recent guidelines by the European Society of Cardiology [(3)] as well as another review article [(4)] provide guidance on these key aspects of a commonly used medicine.

What is Congestion?

Congestion is accumulation of extra cellular fluid leading to increased cardiac filling pressures. It is important to estimate the presence of congestion because administration of diuretics in the absence of congestion leads to adverse effects such as renal dysfunction. Congestion can be due to either fluid overload or fluid redistribution and it is in the former group that diuretics are useful.

How should it be assessed?

Estimation of congestion by direct measurement of cardiac filling pressures in the Evaluation Study of Congestive Heart Failure and Pulmonary artery Catheterization Effectiveness study (ESCAPE) was not found to be accurate [(5)]. Currently assessment of systemic congestion is not based on a single parameter but a combination of clinical, laboratory & radiological features [(3)]. Table 1 provides us a clinical framework on how to estimate and grade the severity of systemic congestion.

Table 1: Multiparametric assessment of Congestion in ADHF

<table>
<tr><td></td><td></td><td>1</td><td>2</td><td>3</td><td>4</td></tr>
<tr><td rowspan="4">Clinical</td><td>Orthopnoea</td><td>None</td><td>Mild</td><td>Moderate</td><td>Severe</td></tr>
<tr><td>JVP</td><td>< 8</td><td>08-Oct</td><td>Nov-15</td><td>> 15</td></tr>
<tr><td>Oedema</td><td>None</td><td>1</td><td>2</td><td>3.4</td></tr>
<tr><td>6 min walk test</td><td>> 300</td><td>200-300</td><td>100-200</td><td>< 100</td></tr>
<tr><td>Lab</td><td>NT pro BNP</td><td>< 400</td><td>400-1500</td><td>1500-3000</td><td>> 3000</td></tr>
<tr><td colspan="2" rowspan="2">Chest X-ray</td><td rowspan="2">No congestion</td><td rowspan="2">Cardiomegaly</td><td>Pulmonary congestion</td><td rowspan="2">Interstitial or alveolar oedema</td></tr>
<tr><td>Small pleural effusion</td></tr>
<tr><td colspan="2">Vena cava imaging</td><td rowspan="3">None of the two</td><td colspan="2">One of the two</td><td rowspan="3">Both of the two</td></tr>
<tr><td colspan="2">- Vena cava diameter >2.2 cm</td><td colspan="2">-</td></tr>
<tr><td colspan="2">- Collapsibility < 50%</td><td colspan="2"></td></tr>
<tr><td colspan="2">Lung Ultrasound
Over 28 fields</td><td>< 15 B lines</td><td colspan="2">15-30 B lines</td><td>> 30 B lines</td></tr>
</table>

Tutorial

Which diuretics are to be selected and where do they act?

Diuretics have been used for treatment of symptomatic congestion for many decades. Recent data provide us guidelines as to how to choose the best agent and titrate them [6]. It is fundamental for us to understand the agent and the mechanism of action. Table 2 provides us the basic pharmaceutical properties of the available diuretic agents.

Choice and initial dose of diuretic:

The most common diuretics given in ADHF is a loop diuretic [7]. The dose of a loop diuretic depends upon whether the patient is diuretic naïve or unresponsive. The starting dose of a loop diuretic in those who are naïve is 20-40 mg furosemide intravenous or equivalent. For those who are already on furosemide, starting dose is 1-2 times the dose of the diuretic the patient was on per 24 hours, given intravenously.

How can we monitor the response to diuretics?

The patient is asked to empty the urinary bladder and collecting of urine is started. After 2 hours, urinary sodium of more than 50-70ml/Hour indicates that the patient is responsive to diuretics.

Urinary output of 100-150 ml at the end of 6 hours also indicates that the patient is responsive to diuretics. This is the early phase assessment of diuretic responsiveness. Assessing this is important, as it will allow for correction of the diuretic unresponsiveness [3].

What if the patient is unresponsive to diuretics?

By the end of 24 hours, urine output has to be more than 3 to 4 liters. If it is less than 3 to 4 liters then the diuretic dose has to be doubled every 6 hours until the maximal dose of loop diuretics has been achieved.

In case of unresponsiveness, a step-wise escalation approach is suggested:

Step 1: Thiazide or thiazide like diuretics (Metolazone)

Step 2: Acetazolamide or Amiloride

Step 3: Sodium Glucose Co Transporter 2 inhibitors (SGLT2 inhibitors)

Step 4: Ultrafiltration

Table 2: Diuretics - Properties and Dosage

	Acetazolamide	Loop diuretics	Thiazide like diuretics	Mineralocorticoid Receptor Antagonist
Location of action	Proximal Nephron	Ascending limb of loop of Henle	Early distal convoluted tubule	Late Distal Tubule
Dose	250-375 mg/day	Furosemide	HCTZ / Chlorthalidone	Spironolactone/Eplerenone
		20-40 mg		25 mg
		Torsemide	25 mg	
Loading		5-10 mg		
Maintenance		Furosemide	100-200 mg	25-50 mg
		40-240 mg		
		Torsemide		
		10-20 mg		
Maximum	500 mg X 3/day	Furosemide	100-200 mg	25-50 mg (Cardiology)
		400-600 mg		
		Torsemide		
		200-300 mg		
Half-life (h)	2.5-5.0	Furosemide	HCTZ – 6-15	Eplerenone
		1-5 - 3-0 h	Chlorthalidone 45-60	
		Torsemide		
		3.0 – 6.0 h		
Potency	4%	20-25%	5-8%	2%

What standard measures have to be taken when managing ADHF?

1. Assessment of body weight at admission
2. Guideline directed medical therapy including ACEI, mineralocorticoid receptor antagonist.
3. Estimation - correction of potassium and magnesium deficiencies
4. Salt and water restriction
5. Draining of pleural and ascetic fluid if any, as well as wearing stockings to reduce the leg edema.
6. Physical rehabilitation

Conclusions

Diuretic therapy has been used in acute decompensated heart failure despite the lack of prospective randomized studies. Clinicians need to understand the physiological effects as well as the pharmacokinetics and pharmacodynamics of diuretics to use them the skillfully in acute decompensated heart failure.

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Journal Scan

Extracts from Major Clinical Trials in Cardiology

From the Editorial desk

The management strategy of chronic stable angina is mired in controversy. The best clinical trials suggest that a non-invasive strategy is not inferior to an invasive approach. However it is the preferential attitude of the cardiologist that mostly determines the strategy. The ischemia trial provides more evidence, regarding the choice of therapy.

International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) Trial:

Reynolds et al / Moran et al
American College of Cardiology Presentation Nov 2019

Camici et al.
International Journal of Cardiology 304(2020) 1-4

- Earlier trials comparing a strategy of optimal medical therapy with or without revascularization have not shown that revascularization reduces cardiovascular events in patients with stable ischemic heart disease (SIHD).
- It remains unknown whether a routine invasive approach offers incremental value over a conservative approach with catheterization reserved for failure of medical therapy in patients with moderate or severe ischemia.
- The ISCHEMIA trial was designed to compare an initial invasive or conservative treatment strategy for managing SIHD patients with moderate or severe ischemia on stress testing.
- Five thousand one-hundred seventy-nine participants were randomized.
- Patients with stable ischemic heart disease and moderate to severe ischemia were randomized to routine invasive therapy (n = 2,588) versus medical therapy (n = 2,591).
- In the routine invasive therapy group, subjects underwent coronary angiography and percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) as appropriate.
- In the medical therapy groups, subjects underwent coronary angiography only for failure of medical therapy.
- Inclusion criteria:
  - Moderate to severe ischemia on noninvasive stress testing (nuclear ≥10% ischemia; echo ≥3 segments of ischemia; cardiac magnetic resonance ≥12% ischemia and/or ≥3 segments with ischemia; exercise treadmill test ≥1.5 mm ST depression in ≥2 leads or ≥2 mm ST depression in single lead at <7 METs with angina)
- Exclusion criteria:
  - ≥50% left main stenosis (from blinded computed tomography)
  - Advanced chronic kidney disease (estimated glomerular filtration rate <30 ml/min)
  - Recent myocardial infarction
  - Left ventricular ejection fraction <35%
  - Left main stenosis >50%
  - Unacceptable angina at baseline
  - New York Heart Association class III-IV heart failure
  - Prior PCI or CABG within last year
  - Over the entire follow-up period, cardiac catheterization was performed in 96% of the invasive group vs. 28% of the medical therapy group
  - Over the entire follow-up period, coronary revascularization was performed in 80% of the invasive group vs. 23% of the medical therapy group.

- The primary outcome was cardiovascular death, myocardial infarction, resuscitated cardiac arrest, or hospitalization for unstable angina or heart failure at 3.3 years.
- This occurred in 13.3% of the routine invasive group compared with 15.5% of the medical therapy group (p = 0.34). The findings were the same in multiple subgroups.
- Invasive therapy was associated with harm (~2% absolute increase) within the first 6 months and benefit within 4 years (~2% absolute decrease).
- Secondary outcomes: Cardiovascular death or myocardial infarction: 11.7% of the routine invasive group compared with 13.9% of the medical therapy group (p = 0.21). All-cause death: 6.4% of the routine invasive group compared with 6.5% of the medical therapy group (p = 0.67) Periprocedural myocardial infarction: (invasive/conservative hazard ratio [HR] 2.98, 95% confidence interval [CI] 1.87-4.74). Spontaneous myocardial infarction: (invasive/conservative HR 0.67, 95% CI 0.53-0.83).
- Quality of life outcomes: [Seattle Angina Questionnaire (SAQ) summary score]. SAQ summary score at 12 months for invasive vs. conservative therapy. 4.2 points (95% credible interval 3.3 to 5.1) overall SAQ summary score at 3 months for invasive vs. conservative therapy: 2.9 points (95% credible interval 2.2 to 3.7) overall.
- There was no association between the degree of ischemia and all-cause mortality (p for trend = 0.33).
- There was a weak association between the degree of ischemia and myocardial infarction (p for trend = 0.04).
- There was an association between extent of coronary disease (modified Duke prognostic score) on all-cause mortality (p for trend < 0.001) and myocardial infarction (p for trend < 0.001).
- The invasive vs. conservative relationship on the primary outcome (death or myocardial infarction) was similar regardless of the degree of ischemia (p for interaction = 0.28).
- Routine invasive therapy was associated with harm at 6 months (increase in periprocedural myocardial infarctions) and associated with benefit at 4 years (reduction in spontaneous myocardial infarction).
- These results do not apply to patients with current/recent acute coronary syndrome, highly symptomatic patients, left main stenosis, or left ventricular ejection fraction <35%.
- Severe ischemia on stress testing was associated with myocardial infarction, while severe extent of coronary disease (modified Duke prognostic score) was associated with both mortality and myocardial infarction.
- But the overall lack of benefit for invasive vs. conservative therapy was similar among those with severe ischemia on noninvasive testing and extensive coronary disease.
- The overall interpretation of this trial was negative.
- There were mixed signals with evidence for both harm and benefit. This signals that:

  1) Invasive therapy for stable ischemic heart disease patients needs to be carefully considered in the context of angina burden and background medical therapy, and 2) Likelihood that optimal coronary revascularization can be achieved with low procedural complications.
- Stress imaging was the qualifying test for 75% of patients. To boost enrollment in countries where cardiac imaging is not commonly performed, the trial allowed entry on the basis of an exercise electrocardiogram (ECG). One-quarter of the participants were enrolled on the basis of non-imaging exercise tolerance testing (ETT).
- ETT is the most common stress test used worldwide, and the [American College of Cardiology/American Heart Association] guidelines recommend treadmill testing when you want to do a stress test for those who are able to exercise and have an interpretable baseline ECG," said Hochman.

- Observational studies suggested that, compared to medical treatment, coronary revascularization with percutaneous coronary intervention (PCI) or CABG improved prognosis in patients with extensive myocardial ischemia.

- Recent randomized trials, however, showed a lack of prognostic benefit of myocardial revascularization, but these studies did not include patients at higher risk such as those with extensive obstructive coronary artery disease and severe myocardial ischemia.

- The open-label real-world design and the lack of a sham procedure, however, are major limitations of the trial.

- Placebo effects are known to be larger for invasive than for non-invasive treatments. This bias could have been mitigated by adding a "sham" group as in ORBITA, which documented that this approach is feasible and informative in angina patients.

- The ISCHEMIA trial asked a fundamental question about the practice of cardiology, challenging clinicians and patients about their preferences for invasive management and revascularization, or not.

- The value of an initial anatomical test using CT coronary angiography followed by functional tests, where appropriate, would be to identify subjects with coronary atherosclerosis and stratify them for preventive medical therapy. A major limitation of a CT-guided approach relates to patients with angina but no obstructive CAD. The prevalence and clinical significance of vasomotor disorders in this setting is being assessed in the Coronary Microvascular Function and CT Coronary Angiography (CorCTCA) trial.

- CTCA strategy doubles the number of angiograms and related exposure to ionizing radiation. The results from ISCHEMIA should arrest this trend.

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As the population ages the number of octogenarians on anti-hypertensive therapy increases. The OPTIMISE trial provides new data to help rationalize therapy in this category of patients.

Effect of Antihypertensive Medication Reduction vs Usual Care on Short-Term Blood Pressure Control in Patients with Hypertension Aged 80 Years and Older: The OPTIMISE Randomized Clinical Trial.

Sheppard et al.
JAMA. 2020;323(20):2039-2051.

Key Points in this studies are:-

Question: Among older adults taking multiple antihypertensive medications, is a strategy of antihypertensive medication reduction no inferior to usual care with regard to short-term blood pressure control?

Findings: In this randomized clinical trial that included 569 patients aged 80 years and older, the proportion with systolic blood pressure lower than 150 mm Hg at 12 weeks was 86.4% in the intervention group and 87.7% in the control group (adjusted relative risk, 0.98), a difference that met the noninferiority margin of a relative risk of 0.90.

Meaning: The findings suggest antihypertensive medication reduction can be achieved without substantial change in blood pressure control in some older patients with hypertension.

Importance: Deprescribing of antihypertensive medications is recommended for some older patients with polypharmacy and multimorbidity when the benefits of continued treatment may not outweigh the harms.

Participants, were aged 80 years and older, had systolic blood pressure lower than 150 mm Hg, and were receiving at least 2 antihypertensive medications.

Interventions: Participants were randomized (1:1 ratio) to a strategy of antihypertensive medication reduction (removal of 1 drug [intervention], n = 282) or usual care (control, n = 287), in which no medication changes were mandated.

Results: 534 (93.8%) completed the trial. Overall, 229 (86.4%) patients in the intervention group and 236 (87.7%) patients in the control group had a systolic blood pressure lower than 150 mm Hg at 12 weeks. Mean change in systolic blood pressure was 3.4 mm Hg higher in the intervention group compared with the control group. Twelve (4.3%) participants in the intervention group and 7 (2.4%) in the control group reported at least 1 serious adverse event.

Conclusions and Relevance: Among older patients treated with multiple antihypertensive medications, a strategy of medication reduction, compared with usual care, was non inferior with regard to systolic blood pressure control at 12 weeks. The findings suggest antihypertensive medication reduction in some older patients with hypertension is not associated with substantial change in blood pressure control, although further research is needed to understand long-term clinical outcomes.

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The use of fish oil supplements is widespread in Sri Lanka. However the appropriate dose for preventive effects is as yet undecided. The REDUCE IT trial gives vital data on this aspects of use of fish oil.

REDUCE-IT

Deepak Bhatt et al.
Circulation 2020;141:367-375)

Triglyceride elevation is a potent marker of residual cardiovascular risk in patients with well-controlled low-density lipoprotein cholesterol (LDL-C) on statin therapy, as shown in both randomized statin trials and observational studies.

REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial) addressed this residual risk.

To qualify, patients were required to have fasting triglycerides of ≥135 mg/dL and <500 mg/dL and LDL-C >40 mg/dL and ≤100 mg/dL. Patients were required to be on stable statin therapy for at least 4 weeks with well-controlled LDL-C.

Because of variability in fasting triglyceride levels, baseline was defined as an average of each patient's qualifying triglyceride level and randomization day level; these baseline values ranged from 81 mg/dL to 1401 mg/dL.

Serious treatment-emergent adverse events occurred in 34.4% of participants treated with icosapent ethyl versus 35.7% treated with placebo (P=0.46).

Regarding treatment-emergent gastrointestinal disorders, there was no treatment difference (40.4% versus 42.6%; P=0.21); diarrhea was less frequent with icosapent ethyl versus placebo (10.3% versus 13.0%; P=0.02), constipation was more frequent (7.8% versus 5.1%; P=0.002), dysphagia was more frequent (2.2% versus 1.1%; P=0.02), eructation was more frequent (1.2% versus 0.4%; P=0.008).

Treatment-emergent atrial fibrillation/flutter occurred in 6.6% of the icosapent ethyl group and 4.5% of the placebo group (P=0.01); positively adjudicated end points of atrial fibrillation/flutter requiring hospitalization for 24 or more hours occurred in 3.6% versus 2.9% of participants (P=0.35).

Bleeding treatment-emergent adverse events of any type (exclusive of positively adjudicated hemorrhagic stroke events which were accounted for as trial end points) occurred in 16.7% of the icosapent ethyl group versus 13.6% of the placebo group (P=0.02), with no significant difference in central nervous system or gastrointestinal bleeding.

Serious bleeding adverse events occurred in 3.6% of the icosapent ethyl group versus 3.3% of the placebo group (P=0.77)

The REDUCE-IT trial showed that use of IPE 2 g twice daily was superior to placebo in reducing TGs, CV events, and CV death among patients with high TGs and either known CVD or those at high risk for developing it, and who were already on statin therapy with relatively well-controlled LDL levels.

Exclusion criteria:

- Severe heart failure
- Active severe liver disease
- Glycated hemoglobin level >10.0%
- Planned coronary intervention or surgery
- History of acute or chronic pancreatitis
- Known hypersensitivity to fish, shellfish, or ingredients of IPE or placebo

Cost-effectiveness analysis: The assumed cost of IPE = $4.16/day.

On-treatment EPA levels via IPE correlated with the primary endpoint, key secondary endpoint, and most other CV endpoints. Benefits noted were beyond those that could be explained by degree of TG or other biomarker changes such as LDL cholesterol, HDL, or hs-CRP.

Impact on revascularization: A total of 920 patients underwent coronary revascularization during the trial. Time to coronary revascularization was significantly lower with IPE compared with placebo (11.4% vs. 16.7%, HR 0.66, 95% CI 0.58-0.76, $p < 0.0001$: number needed to treat = 24). Emergent or urgent revascularization: 5.3% vs. 7.8% ($p < 0.0001$); similar benefit for percutaneous coronary intervention and coronary artery bypass grafting.

Case Report

A 42-year-Old Lady with Takayasu Arteritis, Presenting with In-stent re-stenosis

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Abstract

We report a middle-aged lady with Takayasu arteritis, who presented with in stent re-stenosis of her left main coronary artery and was managed with percutaneous coronary intervention with rotational atherectomy. The technically difficult nature of the interventional approach and the use of specialized revascularization techniques to achieve optimum angiographic results are highlighted.

Keywords: In- stent re-stenosis, Takayasu arteritis

Introduction

The introduction of Drug Eluting Stents (DES) has resulted in significant reduction of In-Stent Restenosis (ISR). ISR has become a frequently encountered clinical challenge due to the increase of percutaneous coronary interventions performed in the management of ischemic heart disease. The percentage of ISR depends on the type of DES, the complexity of the lesion and the duration of follow up. The studies have shown that the first-generation stents (sirolimus /paclitaxel) have an ISR rate of 13 – 16 % whereas it's only 5 - 6.3% with the second-generation stents (everolimus / zotarolimus) in five year follow ups [(1,2)]. In comparison to bare metal stents, the ISR reduction rate is about 75% in DES.

The narrowing of the arterial lumen after stent placement is mainly from the arterial damage succeeded by neointimal proliferation. This process is aided by mechanisms such as mechanical factors (stent under expansion, stent fracture), hypersensitivity, biologic factors (overt inflammation, drug resistance) and technical factors (barotrauma outside the stented segment) [(3)]. ISR is technically challenging as usually there's significant hyperplasia with diffuse lesions. The management depends on the complexity of the target lesion. Due to the complexity & possible significant complications, Left Main Coronary artery (LMCA) ISR management with Percutaneous Coronary Intervention (PCI) is technically difficult.

Rotational atherectomy (Rotablation) is a special revascularization device which uses an olive shaped burr coated with microscopic diamond chips in its front hemisphere. The rapidly rotating burr is used to grind the fibro-calcific plaques in to tiny particles which could easily pass through the myocardial capillary bed. This technique is helpful in successful delivery of the angioplasty balloon and the stent which would otherwise be impossible to push through in highly calcified lesions. The literature is scarce in usage of rotablation in ISR management especially with LMCA lesions.

Case Presentation

A 42-year-old lady, who was a diagnosed patient with Takayasu arteritis, had undergone PCI to the LMCA 14 years back (2005) and Coronary Artery Bypass Graft (CABG) 11 years back (2008), presented with worsening exertional angina. She has been on both steroids and a steroid sparing agent (methotrexate) for the control of Takayasu arteritis. Her compliance to drugs and follow-up was satisfactory.

Her transthoracic echocardiogram showed preserved LV and RV functions. She underwent coronary angiography which showed significant LMCA ostial ISR with diffuse calcific plaque. It was decided to go ahead with rotablation followed by PCI.

Case Report

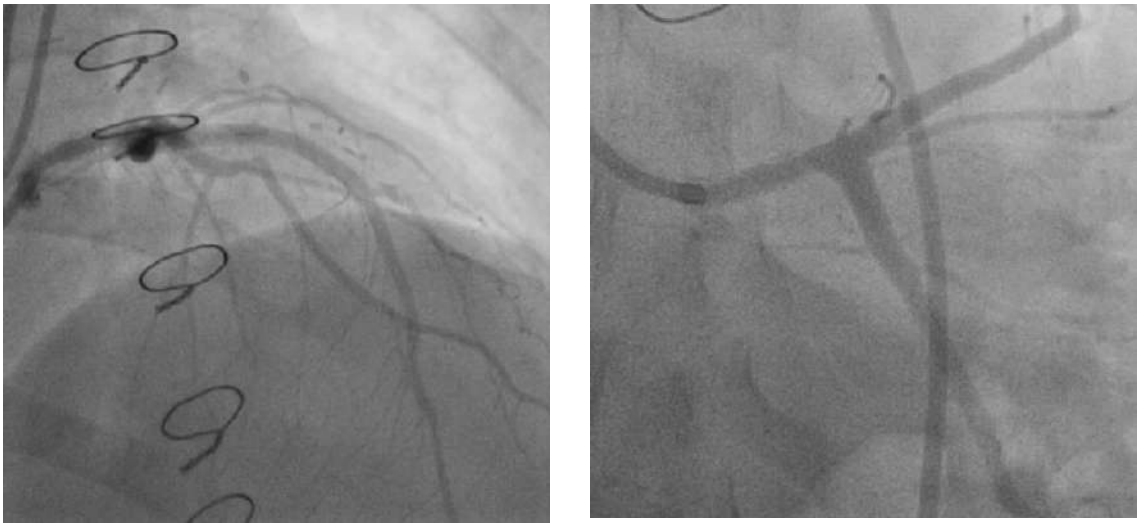

Figure 1: Pre-procedure angiogram of the LMCA showing significant ostial ISR with diffuse calcific plaque.

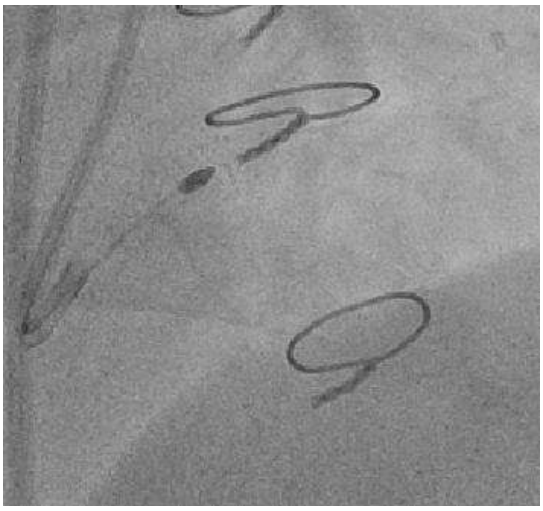

Figure 2: Performing 'Rotational atherectomy' with 1.75 burr size.

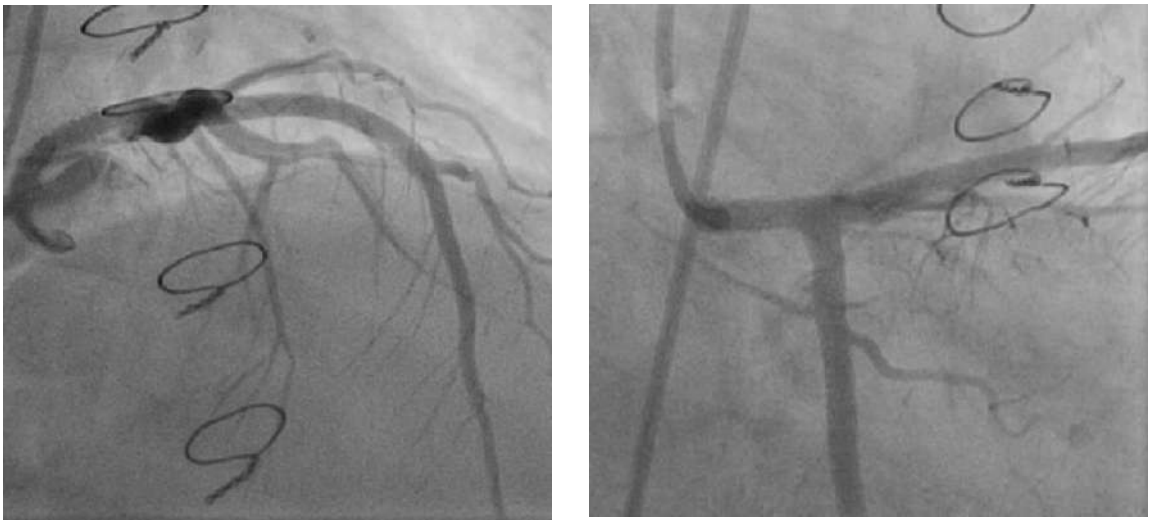

Figure 3: Post procedure angiogram showing excellent stent deployment.

Discussion

LMCA is responsible for at least 75% of blood supply to the left ventricle which explains the significant cardio-vascular risk resulting in a three-year survival rate as low as 37% if left untreated[4]. The treatment of choice for ISR is revascularization with repeat stenting with a newer generation DES, whereas the role of surgery remains uncertain. The clinical outcome has been found to be better with Everolimus Eluting Stents in the management of ISR, when compared to other modalities of treatment[5]. Rotational atherectomy and cutting balloon angioplasty are the two specialized revascularization techniques used here to achieve procedural success which would be technically difficult in ISR, yet useful tools with the availability of expertise.

In this case, the predisposition for ISR is very high with the background of Takayasu arteritis. It is important to achieve and maintain the remission of the inflammatory process in order to minimize the rate of future ISR. In the event of recurrent ISR in a susceptible individual with three or more concentric stents (which could be the predicted outcome in this case), usage of Drug Eluting Balloon Angioplasty would be a reasonable alternative even though this device is not widely available. The recommendations for anti-platelets in ISR remains same as for post stenting population. The priority should be given on proper delivery of post stenting care including optimum drug treatment, management of co-morbid conditions and lifestyle modification which would result in lesser number of ISRs.

Conclusion

PCI is often used over CABG in the management of ISR. Rotational atherectomy is a good tool in appropriate context to achieve proper stent placement and improved outcome. The medical management and the risk factor modification must be given equal priority.

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Case Report

Abnormal Vascular Communication between second Obtuse Marginal branch of Left Circumflex artery and left ventricular cavity

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Abstract

Coronary artery venous (AV) fistula is a rare entity. Mostly AV fistulae drain in to either LV or RV cavity or pulmonary artery. Most of them are congenital in origin though vasculitis is also a known aetiology. Majority are benign and rarely cause clinically significant symptoms. However, some larger AV malformations cause significant coronary steal phenomenon and lead to anigina and ischaemia of the myocardium. Vasodilators will precipitate angina and hypotension in such patients. We report a case of a relatively young patient presenting with acute inferior STEMI and his coronary angiogram showed critical stenosis in right coronary artery and significant AV fistula in second obtuse marginal branch of the left circumflex artery. Percutaneous coronary intervention was done to RCA and subsequent CT coronary angiogram revealed abnormal vascular connection in between circumflex artery and left ventricular cavity. Patient became asymptomatic there after hence no intervention was performed to the AV fistula.

Keywords: Coronary artery venous fistula, circumflex artery, LV cavity

Case report

A 58-year-old male, presented to the emergency treatment unit with burning retrosternal chest pain and mild shortness of breath. He was a diagnosed patient with hypertension and diabetes mellitus. Electrocardiograph showed ST elevations in inferior leads. His cardiac troponin I titer was elevated above normal level. 2D echocardiograph depicted ejection fraction of 50% with inferior and infero lateral wall hypokinesia.

Patient was treated with loading doses of aspirin and clopidogrel. He was treated with 5000 IU of intravenous heparin. He was immediately taken in to the cardiac catheterization laboratory and coronary angiogram performed. There was a 90% long lesion at the mid segment of right coronary artery, which was considered as the culprit vessel (Figure 1).

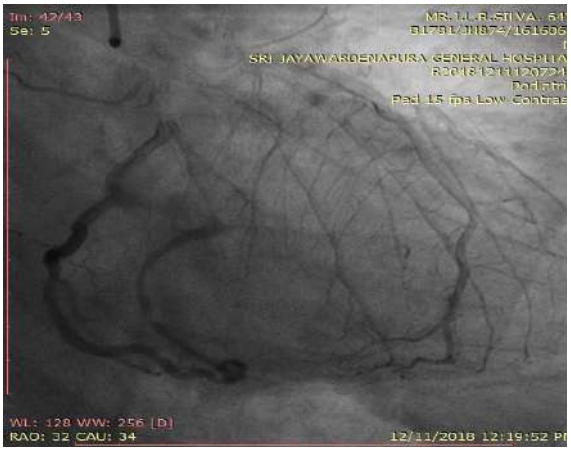

Figure1: Coronary angiogram shows an abnormal coronary AV fistula

In addition, the second obtuse marginal branch of left circumflex artery showed abnormal vascular channel draining in to a cardiac chamber (Figure 2). In addition, there was a 99% stenotic lesion just proximal to the fistula. Primary percutaneous coronary intervention was performed to right coronary artery and patient was commenced on dual antiplatelet treatment.

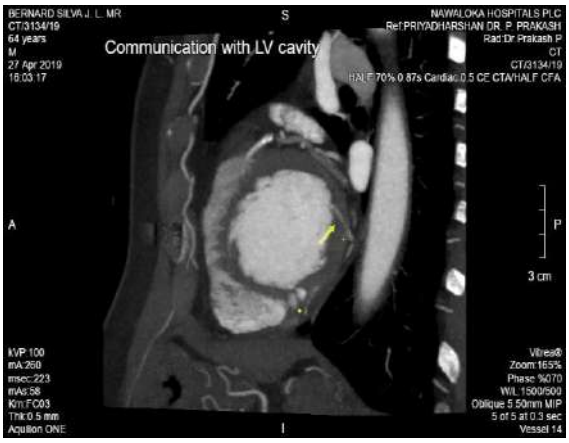

Figure 2: Contrast enhanced cardiac MRI depicted abnormal vascular connection between second obtuse marginal branch and left ventricular cavity.

