Editorial Board

Editor
Stigi Joseph
Little Flower Hospital & Research Centre, Angamaly.

Executive editor
Jonhson Francis, Baby Memorial Hospital, Kozhikode
(Founder and emeritus editor Indian Pacing & Electrophysiology Journal)

Associate editors
Bhim Shankar: VPS Lakeshore Hospital, Kochi
Jo Joseph : Lisie Hospital, Ernakulam
Hisham Ahammed, Amrita Institute of Medical Sciences, Kochi

Past Editors
Rajesh G, Govt. Medical College, Kozhikode
(Founder Editor)
Sanjay G, SCTIMST – Thiruvananthapuram
Sajeev Kalathingathodika, Govt. Medical College, Kozhikode

Editorial Associates
Anand Kumar V, Kochi
Arun Gopi, Kozhikode
Cibi Issac, Kochi
Georgie Thomas, Abudhabi
Mukundan C, Thrissur
Rajasekhar Varma, Kochi
Sajan Ahamed, Thiruvalla

International Editorial Board

Chief International Editorial Advisor
Salim Yusuf. McMaster University. Hamilton Health Sciences (President, World Heart Federation)

International Editorial Advisors
Navin. C. Nanda. University of Alabama, Birmingham
(Editor-in Chief, Echocardiography)
Chandrashekkar, Minnesota University (Deputy Editor JACC Cardiovascular Imaging)
Boban Thomas, Navan, Ireland,
Syamkumar Divakarayanan, Hamilton,
Shahul Hameed, Doha, Qatar
Mithun Jacob Varghese, New York, USA

National Editorial Board
Sandeep Mishra, New Delhi
(Past Editor, Indian Heart Journal)
Ajay Kumar Sinha,(Past Associate Editor, Indian Heart Journal)
Imran Ahammed, Kolkata | Kiron Varghese, Bangaluru | Arati D Lalchandani, Kanpur | Jyotsna M Hyderabad | BP Sing, Patna | MG Pillai, Mumbai | BC Sreenivas, Bangaluru | George Joseph, Velloor | Anita Saxena, New Delhi
## Editorial Advisory Board

### Research
- P. P. Mohanan, Thrissur
- Cibu Mathew, Thrissur

### Preventive Cardiology
- Geevar Zachariah, Thrissur
- Shyam. N, Kollam

### Cardiac Epidemiology
- A. George Koshy, Tvm.
- Jayadeep C Menon, Angamaly

### Clinical Cardiology
- N. Sudhayakumar, Kottayam.
- Prabha Neeni Gupta, Tvm.

### Echocardiography
- Rajan Joseph Manjooran, Thiruvalla
- Balu Vaidyanathan, Kochi

### CT & MRI
- Ajithkumar V. K, Tvm.
- Rajeev. E, Perinthalmanna

### Coronary Imaging
- Rony Mathew, Kochi
- Asharaf, Pariyaram

### Hemodynamics
- Jagan Mohan Tharakkan, Palakkad
- Rajesh Muralideharan, Kozhikode

### Cardiovascular Therapeutics
- Rajalakshmi, Thiruvananthapuram
- Varghese George, Thiruvalla

### Heart Failure
- Jabir.A. Kochi.

### Cardiac Diabetology
- Jayagopal, Palakkad
- Rupeash George, Thrissur

### Geriatric Cardiology
- Venugopal. K, Thiruvalla
- Mathew Abraham, Thodupuzha

### Paediatric Cardiology
- Sivasankaran. S, Tvm.
- Krishnakumar. R, Kochi
- Edwin Francis, Kochi

### Electrophysiology
- K. U. Natarajan, Kochi
- Narayanan Namboothiri KK, Thiruvananthapuram (Editor in chief Indian Pacing & Electrophysiology Journal)

### Coronary Interventions
- Sunitha Viswanathan, Tvm.
- P. K. Ashokan, Kozhikode

### Peripheral Interventions
- M. N. Krishnan, Kozhikode
- Prathap Kumar, Kollam

### Valvular Interventions
- Rajiv. C, Kochi
- Shafeeq Mattummal
- Bijulal, Thiruvananthapuram

### Rheumatic Heart Disease
- Abdul Khader, Thrissur
- K. P. Balakrishnan, Kozhikode

### Cardiac Infections
- Raju George, Kochi
- Saji Subramanyam, Kochi

### Cardiomyopathy
- V. L. Jayaprakash, Kottayam
- Praveen. G. K, Tvm.

### Cardiac Inflammation
- Ramakrishna D, Kozhikode
- Deepa, Thiruvananthapuram

### Biostatistics
- Tiny Nair, Tvm.
- Haridasan, Kozhikode

### Cardiothoracic Surgery
- Nandakumar, Kozhikode
- Rafeeq. A. K, Angamaly

### Cardiac Anaesthesia
- Jacob Abraham, Kochi
- Deepu Antony

---

**Editorial Secretariat:**

**Stigi Joseph**

Little Flower Hospital and Research Centre,
Angamaly, Kochi. 683572.
Mob: +91 9446279889
Email: editorkhj@gmail.com
CSI Kerala Office Bearers

President
Markose K.P
Vice President
Sajeev CG
Secretary
Karunadas CP
Treasurer
Manikandan TV
Imm. Past President
Raju George
Imm. Past Secretary
Syam N

EC Members
Cibu Mathew
Mathew Abraham
Mathew Iype
Mathews Paul
Ramakrishna CD
Shifas Babu
Stigi Joseph
Sunil Shivdas
Table of Contents

- Non-Inflammatory Risk Markers for Cardiovascular Disease
  Ramakrishna C.D. MD,DM, Ish Kalra
  
- Does Serum Uric Acid Fare Similar To Serum High-sensitivity C-reactive protein as Vascular Inflammatory Marker Of Coronary Artery Disease In Young Asian Indians?
  Santanu Guha MD,DM, Imran Ahmed MD,DM
  
- An Interesting Case of Restrictive Cardiomyopathy
  Madhu sreedharn.MD,DM.
  
- Principles and practice of modern endovascular therapy in patients with acute ischemic stroke
  MuneerEesa MD Bijoy K. Menon MD
  
- Endovascular thrombectomy for acute ischemic stroke
  Sajan Narayanan MD. DM.
  
- Image Challenge
  Rajiv C. MD. DM, Hisham Ahammed MD. DM
  
- A simplified approach to wide complex tachycardia in emergency room
  Abhilash SP, MD,DM
  
- Management of arrhythmogenic inflammatory cardiomyopathy: a case based discussion
  
- ECG Challenge
  Bhim Shankar MD. DM.
  
- Spontaneous Coronary Artery Dissection- A Disease of Young Males?
  K J Rainanathul Misiriya MD, DN, Narayanapillai Jayaprassad MD, DM
  Anwar C Varghese MD, DM, K Jayaprakash MD, DM, Suresh Madhavan MD, DM
  V. Sudhakumary MD, DM, V.L Jayaprakash MD, DM, Raju George MD, DM

- Anomalous Origin of Left Coronary Artery from Pulmonary Artery presenting with Atrial Fibrillation and Angina
  CP Karunadas MD, DNB, DM, DNB, FESC, Cibu Mathew MD, DNB, DM, DNB
- An unusual cause of angina................................................................. 62
  Vijin Joseph V F MD, Jo Joseph MD.DM, Jimmy George MD. DM, 
  Jabir Abdullakutty MD. DM
  Jacob Joseph MD.DM, Rony Mathew MD. DM

- Non-Atheromatous Causes of Acute Coronary Syndromes.......................................................... 66
  Deepak Davidson.MD.DM.

- Determination Of Ventilatory Minute Volumes For Normocapnic.................................................. 84
  Chaudhari Anushree A. MD.DNB, Puri Goverdhan D. MD. PhD
  Kumar Bhupesh. MD. DM, Bhalla Anil K.MD

- Ventilation In Postoperative Cardiac Surgery Patients
Non-Inflammatory Risk Markers for Cardiovascular Disease

ABSTRACT

Indians have been reported to have high prevalence rates of coronary artery disease (CAD) even in the absence of traditional risk factors. The use of risk markers has transformed cardiovascular medicine, exemplified by the routine assessment of troponin, for both diagnosis and assessment of prognosis in patients with chest pain. Clinical risk factors form the basis for risk assessment of cardiovascular disease and the addition of biochemical, cellular, and imaging parameters offer further refinement. Identifying novel risk factors may allow greater risk stratification and a steady, but gradual progression toward precision medicine. Risk markers related to atherosclerosis, thrombosis, inflammation, cardiac injury, and fibrosis are introduced in the context of their pathophysiology. Rapidly developing new areas, such as assessment of micro-RNA, are also explored. These markers may be helpful in risk assessment in premature cardiovascular disease and in individuals where traditional risk factors are not present.

INTRODUCTION

Cardiovascular disease is the leading cause of death, accounting for 29% of all deaths in 2017, according to the WHO. The reported prevalence of coronary heart disease (CAD) in adult surveys has risen 4-fold over the last 40 years (to a present level of around 10%), and even in rural areas, the prevalence has doubled over the past 30 years (to a present level of around 4%). CAD strikes Indian population at a younger age and kills many in their productive mid-life years. Deaths due to CAD, in the age group of 35 to 64 years, resulted in 9.2 million potentially productive years of life being lost in 2012.

Studies suggest that most CAD events are noted in individuals with one or more risk factors. However, at least 25 percent of patients have myocardial infarction or sudden death without prior symptoms. The use of risk markers has transformed cardiovascular medicine, as exemplified by routine measurement of troponin, both for diagnosis and assessment of prognosis in patients with chest pain.

Inflammation has a central role in the pathophysiology of atherosclerosis, which is highlighted by the high cardiovascular risk of systemic inflammatory disorders, particularly systemic autoimmune disorders and systemic vasculitis. In the general inflammatory markers like IL-6, CRP and Myeloperoxidase(MPO) are well known for diagnosis and providing additive predictive ability for cardiovascular disease.

More recently, but less clearly established, emerging predictors of coronary artery disease like non-inflammatory markers have come into the light. This article provides insight into non-inflammatory markers associated with increased risk in cardiovascular disease. Combined with an understanding of the pathophysiological role of each marker, this helps to suggest whether each marker could be a simple risk biomarker or may also represent a modifiable risk factor.
LIPID RELATED RISK MARKERS

Coronary artery disease is the leading cause of death worldwide. Atherosclerosis of the coronary arteries is primarily driven by cholesterol and, in particular, low-density lipoprotein cholesterol (LDL-C). The causative role of LDL-C in coronary artery disease is clearly demonstrated by the success of LDL-C lowering drugs, such as statins, and Mendelian randomization studies. Recently, it has been discovered that proprotein convertase subtilisin/kexin type 9 has a significant role in the regulation of LDL-C, and levels of soluble proprotein convertase subtilisin/kexin type 9 have been identified as a new marker of cardiovascular risk. Although traditionally thought to reduce cardiovascular risk, the role of high-density lipoprotein cholesterol has now been brought into question by negative findings from clinical trials of drugs that increase high-density lipoprotein cholesterol and by negative Mendelian randomization studies. Following are lipid-related risk markers.

1. PCSK9: Influenced by the use of statins and diurnal variation. Promotes the degradation of hepatocyte LDL receptors, which have an important role in lowering plasma levels of LDL1

2. OxPL (Oxidized Phospholipids): OxPL are covalently bound to lipoproteins that contain apoB100. Suggested to be a specific biomarker for oxidation 2 and contribute toward atherogenesis.2

THROMBOSIS RELATED RISK MARKERS

After atherosclerotic plaque rupture, platelets adhere to exposed subendothelial components, such as collagen and von Willebrand factor, which promotes platelet activation and aggregation. Besides, platelet activation is potentiated by exposure to released soluble agonists, such as thrombin and ADP. Activated platelets then further release ADP, which acts on platelet P2Y12 ADP receptors and has a central role in amplifying the response of platelets to the initial stimulus. The VerifyNow and Multiplate point of care tests allow for the measurement of platelet aggregation in response to stimulation, and it has been shown that high platelet reactivity is associated with adverse cardiovascular events. Platelet microparticles are released on platelet activation, and their role in cardiovascular disease is an area of active investigation. Circulating microparticles are released from cells undergoing activation or apoptosis and are a type of small plasma membrane vesicle that retains defined properties from their original cell lineage. Platelet activation and aggregation lead to the activation of the coagulation cascade and the formation of a stable cross-linked fibrin clot. The balance between prothrombotic factors and endogenous fibrinolysis determines whether the thrombus propagates or instead proceeds to dissolution. Because thrombosis is central to the pathophysiology of ACS and embolic stroke in atrial fibrillation (AF), both prothrombotic factors and markers of endogenous fibrinolysis have been extensively investigated in these conditions. Following are risk markers related to thrombosis.

1. Platelet reactivity: Assessment of the reactivity of platelet signaling pathways can be used to identify response to antiplatelet therapy in the context of coronary artery disease. Results of the Verify Now and Multiplate tests are well standardized and are predictive of adverse cardiovascular events.4-6

2. Circulating progenitor cells: These cells are inversely associated with cardiovascular risk factors. These are immature bone marrow-derived cells, which are mostly of hematopoietic origin. They are involved in endothelial repair and angiogenesis.7

RISK MARKERS RELATED TO CARDIAC INJURY, HEALING AND FIBROSIS

During acute and chronic cardiac injury, reparative mechanisms must find a careful balance between remodeling the heart to maintain structural integrity while also preserving myocardial function.

1. Troponin T and troponin I: Contained within myocardial contractile apparatus and cardiac muscle tissue. Released via proteolytic degradation on cell death.8

2. NT-proBNP: Released in response to Myocardial stretch. It is Inactive N-terminal fragment of the precursor for BNP 9.

3. MR-proANP: Released in response to Myocardial stretch, derived from cleavage of the mid-regional part of the precursor of ANP104. MR-proADM: Released in response to Myocardial stretch, derived from cleavage of the mid-regional part of the precursor of adrenomedullin.11 Adrenomedullin (ADM) is synthesized by the endothelium and has many cardiovascular effects that are similar to nitric oxide, including potent vasodilation.12

RISK MARKERS RELATED TO HEMODYNAMIC STRESS AND RENAL FUNCTION:

Mechanical stretch and other mediators, such as angiotensin II and adrenergic agonists, induce cleavage of preprohormones and secretion of natriuretic peptides by cardiomyocytes. Both atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) predominantly act on natriuretic peptide receptor A, which leads to the inhibition of the renin–angiotensin–aldosterone system, diuresis, and natri-
uresis. Secretion of both ANP and BNP are increased during hemodynamic overload, and cardiac remodeling and are therefore indicative of heart failure. Additional markers of hemodynamic stress and renal disturbance include cystatin-C.

1. Cystatin-C: Synthesized by all nucleated cells at a constant rate, freely filtered by the renal glomerulus with no reabsorption into the blood.13 Less influenced by diet or muscle mass than creatinine, allowing it to be a reliable marker of renal glomerular filtration rate.13

MICRO-RNA RELATED RISK MARKERS:

There has been much recent interest in the role of micro-RNAs (miRNA) in the pathophysiology of cardiovascular disease. mi-RNAs are short non-coding RNAs that have a significant role in pathophysiological stress responses and mediate many cellular processes by regulating gene expression. miRNAs interact with specific mRNA to regulate their translation, mostly by suppression of protein synthesis. Most miRNAs are located intracellularly while platelets and platelet microparticles are an abundant circulating source.

miRNAs regulate a diverse range of processes in cardiovascular disease, including myocardial remodeling and fibrosis, vascular inflammation, lipid processing, and electric remodeling. It has also recently been shown that miRNAs can act as a novel biomarker for platelet reactivity and that their levels can be manipulated by the administration of antiplatelet therapy. Specific synthetic antagonists of miRNAs (antagomirs) are currently in development, and it is possible that these could prove beneficial in cardiovascular disease. Micro RNA related markers are the following.

1. miR-1: Released in response to ACS. It is associated with cardiomyocyte necrosis14 and inversely associated with cardiac hypertrophy.15

2. miR-133: Released in response to ACS. It is associated with cardiomyocyte necrosis14 and inversely associated with cardiac hypertrophy.15 Also, it has Role in the modulation of VSMC phenotype.16

3. miR-208: Released in response to ACS. It is associated with cardiomyocyte necrosis14 and is regulated during cardiac hypertrophy.17

4. miR-499: Released in response to ACS and Heart failure. Muscle-specific miR that is released during acute MI and levels of miR-499 correlates with levels of troponin.

5. miR-150: It is Reduced by platelet inhibition and inversely associated with left ventricular remodeling after MI.18 It has Role in megakaryopoiesis19 and also Highly expressed in platelets and platelet microparticles.

6. miR-223: It is Reduced by platelet inhibition, and it is inversely associated with subsequent MI.20 It is highly expressed in platelets.

7. miR-197: It is also reduced by platelet inhibition, inversely associated with subsequent MI and highly expressed in platelets.

8. miR-126: It is reduced in diabetes mellitus. It is reduced by platelet inhibition, and it is a regulator of endothelial and vascular integrity.21 It modulates the vascular expression of adhesion molecules22 and is highly expressed in platelets and platelet microparticles. Also, it is predictive of subsequent MI.

9. miR-143/145: Released in response to shear stress. It plays a major role in the modulation of VSMC phenotype.23

10. miR-622: Increased in heart failure and levels correlate with BNP.24

11. miR-21: Released in response to Fibrosis and has Role in myocardial remodeling and fibrosis.25

12. miR-29: Released in response to Fibrosis and has Possible role in myocardial remodeling, hypertrophy, and fibrosis.26 It also Regulates MMP expression.27

13. miR-328: Released in response to Atrial fibrillation, it Regulates

IMAGING RELATED RISK MARKERS:

In recent years, there has been a dramatic increase in the number of imaging modalities that are available for use in clinical practice. Cardiac imaging provides sophisticated measures of many different pathological processes, including quantification of coronary artery disease and the presence of plaque rupture, as well as the determination of myocardial infarct size and the presence of microvascular obstruction.

More recent techniques, such as coronary computed tomographic angiography and optical coherence tomography allow for some assessment of plaque morphology, beyond a simple assessment of luminal stenosis. Further development of imaging technologies may offer the possibility for detailed plaque assessment, including determination of plaque inflammation, which may suggest plaques at high risk of rupture.
Myocardial infarct size (CMR) | Demonstrated by infarcted myocardial tissue in late gadolinium images on CMR imaging
---|---
Microvascular obstruction (CMR) | Demonstrated by regions of myocardial hypoenhancement during the first 2 min of gadolinium-contrast administration
CTCA | Noninvasive investigation for detecting obstructive and nonobstructive CAD, which allows rapid determination of the diagnosis of suspected angina. CTCA correlates well with the findings of invasive angiography, with high accuracy and sensitivity of >97% in several studies, although this may be lower in distal lesions. Coronary artery calcium scoring provides an indicator of the overall prevalence of coronary artery disease.
MR coronary angiography | MR coronary angiography is appealing as it does not involve radiation and provides excellent soft-tissue contrast. However, current applications of MR coronary angiography are limited because of temporal resolution, which is exacerbated by the small caliber and complex motion of the coronary arteries.
Optical coherence tomography | Intracoronary light-based technology that allows for detailed characterization of coronary artery plaque. Plaque rupture can be differentiated from an intact fibrous cap on the basis of a discontinuity in the fibrous cap.

**ENDOTHELIN**
Estimation of plasma endothelin by ELISA using DRG’s human ET-1 enzyme immunometric assay kit can also be used as a marker for CAD.

**HOMOCYSTEINE**
Estimation of Homocysteine was done by using diazyme homocysteine microtitre plate assay (EIA). The assay employs a genetically engineered Homocysteine Binding Protein (HBP) as the capturing agent. LIPROTEIN (a): The plasma Lp(a) can be determined using DRG Elitest assay kit. The amount of color produced is proportional to the amount of Lp(a) present in the sample. NOVEL LIPID BIOMARKER HDL3-C (Predicts severity of CAD): In patients who use statins, severe coronary artery disease (CAD) was associated with low levels of the high-density lipoprotein cholesterol sub particle 3 (HDL3-C) and with high levels of lipoprotein(a) cholesterol (Lp[a]-C).

The investigators sought to identify the association of high-density lipoprotein cholesterol (HDL-C) subparticles with severe CAD. It was seen that patients with severe CAD were associated with a significantly lower total HDL-C and HDL3-C and significantly higher Lp[a]-C.

CONCLUSION: Apart from established inflammatory markers, levels of non-inflammatory markers are also elevated in CAD patients. Thus, they may serve as potential markers of CAD. These biomarkers may be helpful in risk assessment.
in premature cardiovascular disease and in individuals where traditional risk factors are not present.

REFERENCES


18. Devaux Y, Vausort M, McCann GP, Kelly D, Collignon O, Ng LL, WagnerDR, Squire IB. A panel of 4 microRNAs facili-


Does Serum Uric Acid Fare Similar To Serum High-sensitivity C-reactive protein as Vascular Inflammatory Marker Of Coronary Artery Disease In Young Asian Indians?

ABSTRACT

Background: India is estimated to have one of the highest coronary artery disease (CAD) burden in the world. Indians manifest CAD at a younger age. Inflammation plays a key role in CAD progression. Inflammatory marker high sensitivity C-reactive protein (hsCRP) predicts CAD risk either by correlation with CAD extent (disease marker) or as an indicator of inflammatory event that leads to plaque rupture (a process marker). It has been proposed that serum uric acid concentrations can be used as a cardiovascular risk marker in the same way that High-sensitivity C-reactive protein (hs CRP) is being used.

Aim:

To assess the role of vascular inflammation using markers like serum uric acid and hs CRP, and find if it is a cost effective and relevant method for young Indians.

Methods:

Serum uric acid (measured by colorimetry) and serum hs CRP (measured by immune-turbidimetry technique) level was measured in young adults (18–45 years) with angiographic proven CAD (60 patients), and compared with those >45 years age (24 patients), and in controls with no CAD (14 patients). Later, the levels of markers were compared with the angiographic stenosis and extent score in young CAD patients.

