Plaque Passivation: Role of Statins in Acute Coronary Syndromes

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The past decade has witnessed revolutionary changes in the understanding of the pathogenesis and management of acute coronary syndromes (ACS). The major cause of ACS is the rupture or erosion of an atherosclerotic plaque and subsequent thrombosis leading to variable obstruction in the coronary arterial lumen. Clinical strategies for the management of ACS now focus more on creating plaque stability. The culprit plaque is akin to an active volcano that must be made quiescent. “Plaque passivation” is a therapeutic concept by which either the structure or the content of the vulnerable and active atherosclerotic plaque is modified to reduce the risk of subsequent rupture and thrombosis. To better understand the concept of plaque passivation, it is pertinent to understand the composition of vulnerable plaque, and the complex factors involved in its destabilization and rupture.

The Vulnerable Plaque

Vascular biology and not the degree of stenosis determine plaque stability. The process of plaque destabilization begins with endothelial dysfunction against a background of inflammation. Postmortem pathologic studies have revealed that the vulnerable plaque has three hallmark histologic features: (i) a large lipid core occupying more than 40% of the plaque volume; (ii) an abundance of inflammatory cells; and (iii) a thin fibrous cap that lacks proper collagen and smooth muscle cell support. In an unstable plaque, almost every cell type is activated. These cells are mostly monocytes-macrophages, but can also be activated T cells and mast cells. These inflammatory cells secrete certain enzymes (proteases) that degrade collagen. In addition, apoptosis of smooth muscle cells, which are the chief source of collagen, further weakens the plaque. The lipid core is composed of free cholesterol, cholesterol esters, and crystals. In addition, it contains oxidized lipids, and is impregnated with tissue factor derived from macrophages, making it highly thrombogenic. The family of enzymes—matrix metalloproteinases (MMPs)—expressed by macrophages erodes the thin fibrous cap resulting in exposure of thrombogenic subendothelial material to the circulating blood. The acute clinical event is precipitated by the formation of an intimal, platelet-rich thrombus followed in some cases by a fibrin-red cell intraluminal thrombus.

Plaque Passivation Therapy

The biology of plaque instability and rupture suggests that therapeutic strategies must revolve around three potential target sites: (i) platelets and the coagulation cascade leading to dissolution of the thrombus and restoration of luminal patency; (ii) passivation of dysfunctional endothelial cells for the reduction of pro-inflammatory and procoagulant activity; and (iii) modification of plaque contents by an aggressive reduction of serum low-density lipoprotein cholesterol (LDL-c) levels and inhibition of LDL oxidation. These target sites are not mutually exclusive. Therefore, an integrated approach to plaque passivation in ACS is required to reduce future adverse clinical events. Timing is crucial, as the period of greatest risk is during the early hours and days after presentation. Antithrombotic and antiplatelet agents, such as low molecular-weight heparin, aspirin, clopidogrel, and glycoprotein IIb/IIIa receptor antagonists, remain the cornerstone of therapy. Lipid-modifying agents, angiotensin-converting enzyme inhibitors, and perhaps some calcium antagonists may also play a role in plaque passivation. In this editorial, we focus on the role of statins in plaque stabilization, and their utility in the setting of ACS.

Statins in ACS

The concept of plaque stabilization was proposed in the 1990s in an attempt to explain the discrepancy between a small amount of angiographically demonstrated plaque regression, and the large reduction in clinical events in trials of lipid-lowering drugs. In these remarkably successful
secondary prevention trials, patients were enrolled only if they were event-free for several months after the ACS, since it was considered that lipid-lowering drugs could not affect the outcome in the first few months after an acute coronary event. Could statins, which are so effective for stable coronary artery disease (CAD), also reduce the high incidence of coronary events in the early unstable phase after ACS? If so, what are the mechanisms of benefit in this early phase?

**Observational Studies**

The data from observational studies indicate that patients treated early with statin therapy after a coronary event have survival benefits. A large, prospective, cohort study using data from the Swedish Register of Cardiac Intensive Care (RIKS-HIA) demonstrated that early initiation of statin therapy in patients with acute myocardial infarction (AMI) was associated with a reduced 1-year mortality (relative risk 0.75, p=0.001). Post-hoc analysis of two randomized trials—GUSTO IIb (Global Use of Strategies to Open Occluded Coronary Arteries) and PURSUIT (Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy)—showed that patients with ACS discharged on lipid-lowering drugs have a survival advantage in the first 6 months (hazard ratio 0.48, p<0.001). There was clearly a very early separation of curves within days of discharge, and the difference was evident at the end of the first month itself (hazard ratio 0.44, p=0.001). In a preliminary report from the OPUS-TIMI 16 study (Orofiban in Patients with Unstable Coronary Syndromes-Thrombolysis and Myocardial Infarction), mortality at 1 month was reduced in patients treated with lipid-lowering drugs (0.7% vs. 2.4%, p<0.001).

Similarly, an analysis of the databases of two clinical studies—SYMPHONY (Sibrafiban versus Aspirin to Yield Maximum Protection from Ischemic Heart Events Post-Acute Coronary Syndromes) and 2nd SYMPHONY—showed unadjusted mortality benefits at 90 days and 1 year (hazard ratio 0.58 and 0.52, respectively) with early initiation of statin therapy in patients with ACS. Although observational data showed a clinical benefit, the results might have influenced the results. After adjustment for various confounders in these observational studies, survival benefits were attenuated, yet these studies set the stage for the need for randomized trials.

**Randomized Trials**

Myocardial Ischemia with Aggressive Cholesterol Lowering (MIRACL) was the first large-scale clinical trial to examine the rate reduction in clinical events with statin treatment in patients with ACS. More than 3000 patients with non-ST elevation ACS were randomized to high-dose atorvastatin (80 mg) or placebo within 24–96 hours of hospital admission. At 16 weeks of follow-up, the primary end-point of death, MI, or recurrent ischemia requiring rehospitalization was reduced from 17.4% to 14.8% (relative risk reduction of 16% in the primary combined end-point). This benefit was largely driven by a reduction in the end-point of recurrent ischemia requiring rehospitalization, which was reduced from 8.4% to 6.2% (relative risk 0.74, p=0.02). Although death, nonfatal MI, and cardiac arrest occurred less frequently in the atorvastatin group, the differences were not statistically significant. Among patients treated with atorvastatin, there was no significant association between the percentage change in LDL-c levels from baseline to the end of study, and the occurrence of the primary end-point. Also, the reduction of primary ischemic events did not depend on the baseline LDL-c levels. While the relative benefit of treatment observed in the MIRACL trial over 16 weeks is less than that observed in the earlier secondary prevention trials over a period of 5–7 years, the absolute reduction in events (2.6%) in this trial is greater than that achieved during a comparable length of time in stable coronary patients.

The Lipid-Coronary Artery Disease (L-CAD) study was a small trial that randomized 126 patients with ACS to early aggressive treatment with pravastatin alone, or in combination with cholestyramine and niacin, or to usual care. At 24 months, patients who had received early aggressive treatment had a lower incidence of clinical events than those receiving usual care (24% vs. 52%, p=0.005). The Fluvastatin on Risk Diminishing After Acute Myocardial Infarction (FLORIDA) trial randomized 540 patients with AMI to fluvastatin or placebo within 14 days of the index event. This trial failed to show any beneficial effect of statins on major adverse cardiac events or mortality at 1-year follow-up. This was perhaps related to the dose of statin used and timing of drug initiation.

The Pravastatin A Cade Coronary Treatment (PACT) study evaluated early clinical outcomes in 3048 patients with
ACS treated with pravastatin (40 mg/day) or placebo within 24 hours after the beginning of an acute coronary event. At the end of 30 days, there was a 0.8% absolute reduction and 6.4% relative risk reduction for the primary end-points of death, MI, or recurrent unstable angina.1

Taken together, the data from these trials suggest a benefit with regard to early initiation of statin therapy, and represent the best available data on which the hypothesis of early initiation of statin therapy in patients with ACS needs to be examined. These results were not as robust as anticipated after the results of earlier observational studies, but clearly it is not harmful to initiate early statin therapy. In addition, early initiation of therapy helps in attaining better long-term compliance. In one demonstration project, the Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP), in-hospital initiation of lipid-lowering therapy increased the percentage of patients being treated with statins 1 year later from 10% to 91%, and those with an LDL-c level <100 mg/day from 6% to 58%. Similarly, data from patients enrolled in the EPILeG (Evaluation of PTCA to Improve Long-term Outcome by c7E3 Glycoprotein IIb/IIa Receptor Blocker) trial, a retrospective propensity analysis revealed that at 6 months, 77% of patients who started taking lipid-lowering agents before discharge from the hospital continued taking therapy, compared with only 25% of those discharged without these agents (relative risk 3.17, p<0.001). In-hospital initiation of these drugs is a strong and independent positive predictor of subsequent use.18

### Mechanisms of Beneficial Actions

Based on evidence from human and animal studies, it can be assumed that lipid-lowering drugs stabilize plaque by several mechanisms.2,18 Statin-mediated lowering of lipids may stabilize vulnerable plaque by changes in the lipid core itself. There is a reduction in the levels of oxidized LDL in the plaque's core accompanied by reduction in plaque macrophage content, and increase in the volume of collagen and smooth muscle cells with statins.2 In a small, nonrandomized study of patients undergoing carotid endarterectomy, statin therapy given for 3 months resulted in a decrease in the lipid pool and increase in fibrosis in carotid plaque. There was 75% less lipid core, 40% less oxidized LDL and MMP, and twice the amount of collagen.20 In experimental studies, these changes require at least a few months to occur and, therefore, may not fully explain the early benefits observed with statin therapy in patients with ACS.2

Statins have “pleiotropic actions” that go beyond the lowering of LDL-c levels, and are relevant to the pathophysiology of ACS. In comparison to lipid-lowering actions, these pleiotropic effects on vascular and cardiac cells may be effective after early initiation of therapy.21 These effects include: (i) improvement in endothelial function; (ii) reduction in the activity of inflammatory cells; and (iii) decrease in the propensity for thrombosis.

### Endothelial Dysfunction and Statins

Endothelial dysfunction is characterized by impaired bioactivity of nitric oxide (NO) within the vascular wall, resulting in reduced vasorelaxation or abnormal vasoconstriction in response to procoagulant and proinflammatory processes. Several studies have documented the beneficial effects of statins on endothelial function within days of initiation of therapy.22 In a recent publication, Wassmann et al. elucidated the rapid effects of statins (as early as 24 hours) directly on the coronary vasculature as assessed by quantitative coronary angiography (QCA) and measuring coronary blood flow reserve using a Doppler guidewire. In this randomized, double-blind, prospective study, a single dose of 40 mg pravastatin significantly attenuated acetylcholine-mediated vasoconstriction at 24 hours in patients with stableCAD. More importantly, this rapid effect was observed in the absence of any change in the serum concentration of lipid subfractions. An improvement in endothelial function in patients with low pre-treatment cholesterol levels has been observed in other experimental studies as well.24–26 The Reduction of Cholesterol in Ischemia and Function of the Endothelium (RECIFE) trial provides evidence of improvement in endothelial function using statins in patients with ACS.27 In this study, 60 patients with ACS were randomly assigned to either placebo or pravastatin during hospitalization. Flow-mediated vasodilatation of the brachial artery was unchanged with placebo, but improved significantly with pravastatin (p=0.002).

The molecular basis of these direct, lipid-independent, pleiotropic effects of statins on endothelial function has been elucidated in experimental studies. Statins have been shown to interact with the biochemical pathways involved in NO production at the cellular level. The rapid restoration of NO bioactivity is achieved by the upregulation and activation of endothelial NO synthase, and the enhancement of NO release. By virtue of their antioxidant properties, statins also decrease the production of endothelial cell superoxide anions responsible for the inactivation of NO.21,25
Anti-Inflammatory Action of Statins

Inflammation appears to be a pivotal process that transforms stable plaque to ACS. Higher blood levels of inflammatory markers are associated with increased cardiovascular events in patients with ACS. C-reactive protein (CRP) has been correlated with coronary risk more extensively than other markers, and can now be easily measured using a high-sensitivity assay. In addition to an inflammatory marker, CRP may be a direct participant in vascular inflammation and plaque destabilization. Immunohistochemical staining of atherosclerotic plaque has co-localized CRP with complement proteins and macrophages. Also, serum levels of CRP correlate well with the amount of CRP in atheroma and anatomic features of plaque destabilization.

Statin therapy may have powerful anti-inflammatory effects. Recent clinical trials of statin therapy have shown a reduction in the CRP levels, an effect that is independent of lipid lowering. In the Cholesterol and Recurrent Events (CARE) trial, patients with persistent low-grade inflammation, as evidenced by high CRP and serum amyloid A (SAA) levels, were at higher risk of clinical events. Randomization to pravastatin therapy prevented 54% of recurrent events among those with persistent inflammation, compared with 25% among those without it. Kinlay et al. have recently analyzed the effect of a high dose of atorvastatin on inflammatory markers in patients with ACS enrolled in the MIRACL study. In comparison to placebo, CRP was 34% (p<0.0001) and SAA 13% lower (p=0.0006) in patients treated with atorvastatin. These significant beneficial effects were sustained in both the high- (baseline LDL >125 mg/dl) and low LDL-c level groups.

At the molecular level, statins attenuate the inflammatory manifestations of atherosclerosis through a variety of mechanisms. In experimental animals, statins reduce macrophage infiltration and monocyte chemoattractant protein levels in the vascular wall, and inhibit the production of MMPs. However, the dose required for this effect and its relationship with the reduction of clinical events in patients with ACS remains to be clarified. In vitro studies have demonstrated that statins at extremely low concentrations (nanomolar range) block the enzyme HMG-CoA reductase, while inhibition at the molecular level of inflammation requires a higher concentration of statins (micromolar range). Perhaps the results of ongoing studies using various dosing patterns of statins in patients with ACS would provide clearer information.

Antithrombotic Effect of Statins

Statins may favorably influence ACS by reducing plasma viscosity, altering platelet aggregation, and suppressing thrombus formation. In an experimental model using a perfusion flow chamber covered with porcine aortic media, use of pravastatin resulted in reduction of platelet deposition and thrombus formation. These actions are interrelated so that a beneficial effect on one mechanism favorably influences the others, perhaps leading to rapid stabilization of culprit plaque and early clinical benefits.

Concerns

There may be concern regarding the safety of statins in ACS, especially if used at higher doses. However, there was no documented case of myositis, the most serious adverse effect of statins, in the MIRACL study, though levels of serum transaminases exceeding three times the upper limit were seen in 2.5% of atorvastatin- and 0.6% of placebo-treated patients (p<0.001). In the real-world situation, usually such aggressive doses of statins are not used in patients with ACS. Further, it has been shown in experimental studies that statins inhibit migration and proliferation of smooth muscle cells, and may induce their apoptosis. Theoretically, this may weaken the plaque, and result in impaired early healing and plaque destabilization. Platelet function studies have revealed an interaction between clopidogrel and the concomitant administration of lipophilic statins. These statins are metabolized through an isoenzyme CYP3A4, and may competitively inhibit the metabolism of clopidogrel to its active metabolite in the liver. However, recently a post-hoc analysis of the Clopidogrel for the Reduction of Events During Observation (CREDO) trial has failed to substantiate this drug interaction clinically.