Later contrast enhanced cardiac MRI depicted abnormal vascular connection between second obtuse marginal branch and left ventricular cavity (Figure 3). However, there was a flow limiting 99% stenosis proximal to this vascular connection.

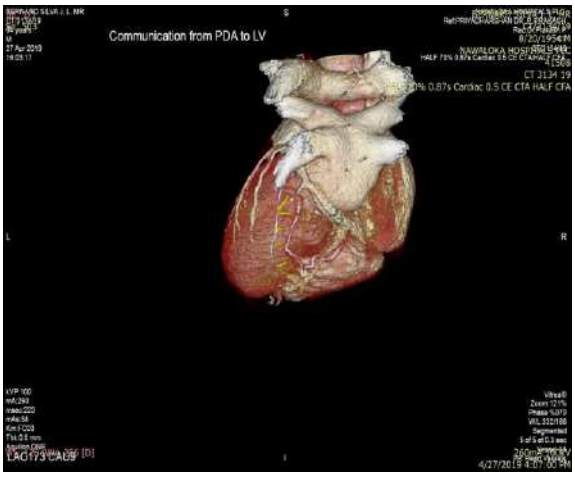

Figure 3: Later contrast enhanced cardiac MRI depicted abnormal vascular connection between second obtuse marginal branch and left ventricular cavity.

Since patient did not show significant clinical symptoms of coronary artery steal syndrome and the abnormal coronary vascular connection was proximally occluded with atherosclerotic plaque, we decided not to perform any intervention to occlude abnormal vascular connection at present. However, the patient will be closely monitored at cardiology clinic for occurrence of new symptoms or signs and intervene accordingly in the future.

Discussion:

Coronary artery fistula is a rare entity. Most of the reported cases were congenital in origin. However a large coronary artery fistula can cause coronary artery steal syndrome and myocardial ischaemia. This can further precipitate cardiac failure. Surgical repair or coil embolization is indicated for haemodynamically significant larger coronary fistulae. Vasodilators such as nitrates are known to precipitate coronary artery steal syndrome hence causing myocardial ischaemia and significant hypotension. Most of the times coronary A V fistulas do not need any interventions other than avoiding precipitating factors of steal syndrome.

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Case Report

Malignant Anomalous Right Coronary Artery

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Abstract

We report a case of a "malignant" anomalous origin of the right coronary artery (MRCA) in a 51 year old man with disabling symptoms of refractory angina and intolerance to medical therapy. This report covers the clinical presentation, diagnostic work up and surgical management. "Malignant" anomalous origin of the right coronary artery (MRCA) runs from the left Sinus of Valsalva with an inter-arterial course, between the aorta and the main pulmonary artery. Following confirmation of the diagnosis with a CT coronary angiography, the patient underwent a successful right coronary artery (RCA) bypass with a vein graft to the posterior descending artery (PDA) which provided sustained symptomatic benefit off anti-anginal therapy.

Keywords: MRCA (Malignant anomalous origin of the right coronary artery), RCA (Right coronary artery), PDA (Posterior descending artery), LV (Left ventricle), Percutaneous coronary intervention (PCI), Coronary artery bypass surgery (CABG)

Introduction

Congenital coronary artery anomalies have an incidence of 1–2 % [(1)]. Anomalous origin of the right coronary artery (RCA) is rare, with a prevalence of approximately 0.25% and reported incidence of less than 1% [(1)]. It can be classified based on the anomalous origin, course & termination and prognostic implications (i.e. presence or absence of hemodynamic significance).

RCA following an anomalous origin from the left sinus of valsalva or from the aortic wall above the sinus of valsalva [(2)] can take an anomalous inter-arterial (between the pulmonary artery and aorta), retro aortic, prepulmonic or septal (subpulmonic) course. The most common course being the inter-arterial course and this variant has been called "malignant" anomalous RCA (MRCA).

Although the patients with MRCA may remain asymptomatic, they may present with angina pectoris, myocardial infarction, syncope or even asymptomatic sudden cardiac death in approximately 25-40% cases and/or physical exertion-related sudden death in approximately 50% cases in the absence of atherosclerosis [(1)]. The other anomalies of RCA origin include those from the pulmonary trunk, the distal ascending aorta, and the left main coronary artery [(1)] have been mentioned as well.

Case

A 51-year-old security guard of Maori heritage had multiple hospitalizations due to unstable angina. He had a five year history of progressively worsening symptoms of angina and intolerance to multiple anti-anginal agents including atenolol, metoprolol, diltiazem, amlodipine and oral nitrates. He therefore required repetitive alterations in medical therapy and adjustment in medication dose. He had no history of dyspnea on exertion, palpitations, pre-syncope or syncope.

His risk factors for coronary artery disease were hypertension controlled on telmisartan, impaired fasting glucose tolerance, obesity (BMI 36), dyslipidaemia, a prior 20 pack per year smoking history and a family history of coronary artery disease. He denied cocaine or other illicit drug use.

His echocardiogram showed normal LV size with moderate LV hypertrophy and normal LV systolic function without any segmental wall motion abnormalities. He underwent an exercise myocardial SPECT scan and dobutamine stress echocardiogram as well. During both studies he experienced non-limiting chest tightness without any ECG evidence of myocardial ischaemia and segmental LV perfusion abnormality.

Coronary angiogram did not show any atherosclerotic disease in the left main, left anterior descending, and left circumflex arteries.

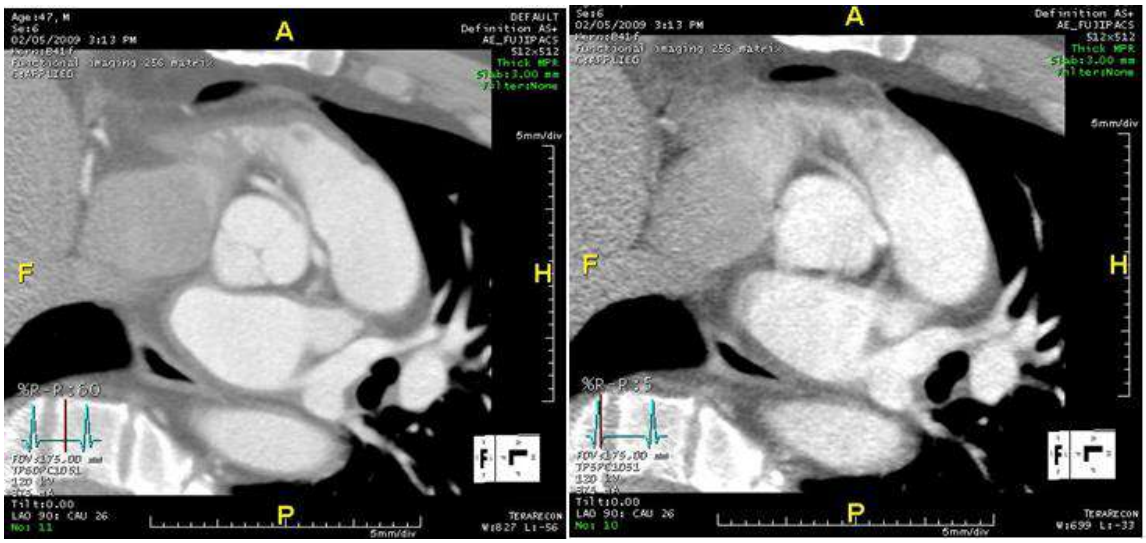

Figure: 51 year old man with a "malignant" anomalous origin of the right coronary artery (MRCA). CT coronary angiography shows RCA originates from the left coronary sinus, slight narrowing of its orifice and cyclic compression as it courses between the aortic root and main pulmonary artery

The origin of the RCA, however, could not be engaged, preventing selective visualization. An aortogram showed anomalous origin of RCA from the left coronary sinus without any obstructive lesion and an LV angiogram showed normal LV systolic function.

Diagnosis was further confirmed with a CT coronary angiogram which revealed co-dominant anomalous RCA originating from the left coronary sinus with slight narrowing of its orifice and cyclic compression as it coursed between the aortic root and main pulmonary artery, providing an example of a classic malignant RCA anomaly without significant atherosclerotic disease.

He therefore was referred for elective CABG. During surgery, the anomalous origin, ostial narrowing and course of the RCA without any significant atherosclerotic disease as seen on the CT coronary angiogram were confirmed. He received a bypass vein graft to the PDA of the RCA. During surgery he required ionotropic support and temporary atrial pacemaker implant. He was transferred to the ICU post operatively.

In ICU he was weaned off the ionotropes, temporary atrial pacemaker explanted and was extubated within 24 hours without incident. His recovery was uneventful and was discharged on day 10 in a stable state with no symptoms of angina on medical therapy with aspirin 100mg, atorvastatin 40mg and metoprolol 25mg twice daily.

He had a clinic review at 6 weeks following successful CABG and remained asymptomatic from angina with no restrictions on physical activity. He was taken off all anti-anginal therapy and since then he has had no recurrence of angina and further hospitalization.

Discussion

"Malignant" anomalous right coronary artery (MRCA) is infrequent and has an incidence of 0.03 - 0.17% among patients undergoing coronary angiography [(3)].

The proposed mechanism of myocardial ischemia in patients with anomalous RCA is mainly dynamic and not atherosclerotic plaques. Various possible mechanisms of obstruction to the blood flow in patients with anomalous RCA are a narrowing of a slit-like small coronary orifice, stretching of intramural proximal segment of the RCA within the aortic wall, compression of RCA between ascending aorta and pulmonary artery, stretching of the RCA with aortic and pulmonary artery distension, kinking and bending of the RCA and spasm of the proximal portion of the RCA [(1)].

Autopsy studies reported diffuse patchy necrosis and fibrosis of myocardium suggesting recurrent events of small myocardial infarctions [(2)].

A proposed mechanism of sudden death during physical exertion is the cyclic compression of MRCA as it courses between the aorta and the pulmonary artery trunk, which may obstruct the

blood flow leading to distal ischemia, sustained ventricular tachycardia and fibrillation arising from an unstable myocardium[1,2]. A proposed mechanism for syncope is ischemia of the sinus node, leading to bradycardia.

Conventional coronary angiography is the gold standard for the assessment of coronary atherosclerotic disease and has an added advantage with its interventional capability. It can identify the anomalous origin of the coronary artery but the course of the anomalous artery and the relationship to the right ventricular outflow tract can be difficult to determine. CT coronary angiogram can be helpful for the diagnosis of coronary anomalies especially by detecting the origin and course of coronary arteries and their relationship to other structures [4].

The management strategy for MRCA remains controversial. The original problem for this congenital anomaly cannot be possibly treated by medical therapy, although the literature does describe some benefits of medical therapy with nitrates, beta or calcium channel blockers.

Percutaneous coronary intervention (PCI) in anomalous RCA can be technically difficult and challenging, as it requires coronary angiographic detection of its anatomic site and selective cannulation which may not be easy. Any blind coronary angiographic procedure will not only increase the duration of the procedure, dosage of the contrast agent and duration of radiation exposure but it can also increase the risk of procedure-related complications such as coronary artery dissection or aortic dissection. Although PCI is advocated in a few case reports with feasible short-term results in selected cases [5], this might not always be a suitable strategy for MRCA as this cannot effectively treat complex ostial issues, long course and its cyclic compression between the aorta and the pulmonary artery trunk.

The 2008 ACC/AHA guidelines for the management of adults with congenital heart disease recommends surgical coronary revascularization in MRCA patients with evidence of ischaemia (class I recommendation, level of evidence B) [6].

Because it has significant hemodynamic consequences and has a high correlation with risk of asymptomatic sudden death, most of the research and studies supports definitive surgical coronary revascularization in all cases.

The different surgical techniques available include CABG, re-implantation of the coronary ostia and unroofing of the coronary artery. The correct surgical repair depends on precise determination of the anatomy and the mechanism of ischemia. The preferred approach by many surgeons is CABG with a vein graft or an internal mammary artery graft. The advantages of CABG with vein graft to RCA over the right internal mammary artery graft to RCA lies in the sparing of the right internal mammary artery as a conduit in a young adult who may develop coronary artery disease (CAD) later.

Conclusion

Our case report highlights the importance of recognition of symptomatic malignant anomalous origin of the right coronary artery (MRCA) and its correct management based on precise determination of anatomy and mechanism of ischaemia.

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Case Report

Spontaneous Coronary Artery Dissection: Two different cases with a typical and an atypical presentation

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Abstract

Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome and sudden cardiac death. It is more common in younger females without major risk factors for obstructive coronary artery disease. In most cases, an associated predisposing arterial disease or cause is identified such as connective tissue disease, oral contraception or postpartum state. Coronary angiography remains the cornerstone of diagnosis. Based on the clinical characteristics, treatment should be individualized to Conservative approach or mechanical revascularization. The present two cases report a young female who presented with an anterior STEMI and a young male who was admitted with a left ventricular thrombus. Coronary angiogram of both cases revealed spontaneous coronary artery dissection in the left anterior descending artery.

Keywords: Spontaneous dissection, OCT, IVUS

Introduction

Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome and sudden cardiac death. In the general population, it accounts for 0.1 - 4% of acute coronary syndrome. There is a non-traumatic and non-iatrogenic separation of the coronary arterial wall leading to distal flow limitation. The clinical presentation of this complication depends on the flow limiting severity of the coronary artery dissection and ranges from acute coronary syndrome to sudden cardiac death.

It is more common in young adults, especially in women without conventional risk factors for coronary heart disease. In most cases, an associated predisposing arterial disease or cause is identified. Potential predisposing factors include fibromuscular dysplasia (FMD), postpartum status, multiparity (>4 births), connective tissue disorders such as Marfan syndrome or Ehlers Danlos type 1V, systemic inflammatory conditions such as systemic lupus erythematosus or Polyarteritis nodosa and hormonal therapy. Precipitating stressors provoking acute spontaneous coronary artery dissection event (especially on the background of predisposing arteriopathy) include intense exercise or emotional stress, labor and delivery, recreational drugs and aggressive hormonal therapy. However, up to 20% of cases are identified as idiopathic.

Case presentation

Patient No1: A 36-year-old woman presented with an acute onset severe retrosternal pain, radiating to the left arm and associated with nausea, vomiting. She had no history of hypertension, diabetes mellitus, dyslipidemia, smoking, familial heart disease or any other systemic illness. She was married with no children. She had been taking combined oral contraceptive pills (OCP) for 6 months duration. Physical examination was unremarkable. The electrocardiogram (ECG) revealed 2 mm ST segment elevation in anterolateral leads (V2-V6, L1, aVL leads). She had elevated troponin levels and apical and anteroseptal hypokinesia of left ventricle. An ejection fraction of 40-45% was displayed on the echocardiography.

Her initial treatment was aspirin, clopidogrel and atorvastatin followed by coronary angiography due to ongoing chest pain. The angiography displayed a type 1 spontaneous dissection of the left anterior descending artery (LAD), involving the middle portion of the artery. She was anticoagulated with intravenous heparin and primary percutaneous intervention was carried out using an appropriate drug-eluting stent.

Two years later she successfully completed her pregnancy and delivered a baby girl without any cardiac complications.