Results:

Both mean serum uric acid and hs CRP were elevated in Young CAD patients more than in those of Old CAD patients and Controls, and this trend was found to be significant by ANOVA (P=0.015/ P = 0.028). Serum uric acid and hs CRP levels were found to be in direct proportion to both stenosis and extent score of coronary artery disease (P <0.01) in young adults.

Conclusion:

Serum uric acid fared similar to hs CRP as vascular inflammation markers and have a positive correlation with the disease burden in the young CAD patient. Premature CAD in
Young Indians could be partly explained by increased vascular inflammation. Further studies to identify & reduce risk factors in an economically and socially relevant section of population of a fast developing country like India is needed.

Keywords:
Angiographic stenosis, Angiographic extent, serum uric acid, hs CRP, Young coronary artery disease. The burden of CAD in developing countries has increased in the last three decades. In India, CAD continues to rise and is now involving middle and lower income class groups. CAD is responsible for an estimated 25% of all deaths in India.1 Symptoms of CAD arise a full 10 years earlier in India than in Western countries.2 However, only a few studies on epidemiological data from angiographically proven cases of premature CAD (≤40–45 years) in native Indians are available. Vascular inflammation plays a key role in coronary artery disease (CAD) and other manifestations of atherosclerosis.

High-sensitivity C-reactive protein , an inflammatory biomarker, has independently proven as one of the most powerful predictors of cardiovascular disease.3 In the search for other novel inflammatory markers, the available evidence has established a link between hyperuricemia and cardiovascular disease and this may be causal. It has been proposed that serum uric acid concentrations can be used as a cardiovascular risk marker.4 As a risk predictor serum uric acid could be additive to other inflammatory markers like hs-CRP. Studies of serum uric acid in angiographically proven CAD in young adults are not known. This study aims to understand the significance of serum uric acid level versus hs CRP levels as markers of coronary artery disease severity (disease marker) or as an indicator of inflammation that leads to an atherothrombotic event that leads to plaque rupture (a process marker).

MATERIAL AND METHODS
Patient population: This study included 100 patients admitted with CAD and underwent coronary angiography (CAG) in the Department of Cardiology, ICVS, IPGMER/ S.S.K.M. Hospital, Kolkata. Sixty patients < 45 yrs of age, both males and females, admitted with CAD were enrolled in this study as the test population of "young adults with CAD". Forty patients (> 45 yrs of age or those with angiographically normal coronary arteries, both males and females, admitted with CAD were enrolled in this study as "controls". The patients with history of coronary angiography in the recent past, on statins for more than one month, any systemic infection, collagen vascular disease, recent trauma, pregnancy and patients with documented extra-cardiac atherosclerosis were excluded from the study.

Study design:
Our Study was a cross-sectional study. Among the selected cases, the test group of patients with age < 45 years were labelled as “Young CAD” group and those with age > 45 years were labelled as “Old CAD” group. The patients who had chest pain but normal coronary angiograms were taken as control subjects (labelled as “controls”). Angiographic estimation of coronary atherosclerosis: Coronary angiography was performed by the femoral approach and included at least 4 views of the left coronary artery and 2 views of the right coronary artery.

Stenosis Score:
Stenosis Score used was a modified Gensini score. 5 Stenosis score provides information related to the bulk of the atherosclerotic lesion and is influenced by episodic processes such as plaque rupture. Each of eight vessel segments was graded according to severity of occlusion; grade 1 for 1% to 49% occlusion in lumen diameter, 2 for 50% to 74%, 3 for 75% to 99%, and 4 for total occlusion. The score in each of the eight segments were added to give a total score out of theoretical maximum of 32. This score therefore, places emphasis on the severity of stenosis, while including some of the extent of CAD.

Extent score:
Extent score used was a David R. Sullivan’s new angiographic score of the extent of coronary artery disease. 6 The score indicates the proportion of the coronary arterial tree involved by angiographically detectable atheroma. The proportion of each vessel involved by atheroma, identified by luminal irregularity, was multiplied by the factor for each vessel. Left main artery, 5; left anterior descending, 20; main diagonal branch, 10; first septal perforator, 5; left circumflex artery, 20; obtuse marginal and posterolateral vessels, 10; right coronary artery, 20; and main posterior descending branch, 10. When a vessel was occluded and the distal vessel not fully visualised by collateral flow, the proportion of vessel not visualised was given the mean extent score of the remaining vessels. When the major lateral wall branch was a large obtuse marginal or intermediate vessel, this was given a factor of 20 and the left circumflex artery a factor of 10. The score for each vessel or branch were added to give a total score out of 100, that is the percentage of coronary intimal surface area involved by atheroma.

hs-CRP estimation:
The CRP test was performed by using UBI MAGIWEL CRP-quantitative AD-401 kit, a solid phase enzyme linked immunosorbant assay (ELISA) as per instructions of the manufacturer (supplied with kit).
Serum uric acid estimation:
Serum uric acid – was measured colorimetrically by xanthine oxidase method. Statistical Analysis: Data were analysed with SPSS for windows statistical package and are presented as mean ± SD. Univariate comparison between groups were made with nonparametric test; Kruskal-Wallis test for multigroup comparison and Mann-Whitney’s test for 2-group comparison. Discrete variables were compared with chi square test. The correlation between levels of hs-CRP/uric acid and angiographic stenosis and extent was assessed by Pearson’s correlation. For all results, a P value of < 0.05 was considered significant.

RESULTS
Out of 60 Young CAD (41 males) patients, 42 presented as acute coronary syndrome and the rest 18 as chronic stable angina. Out of 24 Old CAD (15 males) patients, 14 presented as acute coronary syndrome and the rest 10 as chronic stable angina. There were 16 patients (12 males) in the control group of normal coronaries. The three groups were comparable with respect to age, sex, and other risk factors for coronary artery disease such as diabetes, hypertension, dyslipidemia, obesity and smoking. (Table 1)

TABLE 1: Distribution of risk factors across study groups.

Patients with ACS had the highest mean hs-CRP levels among both young CAD (5.60 mg/l) and old CAD (3.53 mg/l) patient groups. Mean hs-CRP in chronic stable angina patients was 3.89 mg/l in young CAD group and 2.95 mg/l in the old CAD group. Mean hs-CRP was significantly elevated in both ACS Group (P < 0.01) and CSA Group (P = 0.02) of Young CAD patients than in those of Old CAD patients. When compared among age groups in total, mean hs-CRP showed a trend which was highest in the young CAD group (5.0 mg/l), followed by the old CAD patient group (3.40 mg/l) and least in the control group of individuals with normal coronaries (2.30 mg/l). Mean hs-CRP was therefore, elevated in Young CAD patients more than in those of Old CAD patients and Controls, and this trend was found to be significant by ANOVA (P = 0.028). (Figure 1a) Patients with ACS had the highest mean serum uric acid levels among both young CAD (5.93 mg/l) and old CAD (4.88 mg/l) patient groups. Mean serum uric acid level in chronic stable angina patients was 4.25 mg/l in young CAD group and 4.05 mg/l in the old CAD group. Mean serum uric acid level was significantly elevated in ACS Group (P = 0.01) and non-significantly in the CSA Group (P = 0.38) of Young CAD patients than in those of Old CAD patients. When compared among age groups in total, mean uric acid levels showed a trend which was highest in the young CAD group (5.4 mg/l), followed by the old CAD patient group (4.5 mg/l) and least in the control group of individuals with normal coronaries (4.1 mg/l). Mean serum uric acid was therefore, elevated in Young CAD patients more than in those of Old CAD patients and Controls, and this trend was found to be significant by ANOVA (P = 0.015). (Figure 1b)
To see the correlation of disease burden, angiographic stenosis score and extent score were compared with the levels of serum hsCRP and serum uric acid levels in young adults with CAD. Mean stenosis scores were 6.35 in the ACS and 3.67 in CSA group of young CAD patients. The Pearson Chi-square test showed a significant point to point positive correlation between angiographic derived CAD stenosis score (Gensini Score) and levels of inflammatory biomarker – hsCRP (P<0.01, r= 0.6692, 95% CI for r - 0.5003 to 0.7891) and uric acid (P<0.01, r= 0.5223, 95% CI for r - 0.3094 to 0.6853).

(Figure 2a, 2b) The mean extent scores were 36.90 in ACS and 21.67 in CSA group respectively. Similar to stenosis score, the Pearson Chi-square test showed a significant point to point positive correlation between angiographic derived CAD extent score (Sullivan Score) and serum hs CRP levels (P<0.01, r= 0.6067, 95% CI for r - 0.4170 to 0.7457) as well as serum uric acid levels (P<0.01, r= 0.3882, 95% CI for r - 0.1489 to 0.5845). (Figure 3a, 3b)

DISCUSSION
Coronary artery disease (CAD) remains as a leading cause of mortality and morbidity worldwide. Coronary artery disease is devastating precisely because an otherwise healthy person in the prime of life may die or become disabled without warning. CAD in the young (under the age of 45), brings sudden and unexpected distress for the individual, family and his friends. It is now established that CAD is increasingly prevalent in Asian Indians and these people tend to get MI at a younger age in addition to more complex coronary artery abnormalities. Recent research has shown that inflammation plays a key role in coronary artery disease (CAD) and other manifestations of atherosclerosis. In recent years, several studies have shown that CRP is associated with cardiovascular risk. Reports of Serum uric acid as a cardiovascular risk marker are however less, especially in the group of young CAD patients. In our study, mean hsCRP as well as serum uric acid were significantly elevated in Young CAD patients than in those of Old CAD patients. This finding indicates the role of vascular inflammation and endothelial dysfunction in the high incidence of CAD in young Indians. This important data suggests the possible involvement of risk factors that are often not considered in typical risk-stratification schemes. Considering the occasional involvement of these factors in older CAD patients, their involvement in the young CAD group should be further elucidated. Different authors have mentioned that the role of inflammation is understudied and it can be assessed by testing levels of systemic inflammatory markers such as high sensitivity C-reactive protein and upcoming markers like uric acid. Correlation of Inflammation with Angiographic CAD Severity In the present study, out of 60 Young CAD patients, 26 (43.3%) had single vessel disease (SVD), 24 (40%) had double vessel disease (DVD), 10 (16.7%) had triple vessel disease (TVD). Out of the 24 Old CAD pa-
tients, 17 (71%) had SVD, 4 (16.7%) had DVD, 1 (4.2%) had TVD. (Table 2) The high prevalence of DVD and TVD in the Young CAD (56.7%) versus the Old CAD (20.9%) group has also been reported previously. Klein et al. theorized that two distinct populations exist. The more common subgroup is characterized by single-vessel, and often single-stenosis, disease, presumably related to acute plaque rupture, with an excellent three-year outcome. The favourable prognosis was believed to be related to preserved left ventricular function without multivessel involvement. The less common group has extensive three vessel CAD with “galloping” progression unrestrained by coronary artery bypass graft surgery (CABG) and preventive measures. Pearson Chi-square test shows a significant positive correlation between levels of inflammatory biomarkers and angiographic derived CAD stenosis score (Gensini Score) \((P <0.01)\) and extent (Sullivan Score) \((P<0.01)\). Serum uric acid paralleled serum hs CRP for correlation with coronary disease severity and extent. Therefore, both serum uric acid and serum hsCRP may serve as sensitive indicators of progressive increase in stenosis severity and extent of coronary artery disease in Young CAD subjects. Relevance of serum uric acid as a correlate of vascular inflammation and coronary artery disease severity has rarely been reported from India and probably none documented from Eastern India especially among young CAD patients. This is important because type and levels of risk factors may vary from North Indian to South Indian CAD patients.

### Strengths of the Study

There are very few reports of correlation of vascular inflammation with CAD from India, especially among the increasingly relevant young CAD population. This report also highlights the important role of a relatively cheap inflammatory marker – serum uric acid as statistically similar to an established marker like hs CRP in correlating with disease severity and extent of coronary artery disease. The methodology used in the study was similar to international reports of the same nature, thus making it suitable for purposes of comparison.

### Limitations of the Study

It is a cross-sectional study of patients referred for coronary angiography. This study design may not be used to establish causality. It can only establish an association. Therefore, this study must be considered a preliminary yet hypothesis generating rather than hypothesis-proving study. A larger sample study to understand the interaction between role of inflammatory markers like uric acid and hs CRP vis-à-vis CAD is required, to investigate whether there is a ‘threshold effect’ of the markers and also to prove any diagnostic or prognostic value of these markers, especially in the young.

### CONCLUSION

Significantly higher serum uric acid and serum hs CRP levels are found in spectrum of CAD patients through acute coronary syndrome to chronic stable angina than to patients with normal coronary angiography – indicating a role of inflammation in the process of plaque progression. Both serum uric acid and hs CRP levels and inflammation have a positive correlation with the disease burden in the young CAD patient. The findings highlight the relevance of serum uric acid as a novel and relatively cheaper alternative to an already established marker serum hs CRP as a correlate of vascular inflammation and coronary artery disease in young Indians. Premature CAD in Young Asian Indians could be partly explained by increased vascular inflammation. Further observational and interventional studies are warranted in this regard to identify & reduce risk factors in an economically and socially relevant section of population of a rapidly developing country like India.

### BIBLIOGRAPHY


An Interesting Case of Restrictive Cardiomyopathy

A 56-year-old gentleman was admitted to the hospital on 15.12.17 in Cardiogenic shock with bradycardia and a Systolic Blood Pressure of 80 mm Hg. He was admitted to a peripheral hospital a week ago with abdominal pain and vomiting and was referred due to shock, on inotropic support. He had a similar admission ~ 3 months ago in another hospital when an angiogram was normal.

His Hb was 11.4 g/dl with ESR ~ 140 mm/hr. S. Creatinine was 2.1 mg/dl. hs Trop I was 206.4 ng/L, and Nt Pro BNP was 16,439 pg/mL. He was treated as septicemic shock with IV meropenem with which the inflammatory markers came down, and he improved clinically. ECG showed junctional rhythm with HR ~ 60/mt (Fig 1), and an Echocardiogram showed Concentric LVH with speckled appearance (Fig2,3,4) suggestive of restrictive cardiomyopathy.

Specific investigations for the etiology were done with Serum Electrophoresis showing a mild narrow band in the mid gamma region ~ 0.75g/dl implying a monoclonal gammopathy. Serum Immune fixation showed a M band in the gamma region (0.84g/dl). X-Ray showed possible lytic lesions in the skull. Bone marrow aspiration study showed 24% plasmacytosis consistent with a plasma cell neoplasm (Fig 5). A rectal biopsy was negative for amyloid (Fig 6). Thus a diagnosis of Multiple Myeloma with Cardiac Amyloidosis was made though we did not have any tissue diagnosis of Amyloidosis.

The oncologist saw him and started on treatment for myeloma. However, he continued to do poorly and was readmitted again in shock. He expired three months after the initial admission and limited biopsies of the heart (Fig 7,8,) and liver (Fig 9, 10) were done which showed extensive amyloid deposition confirming the diagnosis of Cardiac Amyloidosis.

DISCUSSION

Amyloidosis refers to a collection of diseases in which beta plated sheets of proteins infiltrate the tissues. Based on nomenclature, it is divided into two main types – Light Chain Amyloidosis (AL) and Transthyretin Amyloidosis (ATTR) caused by the deposition of Light Chain or Transthyretin respectively (1). The most common form of systemic amyloidosis is AL. This can get deposited in any organ – the common extra-cardiac sites being kidneys, Liver, GI tract, Tongue and nerves. Cardiac manifestations include heart failure and arrhythmias. Clues to the diagnosis of Cardiac amyloidosis include LVH on echo with low voltage complexes on the ECG.

Transthyretin amyloidosis may be wild type ATTR – due to excess production of transthyretin in the liver or the mutant type. Mutant type results from a pathological mutation in the transthyretin gene leading to amyloid deposition in the heart and nerves.

Though the diagnosis of amyloidosis can be assumed from the clinical features along with the ECG and Echo findings, a definitive diagnosis of amyloidosis requires biopsy. This is difficult to obtain. Though sub-cutaneous fat or rectal biopsies are the easiest to perform, it was negative in this case. The final confirmatory tissue was obtained post mortem.
Fig: 1 ECG - Junctional Rhythm, Low voltage Fig: 2 Echo: Conc LVH

Fig 3: Speckled Pattern

Fig 4: Ventricular Hypertrophy

Fig 5: Bone Marrow-Plasmacytosis

Fig 6: Normal Rectal Biopsy
In either form of amyloidosis, the dominant imaging finding is ‘hypertrophy.’ The hypertrophy is due to amyloid fibril deposition rather than myocyte hypertrophy/hyperplasia which is the reason why the ECG voltages are decreased rather than increased. It causes abnormal patterns of late gadolinium enhancement on Cardiac Magnetic Resonance (CMR) (2) and Strain echocardiography reveals basal > apical impairment in strain (3).

Prognosis in amyloidosis depends predominantly on the degree of cardiac involvement. Though the prognosis is better in ATTR amyloidosis, both forms carry a high annual mortality. Treatment follows two parallel paths: treating the consequence of organ dysfunction and attempting to slow the progression of the disease with chemotherapy against the plasma cells. Cardiac-specific treatment involves volume management (diuretics/salt restriction) and that of arrhythmias. ACE-I / ARB and beta blockers are poorly tolerated and may result in profound hypotension. Pacemakers are frequently required due to conduction disease. AF is common and poorly tolerated. As the disease is irreversible with high mortality, a cardiac transplant may be considered in well-selected patients (4).

**REFERENCE**

Principles and practice of modern endovascular therapy in patients with acute ischemic stroke

The principles of treatment in patients with acute ischemic stroke are simple. A thrombus occludes an artery supplying blood to the brain, tiny collaterals provide some blood supply to the ischemic brain which infarcts over time. If the thrombus is removed before the entire ischemic brain infarcts and the risks of treatment are mitigated, patients benefit. Despite these principles of acute ischemic stroke treatment being so simple, for many years since the first endovascular treatment (EVT) in patients with acute ischemic stroke, the treatment raised skepticism.1 Randomized clinical trials failed to demonstrate the efficacy of EVT, further increasing the scepticism surrounding this treatment.2-4 It took our field many years to understand that selecting the right patients for EVT and administering that therapy early were core to the success of the treatment. These tenets were integral to the success of the MR CLEAN, ESCAPE, REVASCAT, EXTEND IA, and SWIFT PRIME trials.5-9 The HERMES patient-level pooled meta-analyses of these recent EVT trials has finally established EVT as standard care in patients with acute ischemic stroke.10 Trials like ESCAPE, DAWN, and DEFUSE-3 have changed the paradigm in acute ischemic stroke treatment from the time-based selection of patients to tissue based selection.11-13 With many imaging strategies and many devices and techniques, physicians treating patients with acute ischemic stroke need clarity. This review will, therefore, be practical. It will focus on how to select patients for EVT and how to then administer modern EVT safely and efficiently. By applying these simple principles and techniques, physicians will be able to provide their patients with very reasonable chances of recovery from acute ischemic stroke.

Patient selection for Endovascular Therapy (EVT)

Imaging Modality of Choice:

The non-contrast CT (NCCT) of the Head is the work-horse of acute stroke treatment.14 It is inexpensive, fast to acquire and can be done in all patients at all times. We strongly advocate for the use of the NCCT Head as the first line imaging tool in patients presenting with symptoms and signs of acute
stroke. The NCCT Head is used to a) distinguish between a haemorrhagic and ischemic stroke and b) to determine the extent of the infarcted brain. Proponents of Magnetic Resonance Imaging (MRI) suggest that MRI Diffusion Weighted Imaging (MR-DWI) is better at recognizing subtle early ischemic changes (EIC) than NCCT Head. Although arguably true, the purpose of NCCT is not to pick up subtle EICs but only to rule out very large infarcts. We call such very large infarcts “wipe-outs.” (Figure 1) Modern EVT, when administered quickly, is so efficient (Number Needed to Treat of ~2) that the therapy is invariably effective even in patients with infarcts that are moderate to large. Modern EVT, when administered quickly, is so efficient (Number Needed to Treat of ~2) that the therapy is invariably effective even in patients with infarcts that are moderate to large.15 A recent meta-analysis from the HERMES collaboration shows that patients with NCCT ASPECTS (an ordinal 10-point scale to assess the extent of EIC) as low as 3 or infarct volume as high as 100 ml on CT Perfusion continue to benefit from EVT, especially when they are younger than 80 years of age.15, 16 MRI moreover takes more time to arrange and acquire than NCCT. Every minute lost acquiring an MR vs. an NCCT Head results in approximately 2 million neurons being lost forever!17

The CT Angiogram of the Head and Neck (CTA Head and Neck) (Figure 2) should be the next imaging modality of choice after the NCCT Head. As in acute coronary interventions, it is imperative in patients with acute ischemic stroke to understand if there is a target thrombus for EVT. A target thrombus for EVT is an emergent large vessel occlusion (ELVO). An ELVO is a thrombus in the internal carotid artery (ICA), M1 segment Middle Cerebral Artery (MCA), a proximal M2 segment MCA or an intracranial vertebral or basilar artery. ELVOS are less likely to recanalize with intravenous thrombolysis alone.18, 19A debilitating clinical deficit due to a proximal anterior cerebral artery or posterior cerebral artery occlusion may also, in expert hands, be target thrombus for EVT.

The CTA Head and Neck is also useful when planning access for EVT. Knowledge of aortic arch and large vessel help in interventional planning (details described below in the section on interventional techniques and strategies).14, 20 The CTA also helps to identify the extent of collaterals beyond the ELVO (Figure 3).21, 22 Patients with moderate to good collaterals beyond the ELVO are likely to benefit with EVT. If minimal or no vessels are seen beyond the ELVO on CTA, these patients are unlikely to benefit from EVT. Concerns with the use of CTA Head and Neck primarily stem from the use of iodinated contrast and the risk of contrast nephropathy. This risk is so minimal in most patients, and the benefits from vascular imaging are so marked that most stroke centers perform CTA immediately after NCCT without waiting for a serum creatinine; the only exception being in patients with known severe renal insufficiency who is not

---

**Figure 1:**
A non-contrast CT Head showing extensive early ischemic changes (blue arrows) in the left middle cerebral artery territory.

