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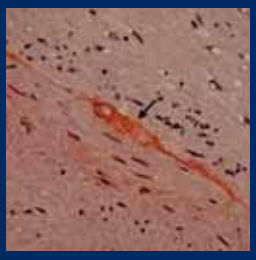

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BENGAL HEART JOURNAL

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Contents

EDITORIAL

Dr. P. K. Deb

A DANGER DISTINCT AND CONTEMPORARY

India is fast proceeding towards the dubious distinction of being the coronary artery disease capital of the world. The Global Burden of Diseases Study projected that disability-adjusted life years lost due to CHD in India by 2020 would be 14.4 million and 7.7 million in men and women respectively.[1] This is more than a clarion call to bring forth the issues related to the pathogenesis,prevention and treatment of coronary artery disease and this issue is dedicated to this discussion.

The review article by Amitava Sengupta et al[2], has highlighted a very interesting pathogenetic role of betelnut in precipitation of coronary artery disease. Though the infliction is particularly common in certain parts of South East Asia and Papua and New Guinea, the very fact underscores an urgent need to investigate its role in at least selected parts of India like Assam, Orissa and some other parts of East and North-East where the usage of betelnut forms a part of local culture.

In developed countries, pre-hospital emergency care plays an important role in bringing down the mortality and morbidity in cardiac patients particularly those suffering from acute myocardial infarction. Sadly, such facility is either lacking or is in a rudimentary state even in metro cities of India. In this issue of the journal, Rajib Sengupta et al[3],describe their award winning innovative emergency care system based in Kolkata. This can provide with a basic mechanism on which the necessary infrastructure for an effective emergency service can be built at least in the major Indian cities.

Cardiac risk markers have a close association with acute exacerbation of chronic obstructive pulmonary disease(COPD).However little work has been done even in developed countries on the relationship of these markers with the spirometric indices of COPD severity. Debojyoti Bhattacharya et al[3], have presented their data from National Medical College, in this issue, establishing the inverse relationship of the markers-homocysteine and hs-CRP with the spirometric indices of COPD severity.

The issue also contains several interesting case reports and an image on coronary artery disease.

Hope these all will make an interesting reading for our members during the Puja recess.

Wishing you all a very happy Durga Puja and Deepavali! Enjoy reading!

References :

1. 1.Ezzati M., Lopez A.D., Rodgers A. World Health Organisation; Geneva: 2004. Comparative Quantification of Health Risks.Global and Regional Burden of Disease Attributable to Major Risk Factors.
2. Sengupta A,Manna K. Betel Nut and Heart Diseas.Bengal Heart J 2016;1:8-11…….
3. Sengupta R , Mahapatra T, Mahapatra S Banerjee A,Bera K, Jha A, BoseS, BanerjeeB, Ghose S, Laha S Bhattacharya R.Kolkata Medical Emergency System (KMES) - an Innovation for Integrating Emergency Services for Better HealthCare Delivery .Bengal Heart J 2016;1: 26-30
4. Bhattacharya D, Bhattacharya K.Biochemical markers of cardiac risk and their relation to spirometric indices of airway obstruction among COPD outpatients in a Medical College and Hospital in Kolkata. Bengal Heart J 2016;1: 16-19 .

Case Report

Acute Limb Ischemia in a Patient with Cardiac Amyloidosis : A Case Report

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Abstract : Introduction: Cardiac amyloidosis is a manifestation of several systemic diseases known as amyloidoses. Arterial thromboembolic complications have not been reported to occur frequently, although the pathophysiology of cardiovascular amyloidosis would theoretically predispose to such manifestations.

We present the case of a 52-year-old woman, who suffered from cardiac amyloidosis and was admitted to our hospital for left acute limb ischemia. An urgent embolectomy was performed, improving her clinical condition and the pathologoanatomic examination of the embolus revealed deposition of amyloid.

Peripheral arterial thromboembolic events in patients with amyloidosis are rare. An antiplatelet treatment is recommended in such patients with cardiac amyloidosis for the prevention of embolism.

Key Words : Acute limb ischemia, cardiac amyloidosis, embelectomy

Introduction : Amyloidosis, despite being a single entity, is a general term covering a wide range of variable diseases, quite though uncommon. Data from Olmsted County, Minn, reflect age-adjusted incidences between 6.1 and 10.5 per million person-years[1]. It is estimated that 1275 to 3200 new cases occur annually in the United States[1-3]. Amyloid disposition can be found in any part of the body associated with variable non-specific symptoms. Particularly though cardiac involvement is one of the causes which can lead to death. The usual pathophysiology involves myocardial infiltration producing slowed diastolic filling. Less frequently, cardiac amyloid may simulate cardiomyopathy, congestive heart failure, coronary heart disease, valvular heart disease or arrhythmia. Arterial thromboembolism is an unusual phenomenon in cardiac amyloidosis. Investigation of contributing causes reveals disorders producing stasis, endothelial disturbance and probably abnormalities in blood coagulability[4]. We herein present a patient with amyloid heart disease complicated by cardiogenic systemic arterial thromboembolism.

Case : A 52-year-old Greek woman was transferred to the Emergency Unit of our Hospital with symptoms of acute left-limb ischemia. The patient reported sudden onset of calf pain, starting five days before. Symptoms rapidly deteriorated on admission day. The clinical examination revealed a cold, pale and painful left leg with absent peripheral pulses but normal ones on the right. The patient was in good general condition, the pulse was 67/min, the arterial blood pressure was 100/50 mmHg and lung examination did not reveal any particular findings. The EKG showed low voltage without atrial fibrillation. Her past medical history indicated cardiac insufficiency due to amyloidosis. A past echocardiogram had revealed restrictive cardiomyopathy with hypertrophy of the left ventricular wall and two years ago myocardial biopsy had shown positive histochemical stains for red of Congo and positive immunohistochemical staining for serum amyloid P component and lamda light chains indicative of primary amyloidosis (AL). As the biopsy was performed elsewhere, adequate information for the site of ventricle punctured, do not exist. An urgent embolectomy was performed following intravenous administration of 5000 IU heparin. Histology of the embolus revealed amyloidosis (Figure 1 & Figure 2). Postoperatively, intravenous heparin and per os anticoagulants (warfarin) were administered. Alongside, low doses of inotropes were required to maintain adequate blood pressure. A new echocardiogram revealed good myocardial function with diastolic dysfunction, calcification of the valves, mild mitral, tricuspidal and aortic valve insufficiency, while also hypertrophy of the left

ventricle and restrictive amyloid cardiomyopathy. The patient was discharged on the 6th postoperative day in good general condition. Three months later oral anticoagulants were discontinued and low dose of aspirin (100 mg/day) was prescribed. To date the patient has not presented any type of recurrence.

Discussion : The exact mechanism by which aggregation of amyloidosis causes damage and consequent dysfunction has been widely studied and discussed. The cardiovascular system is among the common targets of amyloidosis[5]. In clinical practice, amyloidosis is categorized in primary, secondary and hereditary. Primary (idiopathic, systemic) presents without previous or coexisting disease; it may involve the cardiovascular system, the gastrointestinal tract and the muscles. Secondary amyloidosis is linked to chronic diseases and has a tendency to target parenchymal organs such as the liver, spleen, and kidneys[6]. Regarding the heart symptoms of amyloidosis are not concrete. Cardiac amyloidosis can mimic cardiomyopathy, coronary cardiac disease, valvular cardiac disease or arrhythmia. The most common clinical feature though is right cardiac insufficiency, while coronary artery disease manifests predominantly in men by 60-65%, and only 1% of patients are younger than 40 years[7]. Concerning the natural history of thromboembolic disease in patients with amyloidosis, the medical files of 2.132 patients were evaluated in the Mayo Clinic between 1975 and 2000 and forty patients (21 men, median age 65) were selected to objectively evaluate the incidence of thromboembolic disease. Twelve patients had cardiac amyloidosis and 20 had kidney amyloidosis. Neither the extent of amyloidosis nor the type of monoclonal protein was predictive of thromboembolism. Thromboembolism manifested before the diagnosis of amyloidosis in 11 patients, during the diagnosis or within a month after the diagnosis in 11 patients, and one month or more following diagnosis in 18 patients. Twenty nine patients (73%) had vein thrombosis and 11 (28%) had arterial thrombosis. Eight patients (20%) died within a month after the thrombotic formation, and 18 (45%) died within a year. Thromboembolic events in patients with AL amyloidosis anticipated a significant mortality within the first year following the event[8]. The patients with cardiac amyloidosis presented a cardiac insufficiency with impaired diastolic function despite satisfactory systolic function. Such patients, though rarely, can develop cardiogenic thromboembolic disease. The rarity of this complication is impressive taking into consideration the pathophysiological basis of cardiac amyloidosis. Research into the contributing causes reveals that events present on the basis of the classic Virchow triad involving disturbance of blood flow, endothelial damage and possible abnormalities of blood coagulability. These facts lead to concrete proposals for prophylaxis and management of the diseased population[9].

Cardiac amyloidosis is considered a potential cause of systemic embolism. Nevertheless, such events have not been frequently reported. Cardiac mural clot is common in autopsies of patients with amyloidosis. Recommended diagnostic assessment is transoesophageal cardiac ultra-sound to investigate clots within the endocardium. On such high likelihood of thromboembolic episodes, anti-coagulation treatment as a preventive measure should be considered. Low-dose aspirin appears to be safer for thromboprophylaxis than the use of warfarin[4].

Conclusions : Even if amyloidosis is a complex disease, it complies with the triad of Virchow and predisposes the patients to thromboembolic events. This case report presents such an infrequent incidence in a patient who suffered from cardiac amyloidosis complicated by a thromboembolic episode of the lower limb. For such cases, we advocate thromboprophylaxis with low-dose (100 mg/day) aspirin. In patients with atrial fibrillation or arrhythmias we should consider administering anticoagulants (e.g. vitamin K antagonists) in therapeutic doses (INR 2.0-2.5).

Abbreviations : AL, amyloid light chain; INR, international normalized ratio

Consent

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

Competing interests

The authors declare that they have no competing interests.

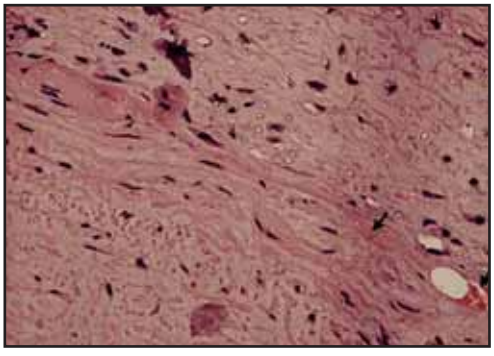

Fig. 1. Partial deposition of amorphous eosinophilic substance in the vascular wall (H&E × 400).

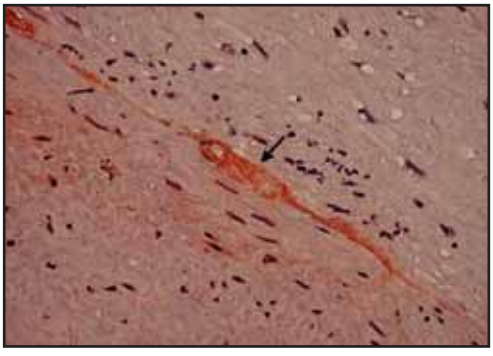

Fig. 2. Deposition of amorphous eosinophilic substance, double direction in polarized light (colored : Congo Red × 400, compatible with amyloid).

References :

1. Feng DL, Edwards WD, Oh JK, Chandrasekaran K, Grogan M, Martinez MW, Syed II, Hughes DA, Lust JA, Jaffe AS, Gertz MA, Klarich KW: Thrombosis and embolism in patients with cardiac amyloidosis. Circulation 2007, 116:2420-2426.
2. Kyle RA, Linos A, Beard CM, Linke RP, Gertz MA, O'Fallon WM, Kurland LT: Incidence and natural history of primary systemic amyloidosis in Olmsted County, Minnesota, 1950 through 1989. Blood 1992, 79:1817-1822.
3. Falk RH, Comenzo RL, Skinner M: The systemic amyloidoses. N Engl J Med 1997, 337:898-909.
4. Browne RS, Schneiderma H, Kaıpini N, Radjlrd MJ, Hager WD:Amyloid heart disease manifested by systemic arterial thromboemboli. Chest 1992, 102:304-307.
5. Gertz MA, Lacy MQ, Dispenzieri A, Hayman SR: Amyloidosis. Best Pract Res Clin Haematol 2005, 18:709-727.
6. Kholova I, Niessen HWM: Amyloid in the cardiovascular system. J Clin Pathol 2005, 58:125-133.
7. Falk RH: Diagnosis and management of the cardiac amyloi-doses. Circulation 2005, 112:2047-2060.
8. Halligan CS, Lacy MQ, Rajkumar SV, Dispenzieri A, Witzig TE, Lust JA, Fonseca R, Gertz MA, Kyle RA, Pruthi RK: Natural history of thromboembolism in AL amyloidosis. Amyloid 2006, 13:31-36.
9. Hausfater P, Costedoat-Chalumeau N, Amoura Z, Cacoub P, Papo T, Grateau G, Leblond V, Godeau P, Piette JC: AL cardiac amyloidosis and arterial thromboembolic events. Scand J Rheumatol 2005, 34:315-319.