Case Report

Patient No 2: A 22-year-old young male presented with atypical chest pain of 3 days. His ECG showed nonspecific T wave inversion in lead V1 to V4. His troponin was marginally positive. Initial TTE showed anteroseptal hypokinesia and the ejection fraction was 55%. In addition, there was a large fragile echogenic mass attached to the LV apex, measuring 30x10 mm (Figure 2). He was immediately referred to the cardio thoracic surgeon for excision of the mass in order to prevent embolization and had an uneventful recovery following surgery. Surprisingly, the histological features of the mass was suggestive of a fibrin clot. He was treated with oral anticoagulation.

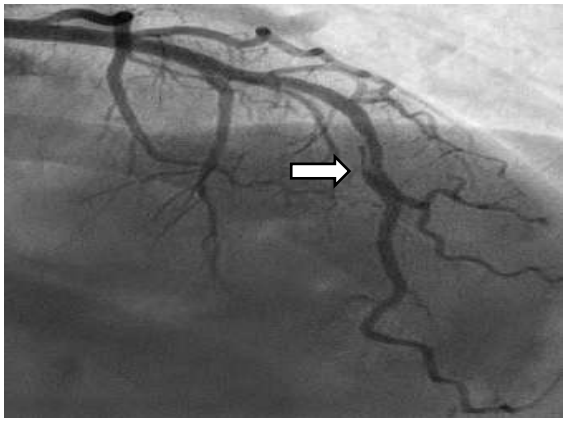

Figure 1: Type A coronary artery dissection in mid LAD

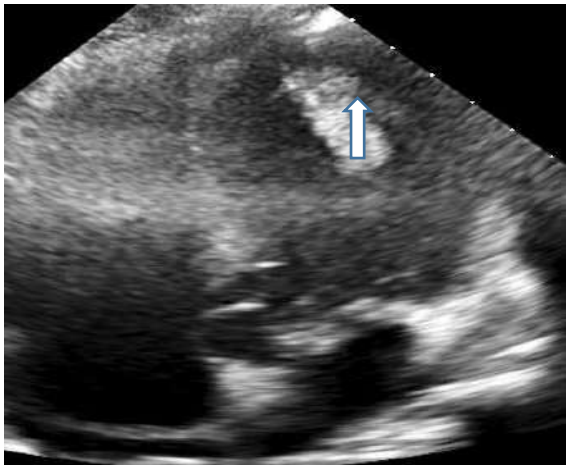

Figure 2: Left ventricular Mass 30 x 10 mm

Thrombophilia screening was performed to rule out hypercoagulability disorders and his lupus anticoagulation assay, anti-thrombin III assay, and genetic mutation studies were negative. Finally, the decision was made to perform coronary angiogram to rule out any coronary pathologies as a cause of the LV thrombus. His coronary angiogram showed a spiral dissection of left anterior descending artery (Figure 3) which was managed conservatively.

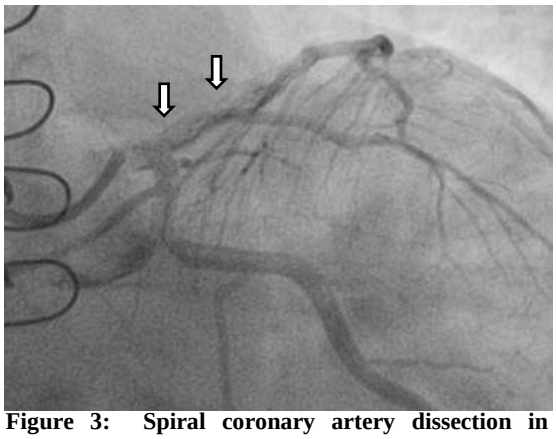

Figure 3: Spiral coronary artery dissection in proximal LAD

Discussion

SCAD is an important cause of acute coronary syndrome, especially in young females which is responsible for up to 25% of all ACS cases in women <50 years of age [(1)]. The underlying mechanism of non-atherosclerotic spontaneous CAD is a separation of intima and media forming a false lumen with an intramural haematoma. The trigger is thought to be either an intimal tear or bleeding from the vasa vasorum, with intramedial haemorrhage. Pressure-driven expansion of the false lumen by the enlarging hematoma causes distal flow limitation of the true lumen leading to myocardial ischemia [(1-4)]. SCAD should be distinguished from dissection caused by plaque rupture in patients with atherosclerosis or catheter-induced iatrogenic dissections. Patients with SCAD have fragile arterial walls with no atheroma or calcification to limit propagation resulting in extensive dissection length. Therefore, cases with SCAD will often have more extensive dissections.

Most patients presenting with SCAD typically do not have risk factors for coronary artery disease but a potential predisposing arterial disease association can be identified. There is a strong association with fibromuscular dysplasia, emotional stress, physiologic stress, and stimulant use. A minority of cases are associated with oral contraceptive pills and pregnancy [1,2,5,6]. Patients with SCAD usually present with symptoms of acute myocardial infarction. 25% - 50% of them present with STEMI and rest with NSTEMI and unstable angina. Life-threatening arrhythmias and sudden cardiac death are reported as early complications. Two largest case series have shown that Coronary angiography remains the cornerstone of diagnosis of SCAD.

The observed coronary angiography findings can be classified into three types. In type 1- there is often contrast staining of the arterial wall with the appearance of a double lumen. Type 2- is diffuse long smooth tubular lesions (due to intramural haematoma) with no visible dissection plane. Lesions are typical >20 mm in length and usually, there is an abrupt change in vessel diameter between normal and diseased segments. There is no response to intracoronary nitrates and there are no atherosclerotic lesions in other coronary segments [1,2]. Type 3 - is multi focal tubular lesions due to intramural haematomas that mimics atherosclerosis, but non-affected coronary artery segments appear smooth and disease-free on angiography. Intravascular imaging is required to make the diagnosis.

At the time of coronary angiography, most patients had only one coronary artery involvement (80%) but multivessel involvement is not rare. LAD was the most frequently affected vessel (40-70%) [1,2]. The most commonly observed angiographic type was 2 (67%).

The treatment of acute MI subsequent to coronary dissection is controversial as clinical trials are lacking due to its low prevalence. Conservative, percutaneous, and surgical management options have all been explored but conservative management is preferred in stable patients with TIMI grade 3 flow as most dissected segments tend to heal spontaneously.

Dual antiplatelet agents, statins, and heparin are used in the initial management to preserve patency of the true lumen and prevent thrombotic occlusion.

Long-term aspirin, and one year of clopidogrel, beta blocker with the addition of statins in patients with dyslipidemia are used in long-term management. Beta blockers are associated with a lower risk of recurrent SCAD. Glycoprotein IIb/ IIIa inhibitors have also been used without complications. However, these agents could potentially delay the healing of the intramural haematoma and lead to dissection extension. Thrombolytic agents should not be used as they can worsen cardiac outcomes due to the same effect.

Revascularization with PCI or CABG should be considered for the patients having symptoms of ongoing ischaemia or haemodynamic compromise [2]. PCI is the preferred re-vascularization strategy in the acute setting but is associated with significant challenges and has reported success rates of <50%. Technical difficulties include negotiating the guidewire into the true lumen, dissection or haematoma extension and side branch occlusion. Stent placement can result in haematoma propagation and loss of vessel flow. Coronary angiography provides poor visualization of intramural hematoma, and intravascular imaging with OCT (Optical Coherence Tomography) or IVUS (Intra vascular Ultrasound) is recommended in all PCI cases. OCT has a superior resolution to IVUS: Additional advantages include that it can confirm the guidewire position in the true lumen, visualize the site of intramural as well as the intimal tear, facilitate appropriate vessel sizing and confirm stent apposition.

CABG is considered for patients with left main stem dissections or when PCI has been unsuccessful or is not technically feasible [2,4,6]. Follow-up studies with angiography have shown high rates of graft occlusion, possibly due to competitive flow in the native vessel or technical difficulties with distal graft anastomosis.

Collectively, Shaw, *et al* and Tweet et al reports suggest excellent in-hospital and long-term survival, with a significant risk of future SCAD events observed in 13% - 17% patients in long-term follow-up. Therefore, patients should be warned about the risks of SCAD recurrence. At present, there is no effective treatment to reduce the long-term risk.

Conclusion

SCAD is a rare entity but should always be considered in the differential diagnosis of chest pain, especially in younger females. Multiple precipitating factors are identified including OCP. Clinical presentation can vary from ACS to sudden cardiac death. Diagnosis is usually made at the time of coronary angiography. Therapy has to be individualized and mainly depend on the hemodynamic status of the patient as well as the distal TIMI flow. Conservative approach is preferred in stable patients whereas mechanical revascularization with either PCI or CABG, although there are technical challenges and limited success rate, should be considered to treat patients with ongoing ischemia in the acute state.

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Case Report

An Unexpected Complication of TAVR requiring entire Paradoxical approach in treatment

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Abstract

Unmasking of Dynamic left ventricular out flow obstruction (DLVOT) is a known complication following surgical aortic valve replacement (SAVR) which was established therapy for tight aortic stenosis prior to the introduction of Transcatheter aortic valve replacement (TAVR). DLVOT is not an infrequent phenomenon after TAVR that may adversely affect outcome. We present a case report of an elderly lady who underwent TAVR complicated with valve migration requiring a valve in valve redeployment and developing dynamic left ventricular out flow obstruction soon after the procedure who was successfully managed despite ensuing complications.

Keywords: DLVOT, TAVR,

Introduction

Dynamic left ventricular outflow tract obstruction (DLVOT) is a condition usually present in patients with hypertrophic cardiomyopathy, but this phenomenon can also be less commonly seen in other conditions including hypotension, catecholamine therapy, anaesthesia, septal anomaly and following valve replacement surgery [(1)]. This phenomenon creates a precarious situation with heamodynamic compromise which can cause confusion as to how to manage the complicated clinical situation where corrective therapy tends worsens the clinical state. The ensuing complications tend to increase in-hospital morbidity as well as mortality but can be salvaged if detected and intervened in a timely manner [(2)]. Aortic valve surgeries have been documented to be complicated with this phenomena [(3)] and with the advent and success of transcatheter aortic valve replacement (TAVR) it's not surprising to note similar cases emerging in documented literature [(4)]. We present a case report of an elderly lady who underwent TAVR complicated with valve migration requiring a valve in valve redeployment developed dynamic left ventricular outflow tract obstruction soon after the procedure and was successfully managed despite ensuing complications.

Case report

A 70-year-old South Asian lady with progressive shortness breath resulting in New York Heart Association class III level of dyspnea and with a history of recurrent presyncopal episodes over several months was investigated and diagnosed to have severe aortic stenosis.

Her trans thoracic 2D Echocardiogram (TTE) revealed calcific tight aortic stenosis with an aortic valve area of only 0.45cm^2 with a maximum pressure gradient of 147mmHg and a mean pressure gradient 75mmHg along with a velocity of 605cm/s across the valve. She was also noted to have grade I aortic regurgitation. In view of the mildly impaired left ventricular (LV) function with an ejection fraction of 50% it was concluded that she fulfilled the criteria for severe aortic stenosis. Remaining valves were morphologically normal and the left ventricle showed concentric hypertrophy (LVH), with the intra-ventricular septum measuring 16mm and the posterior wall measuring 15mm. She underwent comprehensive evaluation including review by the heart team at our tertiary care hospital. When her risk for surgery was calculated with established scoring systems including STS and EURO II she only achieved a score of 1.38 and 1.11 respectively which classified her risk as mild. An initial surgical option was presented to the patient. However non-consent from both patient and family alike along with her symptomatic state prompted the heart team to consider her as a TAVR candidate. She was evaluated accordingly.

Her coronary angiogram was normal. Computed tomographic aortogram was done and based on the measurements of native aortic valve and the root dimensions, the heart team decided to implant a self-expandable 26mm size Medtronic CoreValve™ Evolute™ R-26 TAVI valve for this patient. As her right femoral access was tortuous compared to her left, it was decided to insert the TAVI delivery system along the left femoral artery.

Further inspection of the CT scans revealed a septal bulge and considering the anatomy the TAVR team anticipated potential challenges they may face including placing of the device. A re-evaluation with echo enhanced with Doppler assessment failed to elicit a LVOT pressure gradient despite the septal anomaly.

TVAR was performed under general anesthesia with Trans-esophageal echocardiographic (TOE) guidance. Initial heamodynamic parameters revealed an aortic systolic pressure of 91 mmHg and a LVOT pressure of 221 mmHg giving a 130 mmHg pressure gradient across the stenotic Aortic valve. There was no pressure gradient across LVOT (Left Ventricular end diastolic pressure LVEDP 19mmHg). A self-expandable 26mm Medtronic CoreValve™ Evolute™ R-26 was placed across the native stenosed aortic valve under fluoroscopic guidance after initial predilation with an Osypka 16mm x 4cm balloon. After confirming TAVI valve alignment and coaxiality using multiple fluoroscopic injections and angulations the valve was deployed under rapid pacing at a rate of 120 beats per minute. Immediate post procedure fluoroscopy revealed the deployed TAVI valve had migrated above the annular level in to the most proximal ascending aorta. The septal bulge was considered the culprit cause and the operators decided to implant a second TAVI valve with similar characteristics. While keeping the initially deployed valve snared in place using a 35x120mm single loop goose neck snare the second valve was placed a further few millimeter down into the LVOT in view of the septal bulge while also ensuring the overlap of the first valve. Following deployment of the second valve, fluoroscopic examination revealed a good overlap of both valves as well as a good seating position of 2nd valve across the native aortic valve. Patent coronary perfusion was also demonstrated. Post procedure, the following parameters were recorded:

Aortic systolic pressure 90mmHg and that of LVOT 107mmHg creating a 30mmHg pressure gradient from LVOT to aorta across two TAVI valves (LVEDP 11mmHg).

Final contrast injection showed mild AR with well aligned TAVI valve with preserved coronary perfusion. Based on the outcome and hemodynamics the procedure was considered successful.

Two hours post procedure while in ICU recovery, the patient's blood pressure started dropping. Inotropic support was deemed necessary and a decision was taken to initiate moderate to high doses of dobutamine and noradrenaline together. However failing to sufficiently stabilize the blood pressure an adrenaline infusion was also started. A decision was taken to supplement the blood pressure by inserting an intra-aortic Balloon Pump (IABP). Patient's haemodynamic parameters were: blood pressure of 88/45 mmHg and heart rate of 123beats per minute with variations in time. Alternate causes were excluded with bedside assessment with focused echo to exclude tamponade, electrocardiogram (ECG), chest x-ray, and full blood count including hemoglobin, basic haematological assays and biochemical assays for serum electrolytes, liver and renal functions were all carried out and were found to be within acceptable reference ranges or normal.

In view of the complicated TAVR procedure a comprehensive TTE was done focusing on the implanted valves. The 2nd valve struts were seen at the distal LVOT and a dynamic LVOT pressure gradient ranging from 48 to 91mmHg with a beat to beat variation was observed (Figure 1). TOE revealed both TAVI valves to be in situ, 1st valve at proximal ascending aorta with a few millimeters overlap with the 2nd TAVI valve struts. Both valve cusps were functional and the 2nd TAVI valve placed on the native aortic valve annulus was seen protruding few millimeters into the distal LVOT. Additionally during cardiac cycle, it was noted that the 2nd TAVI valve was compressed by the LVOT bulge causing conformational change of shape from circular during diastole to elliptical in systole. Turbulence across the LVOT was also noted by the color doppler. Very high dynamic LVOT pressure gradients were observed, the maximum being 109mmHg with beat to beat variation (Figure 1).

Based on the imaging findings and correlating the clinical picture, dynamic LVOT obstruction was diagnosed.

Following a cardiac team MDT evaluation, a decision was taken to manage the situation medically with adequate hydration and cessation of exacerbating factors including IABP and tailing off of inotropic support sequentially.

