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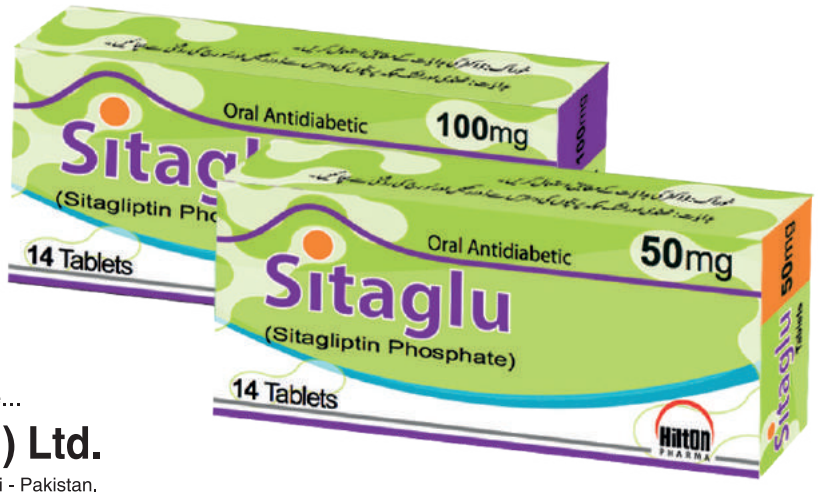

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The third objective is for this publication to be a fruitful avenue of Continuing Medical Education (CME). The lack of time should not be a limiting factor to assimilate knowledge. The journal will utilize reviews, tutorials, journal scans and updates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

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ST Elevation Myocardial Infarction in Young Adults: Clinical Presentation, Risk Factors, Hospital Outcome Index, and Coronary Angiographic Characteristics

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Abstract

Coronary artery disease (CAD) represents a leading cause of death in adults in both developed and developing countries, including Sri Lanka. Fortunately, incidence of myocardial infarction is less common among young adults and its' incidence varies between 2% and 10% of total myocardial infarctions. Interestingly, response and outcomes to treatment are better in younger age groups, than in older age groups, if prompt and timely treatment with current best treatment strategies for acute myocardial infarction [4] is offered. In addition, differences are observed in the clinical presentation, risk factor profile and the coronary anatomy of young patients who develop myocardial infarction compared with those developing it at an older age.

Key Words: STEMI, Younger age groups, risk factor profile, mode of clinical presentation, angiographic characteristics

Introduction

Coronary artery disease (CAD) represents a leading cause of death in adults in both developed and developing countries, including Sri Lanka[1,2]. Myocardial infarction is a lethal manifestation of CAD and may also present as sudden death. Fortunately, incidence of myocardial infarction is less common among young adults and its' incidence varies between 2% and 10% of total myocardial infarctions [3,4]. The higher prevalence of traditional risk factors for ischaemic heart disease in young adults such as smoking, diabetes, obesity and lack of physical activity has almost negated the protection offered by young age. Occurrence of myocardial infarction in the young population has been increasing within the recent times, mainly in Asian countries leading to more young deaths as opposed to the trend in the past when myocardial infarction was considered to be a disease of middle and old age [5].

Interestingly, response and outcomes to treatment are better in younger age groups, than in older age groups, if prompt and timely treatment with current best treatment strategies for acute myocardial infarction [4] is offered. Epidemiological studies done in developed countries show that migrant populations from the Indian subcontinent have a higher risk of coronary artery disease compared to the native population [6]. Moreover, coronary artery disease appears to begin earlier in life, and thus morbidity and mortality rates tend to be higher in the people of South Asian origin compared with other ethnic groups [6,7].

In addition, differences are observed in the clinical presentation, risk factor profile and the coronary anatomy of young patients who develop myocardial infarction compared with those developing it at an older age [4].

To date, few studies have focused on the clinical characteristics and outcomes of young patients with acute ST elevation myocardial infarction and no such studies have been done in Sri Lanka. The cut off age of 40 to 45 years has been used in most studies to define young patients with coronary artery disease or myocardial infarction [4,8,9,10].

There is no universal agreement of the definition for young myocardial infarction. We used 40 years as the cut off age in our study.

Justification

Documented literature on young patients with ST elevation myocardial infarction (STEMI) is not found in Sri Lanka and this is likely to be the first study of this type conducted on a young population in Sri Lanka. Although this study is limited to a single center, findings of this study would help to understand the incidence of the STEMI among patients below 40 years. The clinical presentation, risk factors and hospital outcome would provide invaluable information for formation of guidelines for coronary artery disease preventive strategies.

Material and methods

This is a retrospective cross-sectional study on patients who were under the age of 40 years and admitted with STEMI to the Institute of Cardiology at National Hospital of Sri Lanka (NHSL), Colombo, between July 2019 and June 2020. STEMI was diagnosed when a patient had chest pain and ST elevation in two consecutive leads or with new onset LBB in the ECG [11].

If the diagnosis of STEMI has been changed to another diagnosis (such as myocarditis, electrolyte imbalance etc.) before discharge, patient was excluded from the study.

Hypertension was defined as having a history of high blood pressure diagnosed and/or treated with medication, diet, and/or exercise, with systolic blood pressure more than 140 mmHg or diastolic blood pressure more than 90 mmHg on at least two occasions [12].

Diabetes mellitus (DM) was defined as patients having a fasting blood sugar ≥ 126 mg/dl and/or post-prandial blood glucose ≥ 200 mg/dl or a past history of DM and/or taking medication for diabetes [13]. Dyslipidemia was defined as serum cholesterol of ≥ 200 mg/dl, low-density lipoprotein > 130 mg/dl, triglyceride (TG) >150 mg/dl, HDL-C < 50 mg/dl for females and < 40 mg/dl for males, a total cholesterol/HDL-C value of ≥ 4.5 in patients with dyslipidemia and/or those on medication for dyslipidemia [14].

The lifestyle was categorized as active and sedentary based on occupation and whether patient was doing regular exercises. Professions such as, mechanical engineering, construction engineering, skilled, semi-skilled and manual workers etc. were categorized as having an active lifestyle while professions such as accounting, information technology, legal, administrative, technical and clerical etc. were categorized as having a sedentary lifestyle. Any patient doing regular exercise (30 minutes per day for five days per week) was considered to have an active lifestyle. Overweight was defined as body mass index(BMI) greater than 23 kg/ m^2 and obesity was defined as BMI greater than 25 kg/ m^2 [15]. Current smokers were defined as those who were either currently smoking or recently (within last 4 weeks) stopped smoking. Positive family history of premature coronary artery disease (CAD) was defined as having a diagnosed first-degree relative with ischaemic heart disease i.e.< 55 years of age in malesand < 65 years in females.

Severe coronary artery disease was defined as ≥ 70% lesions in major epicardial arteries or ≥ 50% lesion in left main coronary artery. Moderate coronary artery disease was defined as 50% to 69% stenosis of major epicardial arteries whereas minor coronary artery disease was defined as ≤ 50% stenosis in major epicardial arteries. Normal coronaries were defined as coronary arteries with less than 20% stenosis. Heart failure was defined according to the Killip classification [16] .

Killip I: no clinical signs of heart failure, Killip II: rales in the lungs, third heart sound (S3), and elevated jugular venous pressure, Killip III: acute pulmonary edema (APE), and Killip IV: cardiogenic shock or arterial hypotension measured as systolic blood pressure <90 mmHg), and evidence of peripheral vasoconstriction (oliguria, cyanosis, and diaphoresis).Data was entered into a data sheet and analyzed by Statistical Package of Software Sciences (SPSS version 17).

Descriptive statistics were used to describe the findings. Continuous variables with normal distribution were described using mean and standard deviation. Continuous variables with skewed distributions were described using median and inter quartile ranges. Discrete variables were described using count, percentage and confidence intervals. Independent sample t test was used for comparison of normally distributed continuous variables while an equivalent non-parametric test was used for non-normal distributions. Chi square test was used to compare discrete variables.

Results:

Out of 264 young patients admitted with STEMI 236 (89.4%) were males. Mean age was 36.4 years and the youngest patient was 21 years.

Risk factor profile

Smoking was the commonest traditional risk factor for coronary artery disease among this population and was seen only among males (n=152, 58%). Dyslipidaemia was seen among 47% (n=123). Prevalence of hypertension and diabetes mellitus was 32% (n=85) and 21% (n=56) respectively. 42% (n=110) of the study group had positive family history for CAD. Physical inactivity (sedentary lifestyle) was seen among 55% (n=146). Only 6 patients gave the history of substance abuse (cannabis – 5, heroin -1) within 48 hours of the indexed event. Baseline characteristics of the study population are shown in table 1.

Table 1: Demographic characteristics and risk factor profile

Age	**36.4 (±3.2)**
Male gender	**236 (89.4%)**
Smoking	**152 (58%)**
Dyslipidaemia	**123 (47%)**
Hypertension	**85 (32%)**
Type 2 Diabetes Mellitus	**56 (21%)**
Family history	**110 (42%)**
Physical inactivity	**146 (55%)**

Mode of clinical presentation:

The most common presentation was central chest pain in 242 (92%) patients with radiation (51%), followed by sweating (40%), nausea/vomiting (37%) and breathlessness (16%). Sixteen patients (6%) had atypical symptoms, mainly epigastric discomfort mimicking gastritis. (Table 2).

Table 2: Clinical and ECG characteristics of the patients

Clinical Presentation	
Central chest pain	242 (92%)
Radiation (arm/neck/jaw)	135 (51%)
Sweating	106 (40%)
Nausea/ vomiting	98 (37%)
Breathlessness	42 (16%)
Atypical presentation	16 (6%)
Type of STEMI	
Anterior	159 (60%)
Inferior	72 (27%)
Lateral	27 (10%)
Posterior (without Inferior STEMI)	6 (2%)

Anterior STEMI was the commonest presentation (n=159, 60%) followed by inferior STEMI (n=72, 27%). Only 39 patients were admitted to the cardiology unit for primary PCI and others (n=225) were transferred to the cardiology unit from peripheral hospitals for pharmaco-invasive therapy. 34 patients had late presentation of STEMI and hence were not thrombolysed. Out of the 191 patients thrombolysed, 164 patients had tenecteplase and 27 patients had streptokinase as the thrombolytic agent. All were treated with aspirin 300 mg, clopidogrel 600 mg and high dose statins. At the time of admission to the cardiology unit, 23 patients were in cardiogenic shock requiring one or more inotropes and 6 patients required Intra-Aortic Balloon Pump (IABP).

Angiographic characteristics

All patients but 18 underwent coronary angiography predominantly via right radial approach (n=243). 10 patients had crossover to right femoral due to failed access (n=4) and anatomical difficulties (n=6). In 8 patients right femoral approach was used as they were in cardiogenic shock. 3 patients succumbed to severe cardiogenic shock before undergoing the coronary angiogram.

Out of 261 patients who underwent coronary angiograms, 45 patients had either normal coronaries (n=18) or non-obstructive coronary artery disease (n=27). 216 patients (82%) had obstructive coronary artery disease and 143 of these had single vessel disease. Left anterior descending artery (LAD) involvement was the commonest (n=88) followed by right coronary artery (RCA) (n=32) and left circumflex artery (LCX) (n=23). 35 patients had double vessel disease (DVD) and of these,16 patients had LAD and RCA involvement and 11 patients had LAD and LCX involvement. 38 patients had three vessel coronary artery disease (TVD). Four patients had significant left main involvement. 2 patients (one male and one female) had spontaneous coronary artery dissections involving LAD. The male patient with spontaneous coronary artery dissection underwent PCI with DES and the other patient was managed medically. Left anterior descending (LAD) artery was the culprit artery in 148 patients (56.1%), right coronary artery (RCA) in 51 patients (19.3%) and the left circumflex coronary artery (LCX) in 33 patients (12.6%).

The coronary lesions were classified according to the American Heart Association/ American College of Cardiology guidelines. Type B lesions were the commonest (44%) followed by type A (31%) and type C (25%).

Of the 216 patients with obstructive CAD, 195 patients underwent percutaneous coronary intervention during their indexed admission and 14 patients were referred for CABG and 7 patients were managed medically.

Almost all the patients who underwent PCI received everolimus drug eluting stents (DES) (which was primarily decided by the availability of the specific type of DES rather than operator's choice). 268 DES were used among 195 patients with a median of 1.37 stents per patient. Mean diameter of the stents were 2.88 mm and mean length was 29.62 mm.

Post MI Complications during hospital Stay

The commonest complication encountered was acute left ventricular failure which was seen in 24% of the study population (n=63). 22 patients had Killip II heart failure while 18 patients had Killip III heart failure. 23 patients had Killip IV heart failure requiring inotropes and of these 6 patients required intra-aortic balloon pump support in addition to inotropic support to maintain blood pressure. 17 patients were diagnosed with acute pericarditis during recovery and 8 patients had developed arrythmias including 2 patients who had malignant ventricular tachycardia.

None of the patients developed any mechanical complications such as acute mitral regurgitation, acute ventricular septal defects or free wall rupture.

All patients had echocardiograms performed before discharge. 46% had preserved left ventricular function (n = 122) while 22 %, 16% and 14% had mild (n=58), moderate (n=41) and severe (n=37) left ventricular dysfunction respectively. On discharge, all patients were on aspirin and a P2Y12 inhibitor (clopidogrel or ticagrelor). More than 90% of the discharged patients were on a statin (94% on atorvastatin), a betablocker and either angiotensin converting enzyme (ACE) inhibitor or ACE receptor blocker. Almost all patients with either moderate or severe left ventricular systolic dysfunction were on spironolactone except for few patients who experienced acute kidney injury and electrolyte imbalance. Overall adherence to the guideline directed medical management was seen in more than 90% of the population.

Discussion:

The prevalence of myocardial infarction in young adults < 40 years is 5–11% of all the hospitalized myocardial infarcts and it continues to rise.

Previous studies conducted in many parts of the world have suggested that myocardial infarction in young patients is predominantly a disease of men and the gender distribution of ''young'' myocardial infarction in males is reported to vary between 78 - 95% [17,18,19,20] . The Framingham Heart Study's 10-year follow-up data showed that the incidence of myocardial infarction was 12.9, 38.2, and 71.2 per 1000 in men and 2.2, 5.2, and 13.0 per 1000 in women in the age groups of 30 to 34, 35 to 44, and 45 to 54 years, respectively [21]. A similar gender distribution among males (89.4%) vs females (10.6%) is seen in our study. This is mainlyattributed to the protective effects of estrogens in preventing atherosclerosis and to some extent tothe prevalence of smoking which was much more common amongst males. This has been clearly demonstrated in various epidemiological studies especially in south Asian countries [22] .

Risk factor profile

Smoking was the commonest risk factor identified among the study population and as expected it was exclusively among males. It accelerates all stages of atherosclerosis by inducing endothelial dysfunction and coronary vasoconstriction, hastening thrombotic process, inducing proinflammatory effects and ultimately creating a pro thrombotic milieu. Smoking is identified as one of the strongest modifiable risk factors associated with young myocardial infarctions and Yusuf et al. suggested the association of smoking and MI in the young patients below 45 years has an odds ratio (OR) of 3.33 (99% confidence interval (CI), 2.86-3.87) compared to controls [23]. Aggarwal et al. found a significantly high prevalence of smoking among young patients presenting to hospital with myocardial infarctions and according to their study prevalence of smoking was five times higher among young patients with myocardial infarctions than age and gender matched general population[24]. The number of cigarettes consumed by young patients with myocardial infarctions per day was significantly higher compared to older patients, but as expected smoking pack years was low [25]. According to Larsen et al, 78% of young patients with STEMI were current smokers compared with a smoking prevalence of 23.72% in their age and gender matched general population and he further noted a significant reduction of the smoking prevalence with increasing age in both general population and the STEMI population [26].

The overall OR for smoking in the STEMI population compared with the general population was 3.4 (95% CI, 3.3-3.4), with the highest OR seen in patients aged 18 to 34 years (OR, 11.4 [95% CI, 10.0-12.8]) [26] . These data strongly confirm the enduring detrimental effect of continued smoking. Smoking cessation should be initiated at the primary prevention level. There should be a strong legislation to reduce smoking as it will cut down not only the major risk associated with ischaemic heart disease and other diseases but also, it will cut down the tremendous health expenditure on these conditions.

Dyslipidaemia is a well-known risk factor for ischaemic heart disease and it appears to be strongly linked with STEMI in young adults as well [17,18,19]. The prevalence of dyslipidaemia in our study group was 47%. Some studies demonstrate a similar or lower prevalence of dyslipidaemia among younger patients with STEMI [19,20,28] while others report a higher prevalence [33,35]. Wiesbauer et al. reported relatively high prevalence of familial-combined hyperlipidaemia in young patients with MI, reporting a prevalence of 38% [36] . In addition, endogenous cholesterol synthesis has been shown to be higher among young patients with myocardial infarctions and as a result, they tend to have a higher level of non-HDL cholesterol [37, 38]. The odds ratio for non-HDL cholesterol in young patients with myocardial infarction compared to the control adjusted for age, gender and other traditional cardiovascular risk factors was 5.02 (95% CI, 2.75-9.15) in a recent study [38] .

42% of our study population had a positive family history of coronary heart disease. A family history of premature coronary artery disease is reported in 40% - 72% of young patients with STEMI [17,18,19,20,28]. Young patients with myocardial infarctions appear to have two-fold higher prevalence of positive family history for pre mature coronary artery disease compared to older patients with myocardial infarction [18,19], although some studies suggest even higher prevalence, high as four-fold [17,28]. According to a study done by Oliveira et al, odds ratio for a positive family history of premature coronary artery disease among young men aged 45 years with myocardial infarction was 1.84 (95% CI, 1.07-3.17), in comparison to those who did not [27] .

Prevalence of diabetes and hypertension were reported to vary from 9% - 20% and 16% 46% respectively among young patients with STEMI [17,18,19,20,28].

The prevalence of diabetes and hypertension among young STEMI patients was considerably lower than the prevalence reported among their older counterparts [17,18,20,28]. Untreated hypertension appears to be more prevalent among young patients with STEMI (OR 2.99: 95% CI, 2.00-4.46) suggesting the prevalence of hypertension among young adults is under-reported [29]. The prevalence of diabetes in young patients with STEMI may be relatively low but it is still associated with high risk [27]. A recent study has demonstrated that the adjusted odd ratio for diabetes in patients compared to those who do not have diabetes, was 8.34 (95% CI, 1.67-41.6) [27] .

The clinical presentation of acute MI in young adults differs from their older counterparts. The vast majority (92%) came with chest pain and only a minority had atypical symptoms. The prevalence of chest discomfort suggestive of stable angina within last month of the STEMI was 22% in our study. This is comparable with most of the previous studies. In a study done by Chen et al, two third of the patients with STEMI denied having a chest pain or discomfort suggesting angina prior to the onset of STEMI [32]. He further noted that the majority of patients had chest pain, less than 5 days before they came to hospital. Anterior STEMI was the commonest type of STEMI(60%) in our study group and this is a universal finding in almost all studies done among young patients with STEMIs [17,18,19,20,28].

Angiographic characteristics

Coronary angiography usually reveals less extensive disease in young patients with ST elevation myocardial infarction when compared with their older counterpart [17,19,28]. Significant proportion of patients in our study had obstructive coronary artery disease (82%) and the majority had single vessel disease followed by TVD and DVD respectively. Our findings are consistent with the other studies done in India and other Asian countries [17,20,22,28]. However, studies carried out in western populations showed higher prevalence of normal coronaries and non-obstructive coronary artery disease compared to the Asian counterpart [18,19,31].

This may, at least, partly be explained by the higher prevalence of coronary artery disease risk factors and more aggressive nature of the atheromatous disease found among south Asians.

Hospital outcome (Table: 3)

Occurrence of heart failure varies significantly among studies. 20% of young STEMI patients developed acute left ventricular failure and 17% had cardiogenic shock during the indexed hospital admission in a study done by Chua et al [28]. Our study has comparable findings to the aforementioned studies. However, Pizzaro et al and Hosseini et al observed much lower prevalence of acute left ventricular failure (15% and 6.8% respectively) among young patients with STEMI [19,20]. Acute left ventricular failure is prognostically very important as Killip III or IV heart failure are identified as the strongest predictors of in hospital mortality (OR: 42.15 CI: 8.13– 218.57) and morbidity (OR:31.45 CI:7.22–137.06) [28]. Further a study done by Fournier et al. revealed that the strongest independent predictor of the long-term mortality rate in young patients with STEMI was an ejection fraction less than 45% (odds ratio 4.4, 95% confidence interval 1.6 to 12.4) [33]. Not surprisingly, in-hospital mortality and morbidity rates (except heart failure) were very low in our study and they were comparable to other studies done among young STEMI patients [35].Adherence to the guideline directed medical treatment was excellent in this study as more than 90% of the patients were on aspirin, P2Y12 inhibitors (either clopidogrel or ticagrelor), statin, beta blockers and ACE inhibitor or ARB blocker.

Study limitations

This study has a few limitations. Firstly, the small sample size of 264 does not allow for generalization of these results to the entire country.

Secondly, all study subjects had coronary angiograms and all patients in whom it was indicated, underwent PCI during index hospital admission.

This is not the reality for majority of young STEMI patients living outside Colombo as most of the patients with STEMIs will not get an opportunity for a coronary angiogram before discharge and will be managed medically.

Thirdly, we do not have objective reliable data regarding dietary patterns and psychological stress which could be important risk factors.

Finally, since this study was descriptive, no data was presented regarding statistical significance or correlation.

Conclusions

Our study showed that smoking and dyslipidaemia were important risk factors for STEMI in young patients and therefore more attention should be given for smoking cessation and screening and treatment of dyslipidaemia at primary prevention level. In addition, young patients with STEMI have less extensive coronary artery involvement and lower in-hospital morbidity and mortality.

Table 3: Coronary angiographic characteristics and hospital outcome index of the patients

Obstructive coronaries	216 (82%)
Single vessel disease	143 (%)
LAD	88 (33%)
RCA	32 (12%)
LCX	23 (8.7%)
Double vessel disease	35 (13%)
LAD & RCA	16 (6%)
LAD & LCX	11 (4%)
LCX & RCA	8 (3%)
Three vessel disease	38 (14%)
Non obstructive coronaries	27 (10%)
Normal coronaries	18 (7%)
Spontaneous coronary artery dissection	2 (1%)
Lesion characteristics	
Type A	81 (31%)
Type B	115 (44%)
Type C	65 (25%)
Coronary artery intervention procedure	
Radial	243 (93%)
Femoral	18 (7%)
Primary PCI	39 (15%)
Rescue PCI	156 (59%)
Days in CCU	1.9 □ 1.2
Length of hospital stay (days)	6.8 □ 2.7
In hospital mortality	6 (2.3%)
In hospital morbidity	
LV dysfunction at discharge	
None (EF > 50%)	122 (46%)
Mild (LVEF 40-50%)	58 (22%)
Moderate (LVEF 35-40%)	41 (16%)
Severe (LVEF <35%)	37 (14%)
Heart failure	63 (24%)
Killip II	22 (8.3%)
Killip III	18 (6.8%)
Killip IV	23 (8.7%)
Acute kidney injury	22 (8.3%)
Acute pericarditis	17 (6.4%)
Arrythmias	8 (3%)
Mechanical complications	0

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Research

Influence of Multidisciplinary Approach on Pregnancy and Fetal Outcomes in Women with Heart Disease Complicating Pregnancy

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Abstract

Introduction: Heart disease complicating pregnancy is an emerging clinical entity in both developing and developed countries. In addition to adherence to universally accepted recommendations, it is very important to have data representing different regions of the globe to identify their specific disease patterns and outcomes. When heart disease affects pregnancy, a multidisciplinary approach to manangement involving cardiologists, obstetricians, anesthetists and other relevant specialties has shown to produce overall better feto maternal outcomes.

Objective : To evaluate optimum fetal and maternal outcomes in heart disease complicating pregnancy when using modified World Health Organization (mWHO) risk classification and a multidisciplinary approach in a tertiary care center.

Methods : An observational descriptive study was conducted to evaluate the feto maternal outcome in pregnant patients with cardiac disease referred to the Teaching hospital Kandy, Sri Lanka from the 1st of January 2017 to 31st of December 2018. All consecutive pregnant patients (n=2107) who were referred for cardiac evaluation to the Teaching hospital Kandy were included in the study.

Results : Cardiac diseases were diagnosed in n=351(16.66%) patients. The mean age was 29.02±6.48 years. Out of the 351 patients, primi patients (57.83%, n=203) outnumbered non primi patients (42.17%, n=148). The majority (56.41%, n=198) were represented by valvular heart disease with rheumatic valvular heart disease being noted in 37.60% of the cases. Congenital heart disease, cardiomayopathies, primary pulmonary hypertension and rhythm abnormalities were observed in 30.77%, 9.69%, 1.99%, and 1.14% of cases respectively. Study population was further categorized into mWHO risk group as I, II, II-III, III and IV representing 16.52%, 26.50%, 33.05%, 3.13% and 20.80% respectively. While WHO risk group I and II were referred to the local hospital (43.02%) with a specific management plan, WHO risk group II-III, III and IV were referred to the Multi Disciplinary Meeting (MDM) (56.98%). Fifty two (14.81%) cardiac complications and thirty six 10.26% (n=36) non cardiac complications were observed. Eleven patients had undergone Percutaneous Transvenous Mitral commissurotomy (PTMC) for tight rheumatic mitral stenosis in the second trimester. There were 1.71% (n=6) of pregnancy terminations, 1.71% (n=6) neonatal deaths and 1.42% (n=5) of maternal deaths in the WHO risk group II-III and IV.

Conclusion: This study highlights that cardiac diseases complicating pregnancy is a challenging clinical entity which requires multidisciplinary approach for optimum clinical outcomes. Valvular heart disease is still the dominating cardiac pathology in heart disease complicating pregnancy. Presence of high percentage of primigravida warrants the importance of pre-pregnancy detection of these patients at community level.

Key words: Heart disease, Maternal mortality, Feto-maternal outcome, Multi-disciplinary approach

Introduction

Heart disease is the third most common and the leading non-obstetric cause of maternal deaths in Sri Lanka[(1)]. Pregnancy is physiologically stressful and leads to various hemodynamic adaptations of the body. The effects of these hemodyanamic changes on preexisting cardiac disease are highly variable and can adversely affect feto maternal outcomes.

The incidence of heart disease complicating pregnancy is 0.1 to 4% [(2,3,4)] worldwide. Despite the absence of specific data representing Sri Lanka, in a study by Kaluarachchi *et al.*, the incidence of heart disease complicating pregnancy was found to be 1.46% [(5)]. Rheumatic valvular heart disease (69.8%) was the commonest identified pathology with mitral stenosis taking precedence among others.

Congenital heart disease was encountered as the second most common cause accounting for 30% of cases [(5)].

Another study conducted by Haththotuwa *et al.,* on maternal mortality with reference to heart disease complicating pregnancy in Sri Lanka had shown that rheumatic mitral valve disease was responsible for more than a third of maternal deaths originating from cardiac diseases [(6)]. In addition to the available local data,current literature indicates the worldwide incidence of heart disease complicating pregnancy is increasing [(7)].

The incidence of maternal deaths in Sri Lanka has reduced over the last decade. Maternal mortality ratio in 2007 was 42 per 100,000 live births which dropped in 2013 to 37 per 100,000 live births.

Obstetric haemorrhage was the commonest cause of maternal deaths in Sri Lanka up to 2012. However, from 2013 onwards the most common cause of maternal deaths is due to complications of heart disease in pregnancy[8]. In 2013 maternal mortality ratio from heart disease complicating pregnancy was 8.7 per 100,000 live births [8].

Management of patients with heart disease during pregnancy is clinically challenging. This is mainly attributed to the presence of overlapping of symptoms in heart disease and pregnancy, delayed diagnosis, absence of technical expertise and poor knowledge about alteration of cardio-vascular hemodynamics on pre-existing cardiac diseases. Complications of heart disease in pregnancy depends on the primary cardiac pathology, right and left ventricular function, maternal functional class, pulmonary arterial pressure and co-morbidities which are unrelated to cardiac diseases [7].

Considering all these variables, it is important to have a systematic individualized approach during management to achieve a favorable feto maternal outcome. In the absence of a prior standard disease specific risk assessment tool to mitigate the complex nature of heart disease complicating pregnancy, mWHO risk classification system is highly recommended in developing countries and provides a comprehensive approach to guide management of these patients.

According to the mWHO risk classification system, heart disease complicating pregnancy is classified into five categories; m WHO I, II, II-III, III and IV. mWHO I is defined as no detectable increased risk of maternal mortality and no or mild increased risk of morbidity, mWHO II as small increased risk of maternal mortality or moderate increase in morbidity, mWHO II-III as intermediate increased risk of maternal mortality or moderate to severe increase in morbidity, mWHO III as significantly increased risk of maternal mortality or severe morbidity and mWHO IV as extremely high risk of maternal mortality or severe morbidity [7].This system further emphasizes the importance of adopting a multidisciplinary approach involving obstetricians, cardiologists and obstetric anesthetists and other relevant specialties in the management process.

Through our study, we emphasize on how to utilize the mWHO risk classification system and the multidisciplinary approach during the management of heart disease complicating pregnancy in a developing country to achieve optimum feto-maternal outcomes.

Material and methods

Study design

An observational descriptive study was conducted in Teaching Hospital Kandy (THK) from 1st of January 2017 to 31st of December 2018. All consecutive pregnant patients who were referred for cardiac evaluation were included. These patients were evaluated with clinical history, examination, 12 lead electrocardiogram (ECG) and two dimensional (2D) Echocardiogram. Based on initial evaluation, all patients were categorized into mWHO risk groups I to IV. WHO risk group I patients were referred to local hospitals with echo and clinic follow up, WHO risk group II were followed up once every trimester. WHO risk group II-III, III and IV were discussed in Multidisciplinary Meetings (MDM). MDMs were conducted once a week with the participation of cardiologists, obstetricians and obstetric anesthetists. Other relevant specialists were invited whenever there was an additional problem. The decision on special cardiac or obstetric interventions, mode of delivery and optimal method of contraception were discussed in the MDM. Patients in mWHO risk groups II-III, III were closely followed up by the cardiac team and obstetric team bimonthly and patients in mWHO risk group IV were followed up monthly. If any, special feto maternal events and management were well documented. Following delivery all patients were reviewed throughout the post-partum period up to one year to assess long term clinical outcome. Neonatal outcomes were noted at the end of four weeks of post-partum period.

Study setting

The study was conducted at Cardiology Unit and 3 separate obstetrics units in the Teaching Hospital Kandy, which is a major tertiary care center in Sri Lanka.

Study population

The study population consisted of all pregnant patients who were referred for cardiac evaluation irrespective of the Period of Amenorrhea (POA).

Inclusion criteria

Pregnancy was defined as having a Period of Amenorrhea (POA) with positive test for urinary Human Chorionic Gonadotropin (HCG) hormone and positive fetal ultra sound scan. All the patients who gave consent for the study were included.

Exclusion criteria

Patients who did not give consent for the study, were excluded.

Study instruments

Patients' ECG records, two Dimensional (2 D) echocardiography reports, inhospital medical documents as well as previous clinic records were used to collect data. In addition to those parameters, cardiovascular risk factors, cardiovascular history and relevant family history, as well as the systolic and diastolic blood pressures and heart rate on each clinic visits were obtained by detailed history taking and physical examination.

Plan of data collection

Demographic and other clinical data were collected through an interviewer administered questionnaire. ECG records and 2D echocardiography findings were collected by trained research assistants. At the end of the post-partum period the patients were assessed by a consultant cardiologist or senior registrar in cardiology and data were collected.

Statistical analysis

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

Results

Demographic data

A total of 2107 pregnant patients were referred to the cardiology unit with a suspicion of a cardiac disease during their pregnancy. Only 16.66% (n=351) (mean age= 29.02±6.48) had cardiac abnormalities and were categorized according to the mWHO pregnancy risk group I-IV.

Demographic data of study sample is shown in Table 01.

Characteristics	No of patients
Age (Years)	
15-20	18 (5.13%)
21-25	61 (17.38%)
26-30	140 (39.89%)
31-40	122 (34.76%)
>40	10 (2.85%)
Parity	
Primi	203 (57.83%)
Non- Primi	148 (42.17%)
Gestational age of referral	
T_1	174 (49.57%)
T_2	134 (38.18%)
T_3	41 (11.68%)
Post partum	02 (0.57%)
NYHA class	
NYHA I	182 (51.85%)
NYHA II	92 (26.21%)
NYHA III	47 (13.39%)
NYHA IV	30 (8.55%)
Diagnosis	
Newly diagnosed cases	229 (65.24%)
Previously diagnosed cases	122 (34.76%)
WHO risk group	
I	58 (16.52%)
II	93 (26.50%)
II-III	116 (33.05%)
III	11 (3.13%)
IV	73 (20.80%)
Patients with anticoagulation	30 (8.55%)
Mitral stenosis with atrial fibrillation	20 (66.67%)
Cardiomayopathy	6 (20.00%)
Metallic valve	4 (13.33%)

Table 01: Demographic data of all patients

Signs and symptoms

The commonest indication for cardiac referral was the detection of a cardiac murmur 86.32% (n=303). Tachycardia 47.01% (n=165), peripheral oedema 7.98% (n=28) and clubbing 0.28% (n=01) were the other common causes for referral. Distribution of cardiac symptoms for referral is shown in Figure 01.

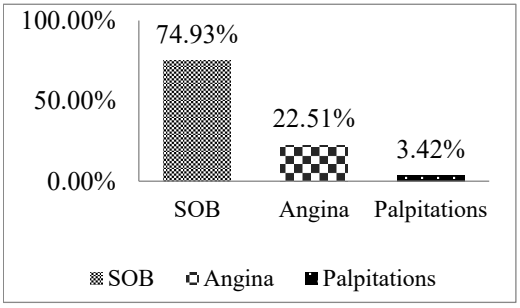

Figure 01: Distribution of symptoms on referral

Sources of referrals

Most referrals 41.03% (n=144) were from obstetricians, whereas community based Medical Officer of Health (MOH) was the next highest source of referrals at 26.78% (n=94). Others were referred by medical officers from Outpatient Department (OPD) (21.37%, n=75) and General Practitioners (GP) (10.83%, n=38) respectively.

Clinical spectrum of cardiac disease

Out of all the cardiac diseases, Valvular Heart Diseases (VHD) were the commonest (56.41%, n=198). There were 30.77%, (n=108) patients with Congenital Heart Diseases (CHD), 9.69% (n=34) with cardiomyopathy, 1.99% (n=07) with Primary Pulmonary Hypertension (PPHT) and 1.14% (n=04) with isolated rhythm abnormalities. (Table 02).