Review Article

Betel Nut and Heart Disease

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Abstract : Betel nut is the fourth most widely used addictive in the world.Numerous studies from South and South-East Asia especially Taiwan and Papua New Guinea have shown a strong relationship between betel nut use and incidence of established cardiovascular risk factors like hypertension, diabetes mellitus, hyperlipidemia, obesity and metabolic syndrome. The betel nut use is also shown to be strongly associated with cardiac morbidity and mortality though the exact mechanism is yet to be discovered.

Key Words : Betel nut, cardiovascular disease

Introduction With the increasing trend of cardiovascular disease world wide, we become more concerned with its pathophysiology and various risk factors for the same. The journey began with the Framingham's study which identified hypertension, smoking, diabetes, and obesity as major risk factors. Subsequently many other risk factors were identified. As per addiction is concerned, apart from smoking and drinking alcohol, betel nut is the fourth most widely used addictive substance in the world[1,2]. However, the link between betel nut use and it's cardiovascular consequences are often not highlighted .The present review is an attempt to explore the effect of betel nut on cardiovascular disease.

Betel nut and cardiovascular events : Betel nut is becoming one of the most frequently used substance of abuse, specially in South Asia, Papua and New Guinea, where people chew betel nut on some cultural occasions. There are different ways of use- eg. fresh or dried nut along with salked lime, betel leaf and tobacco leaves[3,4]. In Taiwan, however people chew betel nuts in combination with Piper betel ((inflorescence leafs and lime). Betel chewing is linked not only to the development of oral and esophageal cancer, hepatocellular cancer and liver cirrhosis[1,5-10] but also to obesity, type 2 diabetes mellitus, hypertension, hyperlipidemia and metabolic syndrome and chronic kidney disease[11-16].

Though betel nut is associated with increased prevalence of established cardiovascular risk factors like obesity, type 2 diabetes mellitus, hypertension, hyperlipidemia and metabolic syndrome, the direct association with CV events is not clear.

During chewing of betel nut four main alkaloids are absorbed in the body, viz. arecolin, arecaidine, guvacine and guvacoline[1]. Those arecal alkaloids have shown to inhibit GABA receptors and affect physiologic and metabolic activities in brain, cardiovascular system, lung and pancreas[1]. Among the alkaloids arecolin is found to be the most active compound. It's an acetylcholine agonist acting on muscarinic and nicotinic receptors. Pharmacological effects are due to parasympathetic stimulation which includes euphoria, CNS stimulation, vertigo, excessive salivation, miosis and tremor[17,18]. It is broken down by pseudocholinesterase and carboxylesterase[19].

In his study of comparison of the heart rate and blood pressure of normotensive and hypertensive betel nut chewer in population of Papua New Guinea, Itaki et al, showed statistically significant increase in the mean heart rate, though transient, two minutes after chewing betel nuts in normotensive subjects. The effects were proposed to be due to stimulation of sympathetic ganglia by Acetylcholine[20].

Similarly Chu et al, showed that there were rise in the heart rate lasting 16.8 minutes in betel nut chewers irrespective of the duration of the addiction[21,22]. He also showed the systolic blood pressure to be increased in nut chewers though Itaki et al ,showed a trend toward hypotension which was not statistically significant. The finding as proposed by him, was due to vasodilatory effects of acetylcholine with intact endothelium. But the use of beta blockers in the study population and presence of other confounding factors were also thought to be behind this contradiction. However

the effects were transient due to rapid metabolism of arecoline by pseudo-cholinesterase.

In the presence of lime, arecoline is hydrolysed to arecaid, which has sympathetic effects via increasing GABA uptake[2 3]. Piper betel inflorescence has been shown to release catecholamine in vitro[1,23], which may also explain the tachycardia in nut chewers. So far we have a link of betel nut use and related cardiovascular activities.

Lan et, al first reported that in an elderly population, people who chewed areca nut were at increased risk of all cause (HR- 1.19, 98% CI; 1.05, 1.35) and CV disease mortality (HR- 1.66, 95% CI 1.19, 2.30) compared to those who did not ever chewed areca nut[4](4A). In the same year Guh et al found that the odds ratio for prevalent heart disease and betel nut consumption rate of ten times per day was 1.37(95%CI- 1.1-1.6) among women.

In a population based prospective study Lin et,al showed that betel nut chewing was associated with greater CVD and all cause mortality in Taiwanese men more than 20 years old , during a 8 year follow up period(baseline cohort of 56116 male). Out of 1549 deaths during the period, 309 were due to CVD. After adjustment for age, BMI, diabetes, hypertension, dyslipidemia, smoking and alcohol consumption and socioeconomic status, the relative risk of CVD and all cause mortality among former betel nut chewers were 1.56 and 1.40 respectively and those among current chewers were 2.02 and 1.40 respectively compared to persons who had never chewed. Current and former betel nut chewers had a higher risk of CVD mortality(RR 2.10, p <0.05) than did current and former smokers[24].

Yen et al. also found an independent dose response effect between chewing betel nut and an increasing risk of incident CVD among men. The betel quid ever chewers were at higher risk of CVD (HR- 1.24, 95% CI- 1.11-1.39) when compared with never chewers[25].

In a case control study from Taiwan, Tsai et al. showed dose dependent relationship between areca nut chewing and obstructive CAD risk[26]. The relation is dose dependent and additive with other established risk factors. Also the Lao-hwa regimen {made by putting a piece of inflorescence of Piper Betle Linn. with red lime paste (slaked lime and some local flavoring) into an unripe areca fruit }was found to be more potent than the betel leaf regimen.(Fig. 1)

Fig. 1. Taiwanese betel quid(BQ). Upper left : BQ wrapped with leaf, Lao-hwa quid ,lower left.

Pathophysiology : Atherosclerosis – surrogate of CAD is related to chronic inflammation. Arecoline, the major alkaloid in betel nut induce Cox 2 upregulation as well as cause higher expression of tissue inhibitor of matrix metalloproteinase in invitro studies[27,28]. Hydroxychavicol, another major phenolic compound in the inflorescence induce reactive oxygen species production via redox cycling, increases superoxide dismutase in mice liver[29] and reduce glutathione in cell line studies[30,31]. Lee et al. reported that betel quid could increase protein kinase C and NFKB expression in mice[32]. The same fact was proved by Ni et al. in human buccal mucosa[33]. Areca nut extract increases TNFα, ILB, IL6, IL8 in human peripheral blood mononuclear cells[34]. The extracts of areca nut, piper inflorescence and betel quid were found to enhance the cytotoxic effects of oxidized LDL toward bovine aortic endothelial cells. This probably explain the additive effects with cigarette smoking.

Conclusion : So far the effects of areca nuts, both acute and chronic, on cardiovascular system ,as reflected in these studies both in vivo and in vitro,were limited in Taiwan and Papua New Guinea. Though direct causal relation is to be established by further large prospective case control studies, it is almost evident that there is association of exposure and its cardiovascular effects. A large population of Indian subcontinent are exposed to various forms of betel nut chewing and datas are lacking. So we are looking ahed for further studies involving various parts of the world and meta-analysis to conclude the causal relation of CAD and Betel chewing.

References :

1. Boucher BJ, Mannan N. Metabolic effects of the consumption of Areca catechu. Addict Biol 2002;7:103–10.
2. Gupta PC, Warnakulasuriya S. Global epidemiology of areca nut usage. Addict Biol 2002;7:77–83.
3. IARC Working Group on the Evaluatin of Carcinogenic Risks to Humans. Betel-quid and areca-nut chewing and some areca-nut derived nitrosamines. IARC Monogr Eval Carcinog Risks Hum 2004;85:1–334.
4. Lan TY, Chang WC, Tsai YJ, Chuang YL, Lin HS, Tai TY. Areca nut chewing and mortality in an elderly cohort study. Am J Epidemiol 2007;165:677–83.
5. Wollina U, Verma S, Parikh D, Parikh A. [Oral and extraoral disease due to betel nut chewing]. Hautarzt 2002;53:795–7 (in German).
6. Zhang X, Reichart PA. A review of betel quid chewing, oral cancer and precancer in Mainland China. Oral Oncol 2007;43:424–30.
7. Sciubba JJ. Oral cancer. The importance of early diagnosis and treatment. Am J Clin Dermatol 2001;2:239–51.
8. Tsai JF, Jeng JE, Chuang LY. Habitual betel quid chewing and risk for hepatocellular carcinoma complicating cirrhosis. Medicine 2004;83:176–87.
9. Wu IC, Lu CY, Kuo FC, et al. Interaction between cigarette, alcohol and betel nut use on esophageal cancer risk in Taiwan. Eur J Clin Invest 2006;36:236–41.
10. Hsiao TJ, Liao HW, Hsieh PS, Wong RH. Risk of betel quid chewing on the development of liver cirrhosis: a community-based case-control study. Ann Epidemiol 2007;17:479–85.
11. Yen AM, Chiu YH, Chen LS, et al. A population-based study of the association between betel-quid chewing and the metabolic syndrome in men. Am J Clin Nutr 2006;83:1153–60.
12. Chung FM, Chang DM, Chen MP, et al. Areca nut chewing is associated with metabolic syndrome: role of tumor necrosis factor-alpha, leptin, and white blood cell count in betel nut chewing-related metabolic derangements. Diabetes Care 2006;29:1714.
13. Chang WC, Hsiao CF, Chang HY, et al. Betel nut chewing and other risk factors associated with obesity among Taiwanese male adults. Int J Obes (Lond) 2006;30:359–63.
14. Tung TH, Chiu YH, Chen LS, Wu HM, Boucher BJ, Chen TH. A population-based study of the association between areca nut chewing and type 2 diabetes mellitus in men (Keelung Community-based Integrated Screening Programme no. 2). Diabetologia 2004;47:1776–81.
15. Guh JY, Chen HC, Tsai JF, Chung LY. Betel-quid use is associated with heart disease in women. Am J Clin Nutr 2007;85:1229–35.
16. Kang IM, Chou CY, Tseng YH, et al. Association between betelnut chewing and chronic kidney disease in adults. J Occup Environ Med 2007;49:776–9.
17. Joan H. Brown, Palmer Talyor. In: Goodman and Gilman's The Pharmacological Basis of Therapeutics, 11th ed. New York: MacGraw-Hill, 2006
18. Osborn P.G, Chou T.S, Shen T.W. Characterization of the psychological, physiological and EEG profile of acute betel quid intoxication in Naïve subjects. PLos One. 2011:6(8); e23874.
19. Giri S, Idle J.R, Chen C, Zabriskie M, Krausz K.W, Gonzalez F.J. A metabolomics approach to the metabolism of the areca nut alkaloids arecoline and arecaidine in the mouse. Chem Res Toxicol. 2006:19(6); 818-827.
20. Rodney I, Isi H. K, Ben M, et al. Comparison of the heart rates and blood pressure of normotensive and hypertensive betel nut (Areca catechu) chewers. Pacific Journal of Medical Sciences; Vol.14, No.2, April 2015
21. Chu N.S. Cardiovascular responses to betel nut chewing. J Formos Med Assoc 1993: 92(9); 835-837.
22. Chu N.S. Effect of betel nut chewing on RR interval variation. J Formos Med Assoc. 1995:94(3);106-110.
23. Chu N.S. Effect of betel nut chewing on the central and autonomic nervous systems. J Bio Med Sci. 2001:8(3); 229-236.
24. Wen-Yuan Lin, Tai-Yuan C, Long-Teng L, et al. Betel nut chewing is associated with increased risk of cardiovascular disease and all-cause mortality in Taiwanese men. Am J Clin Nutr 2008;87: 1204-11.
25. Yen AM, Chen LS, Chiu YH, Boucher BJ, Chen TH. A prospective community-population-registry based cohort study of the association between betel-quid chewing and cardiovascular disease in men in Taiwan (KCIS no. 19) Am J Clin Nutr. 2008;87:70–78
26. Wen-Chung Tsai, Ming-Tsang Wu, et.al. Chewing areca nut increases the risk of coronary artery disease in Taiwanese men: a case control study. MBC Public Health 2012,12:162

27. Tsai C-H, Chou M-Y, Chang Y-C. The up-regulation of cyclooxygenase-2 expression in human buccal mucosal fibroblasts by arecoline: a possible role in the pathogenesis of oral submucous fibrosis. J Oral Pathol Med. 2003;32:146–153. doi: 10.1034/j.1600-0714.2003.00004.x.

28. Chang Y-C, Yang S-F, Tai K-W, Chou M-Y, Hsieh Y-S. Increased tissue inhibitor of metalloproteinase-1 expression and inhibition of gelatinase a activity in buccal mucosal fibroblasts by arecoline as possible mechanisms for oral submucous fibrosis.Oral Oncol. 2002;38:195–200. doi: 10.1016/S1368-8375(01)00045-8

29. Choudhary D, Kale RK. Antioxidant and non-toxic properties of Piper betle leaf extract: in vitro and in vivo studies. Phytother Res. 2002;16:461–466. doi: 10.1002/ptr.1015

30. Chang MC, Uang BJ, Wu HL, Lee JJ, Hahn LJ, Jeng JH. Inducing the cell cycle arrest and apoptosis of oral KB carcinoma cells by hydroxychavicol: roles of glutathione and reactive oxygen species. Br J Pharmacol. 2002;135:619–630. doi: 10.1038/sj.bjp.0704492.