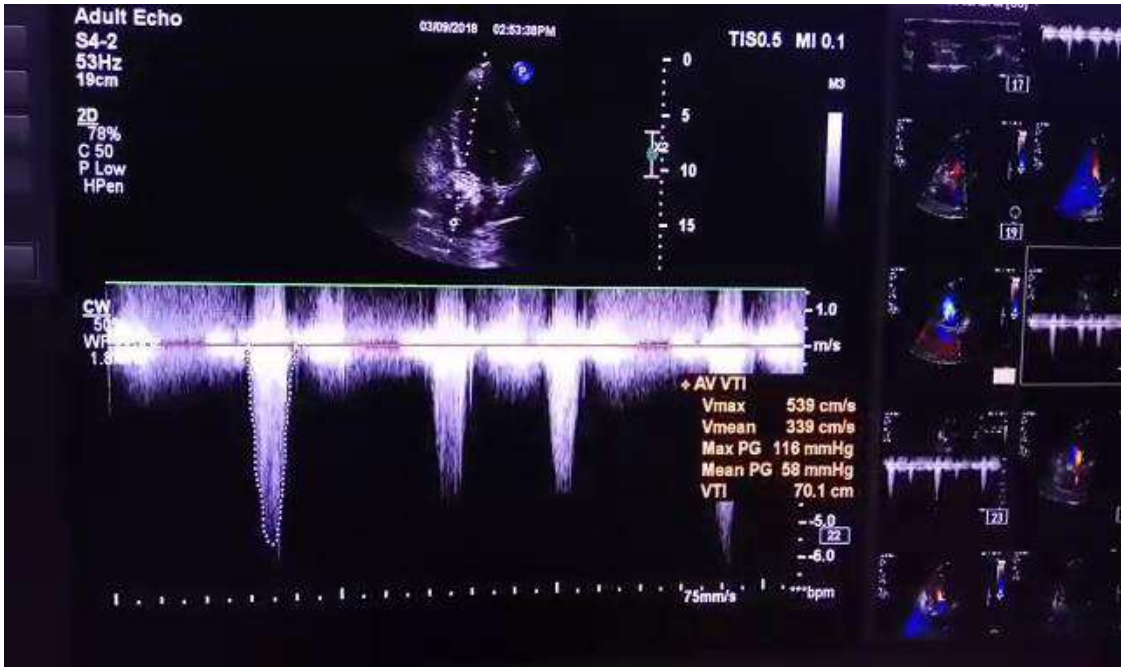

Figure 1

The patient was extubated by day 5 of the procedure and was discharged from the hospital when she was back to her normal health at post procedure day 9. TTE prior to discharge revealed unchanged left ventricular systolic functions (EF 50 - 55%), maximum pressure gradient at aortic valve being 16 mmHg (Aortic valve area 1.78 cm^2) and peak LVOT pressure gradient of 32 mmHg.

Discussion

Dynamic LVOT obstruction following aortic valve intervention either due to surgical valve replacement or TAVR has been documented in literature [5,6]. It's also suggested that sometimes the procedures themselves unmask the already present DLVOT obstruction rather than being the attributable cause [6]. The concept is, severe aortic stenosis when present will prevent DLVOT from manifesting itself by virtue of the high left ventricular pressures needed to overcome the aortic stenosis.

Thus even when the risk factors for dynamic LVOT obstruction are present DLVOT will remain masked. Following valve intervention the LV intra cavitary pressure drops and the hypertrophied LV forcefully contracts against unmasked LVOT obstruction resulting in high pressure gradients across LVOT.

This can be severe enough to cause haemodynamic compromise by reducing the stroke volume [2]. This phenomena can further be worsened when patient has tachycardia and low volume status as the LV filling is impaired. The possible aetiological factors that unmask the DLVOT are many and included general anaesthesia, hypovolaemia, having unfavorable anatomy- i.e. sigmoid shaped intraventricular septum [1]. It's not surprising that most patients undergoing cardiac surgery or complex cardiac intervention such as TAVR by virtue of preparation and induction will be subjected to these factors favoring DLVOT to express itself. Our patient had most of the mentioned risk factors including the unfavourable septal anatomy, which in hindsight should have alerted the cardiac team to be expectant of this potential complication.

Additionally in the absence of an established diagnosis of DLVOT obstruction the management of the haemodynamic compromised state can be a challenging and formidable experience to the managing ICU team.

Though fluid resuscitation maybe the first step in the management, an otherwise incognizant team will initiate inotropes in successive incremental manner to achieve an acceptable blood pressure according to usual protocols.

This will cause the patients to respond poorly if not detrimentally to the initiated treatment. Even IABP can have a counterproductive outcome. Both tend to increase acceleration of the blood jet across the LVOT and aggravate the obstruction and in doing so cause hypotension [7]. Though appearing counter intuitive in a state of cardiogenic shock, withdrawal of inotropic support and IABP and initiation of beta blockers with adequate hydration should be the initial approach in stabilizing the blood pressure in this case scenario. Management beyond combining beta blockers and hydration do exist and include utilization of alpha-adrenergic agonists. The suggested mechanism is by increasing the arterial impedance which then reduces the LV ejection velocity which in turn increase LV volume, this combination is presumed to reduce the dynamic LVOT obstruction[8]. Another mechanism is alcohol septal ablation which is suggested as a salvage method helping to recover from a non-responding DLVOT[6]. Our initial therapeutic path of management gave rise to the alarming situation of worsening haemodynamic instability highlighting the need for greater awareness of this uncommon condition among both intensivists and cardiologists alike.

Another factor is the final state of the TAVR valve, which due to its positioning on the thickened part of the IVS results in a structural conformational change of the inner orifice of the valve from circular to elliptical shape during systole of the cardiac cycle. We are unsure if this was also a factor contributing towards DLVOT obstruction. Very little is documented in literature to support or negate this assumption.

Conclusion

DLVOT is not an infrequent phenomenon. Identifying patient and procedural risk factors that possibly unmask DLVOT will help identify potential candidates who may develop DLVOT. Regardless, managing DLVOT can be both confusing and challenging to an otherwise non-suspecting team and can result in high morbidity and mortality if not recognized and diagnosed immediately.

Contrary to normal recommended protocols, prompt hydration and beta blockers can be lifesaving.

Considering that TAVR remains a modality of therapy in moderate to high risk patients, greater emphasis should go into the identification of potential post procedural complications like DLVOT which may adversely affect the outcome. This case highlights the need for better patient selection, overall vigilance, prompt early anticipation and action when DLVOT occurs.

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Case Report

Bedside basics to the rescue: Acute pancreatitis masquerading as an acute coronary event

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Abstract

Acute Pancreatitis has a reputation for being a great mimicker in internal medicine. Myocardial infarction (MI) in this setting is not only a diagnostic challenge but a therapeutic dilemma too. Standard MI management has the capacity to lead to life threatening complications with concomitant acute pancreatitis.

69-year-old presented with retrosternal atypical chest pain of 1-hour duration. Because of coronary risk factors and the second EKG showing dynamic anterior ST elevation he was rushed to catheterization laboratory with dual antiplatelet loading. Angiography revealed stable triple vessel disease with TIMI 3 distal run off. Portable ECHO showed no regional defects. He developed epigastric guarding and it was decided to arrange for urgent investigations including abdominal scans. Troponin I was 0.765ng/ml (Reference range <0.06). USS-abdomen was negative and serum amylase was 3985 IU/L (Ref. range <80). Full blood count showed WBC of 13100/ul. Patient was urgently referred to surgical casualty unit where after initial management, CT abdomen revealed acute pancreatitis with peripancreatic fluid collection. He had a complicated course and was discharged with a plan of elective stenting once stable. Stenting with acute pancreatitis could have been harmful specially so in complicated pancreatitis necessitating open surgery of abdomen or haemorrhage. Whether this was a stable triple vessel disease with reactive Troponin elevation or an actual ACS with plaque instability (Acute coronary event) is a question of debate, which can be somewhat answered through intracoronary imaging .Customized decisions need to be taken to achieve desirable outcomes.

Keywords: Pancreatitis, MI, electrolyte disturbances, ST elevation, peripancreatic fluid

Introduction

Although acute pancreatitis is known to result in multi organ failure, true acute myocardial infarction in the setting of pancreatitis is very rare. Most ECG changes have been attributed to electrolyte disturbances and systemic rhabdomyolysis [1, 4] but acute ST elevation as in our patient is extremely rare.

Case report

A 69-year-old gentleman was admitted in early hours of the morning with acute onset retrosternal and epigastric atypical pain for 1-hour duration. He divulged that he did attend to a party last evening and engaged in an alcohol binge. Initial management for gastro-oesophageal disease failed to alleviate the symptoms and second EKG showed acute onset anterior lead ST elevation.

Portable 2D Echo did not show any regional wall hypokinesia but Troponin I titre was marginally elevated at 0.765ng/ml (Reference range <0.06). Patient was rushed to catheterization laboratory after antiplatelet loading, assuming it was a developing anterior infarction.

Trans radial angiography revealed triple vessel disease. LAD (Left anterior descending artery) was the closest to being the culprit with complex and hazy 90% mid vessel plaque but all three vessels had TIMI 3 distal run off.

Repeat clinical assessment on table generated some doubts in our minds whether we are tackling a primary cardiac pathology. His symptomatology changed to upper abdominal pain and epigastric tenderness could be elicited. We decided to call off stenting and first exclude abdominal pathology while anticoagulants and antiplatelets are on board. Blood pressure was 110/70mmHg and ST elevations were decreasing in amplitude by this time.

Urgent USS-abdomen showed only a moderately dilated gall bladder but no other features of cholecystitis, pancreatitis or abdominal pathology which could explain his presentation. Then came the pivotal test result of serum amylase which was elevated to 3985 IU/L (Ref. range <80). Full blood count showed WBC of 13100/ul with neutrophilic predominance, CRP < 2, ALP 139, AST 363 IU, ALT 153 IU, Serum Creatinine was 88 µmol/l. Further investigations showed mild systemic acidosis and hypocalcaemia. Patient was urgently referred to surgical casualty where he was kept nil by mouth and given standard surgical care including analgesics, prokinetics, antibiotics and hydration was started.

Case Report

Dual antiplatelets were continued in view of troponin positive unstable plaque disease but anticoagulation and statins discontinued. A CT abdomen contrast was performed the following day which revealed acute pancreatitis with peripancreatic fluid collection and adjacent tissue inflammatory changes. No biliary obstruction, dilated bile ducts, malignant growths and cyst formation were noted.

He eventually made a complete recovery and was discharged on D16 after admission with a plan of elective stenting.

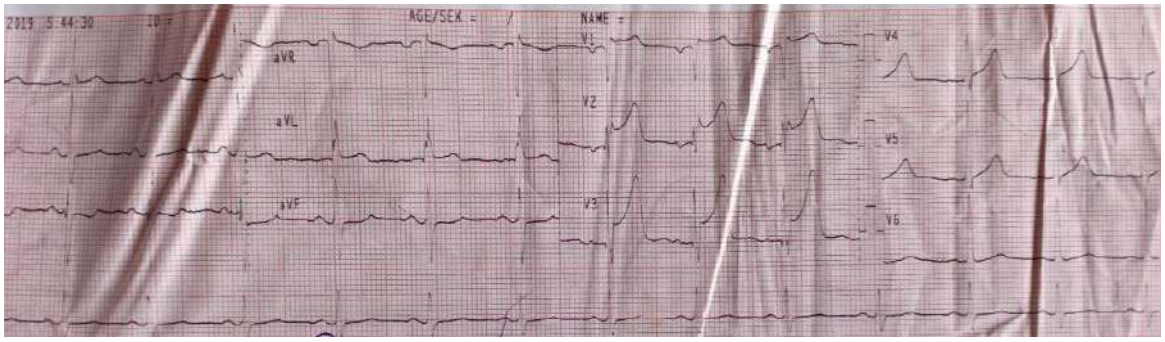

Figure1: Acute anterior ST elevation on presentation.

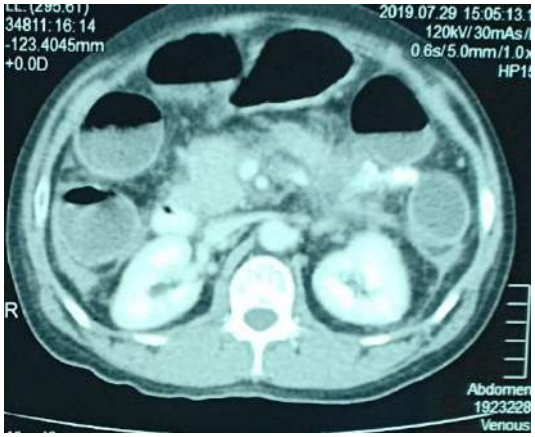

Figure 2: With the given clinical history, CT features are in favour of acute pancreatitis with acute peri pancreatic fluid collection and inflammatory changes in lower lobe of the right lung with associated minimal pleural effusion.

During the next few days he developed slightly deranged clotting profile with positive Grey Turner sign and diffuse ecchymotic patches. Secondary infection of the lung caused a prolonged fever which necessitated a 10-day course of high-end intravenous antibiotics.

Conclusion

Acute pancreatitis could be a great mimicker [2]. Being vigilant on dynamic symptomatology and staying flexible enough to change decisions saved the day on this scenario. Inadvertent stenting in the background of acute pancreatitis could have been harmful especially so if he went in to haemorrhagic pancreatitis [2] or other complications necessitating open surgery of abdomen. Whether he had a stable triple vessel disease with reactive non-cardiac troponin elevation or an actual ACS; as a rare complication [3] is a question of debate, which can only be answered through intracoronary imaging and physiological assessment.

The effect of saponification on coronary atheroma is an interesting area for future research which could explain this kind of clinical presentation.

In the setting of concomitant Pancreatitis and acute true ACS it is preferable to proceed to emergency coronary angiogram avoiding the disastrous consequences of thrombolysis /anticoagulation.

During angiogram if you find flow limiting plaque disease thrombosuction with balloon angioplasty can be utilized as a favourable option. If lesion is found to be resistant, drug eluting stent therapy is necessary with extreme caution in regards to unfractionated heparin and antiplatelets.

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Case Report

Cor Triatriatum Sinister with Osteum secundum Atrial Septal Defect: An Unusual presentation in late adulthood

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Abstract

Cor triatriatum sinister is a relatively rare congenital condition in which the left atrium is bisected by a fibromuscular fenestrated membrane into two distinct chambers. The presentation of patients can be either during infancy, childhood or rarely adulthood. It can present with multitude of symptoms such as dyspnea, faintishness and dependent oedema. We report a case of a patient presented with symptoms and signs suggestive of right heart failure. He was diagnosed to have septum secundum atrial septal defect with left right shunt complicated with pulmonary hypertension and cor triatriatum sinistrum.

Keywords: Cor triatrium, ASD, RV failure

Introduction

Cor triatriatum sinister is a relatively rare congenital condition in which the left atrium is bisected by a fibromuscular fenestrated membrane into two distinct chambers. The presentation of patients can be either during infancy, childhood or adulthood and this is due to variation in both obstruction to pulmonary venous flow and associated cardiac pathology.