Ongoing Trials

Randomized, controlled trials are under way to better delineate the degree of benefit (if any) from the early initiation of therapy in patients with ACS. These trials include the Aggrastat to Zocor (A-to-Z) trial and the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT)-TIMI 22 trial. The A-to-Z trial is an international, multicentric study designed to investigate the hypothesis that the early use of an aggressive dose of a statin (40 mg/day simvastatin for 1 month started within 10 days of the onset of symptoms, followed by 80 mg/day for approximately 14 months) is
superior to the accepted regimen of a lower dose of statin started 3–6 months after an acute event (placebo for 4 months, followed by simvastatin 20 mg/day). Follow-up will continue until the occurrence of 970 primary outcome events defined as cardiac death, MI, or rehospitalization for ACS. The trial is, therefore, the key follow-up trial to the MIRACL study designed to confirm the early benefit of treatment with statins. PROVE IT-TIMI 22 is also an international, multicentric trial that is testing the hypothesis that a lower absolute LDL-c level in patients with ACS is associated with a reduced risk of cardiovascular events. This goal is to be accomplished by comparing the effect of reduction in LDL-c levels to approximately 100 mg/dl with pravastatin (40 mg/day), or to 75 mg/dl with atorvastatin (80 mg/day), initiated within 10 days after the onset of ACS in more than 4000 patients with ACS for a period of 2 years.

Conclusions

The use of statins in patients with ACS remains an area of intense clinical interest. Statin therapy has established secondary benefits in patients with stable CAD, and its extension to ACS seems logical. Larger, randomized trials are being conducted, which would define the role of early aggressive statin therapy in patients with ACS. Meanwhile, it appears logical that physicians should be urged to include statin therapy as an integral part of the treatment plan for patients with ACS while in the hospital, irrespective of the cholesterol levels.

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Who is the Best Candidate for Cardiac Resynchronization Therapy: Implications of Recent Studies

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A central issue in cardiac resynchronization therapy (CRT) is the identification of patients most likely to respond, that is patients with significant atrioventricular (AV) and/or inter- and/or intraventricular mechanical dysynchrony (DYS) who would most likely benefit from CRT.1-4 Almost all prospective, controlled studies on CRT have been conducted on patients with severe congestive heart failure (CHF) presenting with a wide QRS complex5-9 (Table 1). In the original hypothesis of CRT, a wide QRS complex, a marker of electrical DYS, was correlated with mechanical ventricular DYS. While this may generally be correct, it is worth mentioning that some patients with a wide QRS do not have marked mechanical ventricular DYS and, conversely, that some patients with a narrow QRS may be candidates for CRT due to significant mechanical DYS.10 On the other hand, although short-term experimental studies have shown that patients with wider QRS complexes have a greater immediate mechanical response to CRT,11-15 most long-term studies have shown that QRS duration does not predict a response to CRT; and QRS narrowing does not predict a functional improvement following CRT;16-22 although the opposite has been observed in some studies in which the right ventricular (RV) lead was positioned at the RV septum.23-24 In addition, in a series by Ansalone et al.,20 10% of CRT recipients experienced worsening of symptoms and mechanical DYS. This may explain the relatively high percentage of nonresponder (NR) patients who have been selected for CRT based on QRS duration as a surrogate for mechanical ventricular DYS (Table 2). Thus, direct assessment of mechanical ventricular DYS may have greater accuracy in patient selection for CRT, and help to reduce the number of NR patients. We review recent studies on the predictors of long-term response, and their impact on patient selection for CRT.

Definition of Responder and Nonresponder

The definition of a responder has been a major problem in predicting the long-term response to CRT. Different studies have used different criteria to define positive response to CRT (Table 3).22,23,25-27 A consensual definition of a positive response to CRT is needed to better identify potential candidates for CRT, and assess the outcome in various clinical trials.

Table 1. Current criteria for patient selection for cardiac resynchronization therapy

- NYHA class III and IV despite optimal drug treatment (ACE inhibitors, beta-blockers, spironolactone, and diuretics)
- LV systolic dysfunction (LVEF ≤35%)
- QRS duration >130 ms
- LV end-diastolic dimension ≥55 mm

NYHA: New York Heart Association; ACE: angiotensin-converting enzyme; LVEF: left ventricular ejection fraction

Table 2. Factors that can increase the number of nonresponders to CRT

- Improper patient selection (improper assessment of DYS)
- Inadequate medical therapy
- Persistent or worsening DYS after CRT (mostly due to error in lead position and programming)
- Improper lead (RV and/or LV) position
- Improper AV and V-V interval programming (V-V interval can be optimized by using indices of mechanical DYS)
- Lack of regular follow-up and device reprogramming

CRT: cardiac resynchronization therapy; DYS: dys-synchrony; RV: right ventricle; LV: left ventricle; AV: atrioventricular

Table 3. Different definitions of positive response to CRT

<table>
<thead>
<tr>
<th>Reference</th>
<th>Definition of responder</th>
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<tr>
<td>Alonso et al.23</td>
<td>Improved symptoms, at least one NYHA class down, and at least 10% increase in peak VO₂ for at least 6 months</td>
</tr>
<tr>
<td>Reuter et al.22</td>
<td>Improved symptoms and NYHA class with decrease in the QOL score</td>
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<tr>
<td>Cazeau et al.25</td>
<td>Improved NYHA class associated with improved, echocardiographically derived indices of DYS</td>
</tr>
<tr>
<td>Pitzalis et al.26</td>
<td>Reduction in LV end-systolic volume index ≥15%</td>
</tr>
<tr>
<td>Nelson et al.27</td>
<td>Improvement of more than 25% in LV dP/dt max</td>
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QOL: quality of life; DYS: dys-synchrony; LV: left ventricle; CRT: cardiac resynchronization therapy; NYHA: New York Heart Association
Predictors of Long-Term Response

Based on the limitations of QRS duration as a surrogate for mechanical ventricular DYS, various recent studies have assessed different indices of mechanical ventricular DYS in candidates for CRT as predictors of long-term response (Table 4). These studies have prompted a reappraisal of the apparent correlation between conduction disorders and mechanical ventricular DYS, and have shown that the larger the mechanical ventricular DYS, no matter how it is measured or expressed, the greater the benefit from CRT. Thus, direct assessment of ventricular DYS increases the accuracy of patient selection for CRT, and reduces the number of NR. Cazeau et al.25 have recently reported the results of the first prospective study on the selection of candidates for CRT based on mechanical rather than electrical criteria. The study groups included 66 patients with left ventricular ejection fraction (LVEF) ≤35%; NYHA functional class III or IV despite optimum medical therapy; and 1 or more of the following echocardiographic criteria of AV, and inter- and intraventricular DYS: (i) LV filling time <40% of the cardiac cycle; (ii) left pre-ejection interval ≥140 ms with or without interventricular delay ≥40 ms; and (iii) presence of overlap between the end of lateral wall contraction and onset of LV filling. An immediate positive response (Table 3) was observed in 85% of patients with partial or complete correction of the above-mentioned echocardiographically derived parameters of mechanical ventricular DYS. This marked improvement is encouraging, though it must be interpreted cautiously, as these results were observed in the immediate postoperative period, in an uncontrolled study design. Direct assessment of ventricular mechanical DYS could also help in selecting the best timing delay between RV and LV stimulation by minimizing post-implant indices of inter- and intraventricular DYS (Table 4). Further prospective studies are needed to assess and compare different criteria for patient selection in CRT.

Table 4. Predictors of long-term response to CRT

<table>
<thead>
<tr>
<th>Reference</th>
<th>Variable</th>
<th>Findings</th>
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<tr>
<td>Saxon et al.21</td>
<td>Myocardial performance index (MPI)</td>
<td>The degree of abnormality of Doppler-derived MPI strongly predicts a remodeling response with long-term CRT.</td>
</tr>
<tr>
<td>Cazeau et al.25</td>
<td>LV pre-ejection interval (LPEI)</td>
<td>LPEI ≥140 ms, with or without IVD ≥40 ms; LVFT &lt;40% of the cardiac cycle; and overlap between the end of lateral wall contraction and onset of LV filling were predictors of response to CRT.</td>
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<tr>
<td>Pitzalis et al.26</td>
<td>Septal posterior wall motion delay (SPWMD)</td>
<td>In patients with advanced CHF and LBBB, baseline SPWMD is a good predictor of the occurrence of reverse remodeling after CRT, thus suggesting its usefulness in identifying patients likely to benefit from BiV pacing.</td>
</tr>
<tr>
<td>Nelson et al.27</td>
<td>Mechanical dys-synchrony (DYS) measured by tagged MRI; QRS duration; and LV dp/dt max</td>
<td>Mechanical DYS measured by MRI is a key predictor for pacing efficacy in DCM; and combining information about QRS (i.e. QRS duration &gt;155 ms), and basal dp/dt max (&lt;700) provides an excellent tool to identify maximal responders.</td>
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<tr>
<td>Breithardt et al.28</td>
<td>Lateral septal (LS) wall contraction phase difference assessed by echocardiography</td>
<td>This study provides a noninvasive screening method for patients with CHF, so that those likely to have increased contractile function with CRT can be selected, and so that CRT after implantation can be optimized. Baseline asynchrony indicated by LS &gt;25° predicts a contractile function benefit from CRT.</td>
</tr>
<tr>
<td>Sagaard et al.29</td>
<td>Delayed longitudinal contraction (DLC) detected by tissue Doppler imaging (TDI)</td>
<td>The extent of the LV base segments displaying DLC, detected by TDI before pacemaker implantation, predicted the long-term efficacy of CRT. The QRS duration failed to predict efficacy of CRT.</td>
</tr>
<tr>
<td>Yu et al.30,31</td>
<td>DYS index (DI)=SD of LV 12-segment time to peak myocardial systolic contraction measured by TDI</td>
<td>A preimplant DI of 32.6 ms (2 SDs from mean of 88 normal controls) was able to totally segregate responders from nonresponders to BiV pacing.</td>
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<tr>
<td>Breithardt et al.32</td>
<td>TDI-derived strain rate imaging (SRI)</td>
<td>SRI might provide the optimal noninvasive approach to determine the nature of baseline regional contractile DYS, and to assess the changes with pacing to define better patient selection criteria for CRT.</td>
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CHF: congestive heart failure; LBBB: left bundle branch block; BiV: biventricular; CRT: cardiac resynchronization therapy; LV: left ventricular
Effect of Pacing Site on Response to Resynchronization

Initial reports have suggested that the stimulation site within the LV may play an important role in the response to CRT. These studies have suggested that the LV lateral wall is the “preferred site” for CRT in patients with a wide QRS complex and left bundle branch block (LBBB), since the best acute hemodynamic results were obtained by stimulating the LV lateral wall.** Butter et al.** showed that in 30 patients, 18 with dilated cardiomyopathy (DCM) and 12 with coronary artery disease (CAD), CRT with LV free wall stimulation produced significantly better LV systolic performance (LV dp/dt max) compared with anterior stimulation, regardless of the mode of pacing (univentricular or biventricular [BiV]). They suggested that further studies are warranted to prove the clinical superiority of the LV free wall as a preferred site for long-term CRT. Ansalone et al.** compared the efficacy of BiV pacing at the most delayed part of the wall (assessed by tissue Doppler imaging [TDI]) of the LV, and at other areas of the LV wall in 31 patients with DCM. They found that the lateral wall was the most delayed site in 60%, and the anterior wall in 40% of patients. Myocardial performance index, LV end-systolic volume index (LVESVi), LVEF, and exercise load improved significantly in all the patients. However, the greatest improvement was found in patients paced at the most delayed site. They observed no difference between the concordant and discordant groups in long-term improvement of NYHA functional class. Søgaard et al.** evaluated the correlation between the etiology of heart failure and location of the most delayed segments assessed by TDI. In patients with CAD (n=11), the most delayed segments were anteroseptal (10/11), whereas in patients with DCM (n=9), they were lateral (8/9). Ansalone et al.** suggested that (i) according to the anatomic distribution of the left bundle branch fascicles, the greatest delay can be located at the inferior wall, the lateral wall, or the posterior wall; (ii) it cannot be said whether it would be more effective to pace the most delayed or the most dyskinetic region; and (iii) the beneficial effect of CRT on LV volume and dimension did not correlate with acute hemodynamic parameters and/or improvement in functional class. Gasparini et al.** performed the largest single-center, long-term study that evaluated the effect of different pacing sites in 158 patients treated with CRT. Their data surprisingly revealed that LVEF, LVESVi, and exercise load improved significantly during long-term follow-up, regardless of the LV pacing site. Further prospective large-scale studies are warranted to resolve the controversies surrounding this issue.

Unresolved Issues and Future Directions

Although much has been learned over the past several years regarding patient selection in CRT, major unresolved issues remain. First, a consensus definition of the responder, of paramount importance for patient selection, is lacking. New methods for examining regional wall motion hold promise for generating a DYS index that could improve on current, more indirect methods. However, optimal method(s) for the assessment of mechanical ventricular DYS, and prospective identification of responders are important unresolved issues. The optimal method of therapy itself is unresolved. Questions remain as to whether BiV stimulation is needed, whether multisite left heart stimulation would enhance the efficacy, whether the lateral wall is the best LV pacing site, or if an RV lead is to be placed, where the optimal location is, and what is the best timing delay between RV and LV stimulation. Resolving these issues will help to better identify potential candidates for CRT.

References

Prevalence of Rheumatic and Congenital Heart Disease in Schoolchildren of Kathmandu Valley in Nepal

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**Background:** Rheumatic heart disease remains a major public health problem in developing countries with its very high prevalence. Rheumatic and congenital heart disease are significant causes of morbidity and mortality among Nepalese schoolchildren. The aim of our study was to determine the prevalence of rheumatic and congenital heart disease among schoolchildren of the Kathmandu valley in Nepal.

**Methods and Results:** The study included 9420 students, of whom 4466 were male and 4954 were female, with ages ranging from 5 to 18 years. A clinical survey was conducted by the examining team in selected schools, and involved answering standard questionnaires. A total of 83 children were suspected of having heart disease. Out of these 83 children, 23 were confirmed to have heart disease; 11 had rheumatic heart disease, and 12 congenital heart disease, giving a prevalence of 1.2/1000 and 1.3/1000, respectively. The commonest cardiac lesions were mitral regurgitation in the rheumatic heart disease group, and atrial septal defect in the congenital heart disease group. A higher prevalence of congenital heart disease was detected in females.

**Conclusions:** The prevalence of rheumatic heart disease and congenital heart disease among schoolchildren of Kathmandu is 1.2/1000 and 1.3/1000, respectively, with mitral regurgitation and atrial septal defect being the commonest lesions. (Indian Heart J 2003; 55: 615-618)

**Key Words:** Epidemiology, Rheumatic heart disease, Congenital heart disease

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**R**heumatic heart disease (RHD) remains a major public health problem in developing countries, with a prevalence rate varying from 0.8 to 12.6 per 1000 in different countries. RHD and congenital heart disease (CHD) remain significant causes of morbidity and mortality in Nepalese children, and they contribute to the major share of total hospital admissions among patients with cardiovascular diseases.

**Methods**

The study included 9420 students from 7 government schools of the Kathmandu valley in Nepal, which were selected by systematic random sampling methods. Among the 9420 students, 4466 were males and 4954 females. The ages of the subjects ranged from 5 to 18 years, and the mean age was 12.73±3.33 years. The majority of students came from low and low-middle class socioeconomic backgrounds. The study was conducted between May and December 2002.

During the clinical survey, the selected schools were visited by a team of doctors comprising 3 to 5 resident doctors and 1 cardiologist. All the schoolchildren were requested to fill up a proforma prior to the visit of the examining team. The proforma included details of demography, birthplace and current residential address, number of family members, family background, and history of past illness (symptoms, duration, recurrence, and treatment). All the children attending school on the day of the visit were examined by the members of the team, who focused on cardiac examination. Schools were visited repeatedly to cover the maximum number of enrolled students. A record of absentees was maintained, and they were examined subsequently. The attendance rate was 95%.