31. Krol ES, Bolton JL. Oxidation of 4-alkylphenols and catechols by tyrosinase: ortho-substituents alter the mechanism of quinoid formation. Chem Biol Interact.1997;104:11–27. doi: 10.1016/S0009-2797(97)03763-0

32. Lee M-J, Hsu J-D, Lin C-L, Lin M-H, Yuan S-C, Wang C-J. Induction of epidermal proliferation and expressions of PKC and NF-[kappa]B by betel quid extracts in mouse: the role of lime-piper additives in betel quid. Chem Biol Interact.2002;140:35–48. doi: 10.1016/S0009-2797(01)00264-2

33. Ni WF, Tsai CH, Yang SF, Chang YC. Elevated expression of NF-kappaB in oral submucous fibrosis-evidence for NF-kappaB induction by safrole in human buccal mucosal fibroblasts. Oral Oncol. 2007;43:557–562. doi: 10.1016/j.oraloncology.2006.06.007

34. Chang LY, Wan HC, Lai YL, Kuo YF, Liu TY, Chen YT, Hung SL. Areca nut extracts increased expression of inflammatory cytokines, tumor necrosis factor-α, interleukin-1β, interleukin-6 and interleukin-8, in peripheral blood mononuclear cells.J Periodontal Res. 2009;44:175–183. doi: 10.1111/j.1600-0765.2008.01104.

Case Report

LMCA Osteal Stenosis Intervention : Review Through a Case Report

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Abstract : Isolated left main coronary ostial stenosis is a rare condition of unknown etiology. Review of the literature suggests that its natural history is distinct from that usually seen in atherosclerotic coronary diseases.Here we present a 44 year old female who presented with rest angina for one day. On further evaluation, she was diagnosed as having isolated ostial left main coronary stenosis.In a hemodynamically unstable patient with ostial left main stem disease, the primary goal is to do prompt PTCA to restore TIMI 3 flow at the earliest.

Key Words : Coronary ostial stenosis, PTCA, TIMI 3 flow

Introduction : Isolated coronary ostial stenosis is rare. In a previously reported series[1-6], the incidence of ostial stenosis has varied between 0.13 and 2.7%, and in the majority of cases there is a coexisting disease in the multiple coronary vessels. It has been assumed to be atherosclerotic in origin[1–5] but other important causes are coexisting homozygous familial hypercholesterolemia, otherwise normal coronary vessels in patients with syphilis[6–10] or other form of aortitis, congenital anomaly[11] and iatrogenic ostial stenosis[12–16] as a complication of coronary angiography or at the time of cardiac surgery[12–14].

Case report : A 44 year-old female comes to the emergency department complaining of an acute onset chest pain at rest for one day. There was no significant past medical history. There was no history of diabetes, hypertension and hypercholesterolemia or family history of coronary artery disease (CAD).

On examination, she was conscious, oriented to time and place and co-operative. There was no pallor, icterus, cyanosis, edema or clubbing. Pulse was 80/min regular. Her BP was 110/76mmHg with no postural drop. JVP showed normal pressure and waveform. On palpation, normal apex beat. Cardiac Auscultation revealed normal S1 and S2 with no added sound, murmur or pericardial friction rub. The lungs having bilateral basal crepitation. The abdomen was normal; no organ or mass was palpated. Neurologic examination was negative.

Investigation revealed Hb% 13.4gm%, TLC-5430, Platelet-1.22 lac, Urea-23, Creatinine-0.9, Na+ - 139, K+ - 4.0, Sr. Calcium – 10.3, Troponin I – 0.36, CPK- 239, CPK-MB – 54.

On evaluation her ECG showed ST elevation in aVR with ST Depression in anterior and lateral leads (Figure 1). Echocardiography revealed Hypokinetic Anterior Wall with LVEF: 40%. At this point we decided to go for invasive evaluation in the form of coronary angiography (CAG). CAG showed critical left main ostial stenosis with normal Left Anterior Descending and Left Circumflex coronary artery (Figure 2 and Figure 3). The Right coronary artery system was normal (Figure 4).

As the patient was symptomatic, we decided to proceed with Coronary Angioplasty of the Left Main Ostial stenosis by Femoral Arterial Access. JL 3.5 guide was used and coronary wiring was done by BMW wire. Catheter kept just outside the ostium to prevent Pressure Damping (Figure 5). Predilatation was done by 2.5×12 mm Semi-compliant balloon at 14 atm pressure. Guidewire and Balloon advanced simultaneously to reduce time and to restore flow quickly (Figure 6). Simultaneous wiring of LAD and LCX was done to achieve distal protection and to assess the Stent landing zone. Stenting was done with 4.0 × 15 mm DES, 2-3 stent struts should preferably be in the aorta (figure 7). Post-dilatation was done by 4.0 mm Non-compliant Balloon at 18 atm and TIMI III flow achieved as end result.

Patient was symptom free in the post-operative period and discharged after 2 days.

Discussion : Isolated coronary ostial stenosis appears to be a rare lesion and in one series4) occurred with an incidence of 0.2% in a population of patients with coronary heart disease defined by coronary angiography[2-9]. It occurs predominantly in women, usually before menopause (mean age 51 years).

The etiology of isolated coronary ostial stenosis is entirely unknown. Among adults it has been assumed that atherosclerosis, particularly early atheroma, is the most likely cause of this lesion. Other investigations have suggested a congenital arterial hypoplasia complicated by progressive thickening of the aortic intima by advancing age[17] or an inflammatory basis[18]. Histologic studies of non-diseased coronary ostia have suggested the presence of a circumferential sphincter-like muscle in the right coronary orifice of many patients, and it has been proposed that this may offer resistance to blood flow. Occurring predominantly in women, usually before menopause, it is unknoun whether humoral factors are important.

Thompson[4] has suggested that a series of events should alert the cardiologist to the possibility of an ostial stenosis, including: 1) difficulty in cannulation of the coronary ostium; 2) a profound decrease in distal coronary pressure after coronary engagement with or without angina or the appearance of ST segment change in the monitoring electrocardiogram; and 3) failure to observe return of contrast medium into the sinus of Valsalva after intracoronary injection.

Angiography entails some risk because the catheter may readily occlude the stenotic ostium, resulting in a fall in pressure at the catheter tip, chest pain, dyspnea, diaphoresis, and a fall in systemic pressure. Frequently, the catheter and ostium are not viewed in a plane suitable for demonstration of the ostial stenosis. Unless the angiographer is aware of the possibility of ostial occlusion by the catheter, this may occur and lead to hypotension, arrhythmia, and cardiac arrest. When the junction of the catheter and ostium are viewed in the proper obliquity, the stenosis of the left main coronary artery can be observed. Although the ostial stenosis can be appreciated visually, the diagnosis is frequently made by pressure changes and by failure of the contrast medium to be flushed from the coronary artery until the occluding catheter is removed from the ostium.

Some important points regarding Left Main Coronary Artery PCI

- The cannulation of the LMCA ostium from the aorta may require specific technical expedients to prevent pressure damping by deep seating.
- Ostial stenosis in a short LMCA may require treatment of the vessel up to the bifurcation
- Advancement of guidewire and balloon to be done simultaneously so that just after wire passes the lesion, balloon could be inflated without delay.
- A second guidewire is passed through the guiding catheter and then released in the aorta tracing its outline, preventing selective cannulation of the ostium and to precisely determine the LMCA origin
- The stent diameter is selected according to the reference vessel size distal to the lesion or according to the diameter of the vessel measured by IVUS. The stent length should cover the lesion upto ostium with minimal protrusion in aorta.
- During Post-dilatation, because the proximal end of the balloon can lie in the aorta, there is no need to select a specific balloon length .Many operators like to inflate the balloon while it protrudes into the aorta.
- The normal oscillation of the guiding catheter, especially in elderly patients with a dilated sclerotic aorta and high differential blood pressure, increases the risk of stent mal-positioning (hang-out or ostial missing)

Few complications we have to avoid during LMCA Ostial Stenting namely Stent Hangout, Ostial missing, Stent Sliding, Elastic recoil and Proximal-Distal dissection.

Conclusion : In a hemodynamically unstable patient with Ostial Left Main Stem Disease, the primary goal is to do prompt PTCA to restore TIMI 3 flow as soon as possible. Stent sizing in the Left main coronary artery and covering of the ostium with proper post dilatation is equally important to have good long term benefit.

Figure legends:

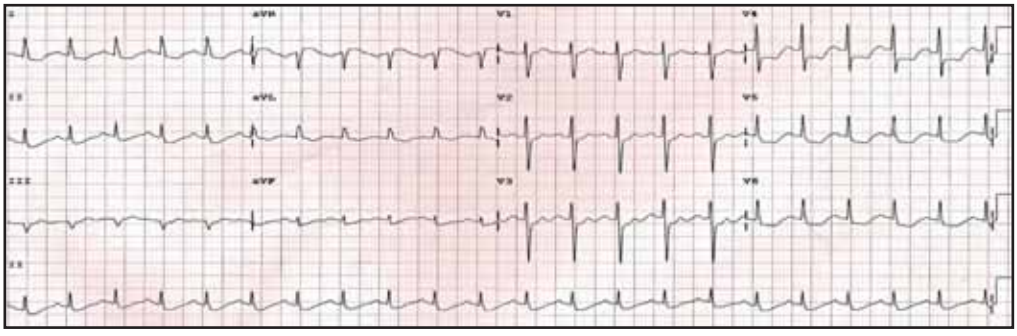

Fig. 1. ECG of the patient

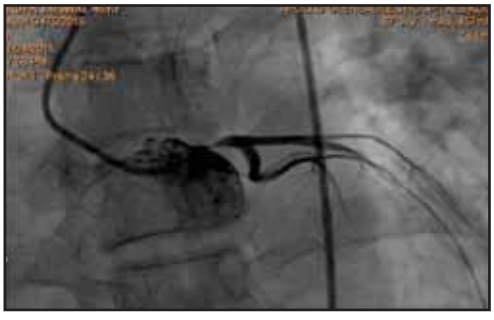

Fig. 2. Coronary angiogram showing the critical left main ostial stenosis (arrow)

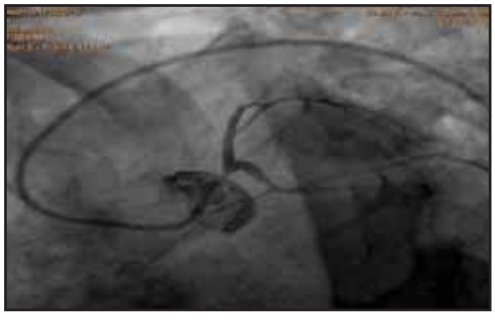

Fig. 3. Left main ostial stenosis in LAO-Caudal view

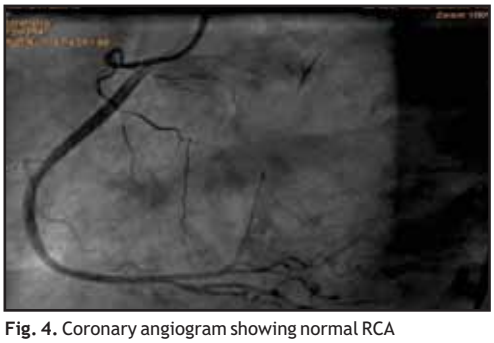

Fig. 4. Coronary angiogram showing normal RCA

Fig. 5. Wiring of the lesion

Fig. 6. Balloon dilatation of the lesion

Fig. 7. Stenting of the lesion

References :

1. Heggtveit HA. Coronary ostial stenosis; Incidence and relation to myocardial infarction (Abstract). Lab Invert 15:1125. 1966
2. Rissanen V. Occurrence of coronary ostial stenosis in a necropsy series of myocardial infarction, sudden death, and violent death. Brit Heart J 37:182. 1975.
3. Pritchard CL, Mudd GL, Barner HB. Coronary ostial stenosis. Circulation 52:46. 1975.Walsh MJ: Systemic sarcoidosis with refractory ventricular tachycardia and heart failure. Br Heart J 1978, 40(8):931-933.
4. Thompson R. Isolated coronary ostial stenosis in woman. JACC 7:997. 1986.Pesola G, Teirstein AS, Goldman M. Sarcoidosis presenting with pericardial effusion. Sarcoidosis 1987; 4:42
5. Enos WF, Beyer JC, Holmes RH. Atherosclerosis of the aortic sinuses. Am J Clin Pathol 29:506. 1963. ACC/AHA/HRS 2008 Guidelines for device-based therapy of cardiac rhythm abnormalities.Heart Rhythm 2008;5:e1-62
6. Barner HB, Codd JE, Mudd JG, Kaiser GC, Tyras DH, Lakes H, Willman VL. Nonsyphilitic coronary ostial stenosis. Arch Surg 112:1462. 1977.
7. Salem BI, Terasawa M, Mathur VS, Garcia E, de Castro CM, Hall RJ. Left coronary artery ostial stenosis; Clinical Marker, angiographic recognition and distinction from left main disease. Catheterization and Cardiovascular Diagnosis 5:125. 1979.
8. Cohen MV, Gorlin R. Main left coronary disease; Clinical experience from 1965–1974. Circulation 52:275. 1975.
9. Malcolm I, Salerno T. Coronary ostial stenosis. Can Med Assoc J 128:371. 1983.
10. Hefflveit HA. Syphilitic aortitis; A clinicopathologic autopsy study of 100 cases, 1950 to 1960. Circulation 29:346. 1964.
11. Kershbaum KL, Manchester JH, Shelburne JC. Complete left coronary obstruction. Chest 64:539. 1973.
12. Gates JD, Kirsh MM, Sodeman TM, Walton JA, Brymer JF. Coronary ostial stenosis. Circulation 49:530. 1974.
13. Bjork Vo, Henze A, Szamosi A. Coronary ostial stenosis: a complication of aortic valve replacement or coronary perfusion. Scand J Thorac Cardiovasc Surg 10:1. 1976.
14. Nakjavan FK, Maranho V, Goldberg H. Iatrogenic stenosis of the proximal portion of the coronary arteries; Report of three cases treated with aortocoronary anastomosis. Am Heart J 83:318. 1972.
15. Midell Al, De Boer A, Bermudez G. Post perfusion coronary ostial stenosis; Incidence and significance. J Thorac Cardiovasc Surg 72:80. 1976.
16. Trimble AS, Bigelow WG, Wigle ED, Silver MD. Coronary ostial stenosis. J Thorac Cardiovasc Surg 67:266. 1974.
17. Rissanen V. Occurrence of coroanry ostial stenosis in a nectopsy series of myocardial infarction, sudden death and violent death. Br Heart J 37:182. 1975.
18. Schoenmackers J. Die Angiomorphologie der Koronarogramme Morphologische Grundlagen, Grenzen der Darstellung and Deutung. Fortscher Geb Rontgenstr Nuklearmed Erganzungsband 102:349. 1965.