Cardiac lesion	No of patients
Valvular heart disease: 198 (56.41%)	
1. Rheumatic valvular heart disease: 136 (38.75%)	
Mixed mitral valves (MS and MR)	58 (16.52%)
Multiple valvular heart disease (MS, MR, AS and AR)	31 (8.83%)
Mitral stenosis (MS)	**26 (7.40%)**
Mitral regurgitation (MR)	11 (3.13%)
Aortic stenosis (AS)	04 (1.14%)
Prosthetic Metalic valve	04 (1.14%)
Mixed aortic valve (AS and AR)	01 (0.28%)
Bio prosthetic valve	01 0.28%)
2. Non- Rheumatic valvular heart disease: 62 (17.66%)	
MV prolapse/MR	40 (11.39%)
Pulmonary stenosis	12 (3.41%)
Bicuspid aortic valve disease	07 (1.99%)
Aortic regurgitation	03 (0.85%)
Congenital heart disease (CHD): 108 (30.76%)	
1. Acyanotic heart disease: 89 (25.35%)	
Atrial septal defect (ASD)	65 (18.51%)
Ventricular septal defect (VSD)	16 (4.55%)
Patent Ductus Arteriosus (PDA)	04 (1.14%)
Coarctation	02 (0.56%)
PDA	02 (0.56%)
2. Cyanotic heart disease: 19 (5.41%)	
Tetralogy of fallot	10 (2.84%)
Eisenmenger's VSD	05 (1.42%)
Transposition of grate vessels (Surgically corrected)	02 (0.56%)
Eisenmenger's ASD	02 (0.56%)
Cardiomayopathies: 34 (9.69%)	
Peipartum cardiomayopathy	09 (2.56%)
Hypertrophic Obstructive Cardiomayopathy (HOCM)	07 (1.99%)
Others	18 (5.12%)
PPHT: 07 (1.99%)	
Isolated rhythm abnormalities: 04 (1.14%)	

Table 02: Clinical spectrum of cardiac disease

Clinical spectrum of WHO Risk group IV

The clinical spectrum of WHO risk category IV where the pregnancy is contraindicated, is shown in Figure 02.

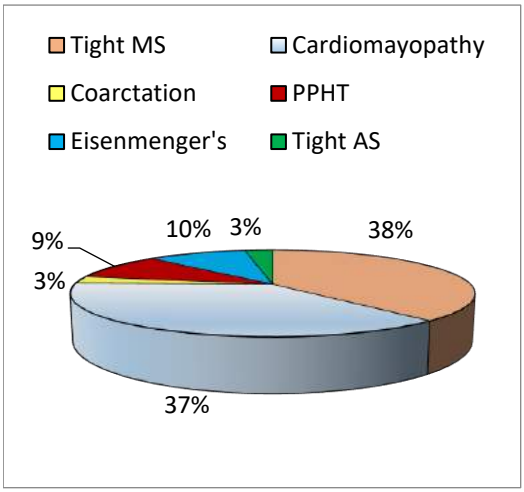

Figure 02: Clinical spectrum of WHO risk group IV

Out of WHO risk group IV, 11 patients (15.07%) with symptomatic tight rheumatic mitral stenosis had undergone percutaneous transvenous mitral commissurotomy (PTMC) during the second trimester and others (23.29%, n=17) were managed medically. Patients with cardiomyopathy (36.99%, n=27), PPHT (9.59%, n=07), Eisenmenger's (9.59%, n=07), Coarctation of aorta (2.74%, n=02) and tight AS (2.74%, n=02) were offered optimal medical management with close monitoring of feto maternal wellbeing. Patients with coarctation had undergone surgical correction during the post partum period.

Six (8.22%) patients in this group had undergone first trimester medical termination due to the presence of PPHT (n=03), Eisenmenger's syndrome (n=02) and peripartum cardiomyopathy (n=01). There were 26 (35.62%) pre term deliveries and 41 (56.16%) term deliveries in WHO risk group IV with an average birth weight of 2.12±0.23 kg. Intra Uterine Growth Restriction (IUGR) of this group was encountered in 21.92% (n=16) patients including 5.48% (n=04) neonatal deaths. In this group 04 (5.48%) maternal deaths were encountered due to tight MS, Eisenmenger syndrome due to VSD, right heart failure with PPHT and peripartum cardiomyopathy.

Complications during pregnancy in the study sample

Complications noted in the study population are shown in Table 03.

Complication	No of patients
Cardiac :	52 (14.81%)
Heart failure	20 (5.70%)
Atrial fibrillation	12 (3.42%)
Isolated high ventricular ectopic burden	07 (1.99%)
Hypertension	05 (1.42%)
Hypercoagulation related	04 (1.14%)
Ventricular tachycardia	02 (0.57%)
Acute pulmonary embolism	01 (0.28%)
Infective endocarditis	01 (0.28%)
Non cardiac:	44 (12.53%)
Anaemia	12 (3.42%)
Postpartum sepsis	09 (2.56%)
Gestational diabetes	08 (2.28%)
Pre-eclampsia	07 (1.99%)
Postpartum haemorrhage (PPH)	06 (1.71%)
Eclampsia	02 (0.57%)

Table 03: Distribution of complications

Maternal Mortality

Only 1.42% (n=05) of maternal deaths were attributed directly to cardiac disease. The main causes of these five maternal deaths were tight MS, Eisenmenger syndrome due to VSD, right heart failure with PPHT, peripartum cardiomyopathy and endocarditis complicating bicuspid aortic disease.

Time of delivery and fetal outcome of the study sample

Time of delivery and fetal outcome of the study sample is shown in Table 04.

Outcome	No of Babies
Term delivery	302 (86.04%)
Preterm delivery	43 (12.25%)
Birth weight	2.31±0.54 kg
Low birth weight	31(8.83%)
Intra Uterine Growth Restriction (IUGR)	24 (6.84%)
Intra Uterine Death (IUD)	02 (0.57%)
Twin delivery	02 (0.57%)
Neonatal death	06 (1.71%)
Termination of pregnancies	06 (1.71%)
Miscarriage	06 (1.71%)

Table 04: Fetal Outcome

Method of delivery

Considering the mode of delivery majority of patients had undergone Lower Segment Caesarean Section (LSCS) 207 (58.97%) in which 117 (56.52%) were due to non cardiac indications while only the 90 (43.47%) were due to cardiac indications (Table 05). Another 37.61% (n=132) had undergone Normal Vaginal Delivery (NVD) with assisted second stage.

Indication for LSCS	No of patients
Cardiac:	90 (43.47%)
Valvular heart disease	59 (28.50%)
Cardiomayopathy	26 (12.56%)
Severe PHT	03 (1.44%)
Coarctation	02 (0.96%)
Non- cardiac:	117 (56.52%)
Previous LSCS	58 (28.02%)
IUGR	20 (9.66%)
Cephalo pelvic disproportion	14 (6.76%)
Gestational Diabetics mellitus	12 (5.79%)
Preclampsia	07 (3.38%)
Eclampsia	02 (0.96%)
Others	04 (1.93%)

Table 05: Indications for LSCS

Contraception

Contraceptive methods used by study sample are shown in Figure 03.

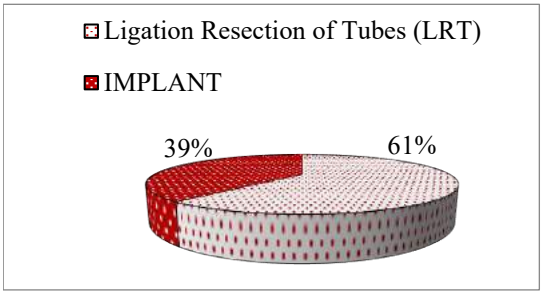

Figure 03: Method of contraception

Discussion

Heart disease complicating pregnancy is one of the leading causes of maternal mortality in Sri Lanka. Our study highlights the complexity of clinical presentations and the importance of a multidisciplinary approach to achieve a favorable feto maternal outcome.

The commonest symptom of the cardiac disease was shortness of breath which can often be overlooked in pregnancy as a symptom. This highlights the importance of taking a detailed history and a thorough physical examination of pregnant patients with symptoms of concern.

The mean age of the pregnant patient in our study was 29.02±6.48 years. Heart diseases were newly diagnosed during the current pregnancy in 65.24% of these patients. This indicates that most of these patients become pregnant without having a prior cardiac diagnosis. Also a cardiac diagnosis was missed in some patients during their first pregnancy and only subsequently noted . This reiterates the importance of pre-pregnancy detection of cardiac disease at the community level. However, majority of patients 49.57% (n=174) were referred during the first trimester. This allowed sufficient time to determine on future course of management in pregnancy, especially concerning the high WHO risk groups. Rheumatic Valvular Heart Disease (RVHD) is the leading cause of cardiac disease complicating pregnancy in developing countries which accounts for 56-89% [9, 10]. According to the prospective study done by Kaluarachchi et al from 1989 -1992 in Sri Lanka, RVHD encompassed 70% of pregnant patients with heart disease.

However, in our study RVHD accounts for only 38.75% of cases which is a low incidence compared to the previous study. Interestingly, this figure may represent an early paradigm shift of our disease pattern towards the western pattern of non valvular etiology. This emphasizes the importance of conducting multi centric similar studies representing the whole country. Among the patients with RVHD, mixed mitral valve disease (16.52%) was the predominant valvular pathology, while multiple valvular lesions accounted for 8.83% of patients. Though isolated moderate and tight mitral stenosis accounted for only 7.40% of patients, it was the dominating valvular lesion manifesting as isolated, mixed and multiple valvular pathologies, accounting for 32.76% (n=115). This is comparable to the study conducted by Asghar et al[11], in which RVHD was seen in 66% of cases, and involvement of mitral valve was seen in all the cases. In our study five patients had previously undergone prosthetic valve replacement in the form of metallic valve in 1.14% (n=04) patients and with bio-prosthetic valve in only one (0.28%) patient. Patients with metallic valves had significant management concerns due to anticoagulation use during pregnancy.

Management of anticoagulation therapy in pregnancy is a very challenging clinical problem. In the present study anticoagulation therapy was entailed in 30 patients, mainly due to the mitral stenosis with atrial fibrillation (66.67%), cardiomyopathy (20.00%) and metallic valve replacement (13.33%).

Pregnant patients with metallic valve replacements carry a high risk of mortality due to valve and anticoagulation therapy related complications including valve thrombosis and hemorrhagic complications. Since Vitamin K Antagonists (VKA) are considered the most effective therapy to prevent valve thrombosis, our strategy was to continue VKA low dose (<5 mg daily) in first, second and third trimester with close monitoring of International Normalized Ratio (INR) up to 36 weeks. At the beginning of 36 weeks of pregnancy, hospital admission was followed by VKA therapy which was substituted with Un-Fractionated Heparin (UFH) or Low Molecular Weight Heparin (LMWH) therapy until 36 hours before delivery.

From this point of time onwards, only UFH therapy was continued to maintain activated Partial Thromboplastin Time (aPTT) ≥ 2 of control and was stopped 4 hours prior to delivery. After 4-6 hours of delivery same regime of UFH was initiated to maintain target aPTT [7,12,13]. In a situation where higher dose of VKA (>5 mg daily) were required during first trimester, the therapy was substituted with LMWH therapy after hospital admission up to 12 weeks. This is then reconverted to VKA during the second and third trimester up to 36 weeks and conventional UFH therapy was followed till the delivery and immediate post partum period.

In contrast to western data, in our study CHD and cardiomyopathies only accounted for 30.76% and 9.69% respectively. However the corresponding data for CHD in western populations were 75-82% [10, 14] .This is due to higher number of women with surgically corrected congenital heart diseases surviving and becoming pregnant and the relative low incidence of rheumatic fever in developed nations. In our study, among the congenital heart diseases, acyanotic heart diseases (82.40%) were responsible for most of the cases. The majority of this group were represented by the patients with ASD (73.03%, n=65). Similar findings were encountered in several studies done in both developed and developing countries [6,15,16,17].

Ischemic heart disease (IHD) is 3-4 times higher during pregnancy [18,19]. In our study, though none of the patients were referred for IHD during the pregnancy, there could be many patients including those in the cardiomyopathy group.

Primary pulmonary hypertension which generally represents pregnancy with poor outcome, accounted for 1.99% of cases. Rhythm abnormalities are more common during pregnancy than during the non pregnant state and were observed in 1.14% of patients. All of these patients were regularly monitored with holter study by consultant electro physiologists.

This study also highlights the importance of categorization of pregnant patients with cardiac diseases according to the WHO modified risk groups in term of streamlining the management strategies. In the present study, WHO risk group I, II, II-III, III and IV consisted of 16.52%, 26.50%, 33.05%, 3.13% and 20.80% respectively.

Interestingly, one fifth of the patients belonged to WHO risk group IV where pregnancy was contraindicated. However the majority of those patients were successfully managed with acceptable feto maternal outcome. Furthermore, in this group 15.49% (n=11) of patients with tight mitral stenosis had undergone PTMC during second trimester representing modification of risk classification from WHO risk group IV to II which further exemplified the iatrogenic modification of WHO risk groups. While the WHO risk group III and IV were being managed in tertiary care hospitals, other groups were safely referred to regional hospitals with a detailed management plan [8]. This helps to reduce the burden on the tertiary care hospital and allows utilization of available health care resources more efficiently.

According to the Guidelines of Cardiovascular disease in Pregnancy published by the European Society of Cardiology (ESC) in 2018, the predictors of future adverse maternal and fetal outcomes were NYHA class III/IV, maternal left heart obstruction (moderate to severe mitral stenosis, aortic stenosis), maternal cardiac medications before pregnancy and mechanical valve prosthesis [10,20,21,22,23,24]. Regarding the maternal complications in our study, cardiac complications were observed in 14.81% of cases, mainly due to heart failure (5.70%) and atrial fibrillation (3.42%) Other non cardiac complications were observed in 12.53% of patients mainly related to anemia (3.42%), puerperal sepsis (2.56%), gestational diabetes (2.28%), pre-eclampsia (1.99%) and PPH (1.71%). A similar finding was observed in a prospective multicentre Canadian study, in which the observed cardiac complications were seen in only 13% of pregnancies [10]. However another study conducted in a country with resource poor settings by Nqana T et al [25] revealed a corresponding figure of cardiac complications was 30%. The number of maternal deaths in our study was 1.42%, but in current literature the maternal mortality in cardiac patients demonstrated variable figures. A study done by Malhotra et al [26] revealed 0.64% of maternal death and Sawhney et al [27] demonstrated that maternal mortality was 2.08%. In our study this low maternal mortality was mainly due to the early referrals and a dedicated multidisciplinary approach during the management process.

Though the Normal Vaginal Delivery (NVD) with assisted second stage is a standard mode of delivery in cardiac patients, only 37.61% of patients had undergone NVD. Majority of our patients had under gone LSCS (61.25%), mainly due to non cardiac indications (56.52%) rather than pure cardiac indications (43.47%). Regarding the cardiac indications, this high figure of LSCS indirectly reflected the number of high risks groups that had been managed in our study. The main recommended cardiac indications for LSCS were coarctation of aorta, pulmonary hypertension, Marfans syndrome and patients with anticoagulation therapy. Another 1.71 % of patients in our study had undergone termination of pregnancy, mainly due to PPHT, Eisenmenger syndrome, peripartum cardiomyopathy. Generally the main indications for terminations were PPHT, Eisenmenger's syndrome and Mafan's syndrome with dilated aortic root [28]. This finding was comparable to the study done by Farhan et al [11], in which the therapeutic termination was done in 2% of cases. However in another study conducted by Warnes et al, the corresponding value was 6.3% [28].

The majority of deliveries (86.04%) were term deliveries whereas preterm deliveries accounted for 12.25% of all deliveries. This high percentage of term delivery re-emphasizes the importance of multidisciplinary approach for the management of these patients. Specially, in cases of high risk pregnancies, our strategy was to admit these patients after the second trimester in order to provide a close monitoring of maternal wellbeing by means of ECG, 2D echocardiogram and fetal biophysical profile by fetal ultrasound scan and cardiotocography (CTG). This provides a maximum time of growing fetus in a natural environment, without compromising maternal hemodynamics. The standard mode of delivery was offered in the presence of feto maternal compromisation irrespective of POA. The mean body weight of the neonate was 2.31±0.54 kg but the corresponding value in the study conducted by Yasmeen et al [29] was 2kg. In the current study, IUGR was observed in (6.84%) of pregnancies and was more common in WHO risk group III and IV. Low birth weight was observed in 8.83% of cases, but the similar study done by kaluarachchi et al [7] in Sri Lanka, the incidence of low birth weight was 4%. Both IUD and twin delivery were noted in 0.57% of each category.

In general, in heart disease in pregnancy18-30 % neonatal complications are observed with a neonatal mortality of 1- 4% [12]. In our study, 1.71% (n=6) of neonatal deaths were observed. These neonatal deaths were mainly attributed to prematurity, respiratory distress syndrome and neonatal sepsis.

The main causes of five maternal deaths (1.42%, n=05) in our study were tight mitral stenosis, Eisemengher's syndrome with VSD, PPHT, peripartum cardiomyopathy and endocarditis complicating bicuspid aortic disease. All maternal and neonatal deaths were observed in the WHO risk group II-III and IV. These findings were consistent with the adverse predictors of maternal and neonatal outcome of ESC 2018 guidelines.

At the end of the pregnancy, the most appropriate contraceptive method was offered to the patient after in depth discussions with the patient regarding the future pregnancy related risks. In our study, 60.97% of patients underwent permanent sterilization by means of LRT while another 39.03 % of patients were offered implant as a temporary contraceptive measures.

Though the majority of patients were referred by obstetricians, the roles played by MOH and medical officers of OPD are also vital for early patient identification. Finally, despite only 16.66% of referred patients having cardiac disease, this low threshold for cardiac referral during pregnancy was considered as a positive attitude of our healthcare setup, especially in the absence of universal screening guidelines.

Conclusion

Heart disease complicating pregnancy is a challenging clinical entity encountered in Sri Lanka. Our study emphasizes the importance of a multidisciplinary approach in the management of these patients by categorization according to the WHO modified risk groups to better streamline the management strategy.

Despite representing higher percentage of RVHD in our study, the incidence was obviously lower than the previous similar studies conducted in Sri Lanka and other developing countries.

This highlights a trend towards transformation of the disease pattern similar to that of western countries. The higher number of primigravida patients and newly diagnosed cardiac patients in pregnancy warrant the establishing a mechanism for pre pregnancy detection of these patients at community level. Nationwide data collection and analysis through research will help in formulation of a plan of management and to develop regional guidelines to institute appropriate care at different levels of healthcare.

Limitations

The study was conducted in one of the major cardiology centers in Sri Lanka. However, expanding the study into a multicenter level would have given more representative values of Sri Lankan population.

In the present study, we have analyzed the data in the context of three years only. However, extension of the study period may represent more consolidated data.

Acknowledgement

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Research

Deep Sternal Wound Infection following CABG with Bilateral Internal Mammary Artery Grafting (BIMA): A Retrospective, Descriptive Study

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Abstract

Coronary artery bypass grafting (CABG) using both internal mammary arteries (BIMA) has been proven to improve long-term survival, reduce the incidence of post op angina, and grant more freedom from repeat revascularization. However, deep sternal wound infection (DSWI) is an infrequent serious complication of harvesting BIMA, which increases morbidity and mortality compared to using a single IMA.

The objective of this descriptive study was to determine the risk of deep sternal wound infection following BIMA harvesting and grafting.

A retrospective study was conducted on patients who underwent BIMA grafting for CABG at Cardiothoracic Unit III of the National Hospital of Sri Lanka from 1st July 2015 to 30th June 2021. A total of 91 patients were reviewed and evaluated. The main outcome was deep sternal wound complications. The preoperative and postoperative characteristics were also recorded.

There was no incidence of deep sternal wound infection in BIMA group. Harvesting BIMA is safe in selected patients.

Keywords: Coronary artery bypass grafting, Bilateral internal mammary artery, Deep sternal wound Infection.

Introduction

Coronary Artery Bypass Grafting (CABG) is the preferred treatment for multi vessel extensive coronary artery disease [(1)].

With the advent of the saphenous vein as a bypass graft in CABG, it became the most commonly used graft because it is readily available, easy to harvest, reproducible and has a favorable outcome [(2)]. After the landmark paper from the Cleveland Clinical group, published in New England Journal of Medicine in 1986, Left Internal Mammary artery (LIMA) became a standard bypass graft to the Left anterior descending artery (LAD). It is reported that LIMA to LAD grafting improved survival, patients became free from recurrent angina and myocardial infraction, further reducing the need for repeat revascularization compared to using only veins as bypass grafts [(3)]. Increasing evidence about the superior outcome of CABG with LIMA graft, prompted cardiac surgeons to start utilizing bilateral internal mammary arteries (BIMA) to achieve a better outcome. Patients who underwent CABG with BIMA had better long-term survival, reduced incidence of recurrent angina and freedom from repeat revascularization compared to using only LIMA [(4)].

However, harvesting BIMA is associated with a higher risk of sternal wound complications. The incidence of superficial sternal wound infections was between I.6% to 6.4%, and the incidence of deep sternal wound infection (DSWI) was 0.4% to 2.7% when using only LIMA. Following BIMA, harvesting the incidence of DSWI increased to 0.6% - 4.2% [(5)].

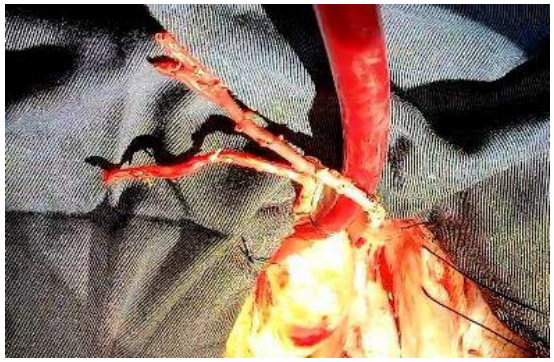
The objective of this study was to assess the effect of BIMA harvesting on the incidence of sternal wound infection after CABG at a single cardiothoracic unit of the National Hospital of Sri Lanka (NHSL).

Methodology

This retrospective study was conducted at Cardiothoracic Unit III of NHSL from 1st June 2015 to 30th June 2021. Patient medical documentation was reviewed to collect data of patients who underwent CABG with BIMA grafts. Patient demographics and co-morbidities were also recorded. Emergency surgery and CABG with concomitant valve procedures were excluded. Additionally, patients with morbid obesity, Chronic Obstructive Pulmonary Disease (COPD) and most patients with severe left ventricular dysfunction with EF of less than 30% were excluded. However, in our study group, patients with insulin dependent diabetes mellitus were also included. Sternal wound infection was defined in accordance with the guideline by the Centre for Disease Control and Prevention. It was classified as superficial sternal wound infection and deep sternal wound infection. Superficial sternal wound infection referred to the definition of superficial incisional surgical site infection, and deep sternal wound infection described the definition of deep incisional surgical site infection and organ/ space surgical site infection.

All patients received standard skin preparation and intravenous cefuroxime as the prophylactic antibiotic. Surgical approach was through median sternotomy.

The LIMA was always harvested in a pedicled manner, along with accompanying veins, pleura, and fascia with electrocautery. Arterial branches were secured with hemoclips and divided with electrocautery. The right IMA was always harvested in a skeletonized manner. It was dissected out from the adjacent veins, muscle, and fascia. Arterial branches were secured with hemoclips and divided. Additional conduits used were saphenous veins or radial artery. Both skeletonized and pedicled IMAs were harvested from their distal bifurcation up to 1cm from their emergence from the subclavian artery as in-situ grafts.



Harvested two Internal Mammary Arteries

Following the grafting, the sternum was closed in butterfly wiring with No 6 stainless steel wires. The subcutaneous tissues and skin were closed with absorbable suture. Patient was advised to wear a chest supporting corset postoperatively.

The data collected was entered in SPSS (version 22.00). Frequencies and means, as appropriate, for the clinical characteristics were obtained.

Results

The data of 91 patients who underwent BIMA grafting were collected. Generally, BIMA patients were younger (Mean age 47.81 years). 57.14% patients were younger than 50 years of age. This study included 81(89%) male and 10(11%) female patients. The mean BMI was 24.4 kg/m^2. All patients had preoperative ejection fraction >30%. Other preoperative clinical characteristics are presented in table1. Hypertension was the commonest co morbidity in this group. Six patients had insulin dependent diabetes mellitus in this study group.

Table1. Preoperative clinical characteristics of patients

Co morbidity	Number of patients	Percentage
Hypertension	64	70.3%
Diabetes Mellitus	33	36.3%
Dyslipidaemia	21	23.1%
Renal Impairment	3	3.3%
COPD	0	0
PVD	0	0
NYHA ≥ 3	27	29.7%

COPD: Chronic Obstructive Pulmonary Disease; PVD: Peripheral Vascular Disease, Renal Impairment: Serum Creatinine >1.5mg/dl, NYHA: New York Heart Association.

Postoperative clinical characteristics were noted in the table 2 and Table 3.

Table 2. Postoperative characteristics of patients

Variables	Number of patients	Percentage
Superficial sternal wound infection	5	5.5%
Deep sternal wound infection	0	0
Pleural effusion required drainage	3	3.3%
Reopening for bleeding	3	3.3%

Table 3. Intraoperative and Postoperative characteristics of patients

Variables	Mean value
Intraoperative blood loss	675.56 ml
Number of ICU days	2.54 days
Postoperative days	9.03 days

ICU: Intensive care unit

The LIMA was always grafted to the LAD. However, the RIMA was grafted to branches of right coronary artery in 6 patients (6.6%), territories of circumflex artery in 70 patients (76.9%), and diagonal branch in 15 patients (16.5%).

The RIMA has taken through the transverse sinus posterior to the aorta and the main pulmonary artery across the midline when grafting to the territories of the left coronary artery.

Intra venous antibiotics were used for superficial surgical wound infections following culture and ABST. Only 2 patients (40%) had positive bacterial cultures. Drainage and wound re-suturing were done for 2 patients (40%) within the same hospital admission.

The deep sternal wound infection was not encountered in any of the patients in this study.

Preoperative and postoperative attributes of patients who had superficial sternal wound infection are presented in table 4 and table 5.

Table 4. Preoperative details of patient who experienced superficial sternal wound infection

Co morbidity	Number of Patients	Percentage
Hypertension	5	100%
Diabetes Mellitus	4	80%
Dyslipidaemia	2	40%

Table 5. Postoperative details of patient experienced superficial sternal wound infection

Variable	Mean
Age	46.4 years
BMI	25.07 kg/m2
Number of ICU days	3.2 days
Postoperative days	18.8 days

ICU: Intensive care unit

Discussion

A large number of observational studies have demonstrated the benefits of BIMA grafts [4]. In comparison to other conduits, physical characteristics of the IMA confer long-term patency, and thereby several survival benefits. Its well-developed non fenestrated internal elastic lamina protects the media from potentially harmful luminal stimuli, as well as the migration of smooth muscle cells to initiate intimal hyperplasia.

The endothelium of the IMA has numerous unique features, which can produce large quantities of Nitric Oxide (NO) and prostacyclin. The NO causes vasodilatation, inhibits platelet activation and neutrophil adhesion to endothelium and reduces the plaque formation, thereby reducing the atheromatous plaque formation [6].

Despite the favorable outcomes, using both IMA was 20% in Europe and less than 5% in the USA [7].

DSWI is a serious complication which increases morbidity, hospital stay and the risk of postoperative mortality [8]. The main reason for this being the devascularization of the sternum, as a result of harvesting both IMAs. Performing skeletonized IMA reduces the risk of DSWI when compared with the standard technique of using pedicled IMA. When the IMA is harvested with the skeletonized technique it increases the length of the IMA by approximately 10 - 25 mm, allowing it to reach the distal vessels, especially when RIMA is used for left sided grafts [9]. However, harvesting skeletonized IMA is also more technically challenging and time consuming [10]. Therefore, to balance both effects, skeletonized right IMA and pedicled left IMA were harvested in this study.

In literature, the incidence of DSWI after open cardiac surgery has been reported as being between 0.8 - 5%. A study in Japan revealed the incidence of DSWI to be 1.8% and the mortality due to DSWI to be 5.2% following isolated CABG. The risk factors for DSWI are advanced age, obesity, Insulin dependent diabetes mellitus, smoking, prolonged operative time, haemodialysis, COPD, NYHA $\geq$ 3, and re-exploration for bleeding [8,11,12].

Hence, patient selection is of paramount importance for successful CABG using BIMA grafts. Among the risk factors, poor control of diabetes was a significant risk factor for DSWI. However, the risk of DSWI can be reduced in diabetic patients by strict preoperative and post operative glycaemic control, and harvesting the IMA in a skeletonized manner [13]. Therefore, in our study we included patients with insulin dependent diabetes. Insulin dependent diabetics are found to immensely benefit from BIMA grafting as the NO produced by the IMA grafts help in controlling the aggressive atheromatous disease in their coronary arteries.

BIMA grafting was generally performed in younger patients. The beneficial effect of cardiac related survival in using BIMA significantly reduced after the age of 60 years [14]. Compared to males, females experienced higher mortality after BIMA harvesting [15]. In addition, BIMA grafts were valuable for patients with normal left ventricular ejection fraction. Patients with impaired ejection fraction had significantly shorter life expectancy [16]. Therefore, young male patients with uncomplicated co-morbidities were more suitable for BIMA grafting.

Other specific measures in this series as sternal closure with butterfly wiring was also a contributing factor in reducing postoperative DSWI [17].

Conclusion

The study showed that, using both internal mammary arteries as a bypass graft in CABG, LIMA in a pedicle fashion, and RIMA in a skeletonized fashion, when combined with good patient selection, good patient preparation, and meticulous surgical technique could effectively avoid DSWI and be a safe procedure.

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Updates

A Digital Experience from a Physician Perspective

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A digital experience from a physician perspective

The global pandemic brought on by COVID-19 infection has been hugely disruptive and upended every facet of life including global educational events. International conferences have been cancelled, rescheduled, relocated or gone virtual.

The European Society of Cardiology organizes over ten large meetings, but its annual flagship event ESC Congress regularly attracts the largest number of participants with attendees from all parts of the world. With international travel restrictions in place and in-person gatherings problematic, the scheduled August 2020 meeting in Amsterdam looked in real danger from been cancelled or postponed, barring a miracle.

In a remarkable technical feat of streaming multiple simultaneous presentations totally online, the organizers set a new benchmark for online conferences. They created a rich digital experience of seamless, educational content that brought cutting-edge cardiology direct to stay-at-home participants.

I was one of the early 116,000 plus registrants from 211 countries that availed of the free offer to savour and enjoy this educational treat. Having confirmed my registration, it was going to be my second participation after presenting a poster at the London congress in 2015, albeit virtual this time. This gesture improved greater global coverage, nearly tripled the total registrations and featured more women and younger participation compared to the 2019 Paris conference. The conference recorded over 50,000 tweets, and images of participants viewing the proceedings in parking lots, and from beach vacations added to the surreal feeling. Despite the inability for networking and peer exchanges, the conference was hailed as a grand success.

I pre-planned to listen in live to much of the presentations knowing that anything interesting that I would miss was available on demand until the end of the month.

The focus of the meeting was undoubtedly to the large cardiology community and ever-expanding subspecialty professionals. As a general physician with an enduring interest in cardiology, I focused my attention on several topics that may have an impact on everyday practice in my specialty avoiding hardcore cardiology topics.

This account summarizes takeaways of eight selected presentations, that excited my interest and was practice changing for a physician, while improving my current understanding of cardiology.

Game changing therapies

The most-awaited presentation of the conference was undoubtedly the results of the EMPEROR-Reduced study [(1)]. The purpose of the study was to find out the safety and efficacy of the SGLT2 inhibitor, **empagliflozin** compared to placebo in patients with heart failure with reduced ejection fraction who were receiving optimal guideline-directed medical therapy. This class of drug was already known to be effective in heart failure in the DAPA-HF study with or without diabetes, the results of which were released at the previous ESC Congress 2019 in Paris and later published [(2)]. However, the patients recruited in EMPEROR-Reduced study were much sicker patients with heart failure with greater impairment of renal function and on more drugs and devices on board. After 16 months of the study, the trial showed significant findings on three pre-specified endpoints in a hierarchical manner: a) reduced risk of 25% of the primary endpoint of composite cardiovascular death or heart failure hospitalization, which was strikingly similar to DAPA HF, b) reduced first hospitalization by 30% - and c) a reduction in the rate of decline of renal function by 50%. The trial was notable for the absence of serious adverse effects. When these data are added to the results of DAPA-CKD study released at the same meeting showing impressive renoprotection in those with chronic renal disease with and without type 2 diabetes, SGLT2 inhibitors have truly come of age for a drug that was first used as a diabetic medication [(3)].

This becomes the only class of drugs to reduce blood glucose, blood pressure, uric acid levels, triglycerides and body weight. While the mechanism of this remarkable benefit will be debated in the years to come, there will be more widespread use of one of the several members of this class of drugs by cardiologists, endocrinologists and physicians.

While empagliflozin was impressive, another novel drug was been hailed a game changer. EXPLORER-HCM study compared **mavacamten**, a first-in-class drug that inhibits cardiac myosin with placebo in a phase 3 randomized double-blind trial in hypertrophic obstructive cardiomyopathy (HCM) patients with left ventricular outflow tract (LVOT) gradient >50 mmHg and run for 30 weeks [(4)]. The was the largest clinical trial to date in HCM and first one to target the underlying molecular defect of HCM to dampen the excess contractility of cardiac muscles seen in hypertrophic cardiomyopathy, the most common heritable cardiomyopathy.

There were impressive improvements in symptoms, exercise capacity, LVOT gradients and patient-reported outcomes and was well tolerated and safe. Given that the currently available drug treatment is limited and do not prevent progression, the positive results of this study herald a new era of medical therapy and change practice and fulfils an unmet need for patients who may have otherwise required surgery. Careful titration and left ventricular ejection fraction monitoring are however needed. The fate of beta blockers in this patient population will no doubt figure in the discussion aftermath of these results.

Comeback of plant-derived drugs

While the newer agents were making waves, two faithful drugs were showing signs of a comeback. The question posed by the investigators in the RATE-AF study was should betablockers or **digoxin** be used for long-term heart-rate control in patients with permanent atrial fibrillation and symptoms of heart failure in older patients (above 60 years) [(5)].

Heart rate control is highly relevant in atrial fibrillation and given that digoxin has been downgraded in rank of choice, this trial look set to answer an important clinical question.

To some but perhaps not to all to see digoxin showing better symptom improvement, lower rise of natriuretic peptide levels and less adverse effects was a surprise. That it did as well as a beta-blocker in controlling heart rate and quality of life indices will indeed help elevate digoxin's status as a frontline agent to control heart rate and resurrect its reputation as a durable and effective cardiac medication. The next prescription for this old workhorse of a drug should not be a giveaway of one's age.

Failure of beta-blockers to reduce mortality in heart failure with atrial fibrillation compared to heart failure with sinus rhythm is intriguing. The lack of efficacy is speculated to be related to greater heart rate lowering.

The other long-standing medication making a comeback was **colchicine**, used to treat attacks of gout which is emerging as an effective and safe therapy for both acute and chronic coronary artery disease. The LoDoCo2 trial was a double-blind, placebo-controlled trial done in patients with stable coronary artery disease with low-dose colchicine and followed up for an average of 5 years [(6)]. The main results showed a 30% reduction of composite four endpoints of the primary outcome in the treatment arm of death, heart attack, stroke or ischemia-driven coronary revascularization and a similar reduction in major adverse cardiovascular events. The drug was well tolerated and builds on the positive COLCOT study results in acute coronary artery disease patients as an inexpensive addition to standard medical therapy in coronary artery disease patients. A matter of concern is a signal of higher non-CV death in the COPS (Colchicine in Patients with Acute Coronary Syndrome) trial. This will call for more data and hold back full adoption. Further, colchicine's potential side effects and drug interactions will require personalized treatment and careful monitoring[(7,8)] .

A sub study presented at the Congress and reported in *Circulation* have shown that low-dose colchicine reduces the serum expression of 37 proteins after 30 days of treatment confirming its marked anti-inflammatory effect [(9)].