A throat swab was taken, and tested with the qualitative rapid antigen detection test (RADT, for Group A beta-hemolytic Streptococcus) in children found to be suffering from pharyngitis. The reagent used was Hexagon rapid strep-A (Human, Germany).
Children suspected of having heart disease or those with a history of rheumatic fever (RF) according to the revised Jones criteria were referred to our institute, and evaluated by a cardiologist. In the hospital, children suspected of having heart disease were subjected to chest X-ray, electrocardiogram (ECG), and two-dimensional and color echocardiography (ALOKA, SSD-5500, Japan). Based on the findings of evaluation (history, physical examination, and investigations), children proven to be free from heart disease were excluded from the study, and those with confirmed heart disease were classified into either the RHD or the CHD group. RHD was confirmed on the basis of previous history of RF (according to the Jones criteria), and echocardiographic findings. CHD was confirmed on the basis of clinical (history of illness since early infancy or childhood, characteristic murmurs, chest X-ray, and ECG), and echocardiographic findings.

Statistical analysis: Demographic data were collected, and expressed as percentage, mean, and standard deviation wherever applicable.

Results

Based on the findings of clinical examination, 83 children were referred to the heart center. Among them, 33 children were found to have innocent murmurs and/or no convincing history of RF or heart disease, and hence were excluded from the study. Fifty students (24 male, 26 female) were suspected of having heart disease on clinical grounds. Out of these 50, 28 students (17 male, 11 female) were clinically diagnosed as having RHD, and 22 (7 male, 15 female) CHD, thus showing a prevalence of RHD of 3/1000, and that of CHD of 2.3/1000. After all relevant investigations, including color Doppler echocardiography, 11 children (7 male, 4 female) were finally diagnosed as having RHD, and 12 (3 male, 9 female) were found to have CHD. Hence, the prevalence rates of RHD and CHD were finally 1.2/1000 and 1.3/1000, respectively. The rest of the children suspected of having RHD on the basis of a grade 2/6 systolic murmur over the precordium were found to have minimal-to-mild TR with normal valve anatomy on echocardiography. Likewise, 10 children suspected to have CHD on the basis of the presence of a grade 2–3/6 systolic murmur over the pulmonary area were found to have no abnormal findings on echocardiography.

Only 1 child was below 10 years of age in the RHD group; the rest were in the age range of 11–16 years. Three children in the CHD group were below 10 years of age, the rest were between 11 and 15 years. Not a single child fulfilled the diagnostic criteria of rheumatic activity as defined by the modified Jones criteria. Six students suffering from RHD did not give any history of past illness compatible with RF. The remaining 5 students gave a past history suggestive of RF. None of the 11 students with RHD were suffering from pharyngitis at the time of examination.

Altogether, 138 students (66 male, 72 female) were suffering from pharyngitis at the time of examination; 57 (41%) (28 male and 29 female) were found to be suffering from group A beta-hemolytic Streptococcus infection as detected by the rapid antigen detection test.

More male than female children were detected as having RHD. Mitral regurgitation was the commonest lesion, followed by mitral stenosis, and aortic regurgitation (Table 1). Among those with CHD, atrial septal defect (ASD) was found to be the most common lesion followed by ventricular septal defect (VSD) (Table 2). All the children with ASD showed ECG manifestations of right bundle branch block.

Only 7 (6 in the RHD and 1 in the CHD group) out of the 23 students had already been diagnosed as having heart disease; the rest were newly detected.

Discussion

The prevalence of RHD in schoolchildren varies considerably throughout the world. Rates ranging from less than 0.02/1000 schoolchildren in the USA to 12.6/1000 in Zambia have been reported. In our study, the prevalence of RHD in schoolchildren was 1.2/1000; which is similar to the results of 2 previous sample surveys done on the outskirts of Kathmandu valley and Kathmandu city. The prevalence is significantly lower than that reported from India, where the mean prevalence rate was 4.54/1000, with an urban area rate of 2.56/1000 and a rural area rate of 7.42/1000. One possible cause of this large discrepancy may be overcrowding, since Indian cities, such as Kanpur, Varanasi, and Delhi, where the prevalence rates were significantly higher than in other parts of India, are much more crowded than Kathmandu. Also, the use of color Doppler echocardiography may have played a role in “reducing” the prevalence of RHD by avoiding overdiagnosis, since out of the 83 children with suspected heart disease, 28 were suspected of RHD without using color Doppler echocardiography, resulting in a prevalence rate of 3/1000. Another important factor pertaining to the lower prevalence of RHD in Kathmandu may be the attempts to create awareness about heart disease and RHD carried out in Kathmandu during the past decade, especially by the Nepal Heart Foundation and other organizations.

In our study, the mitral valve was most commonly
affected, with mitral regurgitation being the most common lesion (Table 1); these findings are consistent with those of previous studies.\textsuperscript{13,14}

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR</td>
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<td>MS</td>
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<td>MR, MS</td>
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<tr>
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<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
</tbody>
</table>

RHD: rheumatic heart disease; MR: mitral regurgitation; MS: mitral stenosis; AR: aortic regurgitation; AS: aortic stenosis

Table 1. Prevalence of RHD in schoolchildren of the Kathmandu valley (n=9420)

There is little information regarding the prevalence of CHD among schoolchildren in Nepal. The real incidence of CHD is difficult to determine; however, it is around 8/1000 live-births.\textsuperscript{15} In our study, the prevalence rate of CHD was 1.3/1000, which is not very different from previous reports.\textsuperscript{13} The finding of ASD being the most common lesion (Table 2) is similar to reports from south India,\textsuperscript{16} but different from several other reports.\textsuperscript{17,18} CHD is more prevalent in females than males.\textsuperscript{17–19} The discrepancy in the spectrum can be explained by the fact that our study population did not include children less than 5 years of age; a large proportion of small VSDs may have closed spontaneously by 5 years of age. In this study, not a single case of cyanotic CHD was detected. This may be due to drop-outs, nonattendance, or a small study population. A similar situation may have arisen among children with a severe form of RHD or active carditis, which may underestimate the true prevalence of RHD. However, inquiry did not reveal any such records of sick children in the schools visited.

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
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</tr>
<tr>
<td>VSD</td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>PDA</td>
<td></td>
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</tr>
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<td></td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
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<td>9</td>
<td>12</td>
</tr>
</tbody>
</table>

CHD: congenital heart disease; ASD: atrial septal defect; VSD: ventricular septal defect; PDA: patent ductus arteriosus; PS: pulmonary stenosis

Table 2. Prevalence of CHD in schoolchildren of the Kathmandu valley (n=9420)

A large proportion of children (66%) were diagnosed for the first time, which may partly be attributed to asymptomatic or mildly symptomatic defects, inadequate medical services, and lack of awareness and funding.

Limitations: This study was conducted only in government schools of the Kathmandu valley with students mainly from low and low-middle class socioeconomic backgrounds. Private schools which enroll students from upper and upper-middle class backgrounds were not included in our study. Hence, this may not completely reflect the real scenario of the prevalence of RF/RHD in the Kathmandu valley. The initial diagnosis and screening process were mainly the goal-directed physical examination (including cardiac auscultation), and the information provided by the subjects in the form of the completed proforma, which is not as reliable as taking history and performing a physical examination in the clinic. Hence, there is a chance of missing cases when inappropriate history is provided by the subjects or physical examination, including cardiac auscultation, is carried out by the physicians in a noisy place.

Conclusions: The prevalence of RHD and CHD in government schoolchildren of the Kathmandu valley is 1.2/1000 and 1.3/1000, respectively. In the RHD group, mitral regurgitation was the most common lesion, followed by mitral stenosis and then aortic regurgitation. Among subjects with CHD, ASD was the most common lesion, followed by VSD and patent ductus arteriosus.

Acknowledgments

We wish to express our gratitude to all members of the Nepal Heart Foundation, Kathmandu Branch, for their valuable assistance and for the coordination of this study. We thank the principals and other teachers of the schools surveyed. Special thanks go to Dr Prabin Adhikari, Dr Hemant Manandhar, Dr Nripesh Pradhan, Dr Ananta Bhakta Upreti, Dr Rajeeb Shrestha, and the staff of the echocardiography laboratory for their assistance.

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Heart Failure: What Proportion of Patients Satisfy the Electrocardiographic Criteria for Cardiac Resynchronization Therapy?

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Background: Cardiac resynchronization therapy has emerged as a new therapeutic modality for patients with congestive cardiac failure and associated intraventricular conduction delay. The purpose of this study was to find out what proportion of Indian patients with congestive heart failure may be candidates for cardiac resynchronization therapy based on electrocardiographic characteristics.

Methods and Results: One hundred twenty-one consecutive patients with congestive cardiac failure due to various etiologies whose left ventricular ejection fraction was less than 40% were included in the study. Standard 12-lead electrocardiogram was recorded in all the patients, and various parameters (rhythm, conduction, QRS axis, chamber enlargement, chamber hypertrophy, and the presence of Q waves) were analyzed. The study population comprised 82 male (67.8%) and 39 female (32.2%) patients with a mean age of 53±13 years. Thirty-nine patients (32.2%) had NYHA class I–II symptoms, and 82 (67.8%) had NYHA class III–IV symptoms. The mean QRS duration was 111±27 ms. Bundle branch block was seen in 43 patients (35.5%), of whom 30 (24.8%) had left bundle branch block, and 13 (10.7%) had right bundle branch block. Of the 30 patients who had left bundle branch block, 19 (15.7%) had a QRS duration of between 120 and 149 ms, and 11 (9%) had a QRS duration ≥150 ms. In the latter group, 7 patients (5.8%) were in NYHA classes III and IV. As the clinical severity of heart failure increased, the mean QRS duration also increased, but this increment was not statistically significant.

Conclusions: Based on our data, it can be estimated that of the patients with heart failure who attend a tertiary care center, 25% of patients present with left bundle branch block. If we use the criteria for NYHA class III and IV congestive cardiac failure with QRS duration of ≥150 ms in patients with left bundle branch block, 6% of patients are likely to need cardiac resynchronization therapy. (Indian Heart J 2003; 55: 619–623)

Key Words: Cardiac resynchronization therapy, Congestive cardiac failure, Electrocardiography

Heart failure is a common sequel of virtually all forms of heart diseases, and is a relatively common disorder. The usual medical therapy for heart failure includes diuretics, vasodilators, positive inotropic agents, and neurohormonal/cytokine inhibitors, while surgical interventions include revascularization, mitral valve repair, left ventricular geometry restoration, and cardiac transplantation.

Recently, cardiac resynchronization therapy (CRT) has been proposed as a new modality of therapy for patients with congestive cardiac failure and associated intraventricular conduction delay. It has been estimated that approximately 25%–44% of patients with chronic heart failure have abnormal ventricular activation leading to interventricular and intraventricular asynchrony, and this plays an important role in the genesis of heart failure.

Currently, there are no Indian data to show what proportion of patients with congestive cardiac failure have intraventricular conduction delay, and may benefit from CRT. The aim of this study was to provide comprehensive and extensive electrocardiographic (ECG) findings in patients with congestive cardiac failure.

Methods

Patient population: We prospectively studied 121 patients with congestive cardiac failure of various etiologies.
and symptom class over a 6-month period. Patients who either had a definite history of myocardial infarction or angiographically proven coronary artery disease were diagnosed to have ischemic heart failure, and all others were considered to have nonischemic heart failure.

Electrocardiography: Standard 12-lead ECG of all the patients was recorded at a paper speed of 25 mm/s with a Hewlett Packard machine.

Rhythm: Sinus rhythm was identified when all QRS complexes were preceded by a P wave, a constant PR interval with an upright P wave in leads I and II, and an inverted P wave in leftward directed leads (leads aVR, V1, and V2), and deep S waves in left precordial leads, and a normal R peak time in leads V1 and aVL, while atrial fibrillation was defined by a rapid, regular atrial rhythm at a rate of ≥120 ms, notched or slurred R waves in leads V5–V6 and ≥50 ms in lead V1. Atrial flutter was characterized by a rapid, regular atrial rhythm at a rate of 200–400 beats/min with no isoelectric segments between the regular, uniformly shaped, biphasic sawtooth-like oscillations, while atrial fibrillation was defined by the absence of P waves, and the presence of small, irregular oscillation, so-called fibrillatory waves with an irregularly irregular ventricular response.

Intervals/bundle branch block: A PR interval ≥210 ms was considered to indicate a first-degree AV block. Left bundle branch block (LBBB) was defined by a QRS duration of ≥120 ms, notched or slurred R waves in leads V6, aVL, and absence of Q wave in left-sided leads except aVL, and a prolonged intrinsicoid deflection (>60 ms) in leads V6 and aVL, but normal in leads V1 and V2. The presence of right bundle branch block (RBBB) was based on a QRS duration ≥120 ms, an rsR’, rsR’ or rSR’ pattern in leads V1 or V2, wide and deep S waves in the left precordial leads, and a normal R peak time in leads V1 and aVL, but ≥50 ms in lead V1. Left anterior fascicular block was based on a QRS axis of –45° to –90°; QRS duration <120 ms with rs pattern in leads II, III, aVF, and qR pattern in leads I and aVL, while the diagnosis of left posterior fascicular block was based on a frontal plane mean QRS axis ≥120°, QRS duration <120 ms with RS pattern in leads I and aVL, and qR pattern in the inferior leads.

Chamber hypertrophy/enlargement: Diagnosis of left ventricular hypertrophy was based on the Sokolow–Lyon voltage criteria while right ventricular hypertrophy was diagnosed by tall R waves in anteriorly and rightward directed leads (leads aVR, V1, and V2), and deep S waves and an abnormally small r wave in leftward directed leads (leads I and aVL, and the lateral precordial leads). The diagnosis of left ventricular hypertrophy in the presence of LBBB was based on the criteria defined by Klein et al. while the presence of left ventricular hypertrophy in patients with RBBB was identified by the usual criteria as defined by Sokolow–Lyon.

Left atrial enlargement was said to be present when the P terminal force in lead V1, was equal to or more negative than -0.04 Vms (Morris index), or notched P wave with a duration of 120 ms or more. Right atrial abnormalities were defined as the presence of peaked and tall P waves in the inferior and right precordial leads with a voltage >2.5 mV.

Q waves/CHF triad: Any Q wave >30 ms was considered abnormal. The congestive heart failure triad was assessed using the criteria of Goldberger.

Echocardiography: Two-dimensional (2-D) echocardiography was performed on all the patients using a Sonos 5500 machine. The left ventricular internal diameter was measured both in systole (LVIDS) and diastole (LVIDD) using the criteria of Goldberger. Determination of the ejection fraction (EF) was based on the modified Simpson’s formula. All the patients were also evaluated for the presence of mitral regurgitation (MR). The severity of regurgitation was based on the absolute MR jet area (MRJA) in the long-axis and apical four-chamber views. MRJA ≤4 cm² was considered as mild regurgitation, while ≥8 cm² was considered as severe MR. Those with an MRJA between 4 cm² and 8 cm² were considered to have moderate regurgitation.

Echocardiographic assessment showed that 84.3% of patients had an LVIDD >55 mm and the mean diameter was 61.65±8.16 mm. The mean LVEF was 33.36±5%. Sixty-six percent of patients had associated MR, which was severe in 15.7% as assessed by color Doppler study.

Statistical analysis: The results were analyzed using SPSS statistical software. All the values for the various durations were expressed as mean (±SD). A p value <0.05 was considered statistically significant.