Original Article

Biochemical markers of cardiac risk and their relation to spirometric indices of airway obstruction among COPD outpatients in a Medical College and Hospital in Kolkata

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Abstract : Very little work has been conducted even in developed countries on the biochemical markers of cardiac risk like homocysteine, lipoprotein a,high sensitivity serum C reactive Protein (hsCRP)in relation to the severity of COPD, as measured by the spirometric indices. In the present study, an inverse correlation could be evaluated between homocysteine and serum hs-CRP and respiratory indices. The biochemical markers assessed had a definite relationship with disease progression.

Key Words : Serm CRP, homocysteine, spirometry, copd

Introduction : There has been an increase in the prevalence of and mortality form Chronic Obstructive Pulmonary Disease (COPD) worldwide. The WHO has predicted that by the year 2020, COPD will rise from its current ranking as the 12th most prevalent disease worldwide to the 5th, and from the 6th most common cause of death to the 3rd. [1]

Several studies suggest that plasma levels of various cardiac biomarkers are often elevated in patients with acute exacerbations of COPD and are associated with increased mortality.[2,3] However, even though such a relation between cardiovascular diseases and COPD is present, very little work has been conducted even in developed countries on the biochemical markers of cardiac risk like homocysteine[1,2,3], lipoprotein a[4], high sensitivity serum C reactive Protein (hsCRP)1 in relation to the severity of COPD, as measured by the spirometric indices. Further, there is a dearth of such studies among patients in a developing country like India where a different outcome is likely owing to the variations in lifestyle as well as risk factors influencing morbidity and mortality of COPD.

Hence, this study was conducted on COPD patients attending the Outpatient Department of the Department of Chest Medicine, Calcutta National Medical College and Hospital, assessing both their cardiac risk factors, as well as their spirometric indices.

Objectives : The study had essentially the following aims and objectives : Primarily, it aimed to test the hypothesis that factors of cardiac risk like plasma homocysteine and serum CRP would be elevated in COPD patients as compared to healthy controls. The study also aimed to realize whether the elevation in the cardiac risk factors is related to severity in the spirometric indices of COPD. The above would be indicative of a positive relation between the severity of COPD and an increased risk to cardiovascular disorders.

MATERIALS AND METHODOLOGY

This was an observational cross-sectional case-control study involving the patients of COPD attending the Outpatient Department of the Department of Chest Medicine at Calcutta National Medical College and Hospital. Research analysis was conducted at the Department of Biochemistry, in association with the Department of Chest Medicine Calcutta National Medical College and Hospital.

Inclusion Criteria for enrollment were-

A prior diagnosis of COPD stated in the patients' medical notes and post-bronchodilator FEV_1/FVC ratio of less than 70%.

Patients were excluded if they had any of the following :

Hemoptysis of unknown origin. pneumothorax. unstable cardiovascular status. recent myocardial infarction or pulmonary embolism. abdominal or cerebral aneurysms. recent surgery. presence of an acute disease process that might interfere with test performance. recent surgery of thorax or

abdomen. acute infection. Inflammatory diseases such as rheumatoid arthritis and history of kidney disease.

The cardiac risk markers were measured as follows-

- Plasma homocysteine levels: Measured by ELISA
- Serum C-Reactive Protein: Measured by immunoturbidimetry

Non-fasting venous blood samples were collected aseptically from the cubital veins of the arms of the patients, for serum CRP analysis and plasma samples with ethylene diamine tetra acetic acid (EDTA) as anticoagulant was used for homocysteine analysis.

A handheld turbine spirometer was used to measure post-bronchodilator FEV_1 and FVC. The spirometer was calibrated appropriately and did not require recalibration. Post-bronchodilator spirometric indices was measured 20 minutes after the subject inhaled two puffs of salbutamol-100 µg.

The levels of the two cardiac risk factors were compared with the spirometric indices of the patient, using a suitable statistical test in order to establish the level of significance and correlation, if any, with each other.

Results : In this study, we had selected at random, 43 COPD patients and 40 relatively healthy subjects as controls.Baseline characteristics were given in Table 1.

Characteristics	Controls (N = 40)	COPD (N = 43)	p-value
Age/yrs mean (SD)	64.8 (6.8)	69.1 (9.8)	0.137
Height/cms	164.3 (9.3)	164.8 (9.2)	0.849
Gender : Male N (%)	16 (64)	23 (79)	0.218
BMI kg/m2 (median (IQR)	27.4 (25.9, 29.9)	24.0 (20.5, 27.0)	0.001
Lung Function (mean (SD))			
FEV1/L	2.25 (0.77)	1.43 (0.60)	<0.001
FVC/L	2.91 (1.02)	2.72 (0.82)	0.18
FEV1/FVC %	78.1 (8.3)	53.1 (14.0)	<0.001
FEV1 % predicted	76.1 (17.2)	49.1 (16.3)	<0.001
tHCY/micromol/L	8.22 (6.63, 9.55)	10.96 (7.56,13.60)	0.006
hsCRP/mg/L	0.890 (0.47, 2.55)	2.050 (0.86, 6.19)	0.023

Table 1. Demographical data, tHCY and hsCRP among controls and COPD patients.

Abbreviations : SD, standard deviation; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; tHCY, total plasma homocysteine; sCRP, serum C-reactive protein; BM

Analyzing this table with Karl Pearson's Correlation Coefficient, we found the following results:

- Inverse relationship between hs-crp level and FEV1/FVC (P value: <0.05){Fig.1}

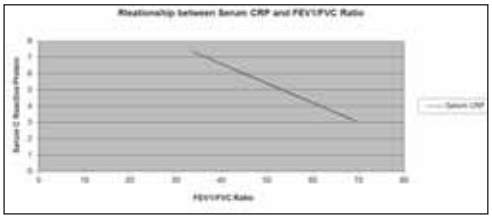

FIGURE 1 : Comparison between Serum CRP levels and FEV1/FVC

- Direct relationship with number of pack years and hs-crp though within a narrow range. (p value: <0.05){Fig.2}

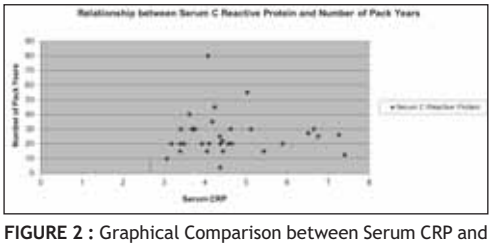

FIGURE 2 : Graphical Comparison between Serum CRP and Number of Pack Years

- Inverse relationship between homocysteine level and FEV1/FVC. (P value: <0.05){Fig.3}

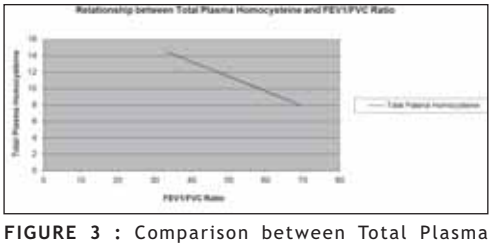

FIGURE 3 : Comparison between Total Plasma Homocysteine and Number of Pack Years

- Direct relationship with number of pack years and homocysteine though within a narrow range. (p value: <0.05){Fig.4}

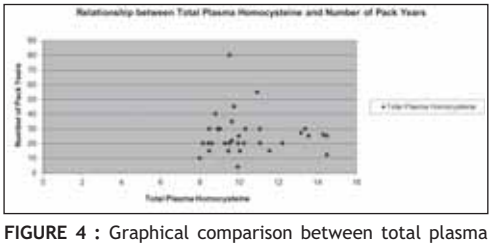

FIGURE 4 : Graphical comparison between total plasma homocysteine and number of pack years

Statistical Data Obtained :

- Karl Pearson's Co-efficient : -0.033
- P value: <0.05

N.B: The scatter pattern is used to avoid confusion from the use of a line graph as the value distribution along the X-axis is within a narrow range.

And with respect to history of smoking we get the following relation, (n=35):

The following data was obtained with resp

Statistical Data Obtained :

- Karl Pearson's correlation co-efficient: -0.030
- P value= <0.05

N.B: The scatter pattern is used to avoid confusion from the use of a line graph as the value distribution along the X-axis is within a narrow range.

Discussion : This study was conducted over a period of two months at Calcutta National Medical College and Hospital. During this time we analyzed the biochemical markers of 43 subjects suffering from COPD, and compared them with those of 40 healthy control subjects.

In the analysis done for serum CRP we found that in general :

Serum hs-CRP was elevated in the COPD subjects at a mean of 4.50 (3.08, 7.41) mg/L than in the case controls.

Compared to the study by Seemungal et al[1], who estimated Serum hs-CRP at 2.05 (0.86, 6.19) mg/l, we obtained a higher value, indicating that altered morbidity and mortality patterns in developing nations do have a bearing on serum hs-CRP levels.

A correlation of r= -0.99 was found with the respiratory indices that showed a strong inverse correlation as hypothesized.

With smoking history, however, we obtained a weaker, but significant r value= -0.033, which indicated that smoking did have a detrimental effect on serum CRP values and might have an impact on its progressive rise among COPD patients.

The analysis was also done for total plasma homocysteine and we found that in general:

Plasma Homocysteine was elevated in the COPD subjects at a mean of 10.15 (8.01, 14.50) micromoles/L than in the case controls.

Compared to the study by Seemungal et al[1], who estimated Plasma homocysteine at 10.96 (7.56, 13.60) micormoles/l, we obtained a lower mean value, which showed that plasma homocysteine was not significantly affected by altered morbidity and mortality conditions of developing nations. In reality, the lifestyle patterns of developed countries, seemed to have a greater impact on it.

A correlation of r= -0.99 was found with the respiratory indices that showed a strong inverse correlation as hypothesized.

With smoking history, however, we obtained a weaker, but significant r value= -0.030, which indicated that smoking did have a detrimental effect on plasma homocysteine values and might have an impact on its progressive rise among COPD patients.

Our results support those of a recent study in a Japanese population who like us showed that a high homocysteine level predicted more rapid FEV_1 decline. However, we had also found that homocysteine is related to COPD severity. Kai and colleagues[1] found that there was a tendency toward a relationship between low arterial oxygen tension and low homocysteine in their COPD patients and speculated that this may cause inhibition of enzymes involved in homocysteine metabolism in the later stages of COPD. However this relationship was not tested in a multivariate analysis. We noted however that the mean FEV_1 of our patients was greater than that in the Japanese study and so, on average, our patients were less severe. Several enzymes are involved either directly or indirectly in homocysteine metabolism and mutations in any of the following- cystathionine beta-synthase, methylenetetrahydrofolate reductase (MTHFR) or methionine synthase reductasemay contribute to hyperhomocysteinaemia in different populations.[6]

Thus, based on the above findings, we could comprehensively state the following facts.

- Biochemical marker of Cardiac disease, homocysteine[1,2] was inversely related to the respiratory indices of a COPD patient.
- Similar inverse correlation could be evaluated between markers of systemic inflammation, serum hs-CRP[1,2,5] and respiratory indices.
- The biochemical markers assessed had a definite relationship with disease progression. Amongst the markers assessed, serum hs-CRP and plasma homocysteine were equivalently sensitive to the progressing disease process. However, in terms of cardiac health analysis, plasma homocysteine was preferred as it was cardio-specific, compared to serum hs-CRP, which might be elevated in several inflammatory conditions, and thus not a true indicator of cardiac health.

- Finally, we had hypothesized that altered morbidity and mortality factors in a developing country like India would affect the status of the biochemical markers[7]. In our study, serum hs-CRP, showed a definitely increased mean value of 4.50 mg/l as compared to the 2.05 mg/l found in other studies done in developed countries. Plasma homocysteine however, gave a surprising result, as the mean value we obtained (10.15 micromoles/L)was less than the values obtained in the studies from developed countries(around 10.96 micromoles/l). This might be attributed to alternative risk factors like altered diets in developed countries, or may be the result of a smaller sample size of study. Hence, this requires further elucidation.