The concept of dampening inflammation to keep atherosclerosis in check was borne out strongly in this study and in the previous CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study) trial with canakinumab that blocks IL-1β [(10)].

Inflammation in atherosclerosis; one cell at a time

Atherosclerosis has gathered acceptance as the most chronic inflammatory disease. A presentation that caught my attention in the section of best of cardiovascular research, was by Claudio Monaco on the topic titled "Myeloid cells in atherosclerosis; one cell at a time" describing a lifetime of her work and new insights in to the subsets of the macrophages that populate two distinct compartments in the atherosclerotic vessel wall. With advances in single cell biology, immune cell subsets involved in atherosclerosis can be identified by new markers using a new mass cytometry technique which is superior to currently used immunohistochemistry or flow cytometry methods [11]. This new knowledge could lead to development of novel therapeutic molecules that selectively target these macrophage subsets responsible for lesion progression, hitherto not attempted.

Four new guidelines

The congress is often the stage to unveil a flurry of new practice guidelines. This year was no different with four new ones published. The chief ones were the updated recommendations on NSTE-ACS where notable recommendations were for the use of hs-Tn assays for rapid rule in and rule out and introduction of new risk categories and risk criteria for early invasive strategy the highlights, one on sports cardiology and exercise in patients with cardiovascular disease and another on adult congenital heart disease [12,13,14,15].

The guidelines can be laborious documents and not easy reads. The new atrial fibrillation (AF) guidelines won praise for simplicity, easy to remember concepts and eye-catching graphics.

Although the document runs into 126 pages with nearly 1500 references the authors have taken pains to simplify the main concept as ABC with an easy-to-recall 4S approach and a catchy "AF never comes alone" phrase.

Some new recommendations include systematic ECG screening for those 75 years and older or at high risk of stroke, structured characterization for 4Ss – stroke risk, symptom severity, substrate assessment, preference of NOACs over warfarin except in mitral stenosis and mechanical heart valves, lenient heart rate control (<110bpm) and aggressive risk factor reduction.

The recommendation of screening with wearables will be controversial without supporting outcome data.

Targeted novel therapies on residual cardiovascular risk

The evolving role of triglycerides with novel opportunities to tackle residual cardiovascular risk is the focus of the next three choices.

It is generally agreed that outcome study results are more valuable for decision making in clinical practice than imaging trials. This was shown with two previous lipid-lowering drugs; niacin and ezetimibe. Despite showing significant atherosclerosis reduction on MRI, niacin produced two negative clinical outcome trials in AIM-HIGH and HPS2-THRIVE [16,17,18]. Ezetimibe on the other hand, showing paradoxical progression of carotid intima medical thickness despite LDL-C reduction and went on to show a positive outcome result in the IMPROVE-IT study [19,20].

The 18-months results of the EVAPORATE trial was presented where **high-dose EPA** as **icosapent ethyl** showed significant plaque regression of all types except those with dense calcium, supporting the findings of REDUCE-IT trial which showed an impressive 30% reduction in first and recurrent events of the primary outcome [21]. Not everyone in the cardiology community agreed with the interpretation of the results with some disputing the statistics and others on the method of quantification of CT angiography-based analysis. The focus now would be to unravel the mechanism of benefit by this therapy given that the triglyceride lowering was relatively modest.

Staying with triglycerides, in an online Late Breaking Clinical Trial Session at the ESC Congress 2020, the results of phase 2 study, **vupanorsen** was presented, one of several recent therapies to target the messenger RNA [22].

Vupanorsen is an antisense angiopoietin-like 3 protein (ANGPTL3) inhibitor targeting lipoprotein lipase developed to treat patients with elevated triglycerides and atherogenic lipoproteins and further reduce the risk of future cardiovascular events.

In the phase 2 study, vupanorsen met the primary endpoint of significant reductions in triglyceride (TG) levels and multiple secondary endpoints compared to placebo, with a favorable safety and tolerability profile. This therapy if proven in outcome studies adds to the excitement of success reported recently with monoclonal antibody, **evinacumab** targeting the gene encoding ANGPTL3 [23].

Covid-19 and ACEI/ARB

Finally, a topical issue and a frequently asked question at the time of the covid-19 pandemic. Do ACEIs or ARBs protect or make one more vulnerable to covid complications in the light of the role the membrane bound ACE2 playing a pivotal entry point for the virus? ACE2 expression may be affected by angiotensin converting enzyme inhibitors and angiotensin receptor blockage and evidence from observational studies is conflicting regarding harm and benefit of these medications. In a randomized clinical trial (BRACE CORONA) involving 659 covid-19 confirmed patients in 29 hospitals in Brazil, ACEI/ARB treatment was either suspended or continued and primary outcome measured at 30 days, a first study to provide answer to this important clinical question [24]. There was no difference in the mortality between the two groups. Based on this study, at least in the mild to moderate covid-19 patients, these drugs pose no risk and may be continued for those with an indication for its use. The uncertainty of using these agents has been abated for now and the full publication of the study is awaited.

Participating virtually in this four-day event has allowed healthcare professionals like me to keep up to date on the latest science and tremendous progress in cardiology research.

This summary is a mere drop in the ocean of presentations made at the congress. Despite, the enjoyable and immensely educationally enriching experience, the fervent wish is that it be my first and last virtual congress.

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Journal Scan

Interventional Cardiology Trials of Importance in the First Half of 2021

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Despite the COVID19 pandemic, international cardiology meetings have continued on virtual platforms, with the results of a number of impactful clinical trials in interventional cardiology being presented. The American College of Cardiology (ACC) Scientific Sessions 2021 provided for extensive new randomized evidence on antiplatelet therapies and insights into interventional cardiology. At EuroPCR 2021, the main highlight was the EBC MAIN trial. This article provides a brief overview of the important late-breaking randomized controlled trials published and presented in the first half of 2021, looking at the aims, PICO (Population, Intervention, Comparator, Outcomes) Criteria, and main results of each trial.

The European bifurcation club Left Main Coronary Stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBCMAIN)

Hildick-Smith, et al., published in European Heart Journal (2021) 00, 1–11
Presented at Euro PCR 2021

Background: There remains some debate over the optimum stenting strategy for left main (LM) bifurcation lesions. The left main is peculiar from non-left main bifurcation lesions given the wide angle of separation between the left anterior descending (LAD) artery and left circumflex (LCx), the fact that neither of these is strictly a side branch, and the greater calcification and fibrosis involving the LM bifurcation, necessitating more lesion preparation [(1)]. While non-randomized data suggest that outcomes are worse with a two-stent strategy, the DK Crush V trial, the only randomized trial of LM bifurcations prior to EBC MAIN [(2)] showed better outcomes with an upfront two-stent strategy by the double kissing (DK) crush technique over a provisional stenting strategy [(3)].

On this background, the EBC MAIN trial, was designed and run through the European Bifurcation Club (EBC) to investigate clinical outcomes in patients with distal LM bifurcation lesions undergoing stenting randomized to receive either a stepwise layered provisional stenting strategy, or a systematic dual stenting strategy. This was an investigator-led prospective randomized multicenter trial, which recruited in 11 European countries.

PICO (Population, Intervention, Comparator, Outcomes) Criteria: 467 patients with true left main bifurcation lesions (Medina 1,1,1 or 0,1,1, with >50% narrowing of both the main branch and side branch and in which both vessel reference diameters were >_2.75mm) were randomized 1:1 to a stepwise layered provisional strategy (n=230) or a systematic two-stent strategy (n=237) at 31 sites in 11 European countries. The primary endpoint was a composite of death, myocardial infarction (MI), and target lesion revascularization (TLR) at 12 months. Secondary endpoints included death, MI, TLR and stent thrombosis.

Main results: There were no significant differences in the primary endpoints between the two groups. The composite of death, MI and TLR at one year was met in 14.7% vs 17.7% in the provisional and dual stent groups respectively (hazard ratio [HR] 0.8, 95% confidence interval [CI] 0.5 – 1.3, p=0.34), with numerically fewer major adverse cardiac events (MACE) occurring with a stepwise layered provisional approach. There was a 22% cross-over to a two-stent strategy from provisional. The use of intravascular ultrasound (IVUS), which was not mandated by protocol was used in only 36% of provisional stenting cases and 31% of systematic dual stent strategy cases (p = 0.3), potentially reflecting real-world practice.

In EBC MAIN, the two-stent strategy of choice was left to operator discretion: the predominant upfront two-stent strategy adopted in EBC MAIN was Culotte (53%), followed by T or TAP (33%), with only a small minority undergoing DK Crush (5%). Of the 22% who were randomized to provisional and required a bail-out 2nd stent, the use of Culotte and TAP were observed in equal proportions (11% each).

Conclusions: This superiority trial found no significant differences in MACE between a stepwise provisional approach and a planned dual stenting strategy in true LM bifurcation stenosis requiring intervention. While a stepwise provisional strategy may be advocated in some subsets of distal LM bifurcation lesions, the results need to be interpreted in comparison with those of the DK Crush V trial, with particular attention to the nuances associated with the respective patient subsets and complexities of the respective LM bifurcation lesions in each trial.

Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease: ADAPTABLE trial (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-Term Effectiveness)

Jones SW, et al. Published in N Engl J Med. 2021;384(21):1981-1990
Presented at ACC Scientific Sessions 2021

Background: With the advent of more novel P2Y12 inhibitor antiplatelet therapies and the definition of a high bleeding risk (HBR) cohort of patients, there is renewed focus on the mortality and morbidity caused by bleeding, and striking an appropriate balance between ischemic and bleeding risk. Thus, the appropriate dosing of the antiplatelet stalwart aspirin in lowering the risk of death, MI and stroke and minimize bleeding in patients with established atherosclerotic cardiovascular disease (ASCVD) remains a subject of controversy.

The ADAPTABLE trial (4) is a multicenter, randomized, open-label trial that sought to evaluate the efficacy of two separate doses of aspirin (325mg vs 81mg) in patients with ASCVD. The trial was unique in that it employed pragmatic methods and quality-by-design guiding principles, and was the first clinical trial to use PCOR net, the National Patient-Centered Clinical Research Network, which is a "network of networks" to conduct comparative-effectiveness research.

True to the pragmatic nature of the trial, there were no in-person visits at the trial Centre during follow up.

PICO (Population, Intervention, Comparator, Outcomes) Criteria: 15,076 patients with established ASCVD were enrolled having being identified with the use of electronic health record data at each institution through a cohort identification query. 96 % of them were already on aspirin. Patients were randomized 1:1 through the patient portal to take either 81 mg (n = 7,540) or 325 mg (n = 7,536) of daily aspirin, which they purchased over the counter. The primary efficacy endpoint was the time to a first occurrence of any event in the composite of all-cause death, hospitalization for MI or stroke. The primary safety outcome was hospitalization for major bleeding with an associated blood-product transfusion. They were followed up for a median duration of 26.2 months.

Main results: The primary efficacy endpoint occurred in 7.28 % of patients in the aspirin 81 mg arm as compared with 7.51 % of the aspirin 325 mg arm (HR, 1.02; 95% CI, 0.91 to 1.14; p = 0.75). The primary safety outcome, hospitalization for major bleeding occurred in 0.63 % and 0.60 % in the aspirin 81mg and 325 mg arms respectively (HR, 1.18; 95% CI, 0.79 to 1.7; p = 0.41). Most notably, patients assigned to 325 mg had a much higher incidence of dose switching than those assigned to 81 mg (41.6 % vs. 7.1 %) and fewer median days of exposure to the assigned dose.

Conclusions: Substantial dose switching to 81mg of daily aspirin and the absence of significant differences in cardiovascular events or major bleeding between patients assigned to 81 mg versus 325 mg of aspirin daily, indicate that a strategy of 81 mg of daily aspirin had similar effectiveness as that of 325 mg in patients with established ASCVD, with better long-term adherence with the 81-mg dosing strategy.

Aspirin versus clopidogrel for chronic maintenance monotherapy after percutaneous coronary intervention (HOST-EXAM): an investigator-initiated, prospective, randomized, open-label, multicenter trial

Koo BK, et al. Published in Lancet 2021 ;397(10293):2487-2496.
Presented at ACC Scientific Sessions 2021

Background: Delving further into the controversies in the antiplatelet (APT) arena, the HOST-EXAM trial, an investigator-initiated, prospective, randomized, open-label, multicenter trial in South Korea sought to compare the efficacy and safety of aspirin versus clopidogrel head-to-head, among patients who have undergone coronary stenting and are in the chronic maintenance phase [(5)]. The optimal antiplatelet monotherapy of choice in this post-PCI subset of chronic patients is not known.

PICO (Population, Intervention, Comparator, Outcomes) Criteria: 5,438 patients who maintained dual antiplatelet therapy (DAPT) without any clinical events for a 6-18 months period after PCI with drug-eluting stents (DES) were included. Those with any ischaemic and major bleeding complications were excluded. Patients were randomly assigned (1:1) to receive antiplatelet monotherapy of either once-daily clopidogrel 75mg (n=2710) or aspirin 100 mg (n=2728) for 24 months. The primary endpoint was a composite of all-cause death, non-fatal MI, stroke, readmission due to acute coronary syndrome, and Bleeding Academic Research Consortium (BARC) bleeding type 3 or greater.

Main results: During 24-month follow-up, the primary outcome occurred in significantly fewer patients in the clopidogrel arm (5·7%), as compared with the aspirin arm (7·7%) [HR, 0·73; 95% CI 0·59-0·90; p=0·0035]. No significant interactions were seen between the treatment effect and subgroups. Indications for PCI in the population of interest included stable angina (25.5 %), unstable angina (35.5 %), non-ST segment elevation MI (NSTEMI) (19.4 %) and ST segment elevation MI (STEMI) (17.2 %). Clopidogrel monotherapy also fared significantly better in terms of secondary outcomes including thrombotic composite outcome (3.7 % vs. 5.5 % for clopidogrel vs aspirin respectively, p = 0.003) and any bleeding (2.3 % vs. 3.3 % for clopidogrel vs aspirin respectively, p = 0.003).

Conclusions: In post-PCI patients stented with DES, and who remained event-free on DAPT for 6-18 months, and requiring indefinite antiplatelet monotherapy, a clopidogrel monotherapy strategy was superior to an aspirin monotherapy strategy in terms of reduced risk of the composite of all-cause death, non-fatal MI, stroke, readmission due to ACS, and BARC bleeding type 3 or greater. Longer-term follow-up of this cohort will yield more definitive results of prolonged single antiplatelet therapy. Given the well-known "East Asian paradox" of antiplatelet therapy, it remains to be seen if these findings are applicable to other ethnicities across the globe.

TALOS-AMI: Ticagrelor Versus Clopidogrel in Stabilized Patients with Acute Myocardial Infarction

Park MW, et al. Protocol published in EuroIntervention. 2021;16(14):1170-1176
Presented at ACC Scientific Sessions 2021

Background: There is very limited data on the de-escalation of DAPT by switching from the more potent P2Y12 inhibitor ticagrelor to clopidogrel in patients with acute MI undergoing PCI. The issue of de-escalation is important because although the risk of ischaemic complications is highest during the first 30 days post-MI, thus necessitating potent DAPT, most bleeding events occur predominantly during the maintenance phase of treatment, thus justifying de-escalation. The TALOS-AMI study, a multicenter, randomized, open-label study also originating from South Korea sought to investigate the efficacy and safety of switching from ticagrelor to clopidogrel in post-PCI patients following an acute MI and who experienced no adverse clinical events during one month post PCI [(6)].

PICO (Population, Intervention, Comparator, Outcomes) Criteria: 2,697 AMI patients who underwent index PCI with a newer-generation DES following an acute MI and in whom no adverse clinical events were noted during the first month after the index PCI, were enrolled. At one month, they were randomized 1:1 to receive either aspirin 100 mg plus clopidogrel 75 mg daily (i.e.de-escalation arm, n = 1,349), or aspirin 100 mg plus ticagrelor 90 mg twice daily (i.e. active control arm, n = 1,348). This de-escalation was uniform and un-guided, with no platelet function tests performed prior. The primary endpoint was a composite of cardiovascular death, MI, stroke, and BARC bleeding type 2, 3 or 5 from 1 to 12 months after the index PCI.

Main results: The composite primary endpoint was observed in 4.6 % of the de-escalation arm (i.e., aspirin and clopidogrel) and 8.2 % of the active control arm (i.e., aspirin and ticagrelor), (p for noninferiority < 0.001, p for superiority < 0.001). There were no significant differences in the secondary outcome of composite cardiovascular death, MI, stroke between the de-escalation and active control arms (2.1 % vs 3.1 % respectively, p = 0.148). However, BARC 2,3, or 5 bleeding was significantly lower in the de-escalation group (3.0% vs 5.6%, p = 0.001).

Conclusion: In acute MI patients who have undergone PCI and remained event-free for one-month post-index PCI, DAPT consisting of a uniform un-guided de-escalation strategy to aspirin and clopidogrel is superior to aspirin and ticagrelor in terms of net clinical benefit, with no increase in ischaemic events and significantly lower bleeding. An East Asian paradox may be in play in this context as well. However, the data are encouraging for low-income countries where most patients are unable to afford novel P2Y12 inhibitors such as ticagrelor in the long-term.

Multivessel PCI Guided by FFR or Angiography for Myocardial Infarction

Flow Evaluation to Guide Revascularization in Multivessel ST-Elevation Myocardial Infarction (FLOWER-MI) trial

Puymirat E, et al. Published in N Engl J Med. 2021 Jul 22;385(4):297-308.
Presented at ACC Scientific Sessions 2021

Background: In patients presenting with STEMI and multivessel disease (MVD), complete revascularization, involving PCI for both culprit and non-culprit lesions, is superior to the treatment of the culprit lesion alone [7,8]. Over half of STEMI patients have MVD. Whether complete revascularization that is guided by physiology, i.e. fractional flow reserve (FFR) is superior to an angiography-guided approach remains uncertain. The Flow Evaluation to Guide Revascularization in Multivessel ST-Elevation Myocardial Infarction (FLOWER-MI) trial sought to answer this question in prospective, multicenter, randomized, open-label study [9].

PICO (Population, Intervention, Comparator, Outcomes) Criteria: A total of 1,171 patients with STEMI and MVD (i.e. >50% stenosis judged amenable to PCI in at least one non-culprit lesion) who had undergone successful primary PCI of the infarct-related artery were randomly assigned 1:1 to receive complete revascularization guided by either FFR (intervention arm; n=590) or angiography (control arm; n=581).

The primary outcome was a composite of all-cause death, nonfatal MI, or unplanned hospitalization leading to urgent revascularization at 1 year. In the majority of patients (97 %) non-culprit lesions were revascularized as staged PCI procedures.

Results: PCI of non-culprit lesions was performed in 66% of the patients with the FFR-guided strategy and in 97% with the angiography-guided strategy. There were no significant differences in the primary outcome between the FFR-guided arm versus the angiography-guided arm (5.5 vs 4.2% respectively, HR, 1.32; 95% CI, 0.78 to 2.23; P = 0.31). No significant differences were observed between the two arms in terms of individual components of the composite primary outcome as well: death (1.5 % vs 1.7 %), non-fatal MI (3.1 % vs 1.7 %) and unplanned hospitalization for urgent revascularization (2.6 % vs 1.9 %) for FFR- guided versus angiography-guided groups respectively. Pertinent to low-income countries, cost-effectiveness and cost utility favoured non-culprit vessel revascularization via an angiography-guided approach, as compared with FFR-guidance (€ 8,322 vs € 8,832 respectively; P < 0.01).

Conclusions: In case of complete revascularization in STEMI patients with MVD, there was no benefit to an FFR-guided strategy over an angiography-guided strategy with respect to the composite ischaemic outcome of death, MI, or urgent revascularization at 1 year. However, the authors inferred that the wide confidence intervals for the estimate of effect do not allow for a conclusive interpretation of the data.

Anti-Thrombotic Strategy to Lower All cardiovascular and Neurologic Ischemic and Hemorrhagic Events after Trans-Aortic Valve Implantation for Aortic Stenosis – ATLANTIS trial

Presented by Jean-Philippe Collet and Gilles Montalescot at ACC Scientific Sessions 2021

Background: Thrombotic and bleeding events post-TAVI are frequent and negatively affect short-term survival. The formation of thrombus on the implanted bioprosthesis is a potential hazard following TAVI.

Currently there is no evidence that a newer oral anticoagulant (NOAC) could replace antiplatelet therapy or a Vitamin K antagonist (VKA) following TAVI. The GALILEO trial demonstrated more harm than benefit with low-dose rivaroxaban compared with anti Platelet therapy (APT).

On this background, the prospective, randomized, open-label ATLANTIS trial sought to assess the efficacy and safety of apixaban 5 mg BID compared with standard care with either antiplatelet therapy (APT) or vitamin K antagonist (VKA) where oral anticoagulation was indicated, among patients undergoing TAVI [10].

PICO (Population, Intervention, Comparator, Outcomes) Criteria: 1,500 eligible patients who underwent a successful TAVI procedure (native or valve-in-valve) were stratified according to having an indication for OAC or not. Stratum 1 (n = 451) comprised of patients with an indication for OAC, and these patients were randomly assigned to either apixaban 5 mg BID or standard of care, i.e., VKA (21 %). Stratum 2 consisted of patients without an indication for OAC (n = 1,049); these patients were also randomized to apixaban 5 mg BID vs standard of care, i.e., single antiplatelet therapy [APT] (14.9%) or DAPT (56.9%). Overall, 749 patients were randomized to Apixaban and 751 to relevant standard of care.

The primary end-point was a composite of death, MI, stroke, systemic emboli, intracardiac or bio prosthesis thrombus, episode of deep vein thrombosis or pulmonary embolism, or major bleedings over one year follow-up.

Main results: The composite primary endpoint was observed in 18.4 % of the apixaban group, and 20.1 % of the SOC group (HR 0·92; 95% CI 0·73–1·16, p for interaction = 0.57). These results did not differ significantly between stratum 1 (apixaban vs VKA: 21.9 % vs 21.9 %) and stratum 2 (apixaban vs APT: 16.9 % vs 19.3 %). Bioprosthetic valve thrombosis was significantly higher in the standard of care group (1.1 % vs 4.7 % for apixaban vs SOC respectively, $p < 0.05$); this was primarily driven by stratum 2, i.e. the antiplatelet stratum of SOC (apixaban vs. APT: 1.1% vs. 6.1%; $p < 0.05$) . In a post-hoc sensitivity analysis looking at the primary endpoint without valve thrombosis, the composite endpoint 17.8 % vs 16.1 % for apixaban vs SOC respectively, (HR 1·12; 95% CI 0·88–1·44; p for interaction = 0.7).

Excluding bioprosthetic valve thrombosis, which was significantly higher in the standard of care group (1.1 % vs 4.7 %, $p < 0.05$, mainly driven by the patients in the APT group), the composite endpoint was found to be occurring higher in the apixaban group (17.8 % vs 16.1 %, p= significant). No between-group differences were seen for the primary safety endpoint of life-threatening (including fatal) or disabling or major bleeding (BARC 4,3a, b and 3c), as defined by Valve Academic Research Consortium-2 (8.5% vs 8.5%; HR 1·02, 95% CI 0·72–1·44)

Conclusions: There is no benefit of apixaban over the standard of care (VKA if an indication for OAC; APT if no indication for OAC) in post-TAVI patients, in terms of net clinical benefit. Safety endpoints were also similar. Albeit not statistically significant, subclinical valve thrombosis is decreased with apixaban driven mainly by the stratum with no indication for OAC.

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Milestones

Post Myocardial Infarction VSD Closure Using a Cribriform Atrial Septal Device Occluder- Two Case Reports with Different Approaches and Outcomes

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Abstract

Acquired ventricular septal defect following myocardial infarction is a dreaded complication. For this complication, Percutaneous device closure is an attractive option but poses its own unique complications and challenges. Improvising with available alternate hardware has shown success, including utilization of ASD occluder devices. We present two case reports with different approaches and outcomes. Case 1: A 54-year-old South-Asian lady developed a VSD on day 1 following thrombolysis after an acute anterior STEMI. Due to the haemodynamic instability and cardiac arrest, she underwent PCI to LAD. Despite maximal inotropic therapy and IABP she was haemodynamically unstable and she was considered unsuitable for open heart surgery, thus device closure was considered as a salvage procedure as we could not postpone the closure of the VSD for 4 weeks due to the deteriorating condition of the patient. Under general anesthesia, an arterio-venous loop was created from left femoral arterial access to right internal jugular vein. Taking internal jugular vein as an access port, using an Amplatzer VSD delivery sheath, a Cribriform ASD device was used to close the VSD which was complicated with acute severe TR, possibly due to chordal rupture. Patient expired on day 2 following procedure. Case 2: A 58-year-old lady developed a VSD on day 2 following thrombolysis for anterior STEMI. She underwent PCI to LAD. Device occlusion of VSD was undertaken on day 23. Right femoral arterial and venous access was taken to create an arterio-venous loop. Using an amplatzer VSD sheath, a 35mm SHASMA cribriform ASD occluder was deployed with a successful outcome. Patient made a good recovery. Post MI VSD device closure can be fraught with challenges and complications. Improvised use of occluder devices and sheaths can yield success. Patient selection and timing plays a key role, especially when considering the outcome regarding morbidity and mortality.

Keywords: Acquired VSD, device closure, complications, ASD occluder, myocardial infarction

Introduction

Acquired ventricular septal defect following myocardial infarction is a dreaded complication as it carries significant morbidity and mortality risk, as high as 50% at day 7. Classically, the common populace afflicted by this complication are elderly females with a single vessel pattern of coronary artery disease, commonly a wraparound left anterior descending artery. Usually post MI-VSD's occur in a sub-acute manner following the STEMI. However, they can also present within 24 hours and these patients often tend to show unpredictable pattern of deterioration despite initial stabilization[(1)]. Considering that most tend to be decompensated with cardiogenic shock and biventricular failure, the clinical state greatly hinders a surgical option of revascularization and VSD patch closure of the defect as it increases the risk of perioperative death. Though urgent revascularization and correction is preferred and is the recommended strategy, study findings have shown contrary results as to the optimal time when it is beneficial and safe to carry out the procedure. Thus, even now uncertainty exists as to the optimal time for coronary artery bypass grafting following MI after thrombolysis [(2)], When complicated with a VSD surgeons prefer a delay/gap period of 4 weeks to ensure that VSD margins are well healed and will hold the sutures and the patch in place firmly [(3)].

This creates a practical problem as patients tend to show poor response to medical optimization and stabilization of cardiac functions in regard to preparation for surgery. Even following surgery, the mortality risk, unfortunately remains high [(3)].

The advent and improvement of percutaneous interventions within a short course of time have fueled cardiac interventionists to venture beyond coronary interventions. Device closure of congenital cardiac septal defects have been successfully carried out with minimal complications. Post MI, VSD closure through percutaneous intervention is still in its infancy. But when compared to open heart surgery, device closure appears to be a safer option and is gaining favor among cardiac interventionists as an alternate feasible option.

Case reports

Case 1

A 54-year-old South Asian lady with diabetes and hypertension presented with acute anterior ST segment elevation myocardial infarction.

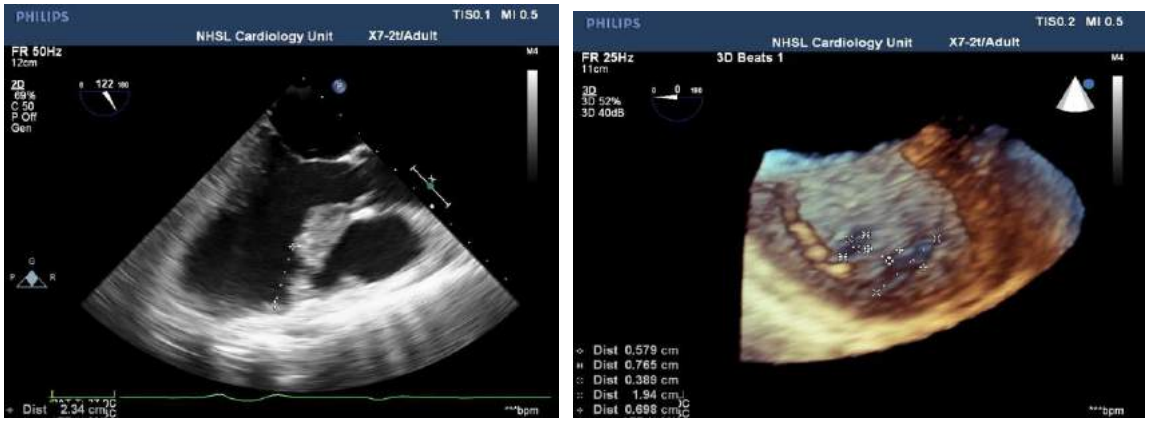
Milestone

Immediate thrombolysis was carried out with streptokinase with rescue percutaneous coronary intervention planned for. However, within the course of the day the patient deteriorated hemodynamically and developed left ventricular failure.

A repeat clinical examination revealed the patient to have marked pulmonary edema and a new onset pan-systolic murmur, suggestive of a VSD. She was transferred to our tertiary coronary care unit for further management. Chest x-ray revealed bilateral gross pulmonary edema. Transthoracic echo revealed an ejection fraction of 40% with regional motion abnormality involving the anterior and anterolateral territories and the presence of two VSD's. Trans-esophageal echo allowed assessment of the VSD, with the largest VSD measuring 10 mm separated by an island of muscle mass of 7 mm with the smaller VSD placed more apically and measuring 7 mm. The total length of the VSD was 23mm (Fig 1). The case was discussed at a multi-disciplinary team meeting (MDT)and a delayed surgical intervention was considered as the preferred modality of treatment. In lieu of the coronary intervention, she underwent a coronary angiogram which revealed a single vessel disease of the LAD with a long segment of diffuse disease. Moderate coronary artery disease involving both right coronary artery and left circumflex artery was also seen. However, during her stay, she deteriorated dramatically, going in to cardiogenic shock followed by cardiac arrest. Though CPR was successful, a decision was taken to intervene with coronary angiogram and stenting of the LAD. This was done with a Xience Xpedition drug eluting stent of 2.75X 48 mm.

This posed an additional restriction on the surgical team as the patient now required the dual antiplatelet therapy to be continued. Furthermore, despite successful revascularization, the patient demonstrated clinical deterioration requiring maximal medical therapy and needed an intra-aortic balloon pump. Considering the unstable nature of the patient and possible mortality risk with or without surgery, a clinical decision was taken to attempt device closure of the VSD.

The procedure was done under general anaesthesia. Left side femoral arterial access was obtained with a 7Fr sheath and left sided venous access with a 6 Fr sheath. Right sided internal jugular (RIJV) access was secured with an 8 Fr sheath. To ensure procedural accuracy, transesophageal echo was also used in addition to fluoroscopy. A repeat assessment of VSD was done prior to the procedure, with TOE and using a 6 Fr marker pigtail catheter positioned at the apex. The VSD was also assessed with a LV angiogram. Using a 0.035" 260cm Terumo wire a Judkins right catheter was advanced into the left ventricle and the VSD was crossed. After which the Terumo wire was exchanged for a 0.035, 260 cm noodle wire which was used to advance into the pulmonary trunk, and the wire was positioned into the left pulmonary artery. Using the RIJV access, an Ensnare 6F catheter was advanced over a 0.035" 260cm Terumo wire and positioned into the left pulmonary artery. Afterwards an Ensnare 20mm snare was inserted via the catheter and the noodle wire was snared and retracted. Initially using the RIJV access, an attempt was made to cross the VSD with a Cook Mullins sheath, which was unsuccessful.



A B

Figure 1: Image A demonstrates TOE assessment of VSD defect in 2D and image B demonstrates the 3D reconstruction of the same.

A 10 Fr Amplatzer ASD delivery sheath was also tried and was found too rigid to cross the VSD defect. The patient developed a brief run of bradycardia which prompted us to insert a temporary pacing wire as a precautionary measure. The second time an Amplatzer Torque Delivery system VSD sheath was advanced successfully over the VSD and kept in the left ventricle. A size 30mm Amplatzer Cribriform atrial septal occluder device was advanced through the catheter and deployed successfully across the VSD defect, under TOE and fluoroscopic guidance and positioned (Figure 2 sequence).

Case 2

A 58-year-old otherwise healthy female developed acute anterior STEMI. In the absence and non-availability of timely percutaneous coronary intervention, she was thrombolysed with tenectaplase, within 4 hours of onset of the chest pain with successful resolution of ST segments elevation. On day 2, clinical examination revealed a pulse of 110/min, with a blood pressure of 120/80mmHg, with a pansystolic murmur on the left sternal edge suggestive of a VSD, in the absence of any features of decompensation. A 13 mm diameter VSD was confirmed on TTE (Fig 3).

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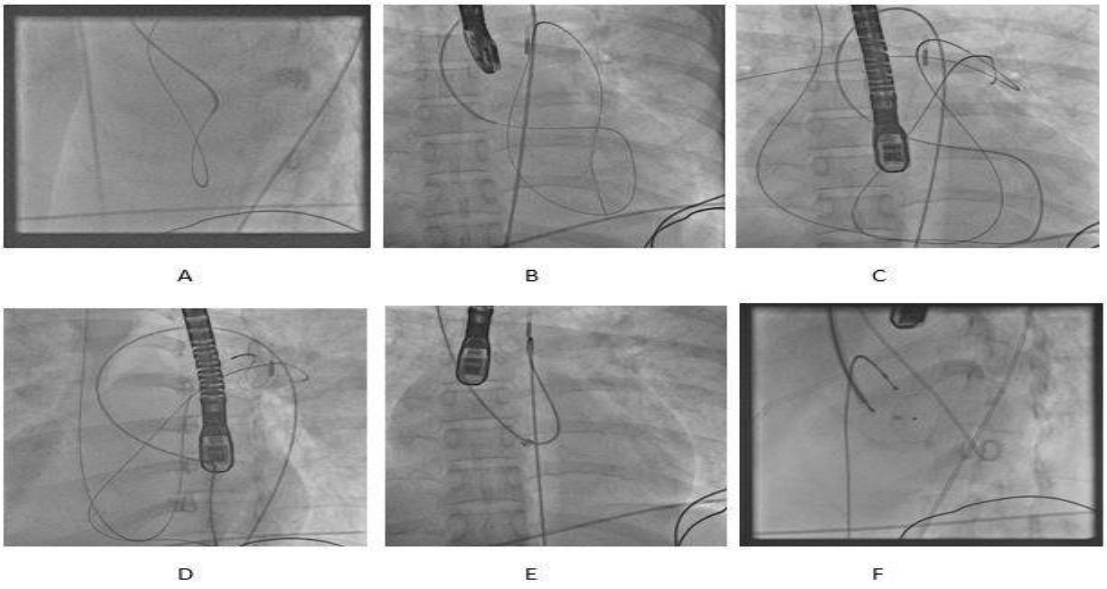


Figure 2: Images A-F demonstrates procedures undertaken to deploy the cribiform ASD occluder device across the VSD

Though procedurally successful and VSD being closed, post procedure TOE revealed severe new onset tricuspid regurgitation (TR) and right atrial dilation. We believe there could have been injury to the sub valvular apparatus during the procedure, resulting in the TR. Despite the Cribriform device showing non displacement, on day 2 post procedure, the patient expired due complications of congestive cardiac failure and cardiogenic shock non responsive to maximal supportive therapy.