**Figure 2:**
A CT Angiography Head showing a left sided L type internal carotid artery occlusion.

**Figure 3:**
Multi-phase CT Angiography Head showing good collaterals beyond a left sided M1 segment MCA occlusion.
Principles of Patient Selection (Imaging vs. time):

Patient selection for EVT has moved on from a time window-based strategy to a brain tissue-based strategy. This means any patient with acute stroke symptoms with an ELVO and salvageable brain on imaging is a candidate for EVT. Common sense suggests that any patient who wakes up with stroke symptoms or whose stroke symptom onset was not witnessed and is brought to the hospital should, therefore, be imaged. Although guidelines suggest the use of 16-24 hours from last known well to define acuteness, we would much rather recommend that physicians use common sense and good history to find out if the stroke may have been acute even if the patient was last known well more than 24 hours earlier. As an example of tissue-based imaging selection, imagine an 80-year-old lady living alone at home. The milkman brings milk every second day in the morning. The lady does not open the door when he knocks. The milkman finds the lady on the floor unable to speak or to move. He calls neighbours and transports the patient to the hospital with EVT facilities. The physician recognizes that the stroke may have happened > 24 hours ago OR may have happened just an hour before he knocked. Ancillary history from the witness (milkman) may provide other clues to stroke onset, e.g. was the breakfast made that day etc. However, in most situations, it is difficult to know when the stroke happened. Imaging of the brain helps in such situations. An NCCT of the brain showed some early ischemic changes in the left MCA territory but no “wipe-out” infarct. A CTA Head and Neck showed a left M1 segment MCA occlusion with good collaterals. The physician takes the patient to the angio-suite for EVT. EVT is successful, and the patient recovers well. The above example illustrates the use of tissue-based rather than time-based patient selection strategy. If a time-based selection strategy had been used, the patient would have been last known well (by the witness milkman) at least 48 hours ago. A life-saving treatment such as EVT would have been denied to a deserving patient! Although the DAWN and the DEFUSE 3 trial used CT Perfusion(CTP) imaging to select patients in the extended time window, the ESCAPE trial used NCCT and CTA to select such patients beyond 6 hours from stroke symptom onset. CTP is technically challenging, especially when patients move and in smaller hospitals. We do not, therefore, recommend the additional use of CTP or MRI in selecting patients for EVT. Principles of Patient Selection (Clinical Variables): The art of medicine is still not lost in the modern era of medical treatment. Variables such as age, frailty, presence of cognitive impairment, cancer or other co-morbidities like heart disease or chronic kidney disease can all affect prognosis in patients with acute ischemic stroke. A pragmatic physician will consider these prognostic variables when making decisions on offering EVT to patients. At our center, not every patient with an ELVO without wipe-out infarct is offered EVT. In the very elderly or those with terminal illnesses or dementia, the likelihood of poor prognosis even with EVT is discussed with families and a considered decision made that often takes into account the patient’s previous wishes, and therefore we desist from offering any recommendations. We do however suggest that the treating physician remembers Charaka’s quote “A physician should first study all the factors including the environment that influence the patient’s disease and only then offer treatment, if necessary.”

Interventional techniques and Strategies

Endovascular techniques for acute ischemic stroke have evolved significantly from earlier case reports of intra-arterial pharmacological clot lysis to thrombectomy in the modern era using stent retrieval devices and aspiration techniques or combinations thereof. Summarized by the aphorism “Time is Brain,” faster techniques to restore intracranial flow after a large vessel occlusion is critical in improving neurological outcomes. Moreover, platelet-rich clots are more resistant to thrombolysis and clot contraction, and low plasminogen content further contributes to likely low revascularization rates. The following sections illustrate the technical aspects of endovascular treatment in acute ischemic stroke.

Anaesthesia:

Most patients with acute ischemic stroke may be treated without the need for a General Anaesthetic. The use of local anaesthesia and conscious sedation if required will suffice in most situations. In agitated patients or patients who have already been intubated either on scene or in the Emergency departments for airway protection, a General anaesthetic may be required.

Access:

Most neuro-interventional practitioners use femoral arterial access for endovascular stroke therapy. The aortic arch
anatomy and use of various selective catheters for Neuro-angiography render this the most preferred access route for acute stroke interventions. However, the use of larger sized access sheaths (typically 8-9 Fr) and concomitant use of intravenous fibrinolytic agents and need for anticoagulation during therapy can lead to increase in the proportion of femoral access site complications. Other access sites are less typically used including radial artery access for both posterior circulation and anterior circulation thrombectomies and direct carotid access in case of tortuosity and difficulty in traversing the aortic arch. Using ultrasound-guided direct puncture and micro-puncture kits can minimize access site complications but should not lead to unnecessary delays in getting the procedure started. The use of a short sheath will suffice in most circumstances, but in elderly patients or tortuous anatomy, the use of a long sheath helps to provide stability for multiple exchanges of devices, and in case there is a need for simultaneous treatment of cervical carotid disease with angioplasty and stenting.

**Guiding Catheter:**
The use of a balloon-tipped guiding catheter to temporarily arrest flow while performing intracranial thrombectomy will decrease the risk of non-target emboli either in distal territories or other vascular territories across a patent circle of Willis (Figure 4). Larger balloon guide catheters such as 8 Fr or 9 Fr guiding catheter will accommodate most intracranial thrombectomy devices including co-axially placed intermediate catheters and stent delivery catheters. All access sheaths, guiding catheters, intermediate catheters as well as intracranial microcatheters should be placed on a continuous pressurized heparinized saline drip. Depending on arch anatomy the guiding catheters may be placed using a simple forward curve such as a hockey stick or Head-hunter curve. Reverse curved catheters such as a Simmons curve or VTK curve might be required to engage challenging type 2/3 aortic arches or bovine configurations (Figure 5). A long hydrophilic coated wire will suffice in most cases for selective engagement of the vessel of interest. Stiffer wires and wires of variable stiffness (softer at the tip and sturdier proximally) might be required in certain cases. In some circumstances, a smaller 5 Fr catheter might be needed to engage the target great vessel, and subsequently, the guiding catheter is placed using an exchange-length wire. A careful review of the pre-procedure CT angiography of the vessels from the aortic arch through the intracranial circulation will help in appropriate selection of the catheters that may be required for arch access. In cases with a severe carotid disease or cervical carotid occlusion the guiding catheters are placed below the level of occlusion and are chosen with the intent of carotid stenting should it be required.
Intracranial access:
A review of the pre-procedural CTA and evaluation of the clot location might determine the specific intracranial access catheters that are required. For distal clots, smaller microcatheters such as a 0.021” or 0.017” microcatheter will be easier to navigate. The use of larger microcatheters or intermediate catheters in vessels more distal than the MCA main trunk should be used with extreme caution as it may lead to complications related to a vessel perforation.37 Smaller distal clots usually do not primarily manifest with a large neurological deficit at presentation, however smaller catheters for access may be required in situations with clinically significant deficits related to a smaller vessel (such as an anterior cerebral artery or a posterior cerebral artery occlusion) or from iatrogenic distal emboli from a proximal occlusion. Various microwires can be used for intracranial access, and most microwires are in the range of 0.012” to 0.016” in thickness and explicitly designed for neurovascular work. The choice of wire will depend on availability and operator preference. Wire manipulation alone may suffice in disrupting distal clots. In rare instances, low dose intra-arterial fibrinolysis may be used for distal occlusions that are resistant to mechanical clot disruption. Mechanical thrombectomy techniques have replaced primary use of pharmacological agents such as tPA or Urokinase for larger proximal clots.

For larger proximal clots involving the intracranial ICA or the MCA main trunk, most practitioners use aspiration thrombectomy, stent-assisted thrombectomy or a combination of both. Earlier devices for mechanical clot retrieval such as the Merci retrieval device and Catch device have been mostly replaced by modern stent retrieval systems.25, 38 There are also previous reports of clot disruption with angioplasty balloons.39 However, these are suboptimal as they result in clot fragmentation and distal embolization. Laser thrombolysis, photoacoustic and micro-infusion sonography transducer systems are near obsolete for intracranial work.

If using an aspiration only technique (0.060” to 0.070” inner lumen systems), an intermediate microcatheter is still required to advance the aspiration catheter to the face of the clot. This will depend on the manufacturer and sometimes are supplied as a single kit. Aspiration may be applied using a specific aspiration pump using a specified protocol. In some instances, manual aspiration with a large capacity syringe may result in revascularization and satisfactory flow restoration. The use of aspiration alone as the first pass technique has been reported to result in faster recanalization rates with decreased puncture to recanalization time.40 However, there is a possibility of clot fragmentation or non-target embolization especially if not used in conjunction with a larger balloon guide catheter.

Stent-retrieval thrombectomy is performed using a non-detachable stent specifically designed for intracranial flow restoration.9, 25 The stent delivery microcatheter is advanced past the clot into a suitably sized vessel distal to the occlusion (Figure 6). Gentle technique and tactile feedback will determine the amount of force necessary to traverse the clot. An atraumatic technique for advancing the microwire is essential to prevent inadvertent perforation from the microwire or the microcatheter. In some instances, the softer tip of the stent delivery microcatheter may suffice to traverse the clot. When working within the MCA an understanding of the size of the distal M2 branches may help in mentally identifying the branch to select, as antegrade flow cannot be evaluated during angiography. Once within a suitable branch distal to the clot, the position of the microcatheter tip and integrity of the vessel is confirmed with a small test injection of contrast. The self-expandable stent at the end of a delivery wire is designed to be advanced through the microcatheter. In cases with tortuous anatomy there can be significant tension within the microcatheter system as well as ovalisation of the lumen of the microcatheter. This can result in difficulty in advancing the stent system through the microcatheter. Partial withdrawal of the microcatheter to decrease the tension within the system can aid in advancing the stent. Sometimes using an intermediate catheter can help in providing an added support. This is usually the case when using combined aspiration and stent retrieval as discussed below. Sizing of the stent in terms of the width and length is usually determined by clot location and length as well as estimation of parent vessel size. Pre-procedure CT angiography with multi-phase imaging for collateral evaluation is sometimes extremely useful in determining the distal end of the clot and thus the size of the distal vessel and length of the clot. The use of longer stent is preferred to ensure stable capture and clot-stent integration at retrieval. Stents are usually placed for a few minutes to allow for clot-stent integration. Sometimes partial re-sheathing of the stent will assist in stable clot-stent interface during retrieval.

The use of a combined aspiration and stent retrieval thrombectomy is being used increasingly wherein a coaxial technique is used to deliver an intermediate catheter (0.060” to 0.070” inner lumen) proximal to the clot, and the stent delivery catheter is placed distal to the clot.27, 28, 41 The stent is then advanced through the stent delivery microcatheter distal to the clot. The added support from the intermediate catheter intended for aspiration makes it easier to advance the stent through the microcatheter. Once the stent is delivered and temporary flow restoration is re-established, the stent delivery microcatheter is withdrawn entirely from the system. This helps in achieving optimal aspiration through the intermediate catheter (Figure 6). The entire system is withdrawn as a system while maintaining aspiration through the intermediate catheter. Sometimes larger bore aspiration catheters may be left in situ, in case multiple passes are anticipated in patients with tortuous anatomy.
In certain populations, there is a high prevalence of the intracranial atherosclerotic disease. There might be a clue to this on the CT angiography if there is concomitant disease elsewhere. A tapered appearance to the occlusion and comparison to prior imaging if available are beneficial as well. In such cases, re-occlusion following thrombectomy may require intracranial angioplasty or even stenting for durable reperfusion. Various intracranial stents for specific indication in atherosclerotic disease are available in both balloon expandable and self-expanding platforms. Control angiography at the end of the procedure is used to document reperfusion and to evaluate for any angiographic complications. In case of suspected complications, intra-procedural cone beam CT may be used to determine the degree of hemorrhage/extravasation or for any mass effect or midline shift.

Cervical carotid disease

In cases with a proximal cervical carotid atherosclerotic disease it might be necessary to simultaneously treat the cervical disease at the time of the thrombectomy procedure. In cases with complete carotid occlusion at the carotid bifurcation the system may be carefully advanced beyond the occluded segment with gentle wire manipulation. In some case, aspiration through the guiding catheter or an intermediate system might be useful in debulking the clot. This can sometimes be anticipated based on information from the pre-procedure CTA, and sometimes the distal aspect of the cervical carotid ICA may be visualized on later stages of a multi-phase acquisition. This can be quite useful in estimating the clot burden. In cases of suspected dissection based on mechanism and pathophysiology, extra care should be taken to traverse the occluded segment. There might be clues to this on the CT angiography as well such as visualization of a flap with thrombi or mid-segment cervical ICA occlusion. Sometimes there is excessive calcification at the level of the carotid bifurcation. This might require angioplasty to advance the guiding catheter into the cervical carotid artery. In some cases, stenting might be required to enable satisfactory placement of the guiding catheter for optimal intracranial access. Ideally, definitive therapy of cervical carotid disease should be deferred to a second procedure. Certain patients may be candidates for carotidendarterectomy, angioplasty alone may be enough to sufficiently revascularize the carotid stenosis in some, and in patients with stenoses resistant to angioplasty, stenting maybe required. Management of antiplatelet therapy can be challenging depending on the extent of ischemia and outcome of intracranial revascularization.

Challenges in Acute ischemic stroke treatment

Although there are numerous challenges in existing pathways and systems for acute ischemic stroke treatment, many are unique in the setting of the new era of endovascular thrombectomy. Some of the questions regarding the treatment of patients beyond existing time windows have been investigated and are being put into practice guidelines based on recent late window trials. Imaging selection remains crucial in that paradigm. Another critical question is the use of the appropriate type of patient sedation and anesthesia in the stroke patient. While traditionally Neuro-angiography procedures were almost always performed in a controlled environment and a fully anesthetized patient, that needs to be balanced with the need for rapid recanalization and avoidance of unnecessary delays in treating patients. There is also increasing debate regarding hemodynamic changes associated with a general anesthetic in the general setting without specific attention to the physiological characteristics in the stroke patient.

Some of the technical and procedural challenges for endovascular therapy have been alluded to in the sections above. Smaller stent retrievers are already in place for distal vessels beyond an ICA terminus or MCA main trunk. However, the incremental gains from going ever more distal in the intracranial vasculature need to be balanced by the procedural risks involved (Figure 7).

The question of simultaneously revascularizing the cervical carotid disease has been alluded to above, however there is extreme variability in the real world and no apparent consensus as to the exact methodology and technique as well as the algorithms for managing antiplatelet therapy in the peri-pro-
The official Journal of Cardiological Society of India, Kerala Chapter

January – June 2019, Volume – 8    Issue – 1

Numerous studies are ongoing comparing the recanalization efficacy of a direct aspiration as a first pass technique versus primary stent retriever thrombectomy as well as procedural and clinical outcomes.28, 44 As mentioned in the sections above a combined approach with aspiration and simultaneous use of stent retrieval devices are being increasingly used. In many situations, the decision is made on a case by case basis with significant influence from practitioner preferences. Ongoing improvements in device development and stent design allow for the use of safer devices for intracranial use and improved recanalization rates while minimizing the complication rates. Some of the challenges relating to vascular access have been described above, and non-femoral access such as trans-radial / trans-brachial or even direct carotid puncture might be useful in the appropriate setting.32, 33 Innovative techniques using imaging-guided access might be needed in certain situations.45

Other challenges include EVT in distal occlusions or in the setting of stroke patients with documented large vessel occlusion with mild stroke scale scores at presentation.19, 46 Use of newer thrombolytic agents such as tenecteplase and ongoing research in the use of ancillary use of neuroprotective agents are looking at improved clinical and imaging outcomes in the era of modern endovascular thrombectomy. 47-49

The future of clinical care in the modern era of endovascular therapy for acute ischemic stroke patients looks promising. However, there remains much work to be done to ensure timely and adequate treatment to all patients who are potential candidates for treatment.

References:


Endovascular thrombectomy for acute ischemic stroke

Background:
Acute ischemic stroke is an important cause of disability. Embolic stroke is a dreaded complication of atrial fibrillation. Intravenous thrombolysis has been the cornerstone of treatment of acute ischemic stroke, presenting within 4.5 hours of onset of symptoms. About 50% of patients who receive thrombolysis are still severely disabled or dead. Delays in recanalization & hemorrhagic transformation are recognized limitations of IV rtPA. Endovascular thrombectomy with stent retrievers has evolved as an important minimally invasive procedure which has shown to improve functional disability in anterior circulation strokes. Here we describe a case of acute stroke treated with endovascular approach.

Case:
57 year old gentleman, hypertensive since last 4 years on telmisartan, has history of surgical closure of ostium secundum atrial septal defect in 1997, presented with palpitations at rest since 2 hours. Initial ECG showed atrial flutter with 2:1 conduction, which degenerated into atrial fibrillation. (Figure 1a&b). He developed dyspnea after admission. Chest X ray revealed pulmonary venous hypertension and prominent interstitial shadows suggestive of early pulmonary edema. Bedside echo showed concentric left ventricular hypertrophy with good LV systolic function. There was no residual shunt at atrial level and resting PA pressure estimated from TR velocity was 34mmHg. He was cardioverted with synchronized DC shock 100J. Patient remained asymptomatic over subsequent 2 days and was discharged on oral metoprolol, telmisartan & amlodipine. Since his CHA2DS2-VASc score was 1 and was cardioverted within 2 hours of onset of AF, oral anticoagulation was not considered. 3 days after discharge, he was readmitted with palpitations at rest. ECG showed AF with fast ventricular response. He was hemodynamically stable during the second admission. Patient was started on intravenous amiodarone with aim of pharmacological cardioversion. 2 hours after admission, he developed sudden onset of weakness of right half of body with global aphasia. Emergency neurology service was activated. Initial neurological evaluation revealed dense right sided hemiplegia suggestive of proximal left middle cerebral artery occlusion. NIHSS score was 24.

Further evaluation:
Patient underwent urgent MRI + angiogram. MRI showed no bleed. MRA revealed occlusion of left middle cerebral artery at M1 level. (figure2)

Procedure:
He was initiated on standard protocol intravenous tPA from imaging suite. A combined neurocardio team decided about possibility of endovascular thrombectomy. Patient was transferred to cath lab for endovascular thrombectomy. Right femoral access. Left carotid angiogram showed totally occluded left MCA at M1 level. (figure3) Left carotid was engaged with 7JR4 guide. Occluded segment was crossed...
with 0.012” X 200cm hybrid wire. Microcatheter was thread-
ed over the wire and parked distal to the occluded seg-
ment. Guide wire was removed and check angiogram con-
firmed distal location of the microcatheter. ( figure4a&b).
A 4X20mm stent retriever was backloaded onto microcath-
eter. Retriever was deployed across the occluded segment
by withdrawal of microcatheter,( Figure 5) Stent retriever
was then pulled back into guide after 2 minutes. (Figure 6)
Repeat angiogram showed good filling of distal MCA and
branches (TICI grade 3).(figure7)

Course in hospital:
There was immediate improvement of motor power of right
upper & lower limbs from grade 0 to 3. Aphasia improved
over ensuing days and had minor word finding difficulty at
time of discharge, Motor power was grade 5 on day 7. He
was initiated on oral apixaban from day 7 .Discharged on
day 7 with NOAC, metoprolol, telmisartan& amlodipine.

Comments:
1) Cardioembolic strokes associated with AF often causes
proximal vessel occlusion and large strokes
2) Performance of endovascular thrombectomy in combi-
nation with intravenous rtPA within 4.5 hours of presenta-
tion of ischemic stroke is associated with improved
neurological outcomes

3) During initial presentation, oral anticoagulation wasn’t
considered since CHA2DS2VASc score was 1. Studies have
shown that presence of risk enhancing features like LV hy-
pertrophy, ethnicity ( south Asians are prone for embolic
complications), CKD, elevated biomarkers echocardi-
ographic indices of LAA emptying velocity should prompt
consideration of OAC even in those patients with low scores.

References :
1) Del Zoppo GJ, Saver JL, Jauch EC, et al., for the Ameri-
can Heart Association Statistics Committee and Stroke
Statistics Subcommittee. Expansion of the time window
for treatment of acute ischemic stroke with intravenous
tissue plasminogen activator: a science advisory from
the American Heart Association/American Stroke Asso-

2) Albers GW, Bates VE, Clark WM, et al. Intravenous tis-
sue-type plasminogen activator for treat- ment of acute
stroke: the Standard Treatment with Alteplase to Re-

3) Powers WJ, Derdeyn CP, Biller J, et al., for the American
Heart Association Stroke Council. 2015 AHA/ASA focused
update of the 2013 Guidelines for the Early Management
of Patients With Acute Ischemic Stroke Regarding Endo-
vascular Treat- ment: a guideline for healthcare profes-
sionals from the American Heart Association/American
Figure 4
a & b: Microcatheter parked distal to occluded segment. Figure 3b showing injection through microcatheter confirming distal position

Figure 5:
4x20mm retriever deployed across the lesion (arrows depict the markers at two ends of the stent retriever)

Figure 6: Stent retriever with trapped embolized clot

Figure 7:
Final angiogram after removal of stent retriever on right showing TICI grade 3 flow in distal left middle cerebral branches
Image Challenge

Echo Quiz
This is the pulmonary artery pulse wave Doppler of a 30 year old lady with CHF. What are the finding? Each deflection in spectral Doppler denotes something which gives a clue to the hemodynamics.
Echo Quiz: Explanation

Interesting finding in this Doppler tracing is the antegrade flow into the pulmonary is not only in systole but also in diastole, to be precise in late diastole, immediately after the P wave on ECG which is a surrogate for atrial contraction. This happens when the RV end diastolic pressure is very high (higher than the pulmonary artery diastolic pressure at that point in time, causing the pulmonary valve to open). If it was a disease affecting the left side of the heart, pulmonary artery diastolic pressure would have been high or at least normal. Hence there should be a combination of normal or low pulmonary artery diastolic pressure and very high RV end diastolic pressure. This lady had isolated right ventricular endo myocardial fibrosis which satisfied both conditions. This could happen in any situation where there is isolated stiff RV.
A simplified approach to wide complex tachycardia in emergency room

A wide QRS complex tachycardia (WCT) is defined as a rhythm with a rate more than 100 per minute with a QRS duration more than 120 milliseconds. The differential diagnosis of a regular, monomorphic wide QRS complex tachycardia is a diagnostic dilemma in emergency room. The proper recognition of the mechanism of WCT is vital not only for acute arrhythmia management, but also for the prognosis and chronic management of the patient. Despite the published numerous ECG algorithms and criteria, the accurate and timely diagnosis in patients with WCT is not straightforward. Many of these ECG criteria are complicated and difficult to recall in an urgent setting. Aim of this article is not to have a comprehensive review of all the complex algorithms but to simplify the assessment in emergency room. The various morphological criteria are avoided purposefully in this discussion since they are not easy to recollect and are complex for most. A relatively simple approach involving 8 steps, focussing on electrophysiological basis of wide complex tachycardia is attempted. Readers are requested to refer to the standard algorithms1,2,3 elsewhere if a comprehensive review is needed. (Refer: Figure 1 - Annexure)

Step 1: Remember a little bit of statistics!