Results

Baseline characteristics: The clinical characteristics of the 121 patients enrolled in the study are given in Table 1. The mean age of the patients was 53±13 years. Heart failure was considered to be due to ischemic heart disease in 26.4%, while the remainder were classified as nonischemic. Twenty-two percent of all the patients had a history of documented prior myocardial infarction, 32.2% had hypertension, and 29.8% had diabetes mellitus. Sixty-five percent had had a prior hospital admission for heart failure. Most of the patients were receiving frusemide, 84% were on digoxin, 76% were receiving an ACE inhibitor, and 47% were on beta-blockers.
12-lead ECG (Table 2): Of the 121 patients, 115 (95%) were in sinus rhythm, while 5 (4.1%) were in atrial flutter/fibrillation. One patient had junctional rhythm. The mean PR interval was 161.84±4.20 ms, and 3.3% of patients had first-degree AV block. A QRS duration ≥100 ms was present in 76 patients (62.8%), while 30 (24.8%) had LBBB, 13 (10.7%) had RBBB, 27 (22.3%) had left anterior fascicular block, and 6 (5%) had left posterior fascicular block. Of the 30 patients with LBBB, 19 (15.7%) had a QRS duration of between 120 ms and 149 ms, and 11 (9%) had a QRS duration ≥150 ms (Fig. 1).

The mean QRS axis was leftward in 44 patients (36.4%). Fifty-one patients (42.1%) had left ventricular hypertrophy while left atrial enlargement was present in 65 (53.7%). A normal Q wave was present in 38 patients (31.4%), and 59 (48.8%) had poor progression of the R wave. The CHF triad was observed in 23.1% of patients in our study population.

LBBB and NYHA class: It was found that as the clinical severity of heart failure increased, the mean QRS duration also increased, but this increment was not statistically significant (Fig. 2). In the group of patients with LBBB and QRS duration ≥150 ms, 3.7% were in NYHA classes I and II while 5.8% were in NYHA classes III and IV (Fig. 3).

Discussion

CRT using left ventricular-based pacing is a new therapy for patients with congestive cardiac failure associated with intraventricular conduction delay. CRT encompasses 2 fundamental mechanisms: the optimization of atrioventricular synchrony, and correction of dys-synchronous ventricular contraction to improve the mechanical efficiency of the left ventricle.

This study was done to determine what proportion of patients in India with congestive cardiac failure may be candidates for CRT based on ECG. Patients with heart failure and LBBB are the best candidates for CRT. In our study, 35.5% of patients with congestive cardiac failure had bundle branch block, with LBBB alone in 25% of patients.
Our findings are almost similar to the results published earlier by Xiao et al., and Wilensky et al. Xiao et al. suggested that 30% of patients with dilated cardiomyopathy had LBBB, while Wilensky et al. demonstrated a 29.4% prevalence of LBBB in patients with dilated cardiomyopathy. In a study by Farwell et al., the prevalence of intraventricular conduction delay was 25%, out of which 15% of patients had LBBB alone.

There is a relationship between QRS duration and benefits from CRT, and the QRS duration selected varies from trial to trial. The cut-off QRS duration in the MUSTIC trial was 150 ms, in the MIRACLE study ≥130 ms, and in the PATH-CHF study ≥120 ms. In our study, 35.5% of patients with heart failure had a QRS duration ≥120 ms.

Reports have suggested that the best candidates for CRT are those who have congestive cardiac failure with LBBB and a QRS duration ≥150 ms. In our study, 19 patients (15.7%) with LBBB had a QRS duration of between 120 ms and 149 ms, and 11 (9%) with LBBB had a QRS duration ≥150 ms (Fig. 2). Gasparini et al. reported that patients with narrow QRS (120–150 ms) also benefited from biventricular pacing.

When we correlated the QRS duration with NYHA class, it was found that as the clinical severity of heart failure increases, the mean QRS duration also increases; however, this increment was not statistically significant. When we analyzed the presence of LBBB with various symptom classes, it was found that 19% of patients with LBBB had NYHA class III–IV symptoms with a QRS duration ≥120 ms, and 6% of patients with LBBB and NYHA class III–IV symptoms had a QRS duration ≥150 ms. Our results are similar to the report by Farwell et al. In their study, which was done in the setting of a district general hospital, 10% of patients were found to be eligible for CRT, using the criteria of NYHA class III–IV, and QRS duration ≥120 ms with LBBB.

Conclusions: In patients with heart failure who attend a tertiary care center, 25% of patients have LBBB. If we use the criteria of NYHA classes III and IV heart failure with a QRS duration ≥150 ms in patients with LBBB, 6% of patients are likely to need CRT.

Limitations: Our study was done in a tertiary care center; thus, the results are not applicable to a wider setting. Only patients who are very ill are likely to be referred to our center. Second, we did not include the echocardiographic criteria for assessing the intra- and interventricular conduction delay to assess the need for CRT, which is a must before proceeding with CRT.

References

Total Anomalous Pulmonary Venous Connection: Helical Computed Tomography as an Alternative to Angiography

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Background: Echocardiographic evaluation of the pulmonary veins is inadequate at times. Cardiac catheterization, especially in sick neonates, may be a high-risk procedure. Helical computed tomography with three-dimensional reconstruction is noninvasive but remains an underutilized modality.

Methods and Results: Between January 2002 and February 2003, 7 computed tomography scans of children 3 weeks to 5 years of age were performed to evaluate the drainage of the pulmonary veins in suspected total anomalous venous drainage. Helical computed tomography (GE High speed Advantage) was performed using 2 mm sections, and rapid bolus hand injections of 2 ml/kg body-weight of nonionic intravenous contrast. Sagittal and coronal reformats, and three-dimensional reconstructions were performed, and reviewed by the radiologist. The findings were discussed with the pediatric cardiologist and surgeon involved in the case. The diagnoses included complex congenital heart disease (n=5), isolated infradiaphragmatic total anomalous pulmonary venous connections (n=1), and transposition of the great arteries with total anomalous pulmonary venous connections (n=1). Cardiac computed tomography accurately demonstrated infradiaphragmatic total anomalous pulmonary venous connections in 4, and supracardiac drainage in 3 patients, in addition to the other cardiac findings. The findings on computed tomography scan correlated with surgical (n=5) and/or angiographic findings (n=2) in 7 patients.

Conclusions: In sick, high-risk patients, cardiac computed tomography can be considered as an alternative to cardiac catheterization for the evaluation of pulmonary venous drainage. (Indian Heart J 2003; 55: 624–627)

Key Words: Congenital heart disease, Total anomalous pulmonary venous connections, Helical computed tomography

Total anomalous pulmonary venous connections (TAPVC) are generally easily diagnosed on echocardiography. However, the exact site of drainage of the pulmonary veins may occasionally be in doubt, especially in association with complex cardiac disorders. Although angiography has been the gold standard for evaluation, it carries certain inherent risks, especially in small and sick infants. Computed tomography (CT) is noninvasive, and has a lower incidence of complications. However, reports of its use in the assessment of TAPVC are limited. We prospectively used helical CT to assess abnormalities of the pulmonary veins diagnosed or suspected by echocardiography in children with complex congenital heart disease. CT findings were correlated with echocardiographic, angiographic, and/or surgical findings.

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Methods
Between January 2002 and February 2003, 7 CT scans were performed to evaluate the drainage of the pulmonary veins in children with suspected TAPVC, aged 3 weeks to 5 years. Informed consent was taken from one of the parents of the child. Helical CT (GE High speed Advantage) was performed using 2 mm sections at a pitch of 1:1, and intravenous rapid bolus hand injections of 2 ml/kg body-weight of nonionic contrast. A delay of 30 s was given between the beginning of the contrast injection and the start of the scan. Each patient was scanned from the apex of the lung to the iliac crests. To avoid motion artifact, children were sedated as required. Sagittal and coronal MPR reformats, and three-dimensional (3-D) MIP reconstructions were obtained. A cardiac radiologist, who was experienced in treating congenital heart diseases and blinded to the echocardiographic diagnosis, reviewed the
cardiac CT scans. After a diagnosis was arrived at, the findings were discussed with the pediatric cardiologist and surgeon involved in the case.

Results

The details and diagnoses of the 7 patients with TAPVC who were studied are given in Table 1. The diagnoses included complex congenital heart disease \((n=5)\), isolated infradiaphragmatic TAPVC \((n=1)\), and transposition of the great arteries with TAPVC \((n=1)\). Cardiac CT scan accurately demonstrated supracardiac drainage in 3 patients (Fig. 1), and infradiaphragmatic TAPVC (Figs 2 and 3) in 4 patients in addition to other cardiac findings. In 7 patients, the findings on CT scan correlated with surgical \((n=5)\) and/or angiographic findings \((n=2)\). Obstruction was suggested on the basis of anatomic narrowing of the pulmonary veins noted on CT scan.

Discussion

According to Darling et al.,\(^1\) there are 4 types of TAPVC: supracardiac, cardiac, infracardiac, and the mixed variety.\(^2\) In most cases, a common chamber is seen posterior to the left atrium. In complex congenital heart disease, where pulmonary blood flow is low, the common chamber is also correspondingly diminutive and easily missed on echocardiography.

In cases in which echocardiography is equivocal, angiography has been used to delineate the pulmonary venous drainage. However, angiography has certain inherent risks and, at times, cannot be performed. Additionally, in complex congenital heart diseases, accurate visualization of the pulmonary venous anatomy may not be obtained even after angiography. During cardiac catheterization in these patients, entry into the pulmonary artery may at times be dangerous, and sometimes impossible. In such a situation, just a ventricular injection may not reveal any discernible dye in the pulmonary venous system even on prolonged levophase. Therefore, a noninvasive and relatively inexpensive alternative to

Table 1. Details of patients and diagnoses

<table>
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<th>Age</th>
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<th>Associated anomalies</th>
</tr>
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<tbody>
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<td>Infracardiac</td>
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</tr>
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<td>Portal vein</td>
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<td>Right SVC</td>
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<td>Infracardiac</td>
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<td>2 years</td>
<td>F</td>
<td>Supracardiac</td>
<td>Right SVC</td>
<td>No</td>
<td>Situs inversus, unbalanced atrioventricular canal, d-malposed vessels, pulmonary stenosis</td>
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</tbody>
</table>

M: male; F: female; TAPVC: total anomalous pulmonary venous connection; CT: computed tomography; VSD: ventricular septal defect; PDA: patent ductus arteriosus; SVC: superior vena cava

Fig. 1. Supracardiac TAPVC draining into the superior vena cava. (a) Right and left inferior pulmonary veins (short arrowheads) joining posterior to the left atrium into a common chamber. (b) Right and left superior pulmonary veins draining into the common chamber (open arrowhead). (c) Vertical vein (short arrow) ascending posterior to the right main stem bronchus. (d) Vertical vein (long arrowhead) draining superiorly into the superior vena cava.
Although there are several case reports on the use of helical CT in complex congenital heart diseases in children,6–11 specific studies evaluating pulmonary venous drainage are limited.12 Kim et al.,12 in their study of 14 patients with TAPVC, demonstrated that the combination of axial and 3-D images in helical CT angiography are helpful in the assessment of TAPVC, and this combination can be a good diagnostic tool for the preoperative evaluation of neonates and infants.

According to Kawano et al.,13 3-D helical CT angiography can clearly demonstrate the shape and spatial relation of the great arteries, the proximal branch pulmonary arteries, and anomalous pulmonary venous connections. However, intracardiac structures could not be visualized because of blurred and/or unclear edges of the ventricular wall, caused by respiratory movement.

CT angiography is a noninvasive procedure, which can provide detailed information on the anatomic features and relations of both the great vessels as well as other extracardiac structures that are very important from the perspective of a cardiac surgeon. Helical CT angiography can be performed considerably quicker than cardiac catheterization; thus, general anesthesia can be avoided, which is a great advantage, especially in the case of a sick baby.

Currently, helical CT angiography cannot visualize intracardiac structures well. In addition, the images of extracardiac structures may have blurred edges because of respiratory and cardiac movements. Another limitation of CT angiography is that it cannot provide pressure gradients; the anatomic configuration of the vessels may suggest pressure effects. However, in most cases, echocardiography gives true estimates of pressure gradients. One of the potential limitations of CT is that in the presence of diffusely small pulmonary veins (<2 mm), CT angiography may not clearly demonstrate the course of these small veins.

In our study, CT accurately demonstrated the pulmonary venous drainage in all 7 patients with TAPVC. Thus, computed helical CT angiography with 3-D reconstructions can be considered a safe and noninvasive alternative to cardiac catheterization in the evaluation of TAPVC, especially in the setting of complex congenital heart disease.

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Dynamics of QT Dispersion in Acute Myocardial Infarction

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Background: We studied the dynamics of QT dispersion in patients with acute myocardial infarction, and compared them with those in controls.

Methods and Results: Serial electrocardiograms of patients admitted to our institute with acute myocardial infarction were analyzed for QT dispersion, and compared with those of healthy age- and sex-matched controls. QT dispersion from 12 leads was measured as maximum QT minus minimum QT interval in ms. The mean QT dispersion of 114±29.6 ms was significantly higher in patients with acute myocardial infarction on admission as compared to 51.45±5.56 ms in controls (p<0.001). QT dispersion showed a dynamic change in patients with acute myocardial infarction who were thrombolyzed, being 109.11±5.77 ms, 87.59±5.88 ms, 75.89±18.33 ms, and 68.20±12.66 ms on admission, post-thrombolysis, and on days 3 and 7, respectively. During a similar time period, nonthrombolyzed patients showed a QT dispersion of 132.38±36.04 ms, 130.47±34.42 ms, 111.11±24.94 ms, and 106.25±27.64 ms, respectively; the difference between the 2 groups at all periods was significant (p<0.01). Mean QT dispersion values in patients who developed ventricular tachycardia or ventricular fibrillation were significantly higher than in patients who did not develop ventricular tachycardia or ventricular fibrillation (p<0.01).

Conclusions: Mean QT dispersion is significantly increased after acute myocardial infarction, and shows a dynamic decrease with time, the difference being more marked in thrombolyzed patients. Mean QT dispersion levels are higher in patients with ventricular tachycardia and ventricular fibrillation compared to patients with acute myocardial infarction without these arrhythmias. The changes in QT dispersion are dynamic, and it may serve as a non-invasive marker of susceptibility to malignant ventricular arrhythmias. (Indian Heart J 2003; 55: 628–631)

Key Words: QT dispersion, Electrocardiography, Myocardial infarction

The incidence of primary ventricular fibrillation (VF) in the early phases of acute myocardial infarction (AMI) depends on various factors: time from onset of symptoms, size of infarction, potassium levels, R-on-T ventricular extrasystoles; however, none of these features has clinically useful positive predictive accuracy.1 Dispersion of repolarization is an important electrophysiologic feature which is considered fundamental to the initiation of VF. With recent evidence suggesting that differences in interlead QT intervals on standard 12-lead electrocardiogram (ECG) did not reflect technical artifacts but regional variations in the recovery of ventricular excitability, a simple method for examining repolarization features as predictors of VF has become available.1,2

This study examines QT dispersion (QTd) in patients with AMI. We examined the dynamic behavior of QTd in patients with AMI, and relates it to thrombolysis and arrhythmias as compared to healthy controls.