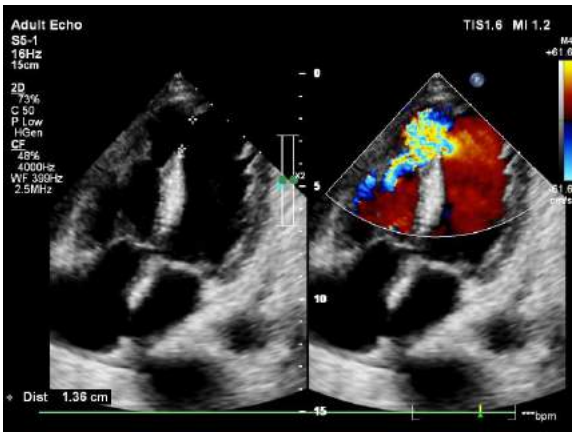
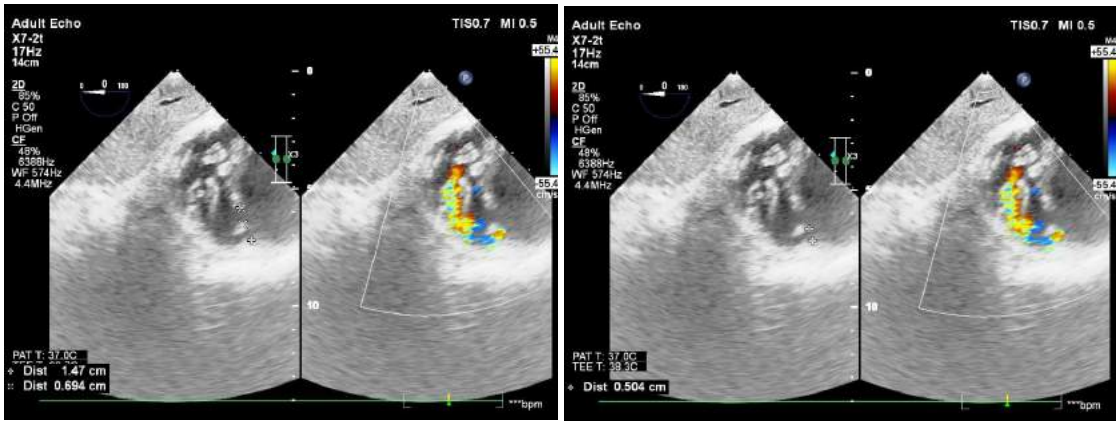


Figure 3: TTE in apical 4 chamber view demonstrates in dual window view the VSD defect and the left to right shunt.

She was transferred to our tertiary care center for evaluation and intervention. On review, she had progressed into pulmonary oedema, with a pulse rate of 96bpm and a blood pressure of 100/70mmmHg. Repeat 2D TTE confirmed the VSD with hypokinesia of the anterior and anterolateral LV territory with moderate left ventricular dysfunction with an ejection fraction (EF) of 35-40%.

TOE demonstrated two muscular VSDs with left to right shunt. The superior defect was 7mm and the inferior defect was 5mm with the overall defect combining both being 14mm (Fig 4).

Figure 4: Modified view in SAX in dual plane mode demonstrates the 2 separate VSD defects and the left to right shunt in color flow.



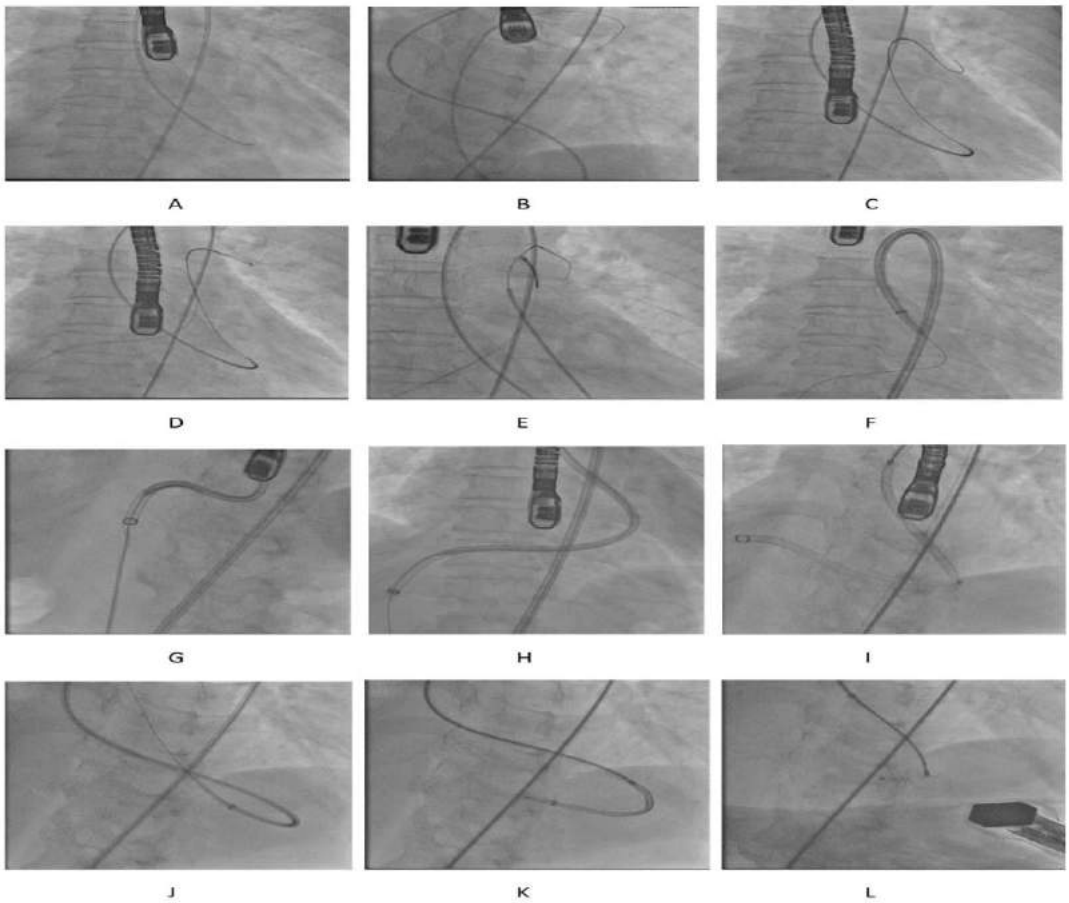


Figure 5: Sequence of cine images from A -L demonstrates the procedures undertaken as explained in text to finally deploy the cribriform ASD occluder successfully across the VSD defect.

There were no features of RV failure. After adequate off-loading, coronary angiogram was performed on 4th day post MI. Severe disease was noted in the LAD with no significant disease of other coronaries. Following MDT discussion, the plan was made to perform percutaneous intervention to the coronary artery with staged device occlusion of the VSD. She underwent successful PCI to LAD with a single drug eluting stent (Xience Prime 3.5x18mm). She remained in hospital under strict observation.

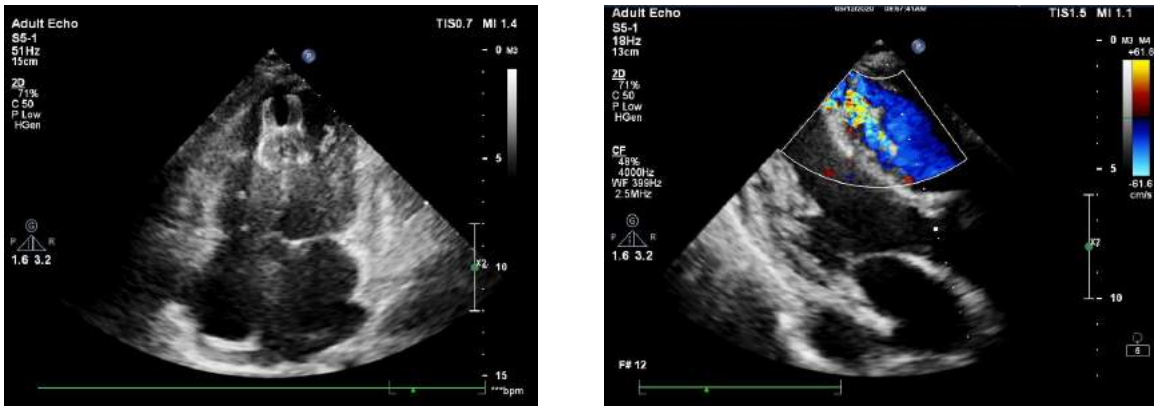
On day 23, under general anesthesia device occlusion was undertaken. Femoral access was obtained via femoral artery and vein using 8Fr and 6Fr sheaths respectively.

Using a JR3 6Fr catheter and a 0.035" 260cm Terumo J tip wire, the VSD was crossed. The Terumo wire was positioned in the main pulmonary artery and was snared using a 6Fr 9-15mm 3 loop Ensnare.

The terumo wire was externalized to the right venous side.

A 12Fr Amplatzer ASD sheath was inserted from the arterial side with the guidance of JR3 catheter (kissing technique). However, as the sheath formed a kink, the 35mm SHASMA cribriform ASD occluder failed reach the RV. Therefore, the whole system was taken out. Subsequently, VSD was crossed with a J tip Terumo guide wire with JR3 6FR catheter. The terumo wire was exchanged with an Amplatzer superstiff. An 8Fr VSD sheath was successfully introduced and the VSD was crossed (Fig 5 sequence).

A 35mm SHASMA cribriform ASD occluder was then deployed, under fluoroscopy and trans esophageal echo guidance with a good outcome (Fig 6). She remained clinically stable and was discharged with a follow up plan as an outpatient. The 6 month post procedural review confirmed the good results (Fig 7).



A B

Figure 6- TTE in apical 4 chamber in A demonstrates successful VSD position post procedure, B in modified PLAX view demonstrates successful occlusion with no color crossing.

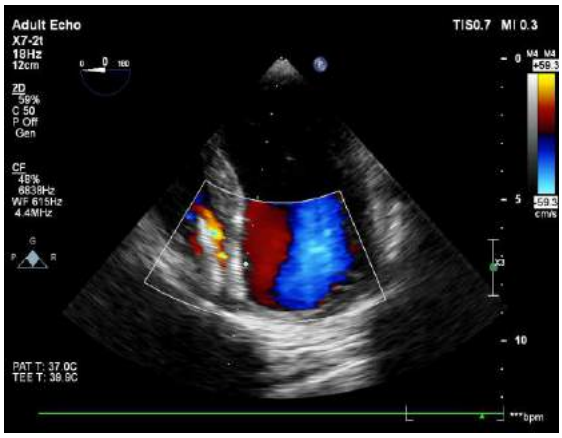


Figure 7- 6 month follow assessment with TOE demonstrates patent occluder in correct position with minimal residual left to right shunt.

Discussion

The cases were challenging in many ways. Both patients had two separate VSD's each, implying the occluder device's disc had to be adequately sized to cover both defects while ensuring a safe disc margin extending beyond the ischemic muscle surrounding the VSD.

In a low resource setting, we unfortunately do not have a range of available devices to choose from, according to patient need criteria. The ability to adapt and improvise is essential.

A clinical decision was taken to use a Cribriform Amplatzer ASD device, as the literature has shown a good success rate [1], furthermore alternate available devices were deemed unsuitable and the ideal/recommended POST MI VSD devices were not available.

The use of an appropriate sheath is essential to ensure success. In case scenario 1, the Mullins sheath was too stiff and in Case scenario 2 the ASD sheath kinked. In both scenarios we found the Amplatzer Torque Delivery system VSD sheath a suitable option with better pliability and curvature for crossing the defect. The correct sheath selection possibly has an impact as it may significantly reduce procedure time and possible unintentional damage to surrounding myocardium.

The 1st patient developed complications peri procedurally, mainly acute severe TR. This is a recognized complication during VSD device closure[1, 4] and was encountered in our patient. Possible mechanism for TR could be due to the wire and subsequently the sheath crossing through the chordae of the tricuspid valve incurring damage. We would like to stress the importance of appreciating the possible range of complications which can have significant impact on morbidity and mortality. Our second patient, who was more stable, was a better candidate and the outcome was excellent.

As the analysis of a case series for VSD device closure has shown , irrespective of the method used the procedural success rate is as high as 85% when carried out on stable patients with established VSD after MI, but carries a high failure and mortality rates in unstable patients during the acute period, especially when hemodynamically compromised[1].These findings highlight the importance of precise patient selection.

Conclusion

Despite VSD device closure appearing as an attractive and relatively minimally invasive option when compared to open surgery in post MI patients, it can be fraught with many challenges and complications.

Though certain case related improvisations can be made, especially in the choice of occluder devices and sheaths, the need to envisage and expect various anatomical obstacles and planning for suitable alternative strategies cannot be over emphasized.

Patient selection and timing of device closure also plays a key role regarding morbidity and mortality of the post MI, VSD device closure.

Learning objective

Post myocardial infarction acquired VSD's tend to increase morbidity and mortality. Percutaneous intervention though possible, has its own fair share of complications which can impact outcome. When anatomy is favorable alternate devices can be used to achieve successful closure. Timing and patient selection is vital as it may determine overall outcome.

Acknowledgements

We would like to acknowledge the dedicated Cath lab theatre staff.

Conflicts of interest

None

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Tutorial

ECG Question

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A 59-year-old man was admitted with a non-ST elevation myocardial infarction. He underwent emergency coronary angiography followed by percutaneous intervention of the proximal left anterior descending artery. During balloon inflation in the proximal left anterior descending coronary artery, the patient developed a non-sustained, wide complex tachycardia (figure 1). This tachycardia terminated spontaneously.

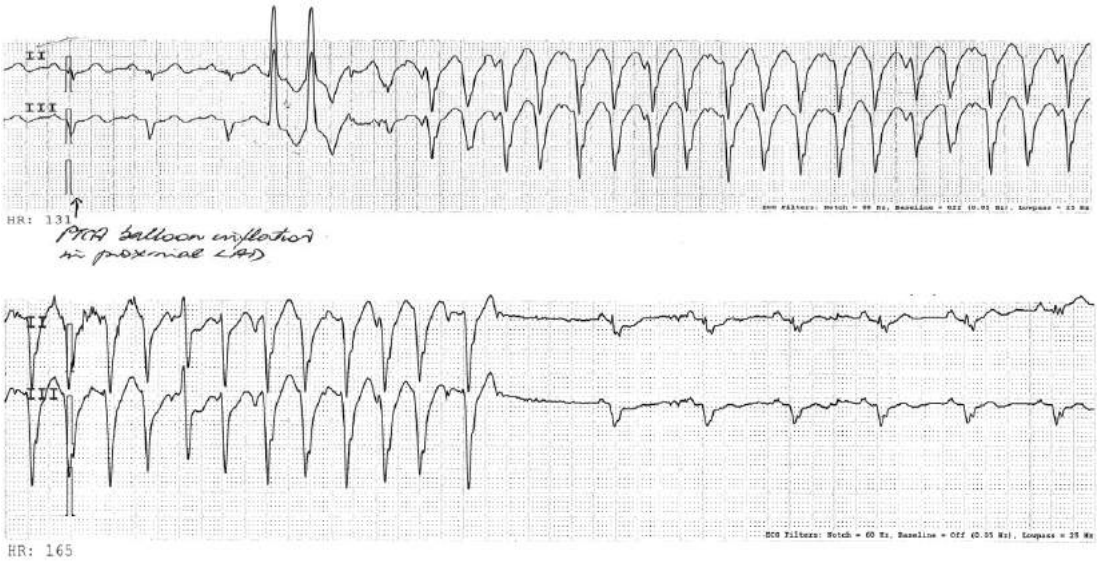
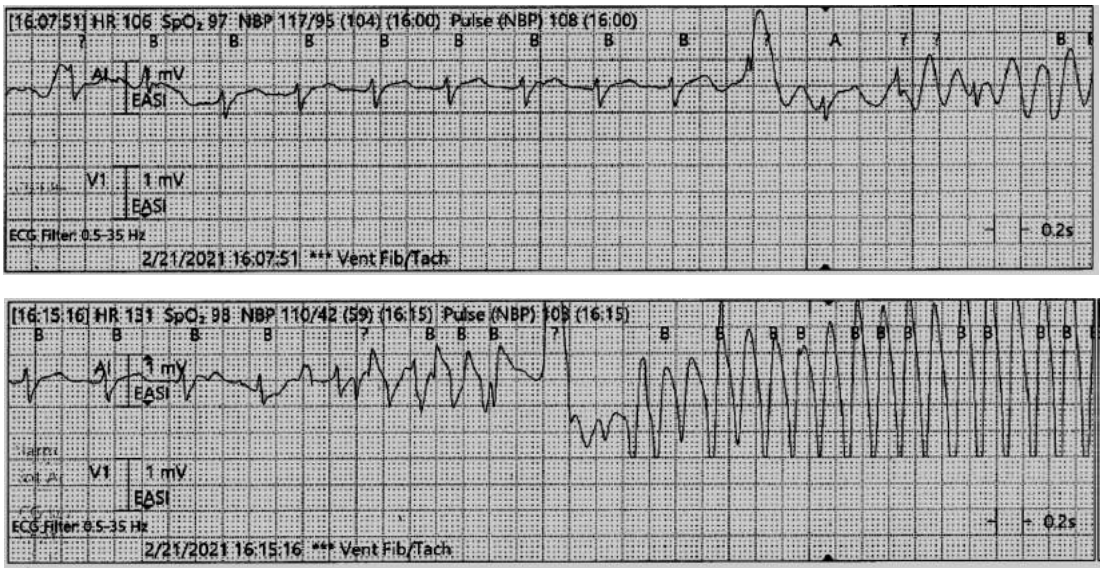


Figure 1: Non sustained, wide complex tachycardia in the cardiac catheterization laboratory.

The patient also had a 60% stenotic lesion in the proximal right coronary artery that was not intervened on. An echocardiogram revealed a left ventricular ejection fraction of 40% with hypokinesis of the mid and apical anteroseptal and anterolateral regions. The patient was placed on aspirin, clopidogrel, metoprolol, atorvastatin and low dose lisinopril.

Telemetry monitoring within the first 12 hours of hospitalization showed recurrent episodes of non-sustained wide complex tachycardia (figure 2).



Tutorial

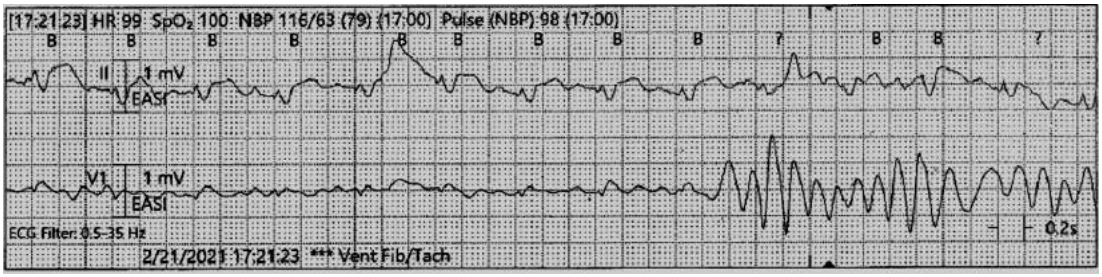


Figure 2: Recurrent, non-sustained, wide complex tachycardia on telemetry.

How do you manage the patient?

(1) Increase the dose of metoprolol
(2) Start intravenous amiodarone
(3) Coronary angiography to assess the patency of the stents and consider intervention on the right coronary artery
(4) Continue to monitor on telemetry
(5) Electrical cardioversion

ECG Analysis:

Figure 1 : Illustrates an episode of non-sustained, wide complex tachycardia coinciding with the inflation of an angioplasty balloon in the proximal left anterior descending coronary artery. Following observations can be made on this rhythm strip (Figure 3).

(a) Tachycardia onset is triggered by a ventricular couplet. This finding per se is not exclusive to ventricular tachycardia, as certain types of supraventricular tachycardia can be initiated by ventricular ectopic beats.
(b) Presence of fusion beats (fusion of a ventricular beat and a conducted sinus impulse).
(c) Atrioventricular dissociation.
(d) Tachycardia terminates with an atrial electrogram. This is likely a result of retrograde conduction of the last ventricular complex.

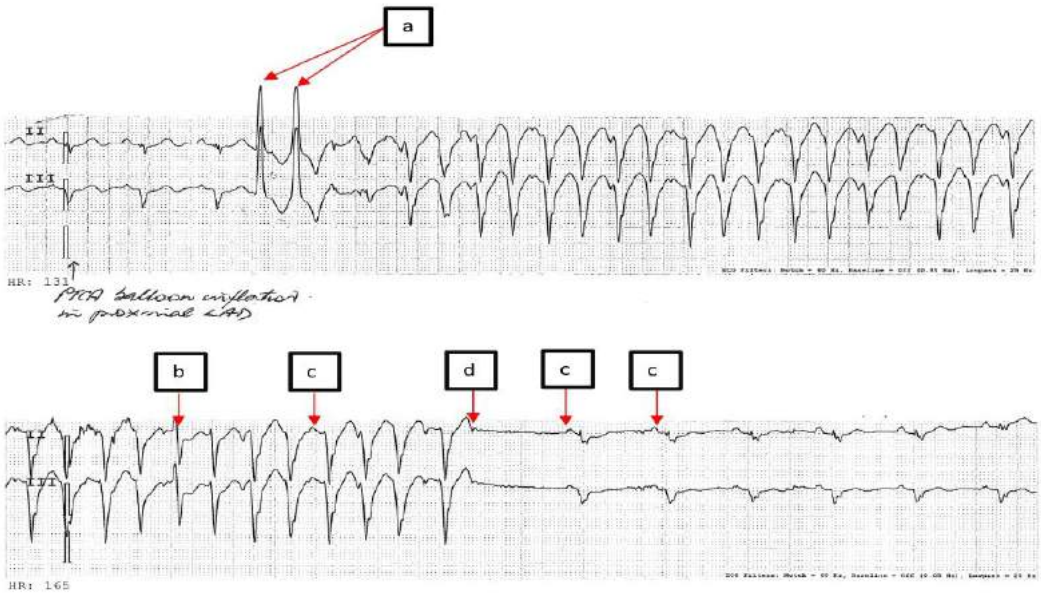


Figure 3: Analysis of the non-sustained, wide complex tachycardia in the cardiac catheterization laboratory. (a= ventricular couplet, b=fusion beat, c= sinus p wave, d=retrogradely conducted p wave of the last ventricular beat)

These observations confirm the diagnosis of non-sustained ventricular tachycardia. It is likely that transient myocardial ischemia induced by balloon inflation triggered this episode of ventricular tachycardia.

Interestingly, figure 2 reveals repetitive occurrence of an ECG artifact on telemetry in the same patient. While the initial appearance is suggestive of polymorphic ventricular tachycardia, several other observations confirm the ECG artifact in these tracings. These observations include(Figure 4) :

(a) An unstable baseline in the ECG before the event.
(b) Presence of normal beats in one of the leads.
(c) Portions of the QRS complexes are visible within the artifact at the sinus / heart rate

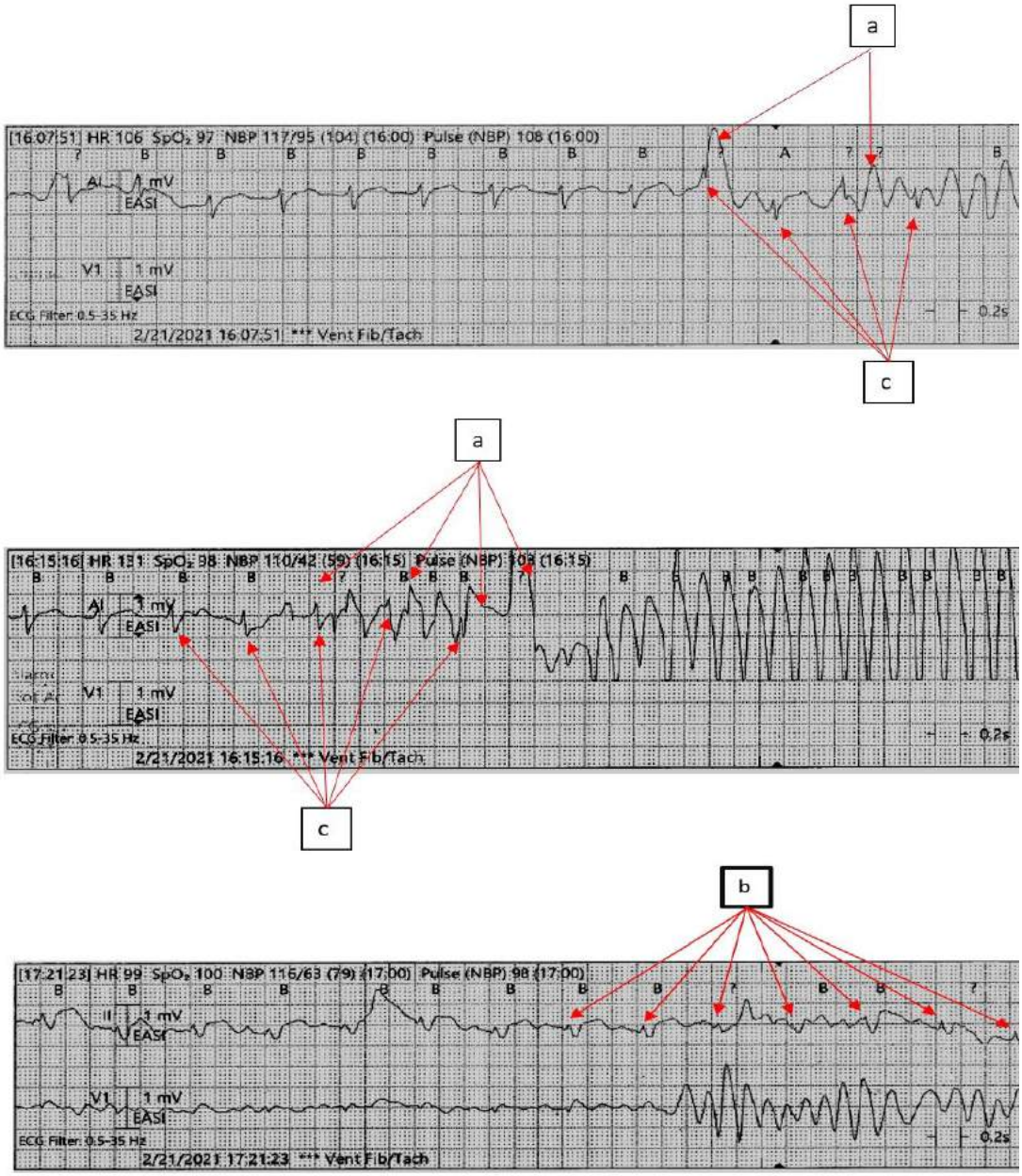


Figure 4: Recurrent, non-sustained, wide complex tachycardia on telemetry. (a=unstable baseline in the ECG before the event, b=normal beats in one of the leads, c=QRS complexes are visible within the artifact at the sinus rate)

Thus, the answer to the question is option (4); continue to monitor the patient on telemetry. [1]

Tutorial

Discussion

ECG artifacts are defined as electrocardiographic alterations, not related to cardiac electrical activity. These alterations result in distortion of the baseline and ECG wave forms. [2] Artifacts due to motion or loosely placed electrodes are not uncommon and constitute the majority of distortions observed on telemetry.

In the ECG question described above, the ECG distortions are due to motion artifacts induced by involuntary or voluntary movements of the patient. In other circumstances, ECG motion artifact has been described in medical conditions such as essential tremor, Parkinson's disease, hyperthyroidism, anxiety, stimulant use, fever associated rigors, hypothermia and chest compressions during cardiopulmonary resuscitation.

ECG artifacts often lead to erroneous diagnoses of cardiac arrhythmias. Failure to detect ECG artifacts can potentially lead to institution of unnecessary and possibly harmful treatment as well as withholding necessary therapeutic options. [3] Electrocardiographic clues, as described above, can help to differentiate ECG artifacts from cardiac arrhythmias.

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Case Report

Cardiac Implantable Electronic Device (Permanent Pacemaker Lead) - Late Infective Endocarditis likely due to Methicillin Resistant *Staphylococcus aureus* as a Nosocomial Infection

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Abstract

Infection of cardiac implantable electronic devices [CIED] e.g., permanent pacemakers [PPM] is a complication with significant morbidity and mortality. PPM lead associated infective endocarditis [IE] is mostly recognized as an early complication following implantation. Late PPM lead IE though reported, is uncommon.

We report an 84-year-old male with type 2 diabetes mellitus, hypertension and paroxysmal atrial fibrillation [PAF] with recurrent transient ischemic attacks [TIA]who had a single chamber AAI PPM implanted 11 years ago for sick sinus syndrome [SSS]. He was admitted for evaluation with fever of 10 days duration and generalized malaise. 3 months prior to his admission he was treated for an acute stoke with a history of having a right forearm intravenous access cannula being inserted with concomitant therapy with IV medication.

On examination he was febrile. Rest of the systemic examination was normal. No cannula site infection was noted. Blood tests showed a neutrophil leukocytosis with high erythrocyte sedimentation rate. Throat swab culture was positive for methicillin resistant *staphylococcus aureus* [MRSA]. Despite starting on antibiotics according to antibiotic sensitivity pattern he continued to have fever. Transthoracic echo [TTE] and subsequently transoesophageal echo [TOE] revealed a mobile homogenous mass of 8x5 mm suspicious of a vegetation attached to the PPM lead in the right atrium [RA] near the superior vena cava [SVC] margin. PPM lead IE was diagnosed according to the Duke's criteria. Intravenous [IV] vancomycin and IV ceftriaxone were started and continued for 6 weeks and he showed a good clinical response with the vegetation reducing in size in subsequent TOE to 1-2 mm. As the current PPM had reached end of battery life, a new AAIR PPM generator was implanted to the same atrial lead under antibiotic cover. Warfarin was restarted at time of discharge and he remains well and fever free at 3 months follow up.

We suspect that the MRSA infection and subsequent vegetation in this patient could be nosocomial related to the right forearm cannulation and IV access during his prior hospital admission as the PPM lead vegetation was in the RA near SVC. This case emphasizes the importance of a high degree of suspicion of CIED related infections in this subset of patients when they present with suggestive symptoms. We also stress the importance of meticulous adherence to aseptic methods during minor invasive procedures such as IV cannulation or IV injections in preventing IE.

Key words: cardiac implantable electronic devices, permanent pacemaker lead vegetation, late infective endocarditis, methicillin resistant *staphylococcus aureus* (MRSA)

Introduction

Cardiac implantable electronic devices [CIED] e.g., permanent pacemakers [PPM], implantable cardiac defibrillators [ICD] and cardiac resynchronization therapy devices [CRT] are lifesaving treatment options for cardiac arrhythmias [(1)]. CIED associated infection is a serious complication with high morbidity and mortality [(2)]. Advances in interventional therapeutics have led to the rising use of CIED and subsequently CIED associated infections [(3)]. The global annual incidence of CIED associated infection is about 0.13- 19.9 % and CIED associated infective endocarditis (IE) is 0.5 - 7%.[(4)]

There are two mechanisms described for pathogenesis of CIED associated infection. Primarily the contamination of the pulse generator and/or leads at implantation or a subsequent manipulation is the most common mechanism [(5)].

The second mechanism is by seeding via the blood stream [(5)] .

CIED associated infections can be classified as early onset (<6 months of insertion) or late onset (> 6 months of insertion) [(6)]. Risk factors for CIED infections are sepsis, immunosuppression (corticosteroids and renal dysfunction), co-existing chronic diseases (malignancy, diabetes mellitus), anticoagulants, device replacements or revisions, high indwelling hardware amount and experience of operator [(7)].

The most common causative pathogen is coagulase negative *Staphylococcus aureus*, of which MRSA accounts for 33.8% of infection [(8)].

CIED associated IE patients tend to have similar symptoms and signs to any other IE with only few exceptions.

Fever is the commonest feature and may present as pyrexia of unknown origin [9] . Patients also commonly complain of generalized weakness. Examination may reveal tenderness over the device. Peripheral stigmata of IE are usually absent and splenomegaly tends to be a rare occurrence. Blood tests tend to show high ESR, leucocytosis, and urine may reveal microscopic haematuria [9].

Patients with CIED who present with fever or other vague symptoms should have a low threshold to be suspected of CIED related infections. Diagnosis of IE is made on modified Dukes criteria.

Another important aspect that emerges through this case is that MRSA may persist for many months after initial acquisition. A recent study has shown that about 40% patients who were MRSA positive took a median time of about 8.5 months for its clearance.

Presentation:

An 84-year-old male was admitted for further evaluation of fever lasting more than 10 days associated with malaise. The fever was of low grade, associated with chills and showed daily spikes despite responding to antipyretics. He also complained of mild non-productive cough of the same duration. He denied night sweats, loss of appetite, loss of weight or contact or previous history of tuberculosis. He had no obstructive or irritative urinary symptoms. His bowel habits were normal and regular with no blood or mucus. He had no neurological symptoms such as prolonged headache, focal neurological weakness or features of meningism.

There were no symptoms suggestive of connective tissue disorders such as joint pain or swelling, skin rashes, digital or oral ulcers or peripheral neuropathy. He had no significant family history of relevance. He consumes alcohol on social basis and is a nonsmoker. He had no recent travel history.

He had type 2 diabetes for 20 years with good glycaemic control and was on treatment for hypertension for 5 years with good control. In 2011, following several syncopal attacks and palpitations he was diagnosed to have sick sinus syndrome and underwent an RA single chamber AAI permanent pace maker. One year prior to his current presentation he was found to have paroxysmal AF and recurrent TIA and was initiated on warfarin.

3 months prior to his current admission he had been admitted to a specialised ward with an acute stoke. His in-hospital details showed a history of a right forearm intravenous cannula being inserted for access and IV medication.

A non-contrast CT brain done at the time showed two lacunar infarcts. An MRI scan was not performed due to the fact that the CIED was not MRI compatible.

Examination:

On general examination the patient's BMI was 21 kg/m2. He was febrile and had a mild pallor. Lymphadenopathy was absent. Cardiovascular system examination was normal with BP-130/80mmHg, pulse rate of 84 bpm. No audible murmurs were noted and there was no evidence of peripheral stigmata of IE. Respiratory findings were, a few rhonchi with normal air entry. Abdominal and neurological examinations were normal. No evidence of connective tissue disorders such as rashes, Raynaud's phenomenon, arthritis, oral ulcers were present.

Investigation	Results
FBC	WBC- 13000/uL (N-70.7 %, L- 18.7 % E- 0.27 %), Hb -10.9 g/d, Plt – 239000 / uL
Blood picture	Features of infection/inflammation Mild anemia could be due to anemia of chronic disease.
CRP	193 mg/L
ESR	80 mm 1st hour

Blood culture	No growth
Throat swab culture	MRSA isolated
UFR	Pus cells- Occasional, Red cells -nil
Urine culture	No growth
Serum Na Serum K Total calcium Mg	136 mmol/L 4.4 mmol/L 8.6 mg/dL 1.9 mg/dL
S.Creatinine	1.22 mg/dL
AST ALT ALP T.Bilirubin D.Bil T. Protein Alb Glob	60 U/L 77 U/L 105 U/L 0.4 mg/dL 0.1 mg/dL 6.9 g/dL 4.4 g/dL 2.5 g/dL
PT(INR) APTT	4.12 34
TTE	Small vegetation (8× 5 mm) attached to the lead at the exit from the SVC to right atrium. AV, MV, TV, PV normal. IAS, IVS intact.
TOE (Figure 01)	Confirmed above findings.
USS abdomen	Possible early diabetic nephropathy. Liver , spleen, gall bladder normal.
Mantoux test	Negative
Sputum gene xpert for TB	Not detected

Investigations were performed to screen for an underlying infection primarily because, the elderly with diabetes mellitus are more prone for infections and can present with vague symptoms as our patient. He had neutrophil leukocytosis with an elevated ESR and high CRP. He had no evidence of urinary tract infection. Although his sputum culture report was positive for MRSA, he didn't have any evidence of severe respiratory infection clinically or radiologically. Urinalysis was normal. Blood cultures were repeatedly negative.