The most common cause of WCT is ventricular tachycardia (VT), which accounts for up to 80% of cases4-7Supraventricular tachycardia (SVT) with aberrant conduction is the secondmost common cause of WCTs, accounting for 15-20% of WCT cases (Table 1). Aberrant conduction refers to widening of the QRS complex due to conduction delay or block along the bundle branches or fascicles. This conduction delay or block could be pre-existent bundle branch block (BBB) or functional, when the BBB is rate dependent (usually tachycardia-dependent). Less commonly conduction delay or block can occur intra-myocardial, due to slowed muscle-to-muscle conduction, as in ventricular hypertrophy, cardiomyopathy and certain congenital heart diseases4,5,8,9 Preexcited SVT (SVT with anterograde conduction over an accessory pathway) is another cause of SVT with wide QRS. It includes antidromic AV reentrant tachycardia (AVRT) with anterograde conduction over a typical or atypical (eg: Mahaim fibre) bypass tract. It also includes AV nodal re-entrant tachycardia (AVNRT), atrial tachycardia or atrial flutter with anterograde conduction over an accessory pathway functioning as a bystander. Ventricular paced rhythm, drugs like class IA, IC, Class III anti arrhythmic agents and electrolyte disorders (eg: hyperkalemia) can also present as WCT. However, pre excited SVTs, drugs, paced rhythms, and electrolyte disorders constitute only a minority of WCTs, and are seen typically in less than 5% of cases. Because the majority (95%) of WCTs are either VT or SVT with aberrant conduction, the main focus of this discussion is to distinguish VT from SVT with aberrant conduction. Remember that when we diagnose VT in a WCT case, we are going to be correct 75-80% of the time and when we diagnose SVT, we will be correct 15-20% of the time! And also note that, a WCT in a patient with history of coronary artery heart disease or heart failure is going to be VT in more than 95% of the time!
Step 2: History and clinical examination do give some clue

Older patients and those with a history of coronary heart disease or heart failure are likely to have ventricular tachycardia, whereas, younger patients and those with long duration of symptoms are more likely to have SVT. Although VT is more likely than SVT to cause hypotension and hemodynamic instability, the hemodynamic stability of a patient does not distinguish VT from SVT, because a significant proportion of patients with VT and most patients with SVT are hemodynamically stable. It is important to note that a patient with structurally abnormal heart (For example: Severe AS, Post Fontan etc) can present with hemodynamic collapse even with SVT. A careful history regarding intake of class IA, IC, III drugs and digoxin is to be obtained. Physical findings that indicate the presence of AV dissociation suggest VT with a very high likelihood. These findings include variable intensity of the first heart sound and the presence of irregular “Cannon” A waves in jugular venous pulse. Irregular Cannon waves occur due to occasional simultaneous atrial and ventricular contraction during AV dissociation. “Cannon” A waves should be distinguished from “frog sign” (Regular, Cannon waves) which occurs during every heart beat due to simultaneous atrial and ventricular contraction that is usually seen in AVNRT and junctional tachycardia. Valsalva manoeuvre, carotid sinus massage or adenosine administration may facilitate the elucidation of WCT mechanism. The termination of tachycardia with these strongly suggests SVT (AVNRT or AVRT). However, VT due to triggered mechanism such as idiopathic outflow tract VT may also be terminated with these manoeuvres.

Step 3: Learn the basic principles behind the major electrocardiographic criteria and apply them to the ECG. (Table 2)

A. If the morphology of the WCT QRS complex fits with typical BBB or fascicular block, the WCT is caused by SVT with aberrancy. If there is no combination of BBB or fascicular blocks that could result in the particular QRS morphology, the WCT is caused by VT or pre-excited SVT.

B. Most VTs are associated with slow initial ventricular activation close to the site of origin due to slow muscle-to-muscle conduction, which results in a more significantly prolonged QRS duration or time to the intrinsicoid deflection, compared to SVT.

C. The relative fastness of initial and terminal ventricular activation is different during SVT with aberrancy and VT. During VT with aberrancy, the initial activation is always fast, because it occurs via the normal His-Purkinje system, and the conduction delay causing the wide QRS occurs in the mid to terminal part of the QRS. During VT the initial ventricular activation is usually slower due to initial muscle to muscle conduction.

D. During SVT with aberrancy, both the initial rapid septal activation (which can be either left-to-right or right-to-left) and the later main ventricular activation wavefront proceed in a direction away from lead aVR yielding a negative or predominantly negative QRS complex in lead aVR. Hence, an initial R or Rs wave cannot be present in lead aVR in a patient with SVT with aberrancy. And the same explanation leads to the assumption that a northwest QRS axis (between +180 degrees and -90 degrees)
degrees) cannot be present during SVT with aberrancy. In addition, this propagation pattern should give rise to an R wave at least in one or several precordial leads during SVT. Therefore the absence of RS complex in the precordial leads strongly suggests VT.

E. The direction of initial septal activation and that of the main ventricular activation wave front during sinus rhythm or SVT are different and results in both positive and negative QRS complexes in different precordial leads. Hence, concordance of the QRS complexes in the precordial leads strongly suggests VT. This finding is very specific for VT (>90%); but seen in only <20% VTs.

F. The presence of AV dissociation (Dissociated P waves, AV ratio <1
VA block (VA ratio >1)
Fusion beats
Capture beats

G. Tell-tale evidence of two foci (sinus and ventricular) like capture beat and fusion beat confirms VT.

Table 2 – Useful traditional ECG criteria for the differentiation of WCTs in emergency room.

| QRS duration | >160 ms with LBBB pattern or >140 ms with RBBB pattern suggests VT
| QRS axis | Right superior (northwest) axis (from -90 degrees to +180 degrees) favours VT
| RBBB pattern with left axis deviation (to the left of -30 degrees) suggests VT
| LBBB pattern with right axis deviation (to the right of +90 degrees) suggests VT
| QRS axis shift >40 degrees between sinus rhythm and WCT suggests VT
| RBBB pattern with a normal axis suggests VT

| Precordial QRS concordance | Positive or negative concordance suggests VT

| AV dissociation (suggestive of VT) | Dissociated P waves
| AV ratio <1
| VA block (VA ratio >1)
| Fusion beats
| Capture beats

Step 4: Look at lead aVR.
(The aVR Vereckei Algorithm)

The following criteria are analysed in lead aVR10. (Figure 2)

A. The presence or absence of an initial R wave

B. Presence or absence of an initial r or q wave of >40 ms width

C. Notching on the descending limb of a negative onset, predominantly negative QRS complex

D. vi/vtratio (See below for description). When any of the first three criteria of the algorithm is met, a diagnosis of VT is made and the analysis is stopped at that step. In the 4th step, a vi/vt <1 diagnosed VT, and if vi/vt is >1 a diagnosis of SVT is made.
because the range of the resultant QRS vector that yields an initial R wave in lead aVR is between -60 degrees and +120 degrees whereas traditional north west axis refers to -90 degrees to +180 degrees. The initial ventricular activation wave front via conduction system of heart during SVT and sinus rhythm should go away from lead aVR yielding a negative QRS (QS) complex. Thus, an initial dominant R wave (such as R or Rs complex) in lead aVR is not normally present in SVT with aberrancy and supports a diagnosis of VT. Similarly notching on the descending limb of a negative onset, predominantly negative QRS complex suggests initial activation wave front does not go through the conduction system of heart but initiates in the relatively slowly conducting ventricular myocardium. This also suggests a diagnosis of VT rather than SVT.

**Vi/Vt Ratio**

The vi/vt criterion is based on the estimation of initial (vi) and terminal (vt) ventricular activation velocity ratio (vi/vt) by measuring the vertical excursion (in millivolts) recorded on the ECG during the initial (vi) and terminal 40 ms (vt) of the QRS complex. (Figure 3) The rationale behind the vi/vt criterion is that during WCT due to SVT the initial activation of the septum should be invariably rapid over the normal His-Purkinje system and the intra-ventricular conduction delay causing the wide QRS complex occurs in the mid to terminal part of the QRS. Thus, the vi/vt ratio is>1 during a SVT. During WCT due to VT, however, an initial slower muscle- to-muscle spread of activation occurs until the impulse reaches the His-Purkinje system, after which the rest of the ventricular muscle is more rapidly activated, thus, the vi/vt ratio is<1 during a VT.
Step 5: Look at lead II.
(R-wave Peak Time – RWPT - Criterion)

In a wide complex tachycardia, the time taken from the QRS onset to the peak of the first positive or negative wave measured in lead II, when >50 ms suggests VT, and when <50 ms suggests SVT. (Figure 4)

This criterion also makes use of the fundamental difference in initial activation pattern between a VT and SVT very similar to aVR criteria.

Step 6: Look at Lead V1 to decide whether LBBB or RBBB wide complex tachycardia. Have a check list for differential diagnosis for LBBB tachycardia as well for RBBB tachycardia

This step helps to refine the differential diagnoses further and gives clues to anatomic localisation of tachycardia origin. (Table 3) Ventricular tachycardia of LBBB morphology suggests origin from right ventricle and positive QRS in inferior leads (II,III,AVF) localises VT to out flow tract (RVOT VT). QRS axis other than right inferior axis in LBBB morphology VT should prompt suspicion of ARVD. A careful examination of basal ECG and echo for evidence of ARVD is mandatory. If in doubt, a cardiac MRI should be ordered.

Similarly VT of RBBB morphology localises the ventricular tachycardia to left side of heart and a positive QRS in II,III, AVF suggests LVOT origin. A relatively narrower QRS and negative QRS in inferior leads suggest posterior fascicular VT. Positive QRS in all precordial leads suggests mitral annular VT and deep S waves in V5-V6 may suggest papillary muscle VT.

Bundle branch re-entry VTs can have both LBBB and RBBB morphology and are usually seen in patients with cardiomyopathy and diseased conduction system. Scar VTs can be of LBBB or RBBB morphology and many a times, multiple morphologies of VT can occur in the same patient. A history of coronary artery disease, or heart failure will clinch the diagnosis. Sarcoidosis is an important differential diagnosis which can present with multiple morphologies of scar VT.

It is useful to be familiar with ECG features of common idiopathic VTs occurring in structurally normal heart and the pattern recognition (For example: LBBB tachycardia with inferior axis – RVOT VT, RBBB tachycardia with left axis – PFVT) helps in easy identification of tachycardia in emergency room.

Detailed description of localisation of accessory pathways, SVTs and Mahaim fibre tachycardia is beyond the scope of this chapter and readers are advised to refer to standard text books for the same.

Step 7:
Remember about irregular wide complex tachycardia

Most commonly a Fast, Broad, Irregular tachycardia (Remember as FBI) occurs due to atrial fibrillation and bundle branch block. However, considering the potential for degenerating to VF, recent guidelines suggest to consider any Fast Broad Irregular tachycardia as atrial fibrillation conducted via accessory pathway (AF with WPW syndrome). Prompt DC version is needed and pre excitation in the basal ECG will confirm the diagnosis.

Polymorphic VT can be irregular but, is not discussed here. Occasionally monomorphic VT due to triggered activity/automaticity can present as irregular WCT. In addition, VTs can be irregular in the initial few seconds of its onset and also when affected by antiarrhythmic drugs.

Step 8:
Importance of sinus rhythm ECG

If the patient has a previous basal ECG with him at the time of presentation, examine it meticulously. It may give a clue to the nature of WCT. Basal ECG after conversion of WCT also gives valuable information on the aetiology of tachycardia.

<table>
<thead>
<tr>
<th>LBBB tachycardia</th>
<th>RBBB tachycardia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular tachycardia</td>
<td>Ventricular tachycardia (Fascicular VT, LVOT VT, Mitral annular VT, Papillary muscle VT, Bundle branch re-entry VT, scar VT)</td>
</tr>
<tr>
<td>(RVOT VT, VT in ARVD, Bundle branch re-entry VT, scar VT)</td>
<td>SVT with fixed or functional RBBB</td>
</tr>
<tr>
<td>SVT with fixed or functional LBBB</td>
<td>Left sided pathway mediated anti-dromic tachycardia</td>
</tr>
<tr>
<td>Mahaim fibre tachycardia</td>
<td>SVT with a left sided bystander pathway</td>
</tr>
<tr>
<td>Right sided pathway mediated anti-dromic tachycardia</td>
<td>SVT with a right sided bystander pathway</td>
</tr>
</tbody>
</table>

Table 3 – Differential diagnosis of wide complex tachycardia according to morphology in V1
Look for pre-existing BBB- Similar QRS morphology suggests SVT with aberrancy whereas different morphology suggests VT

Look for delta wave- A similar morphology of WCT suggests anti-dromic AVRT/pre-excited SVT

Look for QRS axis- A shift >400 suggests VT

Look for markers of VT substrate- pathological Q waves of MI, epsilon waves in ARVD

Look for QRS width- A WCT narrower than the sinus rhythm suggests VT

Above discussion is to simplify the approach to wide complex tachycardia in an emergency room. However, it has to be remembered that no criterion is to be applied in isolation. All the described algorithms in literature are meant to distinguish between VT and SVT with aberrancy. It is very difficult to distinguish VT from pre-excited SVT because in both cases, ventricular activation begins outside the normal intraventricular conduction system. Pre-excited SVT using a typical AV bypass tract behaves as a VT originating from the base of the ventricles. Among the various criteria mentioned above, initial R wave in lead aVR is possibly the only helpful criterion which may help to rule out pre-excited SVT and suggest VT. Luckily pre excited SVTs are rare. Exact identification of a WCT could be difficult occasionally and when in doubt, treat any wide complex tachycardia as VT. Similarly any wide complex tachycardia in a patient with structurally abnormal heart or history of coronary artery heart disease should be treated as VT.

In an unstable patient, it is important to cardio-vert the patient first and think later. At the same time, in a stable patient, we should make every effort to reach the correct diagnosis before treatment.

References


Figure 1

Approach to wide complex tachycardia – ACC/AHA/ESC algorithm.
A 61-year-old male presented elsewhere in December 2016 with an episode of syncope strongly suggestive of arrhythmia. His evaluation at that time showed a left ventricular ejection fraction (LVEF) of 40%, regional wall motion abnormalities (RWMA) in multiple areas of the left ventricle (LV), and normal coronaries. He was treated with beta blockers and angiotensin receptor blockers for dilated cardiomyopathy, and also drugs for late onset seizures. In July 2017, he presented to the same center with an episode of self-terminating presyncopal palpitation. Amiodarone was added to the treatment regime for possible ventricular arrhythmia, and he was implanted with a single chamber implantable cardioverter defibrillator (ICD) (Boston Scientific Inogen VR). He presented to our center in December 2017 for further evaluation, at which time he was asymptomatic. His echocardiogram showed LVEF, LV end diastolic volume (LVEDV), and LV end systolic volumes (LVESV) of 43%, 130 cc and 74 cc respectively, and severe hypokinesia of the entire posterolateral LV. No episodes of arrhythmia were recorded in the ICD. The ECG showed fractionated QRS (fQRS) complexes in inferior leads and lead aVL (Figure 1). This clinical picture - the combination of likely ventricular arrhythmia, reduced LVEF, RWMA not due to coronary artery disease, and fQRS in the region of RWMA suggestive of a mid-myocardial scarring process - was strongly suggestive of an inflammatory cardiomyopathy. Hence he underwent an 18F-FDG PET CT scan from the neck to the abdomen to evaluate for any myocardial inflammation, and any extracardiac focus of hypermetabolism. This showed focal uptake in the basal LV; there was no significant extracardiac uptake. (Figure 2). The same areas showed perfusion defects in a resting 13N-NH3 scan. His Mantoux test was negative. There was no clinical or radiological (chest X-ray, CT scan) evidence of extracardiac disease. Considering that active disease was likely limited to the lateral wall of the LV, an endomyocardial biopsy was not attempted. A diagnosis of arrhythmogenic inflammatory cardiomyopathy (AIC), possibly active cardiac sarcoidosis (CS) was made, and medical therapy was started. Amiodarone was stopped, and he was administered oral Prednisolone 60 mg/day for one month, which was tapered and stopped over the next five months. By February 2018, his LVEF, LVEDV and LVESV had improved to 52%, 108 cc, and 55 cc respectively, though the RWMA persisted. He was advised a repeat 18F-FDG PET CT after 6 months of therapy, which he declined. He presented on 25 July 2018 with three ICD shocks over the past three days. ICD interrogation revealed 13 episodes of ventricular tachycardia (VT) since 22 April 2018, seven of which were terminated by anti-tachycardia pacing (ATP); 7 of the episodes had occurred over the past 3 days, indicating an increasing frequency of VT. (Figure 3) He was initiated on oral Amiodarone 200 mg twice daily, and was scheduled for a repeat 18F-FDG PET CT to evaluate for reactivation of myocardial inflammation. The ICD was programed to deliver therapies for VTs 170 bpm, and record VTs from 140 bpm in a monitor zone. He experienced two more ICD shocks on 26 July 2018 evening, and was admitted late night on 26 July 2018 with heart fail-
ure. At admission, he was in slow VT at 153 bpm which was not treated by the ICD. (Figure 3). This episode of VT had a morphology consistent with a posterolateral LV exit. (Figure 4). Considering that this was the same area involved by inflammation previously, it was reasonable to consider an exacerbation of myocardial inflammation as the possible cause of this VT. Accordingly, he was initiated on enhanced immunosuppression in the form of intravenous (IV) Methylprednisolone 1 gm/day for three days. Simultaneously, he was administered IV Lidocaine, which terminated the VT within 30 minutes. Lidocaine was stopped after a few hours due to bradycardia resulting in VVI pacing and hypotension. Amiodarone was withheld next day due to slightly elevated transaminases.

The dose of oral Metoprolol was increased from the previously administered dose of 50 mg twice daily to 150 mg/day. He remained in sinus rhythm, except for another episode of slow VT of the same morphology on 28 July 2018 morning, which promptly reverted to sinus rhythm after a bolus of Lidocaine which was not followed up with an infusion. After three days of IV Methylprednisolone, he was re-initiated on oral Prednisolone 60 mg/day for one month, followed by a repeat 18F-FDG PET CT guided taping schedule. The follow up 18F-FDG PET CT performed on 11 December 2018 showed complete resolution of myocardial inflammation. (Figure 5). A steroid sparing regime of oral Methotrexate was gradually introduced as per a previously described protocol. He remained VT free until December 30, 2018.

On 31 December 2018, he presented with recurrent VT at 190 bpm requiring three ICD shocks over two days. Considering the findings of the recent 18F-FDG PET CT, it was unlikely that these VTs were due to myocardial inflammation. He was initiated on IV Amiodarone, and remained VT free till 3rd January 2019. Despite beta blockers, Amiodarone and IV Lidocaine, he experienced 14 episodes of rapid VT on 3rd January 2019, 10 of which required ICD shocks for failed ATP, and another 10 episodes on 4th January 2019, 3 of which required ICD shocks for failed ATP. He underwent radiofrequency ablation for VT on January 9, 2019. Endocardial substrate map of the right ventricle (RV) was normal. Endocardial substrate map of the LV showed a large mid posterior wall scar without any late potentials. (Figure 6A).

A posteriorly directed percutaneous subxiphoid epicardial access was obtained under general anaesthesia. (Figure 7) Epicardial substrate map of the LV showed a large mid posterior wall scar, separated from a smaller basal posterior wall scar by a channel of relatively preserved voltage. (Figure 6B) An area of late potentials was identified at the border of the epicardial scar. (Figure 8) Programmed extrastimulation at baseline induced short runs of self terminating VT. Irrigated epicardial radiofrequency ablation was done to connect the basal LV scar to the annulus, transect the channel between the two epicardial scars, ablate the late potentials, encircle the mid posterior wall scar, and ablate areas of low voltage electrograms within the scar. (Figure 9). Irrigated endocardial radiofrequency ablation was performed to connect the annulus to the basal LV scar. Post radiofrequency ablation, programmed extrastimulation at baseline and on Isoprenaline reached VERP using a four extrastimulus protocol without inducing non sustained or sustained VT. There have been no episodes of VT at follow up till 13 April 2018. Amiodarone was stopped 1 month post radiofrequency ablation, and the patient is currently on Metoprolol and Methotrexate.