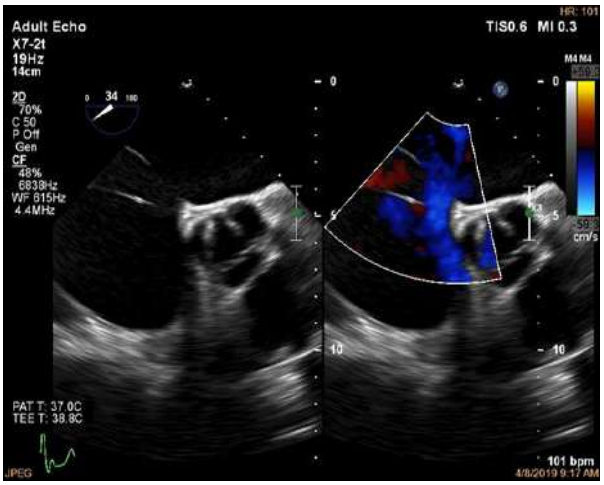
Case

A 66-year-old man presented with worsening exertional dyspnoea, bi lateral lower limb swelling and chest discomfort of 1 weeks duration. On examination his pulse rate was 90/min with a blood pressure of 140/85mmHG. Precordial examination revealed a right ventricular heave, fixed splitting of S2 and loud pulmonary component of the second heart sound. He had basal crepitations in both lungs. Electro-cardiograph showed right bundle branch block and right axis deviation without ST segment changes. Trans thoracic echocardiography revealed pulmonary hypertension with RA, RV dilatation moderate tricuspid regurgitation and dilated pulmonary artery.

Trans oesophageal echocardiogram was performed to delineate further information. This revealed a large osteum secundum type atrial septal defect with prominent left to right shunt and fenestrated thin membrane which was located immediately downstream to the ASD.

This thin membrane divided left atria in to two chambers known as cor triatriatum sinister. All four pulmonary veins were visualized draining in to the left atrium, including one is draining in to the smaller chamber (Figure 1).

Three dimensional TOE elaborated further details regarding additional atrial septum. Right heart catheterization confirmed an ASD with left to right shunt with pulmonary hypertension. Patient had been referred to cardiothoracic team for surgical correction of the ASD with fibro muscular septum



(Figure 1)

Right heart catheterization values

chamber	Pressure	Oxygen saturation
High RA	10/5 mm HG	70%
Mid RA		93%
Low RA	68/42mm HG	92%
RV	70/44mm HG	87%
Pulmonary artery	66/42 mm HG	86%
SVC	8/6mm HG	69%

Discussion

Cor triatriatum sinister can be associated with other congenital abnormalities such as bi cuspid aortic valve, atrial septal defect, and partial anomalous pulmonary venous drainage and AV canal defects. Surgical correction is the management if symptomatic or haemo-dynamically compromised.

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Case Report

Mirror imagery: Percutaneous Coronary Intervention (PCI) in a patient with situs inversus and dextrocardia presenting with anterior STEMI and Ventricular tachycardia (VT) due to acute total occlusion of both the left anterior descending artery (LAD) and dominant left circumflex artery (LCX)

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Abstract

Situs inversus with associated dextrocardia is a rare anomaly. The diagnosis and management of acute myocardial infarction in a patient with dextrocardia can be challenging. Amongst the problems that may be encountered are difficulties in interpretation of the electrocardiogram (ECG) and performing PCI due to abnormal location of the heart, mirror imagery of the aorta and abnormal coronary origin and orientation that may be present. We present the case of a 47year old male patient with previously diagnosed situs inversus and dextrocardia admitted with cardiac arrest due to VT caused by an anterior STEMI. Coronary angiography revealed acute total occlusion of the proximal LAD and a dominant LCX, in effect causing critical ischemia to the left ventricle. Thereafter, he underwent PCI to both the LAD and LCX. The patient had previously been diagnosed with dextrocardia but has been otherwise healthy. The patient having undergone a successful PCI made an uneventful recovery. He is at present receiving long term follow up at the cardiology unit of National Hospital Sri Lanka (NHSL), Colombo. We present this case since the number of reported cases of PCI performed in patients with dextrocardia worldwide is limited. This may be the first documented and reported case of the presence of total occlusion and PCI done to both the LAD and dominant LCX in a patient with dextrocardia in Sri Lanka.

Key words: Dextrocardia, Situs inversus, percutaneous coronary intervention, Anterior STEMI

Case report

A 47-year-old male patient was transferred to the Institute of Cardiology for primary PCI from a private hospital due to unavailability of the PCI facility and financial constraints of the family. The patient had developed typical angina type chest pain and was admitted to the hospital within 30 minutes of the onset of the pain, however he had developed a cardiac arrest upon admission. His ECG revealed VT rhythm (Figure 1). He was successfully resuscitated to sinus rhythm upon delivery of DC shock. An ECG post DC shock revealed changes suggestive of an anterior STEMI. The ECG showed ST elevation in the V1 lead only. ECG also showed right-axis deviation of P wave (negative complexes in I and aVL) and QRS complexes, along with progressive decrement in the amplitude of QRS complexes in precordial leads, which suggested dextrocardia (Figure 1).

A repeat ECG was taken after reversing limb and precordial leads which revealed widespread ST elevation in leads I, aVL, and V1 to V6 suggestive of acute extensive anterior wall MI (Figure 2). A Chest X-ray was also done to confirm dextrocardia.

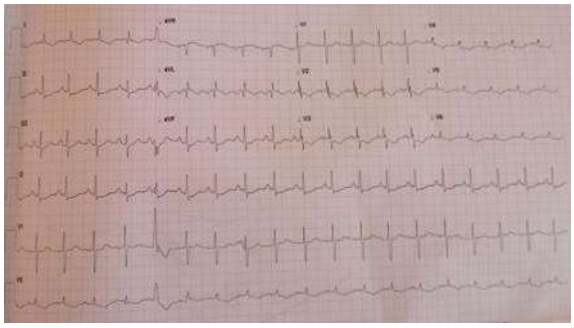

Figure 1: ECG revealed VT rhythm

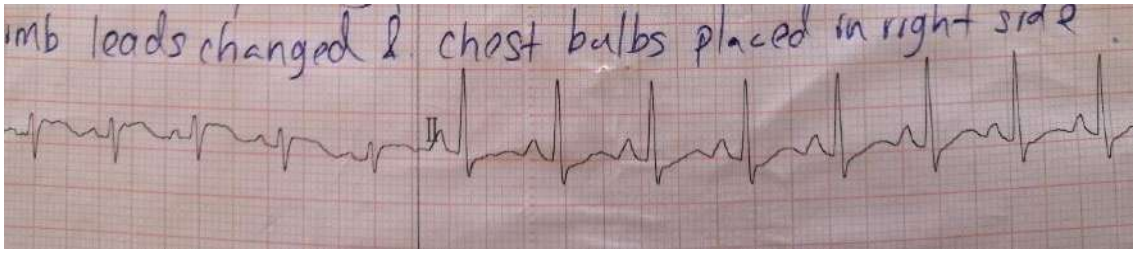

Figure 2: Widespread ST elevation in leads I, aVL, and V1 to V6 suggestive of acute extensive anterior wall

Due to deterioration of his clinical state, his airway was immediately intubated and he was placed on ventilator support along with inotropic support with intravenous (IV) noradrenaline infusion administered to maintain his blood pressure. This patient had a preexisting diagnosis of dextrocardia with situs inversus following an incidental detection on chest X-ray and had undergone a further investigative workup thereafter. He had good exercise tolerence and no symptoms of angina prior to this.

He was transferred to the NHSL cardiology unit within one hour of admission to the initial hospital. An echocardiography examination performed revealed regional wall movement abnormalities as evident by hypokinesia of anterior wall and apex.

Thereafter urgent coronary angiography via right side femoral artery access. A “double inversion technique” was used during radiographic imaging. This enabled the orientation of the patient’s coronaries to simulate the coronaries of levocardia, thereby making the procedure and needful interpretation straightforward.

Coronary angiography performed with 6Fr Judkins left (JL) and 5Fr Judkins right (JR) catheters revealed acute total occlusion of both the LAD and dominant LCX, whilst his right coronary vessel was non dominant. Standard coronary angiographic views were also taken (Figure 3). This revealed unfamiliar anatomy and resultant difficulty of interpretation which was also compounded by the associated total occlusion of both LAD and LCX vessels.

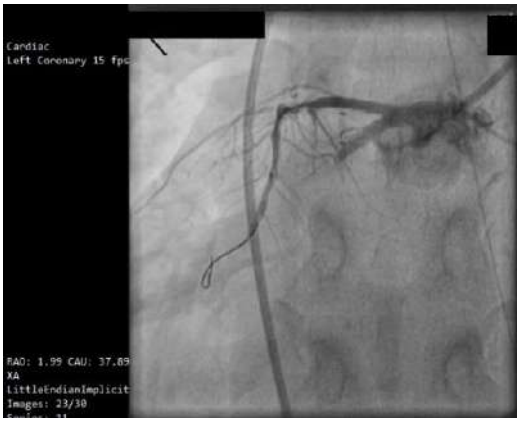

Figure 3: Standard coronary angiographic views

PCI of both the LAD and LCX was done. SION guidewires were used to cross culprit lesions of both vessels simultaneously. PCI of LAD was done with initial pre dilation of the LAD culprit lesion with a MOZEC 2.0 X 8 mm balloon at 6 atm with flow in the LAD established thereafter (Figure 4). The LAD was stented with XIENCE PRIME 3.0 X 38 mm drug eluting stent (DES) deployed at 14 atm with 2 repeated dilations done (Figure 5). Thereafter, the LCX culprit lesion was pre dilated with the MOZEC 2.0 X 8 mm balloon at 6 atm resulting in flow established in the LCX as well. The LCX was stented with XIENCE PRIME 3.0 X 28 mm DES deployed at 14 atm with 2 repeated dilations done (Figure 6). Final angiography revealed TIMI III flow in both vessels with absence of complications such as dissection or wire perforation (Figure 7).

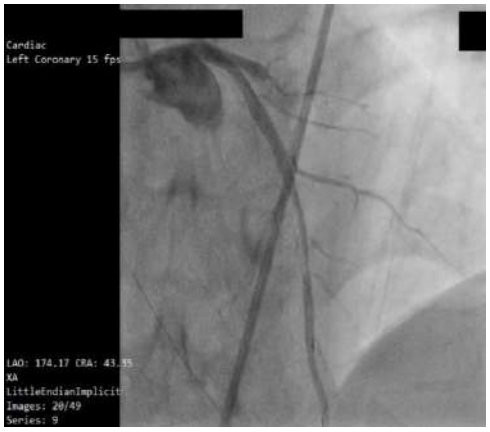

Figure 4: Culprit lesion with a MOZEC 2.0 X 8 mm balloon at 6 atm with flow in the LAD

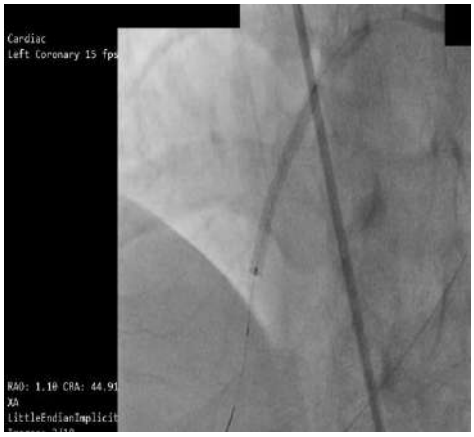

Figure 5: The LAD was stented with XIENCE PRIME 3.0 X 38 mm drug eluting stent (DES) deployed at 14 atm

Case Report

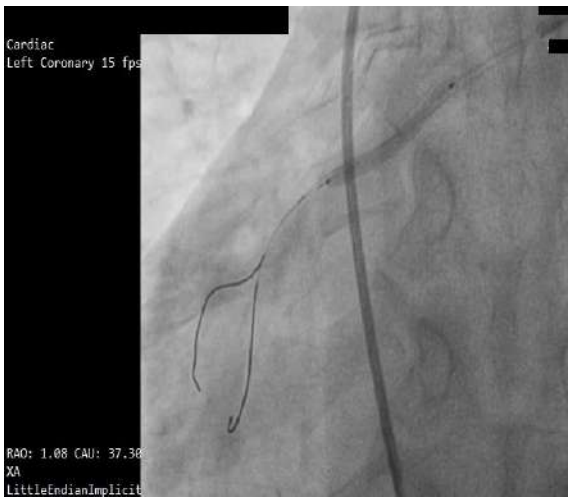

Figure 6: The LCX was stented with XIENCE PRIME 3.0 X 28 mm DES deployed at 14 atm with 2 repeated dilations done.

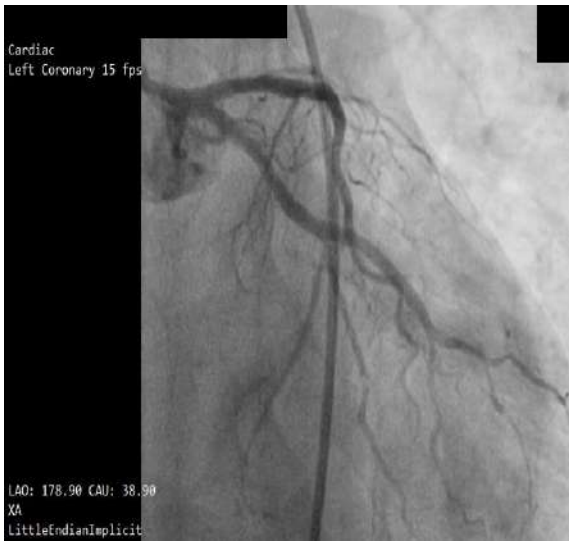

Figure 7: Final angiography revealed TIMI III flow in both vessels with absence of complications of such as dissection or wire perforation

The patient had a good recovery post procedure and was extubated 2 days after the initial procedure. He is at present registered and receiving long term follow up and rehabilitation care at the NHSL cardiology unit.

Discussion

Dextrocardia with situs inversus is a rare congenital disorder that causes a "mirror image" positioning of the patient's heart and viscera. Its incidence is estimated 0.1 to 0.2 per 1000 persons in a population [(1)].

Dextrocardia is characterized by the opposite orientation of the apex and its cardiac axis along with position in the right hemi thorax instead of the left. It may occur as situs solitus but more frequently it is discovered with associated situs inversus (inversion of other organs). It can also be found as situs ambiguous; this anomaly is associated with disordered arrangement of organ systems along with abnormalities of connection between the heart and the viscera [(2)].

STEMI in patients with dextrocardia and situs inversus is even rarer. The combination of both can present challenges in terms of diagnosis and management [(3)].

Performing coronary angiography and PCI in patients with dextrocardia and situs inversus can be a challenge due to the mirror imagery in these patients.

The "double inversion technique" described by PK Goel, was utilized to acquire imagery in-order to ease interpretation and perform the procedure with minimum errors. The "horizontal sweep reversal" feature of the fluoroscopy machine was combined with exact opposite degree to degree image acquisition angulations of LAO/RAO/ CRANIAL/CAUDAL combinations that are used in levocardia coronary angiography in order to generate accurate reversal of the left-right mirror image[(4)].

Eg: "Spider view" that is acquired with LAO 30/ CAUDAL 30 in levocardia, this patient's reversed mirror image "spider view" was generated with RAO 30/ CAUDAL 30 angulation and use of horizontal sweep reversal feature.

Our patient with dextrocardia and situs inversus had critical ischemia of his left ventricle due to acute total occlusion of both the LAD and dominant LCX, each from its respective proximal segments. This most likely caused his cardiac arrest and VT rhythm. With imaging assistance provided by the above technique, he underwent successful emergency PCI to both occluded vessels and subsequent establishment of coronary flow.

His angiographic results were satisfactory and the patient made a steady progressive recovery.

Conclusion

Dextrocardia may be encountered in patients presenting with acute coronary syndrome. Some may have a preexisting diagnosis of the condition due to incidental investigations such as chest X ray or ECG.

Utilization of the "double inversion technique" can provide accurate imaging during coronary angiography with resultant ease of interpretation and decision making. It can provide assistance when performing PCI in patients with dextrocardia.