References :

1. Seemungal TA et al, Plasma homocysteine is elevated in COPD patients and is related to COPD severity. Int J of Chron Obstuct Pulmon Dis 2007;2(3):313-21.
2. Andersson A et al, Hyperhomocysteinemia and changed plasma thiol redox status in chronic obstructive pulmonary disease. Clin Chem Lab Med. 2001 Mar;39(3):229-33.
3. Fimognari FL et al, Hyperhomocysteinaemia and poor vitamin B status in chronic obstructive pulmonary disease. Nutr Metab Cardiovasc Dis. 2009 Nov;19(9):654-9. Epub 2009 Mar 17
4. Ueland PM, Total homocysteine in plasma or serum: Methods and clinical application. Clin chem. 1993;39: 1764-1779
5. Pelegrino NR, Tanni SE, Amaral RA, Angeleli AY, Correa C, Godoy I, Effects of Active smoking on airway and Systemic Inflammation profiles in patients with chronic obstructive Pulmonary Disease. Am J Med Sci 2012 Aug 7.
6. Kluijtmans LA, Young IS, Boreham CA, et al. Genetic and nutritional factors contributing to hyperhomocysteinemia in young adults. Blood. 2003;101(7):2483–8.
7. Anthonisen NR, Connett JE, Enright PL, et al. Hospitalisation and mortality in the Lung Health Study.Am J Respir Crit Care Med. 2002;166:333–89.

Diabetes and Heart

Cardio Vascular Outcomes with New Age Antidiabetics : an Impartial Look

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Abstract : Worldwide there are 430 million diagnosed diabetics, with India contributing 65 millions,; also there is a large population of hidden , undiagnosed patients. Diabetes increases the CVD risk by 1.8 times, heart attacks 1.7 times, and strokes by 1.5 times. Most diabetics die earlier than the general population, often before the age of 70 years. Atleast 60% or more of these deaths are due to cardiovascular causes. Such intimate and fatal relation between these two conditions have prompted the search for that pleuripotentantidiabetic that can halt or reduce cv disease, and/or atleast not worsen or aggravate the already existing cardiovascular pathology in a diabetic. In such context, this article is an attempt to present an unbiased view on the newer antidiabetics and their claims

Key words: Cardiovascular outcomes,newer antidiabetics

Introduction : Globally, diabetes is the 7th leading cause of death[1], with cardiovascular diseases still at number one.

Conversely, more than 60% of diabetics will die from cardiovascular events. Dyslipidimea and hypertension, rising from the same common soil, bind the two together in an almost inseperable manner, and greatly increase the risk of premature death. In fact, diabetic complications are responsible for reduction of mean life expectancy of 12 years in men and 19 years in women.

A clinician treating diabetic patients needs to address three basic issues. These are:

1) Prevent the the metabolic complications, ie hyperglycemia (including its acute manifestations ie diabetic ketoacidosis and hyperglycemic hyperosmolar syndromes) and treat associated hypoglycemia.
2) Prevent/retard/delay the microvascular complications, ie nephropathy and retinopathy, and
3) Prevent the macrovascular complications ie, ischaemic heart disease, stroke, and peripheral arterial disease .

   Neuropathy, with both microvascular and macrovascular components also needs attention, as also a myriad of other complications which are less well defined.

The issue of glycemic control : Strict long term glycemic control, started early, soon after the diagnosis of diabetes, unequivocally reduces microvascular complications. This fact is backed by very strong evidence from DCCT[2] and UKPDS[3] trials. However, good glycemic control achieved later, say after a decade of uncontrolled diabetes, might not show similar benefits. (ACCORD)[5].

However, in contrast to the microvascular benefits seen with tight glycemic control, similar degree of glycemic control failed to give a parallel amount of macrovascular protection. A much smaller(though statistically significant) cv risk reduction was demonstrated in the 10 yr follow up of the DCCT (EDIC) and UKPDS participants. Significantly, the UKPDS and DCCT participants were newly diagnosed patients ,and in the UKPDS, mostly young type 2 diabetics. At this juncture, it will be worthy to note that in the UKPDS a small set of obese type 2 patients did achieve significant cv risk reduction with the use of metformin[4] and the benefits persisted even in the 10 and 15 yr follow up of these patients, an effect which prompted most of the guideline issuing bodies to chose metformin as their first line drug in treating type 2 diabetes.

Subsequent to UKPDS, 3 major glycemic control trials have been completed, targeting tight glycemic control in t2dm patients. these were the ACCORD[5], the VADT[6], and the ADVANCE[7] studies. All were

mega trials involving around 10000 patients each. But, unlike in UKPDS, these were patients mostly having diabetes for more than 10 years, and were elderly (almost10 yrs older compared to the UKPDS population), and most important, had significant cv disease or multiple cv risk factors at the onset (at recruitment). All 3 studies targeted and achieved tight glycemic control. In the ADVANCE , treatment with gliclazide demonstrated some microvascular benefits, mostly arising from reduction in new onset albuminuria. There was no cv benefit of any significance. What happened in the ACCORD and VADT were even more stunning. To the awe and dismay of the investigators, the preliminary and post analysis data of ACCORD and VADT showed the tightglycemic control wing to have significant excess cv events and mortality. In fact, the regulators terminated the ACCORD study prematurely.

Lack of strong cv protection data in the glycemic control trials probably prompted the developers of newer anti diabetic medicines to focus more on glycemic control rather than cv issues.

Side by side, A controversial 2007 meta-analysis[8] questioning the cardiovascular safety of rosiglitazone opened a Pandora's box. The whole rosiglitazone issue became so murky that the FDA and the US senate ordered separate investigations and immediate black box warning was soon followed by calls to withdraw the drug from the market.

Many suchCV safety concerns have been raised with respect to several antidiabetes compounds approved or under development for the treatment of type 2 diabetes.Due to such controversies, and somewhat compelled by the rosiglitazone events, In July 2008, the U.S. Food and Drug Administration (FDA)'s Endocrinologic and Metabolic Drugs Advisory Committee met to discuss the role of CV assessment in the pre- and postmarketing settings. Subsequent to the Endocrinologic and Metabolic Drugs Advisory Committee recommendation, the FDA determined that concerns about CV risk should be more thoroughly addressed during antidiabetes drug development. The 2008 guidelines resulted in profound changes in the ways new antidiabetes drugs are evaluated and brought to market.

An upper bound of the 95% CI for the risk ratio of important CV events of <1.3 should be used as a key criterion for excluding unacceptable CV risk for new treatments of type 2 diabetes.

Study patients must include those with relatively advanced disease, elderly patients, and patients with some degree of renal impairment.

A minimum of 2 years' CV safety data must be provided.

All phase 2 and 3 studies should include a prospective, independent adjudication of CV events. Adjudicated events should include CV mortality, myocardial infarction (MI), and stroke, (collectively called the Major Adverse Cardiovascular Events or the MACE) and can also include hospitalization for acute coronary syndrome, urgent revascularization procedures, and possibly other end points.

For satisfaction of the new statistical guidelines, the analysis of CV events may include a meta-analysis of all placebo-controlled trials, add-on trials (i.e., drug vs. placebo, each added to standard therapy), and active-controlled trials or an additional single large safety trial may be conducted that alone, or added to other trials, would be able to satisfy this upper bound before New Drug Application/ Biologic License Application submission.

Thus, was ushered a new era of mega trials, this time however, focusing on a single drug and focusing on its cardiac safety issues. Most new age antidiabetics like the gliptins, the glp1 analogues , some newer insulins, and the sglt2 inhibitors have already gone through or are being investigated in these trials. One needs to distinguish these studies from glycemic control–focused studies such as the UKPDS, Action to Control Cardiovascular Risk in Diabetes (ACCORD), and Action in Diabetes and Vascular Disease : Preterax and Diamicron MR Controlled Evaluation (ADVANCE), which used multiple treatment modalities to achieve glycemic targets, and have already been mentioned previously.

Prominent among the cv safety trial of the new drugs are the TECOS[9] with sitagliptin, EXAMINE with alogliptin[10], SAVOR TIMI with saxagliptin[11] VIVIDD with vildagliptin, ELIXAwith lixisenatide[12] LEADER with liraglutide[13], and EMPAREG outcomes with empagliflozin[14]. All these trials have been completed and presented. Some more to follow soon are CAROLINA with linagliptin, CANVAS with canagliflozin and DAPA DECLARE with withdapagliflozin.

It should be noted that many of these trials (e.g., EMPAREG, LEADER, CAROLINA[13]) are designed to test for noninferiority first and, if successful, subsequently test for superiority, which, in a way, will appear to be wasteful to many scientists.

Commenting on the latest results to be reported from one of these trials, at the European Society of Cardiology (ESC) 2015 Congress, cardiologist Gabriel Steg, MD, from Hôpital Bichat-Claude Bernard, Paris, France, said: "We have a flurry of trials on the cardiovascular safety of diabetes drugs — I've counted more than 150,000 patients enrolled in [such] completed or ongoing trials. One has to wonder whether this is…diverting [money] from more important tasks.

"I suggest that it is time to stop wasting resources on noninferiority trials and to work on truly improving diabetes care," DrSteg asserted.

"In addition, I'm seeing that noninferiority trials are often being misinterpreted as lack of efficacy trials and they tend, among nonspecialists, to generate skepticism regarding the treatment of diabetes or the need to control glycemia — and this is an important side effect of this whole story in the general public of physicians," he told meeting attendees.

Now, Keeping debates and grey shades away, let us take up the puzzled and confused clinician's concerns and take an objective look at the c.v. issues of these newer antidiabetics.

Probably the most popular and the most prescribed of these newer molecules are the gliptins.

Sitagliptin, Vildagliptin, Saxagliptin, linagliptin, teniligliptin and gemigliptin are in the indian market, with a 7TH , alogliptin, not yet available in india. All of these except lina, gemi, and tenili have completed their cv safety studies (CAROLINA for lina will be completed in20 17/18.none of these studies showed any increase or decrease in the Major Adverse Cardiac Events(ie death/ nonfatal mi/ or non fatal stroke). However , results from SAVOR-TIMI 53 TRIAL showed an unexpected, statistically significant, excess rate of hospitalization for heart failure in the saxagliptin group (hazard ratio 1.27). similarly the EXAMINE trial for ALOGLIPTIN showed a nonsignificant numerical excess of hospitalization for heart failure in the alogliptin group. Data with lina, tenili are still awaited.a post hoc analysis of the vivid data with vilda has cleared vilda, though there have been criticisms about whether there was enough statistical and clinical end point determining power in this study. On the other hand, SITA in TECOS has received a clean chit On all counts of cardiac safety. Thus, as of now, sita appears to be the safest molecule, while treating a cardiac patient with established heart failure, or with chances of heart failure.. it would be pertinent to mention that none of these molecules, sita included , have shown any risk reduction with MACE or other secondary cardiac outcomes.

The gliptin cv outcomes studies were followed by the EMPA REG OUTCOMES, the ELIXA and the LEADER studies,. All 3 have been presented in international fora and duly published. The ELIXA and LEADER were studies carried out with two GLP 1 ANALOGUES , LIXISENATIDE and LIRAGLUTIDE.

The ELIXA study with LIXISENATIDE , like the TECOS, was neutral as regards the MACE , and did not show any superiority or inferiority as compared to placebo. An obvious conclusion is that it might be safely used in diabetics with cvd or heart failure.

The ELIXA was followed by the LEADER , which was carried out with LIRAGLUTIDE, probably the most widely used GLP1 analogue. Even before the final presentation, the top up data had brought exciting news regarding superiority in cardiac outcomes. In the the final presentation at the ADA 2016, the following outcomes were presented:

A) the primary outcomes (1st occurrence of death from CV causes, nonfatal mi, stroke,) occurred 13% less in the liraglutide group., p 0.01 for superiority

B) death from cardiovascular causes reduced by 22% in the liraglutide group compared to placebo.

C) All cause death reduced by 15% in the liraglutide vs. placebo.

D) Nonfatal m.i., nonfatal stroke, and hospitalization for heart failure were nonsignificantly lower in the liraglutide group compared to theplacebo.

These were impressive results , and here is a molecule with clearcut cv safety as well as some amount of cv protective role in some patients with established cvd. However, notwithstanding these novel cardiac and other benefits it is still not clear whether such cv benefits shown in a population with established cvd will also happen with younger patients , particularly those without established cvd or without significant cv risk factors.

In the flipside, adverse GI effects still haunt this molecule causing an average dropout of about 4% even in a controlled study population. Also, there was a numerically increased incidence of pancreatic carcinoma (statisticallynonsignificant) in the liraglutide group in leader. The high cost and the issue with daily injections also stand in the way of its wider acceptance.However, despite

apprehensions,there was no increased numbers with pancreatitis in the liraglutide group.

In the 2015 EASD, Dr. Bernard Zinman and his group presented the EMPA REG OUTCOME trial with empagliflozin, which was simultaneously published online in the NEJM 2015. WORKING with the novel SGLT2inhibitor, Empagliflozin, they recorded the following outcomes:

a) 38% relative risk reduction of death from cardiovascular causes in the empa group.

b) 35% relative risk reduction of hospitalization for heart filure.

c) 32% relative risk reduction of death from any cause.

Such robust risk reductions were never witnessed with any other antidiabetics. In fact the magnitude of risk reduction is almost similar to the statin studies including the seminal 4S SIMVASTATIN TRIAL.