DISCUSSION

This case, where VT due to both the inflammatory and the scar phases of AIC was managed differently, serves to illustrate multiple facets regarding the diagnosis and management of this entity. AIC, defined as focal myocardial uptake on 18F-FDG PET CT causing ventricular arrhythmia (VA), was the cause of VA in 49% of patients in a cohort of patients (n=103) with unexplained cardiomyopathy at a referral center.2 One of the common causes of AIC is cardiac sarcoidosis, which was diagnosed in 36% of cases of AIC in the index report.2 Many of the diseases causing AIC have to be labelled so due to lack of an appropriate tissue for histological diagnosis. Many of them cause granulomatous myocardial inflammation leading to typically non endocardial myocardial scars. Clinically, many of them have a similar presentation, in that they often cause an inflammatory phase and a scar phase, either of which may be responsible for VA.2,5,6 These diseases can be diagnosed based on multiple clues including the following: 1) Unexplained areas of focal uptake on 18F-FDG PET CT, 2) Non endocardial scars on contrast MRI not corresponding to a coronary artery distribution, 3) Association of VT with AV block and/or LV dysfunction.2 In addition, considering that cardiac sarcoidosis is probably the most common cause of AIC, some findings described in cardiac sarcoidosis may serve as clinical clues towards suspecting AIC. These findings include:1) Presence of pleomorphic VT, 2) Recurrence of VT of a morphology different from the index morphology, 8, and 3) Presence of fQRS complexes during sinus beats1. A tissue diagnosis should be sought for in all cases of AIC, and infective causes like myocardial tuberculosis should be ruled out. However, in those cases where a tissue diagnosis cannot be established, it may be reasonable to apply the same treatment principles as outlined for cardiac sarcoidosis, where in VTs due to the initial inflammatory phase and recurrence of inflammation are managed by immunosuppression, and VTs due to the scar phase are managed by radiofrequency ablation in addition to medical therapy.9 Similar to cardiac sarcoidosis, AIC too, seems to have a reasonably good prognosis if therapy is instituted in the early phase of disease wherein the LVEF is relatively preserved.2,8,10
Figure 1. QRS fractionation in leads II, III, aVF and aVL (arrows)

Figure 2. Focal increase in 18F-FDG uptake in the basal lateral LV (arrows)

<table>
<thead>
<tr>
<th>Episode no.</th>
<th>Date and time</th>
<th>Type of episode</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-18</td>
<td>27 Jul 2018 00:19</td>
<td>VT-1</td>
<td>No Therapy</td>
</tr>
<tr>
<td>V-17</td>
<td>27 Jul 2018 01:01</td>
<td>VT-1</td>
<td>No Therapy</td>
</tr>
<tr>
<td>V-16</td>
<td>26 Jul 2018 16:02</td>
<td>VT-1</td>
<td>ATPx4, 26J</td>
</tr>
<tr>
<td>V-15</td>
<td>26 Jul 2018 14:07</td>
<td>VT-1</td>
<td>ATPx4, 26J</td>
</tr>
<tr>
<td>V-14</td>
<td>25 Jul 2018 21:54</td>
<td>VT-1</td>
<td>ATPx3</td>
</tr>
<tr>
<td>V-13</td>
<td>24 Jul 2018 03:06</td>
<td>VT</td>
<td>ATPx3, 41J</td>
</tr>
<tr>
<td>V-12</td>
<td>23 Jul 2018 00:24</td>
<td>VT</td>
<td>ATPx3, 41J</td>
</tr>
<tr>
<td>V-11</td>
<td>23 Jul 2018 00:23</td>
<td>VT</td>
<td>ATPx3</td>
</tr>
<tr>
<td>V-10</td>
<td>23 Jul 2018 00:22</td>
<td>VT</td>
<td>ATPx1</td>
</tr>
<tr>
<td>V-9</td>
<td>22 Jul 2018 23:06</td>
<td>VT</td>
<td>ATPx3, 41J</td>
</tr>
<tr>
<td>V-8</td>
<td>22 Jul 2018 23:05</td>
<td>VT</td>
<td>NoSustV</td>
</tr>
<tr>
<td>V-7</td>
<td>22 Jul 2018 23:05</td>
<td>VT</td>
<td>ATPx1</td>
</tr>
<tr>
<td>V-6</td>
<td>02 Jul 2018 19:53</td>
<td>VT</td>
<td>ATPx3</td>
</tr>
<tr>
<td>V-5</td>
<td>06 Jun 2018 23:53</td>
<td>VT</td>
<td>ATPx3, 41J</td>
</tr>
<tr>
<td>V-4</td>
<td>04 May 2018 19:19</td>
<td>VT</td>
<td>ATPx3</td>
</tr>
<tr>
<td>V-3</td>
<td>28 Apr 2018 17:04</td>
<td>VT</td>
<td>ATPx3</td>
</tr>
<tr>
<td>V-2</td>
<td>28 Apr 2018 17:03</td>
<td>VT</td>
<td>ATPx1</td>
</tr>
<tr>
<td>V-1</td>
<td>22 Apr 2018 00:30</td>
<td>VT</td>
<td>ATPx3, 41J, 41J</td>
</tr>
</tbody>
</table>

Figure 3. Episodes of VT revealed by in-clinic ICD interrogation on 25 July 2018 (episodes V1-V-13), and further episodes of VT revealed at admission late night on 26 July 2018 (episodes V14-V-18). ATP = Antitachycardia pacing, 41J = VT terminated by 41 Joule shock
Figure 4. VT recorded at admission late night on 26 July 2018.

Figure 5. 18F-FDG PET CT showing resolution of initially present myocardial uptake in basal lateral LV (white arrows, left panels) after steroid therapy (right panels). This correlated with resolution of VT.

Figures 6A (left) and 6B (right). Substrate map of the LV showing regional bipolar voltages plotted on a 3 dimensional electroanatomical map. Areas with local bipolar voltage < 0.3 mV are colored grey (“scar”), and those with local bipolar voltage > 1.0 mV are colored purple (“normal area”). Areas of in-between voltage (“peri-scar area”) are colored as per the color bar depicted. Panel A, a posteroanterior view of the LV endocardium, shows a small scar near the basal posterior LV surrounded by a peri-scar area. Panel B, an anteroposterior view of the LV epicardium, shows a larger basal LV scar corresponding to endocardial scar (white arrow), a larger mid posterior LV scar (double white arrow), with an intervening channel of preserved voltage (black arrow).

Figure 7. Left anterior oblique fluoroscopic projection showing intracardiac catheters and the ICD. 1: Ablation catheter on the epicardial basal lateral LV introduced via percutaneous subxiphoid approach. 2: Endocardial ablation catheter (in the left atrium) introduced via the trans-septal approach. 3: Catheter in the coronary sinus. 4: Catheter in the RV endocardium. 5: ICD lead in the RV.
Figure 8. Late potentials in the LV epicardium during sinus rhythm (blue arrows) becoming even later during RV pacing (red arrows). Such discrete areas of late activity, typically found in peri-scar areas, often serve as the critical zones in re-entrant VT circuits.

Figure 9. Sites of epicardial radiofrequency ablation lesions, depicted as brown dots. 1: Lesion set connecting the basal LV scar to the annulus. 2: Lesion set transecting the channel of preserved voltage between the basal and mid LV scars. 3: Lesions encircling the mid LV scar and lesions delivered at sites of preserved electrograms within the dense mid LV scar. Lesions were also delivered within the circled area; this was the site where late potentials were recorded at the scar border.
REFERENCES


Sixty years old lady developed palpitations.
She sought medical attention. Her ECG is shown in Fig 1.

She had a structurally normal heart. Her biochemistry was normal. She was initiated on AV nodal blocking drugs.
She continued to have palpitation. A 24-hour holter was done.
One of the strips is shown in Fig 2.
She had to undergo ablation, as she remained symptomatic. Her ECG post ablation is shown in Fig 3.

**What is the arrhythmia, the possible mechanism, and the location?**

Fig 1. Shows paroxysms of tachycardia, atrial rate of 150 BPM, with isoelectric baseline, suggestive of focal automatic atrial tachycardia with variable conduction to the ventricle.

Fig 2. Discrete P waves and the isoelectric baselines is better discernable at slower AV conduction times. A positive or negative – positive biphasic P wave in V1 suggests left atrial origin. The P wave is positive in Tachycardia. Apart from the V1 p wave, the p waves are not distinguishable from the sinus P wave.

Fig 3; Post ablation ECG shows the V1 P waves positive – negative.

The sinus P wave being positive – negative and tachycardia P wave being positive, is suggestive of RSPV AT. (Right Superior Pulmonary Vein origin of Atrial Tachycardia)
Spontaneous Coronary Artery Dissection-A Disease of Young Males?

Background: Spontaneous coronary artery dissection (SCAD) is the separation of two of the three arterial wall layers without any apparent cause, creating a false lumen. The incidence, epidemiology and risk factors of SCAD has not been well studied in the Indian population.

Aim:
To assess the prevalence, clinical profile, risk factors, management and short term prognosis of patients with spontaneous coronary artery dissection in patients undergoing coronary angiogram (CAG) in a tertiary care center in Kerala.

Methods:
Consecutive patients who underwent CAG and diagnosed to have SCAD were included in the analysis. Demographic, risk factor and clinical profile were analyzed.

Results:
During the study period, out of 7684 patients with coronary angiograms, 28(0.36%) patients were identified to have SCAD. Males constituted 86% (n=24) of the total cases and females constituted 14% (n=4). Young males (<40 years) had the highest prevalence of SCAD (2.2%). The most common risk factor was smoking. Most of the patients presented with acute coronary syndromes (ACS, n=22, 79%) and were managed medically (n=19, 68%). After a mean follow up 8.7 months 85% of the patients remained relatively asymptomatic, whereas 3 (15%) patients had recurrent ACS.

Conclusions:
The overall prevalence of SCAD in the study population was 0.36%. In this study, SCAD was significantly more frequent in males, especially in the younger age group. Most cases presented as ACS and most were managed medically.

Key Words: spontaneous coronary dissection, coronary artery disease, acute coronary syndrome

Introduction
Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome (ACS). SCAD is the sep-
2 of the 3 arterial wall layers, creating a false lumen which may progress resulting in impairment of distal coronary blood flow and cause myocardial ischemia. When this dissection occurs in the absence of severe obstructive coronary artery disease and history of PCI, it is considered spontaneous.\textsuperscript{1,2} It is described that SCAD mainly affects women who have few cardiovascular risk factors. SCAD is associated with various pathophysiological conditions, such as pregnancy, postpartum, collagen diseases, cocaine abuse, severe hypertension, smoking, oral contraceptives, heavy exercise, or vasospasm.\textsuperscript{3,4,5} It was first described in 1931 after necropsy of a 42-year-old woman who died suddenly,\textsuperscript{6} and the first angiographic report occurred almost 50 years later, in a 55-year-old woman with acute myocardial infarction. The diagnosis of SCAD has increased recently as the use of coronary angiography has expanded. Studies on SCAD are limited to isolated case reports and few case series. Therefore its treatment and prognosis are not well established. Case reports and case series on coronary dissection from India have been few. Most cases that have been reported from India involved young men in contrast to the data from other countries.\textsuperscript{7,8,9} This prompted us to look into the epidemiological pattern of this disease in India. In this study, we sought to identify the prevalence, clinical presentation, risk factors, treatment strategies and short term prognosis of SCAD.

**Methods**

We identified all patients diagnosed to have SCAD at Government Medical College Kottayam from January 2010 to December 2013 by reviewing coronary angiograms retrospectively. Two experienced interventional cardiologists read the coronary angiograms. SCAD was identified based on the presence of an intimal flap with a false lumen, and/or stagnation of contrast media in the coronary artery wall. The clinical presentation risk factors and the treatment strategy adopted were identified from the hospital records. Six monthly follow up was carried out through outpatient visits or telephonic interviews. Patients with extensive atherosclerosis, previous PCI or history of recent chest trauma were excluded. Statistical analysis was done by SPSS 19.0 for Windows.

**Results**

**Baseline characteristics**

During the study period, a total of 7684 patients underwent CAG of which 28 cases of spontaneous coronary artery dissections were identified and confirmed. The prevalence of dissection was 0.36%. The population consisted of 4 (14%) women and 24 (86%) males. The incidence of SCAD was more in males (0.41%) compared to females (0.22%, p-value 0.001). The mean age of males was numerically lower (43.5 years) but was not statistically different from that of females (53 years, p-value 0.10). In this series, SCAD was predominantly a disease of males. Among them, the prevalence was more in those below 40 years. The prevalence in males below 40 years was 2.2% (8/362) while no case was reported in females below 40 years (p-value 0.017). Among those above 40 years in males, the prevalence was 0.29% (16/5492) while in females above

The important baseline characteristics are shown in the following table.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Males</th>
<th>Females</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAGs (number)</td>
<td>7684</td>
<td>5854</td>
<td>1830</td>
<td>0.001</td>
</tr>
<tr>
<td>SCAD –number(%)</td>
<td>28(0.36%)</td>
<td>24(0.41%)</td>
<td>4(0.22%)</td>
<td></td>
</tr>
<tr>
<td>Age (mean years)</td>
<td>47.0</td>
<td>43.5</td>
<td>53</td>
<td>0.10</td>
</tr>
<tr>
<td>Age</td>
<td>&lt; 40 years</td>
<td>8(1.3%)</td>
<td>8 (2.2%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 40 years</td>
<td>20(0.28%)</td>
<td>16(0.29%)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Table 1. Baseline characteristics
The official Journal of Cardiological Society of India, Kerala Chapter

40 years it was 0.25 (4/1559) (p-value 0.60). The important baseline characteristics are shown in the following table.

**Risk Factors and Presentation**

Smoking was the most common risk factor noted in 14 patients (50%). Diabetes Mellitus was seen in 7 (25%), systemic hypertension in 6 (22%) and dyslipidemia in 5 (18%). Eight (29%) patients had 2 or more conventional coronary risk factors. Left anterior descending artery was the vessel affected in 14 (45%) patients, Left circumflex artery in 6 (16%) and Right coronary artery in 12 (39%) patients. Most of the patients presented with acute coronary syndromes (79%). Of these 9 (32%) patients presented with STEMI and 13 (47%) patients presented with unstable angina or NSTEMI. Figure 1 shows SCAD in the mid left anterior descending artery (LAD) of a 42-year-old male presented with NSTEMI. A substantial percentage of patients presented with stable angina (21%). Conservative line of management with antiplatelet drugs, statins, nitrates and beta blockers was done in 19 (68%) patients. Eight (28.5%) patients were managed with PCI, and 1 (3.5%) patient underwent CABG.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>14 (50%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6 (22%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>5 (18%)</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>Acute coronary syndrome 22 (79%)</td>
</tr>
<tr>
<td>Management</td>
<td>Stable CAD 6 (21%)</td>
</tr>
<tr>
<td></td>
<td>Medical 19 (68%)</td>
</tr>
<tr>
<td></td>
<td>PCI 8 (28.5%)</td>
</tr>
<tr>
<td></td>
<td>CABG 1 (3.5%)</td>
</tr>
</tbody>
</table>

**Figure 1**: Left coronary angiogram in left anterior oblique cranial view (Panel A) and right anterior oblique caudal view (Panel B) showing dissection in the mid LAD.
Follow up

Follow up data is available for 24 out of 28 patients. The mean duration of follow up was 2.5 years. Three (15%) patients had acute coronary syndromes during this period. Two of these patients were in the medically managed group, and one was in the PCI group. There was no death during the 2.5 years of follow up.

Discussion

In this study, we identified 28 cases of SCAD among 7684 consecutive coronary angiograms with a prevalence of 0.36%. The prevalence in our study is more than that of previous angiographic series reporting prevalence ranging from 0.10% to 0.20%.10,11 In a prospective angiographic series with intravascular ultrasound assistance in ambiguous cases, Hering et al. reported a much higher prevalence of 11.0%.12 In our study 86% of the patients with SCAD were males, and only 14% were females. The incidence of SCAD was 0.41% in males and 0.22% in females. This is in contrast to previous studies where it was more common in females. 1,2,11 The mean age of males was numerically lower (43.5 years) but was not statistically different from that of females (53 years).

This study is also notable for the fact that no case of dissection was identified in females younger than 40 years despite 271 angiograms performed on them. In this study, the maximum incidence was noted in males younger than 40 years (2.2%). These patients had a higher incidence of smoking. In previous studies, SCAD was reported as affecting women in three fourths of the cases,11 one third of them being in the postpartum period,13 with a mean age of onset below 35 years.14 Pregnancy-associated and connective tissue associated SCAD were not identified in this study. One of the reasons for the absence of SCAD associated with pregnancy could be due to selection bias for coronary angiography. Alternatively, it could be that pregnancy-associated SCAD is not frequent in our population due to genetic or social factors. The most common traditional risk factor identified was smoking (50%). Other risk factors were less frequent than in people undergoing a coronary angiogram. The mechanism of SCAD in these patients remains mostly unclear. It is likely that many are probably atherosclerotic, as premature atherosclerosis is common in our country. Plaque inflammation and rupture may disrupt intimal-medial junction resulting in intimal flap and dissection.

The mode of presentation was as an ACS in 79% of patients, 47% with NSTEMI/UA and 32 % with STEMI. The interesting finding was that 21% of patients presented with stable angina. This is in contrast to previously held concept that SCAD almost always presents as an acute coronary syndrome.10,11

Conclusions

The overall incidence of SCAD is 0.36 % and is highest in males less than 40 years in whom it was 2.2 %. Most cases of SCAD seen in this study are in young men who smoke. In contrast to earlier studies, SCAD is rarer in women in this study. The mode of presentation is common as ACS, but it can also present as chronic stable angina. It is usually treated with medical management or PCI with good immediate and short term outcomes. We need more studies to understand the pathogenesis of this disease in the Indian population.

References


CASE REPORT

Anomalous Origin of Left Coronary Artery from Pulmonary Artery presenting with Atrial Fibrillation and Angina

ABSTRACT

Anomalous Origin of Left Coronary Artery from Pulmonary Artery (ALCAPA) is a rare congenital anomaly of coronary arteries usually presenting in early childhood. However, different types of presentation in adults have also been described. Here we present the case of a 55-year-old lady with ALCAPA. She was never diagnosed as having a cardiac disease until this age. She was a manual laborer and had three uncomplicated deliveries. She presented with paroxysmal atrial fibrillation (AF). The diagnosis was ALCAPA, made only after a coronary angiogram was done. CT angiogram confirmed the diagnosis. She opted to continue medical therapy and is being followed up. A brief review of the literature regarding ALCAPA is also added.

KEYWORDS

Anomalous Origin of Left Coronary Artery from Pulmonary Artery (ALCAPA), Atrial fibrillation (AF), CT Angiogram
The official Journal of Cardiological Society of India, Kerala Chapter

January – June 2019, Volume – 8    Issue – 1

Ischemic Heart Disease and Hypertension, Atrial Fibrillation with fast ventricular rate and mitral regurgitation was made. She was started on Digoxin, Diuretics, ACE Inhibitors, Aspirin and Atorvastatin. Amlodipine was stopped. She improved clinically. As atrial fibrillation was persisting, she was started on oral anticoagulation, Warfarin. The dose of Warfarin was titrated up, and upon reaching an INR value of 2.6, she was discharged.

One month later she was again admitted with angina, palpitation and worsening dyspnea. She was having atrial fibrillation with a fast ventricular rate. Oral Amiodarone was added to the other drugs. She had recurrent episodes of symptomatic worsening over the next two weeks along with angina. Echo picture remained the same; global reduction in contractility with moderate LV dysfunction. Because of recurring angina, acoronary angiogram was done. During coronary angiogram left coronary artery could not be cannulated. A left coronary sinus injection did not show any artery originating from the left sinus. RCA was hugely dilated and tortuous. Left coronary artery (LCA) was seen filling retrograde from the right coronary artery. LCA was draining into the pulmonary artery. (Fig 1.A, B, C, D) also, (Videos 1 to 4).

The results of salient blood investigations are given in the table below.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>12.7</td>
</tr>
<tr>
<td>Total</td>
<td>7600</td>
</tr>
<tr>
<td>ESR</td>
<td>23</td>
</tr>
<tr>
<td>RBS</td>
<td>112</td>
</tr>
<tr>
<td>S. Creatinine</td>
<td>0.9</td>
</tr>
<tr>
<td>TSH</td>
<td>2.3</td>
</tr>
<tr>
<td>Serum Sodium</td>
<td>138</td>
</tr>
<tr>
<td>Serum Potassium</td>
<td>4.4</td>
</tr>
</tbody>
</table>

nebivolol, and atorvastatin. Amlodipine and bronchodilators were continued. She was given Enoxaparin for five days. In the hospital she had one episode of palpitation. ECG at that time showed Atrial Fibrillation which reverted spontaneously. She was discharged on the above-mentioned medications with advice to follow up after two weeks.

The patient did not come for follow up and stopped her medications. One month after the first hospitalization she was again admitted with dyspnea, palpitation, and edema. On examination, she had tachypnoea and bilateral pitting pedal edema. Her pulse was 130/mt, irregularly irregular, blood pressure was 150/100 mm of Hg in the right arm, and jugular venous pressure was elevated 12cm from the sternal angle. The apex beat was not located. There was no murmur. There were bilateral rhonchi.

Her blood investigations were normal. Electrocardiogram showed Atrial Fibrillation with a fast ventricular response and non-specific ST segment and T wave changes. Chest X-ray showed mild cardiomegaly. Echocardiogram revealed left ventricular hypertrophy, a global reduction in left ventricular contractility, moderate LV dysfunction with an ejection fraction of 30% and mild mitral regurgitation. A diagnosis of cardiac failure- moderate LV dysfunction - due to Ischemic Heart Disease and Hypertension, Atrial Fibrillation with fast ventricular rate and mitral regurgitation was made. She was started on Digoxin, Diuretics, ACE Inhibitors, Aspirin and Atorvastatin. Amlodipine was stopped. She improved clinically. As atrial fibrillation was persisting, she was started on oral anticoagulation, Warfarin. The dose of Warfarin was titrated up, and upon reaching an INR value of 2.6, she was discharged.

One month later she was again admitted with angina, palpitation and worsening dyspnea. She was having atrial fibrillation with a fast ventricular rate. Oral Amiodarone was added to the other drugs. She had recurrent episodes of symptomatic worsening over the next two weeks along with angina. Echo picture remained the same; global reduction in contractility with moderate LV dysfunction. Because of recurring angina, acoronary angiogram was done. During coronary angiogram left coronary artery could not be cannulated. A left coronary sinus injection did not show any artery originating from the left sinus. Right coronary artery (RCA) was seen originating from the aorta. RCA was hugely dilated and tortuous. Left coronary artery (LCA) was seen filling retrograde from the right coronary artery. LCA was draining into the pulmonary artery. (Fig 1.A, B, C, D) also, (Videos 1 to 4).
Subsequently a CT angiogram was done. It showed RCA originating from the aorta. RCA was dilated and tortuous. Left coronary artery was seen originating from the pulmonary artery. (Fig 2.A,B,C,D). Thus a diagnosis of anomalous origin of the left coronary artery from pulmonary artery was made. The patient refused any form of surgical intervention. Her medical therapy was optimized, and she is under follow up presently.