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Brief Report

An exceptionally rare angiogram

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Brief case presentation & description

Coronary artery abnormalities are seen usually in 1% of the population and it can be 0.3 – 5.6% in studies of patients undergoing angiography(3). Coronary arteries arising from the opposite sinus of valsalva is a rare event. All three coronary arteries arising from a single ostium in the sinus of valsalva is an exceedingly rare event. Its occurrence is less than 0.03% in the general population(1). Left coronary arteries arising from the right sinus of valsalva is reported with a frequency of 0.02% - 0.05% (3) A few cases have been reported worldwide but not reported in Sri Lanka before. These patients are usually asymptomatic and it has little clinical significance(1). It can occur with or without other associated congenital cardiovascular abnormalities and usually have a benign course(2). Sometimes it can be associated with the risk of sudden cardiac death due to external compression of arteries as a result of their anomalous course (1).

A middle age Sri Lankan female presented with class II angina and shortness of breath. No further complaints related to other systems reported. Examination revealed an average built middle aged female with normal general and systemic examinations. Treadmill test was inconclusive as she could not proceed beyond stage II. Her ejection fraction is >60%. Other biochemical investigations were normal.

A coronary angiogram was planned via radial approach. Tiger catheter was used to engage the right ostium. Right coronary artery showed severe mid segment disease in RCA and PDA. Left ostial engagement was difficult and not visible on left root angiogram. Right root angiogram showed signs of left anterior descending artery (LAD) and left circumflex artery(LCX). Angiographic views with right judkin catheter revealed all three coronary arteries arising from a single ostium after right sinus of valsalva. It was a triple vessel disease with severe ostial involvement of LAD and moderate to severe mid vessel disease. Mid vessel near total occlusion of co-dominant LCX. CT coronary angiogram was done for confirmation and to delineate the pathways of arteries.

It demonstrated the anomalous left main artery and LAD running between main pulmonary artery and aorta in the anterior interventricular groove. LCX was running between aorta and left atrium. This patient was referred for coronary artery bypass surgery.

Our patient's course of right coronary artery was normal and usually in the reported cases the course of right coronary artery is normal(1). This patient had a risk of sudden cardiac death due to the course of LAD. Though it may be clinically insignificant and angiographically difficult, it is a rare finding in the population.

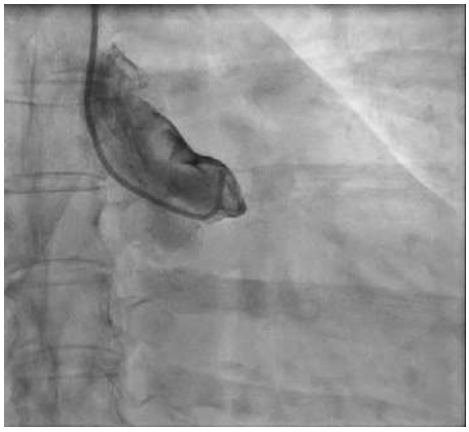

Figure-1: Left cusp cannulation & angiography failed to reveal coronary arteries originating either left cusp or non coronary cusp.

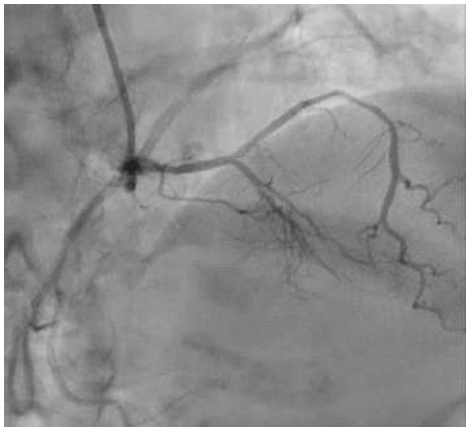

Figure-2: Right ostial engagement showing left sided arteries

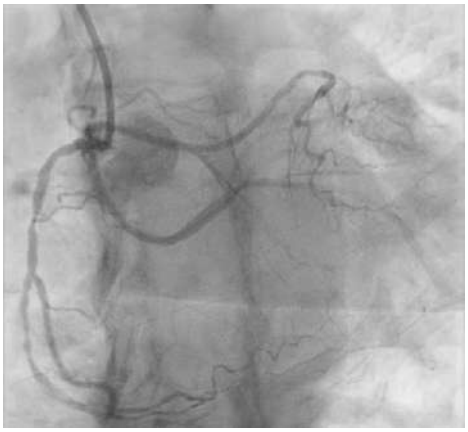

Figure-3: Left anterior oblique (LAO) view Demonstrating single ostium

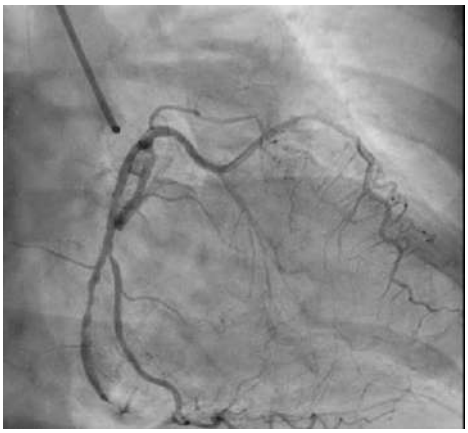

Figure-4: Angiographically triple vessel disease with all three arteries arising from single ostium

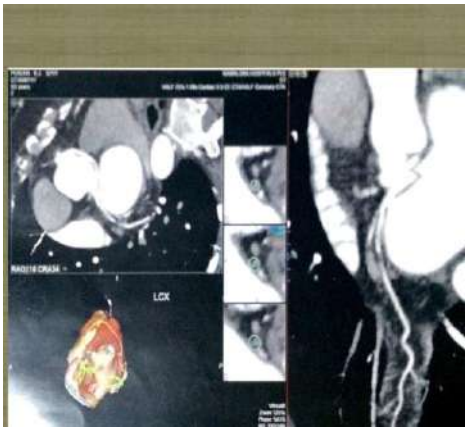

Figure-5: CT coronary angiogram demonstrating LAD And LCX arising from right sinus of valsalva from singleostium and LAD running between aorta and main pulmonary artery and LCX running between aorta and left atrium.

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Clinical Audit

Clinical Audit on Adherence to Antiplatelet therapy in patients on follow-up at a Cardiology Clinic in a Tertiary Care Hospital.

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Abstract

One of the most important aspects of the treatment of Coronary Artery Disease (CAD) is the prescription of antiplatelet therapy. To assess the adherence to antiplatelet therapy, the study focused on several factors, namely, Type of APT, Prior Stopping of APT, Patient Knowledge, and a Patient Adherence Score Determined by a standardized scale. Out of the 500 patients, Females (59%) pre dominated Males (41%). 58.8% of the 500 patients were on single anti platelet therapy and 41.2% were on dual anti platelet therapy. 24.8% of the patients temporarily stopped their antiplatelet therapy prior to the duration prescribed. The most common reasons for prior stopping were cataract surgery (34.68%) and dental procedures (33.87%). The patients' knowledge on correctly identifying which pill is the antiplatelet drug (96% were aware) and when this pill is supposed to be taken (98.6% were aware) was extremely satisfactory. However only 56.2% of the patients were aware of as to why they were prescribed APT and 93.6% of the patients were not aware of how long they were supposed to take these medications for. The patients Adherence Score determined by the standardized scale was classified into High Adherence, Moderate Adherence and Low Adherence. Out of the 500 patients 61.2% of patients had High adherence to APT, and 24.4% had Moderate adherence to APT and 14.4% had Low Adherence to APT.

Keywords: CAD, Single antiplatelet therapy, dual anti platelet therapy, CVD, adherence score

Introduction

Cardiovascular disease (CVD) is the leading contributor to death worldwide [(1)]. In Sri Lanka 22.52% of total deaths in 2017 were due to CVD. An individual surviving the first myocardial infarction (MI) has a substantial chance of suffering a second a MI with an increased risk of dying from such an event [(2)]. Interventions along with medications to modify risk factors in view of prevention of primary or secondary cardiovascular events are supported by a number of clinical trials and epidemiological data [(3,4)].

Number of medications are used in the secondary prevention of CVD, such as, antiplatelet drugs, beta blockers, ACE inhibitors and statins. Out of these, antiplatelet drugs are the most widely used considering availability, cost and effectiveness [(5)]. According to NICE guidelines in secondary prevention aspirin is recommended in combination with clopidogrel or other P2Y12 inhibitor for one year and thereafter aspirin monotherapy indefinitely.

In the past, low dose aspirin (75-100mg) was widely used in primary prevention of atherosclerotic CVD. However, current AHA guidelines 2019 [(6)] does not recommend routine use of aspirin, specially, in the elderly due to the high risk of bleeding. Between 40-70 years of age low dose aspirin can be considered if CVD risk is very high and there is no risk of bleeding.

Medication adherence plays a vital role in management of CVD risk and to obtain the desired effectiveness of the drug therapies and preventive actions[(7)]. Medication adherence can be defined as the level to which patients take medications which corresponds with the prescription by the Health Care provider[(8)]. This can be affected by patient factors, demographic factors and other associated comorbidities[(9,10)]. Adherence to medication is a prime determinant of treatment success. As the burden of disease is leaning more towards chronic illnesses, unsatisfactory adherence affects the optimum clinical benefits, reducing the overall effectiveness of therapy and health system [11].

Thus, evaluation of patient medication adherence provides important feedback on effectiveness and quality of the healthcare system. This information can be used to improve health outcomes of the patient and to optimize the services offered by the health system.

Our main objectives of this audit are as follow;

1. To assess adherence to antiplatelet therapy by the patients.
2. To determine the knowledge of patients regarding antiplatelet therapy.

3. To assess the association between adherence to antiplatelet drugs and patient knowledge regarding therapy.

Method

Study design and setting

A descriptive cross-sectional audit was carried out at the follow-up Cardiology Clinic at Colombo South Teaching Hospital, Sri Lanka with the aim to assess the prevalence of adherence to antiplatelet therapy.

Study Sample

A sample of 500 patients who were currently on any form of antiplatelet therapy was selected randomly during their clinic visits.

Study Instruments

An interviewer administered questionnaire was used to extract data from history and records of the patient which includes demographic data, other comorbidities, information about antiplatelet therapy prescribed to the patient, and patient's knowledge about antiplatelet therapy.

Adherence to antiplatelet therapy was assessed using Morisky's Medication Adherence Scale (MMRS-08) which consists 8 points. Patients were scored 1 point for each question according to their answer as shown in (Figure 1). Patients scoring a total of 0 points are considered to have High adherence, 1-2 points Moderate adherence and more than 2 points Low adherence[12,13].

All data was analysed on PSPP version 1.2.0 and descriptive statistics were used.

Question	POINTS	
	Yes	No
• *Do you sometimes forget to take your anti platelet medication?*	1	0
• *People sometimes miss their medication for reasons other than forgetting. Thinking over the past 2 weeks, were there any days where you did not take your Antiplatelet medication?*	1	0
• *Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?*	1	0
• *When you travel or leave home, do you forget to bring along your antiplatelet medication?*	1	0
• *Did you take your anti platelet medication Yesterday?*	0	1
• *When you feel like your condition is under control, do you sometimes stop taking the medication?*	1	0
• *Taking medication every day is a real inconvenience for some. Do you ever feel hassled about sticking to your antiplatelet treatment medication?*	1	0

• *How often do you have difficulty in remembering to take all your medications?*	Never/Rarely	Once in a while	Sometimes Usually	All time
	0	Any option= 1		

Figure 1: Morisky's 8-point Medication Adherence scale

Grading <1: High adherence

1-2: Moderate adherence

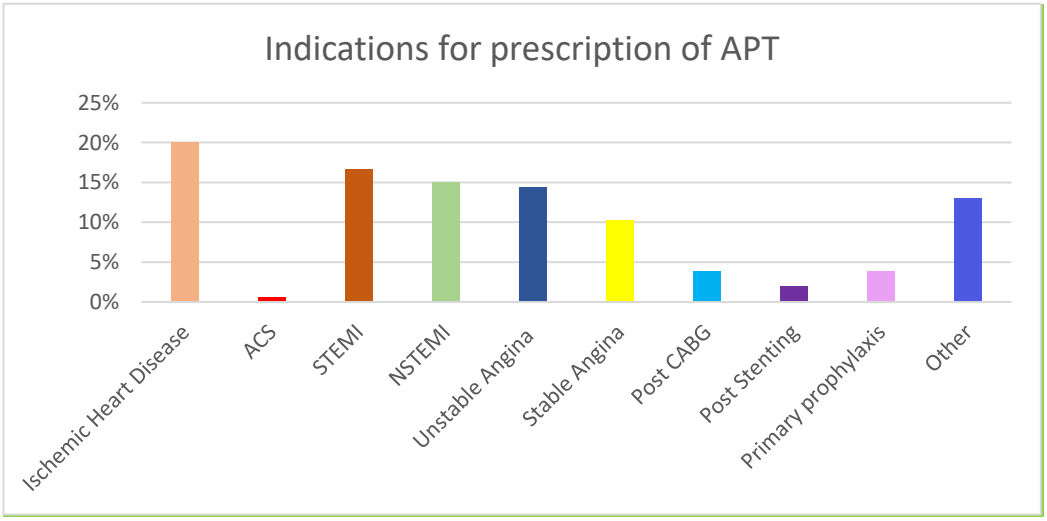
>2: Low adherence

Results

Out of the total of 500 patients who participated in this audit 59% were females and 41% were males. Majority of the patients (73.6%) were above 60 years of age. Mean age was 65±9.66 years. 58.8% of the 500 patients were on Single Anti Platelet therapy and 41.2% were on Dual Anti Platelet therapy for various indications(Figure 2).

Table 1: Demographic data of the participants

Variable name		Results (n,%)
Age (mean ±SD)		65 ±9.66
Age Range (years)	30-40	3 (0.6%)
	40-50	24 (4.8%)
	50-60	105 (21%)
	60-70	180 (36%)
	70-80	167 (33.4%)
	80-90	20 (4%)
	90-100	1 (0.2%)
Gender	Male	205 (41%)
	Female	295 (59%)
Comorbidities	Hypertension	423 (84.6%)
	Diabetes	206 (41.2%)
	Both (Hypertension and Diabetes)	178 (35.6%)
Type of antiplatelet therapy	Single	294 (58.8%)
	Dual	206 (41.2%)



Medication adherence Figure 2: Indications for prescription of Antiplatelet therapy

A Standardized scale was utilized to determine Patients Adherence Score, classifying adherence as High, Moderate and Low. Accordingly, out of the 500 participants, 61.2% of patients had high adherence to APT, 24.4% had Moderate adherence to APT and 14.4% had Low Adherence to APT.