Methods

This prospective study was carried out on patients admitted to the coronary care unit of our hospital. One hundred patients with AMI, and 100 age- and sex-matched controls were studied. Detailed history and clinical examination were undertaken. Apart from routine investigations (including complete blood count, urine analysis, blood sugar levels, liver function tests, renal function tests, lipid profile, and chest X-ray), CPK-MB, troponin-T level estimation, and serial ECG recordings at admission, 6 hours after thrombolysis, and on days 3 and 7, and also whenever the situation demanded, were done. For recording the ECGs, a Schiller ECG machine cardiovit AT-1 model, which has simultaneous 12-lead acquisition, was used. The recordings...
were made at a speed of 25 mm/s, and a setting of 1 mV=10 mm. Two complexes from each lead were analyzed for measurement of the QT interval in ms. QTd measurement was done as suggested in the study by Higham and Campbell. The QT interval was measured from the onset of the QRS complex to the end of the T wave. The most crucial aspect of the methodology is the protocol to define the end of the T wave. Since this definition is especially difficult when T waves merge with U or P waves, we defined the end of the T wave as the point of return to T–P baseline or the nadir between the T and U waves. If a U wave was present, the QT interval was measured till the nadir of the curve between the T and U waves. ECGs in which the QT interval was not measurable in more than 8 leads were excluded. QTd was calculated from the ECG by a blinded, experienced, single observer.

\[ QTd = \text{Maximum QT interval} - \text{Minimum QT interval} \]

The QT interval and QTd were calculated in a similar manner from subsequent ECGs. Arrhythmias studied with respect to QTd were ventricular tachycardia (VT) and VF. Echocardiography was done in all the patients to determine the left ventricular ejection fraction. Thrombolysis was given as per standard indications. This was designed as a case–control study, and cases were further divided as (i) thrombolyzed group and nonthrombolyzed group, and (ii) VT and VF group and nonarrhythmic group.

**Exclusion criteria:** Subjects were excluded from the study on the basis of the following: (i) medical conditions that could affect the QT interval, such as electrolyte imbalance, left and right bundle branch blocks, atrial fibrillation; (ii) patients taking drugs that affect the QT interval.

**Statistical analysis:** All the observations were represented as mean±SD, and significance was calculated using the unpaired t test. The Chi-square test was also used wherever appropriate.

**Table 1. QT dispersion values in various study groups according to time period**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Admission</th>
<th>Post-STK/6 hours later</th>
<th>Day 3</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>100</td>
<td>51.45±5.56</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>AMI</td>
<td>100</td>
<td>114±29.6</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>AMI: STK given</td>
<td>79</td>
<td>109.11±25.77</td>
<td>87.59±25.88</td>
<td>75.89±18.33</td>
<td>68.20±12.66</td>
</tr>
<tr>
<td>AMI: STK not given</td>
<td>21</td>
<td>132.38±36.04</td>
<td>130.47±34.42</td>
<td>111.11±24.94</td>
<td>106.25±27.64</td>
</tr>
<tr>
<td>Nonarrhythmic group</td>
<td>87</td>
<td>105.85±20.24</td>
<td>87.07±22.74</td>
<td>77.07±19.40</td>
<td>70.48±16.09</td>
</tr>
<tr>
<td>VT</td>
<td>7</td>
<td>148.57±32.36</td>
<td>131.42±22.67</td>
<td>125.71±29.92</td>
<td>120±35.77</td>
</tr>
<tr>
<td>VF</td>
<td>6</td>
<td>166.66±30.11</td>
<td>183.33±42.73</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*p<0.01 as compared with the nonarrhythmic group; n: number of patients; AMI: acute myocardial infarction; VT: ventricular tachycardia; VF: ventricular fibrillation; STK: streptokinase

All values are mean ± standard deviation

**Results**

Mean QTd was significantly higher in patients with AMI at admission as compared to age- and sex-matched controls (p<0.001) (Table 1). The mean QTd in patients who were thrombolysed showed a significant decline from the value at admission to that on day 7 (p<0.01). The mean QTd value in patients who were not thrombolysed also showed a significant decline with time but this decline was less than that in the thrombolysed group (p<0.01). The mean QTd in the thrombolysed and nonthrombolysed groups differed significantly at all periods (p<0.01) (Fig. 1). The mean QTd in the VT and VF groups was significantly higher as compared to the nonarrhythmic group (p<0.01), and it increased in the VF group prior to occurrence of VF (Figs 2 and 3).

**Discussion**

The clinical significance of QT interval prolongation has been the subject of much debate, with evidence till date favoring an association between a prolonged QT interval or an increased QTd, and an increased risk of sudden death due to arrhythmia. In our study, the mean QTd noted in controls was in the same range as that established for healthy subjects in the studies by Sylven et al. (54±27 ms),
Mirvis (59 ± 12.9 ms), Cowan et al. (48 ± 18 ms), and Moreno et al. (54 ± 20 ms). In contrast, patients with AMI at admission in our study showed significantly greater mean QTd as compared to controls (p < 0.001). This is also in accordance with the studies conducted by Higham et al., van de Loo et al., and Glancy et al. The main goal of thrombolytic therapy in patients with AMI is the establishment and maintenance of coronary patency to improve left ventricular function and decrease mortality. Although it has been documented that the use of thrombolytic agents reduces mortality rates after infarction, the mechanisms of the benefit continue to be debated, potentially including improvements in both mechanical and electrical functions. However, studies have shown that postinfarction patients with open arteries have a lower mortality rate than patients with closed arteries. Mortality rates as low as 2.5% have been reported in patients with patent arteries compared with 15% in patients with closed arteries.

The mean QTd in patients who were thrombolyzed showed a progressive decline from admission to day 7 (p < 0.01). Thrombolysis was associated with less QTd in post-AMI patients. This is in accordance with the study conducted by Moreno et al., who had similar results. The data support the hypothesis that QTd after AMI depends on the reperfusion status. Moreno et al. attributed the fall in QTd to reduction in the infarct size and improvement in LV contractility. Our findings are consistent with these observations. Reduction in QTd, and the corresponding risk of ventricular arrhythmia, may be a mechanism of benefit of thrombolytic therapy. Patients who were not thrombolyzed had significantly higher values of mean QTd as compared to those who were thrombolyzed (p < 0.01), and they also had a significant fall in mean QTd value with time (p < 0.01), though this fall was less than that in thrombolyzed patients (Fig. 1).

To undertake an in-depth analysis of all these factors, a large study with angiographic, and serial echocardiographic and perfusion studies should be undertaken.

The mean QTd was significantly prolonged in patients with VT (p < 0.01) and VF (p < 0.01), as compared to the nonarrhythmic group (Figs 2 and 3). This is in accordance with a study carried out by Pye et al. The study supports the hypothesis that QTd reflects spatial differences in myocardial recovery time. QTd may be useful in the assessment of risk of arrhythmia. Oikarinen et al. concluded that increased QTd is associated with a susceptibility to VF, and was independent of the extent of coronary artery disease, and the use of beta-blockers.

Figure 4 shows the results of QTd values on admission in healthy controls, in patients with AMI without arrhythmia, and in patients who developed VF. Mean QTd values at admission were greater in patients with VF than in those without VF complicating their AMI (p < 0.01). In their study, Pye et al. concluded that QTd may be an additional noninvasive marker of susceptibility to ventricular arrhythmias. Higham et al. showed that QTd is increased after myocardial infarction, and the levels are higher in patients with VF. The changes in QTd are dynamic, and may reflect the changing pattern of the underlying recovery of ventricular excitability, which is profoundly disturbed in the earliest phase of acute infarction.

Limitations: This study was not designed to be a definitive examination of QTd as a risk factor for VF, but rather to
provide information that would permit the design of such a study. Only 6 of the consecutively included patients with AMI developed with ischemic VF, but even in this small group, significantly higher QTd measurements were seen. Combined monitoring of both QT end-dispersion and R-on-T ventricular extrasystolic activity may be even more sensitive method for the prediction of VF, with one method (QTd), focusing on the arrhythmia substrate and the other (R-on-T extrasystoles) on the arrhythmia trigger. However, automated systems are necessary and improved algorithms for QT end-detection are required to perform such monitoring.

References
Primary Cardiac Tumors: Surgical Experience and Follow-Up

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Background: Primary cardiac tumors are rare. There are only a few reports of such tumors from India.

Methods and Results: We report our experience with 34 patients with primary cardiac tumors operated on at our institute between December 1989 and October 2001. The study group comprised 16 males and 18 females with a mean age of 40.05±13.06 years (range 7–65 years). The predominant symptoms were breathlessness and congestive heart failure. In addition, 1 patient presented with peripheral embolism with impending limb ischemia that necessitated emergency embolectomy. Echocardiography was confirmatory in the diagnosis of all the benign tumors, whereas the malignant tumors were incidentally found during surgery. All the patients survived the operation. Complete resection of the tumor was possible only in benign tumors; however, malignant tumors were partly removed to relieve obstruction. All the excised benign tumors showed no recurrence on a mean follow-up of 54.78±31.30 months (range 3–108 months). Myxoma was found in 31 patients, left ventricular fibroma in 1, and leiomyosarcoma in 2. Both the patients with malignant tumors developed recurrence postoperatively, and succumbed to extensive distant metastases.

Conclusions: The long-term outcome of surgery was excellent in patients with benign cardiac tumors. However, malignant tumors had an unchanged prognosis, although symptomatic relief was achieved. (Indian Heart J 2003; 55: 632–636)

Key Words: Cardiac tumors, Myxoma, Cardiac surgery

Primary cardiac tumors represent 5%–10% of all neoplasms of the heart and pericardium.1 Myxoma is the most common cardiac tumor, comprising about 40% of benign tumors.2 Of the primary malignant tumors, sarcomas are the commonest.3 There has been little surgical experience with primary tumors, and reports include only a small number of patients with a short follow-up. We present our surgical experience of 34 cases, and their long-term follow-up results spanning over a decade.

Methods
Between December 1989 and October 2001, 34 patients with primary cardiac tumors (age range 7–65 years; mean age 40.05±13.06 years; 16 males) were surgically treated at our institute. The patients were divided into 2 groups; the myxoma group comprising 31 patients, and the nonmyxoma group comprising 3 patients, of whom 2 had primary sarcomas (both leiomyosarcoma), and the third a benign fibroma. Their medical records were reviewed, and follow-up data obtained by routine outpatient visits, post, and telephone calls.

Patient profile and surgical techniques
Myxoma group: Table 1 shows the clinical presentation of the patients with myxoma. The commonest clinical presentation included breathlessness on exertion in 23 patients, and congestive heart failure in 12 patients. The majority of patients (96%) were in NYHA class II. One patient presented with peripheral embolism leading to impending limb ischemia. Emergency embolectomy and extraction of myxomatous tissue from the distal vessels were performed. Twenty-nine patients were in sinus rhythm and 2 were in atrial fibrillation. A mid-diastolic murmur was heard in 19 patients (61%). Fourteen patients (45%) had associated pulmonary arterial hypertension.

Routine hematologic, biochemistry, chest X-rays, and
Electrocardiographic studies were performed in all patients for the preoperative assessment. Echocardiography (Table 2) revealed that most of the tumors had a stalk that originated from the interatrial septum (IAS), and grew into the left atrium (LA). All the benign cardiac tumors were diagnosed by echocardiography. It being an institutional policy that any patient above 45 years of age undergoing open heart surgery for any cause should undergo a coronary angiogram, coronary angiography was performed in 4 patients, which revealed normal coronary arteries.

Surgical excision of the cardiac tumors was performed via a median sternotomy with the aid of cardiopulmonary bypass (CPB), which was established using ascending aortic and dual venous cannulation. The approach to the cardiac tumors was trans-septal in 27 patients, while the superior septal approach was used for the removal of 4 large-sized tumors.

The tumors were excised along with a wide margin of tissue surrounding the attachment of the stalk/tumor to avoid recurrence. Most of the tumors could be removed as a single mass but some had to be removed piecemeal as they were very friable. The LA cavity was irrigated with saline to remove any left-over tissue. The defect in the IAS was then closed with a pericardial patch. Macroscopically, the tumors were irregular, greenish-gray, gelatinous or fibrous, lobulated masses, and ranged in size from 5 to 9 cm with weight ranging from 20 to 115 g. Histologically, the tumors were composed of spindle or stellate multinucleated cells with abundant vacuolated cytoplasm in a myxoid or fibromyxoid background (Fig. 1). Some tumors showed patchy areas of calcification. Concomitant procedures included mitral valve (MV) repair in 3 patients, MV replacement in 3, embolectomy in 1, and tricuspid annuloplasty in a patient with severe tricuspid regurgitation. One patient underwent left adrenalectomy for pheochromocytoma a month before myxoma excision. One male patient had multiple myxomas—1 in the right ventricular outflow tract (RVOT), 1 in the right ventricular (RV) body with a short stalk, a single mass in the LA attached to the IAS, and a single mass in the left ventricular (LV) cavity. The masses in the RVOT and RV body were removed by right ventriculotomy on CPB. The mass in the LA was removed via the trans-septal route, and that in the LV through the MV.

Nonmyxoma group: Over a period of 10 years, only 3 patients had nonmyxomatous tumors, of which 2 were leiomyosarcomas, and the third a benign fibroma. Of the 2 patients with leiomyosarcoma, the first patient, a 39-year-old male, presented with cough, dyspnea on exertion, and fever. Echocardiography revealed a mass originating from the LA, suggestive of LA myxoma. The tumor was performed in 4 patients, which revealed normal coronary arteries.
approached via the trans-septal route, and was found to be multilobulated and firm in consistency, involving the major part of the LA. Furthermore, it was adherent to the posterior wall of the LA and the orifices of the right pulmonary veins. The tumor was protruding into the LV cavity through the MV and measured 10×15 cm in size. The incision was extended to the roof of the LA. The tumor was completely excised, including the entire IAS. The atrial septal defect (ASD) was closed with a Dacron patch, and the patient could easily be weaned away from CPB. The postoperative period was uneventful. Histopathology of the tumor (Fig. 2) revealed it to be a sarcoma that proved to be a leiomyosarcoma by immunohistochemistry.

The second patient with a leiomyosarcoma was a 28-year-old male who presented with dyspnea and anorexia. A preoperative diagnosis of myxoma was made in this case also. The patient was taken up for surgery, and a multilobulated solid mass 6×7 cm in size was found to be adherent to the posterior wall of the LA, and occupied the entire left atrioventricular junction; the protrusion outside the LA was partly excised. A sinus venosus ASD was an accidental finding, and was repaired with a patch of autologous pericardium.

The third patient presented only with palpitation. A preoperative diagnosis of LV myxoma was made. The mass was excised by left ventriculotomy, and biopsy revealed it to be a fibroma.

Follow-up: Follow-up was completed in 28 of 34 patients; 6 patients of the myxoma group were lost to follow-up. The follow-up period ranged from 3 to 108 months (mean 54.78±31.30 months).

Results

Early results: All the patients with cardiac tumors survived the operation. Two patients developed postoperative complications. One developed a persistent air leak from the thoracostomy tube due to an accidental lung injury during the operation, which closed subsequently after tetracycline pleurodesis. Two patients required re-exploration of the chest for excessive bleeding. The chest was left open for 24 and 28 hours, respectively, and the sternum was closed when the bleeding stopped.

Late results: There was no late mortality in the myxoma group. However, postoperatively, both the patients with leiomyosarcoma died at 3 and 7 months, respectively, due to distant metastases. All the survivors improved to NYHA functional class I, except 2 who remained in NYHA functional class II. Two patients developed progressive mitral regurgitation necessitating MV replacement—6 years after the initial operation in 1 patient while the other is awaiting surgery. One patient who underwent emergency right lower limb embolectomy with excision of the LA myxoma presented with ischemic contracture of the side of the calf muscle, leading to shortening of the right limb. Serial follow-up with echocardiography demonstrated that none of the patients in the myxoma group showed any evidence of recurrence; however, 1 patient with leiomyosarcoma showed recurrence at 6-month follow-up (Fig. 3), and died after 1 month. The other patient with leiomyosarcoma died 3 months postoperatively due to extensive metastases.
Our series reports the detailed short- and long-term follow-up of patients over a span of 10 years. Primary malignancy is rare, and most series report 1–4 cases over a span of 10–20 years. In their large series, Strause and MerliSS found a 0.0017% incidence of primary cardiac tumors. In most series, benign tumors form approximately three-fourth of all primary cardiac tumors. The exact incidence in India is not known. In the only large series by Bhan et al., an incidence of 0.24% of all cardiac operations performed at their institution was reported. Putnam et al. reported 20 cases of primary sarcoma between 1964 and 1989.