As the elevated ESR indicated the possibility of a chronic infection or an underlying chronic inflammatory disease screening for Tuberculosis was done and found to be negative. The possibility of an underlying malignancy which are common in this age group was also considered and the required screening was carried out. His PSA levels were normal and ultrasound abdomen was also normal.

Case Report

Since his PPM was inserted 11 years ago PPM lead IE was not initially considered a focus of infection. But in the absence of any other obvious foci, TTE was performed and revealed a mobile homogenous mass 8x5 mm suspicious of a vegetation attached to the PPM lead in the right atrium [RA] near the superior vena cava [SVC] margin and was confirmed by TOE. (Figure 01).

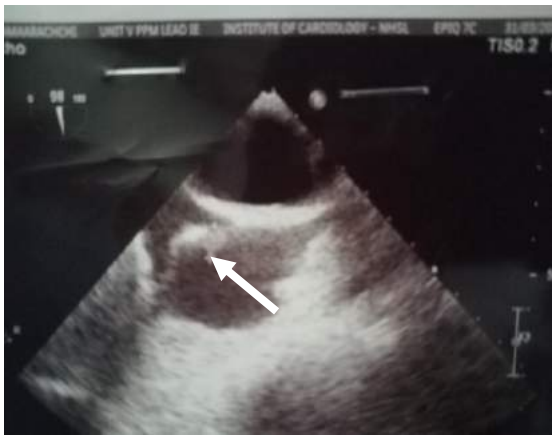

Figure 01: TOE appearance of vegetation at initial diagnosis

Diagnosis:

A diagnosis of possible CIED associated IE was made based on fulfilling 1 major (vegetation) and two minor (predisposing condition and fever) features of Dukes criteria. His blood culture was negative and this was likely due to prior antibiotic treatment. Isolation of MRSA in sputum culture led us to suspect that IE was most likely due to the same organism.

Treatment and outcome:

He was started on IV vancomycin and IV ceftriaxone for likely MRSA, based on the positive throat culture and therapy was continued for a total of 6 weeks. After 2 weeks of antibiotic treatment, a repeat TOE showed reduction in the size of the vegetation (Figure 02).

PPM generator explantation and lead explantation by open heart surgery was initially planned in view of the persistent fever and lead vegetation. However, after 6 weeks of antibiotics the patient clinically improved and repeat TOE showed significant reduction in vegetation size to 1-2 mm. Hence, surgery was deferred.

As the PPM had an elective replacement indication having reached end of battery life, a PPM generator replacement was done with a AAIR PPM being attached to the same atrial lead under antibiotic cover. On discharge warfarin was restarted and maintained at a therapeutic INR range of 2.5.

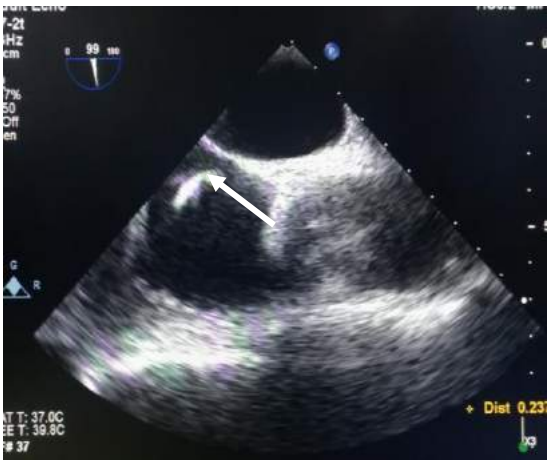

Figure 02: TOE appearance of vegetation after 6 weeks of IV antibiotics

Discussion:

Infections complicating CIED are rising globally with resultant increase in morbidity and mortality [2]. This could be attributable to advances in interventional therapeutics with rising need of CIED [1]. Infections could be pocket infections, device infections, infective endocarditis or abscess formation [10]. CIED accounts for about 0.5-7% of total cases of IE [4].

Patients may present with nonspecific symptoms e.g., fatigue, anorexia, generalized weakness or classical feature such as pyrexia of unknown aetiology. Our patient presented with fever and generalized body weakness. There should be a low threshold for suspecting IE in patients presenting with the above features when having an indwelling CIED. Infrequently the condition may be complicated with embolic phenomenon.

On suspicion, ideally 2 sets of blood samples should be taken for culture and ABST before administration of antibiotics. Isolation of staphylococcal species strongly suggests the clinical picture of infection related CIED. But our patient was treated with antibiotics empirically in the medical ward which most likely explains the negative cultures.

Culture negative endocarditis also should be taken into consideration at this point. Though our patient's IE was detected through TTE, it usually tends to have a low sensitivity particularly in adults. TOE is very useful in diagnosing IE [10] and particularly with lead endocarditis, as it visualizes the lead in the SVC and tissues along the region.

Our patient's throat swab culture was positive for MRSA. The possible route for the acquisition of MRSA infection was suspected to be the use of the IV cannula when the patient was managed for a CVA 3 months ago.

A TTE was done on the patient which showed the vegetation attached to lead positioned in the RA. As TOE confirmed the vegetation being in proximation to the PPM RA lead near the entry of SVC to RA, a causal relationship was suspected.

According to modified Duke's Criteria, our patient had 1 major and 2 minor criteria (he had an oscillating intracardiac mass on the lead of PPM, predisposing heart condition, fever) and was diagnosed to have possible lead endocarditis.

When CIED infection occurs, it is necessary to surgically remove the CIED to contain the infection. In this patient this would necessitate AAI PPM generator removal and major cardiothoracic surgery to explant the intra atrial lead with cardiopulmonary bypass open heart surgery.

A new PPM lead and PPM generator would need to be implanted subsequently. He was deemed high risk for major surgery due to his co morbidities and age. However, since he responded well to IV antibiotics, we did not explant the PPM lead and instead reused same lead for the new AAIR PPM generator. He remains well to date and will be followed up closely for re-emergence of lead vegetation.

Although PPM lead endocarditis is an emerging complication associated with CIED, its occurrence after 11 years of insertion is very uncommon. This case highlights the need to strongly suspect CIED associated infections irrespective of the duration of insertion. Once acquired, MRSA may persist for a long time in patients as carriers.

There are several studies based on this feature and a more recent study has shown it can persist approximately for about 8.5 months while a previous study has shown it to last for about 30 months [11].

All these studies have shown also that the most important determinant of being a carrier is the presence of disruption in skin and tissue e.g., ulcers, bed sores, ileostomy or jejunostomy sites, psoriatic skin lesions etc. However, our index patient did not have any of such lesions of skin break. He most likely acquired the MRSA infection through the IV cannula during his previous hospital admission 3 months before. Thus, another important aspect that needs highlighting in this case is the importance of following strict aseptic measures during any invasive procedure in patients with CIED.

Acknowledgement:

We wish to thank Dr Geethika Patabandige consultant microbiologist NHSL

Consent for publication:

Informed written consent was obtained from the patient to publish his data for this case report.

Conflicts of interest:

The authors declare no conflicts of interests.

Funding:

None

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Case Report

Chest Pain Following an Unidentified Snake Bite

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Abstract

Takotsubo cardiomyopathy or stress cardiomyopathy is characterized by transient left ventricular dysfunction with apical ballooning in the absence of coronary occlusion. This is accompanied by hypokinesia of the left ventricle and ballooning of the apex with hypercontractile base leading to transient decrease in ejection fraction. The underlying pathophysiological mechanism is still unclear but possible causes have been proposed: i.e.: catecholamine cardiotoxicity followed by metabolic disturbance, coronary microvascular impairment and multivessel epicardial coronary artery vasospasm. We report a patient who developed takotsubo cardiomyopathy following a snake bite. *Case Report*. A 66-year-old female with hypertension and dyslipidemia presented following an unidentified snake bite which required antivenom serum. She experienced ischemic type chest pain with T inversion in anterolateral leads and elevated cardiac biomarkers. 2Dechocardiogram showed typical hypokinetic anterior wall with ballooning of apex and hyperkinetic LV base suggestive of takotsubo cardiomyopathy. Coronary angiogram was unremarkable for occlusive coronary artery disease with left ventriculogram showing reduced apical and mid LV wall motions. Patient was treated with a standard treatment regime for LV dysfunction and the followed up 2Dechocardiogram showed complete recovery of LV function at the end of 5 months. *Conclusion*. Our patient had a clear trigger for her overt takotsubo cardiomyopathy. Emotional stress following the snake bite led to excessive sympathetic stimulation resulting catecholamine-induced microvascular spasm or direct myocardial toxicity which is postulated to underly the pathophysiology of takotsubo cardiomyopathy.

Key words: Takotsubo cardiomyopathy, snake bite, antivenom

Introduction

Snake envenomation is a cause of high mortality and morbidity in the suburban and rural areas of the tropical and subtropical world. Envenomation is known to cause cardiotoxicity and multiple case reports of myocardial infarction following snake bites have been reported [(1)]. Snake venom is a complex mixture of proteins and enzymes. Especially, viper venom contains a haemotoxin, a myotoxin, a cardiotoxin and a neurotoxin[(2)]. Although the pathophysiology responsible for myocardial infarction following viper bite is not known, various mechanisms have been proposed including hypovolemia and anaphylactic shock [(3)], coronary thrombosis due to the procoagulant factors in venom[(4,5)], direct toxic effect on cardiomyocytes[(6)], decrease oxygen carrying capacity of blood due to haemolysis, coronary vasoconstriction brought about by endothilins and sarafotoxins in venom[(7)], myocarditis with extensive myocardial necrosis[(8)], myocardial haemorrhage and microvascular thrombosis[(9)]. Takotsubo cardiomyopathy is a rare syndrome that is characterized by a transient decrease in ejection fraction, accompanied by hypokinesis of the left ventricle and ballooning of the apex, with hypercontractile base and non-obstructive coronary artery disease [(10)]. The underlying pathophysiological mechanism of takotsubo cardiomyopathy is still unclear. Possible causes have been proposed- mainly catecholamine cardiotoxicity, followed by metabolic disturbance, coronary microvascular impairment and multivessel epicardial coronary artery vasospasm [(11)].

We are reporting a patient with an unidentified snake bite who developed chest pain with evidence of myocardial damage and subsequently found to have takotsubo cardiomyopathy.

Case report

A 66 yrs. old lady with a background history of hypertension and dyslipidemia was transferred from a local hospital on the 3rd day following an unidentified snake bite for further management of ST elevation myocardial infarction.

She was bitten by an unidentified snake and admitted to the local hospital. Few minutes after the snake bite, she experienced central chest pain. On admission to local hospital, she showed evidence of systemic envenomation (vomiting, abdominal pain, blurred vision and WBCT> 20min). Possible Russel viper bite was suspected. 10 vials of anti venom serum was administered and WBCT reverted to normal. Presence of persistent chest pain warranted an ECG which showed ST elevation in L1 and aVL with T inversion in L2, L3, aVF, V2 to V6. Troponin titer was reported as 1.73 (reference value < 0.12). Treatment was started as for acute coronary syndrome including dual antiplatelets, statins and anticoagulation.

Basic investigations at local hospital are given in table 1.

Basic investigations at local hospital (table 1):

		D1	D2	D3
Full Blood Count	WBC Hb PLT	16.29×10^3 12.1×10^3 126×10^3	13.73×10^3 11.3×10^3 190×10^3	10.47×10^3 9.6×10^3 130×10^3
Renal Function Test	S. Cr	1.39 (0.8-1.2)	1.34	1.02
Liver Function Test	AST ALT ALP Bilirubin	89.5 (0-35) 37.9 (0-45) 63.1 (<110) 0.52	62 28.8	
Serum Electrolytes	Na+ K+	130 (136-145) 3.4 (3.5-5.2)	138 3.6	
PT/INR		2.11	1.54	1.12
Urine Full Report	Proteins RBC Pus cells	3+ 5-8 8-10		

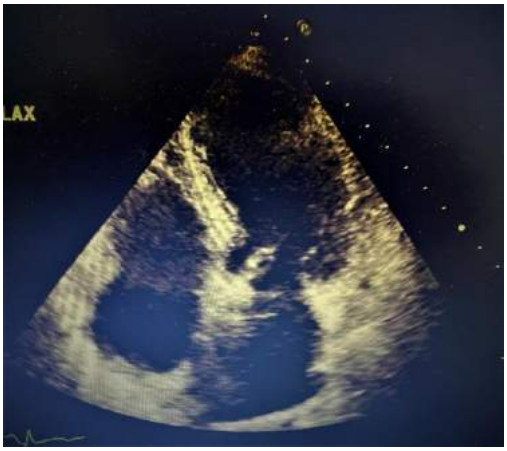
She was transferred to TH Karapitiya on D3 for further management of ACS. On admission to our unit, she was haemodynamically stable and free of chest pain. Further inquiries into the history of the incident revealed that the patient was very frightened and tensed up after the snake bite and that she developed tightening chest pain with autonomic symptoms few minutes later. Apart from that, she gave a history of a transient ischemic attack about 10 years ago and recent in-patient care for acute cholecystitis about 3 months back. She has undergone 2D Echocardiogram during that admission and was found to have evidence of hypertensive heart disease with grade 1 diastolic dysfunction.

2D Echocardiogram performed at our unit revealed hypokinetic mid and apex of LV segments, with ballooning. Base of the LV was hyperfunctioning. Her LV systolic function was around 35% (Figure 1 A, B, C). Above findings made us to suspect the possibility of stress induced cardiomyopathy or so called takotsubo cardiomyopathy.

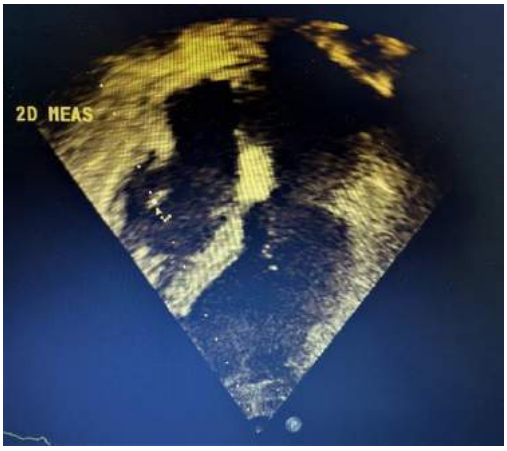
Basic investigation at TH Karapitiya. (Table 2):

		D1	D2	D3
ECG		T Inversion in V2 to V6	T Inversion in V2 to V6	
Troponin titer		11.5 (0-0.12)		
Full Blood Count	WBC Hb PLT	10.27×10^3 9.9×10^3 128×10^3	10.09×10^3 10.1×10^3 142×10^3	8.09×10^3 10.7×10^3 149×10^3
Blood picture		WBC – Mild left shift PLT – Mild thrombocytopenia No evidence of MAHA	WBC – Mild left shift PLT – Mild thrombocytopenia No evidence of MAHA	
Liver Function Test	AST ALT Bilirubin- total	57 (0-35) 26 (0-45) 10 (5-21)		
PT/INR		1.01		
Renal Function Test	S. Cr BU	95 (74-110) 32 (13-43)	75 26	
Inflammatory markers	CRP ESR	99 35	26	
Serum Electrolytes	Na+ K+	140 (136-145) 3.3 (3.5-5.2)	145 4.04	
Fasting Blood Sugar		88		

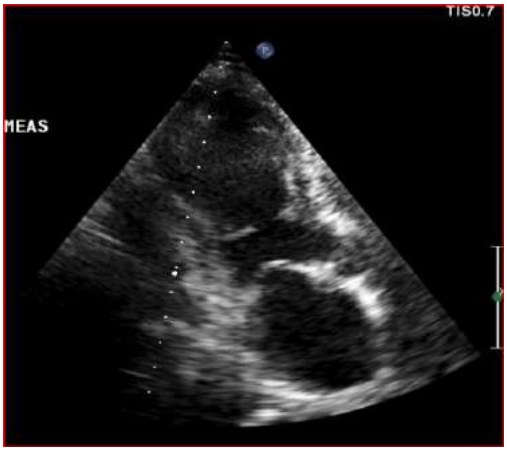
Figure 1:



A. 2D Echocardiographic 4 chamber view on admission showing dilated LV with apical ballooning.



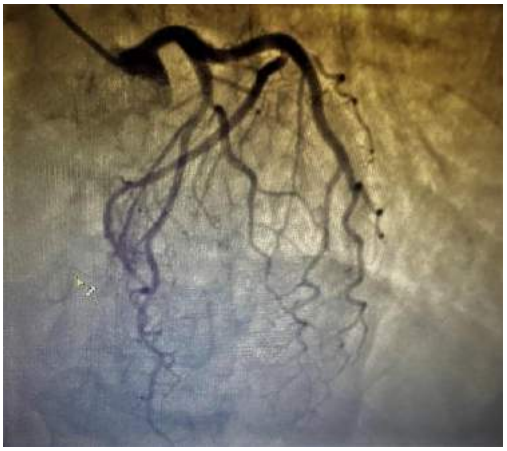
B. 2D Echocardiographic 4 chamber view (inverted) on admission showing dilated LV with apical ballooning.



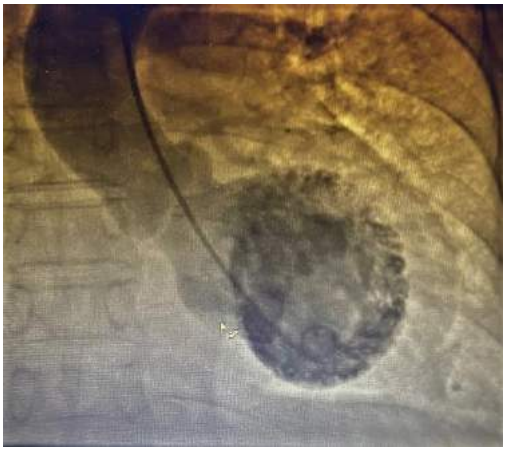
C. 2D Echocardiographic 3 chamber view on admission showing dilated LV with apical ballooning.

Coronary and LV angiogram was performed on D7 and found to have minor coronary artery disease. LV angiogram revealed hypokinetic apex with ballooning and hyperfunctioning LV base (Figure 2 A, B).

Figure 2:



A. Coronary angiogram showing non obstructive left system



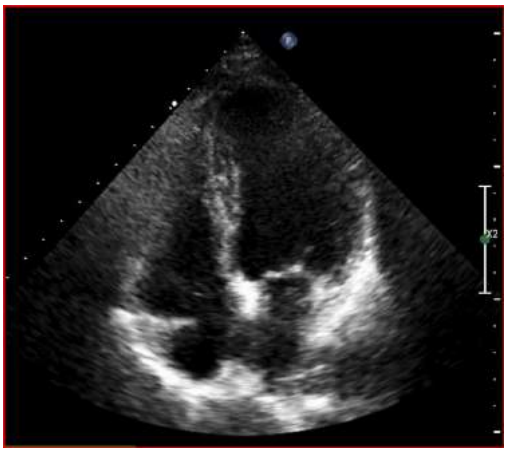
B. LV angiogram showing ballooning of apex.

Diagnosis of takotsubo cardiomyopathy was made on the above findings. She was treated with an ACEI, beta blocker, diuretics and single antiplatelet agent with a statin due to minor coronary artery disease.

Case Report

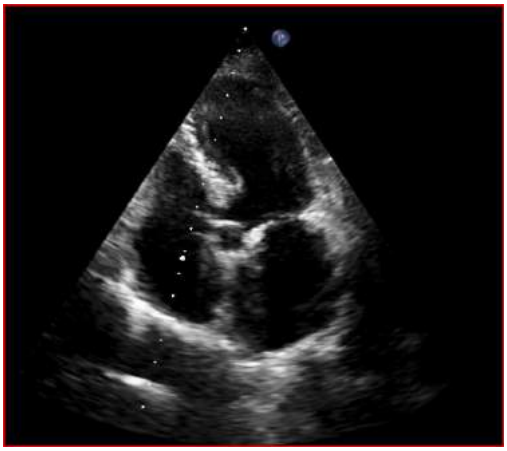
Repeat 2D echocardiogram done 1 month later revealed improved LV function from 35% to 50% with mild apical hypokinesia (Figure 3) and 5 months' time echo showed normal LV function with normal regional wall motions (Figure 4).

Figure 3:



2D Echocardiographic 4 chamber view at 1 month, showing improving LV function and LV size.

Figure 4:



2D Echocardiographic 5 chamber view at 5 months showing fully recovered LV function.

Discussion

Transient cardiac dysfunction in this case can be attributed to the snake venom. Our case met all four of the proposed Mayo Criteria for the clinical diagnosis of takotsubo cardiomyopathy. Therefore, we diagnosed this case as takotsubo cardiomyopathy.

Snake bite is an alarming and frightening experience to the victim. Hence, there may be more cases of snake bite with transient left ventricular dysfunction which probably have gone unnoticed.

The prognosis of patients with takotsubo cardiomyopathy is generally favorable such as the case presented here. However, heart failure is the most common clinical complication. There are no specific treatments for Takotsubo cardio-myopathy, but supportive measures such as administering oxygen and diuretics for pulmonary edema are needed in many cases [(12)]. It is common practice to prescribe ACEIs or ARBs, at least until left ventricular (LV) function is restored. Beta blockers are also indicated and may be useful in the long term [(13)].

Our case report alerts physicians managing snake bite to consider not only cardioinhibitory effect of snake venom but also takotsubo cardiomyopathy as a differential diagnosis if the victim develops cardiac dysfunction.

Conclusion

Myocardial infarction is a well-known and reported complication of snake venom following a snake bite. In the presence of chest pain, suggestive ECG changes and elevated cardiac biomarkers confirm the involvement of the myocardium. Sudden emotional stress along with the snake bite causes excessive sympathetic stimulation leading to catecholamine-induced microvascular spasm or direct myocardial toxicity which manifested as takotsubo cardiomyopathy. Awareness of the possibility of takotsubo cardiomyopathy in a patient with chest pain following a snake bite will be helpful not only to decide on further management but also to avoid complications related to chest pain management specially in the background of venom induced coagulopathy.

Abbreviations

LV: Left ventricle
WBCT: Whole blood clotting time
ECG: Electrocardiogram
ACS: Acute coronary syndrome
TH: Teaching hospital
ACEIs: Angiotensin converting enzyme inhibitors
ARBs: Angiotensin receptor blockers
WBC: White blood cells
Hb: Haemoglobin
PLT: Platelets
AST: Aspartate transaminase
ALT: Alanine transaminase
ALP: Alkaline phosphatase
S. Cr: Serum creatinine
BU: Blood urea
RBC: Red blood cell
MAHA: Microangiopathic haemolytic anaemia
CRP: C-Reactive protein
ESR: Erythrocyte sediment rate

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Disclosure

An approval from the ethics committee was not required to publish this case report. Data sharing is not applicable to this case report as no data sets were generated or analyzed during the current study. All authors were involved in the case management, assessment of cardiac function and writing the case report.

Conflicts of interest

None.

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Case Report

Mystery of an Unusual Cause of Dyspnea: finding an Aorto - Right Atrial Fistula when Operating for a Rare Right Atrial Blood Cyst

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Abstract

Blood filled intracardiac cysts are rare in adults. An intracardiac cyst with an aorto- right atrial [RA] fistula is rarer. Here we report a 57-year-old female investigated for exertional dyspnea, and found to have a cystic mass in the RA cavity on transthoracic echocardiography [TTE]. Cardiac magnetic resonance imaging [CMRI] showed a large blood-filled cyst in the RA. Coronary angiography (CA) demonstrated normal epicardial coronary arteries. During surgery while excising the RA blood filled cyst an aorto-RA fistula [ARAF] was noted. The cyst was excised and the fistula was closed successfully. Retrospective review of the CA revealed an abnormal aorto-RA vascular connection. This case highlights the fact that the contained shunt into the cyst altered the typical clinical and imaging findings of an ARAF through continuous flow into the atrium with high flow velocity in the fistula tract. Echocardiography and CMRI are useful tools to arrive at the initial diagnosis of a RA cyst, but the ARAF part of the diagnosis was missed likely due to the rarity and also altered hemodynamics caused by the flow into the cyst.

Key words: blood filled intracardiac cyst, aorto-right atrial fistula, dyspnea, echocardiography

Introduction

Blood filled intra-cardiac cysts are very rare in adults, though it can be seen in neonates with a low incidence of 0.07% [(1).] These blood-filled cysts tend to be small in size and commonly occur at the atrioventricular valves. However they usually tend to regress[(1)]. Aorto-RA fistula is an abnormal connection between the aorta and right atrium. The formation of the fistula is complex in its origin. It can be congenital or rarely acquired [(2)]. There have been a few documented case reports of atrial blood cysts and ARAF in literature. However, this is the first report of a combined congenital aorto-RA fistula associated with a right atrial blood cyst which was surgically corrected successfully.

Case presentation

A 57-year-old female presented with dyspnea on moderate exertion of 3 months duration. She had no significant past medical history. Clinical examination revealed a pansystolic murmur at the apex with axillary radiation which was initially suspected as mitral regurgitation (MR). Other systems were unremarkable.

Her hematological and biochemical investigations were normal. TTE and transesophageal [TEE] echocardiography showed a large 88 x 86 mm thin-walled cystic mass in the RA that appeared to be attached to the interatrial septum (figure 1). There was moderate mitral and tricuspid regurgitation. Apart from mild aortic regurgitation no abnormality was noted in the aortic root or arch.

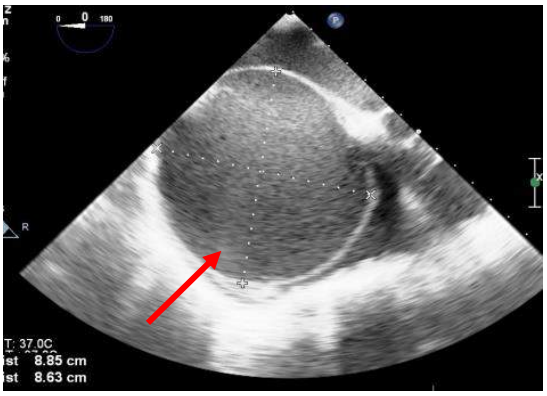

Figure 1: TEE shows right atrial cystic mass cyst (arrow)

Cardiac magnetic resonance imaging (CMRI) also confirmed a large thin walled unilocular cyst and movement of intra-cystic fluid with systole and right atrial inflow obstruction (Figure 2). Cystic contents were isointense suggestive of blood. There was no contrast enhancement seen in the mass or myocardium. The initial CMRI report did not mention the aorto-RA fistula.

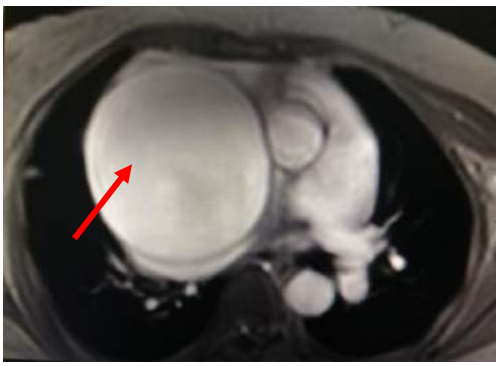

Figure 2: CMR shows a unilocular large right atrial cyst (arrow)

Radial invasive coronary angiogram [CA] demonstrated normal epicardial coronary arteries with separate origins of left anterior descending artery [LAD] and left circumflex artery [LCX]. The CA was done pre-surgically to decide on the need for additional revascularization at the time of cyst excision. Though an abnormal vascular tract was noted draining into RA this was misinterpreted as the venous phase of coronary sinus filling (figure 3).

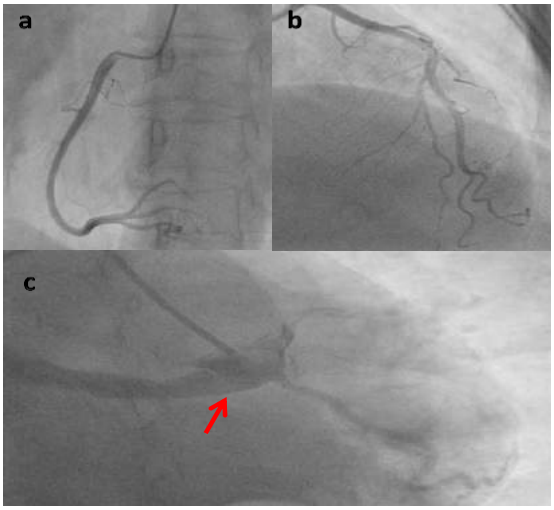

Figure 3: a. Normal right coronary artery (RCA)
b. Normal LAD
c. Abnormal vascular tunnel (arrow) and visible normal LCX

At surgery the fistula tract was identified. It extended from the aortic root to the RA. The cyst was excised and the fistula opening was ligated at both the aortic and the RA ends [figure 4]. Post-operative TTE showed complete excision of cyst with dilated RA (figure 5). She had a good post-operative recovery and was discharged two weeks later.

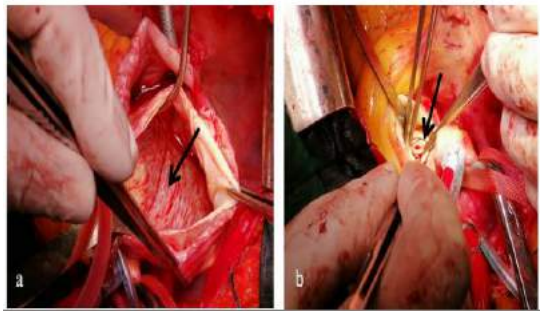

Figure 4- a: right atrial blood-filled cyst excision (arrow) b: fistula opening in the aorta (arrow)

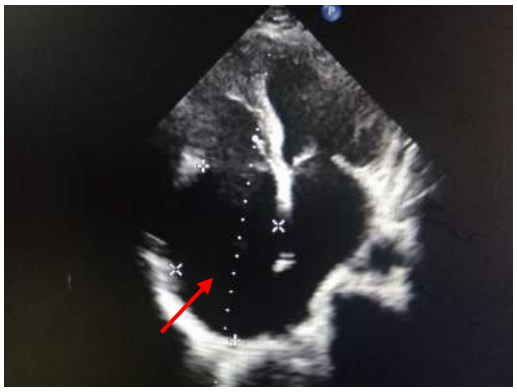

Figure 4: Post-operative TTE shows complete right atrial cyst excision (arrow) and right atrial dilatation.

Discussion

Intracardiac cystic masses are rare and the differential diagnosis include, hydatid cysts, bronchogenic cysts, hemorrhagic cysts, intracardiac varices and cardiac tumors with hemorrhage (myxoma) [3]. Adults with cardiac blood cysts are usually asymptomatic, however it can cause valve dysfunction, thrombus formation, embolic stroke and heart failure [1].

ARAF is characterized by an abnormal intracardiac flow between aorta and atrium. This may lead to heart failure and a spectrum of clinical features such as chest pain, palpitation, dyspnea, orthopnea, oedema and generalized malaise. Physical examination may reveal a continuous murmur at the right upper sternal edge. ARAF is commoner than aorto left atrial [LA] fistulae because of its anatomical position. Aortic valve endocarditis can cause fistula formation between aorta and the LA [4]. Our patient presented with exertional dyspnea without other features of heart failure. On auscultation there was a pansystolic murmur at the apex suggestive of mitral regurgitation. No continuous murmur was detected in this patient and this could be explained by the fact that the ARAF was opening into a contained blood-filled cyst and not the RA. TTE findings were of a cyst in the RA but without significant doppler color flow.

Congenital aorto-atrial fistulae [AAF] can be subdivided into: aorto-atrial tunnel and coronary-cameral fistulas. In aorto-atrial type, there is a weakening in the aortic wall leading to fistula formation usually above or at the sino-tubular junction. In coronary-cameral type, formation of shunt occurs between a coronary artery and the atria [4].

Case Report

Acquired type of AAF is described due to many causes and endocarditis of aortic valve or aortic root complicated with paravalvular abscesses tend to be the commonest cause. Other aetiologies include aortic valve or root surgery, aortic dissection, vasculitis (giant cell arteritis), trauma and erosion of the atrial wall by the occluder used for percutaneous closure of the atrial septal defect, due to oversizing of the device or deficient aortic rim [4].

Both TTE and TEE are useful investigations to evaluate AAF. TEE with colour doppler can give a better visualization, but three dimensional TEE will provide a definitive anatomic assessment and spatial orientation [4,5]. CMR is very useful to quantify shunt fraction and flow measurements. Cardiac catheterization is used to quantify the shunt fraction accurately [4]. In our patient although an abnormal vascular tunnel was visible in CA we did not identify it as an AAF and this highlights the need for better appreciation of such rare entities to understand its implications in unexplained CA findings.

In our patient there was a large right atrial cystic mass detected by both TTE, TEE and CMR but the AAF fistula tract feeding it was only detected while performing surgery. The aetiopathology for this rare congenital form of ARAF and RA blood cyst is unclear but a possible explanation could be ballooning out of soft tissue in RA forming a cyst wall without the tract opening into the RA cavity. It is likely that with time equalization of pressure between aorta and right atrial blood cyst resulted in no audible (continuous) murmur at the aortic area and the absence of a doppler continuous flow signal. Additionally, as the fistula tract had low flow velocities it was not initially detected by color doppler of CMRI.

The dyspnea in our patient was unlikely to be due to the large left to right shunt and was likely caused by the large cyst limiting the flow in the RA. Treatment options for AAF are surgical ligation, percutaneous device closure, covered stent or coil embolization[4]. It is doubtful whether closure of the ARAF alone in our patient would have resulted in sufficient collapse of the RA blood cyst and relieved her of symptoms. A surgical option was decided upon and carried out with successful excision of the RA blood cyst and the closure of the ARAF tract. The probability of recurrence was unlikely and a complete resolution of symptoms was expected.

She was reviewed post surgically and remains well to date and asymptomatic.

Conclusion

Congenital ARAF with RA blood cyst formation is an extremely rare clinical entity and the contained shunt into the cyst alters the typical clinical and imaging findings of an AAF such as continuous flow into atrium and high flow velocity in the fistula tract. TTE, TOE and CMRI were useful to arrive at the initial diagnosis of RA blood cyst in this patient but the AAF part of the diagnosis was missed due to the rarity and also altered hemodynamics. However, fortunately it was detected during surgery and corrected successfully.

Acknowledgement:

We wish to thank Dr Aruna Pallewatta, Consultant radiologist NHSL for CMRI reporting.

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Case Report

How FFR (Fractional Flow Reserve) Changed my Management: A Compilation of FFR Guided Cases

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Abstract

Fractional Flow Reserve (FFR) is now increasingly utilized in the management of patients with chronic coronary syndromes, and it has shown statistically significant, better long-term outcomes compared to the percutaneous coronary interventions (PCI) driven by coronary angiograms (CA) alone. We present two patients, where FFR changed the management strategies. Our first patient was a 50-year-old lady with multiple vascular risk factors including a history of acute coronary syndrome (ACS), who was found to have triple vessel disease (TVD) on conventional angiogram and initially planned for multivessel sequential PCI. Use of FFR made us to select the primary target lesion with significant physiological stenosis irrespective of subjective angiographic stenosis. Second patient was 37-year-old gentleman with high cardio-vascular risk factors who had already undergone PCI to mid right coronary artery (RCA). He was found to have new atheromatous plaque formations in several coronaries. FFR was used to analyze the PCI of a neo-RCA lesion considering his young age and long-term complications that can arise with placing multiple long stents in the same coronary.