There was some increased risk of genital mycotic infections, as expected, in the empa group.

There was no significant difference between the groups as regards rates of nonfatal myocardial infarction or stroke.

The resultsof the empareg and the fact that it is an oral molecule, and its other benefit of weight loss,has made empa and the other SGLT2 blockers immensely popular with the physicians in a short time. This was soon followed by reports of occurrence ofeuglycemic ketoacidosis as a side effect of these drugs. However, this adverse effect seems to be the result of faulty use of this molecule by the physicians in type1 diabetics, either full blown or in evolution, a condition where it is contraindicated., or its use conjoined with drastic reduction of insulin doses in type 2 diabetes with OHA failure. Further, there have been reports of increased incidence of uti of various types and degrees in the users of this group of molecules.

At this juncture, let us look back to the year 2003, and another seminal study , The STENO 2[15], published in the NEJM.

Scientists at the STENO DIABTES CENTRE in SWEDEN assignedEighty patients with type 2 diabetes and microalbuminuria were assigned to receive conventional treatment in accordance with national guidelines, and another 80 were assigned to receive intensive treatment with stepwise implementation of behavior modification and pharmacological therapy that treated hyperglycemia, hypertension, dyslipidemia, and microalbuminuria, along with aspirin. Primary endpoints were Death from CVD, nonfatal myocardial infarction (MI), nonfatal stroke, revascularization, and amputation.

The Steno study has attempted to close the gap in evidence regarding cv outcomes in glycemic control trials by testing an intensive multifactorial intervention against conventional treatment. The intensive intervention consisted of step-wise introduction of lifestyle and pharmacological interventions aimed at keeping glycated hemoglobin < 6.5%, blood pressure < 130/80 mmHg, total cholesterol < 175 mg/dl, and triglycerides < 150 mg/dl. The lifestyle component of the intensive intervention included reduction in intake of dietary fat, regular exercise, and smoking cessation. Participants receiving intensive intervention were also advised to take aspirin, a dietary supplement consisting of vitamins E and C, folic acid, and chromium picolinate and were given an angiotensin-converting enzyme (ACE) inhibitor, regardless of blood pressure.

Results were a pointer to the sceptics. At a mean follow-up of 7.8 years, patients receiving the intensive therapy had a 53% (95% CI: 27–76%) lower risk of CVD, 61% (13–83%) lower risk of nephropathy, 58% (14–79%) lower risk of retinopathy, and 63% (21–82%) lower risk of autonomic neuropathy.

Thus it was shown thatA target-driven, long-term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes and microalbuminuria reduces risk of CVD and microvascular events by about 50%.

It appears that the holy grail of an antidiabetic with anti-cvdproperties , which is safe in all other counts , and is also cheap enough to reach the masses , is still to be found. Till then, the multifactorial approach as practiced in the STENO 2, started soon after diagnosis, as in the UKPDS, is the next best option available to the conscientious physician.

References :

1. WHO | WHO Mortality Database - World Health Organization
www.who.int/healthinfo/mortality_data/
2. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329:977–986. [PubMed]
3. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33) Lancet. 1998;352:837–853. [PubMed]
4. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34) Lancet. 1998;352:854–865. [PubMed]
5. The Action to Control Cardiovascular Risk in Diabetes Study Group*
N Engl J Med 2008; 358:2545-2559June 12, 2008DOI: 10.1056/NEJMoa0802743
6. Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes
William Duckworth, M.D., Carlos Abraira, M.D., Thomas Moritz, M.S., Domenic Reda, Ph.D., Nicholas Emanuele, M.D., Peter D. Reaven, M.D., Franklin J. Zieve, M.D., Ph.D., Jennifer Marks, M.D., Stephen N. Davis, M.D., Rodney Hayward, M.D., Stuart R. Warren, J.D., Pharm.D., Steven Goldman, M.D., Madeline McCarren, Ph.D., M.P.H., Mary Ellen Vitek, William G. Henderson, Ph.D., and Grant D. Huang, M.P.H., Ph.D., for the VADT Investigators*
N Engl J Med 2009; 360:129-139January 8, 2009DOI: 10.1056/NEJMoa0808431
7. Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes
The ADVANCE Collaborative Group*
N Engl J Med 2008; 358:2560-2572June 12, 2008DOI: 10.1056/NEJMoa0802987
8. Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes
Steven E. Nissen, M.D., and Kathy Wolski, M.P.H.
N Engl J Med 2007; 356:2457-2471June 14, 2007DOI: 10.1056/NEJMoa072761
9. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes
Jennifer B. Green, M.D., M. Angelyn Bethel, M.D., Paul W. Armstrong, M.D., John B. Buse, M.D., Ph.D., Samuel S. Engel, M.D., JyotsnaGarg, M.S., Robert Josse, M.B., B.S., Keith D. Kaufman, M.D., JoergKoglin, M.D., Scott Korn, M.D., John M. Lachin, Sc.D., Darren K. McGuire, M.D., M.H.Sc., Michael J. Pencina, Ph.D., EberhardStandl, M.D., Ph.D., Peter P. Stein, M.D., ShailajaSuryawanshi, Ph.D., Frans Van de Werf, M.D., Ph.D., Eric D. Peterson, M.D., M.P.H., and Rury R. Holman, M.B., Ch.B., for the TECOS Study Group*
N Engl J Med 2015; 373:232-242July 16, 2015DOI: 10.1056/NEJMoa1501352
10. Alogliptin after Acute Coronary Syndrome in Patients with Type 2 Diabetes
William B. White, M.D., Christopher P. Cannon, M.D., Simon R. Heller, M.D., Steven E. Nissen, M.D., Richard M. Bergenstal, M.D., George L. Bakris, M.D., Alfonso T. Perez, M.D., Penny R. Fleck, M.B.A., Cyrus R. Mehta, Ph.D., Stuart Kupfer, M.D., Craig Wilson, Ph.D., William C. Cushman, M.D., and FaiezZannad, M.D., Ph.D., for the EXAMINE Investigators*
N Engl J Med 2013; 369:1327-1335October 3, 2013DOI: 10.1056/NEJMoa1305889
11. Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus
Benjamin M. Scirica, M.D., M.P.H., Deepak L. Bhatt, M.D., M.P.H., Eugene Braunwald, M.D., P. Gabriel Steg, M.D., Jaime Davidson, M.D., Boaz Hirshberg, M.D., Peter Ohman, M.D., Robert Frederich, M.D., Ph.D., Stephen D. Wiviott, M.D., Elaine B. Hoffman, Ph.D., Matthew A. Cavender, M.D., M.P.H., Jacob A. Udell, M.D., M.P.H., Nihar R. Desai, M.D., M.P.H., OfriMosenzon, M.D., Darren K. McGuire, M.D., Kausik K. Ray, M.D., Lawrence A. Leiter, M.D., and ItamarRaz, M.D., for the SAVOR-TIMI 53 Steering Committee and Investigators*
N Engl J Med 2013; 369:1317-1326October 3, 2013DOI: 10.1056/NEJMoa1307684
12. Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome
Marc A. Pfeffer, M.D., Ph.D., Brian Claggett, Ph.D., Rafael Diaz, M.D., Kenneth Dickstein, M.D., Ph.D., Hertzel C. Gerstein, M.D., Lars V. Køber, M.D., Francesca C. Lawson, M.D., Lin Ping, M.D., Xiaodan Wei, Ph.D., Eldrin F. Lewis, M.D., M.P.H., Aldo P. Maggioni, M.D., John J.V. McMurray, M.D., Ph.D., Jeffrey L. Probstfield, M.D., Matthew C. Riddle, M.D., Scott D. Solomon, M.D., and Jean-Claude Tardif, M.D., for the ELIXA Investigators*
N Engl J Med 2015; 373:2247-2257December 3, 2015DOI: 10.1056/NEJMoa1509225
13. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes
Steven P. Marso, M.D., Gilbert H. Daniels, M.D., Kirstine Brown-Frandsen, M.D., Peter Kristensen, M.D., E.M.B.A., Johannes F.E. Mann, M.D., Michael A. Nauck, M.D., Steven E. Nissen, M.D., Stuart Pocock, Ph.D., Neil

R. Poulter, F.Med.Sci., Lasse S. Ravn, M.D., Ph.D., William M. Steinberg, M.D., MetteStockner, M.D., Bernard Zinman, M.D., Richard M. Bergenstal, M.D., and John B. Buse, M.D., Ph.D., for the LEADER Steering Committee on behalf of the LEADER Trial Investigators*
N Engl J Med 2016; 375:311-322July 28, 2016DOI: 10.1056/NEJMoa1603827

14. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., ChristophWanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators
N Engl J Med 2015; 373:2117-2128November 26, 2015DOI: 10.1056/NEJMoa1504720

15. Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes
Peter Gæde, M.D., PernilleVedel, M.D., Ph.D., Nicolai Larsen, M.D., Ph.D., Gunnar V.H. Jensen, M.D., Ph.D., Hans-HenrikParving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.
N Engl J Med 2003; 348:383-393January 30, 2003DOI: 10.1056/NEJMoa021778

15. Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes
Peter Gæde, M.D., D.M.Sc., Henrik Lund-Andersen, M.D., D.M.Sc., Hans-HenrikParving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.
N Engl J Med 2008; 358:580-591February 7, 2008DOI: 10.1056/NEJMoa0706245

Review Article

Kolkata Medical Emergency System (KMES) - an Innovation for Integrating Emergency Services for Better Health Care Delivery

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Abstract : Providing integrated emergency healthcare within the golden hour is a challenge in our state where proper referral system is lacking in kolkata. Overburdening of city hospitals and non availability of bed leads to unnecessary harassment on top of delay. KMES is an endeavour to address this problem. Involving general population, paramedics , medical team and hospitals integrated with android technology it will going to be the probable solution to the unmet needs in emergency health care system.

Key Words : Emergency care, cardiac emergencies, Kolkata

Introduction : Pre-hospital emergency care plays a vital role in the management of cardiovascular emergencies particularly myocardial infarction.[1] Several large studies showed that rapid diagnosis and application of thrombolysis reduces morbidity and mortality rates in myocardial infarction[2,3]. Strategies that improve time to treatment in the pre-hospital setting are therefore of fundamental importance in the management of this fatal disease.

With increasing urbanization in low and middle income countries, medical emergencies of cardiovascular etiology as well as stroke and trauma has increased manifold. In the absence of a Government-owned 911-style system, emergency medical services are provided by multiple, isolated providers (Government, semi-Government, private for-profit and non-Government Organizations) with varying capability, resulting in an inefficient & fragmented emergency management system. The patient often needs to wait for an ambulance and/or is transported without proper paramedic support in public transport, and may need to be shuttled from one hospital to another due to unavailability of the required critical care unit (e.g.: NICU, CICU). Also, obtaining emergency resources like blood is a challenge due to shortage and the patient often doesn't receive the life-saving treatment during the golden-hour of emergency, resulting in high mortality. The above issues are multiplied exponentially during any disaster, large or small (e.g: a fire in a public area, train accident, terrorist attack). Currently, there is no central, real-time system for medical emergency (including acute coronary syndrome and other cardio-vascular emergency along with stroke, road traffic accidents, other trauma etc.) in Kolkata, making coordination between disaster recovery agencies and public health services nearly impossible. Kolkata Medical Emergency System (KMES) devised by us offers a solution to this problem.

Kolkata Medical Emergency System (KMES) : The concept

KMES is inspired by North America's 911 systems. However, owing to the huge gap between the delivery of emergency care in India and the US, our operational & business model is different from that of 911. We propose to integrate and enhance the services provided by the isolated emergency providers in urban areas, both public & private, to create a standardized, centralized, integrated, interoperable, real-time Medical Emergency System that seamlessly connects the three cardinal pillars of medical emergency care namely “Sense”, “Reach” & “Care”. The system will be web, mobile and SMS enabled and operated by a state-of-the art emergency control room. Initial site of implementation is Kolkata, India, the most congested metropolitan city in India with an overburdened healthcare system.

Currently, we are developing the KMES Phase I as an availability management platform for Emergency Healthcare Facilities and Products. In partnerships with Kolkata's primary hospitals & blood banks, KMES is gathering and broadcasting the availability of Critical Care Unit (CCU) &

blood. The same information will be available to healthcare providers, emergency responders and disaster management agencies. In Phase II, the plan is to integrate, enhance and organize the existing ambulance services in Kolkata, which is primarily a small fleet of independently operated private ambulances along with few government/police ambulances. After equipping the ambulances with GPS tracking software to capture real-time location and availability information, paramedic training will be provided to the networked ambulance staff. A pool of paramedics will be created from which ambulances, hospitals, police and fire services can recruit. Finally, a state-of-the-art multi-lingual emergency response centre will provide 911 type coordination by dispatching the nearest networked ambulance and paramedic, who after stabilizing the patient will transport him/her to the nearest facility. Further, if an elderly patient staying alone suddenly falls sick, he/she can use a mobile phone and/or a wearable device (prototype being designed) to send an alert to the medical emergency centre for emergency retrieval. (Fig.1)

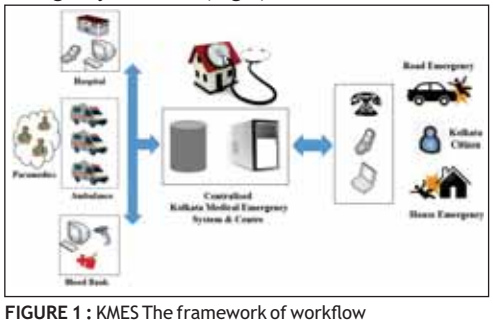

FIGURE 1 : KMES The framework of workflow

Simultaneously, KMES introduces social justice in a deeply divided, two-tier healthcare system by making uniform, highly-relevant emergency medical data available to all citizens, irrespective of their social or economic status.