As in most other series, breathlessness and cardiac failure were the most common presentations in our patients. However, we found a higher incidence of pulmonary artery hypertension and MV pathology in our patients, which could be because of the late referral or progress of the disease. One patient presented with an acute ischemic limb, and required emergency embolectomy along with excision of the LA myxoma. Verkkala et al. also reported a patient who required amputation of the left arm for tumor embolism before cardiac surgery.

Although clinically and echocardiographically it may be difficult to distinguish between benign and malignant primary cardiac tumors, echocardiography is still the most practical diagnostic tool for evaluating an extracardiac mass. Also, 2 masses diagnosed on echocardiography as benign myxomas turned out to be malignant in our series. The diagnosis of myxoma should be critically analyzed when the mass is at a site other than the LA, and when it is sessile. In our series, 2 of the 5 sessile masses were malignant. Also, both the leiomyosarcomas had dense pericardial adhesions, and this may be due to an underlying malignant cardiac tumor.

Our surgical strategy is to approach the tumor through the trans-septal route after establishing CPB by minimal handling of the heart. For better exposure we extended the incision to the roof of LA for complete evaluation of the lesion. There was no recurrence of myxoma during the follow-up. Depending on the pathology and extent of the lesion, 6 patients underwent MV procedures; 3 underwent MV repair, and 3 underwent MV replacement with a Starr–Edwards valve (Edwards Life Sciences). All the patients did well postoperatively. One young female patient underwent a left adrenalectomy for pheochromocytoma, and later underwent excision of the LA myxoma. Carney et al. had reported 3 patients with skin lesions, myxoma, and adrenal disease. In our series, no family members or relatives had a syndrome similar to the patients, as has been suggested by some authors.

Of the primary sarcomas reported by Putnam et al., only 2 cases of leiomyosarcoma were reported; 2 primary tumors in our series were leiomyosarcomas. Preoperatively, we could not distinguish between benign and malignant tumors clinically or echocardiographically. Also, we found dense pericardial adhesions in both the cases.

Primary leiomyosarcomas are extremely rare, and constitute less than 0.25% of all cardiac tumors. Antunes et al. reported 2 cases of leiomyosarcoma, which had a good response to surgery and adjuvant chemotherapy, with both patients surviving up to 22 months after the operation. Of the 2 patients with leiomyosarcoma operated by us, 1 had developed disseminated metastases but refused further adjuvant treatment and died 3 months following discharge from the hospital; the second did well till 6 months postoperatively, but showed a residual/recurrent tumor on follow-up CT scan, and was referred for radiotherapy: he died 7 months postoperatively.

**Conclusions:** Although the commonest presentations are dyspnea and cardiac failure, cardiac tumors may be nonspecific in their presentation. Also, it is difficult to establish the nature of the tumor (benign v. malignant) by echocardiography. A high degree of suspicion is required for masses presenting at sites other than the LA. Surgery for cardiac tumors, both benign and malignant, is an emergency, and the results are satisfactory for benign tumors. The result of surgical treatment for sarcomas are still dismal, partly because the role of adjuvant therapies is not well defined.

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Venogram-Guided Extrathoracic Subclavian Vein Puncture

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Background: Subclavian vein puncture is commonly performed to insert the pacing lead for permanent pacemaker implantation. Our aim was to study the safety and feasibility of venogram-guided extrathoracic subclavian vein puncture for permanent pacemaker lead insertion.

Methods and Results: Sixty patients (32 males, and 28 females) underwent permanent pacemaker lead insertion by extrathoracic subclavian vein puncture at our institute between March 2002 and December 2002. Fifteen patients underwent dual-chamber and 45 single-chamber pacemaker implantation. All the patients underwent extrathoracic subclavian vein puncture guided by venogram, except 1 who underwent dual-chamber pacemaker implantation in whom the ventricular lead insertion was via the cephalic vein on an elective basis. The procedure was successful in all the patients. Inadvertent subclavian artery puncture occurred in 2 patients without any complication. There was no incidence of pneumothorax, hemothorax or pacemaker site infection.

Conclusions: Venogram-guided extrathoracic subclavian vein puncture is safe and successful. It may be adopted as one of the preferred approaches for permanent pacemaker lead insertion. (Indian Heart J 2003; 55: 637–640)

Key Words: Pacemaker, Venography, Endocardial lead

Worldwide, the subclavian vein is the most common route for the introduction of the endocardial pacing lead. It is preferred over the cephalic vein for its speed and simplicity of placement. Also, it allows the placement of multiple leads. However, the classic method of subclavian vein puncture in its intrathoracic course, although reasonably safe, is not free from complications. Pneumothorax, hemothorax, and brachial plexus injury are possible complications, and may rarely be fatal. The long-term integrity of pacing and defibrillator leads may be affected by subclavian crush, related to the entrapment of the lead in the costoclavicular ligament. Extrathoracic subclavian vein puncture avoids most of these risks, and still maintains the advantages of classic subclavian vein puncture. Different methods have been adopted for extrathoracic subclavian vein puncture. We report our experience with permanent pacemaker lead insertion guided by venogram.

Methods

Venogram-guided extrathoracic subclavian vein puncture

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was performed in 60 consecutive patients undergoing permanent pacemaker implantation at our institute between March 2002 and December 2002. There were 32 males and 28 females, with ages ranging from 6 to 76 years. The commonest indication for pacemaker implantation was degenerative complete heart block and sick sinus syndrome (41.6% each). The pacemakers implanted were single-chamber (VVI) in 45 patients (75%), and dual-chamber (DDD) in 15 (25%). The left subclavian vein was accessed in 90% of cases and the right subclavian vein in the remaining. Patients in whom the right subclavian vein was accessed were: (i) left-handed persons, (ii) those with left-sided pacemaker pocket infection, and (iii) those who underwent new lead insertion during pulse generator change at end of life (EOL) in right-sided pacemaker implantation, when lead assessment showed unacceptable parameters.

Technique of extrathoracic subclavian vein puncture: Under aseptic precautions, 10–20 ml of 2% xylocaine with 1:1 dilution was infiltrated at the site of surgical incision. A 4–5 cm surgical incision was made 2 cm below and parallel to the clavicle, with lateral extension up to the deltopectoral groove. Dissection was done up to the level of the prepectoralis fascia, and a pocket for pacemaker placement was created at that level. On the
side of the venous approach, 10 ml of nonionic iodine contrast followed by 10 ml saline flush was injected via a peripheral line inserted in the hand, and a fluoroscopic view acquired. The image of the opacified subclavian vein was stored, and fixed as a guide for subsequent subclavian vein puncture. The subclavian vein usually passed at or just below the angle formed by the outer border of the first rib and the lower border of the clavicle in its extrathoracic course. Care was taken not to displace the table and the fluoroscopic tube any more, till the venepuncture was over. An 18 gauge needle was used for venepuncture. Venepuncture was done at the level of the prepectoralis fascia. During the venepuncture, the needle point was directed towards the extrathoracic part of the subclavian vein, as shown in Fig. 1, with a 30° to 45° angulation to the horizontal plane. The vein was entered at the first attempt in most of the patients. If it was not entered in the first attempt, subsequent attempts were made with a little change in angulation. Upon successful venous access, a 0.035″ J-shaped short guidewire was inserted in the vein. A second puncture was made in a similar fashion, and a second guidewire was left inside the vein for the second lead in case of DDD pacemaker implantation. A subclavian introducer sheath from 7 to 11 F in size, depending on the requirement for lead insertion, was passed over the guidewire for the purpose of lead insertion.

Results

Extrathoracic subclavian venepuncture: Subclavian vein puncture was successful in all the patients. In one case of DDD pacemaker implantation, the ventricular lead was introduced via the cephalic vein on an elective basis. The subclavian vein could be entered in a single attempt in 60 of a total of 74 venepunctures (81%). In case of failure during the first attempt, repeat attempts were usually successful with little change in direction and angulation of the needle. The subclavian artery was inadvertently punctured in 2 cases (3%). Manual pressure over the site of the puncture was sufficient to control the bleeding. Subsequent attempts to puncture the vein were successful. Pneumothorax, hemothorax or brachial plexus injury was not observed in any of the cases. In one obese patient, repeated attempts at subclavian vein puncture were initially not successful from the subcutaneous region. After proper dissection up to the region of the prepectoralis fascia, an attempt to puncture the subclavian vein was successful. In another case, the venogram showed the presence of a left-sided SVC draining to the coronary sinus. The bridging vein was absent. As an incision had already been made in the left side, the subclavian vein was punctured, and the lead negotiated through the left SVC into the right atrium. The stylet was exchanged for another stylet shaped manually to a large pigtail loop at the distal end. The lead could then be directed through the tricuspid valve into the right ventricle after a closed loop in the right atrium. After this case, a routine venogram was attempted to exclude the presence of a left SVC before site preparation.

Complications during the postoperative period and follow-up: There was no clinical evidence of subclavian vein thrombosis in any of the cases. There was a small pacemaker pocket hematoma not requiring surgical evacuation in a patient who was receiving heparin for atrial fibrillation and had a past history of cerebrovascular accident. The anticoagulation therapy was temporarily withheld for 2 weeks, and subsequently restarted without any further complications. There was no incidence of pacemaker pocket infection.

Discussion

In our experience, venogram-assisted extrathoracic subclavian vein puncture is easy, safe, quick, and successful. The high success rate is equivalent to or even better than the classic intrathoracic subclavian method. Extrathoracic subclavian vein puncture has been attempted in different ways by different investigators. In all these series, the success rate is uniformly high. Only in the report by Nash et al., an ultrasonic-guided venepuncture technique had a failure rate as high as 20%. Venogram-guided extrathoracic subclavian venepuncture has been
the subclavian vein commonly passes at or just below the angle formed by the lower border of the clavicle, and the outer border of the first rib, as seen during the venogram in the anteroposterior fluoroscopic view, venepuncture was attempted without a venogram in subsequent cases. If venepuncture failed, a venogram was done to assist puncture. This approach further reduces the chances of infection.

Conclusions: In our experience, venogram-guided extrathoracic subclavian vein puncture is easy, safe, and successful. Puncture-related complications are few.

References


An Unusual Case of Complete Heart Block With Triplet Pregnancy

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A young primigravida presented at 36 weeks of gestation with complete heart block and triplet pregnancy. She underwent a lower segment cesarean section, and was managed successfully. The patient remained asymptomatic and did not require antiarrhythmic drugs or pacing. 

**Key Words:** Complete heart block, Multiple pregnancy, Pacing

**Case Report**

A 26-year-old primigravida presented as an emergency admission at 36 weeks of gestation with labor pains. The antenatal history during the first trimester was normal. Ultrasonography diagnosed triplets at 24 weeks of gestation. She received regular antenatal check-ups and developed high blood pressure at 28 weeks, for which she was put on 250 mg alpha methyldopa 8-hourly. She developed chest pain at 32 weeks of gestation and was found to have complete heart block (revealed on ECG) with cardiomegaly (seen on chest X-ray with abdominal shield). She was given some injections for pain relief and was asymptomatic until 36 weeks, when she presented with labor pains. Examination revealed irregular cannon waves on jugular venous pulse, a blood pressure of 130/90 mmHg, pulse rate of 48/min, regular, and bilateral pitting edema of the feet. Chest examination was normal. Cardiovascular examination revealed that the apex beat was in the 5th intercostal space just outside the midclavicular line and there was no murmur. On palpation of abdomen multiple fetal parts were palpable and three fetal hearts could be auscultated. Other investigations were normal except for 3+ proteinuria. Electrocardiogram showed complete heart block with junctional escape rhythm (Fig. 1). The ventricular rate was 52/min, and there was T wave inversion in leads II, III and aVF. 2-D echocardiography and color Doppler revealed no regional wall motion abnormality. The left ventricular ejection fraction was 68%, with no valvular lesion or clot. The patient had moderate labor pains. Examination per vaginum revealed an inadequate pelvis (android type). The decision to perform a cesarean section was taken along with arrangements for a temporary pacemaker.

A lower segment cesarean section was done under general anaesthesia. Three live babies were extracted weighing 2.4, 2.1 and 1.2 kg, respectively. Postoperatively, the patient had high BP (180/120 mmHg) and was put on 5 mg amlodipine. The first two babies were kept with the mother. The patient's postoperative period was uneventful and she was discharged from the hospital in a satisfactory condition. Her third baby was admitted in the neonatal intensive care unit, receiving incubator care and intravenous fluids.

**Discussion**

Sustained bradycardia may be encountered during pregnancy for a number of reasons. Electrolyte imbalance such as hyperkalemia, metabolic derangements such as hypothyroidism, or medications such as beta-blockers, calcium-channel blockers, or digitalis may be easily remediable causes of bradycardia. Methyldopa is a centrally
acting sympathoplegic drug which lowers the blood pressure, chiefly by reducing the peripheral vascular resistance, with a variable reduction in heart rate and cardiac output. In this patient, the cause of bradycardia was congenital heart block, which was missed during the antenatal check-ups; it persisted in the postpartum period when the patient was no longer on methyldopa. As complete heart block does not cause any special problems during pregnancy, prophylactic placement of a pacemaker is not indicated in asymptomatic patients.

For symptomatic patients in the first and second trimesters, permanent pacemaker implantation is the therapy of choice; it can be performed under echocardiographic control. In symptomatic patients, who present at or near term, temporary pacing followed by the induction of labor at the earliest possible time is suggested, to prevent complications of prolonged temporary pacing. Labor in patients with complete heart block can be complicated by syncope and convulsions due to slowing of the heart rate during the Valsalva maneuver, which may occur during forceful uterine contractions in the second stage of labor when the presenting part descends through the pelvis. It is preferable to deliver these women in a lateral decubitus position to minimize the bearing down, and to shorten the second stage by using a pair of forceps. As volume shifts and blood loss are greater in those undergoing cesarean section, these procedures should be performed only for the usual fetal and obstetric indications.

Women with congenital complete heart block may tolerate pregnancy well, although the limitation in heart rate response may limit their ability to augment cardiac output. This is especially important owing to the fact that such patients have dilated ventricles with chronically high stroke volume in the nongravid state, with a limited capacity to further augment end-diastolic volume and stroke volume, despite the expansion of intravascular volume that occurs in early pregnancy. In women with multiple gestations, cardiac output is increased as compared to singleton pregnancy, and the increased maternal heart rate and contractility in these women suggest that the cardiovascular reserve is reduced.

The hemodynamic changes of pregnancy are known to revert to the prepregnant state after delivery. These altered hemodynamic variables could contribute to the patient's symptoms during pregnancy; hence, the symptomatic status of the patient should be reassessed in the postpartum period before contemplating permanent pacemaker implantation.