Key Words: FFR, Physiological coronary stenosis assessment

Introduction

FFR is defined as the ratio of mean distal coronary pressure to mean aortic pressure. It uses a specialized, 0.014-inch, sensor tipped pressure wire to measure the distal coronary blood pressure across the lesion at maximum hyperaemia. FFR has a near linear correlation between coronary pressure and blood flow. [(1)] Adenosine is used to achieve maximum coronary vasodilatation and doses of 200 mcg for the left coronary and 100 mcg for the right coronary have shown similar efficacy as high dose intravenous infusions. [(2)] Integrating the coronary luminal stenosis severity, myocardial territory and viability in addition to the collateral perfusion, FFR can fully assess the physiological significance of an epicardial coronary vessel obstruction. Studies have elaborated that non-invasive functional testing has desirable overall correlation with FFR. [(3)] FFR cutoff value of 0.80 have been validated in several prospective randomized controlled trials (RCT) as the threshold of significant coronary stenosis responsible for ischemia. [(4,5)]

Case Report- Patient 1

50-year-old lady who had been on treatment for ACS with background type II diabetes mellitus (DM) and hypertension (HT), complained of Class II exertional dyspnea. Her vascular risk factors were marginally controlled with oral medications.

Her 2D-Echo revealed an ejection fraction (EF) of 45% including anterior hypokinesia with a preserved muscle mass. Coronary angiogram showed, distal left main coronary artery (LMCA) 30-40% lesion (Image 1), 50-60% lesion in the mid left anterior descending (LAD) artery (Image 2), 80% stenosis in the high obtuse marginal (OM1) artery (Image 1) and 80% lesion in the proximal posterior descending artery (PDA) (Image 3), which was originating from a dominant RCA. Initial management plan was to go ahead with multivessel, interval PCI to achieve complete revascularization. However, on re analysis a decision was taken to use FFR, to assess the significance of the lesions, considering the myocardial territory supplied by each vessel. FFR of each vessel was recorded as shown below. (Table-1)

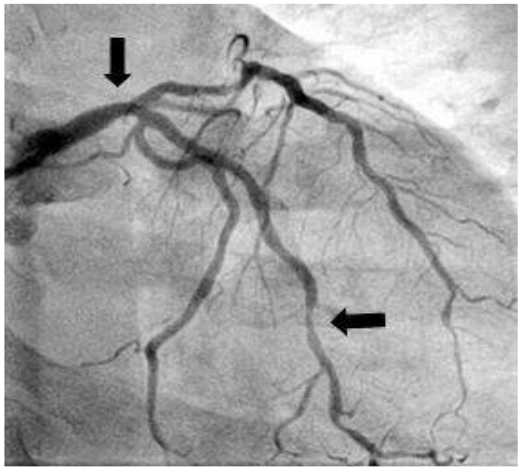

Image 1 – Distal LMCA and High OM1 lesion

Case Report

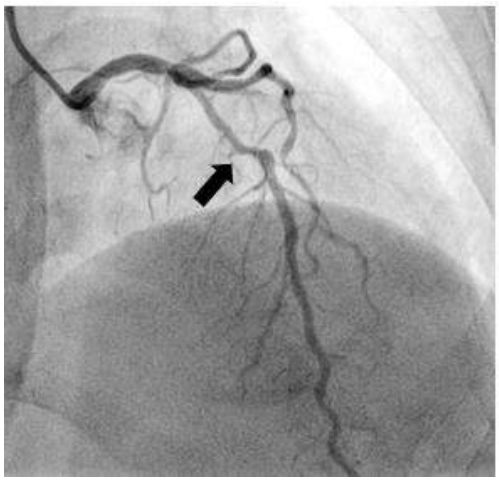

Image 2 – Mid LAD lesion

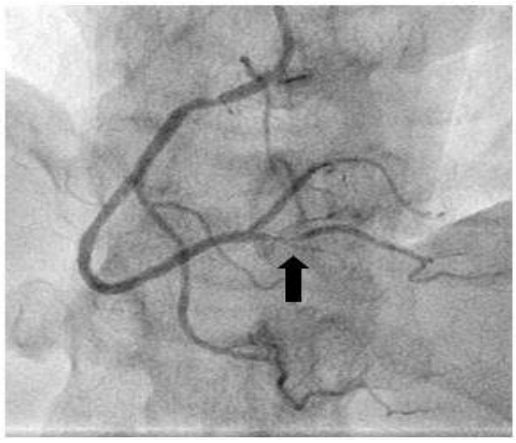

Image 3 – Proximal PDA lesion

Image 4 – FFR value in LAD lesion

Image 5 – FFR value in OM1 lesion

Vessel	Angiographic stenosis (%)	FFR value
LAD	50-60	0.72 (Image 4)
High OM1	80	0.96 (Image 5)
PDA	80	0.94

Table-1: Comparison of angiographic stenosis and FFR values obtained in each vessel

Considering the FFR values we performed PCI to LMCA to LAD, and deferred PCI in high OM1 and PDA. 3.5 X 38 mm Drug Eluting Stent (DES) was deployed to cover both lesions at distal LMCA and mid LAD (Image 6). Kissing balloon technique was used to maintain the carina at the LAD and left circumflex (LCX) artery ostia. Patient was discharged with ticagrelor and aspirin combination. She showed a dramatic improvement in her symptoms during the successive clinic visits.

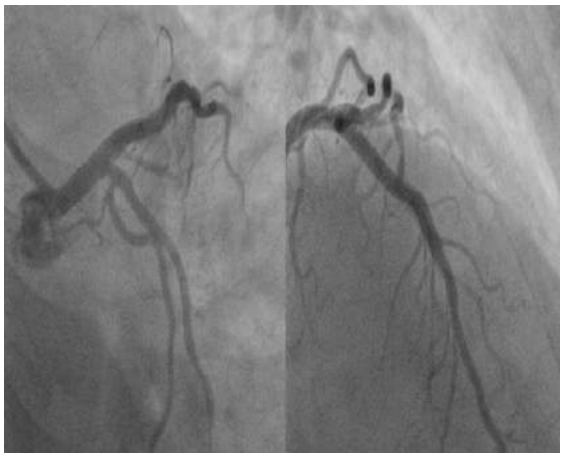

Image 6 – Final angiogram of PCI to proximal LMCA to LAD

Case Report- Patient 2

A 37-year-old gentleman who had undergone rescue PCI to mid RCA in 2013 presented with Class II exertional angina. He had DM, HT and he continued to smoke even after first ACS. His EF remained low at 50% with inferior territory mild hypokinesia. Check CA revealed several new atheromatous plaque formations compared to his first CA. Tight lesions were seen in the LCX (Image 6) and a 50-60% lesion was detected at the proximal RCA, few millimeters proximal to the old RCA stent which showed moderate In-stent Restenosis (Image 7).

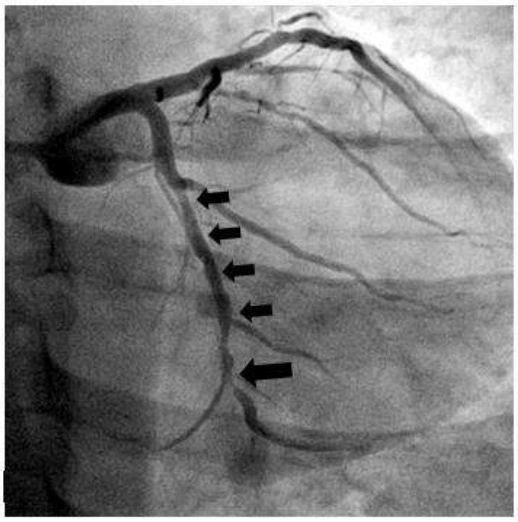

Image 6- Moderate plaque burden with 90% stenosis at distal LCX

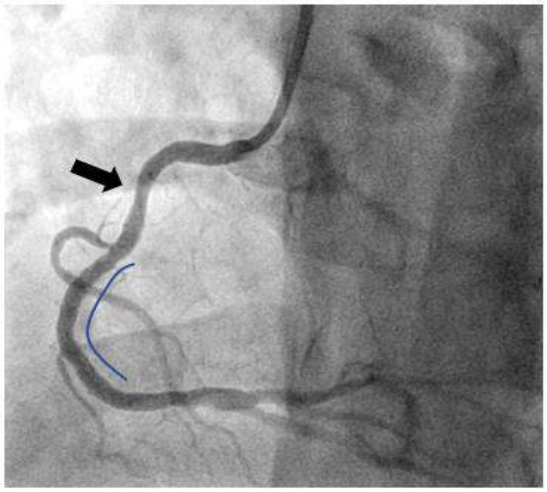

Image 7- Arrow indicates new lesion, Line indicates the old stent with moderate ISR

PCI to LCX done with 3 X 48 mm DES and Plain Old Balloon Angioplasty (POBA) was done to the ISR segment of the old RCA stent. After dilating the RCA stent, we measured the FFR value of the proximal lesion and it revealed 0.78 at maximum hyperaemia with intra-coronary adenosine bolus (100 mcg). Considering his young age and the long-term complications which are expected with overloading metal in the RCA, we opted for optimum medical management for the proximal RCA lesion. Patient was advised with regards to the cessation of smoking and risk factor modification. He is currently being regularly monitored at clinic level and shows an excellent improvement of his symptoms.

Discussion

FFR is a reproducible and reliable indicator of coronary physiological stenosis. Several RCT have evaluated the safety and the efficacy of deferring PCI based on the non-significant FFR. [6,8] It is recommended that in patients with Stable Ischemic Heart Disease (SIHD), FFR is a reliable method to assess the functional significance of intermediate coronary stenoses (50-90%) and optimizes making logical decisions regarding revascularization [7,10] (Class IIa, Level A evidence). Therefore, we deferred the PCI in the RCA and high OM1 in our first patient even though angiographically lesions appeared tight.

Medical treatment is associated with favorable long-term clinical outcomes in angiographically equivocal lesions which are classified as hemodynamically not significant by FFR. [11] Single FFR measurement of between 0.75-0.80, represents a gray zone requiring accurate clinical judgement of the physician. In our second patient, proximal RCA lesion demonstrated-angiographically 50-60% stenosis and FFR value of 0.78. Considering his age and long-term complications that might arise from long overlapping stents, we decided to go ahead with optimum medical management.

FFR guided treatment strategy was associated with favorable long-term outcome with decreased major cardiovascular events. [9] Thus, we have planned to implement long term surveillance and close follow up on these patients with optimal risk factor control.

Conclusion

Current revascularization guidelines have incorporated the use of FFR in the management of SIHD. Multiple studies have shown the significance of utilization of FFR in coronaries to assess the physiological significance of the lesion and improved long-term clinical outcomes.

Therefore, it is of utmost importance to use FFR in contemporary PCI strategies. Knowledge and technical expertise in handling FFR are essential to acquire accurate values which are reproducible.

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Case Report

Exotic Subtype of Reversible Left Ventricular Failure - "Happy Heart Syndrome"

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Abstract

83-year-old lady presented with angina of acute onset. She was having signs of left heart failure. ECG showed diffused ST changes and an urgent coronary angiogram was performed. This showed only a moderate right coronary artery lesion but nothing to account for her symptoms and ECG changes. Bedside ECHO showed apical akinesia with dilatation and both troponin and BNP were significantly elevated. Our working diagnosis was tako-tsubo cardiomyopathy (TTS) which was confirmed later with departmental ECHO and CMRI. We commenced heart failure medication and her symptoms resolved within a week. Throughout she did not need any inotropes/vasopressors and there were no complications related to TTS. Repeat CMRI in 6 weeks showed complete resolution of structural changes. Probable trigger was her birthday party celebration with gathering of all of her extended family. This belongs to a rare subtype of TTS called "happy heart syndrome". Tako-Tsubo cardiomyopathy although rare is an important consideration in a coronary care unit when an angiogram does not reveal a culprit lesion, especially amongst post-menopausal women [(1)]. Generally, it carries an excellent prognosis with 95% complete recovery within 3 months [(2)].

Key words: Happy heart, tako-tsubo, Cardiomyopathy

Introduction

First description and coining of the term Tako-Tsubo cardiomyopathy (TTS) was in 1990 by Sato et al. It was exclusively reported in Japan initially until the end of 1990's [(3)] when a small number of cases were recorded from the western countries. In Japanese language the term means "fishing pot to trap Octopus" and this has a very similar appearance to the shape of the heart during a ventriculogram in the acute phase of TTS. Generally, TTS is a reversible left ventricular dilatation specially of the apex without culprit coronary artery disease. A vast majority of the cases are documented in post-menopausal women with onset consequent to an acute emotional or physical stress. Common presenting symptoms are angina, subacute difficulty in breathing, and left heart failure with arrhythmias, which makes it extremely difficult to distinguish from acute coronary syndrome (ACS). Generally, it is believed 1% of all ACS presentations worldwide are possibly due to TTS. Until recently, events triggered by positive emotions were not entertained and this particular rare subtype is called "happy heart syndrome" which comprises approximately 1% of all TTS cases [(4)].

Abe et al in 2003 first introduced TTS diagnostic criteria and since then, there has been multiple modifications to the accepted criteria [(5)]. Currently modified Mayo clinic and International TTS criteria are recommended for clinical use. Generally, almost all cases (95-97%) recover completely. It is important to plan and repeat CMRI in 6 weeks to reassess for retrospective confirmation as well as for identification of scarring/fibrosis.

Case report

An 83-year-old lady with no past medical history of note presented to our coronary care unit (CCU) brought in by paramedics. She gave a 2-day history of subacute shortness of breath which had worsened with acute onset of angina on the day of admission. Oxygen saturations were maintained at 92%without the need of supplementary oxygen but there was left ventricular failure and tachypnoea on clinical examination. Pulse rate was paradoxically on the lower side at 75/min with intermittent bradycardia and BP was 100/70mmHg. ECG showed marginal yet diffuse ST elevations in antero-inferior regions with prolonged QT.

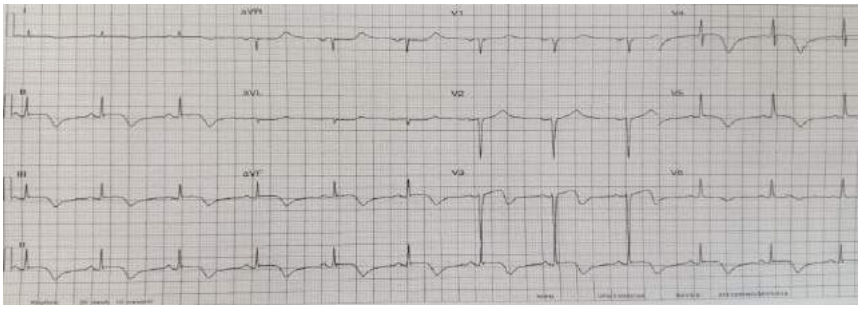

Figure1: ECG on admission showing anteroinferior mild ST changes with prolonged QTC (>500)

Case Report

She was taken up for urgent cardiac catheterization. The right radial angiogram revealed a moderate stable plaque in the right coronary but the left coronary was relatively normal. Bedside ECHO showed an overall EF of 40% with apical dilatation (nonregional) and good basal contraction. There was no evidence of myocarditis, embolism, pericardial fluid collection or valve disease. Thinking of possible TTS, we performed a Pigtail-Injector ventriculogram which showed a characteristic TTS apical ballooning and akinesia similar to a Japanese Octopus pot.

Fortunately, her blood pressure throughout was above systolic of 90mmHg and without LVOT obstruction, which meant that she did not require any vasopressors or mechanical left ventricular assistance such as IABP or IMPELLA. Due to the prolonged QT (classic feature in TTS) we prophylactically treated with magnesium and calcium supplementation but she did not have any ventricular arrhythmias at any point.

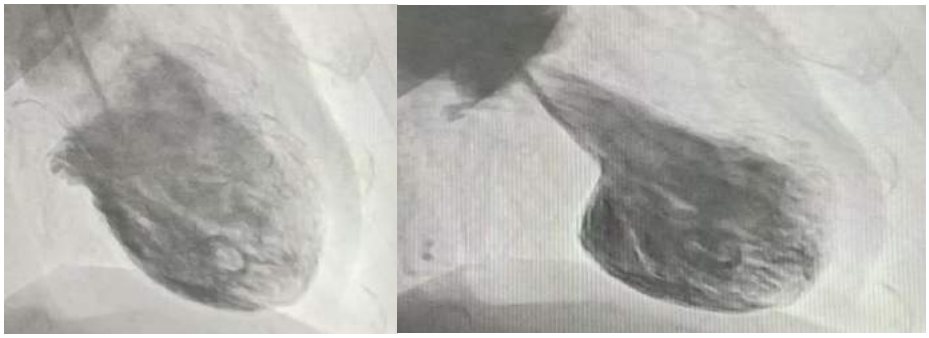

Figure 2: Ventriculogram during early and late systole. "classical Octopus catcher"

Further questioning revealed that she had celebrated her 83rd birthday few days back with participation of all her relatives, which was a long-awaited reunion. As she was negative for over indulgence of alcohol and drug abuse, we entertained the working diagnosis of "happy heart syndrome".

Properly detailed ECHO confirmed our suspicion of apical ballooning syndrome and importantly no left ventricular outflow (LVOT) obstruction was noted. We managed her in CCU with heart failure medication including IV frusemide infusion, 2 L/min mask oxygen, low dose angiotensin converting enzyme inhibitors, beta blockers, spironolactone and on demand noninvasive pressure ventilation.

Amongst important test results were white cells (WBC) 12,000/ul with neutrophilic predominance, CRP-35, BNP 940(<30), Troponin 2692(<21), creatinine 104(<90), COVID PCR-Negative, d-dimer-220(<120) and normal clotting profile. MRI was performed once she was stable enough which showed: Preserved LV volumes with moderate ejection fraction (LVEF 45%), no LVH, mildly increased RV volumes with preserved function, mid-ventricular to apical near-akinesia with preserved basal contractility, myocardial oedema in the mid-ventricular to apical segments and no overt myocardial thrombus, significant fibrosis or infarction.

These findings were highly suggestive of acute phase of a takotsubo cardiomyopathy.

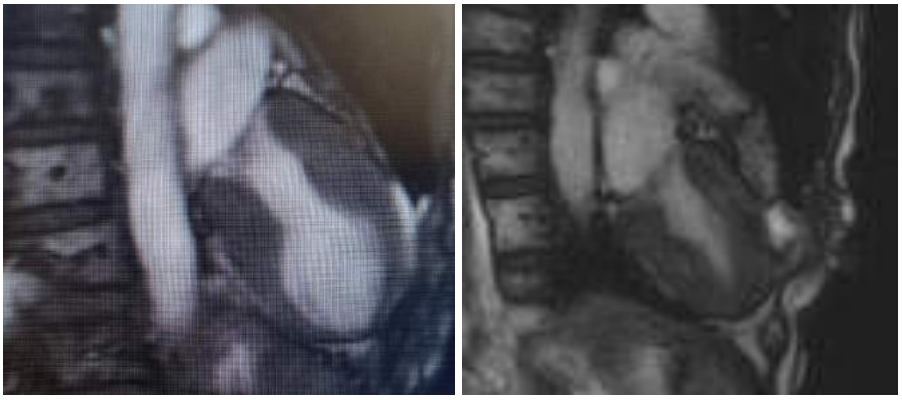

Figure 3: The CMRI in our patient with acute phase apical ballooning Vs resolution 6 weeks after.

On day four of admission, she was off oxygen, with significantly better symptoms. ECHO showed non progression. Although there was no obvious clot, as an akinetic ventricular apex with TTS has high thrombotic risk we discharged her on low dose bisoprolol as well as apixaban for anticoagulation in addition to her general medication. Post discharge 6 weeks evaluation CMRI showed resolution of apical changes with normal biventricular function and no significant scar formation.

Discussion

TTS is an exotic diagnosis in cardiology. There has been much debate and uncertainty with regards to its etiology, pathophysiology and diagnostic criteria. The current international tako-tsubo diagnostic criteria is broad and in cooperates most of the atypical features and subtypes within the umbrella term. Three main points deserve special mention regarding inclusion criteria. Firstly, pheochromocytoma and central nervous system (CNS) events can trigger TTS and are not considered as exclusion criteria currently. Second point is that concomitant significant coronary plaque disease is seen in 10-30% of cases and presence of these lesions do not rule out TTS [6]. Last point is that, although traditionally TTS changes are not limited to a single coronary distribution, rarely you may find a case with changes predominant in a territory subtended by a single artery. There are four main types of TTS; Apical, mid ventricular, basal and focal (single artery) pattern. In addition to this, global form and isolated right ventricular forms are also reported very rarely [7].

Traditionally the trigger is either a physical or psychological stressor. Commonest physical triggers are acute asthma/COPD exacerbation, CNS catastrophe, seizure disorders, surgery and phaeochromocytomas. Emotional triggers could be the death or the loss of a family member or close friend , interpersonal conflict such as divorce, fear (e.g.: robbery, kidnap), and financial strains (bankruptcy, gambling loss, loss of job) [8]. It is also identified that positive emotions can result in sympathetic plus parasympathetic activation and this contributes to a mere 1% of all TTS cases further cementing psychological background as a trigger.

Hence, birthday celebrations, weddings, successful job interview, major sports win are classically known to be trigger events for “happy hearts syndrome” in that order of importance.

It is estimated that one has a 27% higher chance of TTS on a birthday compared to other days of the year [9]. Importantly pure apical type is less commonly seen in happy hearts (65%) whereas in broken hearts the subtype is seen in 80% [8]. Generally, 52% have physical stressors, 31% psychological and 17% no cause identified.

Pathophysiology of TTS is a major dilemma. There are five main mechanisms put forward:

1. Epicardial coronary spasm [10]- Mixed results in studies. Not generally accepted.
2. Microvascular spasm disease [11]- Again non conclusive study results.
3. Type 2 MI with generalized ischaemia [12] (The histopathology is different to ischemic damage)
4. Stunned myocardium [12] (Emotional/CNS or catecholamine surge)- Most widely believed.
5. Transient infective myocarditis [12] - blood testing, biopsy and CMRI was not suggestive.

The classical histopathological changes [13] seen in TTS are not coagulative necrosis as seen in infarctions but contraction band necrosis, interstitial lymphocytic-macrophage infiltration and hypercontracted sarcomeres. High levels of circulating catecholamines are identified in acute phase and most histological features are similar to the ones seen in phaeochromocytoma and CNS catastrophes. FDG PET imaging has shown microvascular reduced uptake but cause-effect relationship is a major question with regards to it. Apex is predominantly affected because it lacks the characteristic three-layer myocardial architecture, limited elastic reserves and has highest density of adrenoreceptors in the heart [14]. The relative ratio of noradrenaline: adrenaline receptor is a determining factor in disease as well as treatment of TTS. Generally, TTS patients have troponin and BNP elevation less than when compared to ACS patients but our patient is a good example that these features are not infallible.

TTS although benign in prognosis is known to result in some life-threatening complications in a minority. Refractory heart failure, stroke/TIA d ue to thromboembolism, ventricular tachy-arrhythmias are some of them [15].

In hospital mortality is around 2-5%. In patients with stable haemodynamics treatment involves general HFrEF medication including ACE inhibitors (ACEI), beta blockers (BB), nitrates, mineralocorticoid receptor antagonist (MRA), and treatment to control BP. On demand use of non-invasive ventilation is well accepted. If BP is low, management depends on whether LVOT obstruction is present or not [16] .

If obstruction >50mmHg is present no inotropes should be used and selective adrenoceptor agonists, vasopressors without inotropism, beta blockers and ECMO are the main treatment modalities. If no LVOT obstruction one may use inotropes plus mechanical assist devices such as IABP and IMPELLA. Special consideration should be given to prolonged QT related Torsade's de pointes tachycardia as well as mural embolism due to akinetic apex. Anticoagulation is prophylactically recommended during acute stage. Concomitant atrial fibrillation is an independent risk factor for inpatient mortality.

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Case Report

Uncommon Manifestation of an Uncommon Disease: Pyogenic Infective Endocarditis Complicated by Ruptured Aortic Root Abscess

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Abstra

A 16-year-old boy presented with fever for 03 days, left sided sudden loss of vision and chest discomfort diagnosed as pyogenic infective endocarditis caused by *Streptococcus viridans*, complicated by aortic root abscess which had ruptured into the sinus of valsalva and right ventricle and resulted in multiorgan dysfunction. This patient was treated as acute pyogenic endocarditis. Acute endocarditis is an uncommon disease nowadays. And it is rare that the pyogenic endocarditis is caused by *Streptococcus viridans*. We discuss the possible complications and review the available literature on this disease.

Key words: Pyogenic, acute, infective endocarditis, *Streptococcus viridans*, Aortic root abscess, sinus of valsalva

Introduction

A 16-year-old previously healthy boy presented to Base Hospital Kalmunai (North) with 03 days history of intermittent fever, vomiting, giddiness and blurring of vision. He had no significant past medical or surgical history. No preceding history of oral infection, recurrent gingivitis, tooth extraction or any significant invasive procedures were reported. There was a history of a completely healed superficial wound before one month. No history of drug abuse. There was no consanguinity.

On examination, he was febrile; conjunctiva was pink, GCS 15/15, mildly confused, especially in right left orientation. Oral hygiene was good and no dental caries were detected. There was no neck stiffness, ophthalmoplegia or diplopia. He had splinter haemorrhages on right middle finger. Blood pressure was 75/55mmHg, pulse rate was 100bpm and no significant murmur was heard. Other systems were clinically normal.

On the second day after admission, he developed right sided sudden loss of vision and confusion. His examination revealed that he was confused and disoriented. There was a splinter hemorrhage on his left thumb. Heart sounds were muffled with a faint diastolic murmur, best heard over the aortic area clinically suggestive of aortic regurgitation. ECG revealed widespread concave ST elevation suggestive of pericarditis. His bed side 2D echo showed a mobile vegetation on non-coronary aortic cusp measuring 6.8×4.4mm (Figure A, D) with a thin rim of pericardial effusion [1,2] without right atrial or right ventricular collapse.

The boy was empirically treated with IV co-amoxiclav and IV gentamycin. The first blood culture showed a growth of *Streptococcus viridans*.
The following day the patient developed cardio respiratory arrest and was managed in the ICU.

The repeat bed side 2D echo on day 03 of admission revealed aortic root abscess (Figure B) with ruptured sinus of Valsalva giving rise to a pericardial pus collection leading to cardiac tamponade and aortic regurgitation (Figure C,D,E).

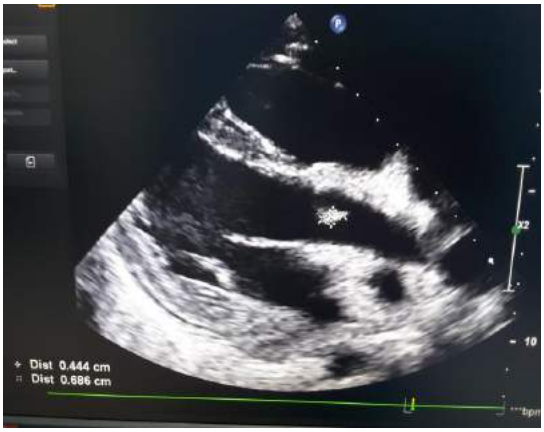
The patient was transferred for urgent cardiothoracic intervention to Cardiothoracic unit Teaching Hospital Kandy where the trans esophageal echocardiogram confirmed the above echo findings and in addition to that they also found another abscess which had ruptured into the right ventricle. He underwent aortic valve replacement with a mechanical prosthetic valve and aortic root repair was also done.

Post-operatively, the patient was managed at the cardiothoracic ICU. Although the patient showed signs of clinical improvement, during the post-operative phase, he was found to have short term memory impairment, disorientation and some behavioral changes. His non contrast CT brain revealed a frontal and occipital lobe infarction.

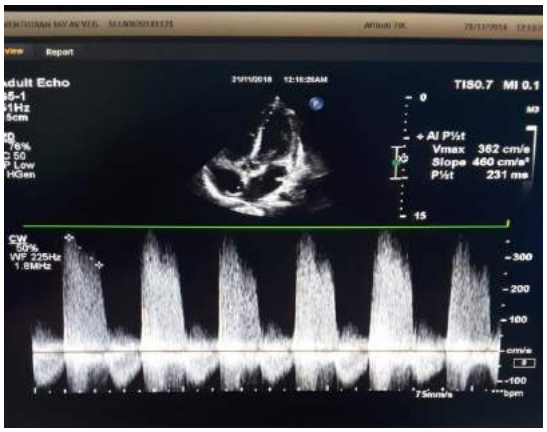
He was on ventilator support for 03 days and then returned to spontaneous breathing with temporary pacemaker support.

Multiple regimens of antibiotics (IV ceftriaxone, IV linasolid, IV. teicoplanin and IV meropenum) were started with the opinion of consultant microbiologist.

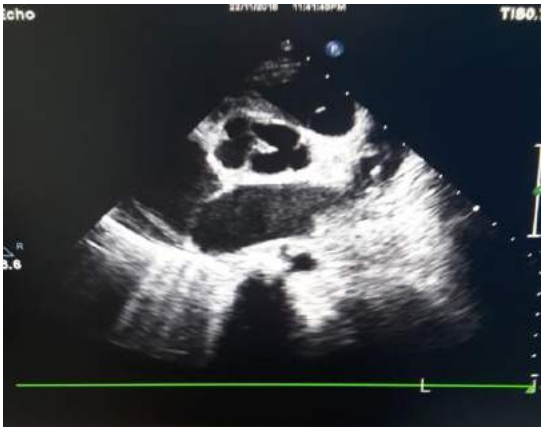
Case Report



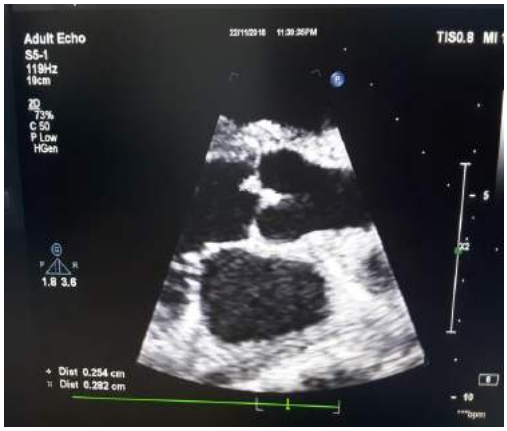
A – Aortic Valve vegetations



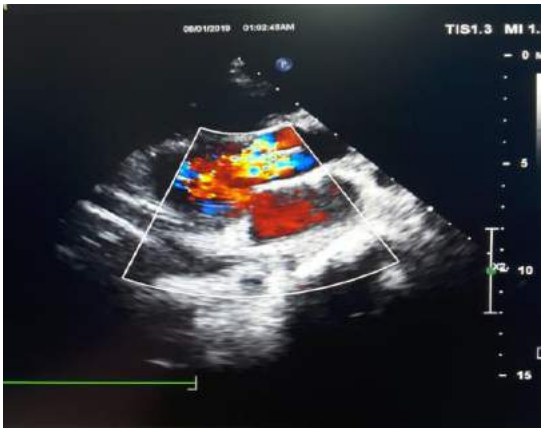
D – Aortic regurgitation



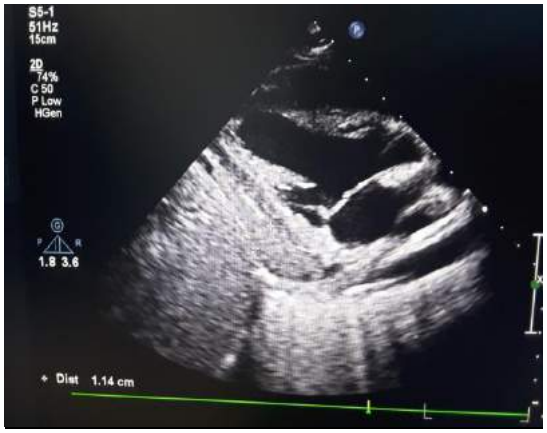
B – Aortic root abscess



E – Aortic valve vegetation



C – Aortic regurgitation



F – Pericardial Abscess

The collected pus, several blood samples, the CVP line tip, part of aortic valve with vegetations and urine samples were sent for culture and ABST. However, all these cultures did not show any growth of a bacterium.

Antibiotics were stopped on day 34 of admission according to consultant microbiologist's advice as the boy had improved clinically and biochemically.

Later, the patient underwent Holter monitoring and due to AV nodal blocks, a permanent pacemaker was implanted.

Discussion

Streptococcus viridans is the most common causative organism for sub-acute infective endocarditis and it is not commonly pyogenic. *Staphylococcus aureus* is a common causative agent of acute pyogenic infective endocarditis. [4,5]. It carries a very high morbidity and mortality rate. Early diagnosis and surgical intervention are the key features in the management.

Pyogenic infective endocarditis involving the aortic valve is often complicated with aortic root abscess formation which may worsen the clinical condition by rupturing into the systemic circulation, sinus of valsalva or invading the myocardium and pericardium.

Rupturing into the systemic circulation may cause persistent sepsis, septic shock and multi organ failure. [2]

A perivalvular invasion into the myocardium, aortic valvular annulus or pericardium can occur [5] .

Transthoracic echocardiography is of diagnostic value in infective endocarditis regarding vegetations, valvular regurgitations and presence of aortic root abscess.

Infective endocarditis should be suspected in patients with a history of high-grade intermittent fever and new onset regurgitation murmurs with peripheral signs suggestive of thromboembolism.

Conclusion

Ruptured aortic root abscess is a devastating complication of infective endocarditis. Transthoracic echocardiography plays an important role in the early detection of aortic root abscess. Early diagnosis and timely surgical intervention are the keys for the successful management.

Conflict of interests

The authors declare that there is no conflict of interests.

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Case Report

Tricuspid Transcatheter Therapy to the Rescue- A Patient with Refractory Carcinoid Syndrome

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Abstract

Tricuspid valve (TV) intervention has been a grey area for interventionists and surgeons alike until recently. Nowadays, threshold to correct TV pathologies has been significantly lowered and this will lead to more and more TV repairs as well as bioprosthetic replacements. A 76-year-old lady presented to us with symptomatic and failing Perimount™ bioprosthetic TV with severe TR. She has carcinoid syndrome, which is the driving factor and detailed imaging shows primary leaflet failure as the reason for the TR. Due to imminent risk of profound right heart failure combined with the risks of redo open heart surgery, we decided to proceed with transcatheter percutaneous ViV (Valve in Valve) therapy using Edwards™ TAVR valve matched to the failing bioprosthesis. With careful planning and innovative operative strategy, we successfully implanted the valve in position relieving her of the TR. We also managed to keep the pacemaker lead to RV intact, as she was in dependent rhythm following initial surgery. Post operatively she recovered with good haemodynamics and the 3-month clinic visit showed much improved functional status as well as improved ECHO parameters from this relatively novel treatment strategy.