Implementation of KMES : the preparatory phase

We undertook extensive public communications via major local media houses including Times Of India (highest circulated daily in India), The Telegraph (highest circulated English daily in Kolkata) and Anandabazar Patrika (highest circulated Bengali newspaper in India and Kolkata), Weekly Magazines (Mint and Femina) as well as social media (Facebook, Twitter) and direct public interactions. As a result we received enquiries from interested citizens, as well hospitals not included as pilot sites. We reached out to the Traffic Police department, who showed eagerness to use the system across Kolkata Metropolitan area, as this would immensely help them during road accidents.

Based on our interactions, we realized that including hospitals from different parts of the city beyond the pilot sites would have a significant public health impact. We also realized that including only 3 pilot sites was creating the false perception that KMES was advertising these private hospitals. Since initial public response is critical for the adoption of the system, we would not want users to be put off by not finding major hospitals near his/her neighborhood included in the network during initial enquiries through phone or the web.

On the other hand service standards are not uniform across all Kolkata hospitals. Some hospitals claiming to have Critical Care Units (CCU/ICU) lack proper facilities such as Ventilators in all the ICU beds or Cath Lab with a Cardiac ICU (CICU). So a proper vetting of hospitals is required for inclusion in the KMES network to ensure integrity of the information provided by KMES. So we visited each hospital that had shown interest to join the network and have decided to include only those hospitals, which have ICU beds with proper facilities and categorization, as applicable (e.g.: Neo Natal ICU, Cardiac Care ICU, Neuro ICU etc).

Although initial plan was to scale KMES across the major hospitals of Kolkata in a two to three year plan after completing the pilot project, due to the reasons above, we decided to expand our reach from the 2 to 3 pilot hospitals to about 20 major hospitals in Kolkata in the initial phase itself.

Lessons Learned : During the preparatory phase, we have learned the following lessons-

1. To make the KMES system useful to the public, it will be important to include as many as hospitals possible with good critical care facilities in the initial phase. As such, we have decided to implement KMES for all the major hospitals in and around Kolkata.
2. We started to build the system with a globally dispersed team but realized that the detailed requirement needs to be gathered on-site in the Hospitals before we can embark in any system development
3. Communication with the hospitals and blood banks over telephone and though emails is ineffective. It is necessary to have face-to-face interaction with the administration.

The challenges : The primary challenge for KMES is its adoption by all major hospitals in Kolkata. Few hospitals in Kolkata have a fully digitized system for patient and bed management. Hospitals, which do have digitized systems are not keen to share patient information or allow direct integration with their system for security, privacy concerns etc. Hospitals lacking digitized systems do not have the finances to build a complete Bed Management system. However most hospitals have registration desk with internet connections and have agreed to update the bed availability information manually, provided it can be done easily. As such we have decided to build a minimally invasive, intuitive system which will be available via internet using web-browser, phone app, as well as keep the option of automated integration with internal system.

KMES Hospitals Network Development and Implementation : Phase1

We identified the following issues in medical emergency system implementation in large cities like Kolkata, where emergency care is provided by many Hospitals with varying capability:

- Each Hospital has different workflow and it is very difficult to standardize Bed Management
- Service providers have heterogeneous data & information management systems.
- Hospitals typically have proprietary, closed and isolated information systems and lack internal IT staff to integrate the internal systems.
- Though several standards exist for interoperability of clinical data (HL7, CCR etc), none exists for medical emergency services.
- No hospital wants to share its patient data due to privacy and financial reasons
- Several hospitals do not want any automated interface between their internal system and KMES for several reasons, ranging from fear of data theft (of customer and other data) to logistic considerations
- Several hospitals manage beds using paper tickets (known as bed-tickets) and do not have any electronic system in place.

We tackled these issues by following a few pragmatic approaches :

- Multiple options to integrate with KMES by providing customizable solutions for each Hospital/Blood Bank to integrate its own data source with minimal intrusion.
- KMES central software, Medical Emergency System (MES) to be exposed via APIs (eg. XML and JSON format), to enable real time integration if the hospital agrees.
- Easy update using web-portals and smart phone apps for hospitals lacking or not willing to integrate their electronic bed management system.
- Only capturing supply chain information (ICU/CCU, BSU) without any patient record. Prototype is demonstrated to the hospitals.
- Efficient implementation framework with significant usage of Open Source technologies to minimize reinventing the wheel. Focus is on implementation rather than on technology.

Medical Emergency System (MES) Development :

The two primary system components have been developed with above design principles in mind:

1. Secured, backend hospital bed management system on top of the Open source DHIS system (180.149.243.108:8080/kmes/). Customized, secure bed management system being developed for each of the 20 hospitals in collaboration with the Hospital
2. An open portal readily accessible to the public and to the Emergency Inquiry Centre (http://kmes.in) along with mobile website (m.kmes.in) and smart phone App (tinyurl.com/kmes-in).

If the user types in an address such as South City, Kolkata , which is a popular land-mark and clicks on “Find Nearest Hospitals”, the nearest Hospitals where the system is implemented will be shown. The MES has been developed as a generic emergency (acute coronary syndrome and other cardio-vascular emergency along with stroke, road traffic accidents, other trauma etc.) system platform that can be configured for any city, with the following design principles:-

a. Use of stable, community supported, open source, JEE based DHIS2 and Open MRS platforms as base for the backend system

b. The back-end system is exposed via REST based APIs through which bed and blood availability information can be pushed from hospitals and blood banks.

c. If no internal system is available, internet based secured portal is available for the Hospital.

The salient system features are:

- One click update when a patient is admitted to or discharged from a specific ICU bed.

- Sensible default values (such as current date, type of ICU beds etc) will be chosen as per hospital minimizing the data entry required by hospital staff.
- Data for reporting, evaluation and research will be updated at midnight in batch mode
- Customized portal for each Hospital, with update access for respective Hospital staff only
- Portal can be customized to maintain not other relevant information, such as total number of beds by type, reserved beds etc, apart from availability information.
- The system is available in offline mode allowing update of availability information even when internet connection is down. The data is stored locally and synced with the central server as soon as internet connection becomes available.

d. The public portal and mobile site, built using PHP, and smart phone apps invoke the REST APIs to expose the availability information. The salient features are:

- Use Google Map API to find and provide driving directions to the nearest hospitals.
- Availability information by Hospital and by type of beds
- The date and time of the last update by the Hospital is displayed, to enable informed decision (For example, if the last update was a day earlier, the information may not be valid any more)
- Capabilities not available (for example, Emergency Neuro Surgical Facility or Emergency Coronary Angiography) at a particular hospital are also displayed when displaying ICU availability to allow informed decision making.

Implementation in the Major Hospitals of Kolkata

In the first year of the project, we concentrated on building the Hospital network of KMES and implementing it in all the major hospitals in Kolkata. We followed a simple, robust, legally & ethically binding process for this collaboration between KMES and the Hospitals. Although there were initial struggles with a few hospitals, we were able to create a streamlined and efficient process, with which, it is only few weeks' effort to bring any Hospital in the network.These are-

1. An email is sent with the salient points of the system, requesting a meeting with the concerned authorities of a specific Hospital
2. A power point presentation along with a demonstration of the system (often needed multiple times to various management stakeholders and physicians involved in the critical care process), showing the multiple options of integration as well as ease of creating a customized, independent, secured portal for the Hospital. During this presentation, the critical care facilities are visited by our organization to confirm the minimal requirement criteria. Only when the concerned hospital authorities are convinced, do we move to the next step. (On average, we have met with individual Hospitals at-least five to six times in-person and numerous times over phone)
3. A formal MOU (Memorandum of Understanding) outlining the responsibility of the Hospital and our organization is countersigned by both organizations to start the implementation.
5. A questionnaire on Critical Care facilities, emergency work-flow and hospital information system is filled up by face to face interview with respective departments.
6. The final implementation for each hospital. This is simple from a technological perspective. However we realized that this stage may be quite lengthy due to varied reasons ranging from not having all the ICU in-charge in one session to the solitary internal IT staff of the Hospital leaving the hospital.

Still, with all these challenges, we have been able to complete implementation for most of the major Hospitals of Kolkata in the very first year.

Primary Challenge identified in Phase I and Solutions

In Phase I, setting up the Emergency Inquiry Centre and making it sustainable, was the biggest challenge. The primary operational cost of KMES was the 24 X 7 emergency inquiry center.

First, we requested the government to adopt the Kolkata medical emergency system within their existing emergency response center but as the current emergency center is run by the Police rather than Health department, we were not able to convince them to take up the Medical Emergency System. As that effort failed, we decided to convert our software into self-service based smart phone Apps and Mobile web-sites, minimizing the need of human resources which is the primary cost of KMES operation. As availability of internet/data in phone is not so common in India we continued to receive many calls. So, initially we had decided to

makeKMES, IVR (Interactive Voice Response) enabled. But over time, specifically in the last one year, due to significant reduction in internet/data costs over mobile network we have seen a surge in the usage of the KMES mobile website, with significant reduction in call volume. As such, we have currently shelved the idea of IVR enabling and decided instead to invest the effort in more automation, technology enablement and new services.

Emergency Service Innovation Award in India

The first phase of KMES project, KMES 1.0 had been awarded the Health Care innovation award in the country's (India) leading Emergency Service Award program conducted by AIIMS (All India Institute of Medical Sciences), New Delhi, due to a very innovative yet practical and feasible concept, which can be replicated across cities in India with varied emergency service providers with varying capability.

References :

1. Johnston S, Brightwell R, Ziman M Paramedics and pre-hospital management of acute myocardial infarction: diagnosis and reperfusion.Emerg Med J 2006;23:331–334. doi: 10.1136/emj.2005.028118
2. Bett N, Aroney G, Thompson P. Delays preceding admission to hospital and treatment with thrombolytic agents of patients with possible heart attack. Aust NZ J Med 1993;23:3121–3.
3. Gibler WB, Kereiakes DJ, Dean EN. Prehospital diagnosis and treatment of acute myocardial infarction: a North-South perspective. Am Heart J 1991;121:1–11.

Case Report

Ventricular Pseudoaneurysm in a Case of Silent Myocardial Infarction

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Abstract : Contained rupture of myocardial wall after infarction can give rise to pseudoaneurysm. This is in fact one of the less common causes of LV pseudoaneurysm. Here a case of silent myocardial infarction giving rise to LV pseudoaneurysm due to contained rupture of posterolateral wall has been reported.

Key Words : LV pseudoaneurysm.silent myocardial infarction

Introduction : A pseudoaneurysm is a contained rupture of a blood vessel or the myocardial wall.

Pseudoaneurysms of left ventricle will have to-and-fro blood flow into a cavity contained by pericardium, thrombus, scar tissue or adhesions. True aneurysm results forms weakness of the wall that is thin and has an outer layer of the myocardium. Left ventricular(LV) pseudoaneurysm contains no endocardium or myocardium. Wall stress, which is related to LV pressure and radius, and loss of myocardial integrity (e.g., from myocardial infarction) are the likely determinants of cardiac rupture. Free intrapericardial rupture usually causes cardiac tamponade and death. Less commonly, cardiac rupture is contained and LV pseudoaneurysm is formed.

Case report : A 52-year-old lady presented with dyspnea (New York Heart Association functional class III), which had been insidious in onset and slowly progressive. She had also paroxysmal nocturnal dyspnea, palpitations and easy fatiguability during walking but without any angina or syncope. She is a known diabetic for ten years and had high triglyceride, low HDL cholesterol. The physical examination revealed a regular pulse rate of 110 beats/min, a blood pressure of 90/70 mmHg, and an elevated jugular venous pulse with prominent *v* waves and a sharp *y* descent. Apical impulse was felt in the 6th intercostal space. Another diffuse pulsations were also felt in the 3rd and 4thintercostal spaces lateral to the midclavicular line. There were both S3 and S4, early systolic murmur with soft S1 and loud P2. Basal crepitations and tender hepatomegaly were present.Electrocardiography showed QS complex in lead 11,111 and AVF.Chest radiograph showed cardiomegaly with a bulging of the left border of the heart. Echocardiogram revealed a left ventricular ejection fraction of 35% with akinesia of the inferior septum, posterior wall and basal lateral wall. There was a large LV pseudoaneurysm measuring 10 × 5.5 cm posterolateral to the left ventricle, communicating through a narrow neck of 10 mm in diameter. Color-flow Doppler echocardiography showed turbulence across the neck of the aneurysm with systolic flow into the pseudoaneurysm and diastolic flow away from the aneurysm into the LV cavity. The patient had moderate mitral regurgitation (grade 2/4) and moderate tricuspid regurgitation.