References

Fig. 1. ECG showing complete heart block with junctional escape rhythm. Ventricular rate 52/min, T wave inversion in leads II, III, and aVF.
Post-Stenotic Dilatation: Challenge in Renal Ostial Stenting—A Simple Solution

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Stenting is the treatment of choice for treating stenotic renal ostial lesions. During the stenting of an ostial lesion in a renal artery with post-stenotic dilatation, we were faced with the problems of unavailability of a balloon of appropriate length and diameter, and determining the real reference vessel diameter. The problem was solved by a simple technique. (Indian Heart J 2003; 55: 643–645)

Key Words: Renal ostial stenosis, Stenting, Post-stenotic dilatation

Percutaneous transluminal renal angioplasty (PTRA) and stent placement have become widely used modalities for the treatment of symptomatic renal artery stenosis causing renovascular hypertension. For ostial renal lesions, stenting, compared to plain balloon angioplasty, has been shown to be associated with a higher technical success (of up to 97%),1–3 and longer patency rates.4 We report a problem faced during the stenting of an ostial renal artery stenosis with post-stenotic dilatation that was solved by a simple technique.

Case Report
A 38-year-old male, a chronic smoker, was detected to be hypertensive 6 months back after suffering a hemorrhagic cerebrovascular accident. In spite of being on regular treatment with a combination of the maximum recommended dosage of an ACE inhibitor, diuretic, and calcium-channel blocker, his blood pressure remained around 160/100 mmHg. His renal function tests were normal (BUN 15 mg/dl and serum creatinine 1.1 mg/dl). Ultrasound study showed a normal-sized right kidney, and a small left kidney (vertical dimension 8 cm) with evidence of left renal artery stenosis on Doppler examination.

An aortogram (LAO 4°, cranial 10°) revealed ostial stenosis of the left renal artery. The right renal artery was normal. Selective angiogram of the left renal artery revealed a 9 mm long concentric 90% lesion extending from the ostium followed by dilatation of the artery (Fig. 1). As the ostial stenosis was followed by dilatation, the diameter of the left renal artery (5 mm) just before its trifurcation was taken as the reference vessel diameter for angioplasty. The left renal artery was cannulated with an 8 F renal guiding catheter (Cordis, Miami, Fl, USA), and the lesion was crossed with a 0.018" wire (Platinum plus, Boston Scientific, Watertown, MA, USA) having a floppy tip. It was then dilated with a 4×10 mm cutting balloon (Boston Scientific, Watertown, MA, USA) at 8 atm pressure. Following dilatation, there was significant residual stenosis, which was addressed by a 17 mm long JoMed stent (JoMed, Germany) mounted on a 5×20 mm Bluemax balloon (Boston Scientific, Watertown, MA, USA) positioned across the ostium of the left renal artery. Following deployment at 12 atm pressure, the stent was well apposed to the vessel wall in its proximal part, while the distal part of the stent in the post-stenotic dilated segment of the artery was lying unapposed and hanging freely in the lumen, thus posing a risk of subacute thrombosis (Fig. 2). To appose this portion...
of the stent to the arterial wall, we needed a balloon 8–10 mm in diameter. However, there was a peculiar problem; the length of the stent in the dilated segment was about 6–7 mm, which required a 7 mm long balloon, with a diameter of 8–10 mm. Unfortunately, no short balloons of length ≤ 10 mm and a diameter of 8–10 mm are presently available. Since the minimal available length of a balloon with a diameter of 8–10 mm is 20 mm, such a balloon, when used to appose the underdeployed distal part of the stent, would have to be kept either in the proximal segment of the stent or distal to the stent in the unstented segment. Whereas a balloon 8–10 mm in diameter could have led to rupture of the vessel in the proximal stented segment (reference vessel diameter 5 mm), such a balloon in the distal unstented segment carried the risk of causing dissection of the vessel. The guiding catheter was thus advanced deep into the renal artery, with its tip just proximal to the dilated part. An 8×20 mm Bluemax balloon was then advanced, so that only half of this balloon was protruding from the tip of the guiding catheter, with its tip just beyond the unapposed stent, with the rest of the balloon remaining in the guiding catheter. During inflation of the balloon, a negative traction was maintained on the balloon to prevent the constrained portion of the balloon from migrating distally during inflation. Inflation of this balloon (Fig. 3) at 10 atm resulted in apposition of the upper margin of the stent while its lower margin was still lying unapposed against the arterial wall. A 10×20 mm Bluemax balloon was then placed similarly with its proximal half within the guiding catheter, and its distal half protruding from the guiding catheter with its tip just distal to the unapposed stent. Inflation of this balloon at 10 atm resulted in apposition of the lower margin of the stent to the arterial wall (Fig. 4). A check angiogram showed a wide open left renal ostium, and a well apposed and nicely flared stent (Fig. 5).

Discussion

An aorto-ostial stenting demands precision, especially at its aortic end. Our patient, who had a post-stenotic dilatation with the reference vessel diameter available only just proximal to the renal artery trifurcation, thus posed the dual challenge of precision at both the proximal and distal ends, which was further compounded by the nonavailability of the real reference vessel diameter. In normal practice, the reference vessel diameter on angiogram is obtained by calculating the mean of the diameters of the vessel just proximal and distal to the lesion in the normal/healthy segment. In our case, proximal to the lesion was the aorta and distal to the lesion was a dilated segment. Hence, none of them could be used for calculating the reference vessel diameter. In this situation, an
intravascular ultrasound (IVUS) would have helped us in estimating the reference vessel diameter. However, at that point of time, due to a technical problem in our IVUS machine, we could not use it for estimating the reference vessel diameter. In this scenario, we used the diameter of the left renal artery segment just before its trifurcation as the reference vessel diameter, which was equal to the reference vessel diameter of the right renal artery.

During the stenting of a lesion having marked post-stenotic dilatation, where the dilated segment was twice the reference vessel diameter, a self-expanding stent was likely to achieve a better apposition to the vessel wall conforming to the contour of the vessel. However, with self-expanding stents, precise ostial positioning is difficult, and also, any attempt towards post-dilatation, if needed, was likely to result in distal migration of the stent. The balloon-expandable stent was thus chosen to address the precision required for ostial positioning. However, the length of the stent chosen was longer than that of the stenosed segment. As 1–2 mm of the stent had to be in the aorta for ostial flaring and the lesion length was about 9 mm, we had to use a stent longer than 11 mm. We decided to use a 17 mm stent, though a stent of 12 mm was also available at that time—since we had to use a longer balloon, a portion of which had to be constrained in the guiding catheter, if only 2 mm of the 20 mm balloon protruded outside, then inflating this balloon would not have caused the distal 2 mm to attain the desired diameter of 10 mm (Fig. 6). We chose a longer stent with 6–7 mm protruding freely, so that around half of the 20 mm long balloon protruded beyond the guiding catheter. When this balloon was inflated, though the proximal part constrained within the guiding catheter did not inflate, the distal 7–8 mm of the 10 mm lying beyond the guiding catheter attained the desired diameter of 10 mm (Fig. 7).

Thus, when dealing with stenotic lesions followed by dilatation of the artery that required distal flaring of the stent with balloons of a larger diameter, our technique can be safely and effectively applied if the guiding catheter can be taken deep into the stented segment.

References
Combined Presence of Coronary Artery Ectasia and Descending Aortic Dissection in Polycystic Kidney Disease Presenting as Acute Coronary Syndrome

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We report the unusual case of a 55-year-old man with a history of hypertension and dyslipidemia who presented with acute coronary syndrome. Examination revealed that he had coronary artery ectasia and descending aortic dissection along with polycystic kidney disease. (Indian Heart J 2003; 55: 646-648)

Key Words: Coronary artery ectasia, Aortic dissection, Acute coronary syndrome

Cardiovascular manifestations of polycystic kidney disease (PKD) include hypertension, mitral valve prolapse (MVP), mild dilatation of the aortic root, abdominal aneurysms, and predisposition to aortic, mitral, and tricuspid valve regurgitation reminiscent of Marfan syndrome.1-4 We report a patient who had a combination of coronary artery ectasia and descending aortic dissection with PKD. The presenting feature was acute coronary syndrome, which, to the best of our knowledge, has not been reported so far.

Case Report

RS, a 55-year-old man was referred to our institute for coronary angiogram. He had been detected to have high blood pressure and dyslipidemia 6 years back on a routine health check-up, and was on regular medication. Apart from smoking 4-5 cigarettes a week, he did not have any other risk factors for coronary artery disease (CAD). Two weeks prior to admission the patient had chest and back pain, which lasted for half-an-hour, and was diagnosed to have non-Q anterior wall myocardial infarction (MI) at a local hospital. He was treated with low-molecular weight heparin (LMWH), beta-blockers, antiplatelet agents, and nitrates. After 5 days of hospitalization, he stabilized and was referred for coronary angiography.

Clinical examination revealed a moderately built male with a pulse rate of 70/min, and blood pressure of 140/90 mmHg. All the peripheral pulses were palpable. Bilateral cystic renal masses were palpable, later confirmed by ultrasonogram as PKD. All hematological and biochemical parameters, including renal function tests, were within normal limits. Echocardiogram showed a normal-sized left ventricle with normal systolic function. There was no regional wall motion abnormality. The aortic root was dilated (4.1 cm), and there was a suspicion of dissection of the descending thoracic aorta. There was no aortic regurgitation.

Ultrasound examination of the abdomen showed an enlarged liver with multiple cysts of varying sizes in both lobes, more in the left lobe, with the largest measuring 2.3 cm. The right kidney measured 14.3 cm, and the left 16.2 cm. Both kidneys showed multiple cysts of varying sizes in the cortex and medulla, the largest measuring 5.7 cm in the lower pole of the left kidney. The abdominal aorta showed evidence of dissection extending up to its bifurcation. Computed tomographic (CT) angiogram of the chest and abdomen showed evidence of dissection of the aorta starting from the arch with involvement of the left subclavian artery, up to the level of the bifurcation of the aorta with bilateral involvement of the common iliac arteries at their origin (Fig. 1). There was no evidence of a thrombus. The major branches of the abdominal aorta, viz. the celiac axis, superior mesenteric artery, and bilateral renal arteries, were seen to arise from the true lumen. The ascending aorta and the arch of the aorta proximal to the origin of the left subclavian artery were normal. The retroperitoneal spaces were clear. There was evidence of polycystic disease of both the kidneys and liver.

The patient underwent coronary angiogram through the right brachial route. The left anterior descending artery was type III, and showed a proximal ectatic segment just after its origin. The left circumflex artery was dominant,
and showed proximal ectasia. The right coronary artery was nondominant and normal. There was no luminal narrowing of any of the coronaries. Aortic arch injection showed a spiral dissection extending from just after the origin of the left subclavian artery up to the right external iliac artery. The benefits and risks of surgical treatment were explained to the patient. He refused surgery, preferring medical treatment. At 5-month follow-up, the patient remained asymptomatic. MRI (magnetic resonance imaging) and MR angiogram of the aorta were done, which revealed no extension of the dissection.

**Discussion**

The advent of molecular medicine has seen a resurgence of interest in pathophysiologic study, and the palliative and definitive treatment of PKD. PKD may be hereditary or acquired. The major inherited types are autosomal dominant (AD), and autosomal recessive (AR). AD PKD is caused by at least 2 (and possibly 3) genes located on separate chromosomes. AR PKD is due to a mutated gene on both copies of the long arm of chromosome 6. AD PKD is a systemic disease; cysts appear with decreasing frequency in the kidneys, liver, pancreas, brain, spleen, ovaries, and testes. The systemic involvement as well as experimental data, which suggested a disordered synthesis of extracellular matrix, led to the hypothesis that AD PKD is a disorder of the connective tissue. Marfan syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta, and pseudoxanthoma elasticum—all disorders of the extracellular matrix—are associated with an increased frequency of cardiac valvular abnormalities. Cardiac valvular disorders, abdominal and inguinal hernias, and aneurysms of the cerebral and coronary arteries, and aorta have also been reported with AD PKD.

Hossack et al. echocardiographically analyzed the prevalence of cardiac abnormalities in AD PKD. They assessed 163 patients with AD PKD, 130 unaffected family members, and 100 control subjects. The prevalence of MVP in AD PKD was 26%. Mitral incompetence (31%), aortic incompetence (8%), and tricuspid valve prolapse (6%) were also noted. This supports the hypothesis that AD PKD involves a defect in the extracellular matrix, and that the cardiac abnormalities are an expression of that defect.

Aortic dissection in AD PKD has been reported in the literature. Additionally, patients with AD PKD have increased aortic fragility. Biagini et al. have reported familial clustering of aortic dissection in PKD. Patients with AD PKD have an increased risk of intracranial aneurysms. Intracranial saccular aneurysms in AD PKD tend to rupture more frequently and earlier than the sporadic variety, with a tendency to cluster in families. Dissecting intracranial aneurysms have also been reported. Our patient had many unusual features. Both aneurysms/ectasia of the coronary arteries and dissection of the aorta are uncommon associations of AD PKD. A Medline search did not reveal any report of the combined presence of coronary artery ectasia and aortic dissection in a patient with AD PKD. Moreover, aortic dissection, which was mistaken as an acute coronary syndrome, was the presenting feature of AD PKD, which has not been reported before.

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Off-Pump Bidirectional Glenn Shunt by Active Decompression of the Superior Vena Cava

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We report 2 cases of infants in whom off-pump bidirectional Glenn shunts were performed. A technique of decompressing the superior vena cava by active manual aspiration has been described. The challenges of maintaining the hemodynamic status, and cerebral protection maneuvers in association with mild hypothermia and a high transcranial pressure have been highlighted. (Indian Heart J 2003; 55: 649-651)

Key Words: Congenital heart disease, Cavopulmonary shunt, Off-pump surgery

Palliative surgery in patients with a functional single ventricular physiology can be performed, avoiding cardiopulmonary bypass (CPB). There are many advantages of this procedure, such as early extubation and decreased need for inotropic support due to improved hemodynamic status.

Case Report

We present our experience with 2 infants with complex cardiac anomalies (Table 1). Both had an unrestricted atrial septal defect (ASD) with no atrioventricular (AV) valve regurgitation. An off-pump surgical procedure—anastomosis of the superior vena cava (SVC) to the right pulmonary artery (RPA)—was chosen, with transient cross-clamping of the SVC. The procedure was performed under general anesthesia. Electrocardiogram (ECG), SaO2, EtCO2, and nasal/skin temperatures were monitored continuously. Blood glucose levels were measured, and arterial blood gases analyzed at regular intervals. Invasive hemodynamic monitoring included cannulation of the radial artery (RA) and left internal jugular vein (IJV). The femoral vein was cannulated with a 5.5 F triple-lumen central venous catheter 13 cm in length for the administration of vasoactive drugs and fluids, as well as monitoring of the inferior vena caval pressure (IVP), which subsequently measured the left atrial pressure (LAP). We presumed that in case of an unrestricted ASD, a properly placed femoral venous line reflected the LAP during and after SVC-pulmonary artery (PA) anastomosis. The surgical procedure involved clamping and division of the SVC near the RA with a wide anastomosis between the SVC and RPA.

After heparinization (1 mg/kg), a temporary shunt was created between the SVC and RA by the insertion of two 6 F cannulae to decompress the SVC. One cannula was placed in the junction of the SVC and innominate vein, the other into the RA, below the site of the proposed clamp. These two cannulae were connected by 2 large-bore blood transfusion tubings, each 100 cm in length. Four 3-way stopcocks were interposed, and four 50 ml syringes were connected, one for each 3-way stopcock (Fig. 1).

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The left IJV pressure was monitored continuously, and reflected the central venous pressure (CVP) proximal to the clamp. The femoral cannula reflected the IVP. Once the SVC–RA junction was clamped, elevation in SVC pressure was prevented by smooth and continuous manual aspiration of blood, which was then returned to the RA. Ample care was taken to prevent air entrainment. In each case, the anastomosis was completed within 10 min.