Key words: Transcatheter, Tricuspid valve, Severe TR, ViV, Bioprosthesis, Carcinoid syndrome

Introduction

Recent consensus documents and guidelines shed light on the importance of tricuspid valve (TV) as a separate entity and the importance of the right heart as a whole. Because of this paradigm shift, tricuspid interventions have achieved a rapid expansion in number of cases, all over the globe and cardio thoracic surgeons have had comparatively lower numbers referred for surgical corrections of TV pathology. Majority of TV interventions are commonly performed in combination with left heart valve interventions. Tricuspid regurgitation (TR) is rather common and is broadly categorized into primary and secondary TR. If the cause of TR is deemed to be functional/secondary, surgeons frequently proceed with TV and annuloplasty repair, preserving the native valve elements. However, if the cause is found to be organic especially with elements such as degeneration and vegetations, repair of the native valve is found to be unsuitable. Therefore, under these circumstances the correct treatment is valve replacement as a whole, exclusively using a bioprosthetic valve unless indicated otherwise. Acquired organic TR is a definite minority, but one of the important causes is carcinoid syndrome. We present a patient with refractory carcinoid syndrome presenting with failing TV bioprosthesis and severe TR, undergoing transcatheter therapy as a treatment modality.

Case report

74-year-old lady of Asian origin was referred to us for failing TV bioprosthesis with progressive severe TR.

Importantly she had a history of being diagnosed with carcinoid syndrome, with relapsing disease spells since 2004 and liver metastases as of 2011. She was being managed in a specialized endocrine unit with treatment including but not limited to octreotide. At presentation she was not having gross right heart failure symptoms. The classical triad of elevated jugular venous pressure, mild ankle oedema and hepatomegaly were present, functional class was NYHA 2-3 but dependent swelling was not profound. She was self-reliant, ambulant with a BMI of 22 and did not have features of left heart failure. Due to carcinoid complications, she had undergone TVR with Perimount 25mm Bioprosthetic and a PV replacement (Perimount™ 21mm) + pulmonary artery patch augmentation in 2017. Immediate postoperative period was complicated where she had to undergo permanent dual chamber pacemaker for complete heart block (CHB). Due to change of symptomatology 2D echo study was undertaken in October 2018 which first showed a failing TV bioprosthesis where the valve had progressively given away and the latest 2D echo showed severe TR with imminent threat of affecting right ventricular function irreversibly. Initially it was thought that the RV pacing lead was the culprit. We first of all wanted to delineate the aetiology of the bioprosthetic failure. Detailed 3D transthoracic (TTE), CT as well as trans-oesophageal (TEE) imaging were undertaken. These showed that tricuspid valves septal cusp had degenerated and shrunk creating a massive TR flow over the septal cusp. The pacing lead was non adherent and non-obstructive where it was lying between the septal and posterior cusps without impeding the cusp movements.

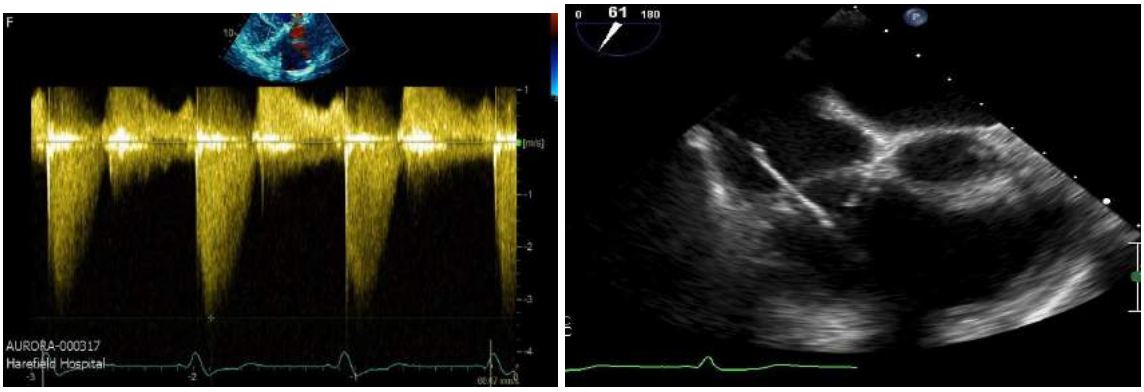


Figure 1: Severe primary TR across the failing bioprosthetic valve and PPM lead.

RV tricuspid annular plane systolic excursion (TAPSE) was impaired at 7mm and also the fractional contraction. However, mid-basal cavity dimensions were not dilated significantly. PV was stable with mild PR, pulmonary artery was mildly dilated, and the left heart was normal with an EF>65%. As the problem was with TV leaflets itself without mechanical impedance, laser extraction of RV lead was excluded as a possible remedy.

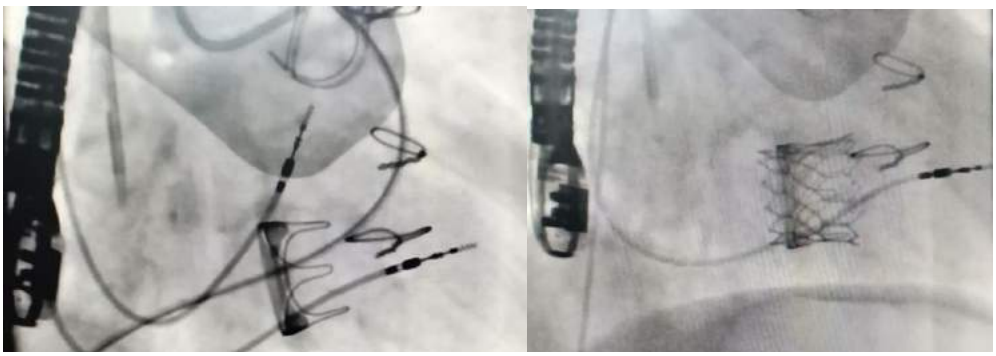
After careful consideration and discussion with family members and in-depth discussions with the multidisciplinary team, we decided that redo open heart surgery is not suitable and to proceed with valve in valve trans-catheter therapy. The corrective measures to be carried out was meticulously planned and prepared for, assiduous attention to details was applied, as this kind of procedure is not common even in a major center like ours. The procedure was performed with access via the right femoral vein with use of two Proglide preclosure sutures. The tricuspid valve was crossed using an MPA catheter and a J wire positioned in the left upper pulmonary artery. We then exchanged this for an Amplatz ST-1 Super Stiff wire and advanced the Edwards SAPIEN™ size 26mm TAVI valve within the guiding system and into position within the existing Perimount bioprosthetic valve.

It was challenging due to the interaction with the atrial pacing lead and the angle between inferior vena cava (IVC)-TV, but we were able to deploy the valve under rapid pacing at 180 bpm using RV PPM lead with an excellent positioning and haemodynamic result.

The proper skirt positioning to get the leaflet opening towards the RV and the use of sewing ring of the original bioprosthetic valve for placement are important tips to note. Valve leaflets should open in the opposite direction to a standard TAVI.

Unfortunately, the atrial lead got displaced on withdrawing the system, initially prolapsing into the right ventricle. Nonetheless, we were able to retract the lead into the IVC. We carefully extracted this from left pre pectoral pocket and placed a new RA lead and also replaced the pulse generator later on. Due to the worry of losing capture of dependent RV during procedure or after jailing between two valves at high pressures we had back up pacing set up through a stiff wire in unipolar fashion which was confirmed prior to deployment.

Figure 2: Pre op and post op ViV RAO projection



Case Report

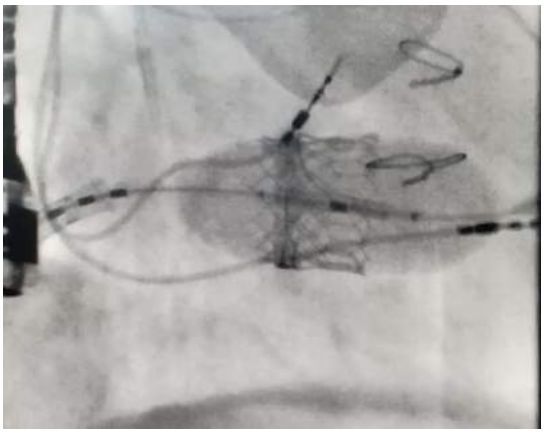


Figure 3: During balloon inflation with rapid pacing.

Post operatively she recovered well with stable haemodynamics and octreotide was continued throughout the perioperative period in case of a carcinoid crisis. Discharge 2D echo study showed stable and well placed ViV Edwards valve with no traceable TR and no features of right heart decompensation syndrome. Pacemaker parameters through the jailed RV lead were also stable with excellent impedance and unchanged thresholds. At three-month follow-up clinic visit patient was found have better RV dimensions and contractions, a TAPSE of 12mm and only NYHA class 2 symptoms.

Discussion

80% of tricuspid regurgitations are secondary/functional with dilated TV annulus mostly as part of left heart disease. Out of the primary TR patients the congenital group consists of atrioventricular defects and Ebstein anomaly patients. Causes for acquired primary defects are infective endocarditis, rheumatic fever, carcinoid syndrome, pacemaker lead and trauma related aetiologies [1]. When TV repair with annuloplasty ring is insufficient surgeons go for TV replacement. Bioprosthetic valves are preferred over metallic devices due to, lack of need for anticoagulation and freedom from associated bleeding risks in elderly patients. Higher rate of prosthetic valve thrombosis is seen with metallic valves and also the metallic valve may form an obstruction when traversing and implanting the PPM lead to RV [2].

TV bioprosthetic longevity is generally considered less than similar valves in left side of the heart. Usually only 75% are functioning properly at 10 years [3].

The usual reasons for failure are leaflet degeneration as observed in this case, calcification, endocarditis, pannus and valve thrombosis[4]. When it necessitates a redo operation, open heart surgery carries a very high operative mortality in the range on 37% on an average[5]. Because of this, percutaneous transcatheter therapies have gained a popularity as a safer treatment modality.

First case of ViV TV intervention was performed in 2015 by Wenaweser et al using a Core valve™ (Medtronic) in a failing Mitroflow™ (Medtronic) device. In the same year United states FDA gave approval for both Medtronic and Edwards TAVR valves to be used as ViV in TV position due to the initial success [6]. In multicenter registry data of an international study, it was shown that outcome data were very promising where 1-year survival was >80%. The percentage (71%) of patients who were NYHA class 3/4 preoperatively, were reduced to 14% at one year with improvement of right heart 2D echo study dimensions in the majority [7].

As per the procedure, preprocedural detailing with 3D to identify clear pathology is crucial. In addition, use of preop CT scans, intra-op TEE and intracardiac 2D echo (ICE) with fluoroscopy coordination is very important [8]. The procedure could be performed under sedation or general anaesthesia (GA) but GA helps when intraoperative TEE is used and also ameliorates the technical difficulties of valve placement. True internal diameter of the failing bioprosthesis should match the new Trans catheter Heart Valve's (THV) external diameter and this is calculated with the help of standardized THV charts which are readily available [9]. If necessary, operator can perform post dilatation with a 6 balloon to achieve good apposition similar to TAVR. There have been case reports showing acute RV failure due to higher afterload once the ViV starts to function, a phenomenon observed in 25% of successful Mitra clips procedures [10], but careful titration of fluids and inotropes counteracted this effect in our patient. Extra attention should be given to access closure of the 23FR guiding sheath and suture based Proglide is very effective for this according to our experience in using it for Mitra clip procedures. As far as the pacing function is concerned in a patient 100% dependent on RV pacing, intraoperative pacing can be achieved via RV lead itself as well as unipolar pacing through the stiff wire in an emergency. Floating a temporary wire in coronary sinus is also another possibility. Post operatively if jailed lead fails, epicardial pacemaker or leadless to RV are plausible options.

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Case Report

A Rare Cardiac Tumor with Chronic Liver Cell Disease and Ascites Simulating Cardiac Myxoma

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Abstract

While most intra cardiac tumors are benign, metastatic tumors to the heart are also seen occasionally. We report a patient with a fatal, rare malignant cardiac tumor, which was metastatic in origin, mimicking a cardiac myxoma. A 63-year-old male with long standing diabetes and background short history of bronchial asthma presented with angina and exertional shortness of breath. He also had anemia and thrombocytopenia with normal liver and coagulation profile. Ultrasonography of the abdomen showed cirrhosis of liver with mild ascites with no focal lesions or portal hypertension. Endoscopic studies were normal except for mild antral gastritis. Transthoracic echocardiography [TTE] showed a large elongated pedunculated right atrial mass extending in to the right ventricle [RV] through the tricuspid valve [TV] with significant right atrial outflow obstruction at tricuspid valve and a mild pericardial effusion. Computed tomography pulmonary angiogram [CTPA] showed pulmonary embolism [PE] with mild bilateral pleural effusions. The typical triad of constitutional symptoms, obstructive effects and embolic phenomena were suggestive of a cardiac myxoma and he underwent cardiac mass excision. The tumor was attached to the IVC margin and extended to the RV through the TV and was removed piecemeal. The histological diagnosis was hepatocellular carcinoma [HCCA] with Hep Par 1 immuno-histochemical marker. Clinically silent HCCA is recognized. This patient additionally had intra-cardiac metastasis with RV out flow tract obstruction and PE likely to be lung secondaries. This case report highlights the importance of considering HCCA as a differential diagnosis of right sided intra-cardiac tumors and the value of histological diagnosis in establishing the final diagnosis.

Key words: Cardiac myxoma, hepatocellular carcinoma, ascites, chronic liver cell disease

Introduction

Most cardiac masses are benign [(1)]. Out of the benign cardiac mases atrial myxomas are the commonest[(2)]. Patients present with constitutional symptoms, embolic phenomena and intracardiac obstruction which are considered the typical triad of symptoms caused by a cardiac myxoma[(3)]. Metastatic tumors to heart can occur with hematogenous, trans-venous and lymphatic spread and also by direct invasion[(4)]. They can be clinically silent or present with fatal complications like embolic phenomena, cardiac out flow tract obstructive symptoms, cardiac tamponade and arrhythmias[(4)]. All above signs and symptoms are nonspecific and clinicians need extra vigilance to identify these in the correct clinical context. We report a patient with a fatal rare metastatic malignant cardiac tumour which mimicked a cardiac myxoma. This case report will raise the awareness of associated clinical findings of cardiac masses and the need to arrange appropriate investigations to arrive at an accurate diagnosis and the definitive management of the patient.

Case report

A 63-year-old male with long standing diabetes mellitus with satisfactory glycemic control presented with progressive shortness of breath NYHA class III of one-year duration and significant unintentional weight loss, malaise and easy fatiguability.

There was no history of any febrile illness. He was a nonsmoker and ex alcoholic with complete abstinence for over 6 months. He had symptoms of anemia without overt bleeding manifestation. He was managed as bronchial asthma with regular inhalers.

He was pale without peripheral stigmata of chronic liver cell disease and had mild ankle edema. Pulse rate was 92 /min and blood pressure were 140/90 mmHg. Jugular venous pulse was elevated with engorged neck veins. Cardiac apex was not displaced and there were no murmurs. Patient had occasional bilateral rhonchi on auscultation. There was mild ascites without organomegaly.

His ESR was 55mm/1st hour and CRP was normal. He had a hypochromic microcytic anemia (10.4 g/dl), thrombocytopenia (109x10^3 /dl). His serum protein level was normal without reversal of albumin /globulin ratio. Liver profile and coagulation studies were within normal limits. Retroviral screening, Hepatitis B and C serology were negative. Ultrasound abdomen showed chronic liver cell disease and mild ascites without portal hypertension. Endoscopies showed mild antral gastritis without varices.

TTE showed a pedunculated 70x 65 mm size homogenous mass arising from right atrium extending to the RV through the TV with mild pericardial effusion.

The mass was somewhat tightly fitting through the TV annulus with obstruction to the RA out flow **(figure 1).**

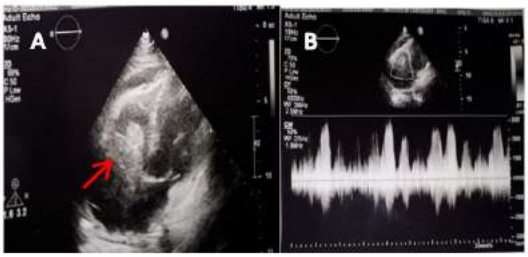

Figure 1: Trans thoracic echocardiogram showing (A) right atrial [RA] mass protruding to the right ventricle [RV] (arrow) through the tricuspid valve annulus causing RA outflow obstruction seen in (B) with continuous wave CW Doppler across tricuspid valve [TV].

LV function was good. As the patient was dyspneic a CTPA was done which showed pulmonary embolism with bilateral pleural effusion (**figure2**).

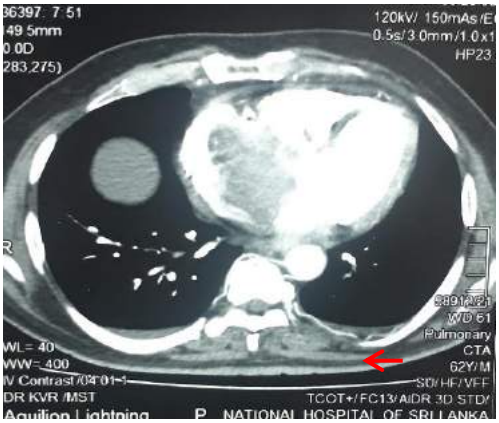

Figure 2: CTPA showing focal pulmonary embolism [arrow] involving the left descending pulmonary artery.

A clinical diagnosis was made of a right atrial myxoma complicated with obstructive and embolic phenomena. He was given enoxaparin for possible venous pulmonary embolism and cardio thoracic surgical consult was done for excision of cardiac mass and coronary artery bypass grafting (CABG) for double vessel disease. During surgery the mass was observed to arise from the site of insertion of inferior vena cava (IVC) raising the suspicion of tumor metastasis along the IVC and IVC was explored but no tumor was found. The mass was removed piecemeal and fragments showed a polypoidal appearance **(figure 3).**

Figure 3: Parts of right atrial mass with polypoid appearance after removal

The post-operative period was complicated by recurrent left pleural effusions, acute liver failure, septic shock, atrial fibrillation and acute kidney injury and he succumbed on post-operative day 15. Histology of intra cardiac mass showed infiltrative malignant tumor composed of cords, nests and sheets of malignant cells with sinusoidal vasculature and some of the cells showed cytoplasmic brown pigment resembling bile with frequent mitoses **(figure 4).**

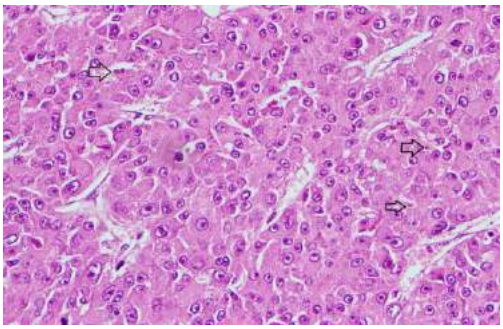

Figure 4: Some of the cells show cytoplasmic brown pigment resembling bile and there are several canalicular like spaces contain bile plugs (arrow).

Positive Hep Par 1 immunohistochemistry was diagnostic of metastatic extension of hepatocellular carcinoma **(figure 5).**

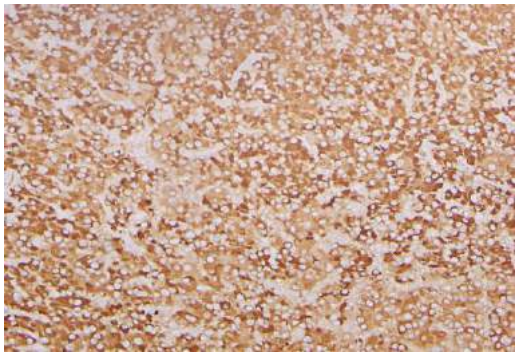

Figure 5: Hep Par1immunohistochemistry: The tumor cells show strong granular cytoplasmic positivity.

Case Report

Discussion

Our patient's main symptom was progressive exertional dyspnea for which he was managed previously as bronchial asthma with inhalers without evaluation with lung function tests. Anemia and RA outflow obstruction due to the cardiac mass causing elevated RA pressures and low RV cardiac output were main contributory factors for his exertional dyspnea. Although he had a long history of chronic unsafe alcohol consumption, he was not diagnosed with chronic liver cell disease (CLCD) until this admission. Normal liver profile, coagulation studies, absence of portal hypertension and absence of gastric or esophageal varices did not alert us for the possibility of hepatocellular carcinoma (HCCA). Additionally radiological imaging did not show any focal liver lesions [5].Our clinical diagnosis was right atrial myxoma which present with typical triad of constitutional symptoms, embolic phenomena and intracardiac obstruction[2]. Patients with cardiac myxoma can also present with cardiac asthma, high ESR, anemia, thrombocytopenia [2,6]. Atrial myxomas originating from IVC are reported to present with chronic ascites [3].

The patient underwent surgical excision of the cardiac mass to relieve the right atrial outflow obstruction along with CABG. Histology report showed HCCA with positive Hep Par 1 immunohistochemistry. HCCA patients commonly present with chronic decompensation of CLCD and focal liver lesions[5]. Liver profile was normal in our patient and he did not have ultrasound evidence for HCCA. HCCA with a background history of CLCD and ascites is reported[7].There are very few case reports of intra-cardiac metastasis of silent HCCA with poor prognosis[8,9]. Most common extrahepatic metastatic sites of HCCA are lung, intra-abdominal lymph nodes and bone [10]. Atrial fibrillation, pericardial effusion, recurrent pleural effusions and pulmonary embolism in our patient is compatible with cardiac and pulmonary metastasis of HCCA. Renal cell carcinoma can also present with a similar clinical picture with trans-venous metastasis[4].

Conclusion

This patient had HCCA with metastasis to the heart presenting as an RA mass extending to the RV causing obstruction at the TV annulus mimicking an RA myxoma. Diagnosis of HCCA was confirmed by histology of the excised specimen at surgery.

Although most intra-cardiac tumors are benign tumor metastases to the heart are seldom seen. Histology of excised tumor after surgical procedures usually help arrive at the diagnosis.

Consent

Prior informed consent was given by the patient for publication of this case report.

Conflict of interest

Authors declare no conflict of interest in the publication of this case report.

Acknowledgement

We thank Dr. Chandima Amarasena consultant cardiothoracic surgeon and his team at the National Hospital of Sri Lanka, Colombo for their contribution in managing this patient.

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Case Report

A Rare Case of a Single Coronary Artery with Atherosclerotic Obstruction causing Acute Coronary Syndrome in an Adult: Successfully Treated with Stent Implantation

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Abstract

Background: A single coronary artery (SCA) is an extremely rare congenital anomaly. Atherosclerotic obstruction of an anomalous left main coronary artery (LMCA) can be successfully treated with percutaneous intervention (PCI) and stent implantation depending on its course.
Case summary: A 54-years-old female with hypertension and dyslipidemia presented with acute onset ongoing ischaemic chest pain of 5 hours duration. Her ECG showed an acute inferior ST elevation myocardial infarction (STEMI) which was successfully thrombolysed with intravenous (IV) tenectaplase. She underwent routine coronary angiography the next day which showed a single coronary artery originating from the right coronary cusp. LMCA was long and showed mild disease. Left anterior descending (LAD) artery had ostial moderate stenosis. Left circumflex (LCX) had ostial and mid vessel 90% stenosis. Right coronary artery (RCA) had a proximal 60% and mid vessel 90% stenosis. A computerized tomography coronary angiogram (CTCA) confirmed a benign course of the LMCA over the right ventricular outflow tract (RVOT). The patient was successfully treated with multivessel PCI and stent implantation.
Conclusion: Our case represents a very rare case of a single coronary artery with an acute inferior STEMI due to atherothrombosis which was successfully treated with thrombolysis and subsequent multivessel PCI. PCI of a SCA is a difficult and technically challenging procedure that requires operator skill and expertise. PCI of an anomalous LMCA originating from right coronary cusp is considered a reasonably safe and feasible option in those with a benign course of the LMCA.

Key words: single coronary artery, Anomalous LMCA, percutaneous intervention, case report

Introduction

A single coronary artery (SCA) is a rare congenital anomaly where an isolated coronary artery originates from the aortic root through a single ostium and is responsible for the blood supply of the entire myocardium. The incidence of anomalous LMCA arising from right coronary sinus is reported as 0.024% in angiographic series [1,2]. The clinical manifestations and the pathophysiological mechanisms are also highly variable irrespective of its course [3]. Though coronary artery bypass grafting has been recognized as the conventional treatment for atherosclerosis of aberrant LMCA, PCI is considered a reasonable and safe option when the LMCA follows a benign course and PCI is performed by experienced operators.

We report a patient with a single coronary artery originating from the right coronary sinus and atherosclerotic obstruction, who underwent multivessel PCI successfully following thrombolysis for acute STEMI.

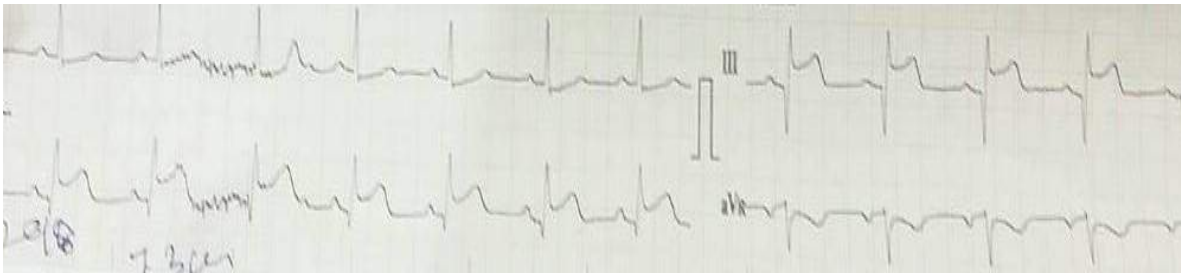
Case Presentation

A 52-year-old female with a history of hypertension and dyslipidemia presented to a local hospital with acute onset ischemic chest pain of 5 hours duration. Her BMI was 23 Kg /m^2. Her pulse rate was 84 bpm. Blood pressure was 120/80 mmHg. Lung bases were free of crepitations.

Her initial ECG showed ST segment elevation in inferior leads LII, LIII and AVF [Figure 1]. Considering the transport delay for primary PCI she was thrombolysed with tenecteplase 35 mg intravenously. Post thrombolysis ECG showed 50% resolution of ST segment elevation in the inferior leads. She was transferred to our tertiary care PCI center for routine coronary angiogram. Her 2D echocardiogram showed inferior wall hypokinesia and EF was 50%. Hemoglobin and creatinine levels were normal.

Thereafter, Coronary angiogram was done.

Figure 1: Patients ECG showing an acute Inferior STEMI



Coronary angiogram [Figure 2] showed a single coronary artery originating from the right coronary cusp. LMCA was long and showed mild disease. LAD showed ostial moderate stenosis. Left circumflex (LCX) showed ostial 90% and mid vessel 95% stenosis. RCA showed a proximal 60% and mid vessel 90% stenosis.

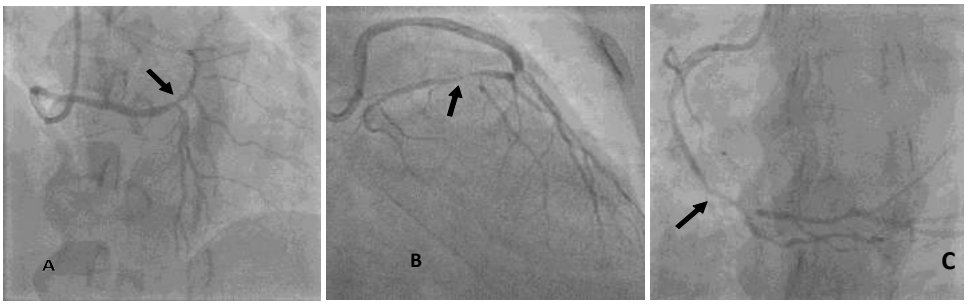


Figure 2: Invasive coronary angiogram showing the anomalous LMCA from RCA cusp and stenosis in LCX and RCA. A- LAO 33 CRA 23 view showing ostial LCX 90% stenosis, B- RAO 26 CRA 27 view showing Mid LCX 95% stenosis, C- LAO 45% showing RCA -80% stenosis

A computerized tomography coronary angiogram (CTCA) confirmed a single coronary artery arising from the right coronary cusp [Figure 3A]. A benign course of LMCA over right ventricular outflow tract (RVOT) was visualized [Figure 3B]. Therefore, PCI and stent implantation was considered as a treatment option.

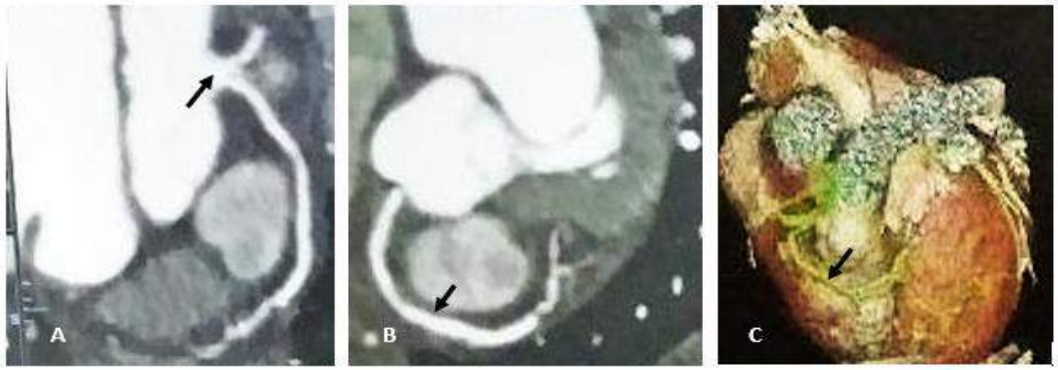


Figure 3: CTCA confirming SCA origin from right cusp [A] and course of LMCA over RVOT [B, C]

The patient was unwilling to undergo CABG and since the LMCA showed a benign course over RVOT we offered PCI as an option to her. With her informed consent we proceeded to PCI.

Right radial access was obtained and 7F sheath was inserted. LMCA was cannulated with a 6F Judkins Right (JR) 3.5 guide catheter. LMCA to LCX was wired with a Runthrough (Terumo, Japan) 0.014" guide wire. LCX lesion was predilated with a 2x 20 mm PTCA balloon. Mid LCX was stented with a Xience Prime 2.5x 23 mm (Abbott, USA) drug eluting stent (DES) at 16 atmospheric pressures (ATM) to a final diameter of 2.7 mm. LMCA to LCX was stented with a Xience Prime 2.75x 23 mm (Abbott, USA) DES at 18 ATM to a final diameter 3.04 mm overlapping the distal stent. Overlapped segment was post dilated with the proximal stent balloon.

Post procedure angiogram showed TIMI 3 flow in LMCA and branches **[Fig. 5].**

RCA was cannulated with the same 6F JR 3.5 guide catheter with rotational manipulation and wired with the same guide wire. Mid RCA lesion was predilated with a 2 x 15 mm PTCA balloon and stented with a Xience Prime 2.75x 38 mm (Abbott, USA) DES at 18 ATM to a final diameter 3.04 mm. Proximal RCA stented with a Xience Prime 3x 23 mm (Abbott, USA) DES at 18 ATM to a final diameter 3.5 mm overlapping the distal stent [Fig 7]. Post procedure angiogram showed TIMI 3 flow in RCA and branches [Fig. 5]. Patient was discharged after three days of inward care with aspirin, clopidogrel, atorvastatin, bisoprolol and losartan.

Case Report

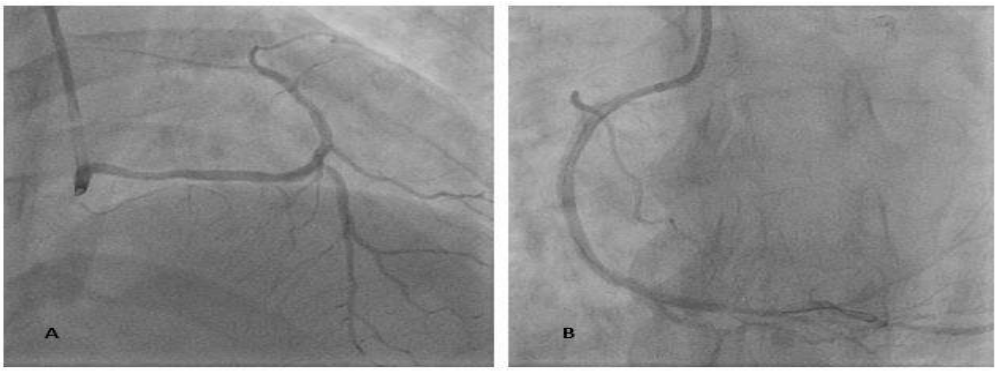


Figure 6: Post procedure angiogram showing A- revascularized LMCA and LCX with two overlapping DES and B- RCA with two overlapping DES.

Discussion

SCA is the rarest form of anomalous aortic origin of a coronary artery (AAOCA) characterized by both left and right coronaries arising from a single aortic coronary ostium. AAOCA can be classified in several ways.

The classification of SCA by Lipton et el. is based on the site of origin and the proximal course of the SCA in relation to greater arteries [4].

Four courses of anomalous LMCA are identified in respect to its anatomic relationship to the aorta and pulmonary trunk namely a). inter-arterial or intramural b). retro aortic c). pre-pulmonic and d). septal or sub-pulmonic [5].

In our patient both coronaries originated from the right coronary sinus from a single origin and divided into right and left coronary arteries and the anomalous LMCA followed an anterior pre-pulmonic course classifying it as R II A type (Table 1).

Ostial Location	**R**	**Right sinus of Valsalva**
	L	Left sinus of Valsalva
Anatomical Distribution	I	Single coronary artery with normal right or left course (RC or LC)
	II	After leaving the right or left sinus the single coronary artery crosses at the base of the heart as a large transverse trunk in order to supply the contra lateral coronary artery
	III	SCA origin from the right sinus with LAD and LCX arising from separate coronary artery trunks instead of a single trunk immediately at the exit
Course of the transverse branch	A	Anterior to great arteries and right ventricle
	B	Between aorta and pulmonary artery
	P	Posterior to large vessels
	S	Septal type (Above the interventricular septum)
	C	Combined type

Table 1: Classification of SCA based on anatomical distribution of coronaries

Most adults with SCA are usually asymptomatic but acute coronary syndrome [ACS] has been reported in adult symptomatic patients with SCA. Other presentations include syncope and sudden cardiac death [6,8].

CTCA is recommended as the primary imaging tool in evaluating anomalous coronaries and was performed to delineate the coronary anatomy and for risk stratification. It is considered superior to ICA and cardiac magnetic resonant imaging (CMRI) to delineate the course and to assess high-risk anatomical features such as coronary orifice configuration and proximal angulation. ICA remains the gold standard for identifying atherosclerotic obstruction. CTCA of our patient revealed a benign pre-pulmonic course of the LMCA without any high-risk features. Therefore, as our patient needed revascularization for ACS we offered PCI since the patient was not willing for CABG and the anatomy was favorable for stenting. PCI to anomalous LMCA is technically challenging due to its anomalous origin, long aberrant course and requires operator experience for successful engagement and to minimize complications such as ischemia and dissection of the single coronary artery [9,11]. Topazet al. has reported five patients with coronary anomalies who underwent PCI for atherosclerotic coronary obstruction [12]. We managed to complete the stenting procedure successfully in our patient using a JR guide catheter maintaining the direction of tip towards LMCA or RCA without much difficulty.