Patient Adherence Grade (Based on Morinski scale)

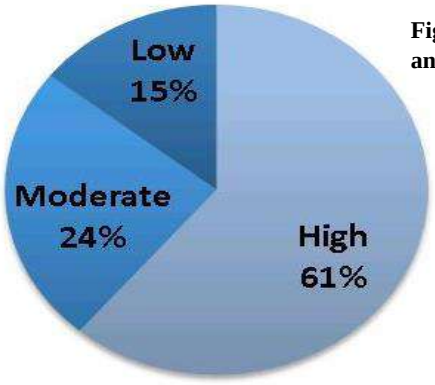


Figure 3: Adherence to antiplatelet medication

Table 2: Descriptive analysis of variables and level of adherence

Variable	Adherence Results (n, %)		
	High	Moderate	Low
Type of antiplatelet therapy			
Single	*175 (59.52%)*	*76 (25.85%)*	*43 (14.63%)*
Dual	*131 (63.59%)*	*46 (22.33%)*	*29 (14.08%)*
Gender			
Male	*135 (65.85%)*	*45 (21.95%)*	*25 (12.2%)*
Female	*171 (57.97%)*	*77 (26.1%)*	*47 (15.93%)*
Indication			
Ischemic Heart Disease	*63 (61.17%)*	*23 (22.33%)*	*17 (16.5%)*
ACS	*2 (66.67%)*	*1 (33.33%)*	*0*
STEMI	*55 (66.27%)*	*20 (24.1%)*	*8 (9.64%)*
NSTEMI	*40 (53.33%)*	*22 (29.33%)*	*13 (17.33%)*
Unstable Angina	*38 (52.78%)*	*21 (29.17%)*	*13 (18.06%)*
Stable Angina	*30 (58.82%)*	*13 (25.49%)*	*8 (15.69%)*
Post CABG	*11 (57.89%)*	*5 (21.05%)*	*3 (21.05%)*
Post Stenting	*8 (80%)*	*2 (20%)*	*0*
Primary prophylaxis	*14 (73.68%)*	*3 (15.79%)*	*2 (10.53%)*
Comorbidities			
Hypertension	*264 (62.41%)*	*104 (24.59%)*	*55 (13%)*
Diabetes	*121 (58.74)*	*56 (27.18%)*	*29 (14.08%)*
Both	*103 (57.87%)*	*53 (29.78%)*	*22 (12.36%)*
Duration of Treatment			
<1 year	*71.25%*	*63.51%*	*55.56%*
1-2 years	*16.25%*	*22.3%*	*33.36%*
>2 years	*12.5%*	*14.19%*	*11.08%*

Patient's knowledge regarding antiplatelet therapy

Patient's knowledge was assessed on correctly identifying which pill is the antiplatelet drug, why it is prescribed, duration of treatment and when to take the pill (Table 3). No substantial relationship was discovered between adherence to medication and patient's knowledge based on the questions asked in the questionnaire. Adherence patterns remained to be moderate to high in most patients irrespective of their knowledge regarding the drug (Figure 4).

Table 3: Patient knowledge regarding antiplatelet medication

		YES	NO
Q1	Do you know which pill is given to you as an Antiplatelet drug?	96%	4%
Q2	Do you know why you take this medication?	56.2%	43.8%
Q3	Do you know for how long you have to take this medication?	6.4%	93.6%
Q4	Do you know when to take this medication?	98.6%	1.4%

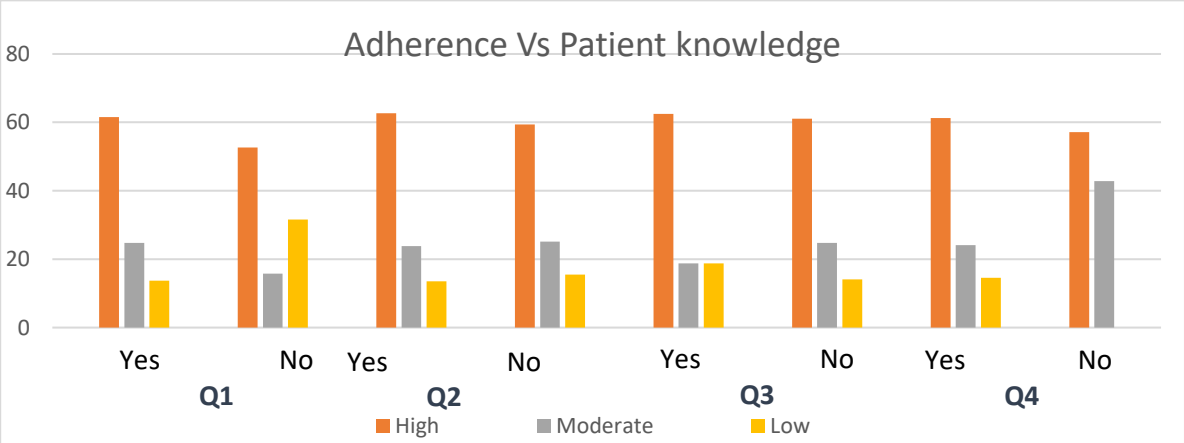
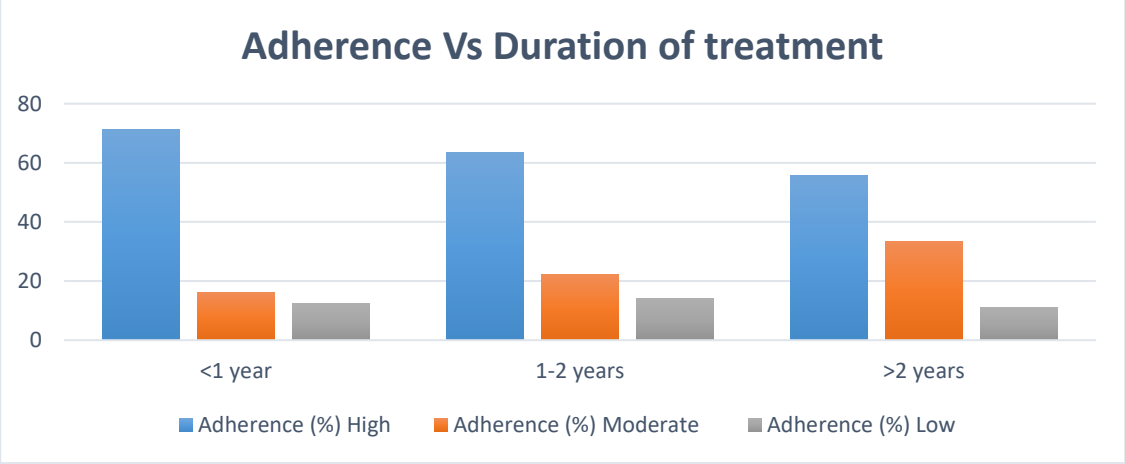


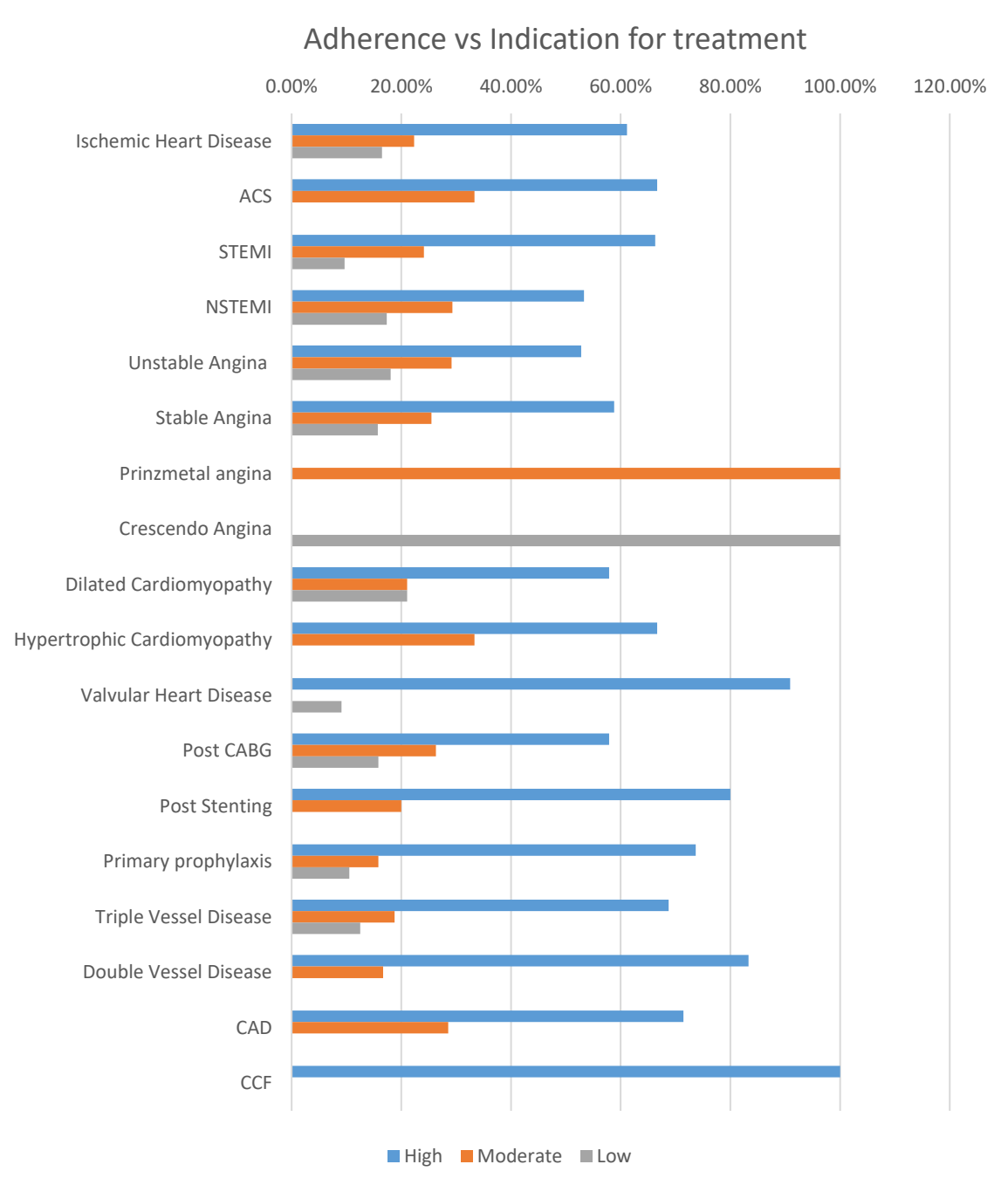
Figure 1: Adherence Vs Patient knowledge

During the analysis it was observed that level of adherencewas deemed to reduce, with increase in duration of treatment. Out of the patients who were on theirfirst year of treatment Antiplatelet therapy, 71% of the population had High adherence.63.5% of those on APT for 1-2 years had High adherence, and 55.5% of the patients had High adherence while on APT for more than 2 years(Figure 5).



Adherence vs indication for Antiplatelet therapy

Differences in adherence were analyzed in the background of different indications for antiplatelet therapy. Results showed post stenting 80% of the patients had High adherence and the rest had moderate adherence *(Figure 6)*.



Discontinuation of medication

Patients were also assessed on discontinuation of medication. Out of the 500 participants 124 (24.8%) patients admitted having discontinued APT temporarily, and 376 patients did not report of discontinuation of therapy. Most of the patients had discontinued treatment prior to cataract surgery and dental surgery (Table 4).

Table 4: Discontinuation of treatment

Variables	N	%
Continued treatment	376	75.20
Discontinuation of treatment	124	24.8
Reasons for Discontinuation		
Dental Surgery	42	8.40
Prostate Surgery	1	0.20
ENT Surgery	2	0.40
Cardiothoracic Surgery	2	0.40
Cataract Surgery	43	8.60
Abdominal Surgery	18	3.60
Orthopeadic Surgery	3	0.60
Trauma	5	1.00
Dengue	3	0.60
Breast Surgery	3	0.60
Endoscopy	2	0.40
Total	500	100.0

Discussion

This audit was conducted to determine the patient adherence to antiplatelet therapy and to assess and determine the patient's knowledge regarding APT and relationship between knowledge and adherence practices. Approximately 86% of the participants showed moderate to high adherence to antiplatelet medication. Incidence of low adherence was only 14%.

In a previous study [8] conducted on post PCI patients' adherence to medication, was as high as 97%. In contrast, post MI 25% of the patient population was highly adherent and nearly 50% the population had moderate adherence. In our audit, post-stenting 100% of the patients had moderate-high adherence. In addition, following MI, patients who had NSTEMI 53% had high adherence, 29% had moderate adherence and nearly 20% had low adherence. But patients with STEMI had more satisfactory adherence with only 10% of the population with low adherence.

A study conducted in a Tertiary-Care Cardiac Center [14] in Sri Lanka regarding medication adherence following PCI determined that high adherence to medication following PCI is greatly due to patients 'perception, as majority of the patients consider continuation of medication following PCI as of utmost importance, whereas in most other circumstances medication are consumed as enforced upon by the medical personnel. Latter study connotes that, to gain maximum compliance with medication it is important to educate the patients regarding the importance of treatment with APT and other medications before and after PCI.

Though the analysis in our audit showed little significance in level of adherence between patients who were aware about therapy and who were unaware, there was a clear lack of knowledge regarding the antiplatelet medication consumed by the patients.

Nearly half the population were unaware as to why they were prescribed antiplatelet drugs and 93.6% of the population did not know for how long they were prescribed the drugs. But majority of the patients were able to identify which drug is the antiplatelet drug (Aspirin/Clopidogrel) and knew when to take it.

WHO Report on Adherence to long-term therapies in 2003[11], identifies doctor factors, health system factors and patient attributes as main determinants of adherence to medication. Evidence from number of studies show that Doctor-patient relationship, and communication between the doctor and patient in disease condition and treatment enhances positive outcomes [15,11] . A study carried out among public and private hospitals concluded that, though the overall quality of clinical care is high and equal in both sectors, patient education and interpersonal satisfaction was high in the private sector, due to the increased time spent with a patient in private sector [16] . But in the public sector there are time constraints due to high demand in healthcare and financial burdens reducing the time spent with patients by the doctors. This is understood by the patients as well, thus, due to the trust in doctors and respect towards the free healthcare system, majority of the patients seem to adhere to the treatment even without adequate knowledge, which was evident by our audit.

Another important factor is regular follow-up at the clinic which augments medication adherence[17]. In the setting this audit was carried out patients are given the date for next clinic visit at each visit, and medication is issued for the set time period, it regulates continuity of care [11]. In this audit, data is collected from follow-up patients, most on regular follow-up over years, which could be another reason for High adherence in the study population.

When analyzing reasons for discontinuation of treatment it was detected that the reasons were mainly prior to surgical procedures. All patients who stopped have recommenced therapy after an interval. This could be due to regular follow-up in the clinics. It also reflects on the efficiency of clinical care provided by the doctors in recommencing antiplatelet therapy effectively following surgery, improving medication adherence by the patient.

Level of adherence among patients on SAPT and DAPT also did not show a comparable difference. Approximately 60% of the population had High adherence. It is important to further improve this adherence level by educating both groups of patients, more importantly those on Dual antiplatelet therapy regarding importance of compliance in order to avoid further thromboembolic events leading to reinfarction or sudden death [18].

According to Aghabekyan et al [19] of the many factors that lead to non-adherence to medication, financial difficulties portray as the biggest burden. In this audit this factor is eliminated as the patients are provided medication at no cost due to Free Healthcare policy[20]. Nevertheless, though there is no cost, if there is difficulty in approaching the health services regularly which affects obtaining medication from the state sector and inability to pay for medication in that case is an area to be explored.

This is a single centre audit, though there is a high patient turnover from certain parts of the country, for further generalization of results more multicentric studies may be necessary. Qualitative studies may allow to discover reasons for low adherence, and results can be used to improve on the necessary areas.

Conclusions

In conclusion, vast majority (85.6%) of the patients had moderate to high adherence to antiplatelet therapy. There were no significant reasons identified in this audit for low adherence. Even though, the patients' awareness regarding indication of antiplatelet therapy and duration of treatment were poor, adherence to antiplatelet drugs remained high.

Overall medication identification was satisfactory in the population and majority of the participants were aware on when to take the drug. Patients who had discontinued treatment temporarily, mostly prior to surgery have recommenced treatment successfully.

Regular follow up at the clinics and drugs issued free of charge may play a key role in medication adherence mitigating the effects on adherence by factors such as lack of knowledge regarding therapy and duration of treatment.

Recommendations

- To overcome time constraints in patient education an information booklet can be developed with all relevant information and given to the patients and the audit can be repeated to see improvement in knowledge and adherence.
- Health education seminars
- Posters can be displayed in the clinic area for self-education of patients regarding antiplatelet therapy

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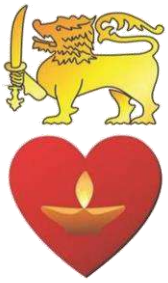

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