**DISCUSSION**

In the general population, anomalies of coronary arteries may occur in around 1%. Many of these anomalies are benign and often found incidentally. However, some of these anomalies can be associated with life-threatening cardiac complications like ischemia, arrhythmias, heart failure, and even death. Anomalous origin of the left main coronary artery from the pulmonary artery (ALCAPA) is one of the anomalies with high mortality. The initial description of this anomaly came in the 1860s by Krause and later in 1885 by Brooks. However, these cases were later attributed to coronary AV fistula. The earliest complete clinical description was in 1933. Bland, White, and Garland reported a three-month-old infant who had paroxysmal attacks of acute discomfort along with profound vasomotor collapse. The ECG findings were similar to that of an adult with myocardial infarction. The autopsy confirmed the anomalous origin of the left coronary artery from the pulmonary artery. So this disease is also known as Bland–White–Garland syndrome. The incidence of ALCAPA is considered to be 1 per 300,000 live births. Embryologically it is believed to be due to either an abnormal division of the conotruncus into the aorta and pulmonary artery or the persistence of the pulmonary buds together with involution of the aortic buds that form the coronary artery.
In the intrauterine period, the left coronary system has normal blood flow (antegrade) from pulmonary artery due to the high pulmonary artery pressure. Pulmonary vascular resistance and pulmonary artery pressure fall in the neonatal period so that the flow into left coronary artery decreases. Collaterals develop from the right coronary artery to supply the branches of the left coronary artery. Finally, a reversal of flow in the left coronary system occurs, and blood starts flowing into the pulmonary artery. Depending on the degree of collaterals clinical presentation varies.

The clinical presentation may be of four types:

1. Infants: Around 85-90% of cases present between 2 and 4 months of age. There is poor growth, tachypnea, profuse sweating, and angina-like episodes. This is observed as a sudden onset of distressed state with pallor during or after feeding. About 90% of these infants who are symptomatic die in the first two years of life if untreated.

2. Asymptomatic adults: Most cases of ALCAPA who survive infancy will have extensive collateralization of LCA and a dilated RCA. These cases may be picked up because of a soft continuous murmur or mild mitral regurgitation or incidental cardiomegaly on chest X-ray.

3. Symptomatic adults: These cases present mainly with angina, heart failure or arrhythmias.

4. Sudden cardiac death: ALCAPA is one of the causes of sudden death in a previously asymptomatic person. Pathologic studies show a variable degree of fibrosis in myocardial tissue, which can trigger fatal ventricular tachyarrhythmias.

ECG abnormalities are noted in a large number of patients. Q waves are seen in anterior leads in 50% of patients and left ventricular hypertrophy in 28% of cases. Colour Doppler echocardiography may show the dilated RCA. Rarely the
retrograde flow into the left coronary artery is seen. Coronary angiography and cardiac CT scanning can be diagnostic. Cardiac MRI picks up the amount of scar tissue.

Surgery is the only definitive treatment. ALCAPA has to be surgically treated in the first year of life. Several surgical techniques have been described. LCA ligation at origin was practiced in the initial days. But there was a high incidence of late deaths. The restoration of blood flow in the left coronary artery from the aorta was considered in subsequent techniques. Direct reimplantation of the left coronary artery on to aorta can be done. In the first year of life, great arteries are not fully developed, and tissues are more flexible, which allows coronary reimplantation. The Takeuchi procedure is often used in the pediatric population. This procedure, introduced in 1979, involved the creation of an aortopulmonary window and intrapulmonary tunnel extending from the anomalous ostium to the window. This procedure is now unpopular due to late complications; especially the high incidence (> 21%) of supravalvular stenosis of the pulmonary artery. In the 10–15% of patients who reach adulthood, surgical correction is burdensome, due to the heart dimensions and compensatory disorders in coronary circulation to the left ventricle.

Cardiac function normalizes within one year in the majority of cases. Mild to moderate MR also gets corrected due to reverse LV modeling. Severe MR due to irreversible myocardial necrosis or papillary muscle infarction will need concomitant repair. ICD implantation has been done in patients who present with fatal ventricular arrhythmias.

**CONCLUSION**

ALCAPA is a rare congenital anomaly. It can remain asymptomatic and may present with atypical symptoms like atrial fibrillation. A high index of suspicion should be kept even in adult patients regarding ALCAPA as the underlying cause of heart failure or arrhythmias. Coronary angiogram or CT Angiogram can provide a definite diagnosis. Management options will have to be discussed especially in adult patients and individualized for each patient.

**References:**


2. W. Krause- About the origin of accessory coronary artery from the pulmonary artery: Ztschr Rat Med;1865 vol. 24, pp. 225–227

3. S. J. Brooks-Two cases of an abnormal coronary artery of the heart arising from the pulmonary artery with someremarks upon the effect of this anomaly in producing cir
doid dilatation of the vessels: Journal of Anatomy and Physiology, 1886 vol. 20, pp. 26–32


5. J. D. Keith- Anomalous origin of the left coronary artery from the pulmonary artery: British Heart Journal, 1959 vol. 21, no. 2, pp. 149–161


CASE REPORT

An unusual cause of angina

Introduction:
Kounis syndrome is the coincidental occurrence of an acute coronary syndrome (ACS) with hypersensitivity reactions involving activation of interrelated and interacting inflammatory cells and including allergic or hypersensitivity and anaphylactic or anaphylactoid insults [1]. It is caused by inflammatory mediators such as histamine, neutral proteases, arachidonic acid products, platelet activating factor, and a variety of cytokines and chemokines released during the hypersensitivity insult [2–4]. There are three types of variants of which, Type II variant includes patients with culprit but quiescent pre-existing atheromatous disease in whom the acute release of inflammatory mediators can induce either coronary artery spasm with normal cardiac enzymes or plaque erosion or rupture manifesting as acute myocardial infarction.

Case Report:
AA 44-year-old male with a two-year history of type 2 diabetes mellitus and systemic hypertension was admitted with rest angina. He had effort angina class II for two weeks and was evaluated outside with TMT which was positive. Admission ECG showed minor ST depression in inferolateral leads, and the Troponin T was borderline positive (0.05ng/ml), the 2D echo showed No RWMA with Normal LV systolic function. Hence he was diagnosed as an acute coronary syndrome, non ST elevated myocardial infarction and treated as per standard ACS protocol. He was taken up for coronary angiogram which revealed non-obstructive coronary artery disease. He also gives a history of allergic to aspirin and dust. He was discharged with single antiplatelet (Clopidogrel) and statins.

He was readmitted ten days later with complaints of rest angina for three days which was relieved with sublingual nitrates. His ECG showed dynamic ST- T changes in anterior leads and troponin T was mildly elevated, which was not progressive in subsequent days, and 2D echo showed no RWMA and Normal LV systolic function. His coronary angiogram was reviewed, and there were no significant obstructive lesions to account for his recurrent symptoms.
During the course in hospital his vitals were stable, and investigations showed Hb- 13gm%, ESR- 26mm/hr, Eosinophil- 1, absolute eosinophil count- 142cells/mm³, Serum IgE- 1379, Radioallergosorbent test (RAST) showed allergy to house dust and dust mite and rest of the investigations were within normal limits.

Given the strong allergic symptoms, recurrent episodes of angina and no significant obstructive lesions on his recent coronary angiogram the possibility of Type 2 Kounis syndrome was considered, and he was treated with vasodilators, antianginals, calcium channel blockers, mast cell stabilizers, and intravenous steroids. (Steroids were tapered and subsequently stopped).

Throughout his stay, he was asymptomatic and discharged with antianginals, calcium channel blockers, and mast cell stabilizers.

Fig 2- ECG after 10 days with Dynamic ST-T changes in anterior leads, marked with red arrow
Fig 3: M mode across Left ventricle

Fig 4: Coronary angiography image showing Left anterior descending artery, Left circumflex and Right coronary artery. Red arrow showing minor plaque in LAD

Discussion:
Kounis syndrome has been defined as an ACS that manifests as vasospastic angina or ST-elevation myocardial infarction/ non ST-elevation myocardial infarction triggered by the release of inflammatory mediators following an allergic insult [2].

The mechanisms of this syndrome are characterized by coronary artery vasospasm due to mast cell degranulation and the subsequent release of vasoactive mediators [5]. The most important vasoactive mediators responsible for coronary artery spasm and consequences of Kounis syndrome are histamine, serotonin, and leukotrienes.

There are 3 variants of Kounis syndrome. The Type-I is observed in patients with no cardiovascular risk factors & healthy coronary arteries, in which the inflammatory cascade triggered by the allergic insult causes coronary vasospasm accompanied by elevated or normal levels of cardiac enzymes. Type II is observed in patients with the pre-existing atheromatous disease (whether known or not) in whom the release of these mediators would also produce coronary vasospasm which occurs with normal cardiac enzymes or rupture of the atheromatous plaque, manifesting as an acute myocardial infarction. Type III includes patients with coronary thrombosis (including stent thrombosis) in whom aspirated thrombus specimens stained with hematoxylin-eosin and Giemsa demonstrate the presence of eosinophils and mast cells respectively [4, 6, 7]. Our patient’s coronary angiography revealed non-obstructive lesions in the coronary vasculature and was diagnosed as atype II variant.

Etiology of Kounis syndrome include drugs (antibiotics, analgesics, antineoplastics, contrast media, corticosteroids, intravenous anaesthetics, non-steroidal anti-inflammatory drugs, skin disinfectants, thrombolytics, anticoagulants), various conditions (angioedema, bronchial asthma, urticaria, food allergy, exercise-induced allergy, mastocytosis, serum sickness), and environmental exposures (stings.
of ants, bees, wasps, jellyfish, grass cutting, millet allergy, poison ivy, latex contact, shellfish eating, viper venom poisoning). [8]

There are no specific diagnostic criteria to differentiate Prinzmetal angina from Kounis syndrome, and the diagnosis of Kounis syndrome is based on the patient's signs and symptoms of a systemic allergic reaction associated with clinical, laboratory and electrocardiographic findings of acute myocardial ischemia.

The Management of patients with Kounis syndrome differs from those for non-allergic common ACS [9]. These patients need treatment with steroids, antihistamines, fluid replacement, possibly epinephrine, oxygen, and antithrombotics for transfer to the cardiac catheterization laboratory. Treatment should be both treating coronary lesions and suppressing the allergic reaction. Vasodilator drugs, including nitrates and calcium channel blockers, should be considered as a first line therapy since vasospasm is the primary mechanism [9]. Aspirin is among the most frequent causes of drug-associated anaphylactic reactions [2]. Both fractionated and low molecular weight heparins are derived from animals which are potentially antigenic and can cause allergic reactions. Epinephrine is a life saving medication in anaphylaxis; however, it can aggravate the ischemia, and induce coronary vasospasm and arrhythmias. Therefore, given a narrow therapeutic window, the recommended dose is 0.2–0.5 mg of intramuscular injection [9].

Corticosteroids are agents playing a significant role in the treatment of allergic reactions, but they are well known to impair wound healing and scar formation which may cause myocardial wall thinning, cardiac aneurysms, and wall rupture [10]. Successful use of corticosteroids in allergic ACS has been reported and is thus probably safe and appropriate.

Conclusion:
The Kounis syndrome is probably not an uncommon disease but rather an under diagnosed one. Regarding the complex course of ACS associated with allergic reactions, high awareness, rapid diagnosis, and appropriate treatment are of utmost importance.

References:
Non-Atheromatous Causes of Acute Coronary Syndromes

Summary:
Approximately 5% of patients with acute coronary syndrome do not have atherosclerotic coronary artery disease but have other causes for their luminal narrowing. This article reviews non-atherosclerotic causes of ACS.

Introduction:
Atherosclerosis is the commonest cause of luminal narrowing and coronary heart disease, but there are multiple non-atherosclerotic (congenital and acquired) causes of severe luminal narrowing and subsequent clinical coronary events.

Approximately 4 to 7% of all patients with ACS do not have atherosclerotic coronary artery disease in coronary angiography, at necropsy or both. This percentage is 4 times in in patients aged <35 years. Since Coronary angiography represents a “lumenogram,” the specificity for the etiology of the coronary luminal narrowing is extremely low. Review of necropsy studies suggests that approximately 95% of patients with fatal AMI have severe luminal narrowing or total occlusion of at least one of the major epicardial coronary artery. The remaining 5% of patients have normal epicardial coronary arteries. In those with severe coronary luminal narrowing, 95% have the typical atherosclerotic plaque with (85%)or without (15%) superimposed thrombus. The remaining 5% with severe coronary luminal narrowing has a host of etiologies, including coronary arteritis, systemic metabolic disorders, intimal fibrous proliferation, coronary emboli and trauma. Of the 5% necropsy patients with fatal AMI with normal or nearly normal epicardial coronary arteries, perhaps 50 - 60 % represent coronary spasm, but the remaining 40 - 50 % may have congenital coronary artery anomalies, spontaneous recanalization, or coronary supply-myocardial demand mismatches.

Acute Coronary Syndromes with Non-stenotic Coronary Arteries.
Myocardial infarction with nonobstructive coronary arteries (MINOCA) and Stress Cardiomyopathy will be discussed towards the end of this article.

1. Congenital Coronary Artery Anomalies
Coronary anomalies like variation in the origin, course, or distribution of the epicardial coronary arteries are found in 1-2% of the population. In young patients (<20 years of age) with angina pectoris or acute Myocardial Infarction, a congenital coronary artery anomaly or a congenital coronary artery aneurysm should be suspected.
a) Origin of Both Coronary Arteries from the Same Sinus of Valsalva.

When both the coronary arteries arise from the left or right sinus of Valsalva, the anomalous vessel transverses the base of the heart in a course anterior to the pulmonary trunk, posterior to the aorta, or between the aorta and pulmonary trunk. Ischemia, infarction, and sudden death in this coronary anomaly appears related to the shape of the coronary ostium of the anomalous vessel (Fig. 1). Typically, the coronary ostia are round to oval in shape, but in this anomaly, the coronary artery has an acute take-off angle. This results in slit-like coronary ostium. With increased cardiac output as in exercise, the aorta dilates, and this slit-like ostium becomes severely narrowed due to the aortic wall stretching. The “compression” of the anomalous coronary artery by the aorta and pulmonary trunk is an unlikely cause for the clinical symptoms given the marked differences in diastolic pressures. 12, 14 reported morphologic evidence of chronic ischemia (13) in a patient with high-takeoff right coronary artery who had right and left ventricular wall scarring. High-takeoff position of the coronary ostium also has been postulated as a cause of sudden coronary death. 17 In a series of 54 major and minor coronary artery anomalies by Alexander (18), high takeoff of both coronary arteries were seen in two, right coronary artery alone in five, and left coronary artery alone in three patients.

b) Single Coronary Artery

Origin of the entire coronary circulation from a single aortic ostium has been termed “single coronary artery.” This is usually associated with other congenital anomalies of the heart like pulmonary artery atresia, tetralogy of Fallot, and patent truncus arteriosus. One or more branches of the single artery may cross the base of the heart in a fashion described above and thus may be exposed to the risks of ischemia due to acute angulation. 17

c) High-takeoff Coronary Ostia

Typically, the coronary ostia are located within the sinuses of Valsalva, which permits the maximal opportunity for coronary artery diastolic filling. In high takeoff, the coronary ostia is in the tubular portion of the aorta and may be associated with decreased coronary perfusion. 16 Menke et al. reported morphologic evidence of chronic ischemia (13) in a patient with high-takeoff right coronary artery who had right and left ventricular wall scarring. High-takeoff position of the coronary ostium also has been postulated as a cause of sudden coronary death. 17 In a series of 54 major and minor coronary artery anomalies by Alexander (18), high takeoff of both coronary arteries were seen in two, right coronary artery alone in five, and left coronary artery alone in three patients.

d) Ostial Narrowing.

Nonatherosclerotic causes of coronary ostial narrowing include syphilis, 20 Takayasu’s disease, 21 fibromuscular hyperplasia associated with methysergide therapy, 22, 23 aortic valve surgery with or without coronary artery canulation, 24 and ostial valve-like ridges. 25 Baroldi has summarized other rare diseases that may narrow or occlude the coronary ostia: 26 (1) a nonatheromatous, calcific protrusion from the sinotubular junction into the right or left ostium; (2) saccular aneurysm of the aorta; (3) aortic dissection extending into the coronary ostium (right ostium more common than left); (4) supravalvular aortic stenosis with severe intimal thickening; (5) obliteration of the ostium due to adhesion of the free edge of an aortic cusp to the aortic wall above the coronary ostium; (6) occlusion by embolus and (7) occlusive fibroelastosis.
**e) Anomalous Origin of One or two coronaries from the Pulmonary Trunk.**

Anomalous origin of a coronary artery from the pulmonary trunk may be responsible for myocardial ischemia and infarction in infants and children. In more than 90% of cases, the left main is the anomalous artery, and thus the antero-septal and anterolateral left ventricular myocardium may be at jeopardy. Asymptomatic older patients with this coronary anomaly usually are discovered by having an abnormal ECG, a precordial murmur, or by the occurrence of sudden death.9

**f) Coronary Artery Fistula**

A direct connection between a major epicardial coronary artery and a cardiac chamber or major vessel (vena cava, coronary sinus, pulmonary artery) is another coronary artery anomaly.7 Right coronary artery fistulae are more common than left coronary fistulae. Over 90% of the fistulae drain into the venous circulation.7 Myocardial ischemia has been documented in patients with coronary artery fistulae.7

**g) Myocardial Bridges (“Tunneled” Epicardial Coronary Artery)**

The coronary arteries which normally course over the epicardial surface of the heart may dip into the myocardium to travel for varying lengths and then reappear on the heart’s surface (Figs. 3-6). The muscle overlying the intramyocardial segment of the epicardial coronary artery is the “myocardial bridge,” and the artery coursing within the myocardium is the “tunneled” coronary artery.
Tunneled coronary arteries have been recognized anatomically for more than two centuries, but recent reports indicating an association with myocardial ischemia and myocardial bridges have heightened clinical relevance. Tunneled coronary arteries have been presumed congenital in origin. Visscher and colleagues reported a tunneled left anterior descending artery in a 42-day-old infant, supporting the presumption that myocardial bridging of coronary arteries exists at birth. At least three factors have been postulated to account for differences between the high frequency of tunneled major coronary arteries observed at necropsy (32,7) and the lower frequency of tunneled coronary arteries observed angiographically (29,34,35) or associated with symptoms of myocardial ischemia (18%): (1) length of the tunneled coronary segment, (2) degree of systolic compression, and (3) heart rate (Fig. 4). Isolated reports have suggested that longer tunneled segments of coronary arteries (29) more severe systolic diameter narrowing of the tunneled segment (30) and tachycardia (36) are contributing factors in the production of myocardial ischemia in association with myocardial bridging. The length of coronary tunneling in causing myocardial ischemia has been challenged by two recent reports. Although the left main coronary artery was tunneled, none of the patients had clinical or morphologic evidence of myocardial ischemia.

h) Coronary Aneurysms

Congenital coronary artery aneurysms are found most commonly in the right coronary artery. Abnormal flow patterns within the aneurysm result in thrombus formation with subsequent vessel occlusion, distal thromboembolization, and myocardial infarction (MI). The incidence of coronary arterial aneurysms is about 1.5% of patients studied at necropsy or by coronary arteriography. Aneurysms may be multiple and be acquired or congenital in origin. Causes for coronary arterial aneurysms include congenital origin, atherosclerosis, angioplasty, atherectomy and laser procedures, arteritis (including syphilis), mycotic emboli, mucocutaneous lymph node syndrome, dissection (sponta-
neous or secondary) and trauma. Atherosclerosis induced aneurysms/ectasia represent the majority (up to 50%) of coronary aneurysms and results from primary thinning and destruction of media.

**i) Spontaneous recanalization:**

Eg: Coronary Artery Emboli

Coronary arterial emboli are clinically suspected in patients who develop angina under the following circumstances: in the presence of a left-sided prosthetic valve, left-sided native valve stenosis, active infective endocarditis, atrial fibrillation, left ventricular aneurysm, dilated cardiomyopathy, cardiac tumor, or during cardiac catheterization or cardiac surgery. The etiology of coronary emboli can be classified as natural causes, iatrogenic causes, and “paradoxical” causes. Coronary embolism most often involves the left anterior descending coronary artery. Coronary embolisms is suspected as the cause of acute MI when the zone of necrosis is large but discrete lesions at necropsy (there would have been little time to develop effective collaterals). Embolic coronary artery lesions may resolve completely and and result in angiographically normal coronary arteries several months after an acute MI.

The size of the embolus and the size of the lumen of the artery in which it becomes impacted are determinants of clinical consequences. The smaller the embolus, the higher the chance that it will travel distally to a small coronary arterial segment and the likelihood of MI or fatal arrhythmia is less. A very small embolus that travels distally and impacts in a single intramural vessel is clinically silent and may be observed only at necropsy. The status of the coronary lumen before the embolus also determines the subsequent myocardial consequences.

**Acute Coronary Syndromes in patients with non-atheromatous obstructive coronary lesions:**

1. **Spontaneous Coronary Artery Dissection. (SCAD).**

Spontaneous coronary artery dissection (SCAD) is defined as an epicardial coronary artery dissection that is not associated with atherosclerosis or trauma and not iatrogenic.71

The reported prevalence ranges from 0.07% to 1.1%,71-74. SCAD is more common in women,77,78,79,80,81,82,83,84,85 and may be the cause of ACS in up to 35% of MIs in women <50 years of age. It is the most common cause of pregnancy-associated MI.71 SCAD causes myocardial ischemia and infarction (MI) due to obstruction of coronary blood flow from intimal dissection and intramural hematoma formation.