Inter-arterial course is the primary limitation for PCI where surgical correction is recommended as it is associated with sudden cardiac death due to the acute angle of the ostium and compression between the commissure of right and left coronary cusps during its aberrant intramural course [13,14]. Guidelines recommend surgical correction for both asymptomatic and symptomatic patients with this type of anomaly. Unroofing of the intramural segment and neo-ostial formation is the commonly performed surgical correction. Additional coronary bypass grafting is indicated if stenosis is also present as the normal coronaries may cause competitive flow steal.

Given the rarity of its occurrence no specific guidelines are available on the management of anomalous LMCA with coronary stenosis. Moreover, despite favorable immediate results limited data is available on the long-term outcome of stent placement for such patients. Our patient had a favorable immediate result and is asymptomatic up to two years follow up at present.

Conclusion

SCA is an extremely rare congenital anomaly and ACS has been reported as a presentation during adult life. CTCA is useful for accurate delineation of the coronary anatomy and risk stratification. PCI and stenting can be a safe and feasible option to revascularize SCA and anomalous LMCA with a benign course when indicated in ACS by appropriately experienced operators.

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Case Report

A Case of Recurrent Unstable Angina with LMCA In-stent Restenosis (ISR)

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Abstract

We report a case of a young male who presented with recurrent angina and was found to have severe LMCA in- stent restenosis which was treated with a cutting balloon and a drug eluting balloon successfully.

Key words: Unstable angina, LMCA, in-stent restenosis, ISR, cutting balloon

Introduction

In-stent restenosis (ISR) is a challenging complication of both bare metal and drug eluting stents.

However, in this regard, the possibility of ISR is less in drug eluting stents when compared to the bare metal stents. There are several mechanisms which can result in ISR, such as mechanical, biological and mixed.

The treatment modality is decided according to the mechanism which resulted in the ISR.

Case report

Our patient, a 43-year-old postman, married, with 3 children had a past history of type 2 diabetes mellitus and an inferior STEMI 6 months previously. Subsequently, the patient was admitted for a routine coronary angiogram and was found to have triple vessel disease with left main involvement and CABG option was offered. But patient refused CABG and underwent PCI to LMCA to LAD. After that he had regular clinic follow ups at the local hospital.

One year after the PCI, he presented with NYHA class 3 to 4 dyspnea and a check coronary angiogram was planned. At that time his BMI was 28. His blood pressure was 120/70 mmHg and pulse rate was 90 beats per minute. Blood investigations including FBC, serum creatinine, serum electrolytes and liver function tests were all normal.

Check coronary angiogram was performed from right radial access with 5 FG TIG catheter and this revealed a severe in stent restenosis of LMCA stent with proximal 99% lesion and a new LAD lesion beyond the stent.

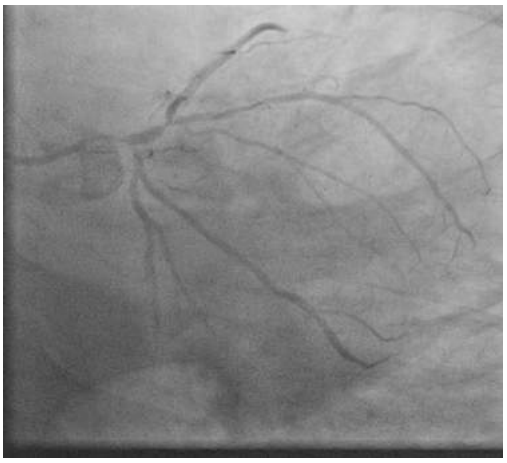

Figure 1: AP caudal view.

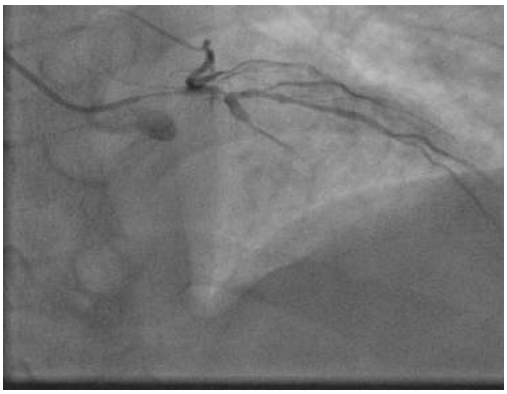

Figure 2. AP cranial view

As the patient was severely symptomatic and not willing for CABG we planned for PCI. LMCA was engaged with 7 FG EBU guide catheter and both LAD and LCx wired with Sion blue and Sion black 0.014”GW guide wires, respectively. LAD was pre dilated with EMERGE 2×15 mm NBP at 12 atm. LMCA previous stent was found to be re stenosed and segment POBA was done with EMERGE 3.25×8 mm HBP at 20 atm followed by FLEXITOME 3.75×10 mm cutting balloon at 6 atm.

Case Report

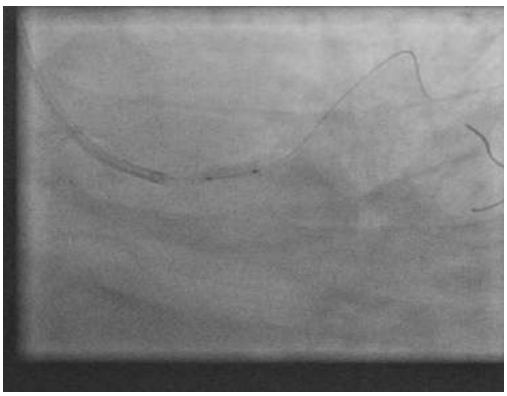

Figure 3: LMCA POBA with HPB

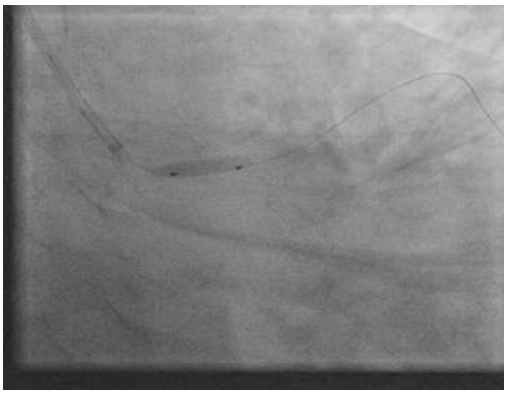

Figure 4: LMCA POBA with CUTTING BALLOON

LCx ostium to proximal was pre dilated with EMERGE 2×15 mm NPB at 6 atm. Proximal LAD was stented overlapping previous LMCA stent with Coroflex 2×15 mm Drug Eluting Stent (DES) deployed at 10 atm. Stent was post dilated with EMERGE 2.75×8 mm HBP at 12 to 20 atm. Entire LMCA stent was post dilated with INPACT FALCON 320 mm Drug Eluting Balloon (DEB) at 7 atm for 2 minutes. Finally, LCx was re crossed and ostium to proximal pre dilated with EMERGE 2×15 mm NPB at 6 atm. Final results showed excellent TIMI 3 flow in LAD and its branches.

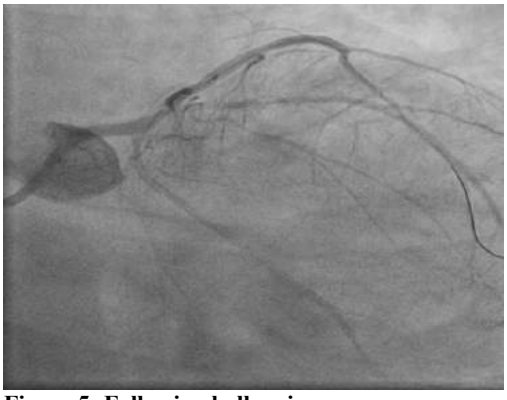

Figure 5: Following ballooning

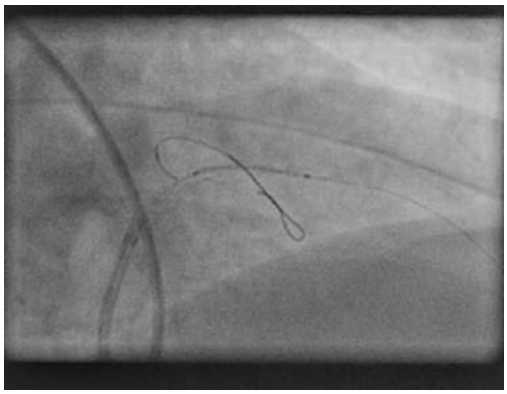

Figure 6: LAD stenting

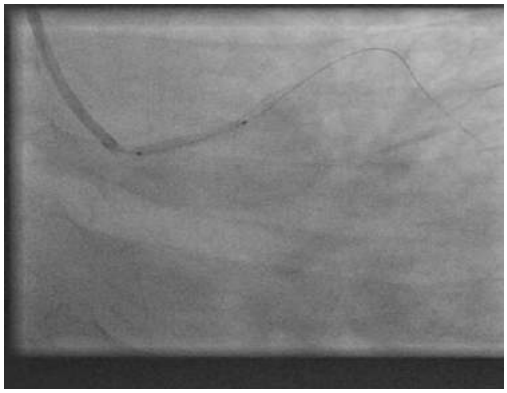

Figure 7: DEB application

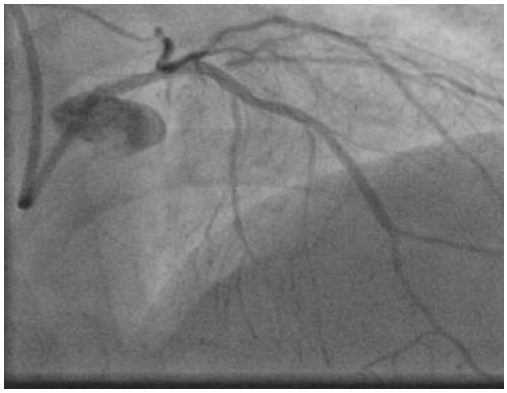

Figure 8: Final angiogram

Discussion

In-stent restenosis following LMCA stenting is a known complication. With advancement in technology in-stent restenosis is significantly reduced, but still occurs in 10 % to 20% cases [(1)]. In-stent restenosis is the gradual narrowing of a stented segment within three months to one year duration. Usually, it presents as recurrent unstable angina as in our patient and sometimes presents with an acute myocardial infarction also.

There are several mechanisms of ISR. After the stent deployment due to micro tears that occur in the vessel intima and media, complex immune reaction occurs which leads to smooth muscle proliferation and protrusion into the stent. [2,3] This process reduces the minimum luminal diameter over time resulting in-stent restenosis. Stent malapposition, diabetes mellitus, hypertension and dyslipidemia are contributory factors for ISR.

There are several treatment modalities for treating ISR depending on the mechanism and the extent of the lesions. PTCA and stenting, use of cutting balloon, use of DEB, rotational atherectomy and CABG are common treatment options at present. Use of drug eluting balloons have a significant survival benefit compared to normal balloons which was proved by several randomized controlled trials such as PACCOCATH ISR 1, PACCOCATH ISR 11, REPCAD 2 and ISR DESIRE 3. All these studies showed superiority over POBA and non-inferiority over PTCA and stenting.

DEBs are coated with paclitaxel and sirolimus which are anti-proliferative agents, which prevents neointimal hyperplasia. [4] There are several advantages of DEB over re stenting. [5] One is that with the balloon there is an even drug distribution and does not leave a metal grid which causes further inflammation leading to the thrombosis. Secondly it does not change vessel anatomy and ensures the chance of future treatment if necessary. Lastly it is very suitable for patients with a high risk of bleeding tendency.

For tight LMCA lesions plaque modification with an atherectomy device is needed. Therefore, we used a cutting balloon in our case. Cutting balloon is a device that consists of 3 longitudinal sharp micro blades attached to the balloon which cuts the calcium plaques. [6]

Conclusion

In our patient we didn't use PTCA and stenting strategy for treatment of ISR as there is a high risk of restenosis. Use of cutting balloon and DEB was very useful in achieving excellent results in this young patient.

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Updates

Updates from Recent Publications.

From the editorial desk

Vulnerable plaques and patients: state-of-the-art

Mariusz Tomaniak
European Heart Journal (2020) 41, 2997–3004

Despite advanced understanding of the biology of atherosclerosis, coronary heart disease remains the leading cause of death worldwide. Progress has been challenging as half of the individuals who suffer sudden cardiac death do not experience premonitory symptoms. Furthermore, it is well-recognized that a plaque that does not cause a haemodynamically significant stenosis can trigger a sudden cardiac event. Yet the majority of ruptured or eroded plaques remain clinically silent. In the past 30 years since the term 'vulnerable plaque' was introduced, there have been major advances in the understanding of plaque pathogenesis and pathophysiology, shifting from pursuing features of 'vulnerability' of a specific lesion to the more comprehensive goal of identifying patient 'cardiovascular vulnerability'. It has been also recognized that aside a thin-capped, lipid-rich plaque associated with plaque rupture, acute coronary syndromes (ACS) are also caused by plaque erosion underlying between 25% and 60% of ACS. While there have been advances in preventive strategies and in pharmacotherapy, (with improved agents to reduce cholesterol, thrombosis, and inflammation), events continue to occur in patients receiving optimal medical treatment. Although at present the positive predictive value of imaging precursors of the culprit plaques remains too low for clinical relevance, improving coronary plaque imaging may be instrumental in guiding pharmacotherapy intensity and could facilitate optimal allocation of novel, more aggressive, and costly treatment strategies. Recent technical and diagnostic advances justify continuation of interdisciplinary research efforts to improve cardiovascular prognosis by both systemic and 'local' diagnostics and therapies.

Management of non-culprit coronary plaques in patients with acute coronary syndrome

Rocco A. Montone
European Heart Journal (2020) 41, 3579–3586

Based on current evidence, a strategy of Staged PCI of obstructive non -culprit lesions, when technically feasible, should represent the gold standard for the management of STEMI patients with multivessel CAD. Evaluation of intermediate non-culprit lesions represents an area of uncertainty, as best technique and optimal timing for functional assessment are not still clearly defined. It is conceivable that in most cases a delay of 5—7 days may be sufficient for a reliable assessment using both FFR and iFR. However, in case of larger MI (i.e. culprit lesion in the proximal left anterior descending coronary artery), a longer delay might be considered. At the same time, the role of functional assessment in improving prognosis of ACS patients is limited, as pressure-wire indexes are less accurate in the identification of patients in whom deferral is safe as compared to what is the case in stable patients. Intracoronary imaging may help identifying untreated non-culprit lesions containing vulnerable plaques, but the positive predictive value of imaging-derived vulnerable features for the occurrence of future cardiovascular events is low. Thus, based on current available evidences, its use cannot be routinely recommended in clinical practice, The PREVENT study is currently ongoing and will evaluate whether preventive PCI of functionally nonsignificant non-culprit stenosis (FFR > 0.80) with vulnerable plaque characteristics plus optimal medical therapy may improve clinical outcome compared with optimal medical therapy alone. On the other hand, it should be considered that obstructive non-culprit stenoses harbor most of the vulnerable plaques, thus the benefit deriving from treatment of these lesions in the COMPLETE trial might be related to the sealing of vulnerable plaques along with the reduction of residual ischaemia.

Whilst there is no evidence supporting a role of a preventive PCI for the treatment of non-obstructive vulnerable plaques, several studies performed with serial intracoronary imaging demonstrated an important role for lipid-lowering therapies to stabilize these lesions. In particular, in patients with unstable angina atorvastatin 20 mg/day provided a greater increase in fibrous cap thickness in coronary plaques compared with 5 mg/day of atorvastatin, along with a decrease in serum atherogenic lipoproteins and inflammatory biomarkers (ie. C-reactive protein, matrix metalloproteinases-9).

Moreover, an analysis of the OCTAVIA study demonstrated that in STEMI patients undergoing primary PCI and OCT imaging of the culprit vessel, most of the untreated Thin Cap Fibro Atheroma (TCFA) along the infarct-related artery exhibited a more stable phenotype after 9months of statin therapy when compared with baseline OCT assessment, with more TCFA converted into non-TCFA lesions particularly when higher doses were used. Accordingly, an OCT study by Xie et al. demonstrated that three-quarters of coronary plaques did not progress over time with contemporary medical treatment and this stabilizing effect of statin therapy was particularly evident in ACS patients.

In addition, the use of ticagrelor or prasugrel compared with clopidogrel may reduce the risk of recurrence of ACS arising from untreated non-culprit lesions as well as prolonged dual antiplatelet aggregation, and this may be particularly true in patients with vulnerable plaques. Finally, patients with local (as detected by OCT defined macrophage infiltration) or systemic signs of inflammatory activation may probably have a benefit targeting specific cytokine path ways, such as the interleukin (IL)-18 pathway by administration of canakinumab.

Finally, it is worth mentioning that in spite of the new light shed by several recent studies on the management of non-culprit lesions in STEMI patients, several knowledge gaps, still remain that should be addressed in appropriate controlled randomized studies.

Return to sports after COVID-19 infection Do we have to worry about myocarditis?

Philipp Schellhorn et al.
European Heart Journal (2020) 41, 4382-4384

Updates

Are athletes at risk for COVID-19?

Despite the fact that athletes do not belong to the risk group for severe COVID-19, numerous individuals and occasionally entire sports teams have been affected by COVID-19 infections. In this context, the question arises as to what extent a SARSCoV-2 infection with or without symptoms can affect eligibility for sport, particularly the point of return to training or competition.

Keep in mind that myocarditis is one of the leading causes of sport associated sudden cardiac death in the group of athletes under 35 years of age. The clinical presentation of myocarditis in general shows a wide and heterogenic spectrum of symptoms. Athletes frequently present with non-specific symptoms such as fatigue, malaise, reduced performance, muscle soreness, or increased resting heart rate, which can often be misinterpreted in the context of other differential diagnoses (e.g., training-related exhaustion/ overtraining, depression, or psychosomatic disorders). Thus, athletes are often not subjected to a COVID-19 test (e.g., nasopharyngeal swab), so that the diagnosis of a COVID-19 infection and a potential COVID-19- associated myocardial involvement or myocarditis cannot be made. In this case, further diagnostic or therapeutic measures can be delayed or even completely neglected.

Myocarditis associated with COVID-19 in athletes

In the reports of severe COVID-19 cases, data on cardiac examinations are often missing. However, a report by Inciardi et al., describing the case of an otherwise healthy 53-year-old white woman with cardiac involvement, lists numerous diagnostic anomalies. Remarkably, cardiac pathology developed 1 week after recovering from influenza like symptoms. Moreover, there are reported cases of sudden cardiac death in non-hospitalized COVID-19-positive individuals with only mild symptoms.

Descriptions of mild COVID-19-associated myocarditis are very rare or even non-existent.

Nevertheless, in the assessment of eligibility for participation in sport for athletes in recovery from COVID-19, these might be very helpful for further risk stratification and for guiding reintegration to training and competition.

Eligibility for sport in situations of possible myocardial involvement:

The question of how to deal with athletes following COVID-19 and how to reintegrate them safely into sports is difficult to answer at the moment. A helpful orientation for guiding clinical processes are the recommendations proposed by the European Society of Cardiology, the American Heart Association/American College of Cardiology, or the 36th Bethesda Conference (2005).

From other virus infections, it is known that viral replication can be enhanced during vigorous activity, resulting in greater structural damage of the heart tissue. Thus, in the case of an athlete diagnosed with COVID-19, but without any symptoms, we would also recommend refraining from intensive or competitive-like exercise for at least 2 weeks. In the absence of symptoms and abnormalities in the resting ECG at the end of this time period, return to sport can be recommended without restriction.

Re-purposed antiviral drugs without a purpose in COVID-19: a valuable lesson for clinicians

Giovanna Liuzzo and Carlo Patrono
European Heart Journal (2021) 42, 882-883

Key Points

- The World Health Organization (WHO) Solidarity Trial is an adaptive, randomized, open-label trial designed to help determine whether any of four repurposed antiviral drugs (Remdesivir, Hydroxychloroquine, Lopinavir, and Interferon-β1a) could have an effect on in-hospital mortality of COVID-19 patients.

- In 405 hospitals in 30 countries, 11 266 adult patients (81% younger than 70 years, and 62% male) were randomized equally between whichever study drugs were locally available and open control (up to five options: four active and local standard-of-care).

  The intent-to-treat primary analyses were of in-hospital mortality in the four pairwise comparisons of each drug-treated group vs. its control (concurrently allocated the same management without that drug, despite availability). Secondary endpoints were initiation of ventilation and hospitalization duration.

- Overall, 1253 deaths were reported (at median day 8, interquartile range 4-14). Kaplan–Meier 28-day mortality was 11.8% (39% if already ventilated at randomization, 9.5% otherwise). Log-rank death rate ratios (RRs) [with 95% confidence intervals (CIs) and numbers dead/randomized, each drug vs. its control] were stratified for age and ventilation at entry: Remdesivir, RR = 0.95 (0.81–1.11, $P = 0.50$; 301/2743 active vs. 303/2708 control); Hydroxychloroquine, RR = 1.19 (0.89-1.59, $P = 0.23$; 104/947 vs. 84/906); Lopinavir, RR = 1.00 (0.79–1.25, $P = 0.97$; 148/1399 vs. 146/1372); Interferon, RR = 1.16 (0.96–1.39, $P = 0.11$; 243/2050 vs. 216/2050).

- No study drug definitely reduced mortality (in unventilated patients or any other subgroup of entry characteristics), initiation of ventilation or hospitalization duration.

Controversies in revascularization for stable coronary artery disease

Alexandra N Nowbar
https://doi.org/10.7861/clinmed.2020-0922
Clin Med March 2021

Summary

Urgent revascularization remains a cornerstone of the management of acute myocardial infarction, because of the proven survival benefits. However, for patients with stable coronary artery disease or stable angina, it should no longer be assumed that a mechanical solution to 'fix' a narrowed artery is obviously beneficial. In angina, every licensed anti-anginal (of which there are many) has been proven to reduce angina by placebo-controlled trial.

Placebo-controlled trials of PCI for angina are only now evolving.

It is biologically plausible that PCI alleviates exertional angina, but this was not demonstrated in the only placebo-controlled trial completed so far and this remains an area of active study. Likewise, it has been considered biologically plausible that revascularization reduces mortality, but the ISCHEMIA trial and a meta-analysis of all such trials, shows no such effect.

What would we do with a patient today with stable angina despite anti-anginal medication? We believe PCI may relieve their angina but have not been able to demonstrate this so far. Therefore, we would enroll the patient into ORBITA-2. This is the rational approach in modern medicine when there is a treatment that has good theoretical grounds for relieving symptoms, but which has not yet been proven to do so, and for which a clinical trial exists.

In the modern era, the absolute priority in chronic stable coronary artery disease management is cardiovascular event prevention with medication and lifestyle measures. This is the responsibility of all physicians, and the prevention of cardiovascular disease remains a key goal of the NHS Long Term Plan.

COVID-19 is, in the end, an endothelial disease

Peter Libby
European Heart Journal (2020) 41, 3038–3044

The vascular endothelium provides the crucial interface between the blood compartment and tissues, and displays a series of remarkable properties that normally maintain homeostasis. This tightly regulated palette of functions includes control of haemostasis, fibrinolysis, vasomotion, inflammation, oxidative stress, vascular permeability, and structure. While these functions participate in the moment-to-moment regulation of the circulation and coordinate many host defense mechanisms, they can also contribute to disease when their usually homeostatic and defensive functions over-reach and turn against the host.

SARS-CoV-2, the aetiological agent of COVID-19, causes the current pandemic.

It produces protean manifestations ranging from head to toe, wreaking seemingly indiscriminate havoc on multiple organ systems including the lungs, heart, brain, kidney, and vasculature.

This essay explores the hypothesis that COVID-19, particularly in the later complicated stages, represents an endothelial disease. Cytokines, protein pro-inflammatory mediators, serve as key danger signals that shift endothelial functions from the homeostatic into the defensive mode. The endgame of COVID-19 usually involves a cytokine storm, a phlogistic phenomenon fed by well-understood positive feedback loops that govern cytokine production and overwhelm counter-regulatory mechanisms. The concept of COVID-19 as an endothelial disease provides a unifying pathophysiological picture of this raging infection, and also provides a framework for a rational treatment strategy at a time when we possess an indeed modest evidence base to guide our therapeutic attempts to confront this novel pandemic.

COVID-19 kills at home: the close relationship between the epidemic and the increase of out-of-hospital cardiac arrests

Enrico Baldi
European Heart Journal (2020) 41, 3045-3054

An increase in out-of-hospital cardiac arrest (OHCA) incidence has been reported in the very early phase of the COVID-19 epidemic, but a clear demonstration of a correlation between the increased incidence of OHCA and COVID-19 is missing so far. We aimed to verify whether there is an association between the OHCA difference compared with 2019 and the COVID-19 epidemic curve.

Conclusion: The increase in OHCAs in 2020 is significantly correlated to the COVID-19 pandemic and is coupled with a reduction in short-term outcome. Government and local health authorities should seriously consider our results when planning healthcare strategies to face the epidemic, especially considering the expected recurrent outbreaks.

Updates

Pulmonary embolism in COVID-19 patients: a French multicenter cohort study

Charles Fauvel
European Heart Journal (2020) 41 :3058-3068.

While pulmonary embolism (PE) appears to be a major issue in COVID-19, data remain sparse. We aimed to describe the risk factors and baseline characteristics of patients with PE in a cohort of COVID-19 patients.

Conclusion: PE risk factors in the COVID-19 context do not include traditional thrombo-embolic risk factors but rather independent clinical and biological findings at admission, including a major contribution to inflammation.

Myocardial injury after non-cardiac surgery: diagnosis and management

P J Devereaux
European Heart Journal (2020) 41 :3083-3091.

Myocardial injury after non-cardiac surgery (MINS) is due to myocardial ischaemia (i.e. supply-demand mismatch or thrombus) and is associated with an increased risk of mortality and major vascular complications at 30 days and up to 2 years after non-cardiac surgery.

Patients undergo non-cardiac surgery to improve or prolong their quality or duration of life. In contrast to these potential benefits, noncardiac surgery is associated with haemodynamic compromise, hypercoagulability, inflammation, sympathetic stimulation, and bleed, all of which can pre-dispose patients to ischaemic injuries.

Large studies have also established troponin thresholds for MINS based on iterative processes that explored potential troponin thresholds after non-cardiac surgery using multivariable analyses to determine what thresholds were independently associated with 30day mortality. These analyses identified the following peri-operative troponin thresholds: (i) a non-high-sensitivity troponin T >30 ng/L and (ii) a high-sensitivity troponin T (hsTnT) of 20 to <65 ng/L with an absolute change of at least 5 ng/L—this change threshold is independently associated with 30-day mortality [hazard ratio (HR) 4.69; 95% confidence interval (Cl) 3.52-6.25]—or an hsTnT level >65 ng/ L.

Although no study has established optimal troponin I thresholds for MINS, there is no preference for troponin T over I. Until research establishes MINS troponin I thresholds, physicians should define an elevation as any value above the 99th percentile upper reference limit for each specific troponin I assay.

How should physicians manage myocardial injury: after non-cardiac surgery?

Medical management:
Aspirin, statin, beta-blocker, and angiotensin-converting enzyme inhibitor

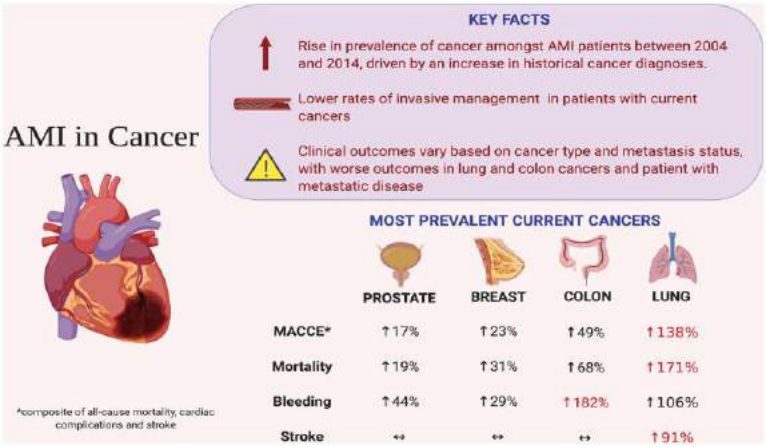
Peri-operative, risk-adjusted, observational data suggest that patients with MINS benefit from aspirin and statin therapy. In a sub study of 415 patients who had a peri-operative myocardial infarction in the POISE trial, a multivariable analysis demonstrated a lower risk of death at 30 days if patients received aspirin (adjusted HR 0.54; 95% C\ 0.24-0.99) and a statin (adjusted HR 0.26; 95% C1 0.1 3-0.54)

The publication of the MANAGE trial results, which highlighted risk of major thrombotic complications in patients with MINS, also supports the use of secondary prophylactic interventions.

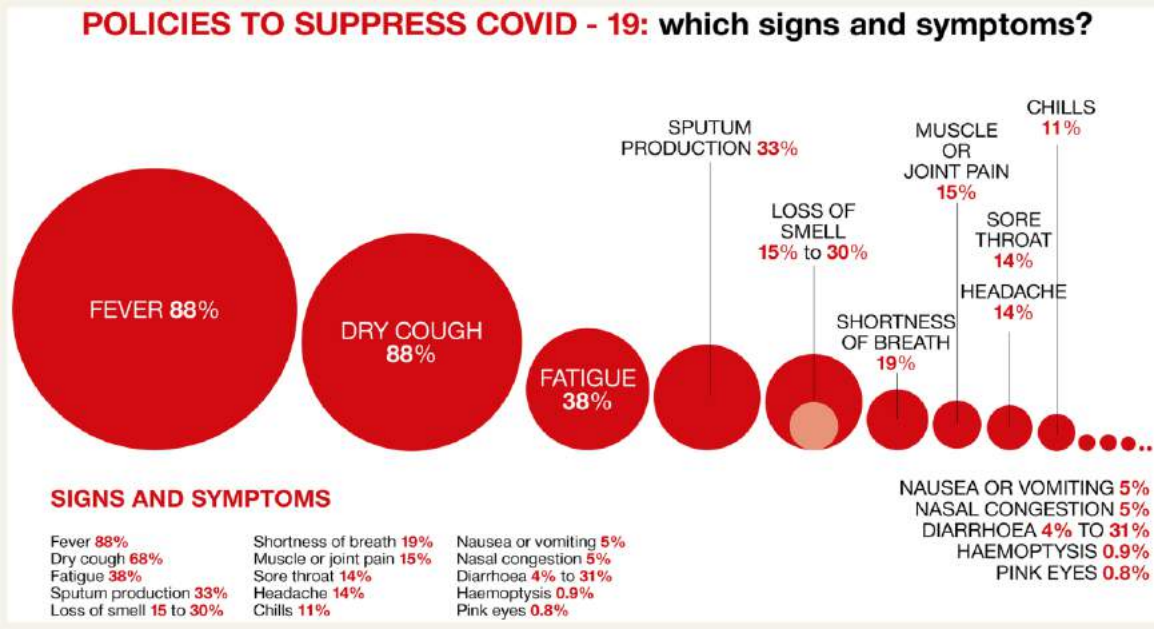
The MANAGE trial, conducted at 84 centres in 19 countries, randomized 17554 patients who had MINS to dabigatran 110mg twice daily (n. = 877) The results of COMPASS also support the results of MANAGE. COMPASS randomized 27 395 patients with stable cardiovascular disease in the non-operative setting, and demonstrated that rivaroxaban and aspirin compared to aspirin alone lowered the risk of a composite of cardiovascular death, stroke, and myocardial infarction (HR 0.76; 95% Cl 0.66—0.86) and also decreased the risk of venous thromboembolism, acute limb ischaemia, and amputation.

COMPASS and MANAGE provide evidence of the benefits of a very low-dose antithrombotic (i.e. rivaroxaban 2.5 mg twice daily) and an intermediate-dose anticoagulant (i.e. dabigatran 110 mg twice daily) in patients with atherosclerotic disease who are at risk of major vascular complications.

Large observational studies demonstrate that only 8% of patients who have MINS and 21% of patients who have a peri-operative myocardial infarction undergo coronary angiography. This low utilization of coronary angiography highlights that physicians are not yet convinced there is a net benefit to an invasive strategy in patients with MINS and identifies the need for a large randomized trial to inform the potential benefits and risks. Based on current knowledge, it seems reasonable to restrict cardiac catheterization referral to patients with MINS who demonstrate recurrent instability (e.g. cardiac ischaemia, heart failure).



Management and outcomes of myocardial infarction patients with cancer. Figure taken from *Eur Heart J* 2020;**41**:2183–2193.



Author guidelines

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The manuscript should contain an **abstract**, limited to 250 words, with sections on *introduction, methods, results, discussion and conclusions and keywords* (format may vary according to the type of manuscript).

The body of the manuscript should include a) introduction, b) results and findings or case report, c) discussion d) conclusion e) references. Where applicable please include a) acknowledgements b) conflicts of interest statement, c) consent d) ethical approval.

In regard to references, please utilize an accepted referencing software and avoid manual input. The style to be utilized is "numbered". Use a (..) for the reference within the text with a relevant number. Example of reference is as follows.

Bitigen, A., et al., *Mitral regurgitation and ventricular septal defect as a complication of penetrating cardiac trauma: a case report.* Turkish Thoracic Cardiovascular Surgery Magazine, 2010. 18(1): p. 058-060.

Additionally, patients suffering from anxious and depressive disorders are more likely to have increased activity of sympathetic nervous system (23) and subsequently catecholamine overload (23, 25).

The manuscript should be typed in

- Font: Times New Roman.Size12
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- with double line spacing
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File formats which are accepted for submission include Microsoft word (DOC, DOCX).

In regard to preparing figures, please follow the formatting instructions below.

- Figures should be provided embedded *in the main manuscript file in the correct position.*
- Figures should **ALSO** be provided as separate files (not embedded in the main manuscript file).
- Each figure of a manuscript should be submitted with acceptable quality.
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- Multi-panel figures (those with parts a, b, c, d etc.) should be submitted as a single composite file that contains all parts of the figure.

Author guidelines

- Figures should be numbered in the order they are first mentioned in the text, and uploaded in this order along with an appropriate title.
- Figure titles (max 20 words) and legends (max 200 words) should be provided in the main manuscript, and also in the graphic file.
- Each figure should be closely cropped to minimize the amount of white space surrounding the illustration.
- Individual figure files should be within 5 MB if *possible*. If a suitable format is chosen, this file size is adequate for extremely high-quality figures.
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- Tables should be numbered and cited in the text in sequence using Arabic numerals (i.e. Table 1, Table 2 etc.).
- Tables less than one A4 or letter page in length can be placed in the appropriate location within the manuscript.
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- Table titles (max 20 words) should be included above the table, and legends (max 200 words) should be included underneath the table.
- Tables should not be embedded as figures or spreadsheet files, but should be formatted using 'Table object' function in your word processing program.
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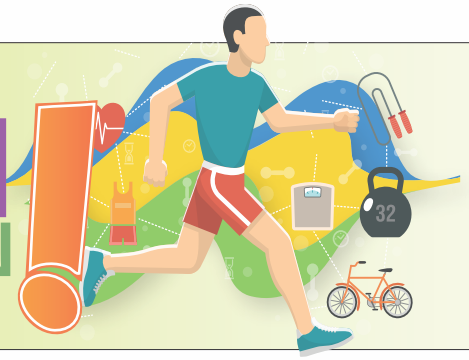

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