Coronary angiogram revealed occluded left circumflex artery and left ventricular angiography showed grade 2 mitral regurgitation and a large LV pseudoaneurysm originating from the lateral wall of the left ventricle. Cardiac magnetic resonance imaging (MRI) confirmed the presence of a transmural myocardial infarction with apseudoaneurysm of the basal inferolateral wall.We made a diagnosis of silent myocardial infarction with rupture of the posterolateral wall, resulting in a LV pseudoaneurysm. At surgery, a large nonruptured posterolateral pseudoaneurysm was seen to communicate beneath the posterior papillary muscle.

The pseudoaneurysm was resected, and the rupture in the posterolateral wall of the left ventricle was repaired with a polytetrafluoroethylene patch.Venous graft was placed in major obtuse

marginal artery. Mitral valve was also repaired in the same period.

Discussion : Cardiac pseudoaneurysm is usually seen in the left ventricular myocardium. The most common etiology of LV pseudoaneurysm is myocardial infarction. Inferior infarcts were approximately twice as common as anterior infarcts. Other cardiac sites include mitral-aortic intervalvular fibrosa,the right ventricular outflow tract, native and grafted coronary arteries and the atria. Prior aortic valvular surgery and endocarditis predispose pseudoaneurysms at the mitral-aortic intervalvular fibrosa.

Less commonly, blunt or penetrating trauma may cause pseudoaneurysm. (Table 1)

Pseudoaneurysms of the Heart	
Location	**Common Predisposing Conditions**
Left ventricle	Myocardial infarction; ablationprocedures; trauma
Right ventricle	After surgery to repaircongenital heart disease
Mitral aortic intervalvular fibrosa	Prior valvularsurgery;endocarditis; abscess
Coronary arteries	Prior PCI; spontaneousdissection; vasculitis
Bypass grafts	Infection; suture sites; prior PCI
Atria	Ablation procedures; trauma

Table 1. Location and common predisposing conditions of pseudoaneurysms

Pseudoaneurysms of the native coronary arteries tend to occur after stenting or spontaneously. The median patient age is around 60 years. More than two thirds of patients are usually men . The most common presentingsymptoms are heart failure (36%), chest pain (30%) and dyspnea (25%). Sudden death may be the presenting symptom in 3% of cases. Approximately 12% of patients are asymptomatic at the time of diagnosis. Murmurs are found in more than two thirds of patients and more than 95% of patients may have electrocardiographic and chest X-ray abnormalities. ST segment elevation are seen in 20% of patients.[1] Nonspecific ST segment changes are seen in around 75% of patients. More than half of the patients have evidence of a mass on chest X-ray and 65% may have cardiomegaly. If the rupture is not entirely contained or a previously contained pseudoaneurysm ruptures, a patient may present with tamponade, shock, or sudden death. Ventricular pseudoaneurysms are more likely to rupture when they are relatively acute (3 months), large, or located within the anterior or lateral ventricular wall[2]. They are more often located in the posterior and lateral wall segments, in contrast to true aneurysms, which are more often seen in the anterior wall and apex. It was found that the ratio of the maximum diameter of the orifice to the maximum internal diameter of the cavity was between 0.25 and 0.50 for pseudoaneurysms while the range for true aneurysms was between 0.90 and 1.0.[3] The presence of turbulent flow by pulsed Doppler at the neck of a cavity or within the cavity itself also suggests presence of a pseudoaneurysm. MRI is very useful for differentiating between true and pseudoaneurysms. In contrast to LV pseudoaneurysms, only about 4% of true LV aneurysms are located at the posterolateral or diaphragmatic surface[4]. (Table 2)

	Aneurysms	**Pseudo-aneurysms**
Location	3% posterior	Posterior or inferior
Echocardiography		
Anatomy	Thinned myocardium, broad base	Ruptures with narrow neck
Contractility	Non contractile	Dyskinesia
Consequences/ Complications	Congestive heart failure Embolic eventsSame Ventricular arrhythmias	
Therapy	Medical or Surgical therapy	Surgery or Device therapy

Table 1. Differences between aneurysms and pseudo - aneurysms.[9]

One proposed explanation for the relative lack of anterior LV pseudoaneurysms is that anterior rupture may be more likely to result in hemopericardium and death than posterior rupture. Because hospitalized patients usually are in the recumbent position, an inflammatory reaction of the posterior pericardium may result in pericardial adhesions and the formation of a posterior LV pseudoaneurysm rather than cardiac tamponade. Coronary and LVangiogram isessential for the diagnosis of LV pseudoaneurysm. Angiographic findings include a narrow orifice leading into a saccular aneurysm and the lack of surrounding coronary arteries. LV angiography may be normal in 2% of patients.[5] Cases that are missed may occur when the angiographicprojection is not perpendicular to the pseudoaneurysm (resulting in overlap with the left ventricle) or when insufficient contrast is used. A definitive diagnosis was made in 26% of patients by transthoracic 2D echocardiography[6]. The most important and difficult finding is the detection of continuity in the myocardium. In clinical practice, distinguishing true from false aneurysms often proves difficult because a true aneurysm may present with a narrow neck and false aneurysm at times may have a rather broad base[7].The high spatial resolution and tissue characterization of cardiac MRI make it ideal for evaluation of pseudoaneurysm of the left or right ventricles and also for distinguishing pseudoaneurysm from true aneurysms. Use of late gadolinium enhancement may be helpful to identify

the location and transmural extent of prior infarcts. Ventricular pseudoaneurysm may also serve as a focus for arrhythmia and result in decreased cardiac output. Historically, ventricular pseudoaneurysmhas a high risk of rupture varying from 30% to 45% with a mortality of almost 50 percent[7]. The main goal of therapy is to reduce the risk of expansion or rupture. No randomized controlled trial exists to guide treatment decision. Surgical repair is the gold standard of treatment. Apart from usual statins, anti platelets, beta blockers, ACE inhibitors, diuretics including spironolactone, anticoagulation may be required to reduce the risk of thromboembolism in some cases. There are reports of successful percutaneous closure by using septal occluderdevices in atria and ventricles. Current surgical perioperative mortality is less than 10 percent[8]. The risk is greater among patients with severe mitral regurgitation requiring concomitant mitral valve replacement.

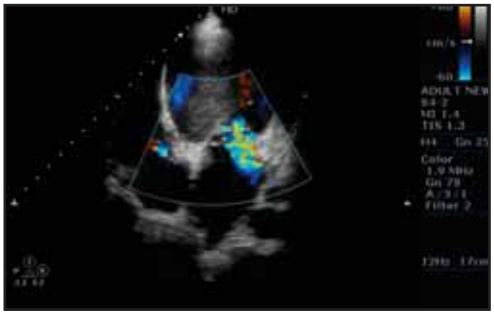

Fig. 1. Echocardiography showing moderate Mitral Regurgitation

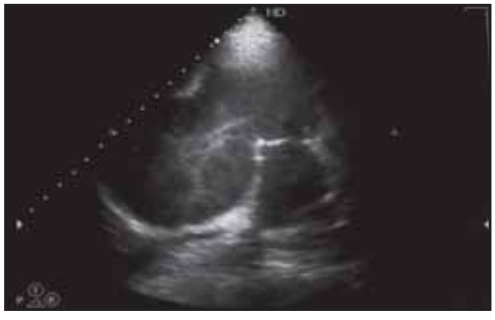

Fig. 2. Spontaneous echocontrast across the communication between pseudo-aneurysm and LV cavity.

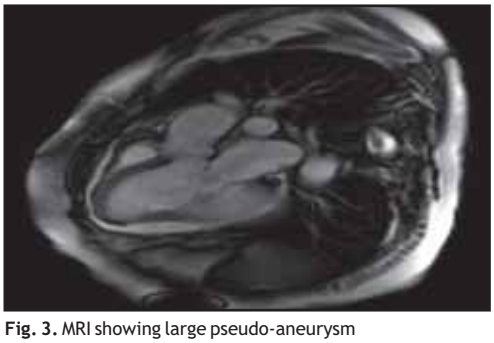

Fig. 3. MRI showing large pseudo-aneurysm

Fig. 4. Occluded left circumflex artery

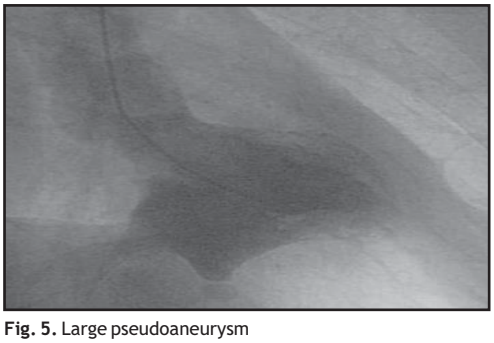

Fig. 5. Large pseudoaneurysm

References :

1. Treasure T. False aneurysm of the left ventricle. Heart 1998;80:7–8.
2. Hung MJ, Wang CH, Chang WJ. Unruptured left ventricular pseudoaneurysm following myocardial infarction. Heart 1998;80:94–7.
3. Gatewood R Jr, Nanda N.C; Differentiation of left ventricular pseudoaneurysm from true aneurysm with two dimensional echocardiography. Am J Cardiol. 1980: 46 :869-878.
4. Loperfido F, Pennestri F, Mazzari M, Biasucci LM, Vigna C, Laurenzi F. Diagnosis of left ventricular pseudoaneurysm by pulsed Doppler echocardiography. Am Heart J 1985;110:1291–3.
5. Dachman A.H, Spindola-Franco H, Solomon N; Left ventricular pseudoaneurysm. Its recognition and significance. JAMA. 1981: 246:1951-1953.
6. Craig Frances, Anthony Romero, Deborah Grady.Left ventricular Pseudoaneurysm.J Am CollCardiol. 1998;32(3):557-561.
7. Edward A. Hulten and Ron Blankstein. Pseudoaneurysms of the Heart.Circulation. Apr 17, 2012. 10.1161
8. Pretre R, Linka A, Jenni R, Turina MI. Surgical treatment of acquired left Ventricular pseudoaneurysm. Ann ThoracSurg 2000;70:553–7.
9. J Tuan , Farhad Kaivani, Hilary Fewins.Left ventricular pseudoaneurysm.EHJ:2007:03:043; 107-109

Image Corner

Ruptured Papillary Muscle

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Rupture of papillary muscle (PM) after acute myocardial infarction (MI), although rare, has an unacceptably high mortality if surgical intervention is delayed. It has been reported that without surgery, 50% of patients with this complication are dead within 24 hours.[1,2] This is nearly twice the mortality seen in those with a VSD after an acute MI. Since prompt surgical management can be successful, it is crucial to arrive rapidly at a definitive diagnosis in these patients. Echocardiography (Echo) both transthoracic (TTE) and Transesophageal echo(TEE) have an invaluable role in making quick diagnosis.

Echocardiographic features of importance include location of the papillary muscle rupture which may be partial or complete and leaflet involvement, direction and severity of mitral regurgitation and hemodynamic complications. A disruption in either papillary muscle in the setting of myocardial injury can result in dysfunction of either the anterior or posterior leaflet of the mitral valve as each leaflet is attached to both the PMs by chordae tendinae.[3]

We report a case of an individual in whom both TTE & TEE demonstrated a posteriorly directed eccentric jet of severe MR (Fig:1) due to a flail AML with papillary muscle rupture (Fig:2). Intraoperative findings confirmed rupture of the posteromedial papillary muscle attached via chords to the flail AML.

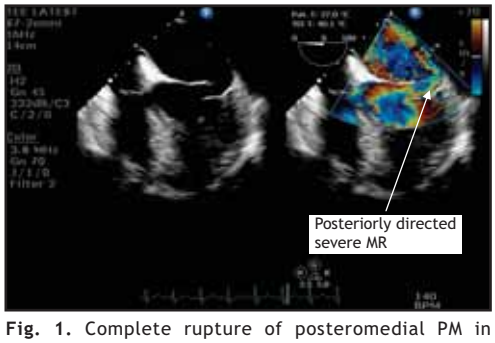

Fig. 1. Complete rupture of posteromedial PM in transgastric view of TEE

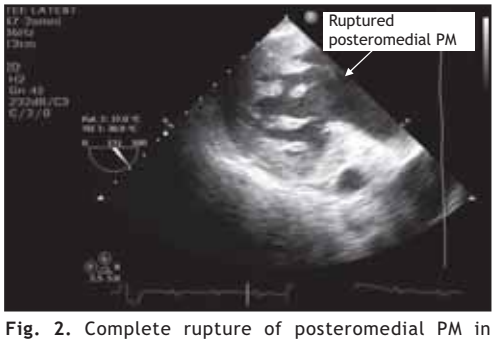

Fig. 2. Complete rupture of posteromedial PM in transgastric view of TEE

References :

1. Yuan S, Jing H, Lavee J. The mechanical complications of acute myocardial infarction: echocardiographic visualizations. Turkish J Thorac Cardiovasc Surg. 2011;19:36.
2. Lavie CJ, Gersh BJ. Mechanical and electrical complications of acute myocardial infarction. Mayo Clin Proc.1990;65:709. [PubMed]
3. Czarnecki A, Thakrar A, Fang T, et al. Acute severe mitral regurgitation: consideration of papillary muscle architecture. Cardiovasc Ultrasound. 2008;6:5. [PMC free article] [PubMed]
4. Sochowski RA, Chan KL, Ascah KJ, Bedard P. Comparison of accuracy of transesophageal versus transthoracic echocardiography for the detection of mitral valve prolapse with ruptured chordae tendinae (flail mitral leaflet) Am J Cardiol. 1991;67:1251. [PubMed]

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