Although SCAD can be a fatal event, most series suggest that early and long-term survival is good.75,80 However, the burden of subsequent complications is notable,75,80 with 10-year Kaplan-Meier estimated rates of major adverse cardiovascular events, including recurrence, congestive heart failure, MI, and death as high as 47% and SCAD recurrence rates as high as 29%.75 The natural history of SCAD is markedly different from atherosclerotic coronary disease.75 The precipitants of coronary dissection are uncertain, a different pathophysiological mechanism from atherothrombotic ischemic MI is likely.75,78,81-83 Accordingly, short-term and long-term management strategies also differ substantially.84,85

**SCAD Presentations and diagnosis**

SCAD presents primarily as Acute Coronary Syndromes or sudden cardiac death.75,80 Patients are usually women (74%-92% in published series72-73,75,80) with a mean age of 42 to 52 years. Typical presenting symptoms include chest pain, dyspnea, diaphoresis, and/or nausea. Diagnostic findings include abnormal electrocardiographic findings, elevated cardiac biomarkers, and regional wall motion abnormalities on echocardiography. Because these patients are often young, fit, and otherwise healthy, SCAD may not be considered in the initial differential diagnosis and may preclude or delay proper diagnosis if serial electrocardiograms and troponin levels are not included in the evaluation.

When ACS is recognized, coronary angiography should be immediately performed.

Angiographically, SCAD is of three types. 79

**Type:** recognizable as a double lumen or ‘flap.’ There is open communication of the true lumen with the dissected plane (false lumen). Although being the classic finding, angiotype 1 only accounts for 26%–43% of the cases in SCAD series. This pattern, when identified, is considered diagnostic itself.

**Type 2:** when the dissection plane (false lumen) encompasses a contained intramural hematoma that does not allow contrast to enter in it (with or without intimal tear). In Angiography there is an abrupt change in the diameter of the vessel (narrowing or tapering). This narrowing is long with smooth borders, with or without distal recovery of vessel’s diameter. It shows no response to intracoronary nitrates. This pattern is the most common according to SCAD, accounting for 55%–78% of the cases.

**Type 3:** is the ambiguous pattern and is the least common angiographic presentation, although very likely is under-represented (misdiagnosed). It corresponds to a discrete,
not propagated intramural hematoma that gives the appearance of a focal (single or multiple) lesion, sometimes mimicking atherosclerosis. Its ambiguity makes diagnostic confirmation with intravascular imaging mandatory.

2. Coronary Artery Spasm

Coronary artery luminal narrowing produced by spasm has been associated with acute coronary syndromes and sudden death. Despite the extensive clinical information about coronary artery spasm, relatively few necropsy data are available from these patients. Contraction of the medial smooth muscle cells in the coronary artery wall may be a response to various neurologic and pharmacologic stimuli. Various postulates for the exact mechanism of spasm exist, but the specific pathogenesis of this disorder is unknown. Enhanced alpha adrenergic tone and various vasoactive substances (histamine, catecholamines, prostaglandins, thromboxaneA2) are presently thought to be relevant factors. Roberts and colleagues have reviewed the necropsy findings in 13 previously reported cases of coronary artery spasm. Although coronary angiograms during life did not recognize any fixed lesions, most of them had associated atherosclerotic plaque, (identified at necropsy). In one of the original patients described by Prinzmetal and colleagues, both major epicardial coronary arteries were “markedly sclerotic”, and the “posterior coronary artery” was 80% narrowed. Recently Isner and colleagues have demonstrated that coronary artery smooth muscle depletion (medial attenuation) accompanies advanced degrees of luminal narrowing by atherosclerotic plaque. This medial attenuation diminishes the potential for augmentation of coronary wall tone at the sites of severe luminal narrowing. Factor and colleagues have recently suggested that medial “contraction” bands may represent a morphologic-histologic marker for arteries that have spasm during life. Eccentric atherosclerotic plaques have a segment of disease-free wall that has preserved media and presumably has the potential for spasm. Hangartner, and colleague have recently evaluated this form of stenosis in patients with clinical coronary spasm and ACS. Of 448 segments narrowed >75% in cross-sectional area by plaques, 15% had a variable arc of a disease-free wall (normal media). Quyyumi and colleagues (15%) and Hort and associates (20%) report similar data. Freudenberg and Lichtlen report a higher percentage of disease-free wall (70%). This disease-free coronary segment represents a site of “vasospastic potential” and could convert a hemodynamically insignificant lesion or one of borderline significance to a hemodynamically significant lesion.

3. Coronary Artery Trauma

Coronary artery trauma may produce myocardial ischemia and or acute MI. Traumatic injury may result from non-penetrating blunt chest wall injury (e.g., steering wheel injury). Penetrating trauma (e.g., laceration from stab wound or bullet), or during coronary angiography. Nonpenetrating trauma may produce coronary injury and subsequent MI as a result of coronary dissection, contusion and thrombosis, fistula formation and or coronary artery aneurysm formation.

4. Coronary Artery Arteritis (Vasculitis)

Coronary arteritis (vasculitis) is a rare event. The coronary injury in arteritis may directly lead to myocardial ischemia/infarction with or without associated coronary artery thrombosis. According to Baroldi arteritis may be classified into three groups. a) Coronary arteritis that results from direct extension from an adjacent organ or tissue infections (e.g., epicardial or myocardial abscess from aortic valve endocarditis, pericardial tuberculosis). In this situation, the coronary artery adventitial layer is initially involved. b) Coronary arteritis resulting from a hematogenous spread through the coronary lumen or through vasa vasorum. In this situation, the intimal layer is initially involved. c) The exact mechanism of vascular origin is not understood. Specific coronary lesions a may be seen in systemic diseases like polyarteritis nodosa..

Tuberculosis

Tuberculous arteritis is seen chiefly in patients with pericardial or myocardial lesions. Specific coronary artery granuloma may involve the adventitia, the intima, or the entire wall.
Polyarteritis Nodosa

Polyarteritis nodosa is probably the most common cause of coronary arteritis. It is a systemic necrotizing vasculitis that affects medium and small vessels. Of 66 cases studied by Holsinger et al. 41 (62%) had involvement of the epicardial coronary arteries and 41 also had myocardial infarcts of varying size.(83) The coronary lesions resemble the necrotizing vascular lesions elsewhere, with an acute cellular phase with the destruction of the media and internal elastic membrane and subsequent intimal proliferation and scar in the healed phase. The coronary artery may dilate to form small berry-like aneurysms, become occluded by thrombus, or rupture (producing fatal pericardial tamponade).(84).

Giant Cell Arteritis

Giant cell arteritis affects chiefly the temporal and other cranial arteries, but Ainsworth et al. have reported coronary artery involvement and myocardial infarction,(85,86) The arterial wall lesion is a granulomatous inflammation with giant cells found along a degenerated internal elastic membrane.85 The intima becomes much thickened, and ultimately the vessel is converted into a fibrous cord. The Luminal thrombus may also be present. Of 16 cases of temporal arteritis reported by Harrison,” only 1 case involved the epicardial coronary arteries.

Systemic Lupus Erythematosus

Pericardial and myocardial involvement are common complications in systemic lupus erythematosus. Several young patients with lupus and absent coronary atherosclerosis have suffered acute myocardial infarction (AMI). 88-91 Necropsy examination of the coronary arteries in these patients showed intimal fibrous proliferation, which may represent healed arteritis. In a 16-year-old girl with lupus studied by Bonfiglio et al.,90 AMI was associated with recent thrombotic occlusion of all three major arteries. Tsakraklides et al.92 Studied a 29-year-old woman with lupus and fatal AMI who had severe coronary atherosclerosis. This case suggested that lupus and other conditions causing arteritis might predispose to premature coronary atherosclerosis. Smaller intramyocardial coronary arteries are involved frequently in the diffuse vasculitis with fibrinoid necrosis and fibrosis.94

Burger’s Disease

(Thromboangitis Obliterans)

In a few patients with Burger’s disease, the epicardial coronary arteries have shown focal polymorphonuclear infiltrates, histiocytes, and giant cells with or without coronary artery thrombosis(95) or only coronary thrombosis. In 30 cases studied by Saphir,(94) only one patient had coronary involvement, whereas in 19 cases studied by Averbuck and Silbert 6 patients had coronary thrombosis.

Wegener’s Granulomatosis

Wegener’s granulomatosis is a necrotizing vasculitis commonly affecting renal and pulmonary systems. Parrillo and Fauci have reported Fibrinoid necrosis of the small and medium-sized coronary arteries.87 Larger epicardial coronary artery occlusion, and MI was reported by Gatenby et al. 96

Infectious Diseases

Various infectious diseases have been associated with coronary arteritis: syphilis79.93-97 infective endocarditis, 98 salmonelloses, 99,100 typhus,101 and leprosy.100 Syphilis is stated to be one of the most common infectious diseases affecting the coronary arteries.102 Up to one-quarter of patients with tertiary syphilis may have ostial stenosis.98 The first 3 to 4 mm of the left and right coronary arteries may be involved with obliteratorive arteritis.93 Rarely a coronary artery contains a gumma.93 Angina and AMI may result from syphilitic coronary disease.97 Malarial parasites and parasitized red blood cells also may plug larger coronary arteries.110,110a Schistosoma hematobium has been found in a major epicardial coronary artery unassociated with MI.106

Mucocutaneous Lymph Node Syndrome (Kawasaki’s Disease)

This acute febrile illness affects infants and young children. In about 20% of patients, vasculitis of the coronary vasavasorum leads to coronary arterial aneurysm formation, thrombosis, and MI. Death may result from MI or ventricular arrhythmia in 1-2%. Late presentation with MI secondary to dislodged aneurysmal thrombus may also occur.79:107-108 Occasional death may result from coronary artery aneurysm rupture.

Takayasu’s Disease

(Pulseless Disease)

This disease results in granulomatous pan arteritis and fibrosis of the aorta and its large branches, which in turn lead to luminal narrowing.25 Involvement of the coronary artery ostia and proximal main coronary artery segments has been described in several patients.88, 110,111 Angina pectoris and AMI may result from these coronary lesions.
Rheumatoid Diseases
Rarely, arteritis and intimal thickening associated with rheumatoid disease severely narrow major epicardial coronary arteries. More commonly, diffuse arteritis involves smaller coronary arteries (including conduction system vessels) in 10-20% of necropsy patients with rheumatoid arthritis.112-114 Small myocardial vessels may also be narrowed severely in patients with ankylosing spondylitis. Grismer et al. have described a patient with ankylosing spondylitis who had occlusion of the left main ostium.

5. Metabolic Disorders Narrowing Coronary Arteries
Specific metabolic substances may accumulate in the walls of large and small coronary arteries as a result of inborn errors of metabolism. The deposition of this material may severely narrow the coronary artery lumen and produce AMI.102 Inherited inborn errors of metabolism that are known to affect major epicardial coronary arteries include Hunter’s and Hurler’s diseases (mucopolysaccharidoses).115-117 The involvement of the coronary arteries in these disorders may be so severe as to occlude the vessel totally and to produce myocardial ischemia/Infarction. Other disorders of metabolism such as primary oxalosis, Fabry’s disease, Sandhoff’s disease (gangliosidoses), homocystinuria may affect smaller coronary vessels by severe intimal proliferation.

6. Intimal Proliferation
Fibrous hyperplasia of the coronary arteries may severely narrow the lumen and produce myocardial ischemia/infarction. The process may be associated with mediastinal irradiation, fibromuscular hyperplasias of the renal arteries, the use of methysergide, ostial cannulations during cardiac surgery or following aortic valve replacement. Up to 50% of patients undergoing cardiac transplantation develop significant epicardial coronary artery luminal narrowing or total occlusion by intimal fibrous proliferation within 3 to 5 years after transplantation. 126 Myocardial infarction and sudden death may result from this chronic rejection process. Fibrosis of the intramural vessels may also occur. Intimal damage from immunologic rejection is believed to be the basis for the accelerated intimal fibrous hyperplasia involving the coronary arteries. 79

A similar histologic picture of intimal fibrous proliferation is seen in epicardial coronary arteries late after undergoing percutaneous balloon angioplasty. Waller et al. recently reported intimal fibrous proliferation of the left main coronary artery occurring late after balloon angioplasty of a lesion in the proximal left anterior descending coronary artery. They postulated that the left main intimal reaction (identical to that seen at the left anterior descending coronary artery angioplasty site) resulted from balloon rubbing of the intimal surface and/or extension of the fibrous process from the angioplasty dilation site.

7. External Compression
External compression of the epicardial coronary arteries may result in severe luminal narrowing and progressive myocardial ischemia. External compression of a major epicardial coronary artery has been reported in patients with sinus of Valsalva aneurysms and epicardial tumor metastases. Myocardial bridging (external muscle compression during ventricular systole) has been reviewed earlier.

8. Metastatic Implants
Myocardial metastatic lesions from various tumors (carcinomas, sarcomas, lymphomas) may mimic a healed myocardial infarct at necropsy. The discrete location or locations of these metastatic deposits generally are unrelated to specific coronary arterial supply zones, and the lesions are usually surrounded by normal myocardium. These two gross observations suggest the lesions are metastatic tumor implants rather than healed myocardial infarcts.

9. Coronary Artery Thrombosis without Underlying Atherosclerotic Plaque (Thrombosis In Situ)
Thrombotic occlusion of the coronary system unassociated with underlying atherosclerotic plaque may be seen with several hematologic diseases: thrombocytopenia purpura, leukemia, polycythemia vera, sickle cell anemia, and primary thrombocytosis. Occasionally, AMI may be the initial manifestation of these hematologic disorders. The main factor responsible for the myocardial ischemia in this condition is blockage of small intramural coronary vessels by platelet aggregates. These platelet aggregates initially form in the major coronary arteries and then embolize distally.

Substance Abuse (Cocaine)
Cocaine abuse is a major health hazard. More than 22 million Americans have tried cocaine at least once in their life, and five million are current users. Recent reports have documented that cocaine abuse can result...
in myocardial ischemia and MI in the absence of coronary atherosclerotic disease. Several instances of coronary artery thrombosis and spasm have been reported in patients with cocaine abuse. Coronary thrombosis occurring in coronary arteries free of atherosclerotic plaque suggests the role of cocaine-induced spasm or possible primary thrombogenicity of cocaine or its metabolites.

Coronary spasm has been associated with cocaine usage and has been postulated as a mechanism of MI in those users with clean coronary arteries 136,147-152 Simpson and Edwards 153 reported coronary artery narrowing in a young patient without underlying atherosclerotic plaque. The coronary artery was severely narrowed by fibrointimal proliferation that was attributed to underlying coronary artery spasm that caused focal vessel endothelial injury, and platelet adherence and aggregation. Platelets liberate platelet-derived growth factor (PDGF), which induces intimal proliferation. In patients with underlying coronary plaque, cocaine-induced spasm also may produce endothelial disruption at the surface of the plaque and promote platelet aggregation and further vasoconstriction from the release of platelet prostaglandins.

Takotsubo cardiomyopathy: Apical Ballooning Syndrome. (Stress Cardiomyopathy)

A specific syndrome of stress-related reversible cardiomyopathy, has recently been observed with greater frequency. Increasingly referred to as the “broken heart syndrome,” this condition mimics myocardial infarction in patients without obstructive coronary artery disease. Initial signs and symptoms resemble those of acute coronary syndrome; chest pain, dyspnea, electrocardiographic (ECG) changes, and elevated levels of cardiac biomarkers. 160 Takotsubo is the Japanese name for the traditional octopus trapping pot that has a round bottom and narrow neck, resembling the appearance of the left ventricle during systole. (see Figure 161).

Aetiology and pathogenesis:

The exact aetiology is not known. Normal myocardium utilizes 90% of its energy from fatty acid metabolism and only 10% from glucose metabolism. In Stress Cardiomyopathy, there appears to be a shift towards glucose pathway with impaired fatty acid metabolism. Several mechanisms have been proposed to explain the pathogenesis of Takotsubo cardiomyopathy characterized by apical ballooning of left ventricle.

**Catecholamine theory:**

Due to severe emotional or physical stress, overstimulation of hypothalamus pituitary adrenal axis occurs and results in excessive release of catecholamine. Elevated plasma levels of epinephrine and norepinephrine have been demonstrated during the acute phase. Acute onset of a
Investigations:
Electrocardiogram (ECG)
ECG reveals abnormal findings in over 95% patients in the form of ST elevation (43%) or ST depression (8%), T wave inversion (50%) and prolonged QTc interval (400ms).

Cardiac biomarkers
During acute phase, serum natriuretic peptides (BNP and NT-proBNP) are always increased along with troponin. BNP and NT-proBNP may be increased 3–5 times (much more than troponin) and are considered more useful diagnostic biomarkers for the diagnosis of Takotsubo cardiomyopathy. In a recent study of cardiac biomarkers in Takotsubo cardiomyopathy and STEMI patients, the concentration of NT-proBNP was greater in Takotsubo cardiomyopathy versus STEMI (4702 pg/ml vs 2138 pg/ml respectively) while troponin and CKMB mass were lesser in Takotsubo cardiomyopathy vs STEMI (Troponin 2.1 ng/ml and CKMB Mass 9.5 ng/ml v/s Troponin 19 ng/ml and CKMB mass 73.3 ng/ml (172).

Echocardiography (ECHO)
Transthoracic echocardiography with colour Doppler is always the first imaging procedure in the diagnosis of Takotsubo cardiomyopathy. Transthoracic echocardiography with colour Doppler is always the first imaging procedure in the diagnosis of Takotsubo cardiomyopathy. The key ECHO findings consist of a large area of regional wall motion (akinesia) of LV extending beyond the territory of single coronary artery. The dyskinetic/ akinetic myocardial area usually involves apical portion of LV resulting in acute apical ballooning along with dilatation of mid ventricular area. Left ventricle ejection fraction (LVEF) is always compromised (20–45%).

Angiography:
Coronary angiography is urgently indicated to rule out obstructive ACS (STEMI/NSTEMI). There is no obstructive pathology is found; thrombus or plaque rupture is absent. Co-existing mild atherosclerosis without obstruction has been described in <10% cases.

Cardiac magnetic resonance (CMR)
CMR provides 3-dimensional view of the anatomy of LV as well as RV. Four major anatomic patterns of regional wall motion abnormality (RWMA) have been recognized apical ballooning (81.7%), midventricular (14.6%), basal or inverted (2.2%) and focal (1.5%). CMR is indicated, first within 7 days and then at 2–6 months to judge the recovery of RWMA.174

Hormonal and genetic factors:
A recent update on Takotsubo syndrome confirmed female preponderance (88.7%) which suggest a role of various reproductive hormones in the pathogenesis.169

Classification.
1. Primary Takotsubo cardiomyopathy with/without stress trigger: More common in postmenopausal elderly women. The patients presents with cardiac symptoms of ACS. Physical and emotional stresses are responsible for Takotsubo cardiomyopathy in over 70% patients. However more than one quarter have no clear triggers. Patients have a higher rate of co-existing neurological and psychiatric disorders.170, 171
2. Secondary Takotsubo cardiomyopathy: Patient with clinical evidence of serious medical/surgical/obstetric and psychiatric disorders develop Takotsubo cardiomyopathy during the course of primary illness.
Treatment
Treatment of Takotsubo cardiomyopathy during the acute phase is mainly symptomatic treatment. Intra-aortic balloon pump equipment is required for hemodynamically unstable patients in addition to cardiopulmonary circulatory support and continuous veno-venous hemofiltration. There is controversy on the use of cardiac stimulants because of increased circulating catecholamines[175]. However, cardiac stimulants are used in 20%-40% of patients. Levosimendan may be beneficial because of its inotropic action and vasodilator effect[176]. Usage of anticoagulants may be considered at least until systolic function is recovered. For patients with severe LV outflow tract obstruction with hemodynamic compromise, treatment with a β-blocker should be considered. For patients with suspected vasospasm, the use of calcium channel blockers such as verapamil or diltiazem is suggested[177].

Prognosis.
Patients usually have a good prognosis, and almost perfect recovery is observed in 96% of the cases[178]. In hospital mortality rate vary from one to two percent[179]. Takotsubo cardiomyopathy, though thought to follow a relatively benign course, have a greater risk [178] of death at the time of initial onset. Their long-term survival rate is the same as that in healthy subjects,

Myocardial infarction with nonobstructive coronary arteries (MINOCA):
Myocardial infarction with nonobstructive coronary arteries (MINOCA) is clinically defined by the presence of acute myocardial infarction (AMI), absence of obstructive coronary artery disease (≤50% stenosis), and no overt cause for the clinical presentation at the time of angiography[180]. MINOCA refers to approximately 5%-10% of acute myocardial infarction.

Aetiology:
Potential underlying mechanism includes coronary causes such as coronary spasm, coronary microvascular dysfunction, plaque disruption, spontaneous coronary thrombosis/emboli, and coronary dissection; myocardial disorders, including myocarditis, takotsubo cardiomyopathy, and other cardiomyopathies & noncardiac causes like pulmonary embolism.

Prognosis:
Contemporary research studies of MINOCA have evaluated the prognosis of these patients, reporting a 12-month all-cause mortality of 4.7%[181]. Patients with MINOCA frequently had manifestations of atherosclerotic disease in other territories (eg, peripheral vascular disease)[182]. Moreover, mortality rates were substantial in the years following the MINOCA event. In the nationwide Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDHEART) registry, 14% died during a 4.5-year follow-up[182].

References
6. Elliot RE, Baroldi G: Necropsy studies in myocardial infarction with minimal or no coronary luminal reduction due to atherosclerosis Circulation 1974;49:1127-1131
12. Roberts WC, Siege1 RJ, Zipes DP: Origin of the right coronary artery from the left sinus of Valsalva and its func-
The official Journal of Cardiological Society of India, Kerala Chapter


33. Polack P: Relation of myocardial bridges and loops in the coronary arteries to coronary occlusions. Am J Cardiol 1961;61:44-52


37. Roberts WC, Dicicco BS, Waller BF, Kishel JC, McManus BM. Dawson SL. Hunsaker JC. Luke JL: Origin of the left main from the right coronary artery or from the right aortic sinus with intramyocardial tunneling to the left side of the heart via the ventricular septum: The case against clinical significance of myocardial bridge or coronary tunnel. Am Heart J 1982;104:303-305

38. Schulte MA. Waller BF, Hull MT. Pless JE: Origin of the left
anterior descending artery from the right aortic sinus with intramyocardial tunneling to the left side of the heart via the ventricular septum: A case against clinical and morphologic significance of myocardial bridging. Am Heart J 1985;110:499-501


100. Tsakraklides VC; Blieden LC, Edwards JE: Coronary atherosclerosis and myocardial infarction associated with lupus erythematous. Am Heart J 1974;87:637-641


110 a. Merkel WC: Plasmodium falciparum malaria: The coronary and myocardial lesions observed in autopsy in two cases of acute fulminating Pfapicarum infection. Arch Pathol 1946:41:29a298


126. Brosius FC 111, Waller BF, Roberts WC: Radiation heart disease. Analysis of 16 young (aged 15 to 33 years) necropsy patients who received over 3500 rads to the heart. Am J Med 1981;70:519–530


130. Billingham M: Personal communication, 1988


137. Wirth L: Myocardial infarction as the initial manifestation of Polycythemia Vera. Milt Med 1960;125:544–548


146. Waller BF: Cocaine and the heart. Indiana med 1988;81:956–959


177. Ibanez B, Navarro F, Cordoba M, M-Alberca P, Farre J. Takotsubo-
bo transient left ventricular apical ballooning: is intravascular ultrasound the key to resolve the enigma? Heart 2005; 91: 102-104 [PMID: 15604352 DOI: 10.1136/hrt.2004.035709]


Chaudhari Anushree A. MD.DNB*
Puri Goverdhan D. MD. PhD**
Kumar Bhupesh. MD. DM***
Bhalla Anil K.MD****

*Assistant Professor, Department of Anaesthesia,
Miraj Medical College and Hospital, Sangli-Miraj,Maharashtra

** Professor & ***Additional Professor, Department of Anaesthesia
and Intensive care, Advance Cardiac Center, PGIMER, Chandigarh

****Professor, Paediatric Medicine, PGIMER
Correspondence:annushree2402@gmail.com

ABSTRACT

**Determination Of Ventilatory Minute Volumes For Normocapnic Ventilation In Postoperative Cardiac Surgery Patients**

**BACKGROUND:** Following cardiac surgery under cardiopulmonary bypass (CPB) there is an increase in the extravascular lung water. So a prospective study to quantify minute ventilation (VE) for normocapnic ventilation in postoperative cardiac surgery patients was carried out.

**METHODS:** 50 NYHA II cardiac surgery patients 20 to 60 yrs of age with postoperative nasopharyngeal temperature (NPT) 36.5̊C-37.5̊C, sedated to Ramsay score three were electively ventilated at a respiratory rate of 15. Tidal volume (VT) was set initially as per the available published normogram for healthy subjects for normocapnic ventilation. It was further titrated to end-tidal CO2 concentration (PETCO2) of 35 to 40 mm Hg and cross-checked after 20 min with arterial blood gas analysis. VT was re-adjusted if PaCO2 was outside 38 to 42 mm Hg. VE, minute CO2 production (VCO2), respiratory system compliance (Crs) and end-inspiratory pause pressure (Pst) were measured and physiological dead space (VDPHYS) was calculated from Enghoff’s modification of Bohr’s equation.

**RESULTS:** VE requirement was significantly higher than those calculated based on data in healthy subjects while the Crs was lower (26 ± 6.7 vs 50.8± 13.82 ml/cm H2O) and Pst (15.32 ± 2.57 vs. 7.6 ± 2.4 cmH2O) and VDPHYS/kg (3.34 ± 1.08 vs. 2.35 ± 0.63 ml/kg) were higher.

**CONCLUSION:** Higher VE is required in cardiac surgery patients as compared to healthy subjects in the immediate postoperative period to maintain normocapnia which may be due to higher VDPHYS/kg resulting from the pulmonary injury seen post-bypass.

**Key-words:** minute ventilation, normocapnia, postoperative cardiac surgery, physiological dead space.
Introduction:
In the postoperative period following cardiac surgery under cardiopulmonary bypass (CPB), there is an increase in the extravascular lung water. Intermittent positive pressure ventilation (IPPV) forms an integral part of the postoperative management of cardiac surgery patients as it decreases the work of breathing[1] and improves ventilation-perfusion matching. The minute ventilation requirement in these patients depends on physiological-dead space (VD\textsubscript{PHYS}) and minute carbon dioxide production (V\textsubscript{CO2})[2] both of which are altered in the immediate postoperative period due to effects of anesthesia [3-8] and cardiac surgery itself.[9,10] There is a need to maintain normocapnia while controlling ventilation given the harmful effects of both hypercapnia as well as hypocapnia.[11-13] Several nomograms/guidelines [14-18] defined in literature have been derived about healthy patients or non-cardiac ICU patients.

In view of the absence of any controlled clinical study for normocapnic ventilation in post-cardiac surgery patients postoperatively we evaluated the minute ventilation requirement for the same and studied its relation to various preoperative patient demographic variables like weight (W), height (H), body surface area (BSA) and body mass index (BMI).

Materials and Methods:
Fifty New York Heart Association (NYHA) II patients 20 to 60 years of age undergoing elective open heart surgery and having a post-operative nasopharyngeal temperature of 36.5°C to 37.5°C were included in this study ensuring at least ten patients in each age group of 20-30, 31-40, 41-50 and 51-60. The study was approved by the Ethics committee and written informed consent was obtained from all subjects.

Patients with NYHA III and IV, BMI < 18.5 kg/m\textsuperscript{2} or >30 kg/m\textsuperscript{2}, congenital cyanotic heart disease, pre-operative severe compromised respiratory function i.e. predicted FEV\textsubscript{1} ( Forced expiratory volume in one second) <50% and predicted FVC ( Forced vital capacity) <50%,[19] severe pulmonary artery hypertension, high inotropic score,[20] hypothermia patients and those with fever were excluded.

Patients were sedated with propofol with Ramsay score 3 and electively ventilated using Maquet Servo i V.3.1 ventilator (Maquet Critical Care AB, SE-171 95 Solna, Sweden) with 4 sec cycle time, I: E ratio 1: 2 and 10% inspiratory pause at a respiratory rate of 15 breaths per minute (bpm). Tidal volume (VT) was set initially as per the earlier normogram for normocapnic ventilation[18] and further titrated to PET\textsubscript{CO2} of 35 to 40 mm Hg. At least 20 min were allowed at a given VT for the PET\textsubscript{CO2} to get stabilized (not more than ±1 change in PET\textsubscript{CO2} value in 20 min) after which arterial blood gas (ABG) analysis was performed. The VT was re-adjusted if PET\textsubscript{CO2} was outside 38 to 42 mm Hg. At the time of sampling, PET\textsubscript{CO2}, V\textsubscript{CO2}, VE, respiratory system compliance (Cr\textsubscript{s}) and end-inspiratory pause pressure (Pst) were obtained. Mainstream, dual-wavelength, non-dispersive infrared \textsubscript{CO2} analyzer module was used with a sensor and an airway adapter (Standards: EN 864, ISO 9918). Each variable was measured at four hours post CPB. Ambient temperature was maintained at 24°C to 26°C. The V\textsubscript{DPHYS} was calculated from the Enghoff’s modification of the Bohr’s equation: V\textsubscript{DPHYS} = VT x (Pa\textsubscript{CO2} - P\textsubscript{E\textsubscript{CO2}})/Pa\textsubscript{CO2}, where the mixed expiratory carbon dioxide tension (P\textsubscript{E\textsubscript{CO2}}) was calculated from (V\textsubscript{CO2}/VE) x PB.

The volume of extraoral apparatus dead space (VD\textsubscript{app}) was calculated by finding the volume of the connector, cuvette, the size and length of the extraoral endotracheal tube and the same was subtracted from VT and V\textsubscript{DPHYS}. The same corrections were applied while calculating VD/ VT. Each subject was also measured for body weight and height using standardized anthropometric measurements given by Weiner and Bourlie. The W was measured with the help of an electronic weighing machine (Make: Avery India Limited, Capacity: 150kg machine least count: 20gm) while height was measured by using anthropometer (make: Hol-tain Limited up to the accuracy of 1mm). These two measurements were used to compute BMI for every subject before surgery. BSA was calculated using a standard formula.[21] Similarly, the V\textsubscript{CO2} was calculated from available BMR studies.[22,23] Alveolar ventilation requirement (VA) was calculated by subtracting V\textsubscript{DPHYS} from VT and multiplying it with respiratory rate.

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 15.0 for Windows). Mean, and SD for W, H, BMI, BSA, VE, V\textsubscript{CO2}, and V\textsubscript{DPHYS} was calculated at each age for both males and females. The magnitude of gender and inter-group differences were quantified by applying ANOVA and students unpaired ‘t’ test for each variable in each group and subjects combined. Comparative assessment of different volumes with each type of different values of age (A), sex (S), H, W, BMI, BSA, VE, V\textsubscript{CO2}, and V\textsubscript{DPHYS} was calculated at each age for both males and females. The magnitude of gender and inter-group differences were quantified by applying ANOVA and students unpaired ‘t’ test, p < 0.05 was considered to be statistically significant.
Results:
As the magnitude of inter-age differences obtained for each of the anthropometric and physiological traits was found to be statistically insignificant, the data for different ten year age groups were pooled to have estimates for the larger sample size to arrive at more meaningful scientific inferences. There were 25 male patients and 25 female patients. There were relatively more number of patients in the age groups of 40 to 60 (TABLE 1).

Males and females were found to be comparable for the obesity indices of BMI and H/W1/3 as well as age, BMI, CPB time, PaCO2, and PETCO2. End-tidal CO2 tension matched arterial CO2(r=0.365, p=0.009) with P(a-ET)CO2 of 4.36 ± 1.54mm Hg in males and 4.34 ± 1.68mm Hg in females and the difference between the two sexes insignificant (p=0.970). The mean CPB time was 133.96 ± 76.14 min. Male patients were taller (p<0.0001) and heavier (p<0.0001) than their female counterparts with higher BSA (p<0.0001) (TABLE 2).

<table>
<thead>
<tr>
<th>Age group (yrs)</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>31-40</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>41-50</td>
<td>5</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>51-60</td>
<td>10</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
<td>50</td>
</tr>
</tbody>
</table>

TABLE 1: Age distribution of subjects

<table>
<thead>
<tr>
<th>AGE GROUPS</th>
<th>INDEPENDENT VARIABLE</th>
<th>FEMALES</th>
<th>MALES</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30</td>
<td>W</td>
<td>52.20 ± 1.49</td>
<td>65.20 ± 16.03</td>
<td>0.179</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>124.80 ± 5.07</td>
<td>168.60 ± 9.20</td>
<td>0.019*</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>21.78 ± 4.71</td>
<td>22.73 ± 4.17</td>
<td>0.744</td>
</tr>
<tr>
<td></td>
<td>BSA</td>
<td>1.48 ± 0.14</td>
<td>1.73 ± 0.24</td>
<td>0.097</td>
</tr>
<tr>
<td>31-40</td>
<td>W</td>
<td>46.30 ± 7.66</td>
<td>63.00 ± 10.97</td>
<td>0.024*</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>149.70 ± 3.11</td>
<td>166.60 ± 5.94</td>
<td>0.009*</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>20.67 ± 3.58</td>
<td>22.80 ± 4.76</td>
<td>0.447</td>
</tr>
<tr>
<td></td>
<td>BSA</td>
<td>1.38 ± 0.99</td>
<td>1.68 ± 0.12</td>
<td>0.002*</td>
</tr>
<tr>
<td>41-50</td>
<td>W</td>
<td>55.67 ± 10.66</td>
<td>55.20 ± 4.76</td>
<td>0.929</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>155.67 ± 5.54</td>
<td>158.40 ± 6.84</td>
<td>0.432</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>22.92 ± 3.89</td>
<td>22.03 ± 2.05</td>
<td>0.649</td>
</tr>
<tr>
<td></td>
<td>BSA</td>
<td>1.53 ± 0.14</td>
<td>1.55 ± 0.09</td>
<td>0.807</td>
</tr>
<tr>
<td>51-60</td>
<td>W</td>
<td>51.33 ± 10.50</td>
<td>70.50 ± 10.17</td>
<td>0.003*</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>152.50 ± 6.80</td>
<td>169.80 ± 7.02</td>
<td>0.000*</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>21.93 ± 3.47</td>
<td>24.72 ± 3.72</td>
<td>0.160</td>
</tr>
<tr>
<td></td>
<td>BSA</td>
<td>1.46 ± 0.16</td>
<td>1.80 ± 0.13</td>
<td>0.008*</td>
</tr>
<tr>
<td>COMBINED</td>
<td>W</td>
<td>52.06 ± 10.22</td>
<td>64.88 ± 11.79</td>
<td>0.006*</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>153.54 ± 3.58</td>
<td>166.32 ± 7.96</td>
<td>0.000*</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>22.00 ± 3.75</td>
<td>23.40 ± 3.72</td>
<td>0.193</td>
</tr>
<tr>
<td></td>
<td>BSA</td>
<td>1.47 ± 0.14</td>
<td>1.71 ± 0.17</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

TABLE 2: Inter age group comparison between males and females for the patient variables of W, H, BMI, BSA
linear correlation with W, H, BSA, and S, with BSA showing the best relation ($r=0.751, p=0.000$). VE/kg showed significant negative correlation with BMI ($r=-0.464, p=0.001$) (TABLE 5). This indicates that for similar weights, taller patients require higher VE. Study in Healthy subjects VCO2 though significantly higher in males ($p=0.000$) was not different if indexed to weight ($p=0.576$) (TABLE 3). VCO2/kg measured in the present study though similar to healthy subjects intraoperatively under general anesthesia [18] ($p=0.757$) (TABLE 4) was significantly higher than that calculated according to Benedict and Talbot [22] ($p=0.000$) and Kleiber’s formula [23] ($p=0.000$). VCO2 showed significant correlation with W, H, BSA best with BSA ($r=0.661, p=0.000$). VCO2/kg showed significant negative correlation with BMI ($r=-0.298, p=0.035$) (TABLE 5). VCO2/BSA was 109.85 ± 21.60 ml/m2.

VDPHYS was significantly higher in males as compared to females ($p<0.001$) (TABLE 3). VD/VT was 0.45 ± 0.10, compliance of lungs was 26.02 ± 6.73 ml/cm H2O and airway pressure was 15.31 ± 2.54 cm H2O (TABLE 4). VDPHYS/kg was significantly higher as

<table>
<thead>
<tr>
<th>Sex</th>
<th>$V_e$ (litres)</th>
<th>$V_e$ (ml/kg)</th>
<th>$V_{co2}$ (ml)</th>
<th>$V_{co2}$/kg (ml/kg)</th>
<th>$V_{phy}$ (ml)</th>
<th>$V_{phy}$/kg (ml/kg)</th>
<th>$V_{v}$/Vr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>7.02 ± 0.56</td>
<td>110.94 ± 17.46</td>
<td>198.85 ± 34.77</td>
<td>3.10 ± 0.52</td>
<td>219.84 ± 46.31</td>
<td>3.51 ± 1.12</td>
<td>0.46 ± 0.09</td>
</tr>
<tr>
<td>Females</td>
<td>5.48 ± 1.17</td>
<td>106.08 ± 17.78</td>
<td>153.84 ± 37.80</td>
<td>2.99 ± 0.78</td>
<td>165.58 ± 61.17</td>
<td>3.16 ± 1.03</td>
<td>0.44 ± 0.12</td>
</tr>
<tr>
<td>Total</td>
<td>6.25 ± 1.19</td>
<td>108.51 ± 17.61</td>
<td>176.35 ± 42.53</td>
<td>3.04 ± 0.66</td>
<td>192.71 ± 60.29</td>
<td>3.34 ± 1.08</td>
<td>0.45 ± 0.10</td>
</tr>
<tr>
<td>T</td>
<td>5.945</td>
<td>0.973</td>
<td>4.381</td>
<td>0.562</td>
<td>5.356</td>
<td>1.173</td>
<td>0.698</td>
</tr>
<tr>
<td>P</td>
<td>0.000**</td>
<td>0.335</td>
<td>0.000**</td>
<td>0.576</td>
<td>0.001*</td>
<td>0.247</td>
<td>0.488</td>
</tr>
</tbody>
</table>

$p<0.001$ significant, **highly significant.

operatively under general anesthesia [18] ($p=0.757$) (TABLE 4) was significantly higher than that calculated according to Benedict and Talbot [22] ($p=0.000$) and Kleiber’s formula [23] ($p=0.000$). VCO2 showed significant correlation with W, H, BSA best with BSA ($r=0.661, p=0.000$). VCO2/kg showed significant negative correlation with BMI ($r=-0.298, p=0.035$) (TABLE 5). VCO2/BSA was 109.85 ± 21.60 ml/m2.

VDPHYS was significantly higher in males as compared to females ($p<0.001$) (TABLE 3). VD/VT was 0.45 ± 0.10, compliance of lungs was 26.02 ± 6.73 ml/cm H2O and airway pressure was 15.31 ± 2.54 cm H2O (TABLE 4). VDPHYS/kg was significantly higher as

$\text{TABLE 4: Comparison of ventilator data in cardiac patients with healthy subjects}^{18}$

<table>
<thead>
<tr>
<th></th>
<th>Study in Healthy subjects</th>
<th>Present study post CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>VE/kg</td>
<td>99.72 ± 7.42</td>
<td>108.51 ± 17.61**</td>
</tr>
<tr>
<td>VCO2/kg</td>
<td>3.02 ± 0.49</td>
<td>3.04 ± 0.66</td>
</tr>
<tr>
<td>VDPHYS/kg</td>
<td>2.35 ± 0.63</td>
<td>3.34 ± 1.08**</td>
</tr>
<tr>
<td>Pst</td>
<td>7.6 ± 2.4</td>
<td>15.32±2.57**</td>
</tr>
<tr>
<td>Crs</td>
<td>50.8 ± 13.82</td>
<td>26.02±6.73**</td>
</tr>
</tbody>
</table>

Values are mean ± SD,* $p<0.001$ significant, **highly significant
Discussion:

As we had expected, the VE requirement in cardiac patients post cardiac surgery was significantly higher than that in available published data in healthy subjects intraoperatively[18](p=0.000). This can be attributed to higher VDPHYS/kg found in the present study which may be due to the increase in anatomical (VDAW) or alveolar dead space [26-30] (VDALV). This may be due to pre-existing pulmonary dysfunction in cardiac patients or due to the effects of cardiac surgery or CPB on lung function. Once CPB commences, microembolism and contact activation of blood by extracorporeal circuit results in activation of the complement system, anaphylatoxins, and neutrophils. This leads to capillary leak syndrome increasing extravascular lung water and closure of smaller airways colloquially referred to as “pump lung” and increases the VDALV. The Pst measured was significantly higher, and Crs was lower in the postoperative period in these patients (TABLE 4). Increase in static airway pressure can increase airway dimensions and so increase VDAW while decreasing respiratory system compliance may increase ventilation-perfusion mismatch by resulting in increased VDALV. Perez and colleagues [25] reported still higher VDPHYS/kg of 4.8 ±0.6 ml(p=0.000) in their study. This may be due to the inclusion of patients who already had some pulmonary dysfunction before they underwent surgery and also because their patients were hyper-ventilated as compared to our study to a PaCO2 of 28 to 32 mm Hg requiring larger tidal volumes which are associated with larger dead space values. Higher VE requirement for normocapnic ventilation in post-cardiac surgery patients may also be due to increased VCO2 which can be due to the stress response of anesthesia, surgery, CPB and rewarming. The resting energy expenditure is markedly elevated in the first 6 hours post CPB.[30] As compared to an earlier study in healthy individuals under anesthesia VCO2 in the present study was not significantly higher (Table 4). This may be because of the difference in the time of samplings in two studies as 20 minutes were allowed to elapse before we took samples whereas in the control study samples were taken after 10 minutes. Hence the earlier study might
have overestimated the VCO2. Nunn and Mathews[31] stated that CO2 output during anesthesia might not become constant until 60 minutes after a step change in ventilation. However, this will not affect PaCO2 values as it has been shown previously that during the fall of PaCO2 with an increase in ventilation, half of the total change in PaCO2 is completed in 3 minutes.[32] The measurements in the present study were also performed under controlled conditions with the patients sedated to Ramsay score 3 and adequately rewarmed to mean temperature 37°C. This might have led to better equilibration in PaCO2, and so VCO2 was comparable yet higher than that of the published study. It was also higher than the estimated norms of Benedict and Talbot[23]and Kleiber[24] (p=0.000) thus showing that nomograms from the nonsurgical setups cannot be applied to the perioperative period.

Ralley and colleagues[33]reported similar VCO2/m2n non-shivering patients scheduled for cardiac surgery at the end of 4 hours post CPB as compared to present study(111.36 ml/min/m2n± 21.60 ml/min/m2p=0.624). Our VCO2 was at variance with that of Damask and colleagues[34] who reported higher values (3.2 ± 0.53 ml/min/kg) amongst patients with open heart surgery which can be because of the inadequate and ongoing rewarming in their subjects and metabolism of recirculated blood lactate.[35] These findings were also at variance with Cruise et al[35] who reported lower values (2.54 ± 0.10 ml/min/kg, p<0.000) in non-shivering patients after cardiac surgery may be due to higher BMI and extended rewarming done before the end of CPB that may have decreased the postoperative BMR and VCO2. We found an inverse relationship between BMI and VCO2.

It emerges from the aforementioned discussion that cardiac patients undergoing surgery under CPB appear to require significantly higher VE for maintenance of normocapnia during the postoperative period. This may be attributed to the influence of increased respiratory physiological dead space owing to its lower respiratory system related compliance in the cardiac surgery patients post CPB.

References:
20. Zaccaria R, Stefano M, Claudio R, Angelo P et al. Inotrope support and peritoneal dialysis adequacy in ne-


In uncontrolled stage 2 & 3 HT with comorbidities

**TriOlmezest- CH**
Olmesartan Medoxomil 20/40 mg + Amlodipine Besilate 5mg + Chlorthalidone 12.5mg

Get results every mm of Hg*

**MAJOR HT GUIDELINES RECOMMEND:**

**Olmezest**
Olmesartan Medoxomil 10/20/40 mg

⚡ Strong on BP control, Strong on Vascular protection

**Olmezest- CH**
Olmesartan Medoxomil 20/40 mg + Chlorthalidone 12.5mg

Scored tablet even in combination
Proposed Kerala Heart House