We stipulated that adequate cerebral perfusion would be maintained if the transcranial pressure (the difference between the arterial systolic pressure and the jugular venous pressure) was above 30 mmHg. Hemodynamic parameters were recorded at 5-min intervals before and after clamping, and every 3 min during clamping. The mean values are displayed in Table 1. High transcranial pressures were maintained throughout at approximately 50 mmHg during SVC clamping. In both the patients, neither volume expanders nor inotropes were required to achieve high transcranial pressures.

Both the infants were cooled to 33°C and 34°C, respectively, at the time of SVC cross-clamping with a cooling blanket, and 17°C ambient temperature. Prior to SVC clamping, an injection of dexamethasone (0.5 mg/kg) was administered. Ice packs were applied to the head of each child, and blood sugar levels were kept strictly below 8 mmol/L. The children were rewarmed to normothermia, and extubated within 4 hours of surgery. After a neurological examination revealed no major or minor deficit, they were discharged from the hospital on postoperative day 7.

### Discussion

Various techniques have been suggested for establishing transient shunts without CPB support to decompress the SVC during an off-pump bidirectional Glenn (BDG) shunt. The best results were achieved with an external shunt that was constructed between the SVC and left pulmonary artery (LPA) using a single, short venous cannula compared to shunts constructed between the SVC and RA. Murthy et al. established a temporary shunt between the SVC and a contralateral branch of the PA with a good outcome. Some authors have even suggested cavopulmonary anastomosis through a thoracotomy incision without CPB support or any type of SVC–RA or SVC–PA shunt.

At the same time, there has been criticism of the BDG shunt being performed without CPB support. Clamping the SVC without decompression exposes the brain to the effects of reduced cerebral perfusion pressure, producing Doppler flow changes and electrocortical alterations. An off-pump procedure does levy stress on the brain, and on the operating surgeon, in terms of time limitation.

Mild-to-moderate hypothermia, along with a reduced cerebral metabolic rate, can attenuate the excitotoxic cascade associated with cerebral hypoperfusion. We hoped that the hypothermia associated with the short SVC clamp time, and a high transcranial pressure, in spite of high filling pressures during the cross-clamp period, would minimize the risk of neurological damage. As for criticism of the incompleteness of anastomosis and time restriction,
an experienced surgeon operated on both the cases presented here, and could establish a wide anastomosis in the shortest time possible. By active aspiration, we were able to enhance the decompression of the SVC. This may not be possible in the case of the external shunts mentioned above,\(^1\)\(^2\) where the flow depends on the pressure gradients across the shunt.

The technique described here should be implemented keeping in mind certain limitations. This procedure does not afford the benefit of oxygenation, and cannot be applied to children with considerable hypoxemia. There is a risk of inadequate SVC drainage, and potential long-term adverse neurocognitive malfunctions. Both infants had no apparent neurologic problems. However, long-term neurocognitive evaluation might be necessary for establishing the safety of the procedure as suggested by Jahangiri et al.\(^2\) and Rodriguez et al.\(^6\) We propose that prior to adopting this technique in clinical practice, its safety should be further established through animal experiments.

In conclusion, we propose a simple technique for performing a cavopulmonary shunt without CPB support. This technique may offer the advantages of avoiding blood transfusions, shortening ventilator dependency, and decreasing the use of inotropic drugs.

**References**


Radiofrequency Ablation of Incessant Orthodromic Tachycardia in a Young Child With a Univentricular Heart

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The incidence of supraventricular tachycardia is high in infants and children with congenital heart disease. We report a case of incessant orthodromic tachycardia in a child with a univentricular heart, which was successfully treated with radiofrequency ablation. (Indian Heart J 2003; 55: 652-654)

Key Words: Supraventricular tachycardia, Congenital heart disease, Catheter ablation

Supraventricular tachycardia (SVT) occurs in approximately 1 in 250 to 1000 children, commonly appearing before the child is 1 month old. The incidence of SVT is higher in patients with congenital heart disease (CHD), especially those with Ebstein’s anomaly, and corrected transposition of the great arteries (c-TGA). The management of patients with CHD may be complicated by serious arrhythmias due to the Wolff-Parkinson-White (WPW) syndrome, or by atrial arrhythmias after cardiac surgery.

During the past decade, a number of new options have evolved for managing SVT, including class IC and III antiarrhythmic agents, and radiofrequency catheter ablation (RFCA). We report the case of an 18-month-old child with CHD who underwent successful RFCA for incessant tachycardia mediated by an accessory pathway.

Case Report

A 10-month-old child was referred to our center from a tertiary pediatric hospital for cardiac work-up in view of cyanosis and effort intolerance since birth. The child was diagnosed to have complex congenital cyanotic heart disease, viz. single ventricle with severe pulmonary stenosis on echocardiography. The child also had a few episodes of SVT, which were terminated with adenosine. There was no evidence of pre-excitation on the surface ECG (Fig. 1a). A surgical opinion was taken, and staged repair was planned.

A bidirectional Glenn shunt was performed as the first stage of univentricular repair. Following surgery, the child had several episodes of rapid SVTs (Fig. 1b), which persisted during the recovery period. These episodes were terminated...
with intravenous adenosine (0.2 mg/kg bolus dose). Subsequently, the child was put on amiodarone 5 mg/kg/day after the initial loading dose, in addition to propranolol. Class IC agents and calcium-channel blockers were not used in view of the structural heart disease. However, despite amiodarone and beta-blockers, the child had recurrent episodes of SVTs. The child had an episode of SVT which was not responding to antiarrhythmic drugs and DC cardioversion. RFCA was planned in view of the incessant tachycardia.

The child was taken up for electrophysiology study (EPS) after taking informed consent from the parents. The procedure was performed under general anesthesia. Two venous accesses (5 F and 6 F) were taken from the femoral route. A 5 F diagnostic quadripolar catheter (USCI, Bard, MA, USA) was placed inside the right ventricle, and a 6 F ablation catheter (Mariner, Medtronic, MN, USA) was placed inside the right atrium.

Atrial and ventricular stimulation protocols were performed, and tachycardia was easily induced with extrastimuli and incremental pacing. An extraventricular premature complex given during the His bundle refractoriness showed advancement of the atrium (Fig. 2), which was suggestive of accessory pathway-mediated tachycardia. Mapping was performed during the tachycardia, which revealed earliest activation in the left lateral region along the mitral annulus. The left atrium was entered through the patent foramen ovale.

The tachycardia was terminated, and mapping performed trans-septally during sinus rhythm revealed a continuous activation signal along the annulus in the left lateral region (Fig. 3), indicating “local” pre-excitation. The RF energy was delivered during ventricular pacing; the pathway was eliminated immediately (within 2 s) after the application of RF energy (VA dissociation). The maximum temperature was 65°C with an impedance of 112 ohms, and the total duration was 60 s. There was no local pre-excitation during sinus rhythm after the ablation. VA dissociation persisted after RF ablation, and no other tachycardia could be induced despite a vigorous stimulation protocol. There was no complication during the procedure. The child was asymptomatic at the time of discharge, and doing well at 6-month follow-up.

**Discussion**

Although RFCA is potentially “curative,” it may not be a reasonable first-line therapy for the younger age group, since 30%-40% of young patients with an accessory atrioventricular pathway may “outgrow” the predisposition to tachycardia with age. Additionally, there is a higher likelihood of complications related to an ablation procedure in very small children. Our patient was subjected to RFCA since he had a breakthrough on amiodarone and beta-blockers.

Catheter ablation of the concealed left free wall accessory pathway is most commonly performed with the placement of an electrode catheter in the coronary sinus. Electrograms recorded from within the coronary sinus provide useful diagnostic and mapping data, and the coronary sinus catheter aids in visually identifying the valve ring. However, studies have shown that good results (ablation) can be achieved without a coronary sinus catheter. In our case, placement of a coronary sinus catheter was not attempted because of the following...
reasons: (i) the possibility of anatomic distortion or anomalous position in view of the associated complex congenital heart disease, and previous surgery; (ii) the inability to advance the catheter from the internal jugular and subclavian veins (bidirectional Glenn performed); (iii) the potential complication of an additional venous line in a small child; and (iv) the possibility of an increase in procedural and fluoroscopic time.

The concealed WPW syndrome is diagnosed by electrophysiologic evidence of a persistent unidirectional (antegrade) block through the accessory pathway. High-resolution ECG recording using the signal averaging technique can detect the low amplitude component preceding the QRS complex in half the patients with concealed WPW syndrome. The possible mechanism of the local potential preceding the QRS complex is a reflection of atypical electrical activation of the localized ventricular muscle adjacent to the accessory pathway-ventricular junction. However, differential diagnosis of far-field activity, and previous radiofrequency current application should be considered with local potential. In our case, a pre-QRS potential (-14 ms) was seen, which possibly corresponded with the accessory pathway-ventricular attachment. In their study, Miyauchi et al. documented pre-QRS local potential in 32% of patients (12/38) at the site of successful ablation.

In patients with congenital heart disease and SVT, catheter ablation during preoperative cardiac catheterization is recommended. Ablation therapy could have been successfully incorporated into the concomitant repair of CHD in this case, but we did not have the facility for intraoperative mapping. In our case, the child was subjected to ablative therapy because of worsening of symptoms on medical management.

References
Spontaneous coronary artery dissection has rarely been reported as a cause of acute coronary syndromes. Although spontaneous coronary artery dissections are most common in young patients without atherosclerosis, they could also occur in elderly patients with underlying atherosclerosis. An unstable atherosclerotic plaque is most likely central to the pathogenesis of dissection in these cases. We report the case of an elderly hypertensive man who presented with unstable angina and impaired left ventricular function. Coronary angiography revealed dissection of the left anterior descending as well as the circumflex arteries. This case supports the occurrence of spontaneous coronary dissection as a cause of acute coronary syndromes in patients with underlying atherosclerosis, which has rarely been reported. (Indian Heart J 2003; 55: 655-657)

**Key Words:** Coronary artery disease, Unstable angina, Coronary dissection

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**Case Report**

A 59-year-old retired man presented with symptoms of dyspnea on exertion of 12 days' duration. The dyspnea appeared on climbing a flight of stairs or walking for about 50 m. It was accompanied by severe diaphoresis, and an unpleasant epigastric discomfort which he described as "acidity," and was completely relieved by resting for a few minutes. He had no precordial pain, dyspnea at rest, orthopnea or paroxysmal nocturnal dyspnea. He had been diagnosed to have hypertension 7 years back, and was on treatment with atenolol (50 mg) daily. He regularly chewed tobacco, and was non-diabetic, a nonsmoker, and a social drinker. He denied any family history of ischemic heart disease. On physical examination, the heart rate was 86/min and regular, and blood pressure was 160/100 mmHg in the supine position. Jugular venous pressures were 5 cm above the sternal angle. The patient had mild pitting edema bilaterally. Cardiovascular examination revealed a laterally displaced left ventricular apex, normal heart sounds and no murmur, gallop or rub. There were fine basal crepitations in both lung fields. The remainder of the physical examination was unremarkable. Electrocardiogram (ECG) revealed normal sinus rhythm, a PR interval of 0.22 s, left ventricular hypertrophy by voltage criteria, left atrial enlargement, and an incomplete left bundle branch block pattern. Cardiac enzymes were not elevated. Chest X-ray showed cardiomegaly with bilateral hilar flaring.

The patient was treated with aspirin, nitrates, diuretics, and antioxidants. Two-dimensional echocardiography revealed global hypokinesia with an estimated left ventricular ejection fraction of 25%, intact septae and normal valves, type I diastolic dysfunction, and a pulmonary arterial systolic pressure of 52 mmHg. Doppler studies revealed grade I aortic and mitral insufficiency. The lipid profile and lipoprotein (a) levels were normal. Serial ECG revealed no changes. Coronary angiography done 5 days later revealed spontaneous dissection of the left anterior descending as well as the left circumflex arteries (Figs 1 and 2). The patient was treated with ticlopidine (250 mg) twice daily and simvastatin (20 mg) daily, and discharged after observation for 5 more days. On follow-up in the outpatient clinic 6 months after his initial presentation, he was free of symptoms, and clinically stable.

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Discussion

Spontaneous coronary artery dissection has been most commonly described in middle-aged, otherwise healthy women in the peripartum period, with no coronary atherosclerosis and no apparent risk factors for atherosclerosis or coronary artery disease. Sudden death has been reported commonly, and nearly 69% of cases are diagnosed in post-mortem studies. Coronary dissection has been associated with pregnancy, the puerperium, and the use of oral contraceptives. This is possibly due to fluctuations in the hormonal milieu, causing weakening of the media of the vessel wall. Systolic hypertension, intense physical activity, and cocaine abuse are other known associations.

Celik et al. proposed that spontaneous coronary artery dissection is not a disease just of middle-aged women but can also be found in older patients with risk factors for atherosclerosis. They described a series of 9 patients with spontaneous coronary artery dissection. The mean age in this group was 55.7 years, and 7 patients were males. All these patients had multiple risk factors for atherosclerosis. None of them had acute myocardial infarction on admission. The authors also proposed that patients with atherosclerotic coronary dissection have a more benign course compared to patients with nonatherosclerotic coronary artery dissection, owing to the development of improved collateral circulation. None of the patients in this study had dissections affecting more than 1 vessel.

Our patient presented with unstable angina, depressed left ventricular function, and spontaneous coronary dissection of 2 vessels. He had risk factors for atherosclerosis, such as hypertension and tobacco consumption. In atherosclerotic arteries, plaques are central to the pathogenesis of dissection. Plaques could bleed or rupture, leading to dissection of the adventitia from the media, and subsequent rupture of the media. They could also cause an intimal tear progressing into the media. Most likely, our patient had a similar pathogenesis. Intravascular ultrasound is an excellent modality that could yield important diagnostic information about the precise pathophysiology involved in such events.

There are no guidelines available on the best treatment of patients with coronary artery dissection. Conservative treatment in the form of aspirin, nitrates, beta-blockers, and antiplatelet agents has been associated with clinical and angiographic resolution. Low-molecular weight heparin has been found to be beneficial. Immunosuppressive therapy has been tried because of the presence of eosinophilic inflammatory infiltrates. Percutaneous coronary interventions have also had favorable outcomes. Cardiac transplantation, and total artificial heart implantation have been attempted as temporary measures in patients with catastrophic
presentations. Our patient was managed medically, and had a stable course on follow-up after 6 months.

In conclusion, to the best of our knowledge, this is the only case report describing spontaneous 2-vessel coronary artery dissection in a patient with risk factors for atherosclerosis. This report supports the proposition that spontaneous coronary artery dissection could occur in patients with atherosclerosis too, and that this group of patients has a better prognosis compared to patients with nonatherosclerotic spontaneous coronary artery dissection. Definitive guidelines for the management of spontaneous coronary artery dissection can evolve only after the etiopathogenetic factors of this rare clinical condition are completely understood.

References
Noncoronary Cardiac Interventions
The 3rd Report of the Non-Coronary Cardiac Interventions Registry of India
The Cardiological Society of India

AK Kar, PC Rath, Nakul Sinha, KK Haridas, A Dasbiswas, Prafulla Kerkar, Rajinder Kumar
On Behalf of the Non-Coronary Cardiac Intervention Registry of India

Data from various centers in India where noncoronary cardiac interventions are actively being performed were collected on behalf of the Subcommittee on Interventional Cardiology, Cardiological Society of India (CSI). The procedures considered were balloon valvuloplasties of stenosed mitral, tricuspid, aortic, and pulmonary valves; device closure of various intracardiac and extracardiac defects, such as patent ductus arteriosus (PDA), atrial septal defect (ASD), and ventricular septal defect (VSD); dilatation of surgical shunts; coil embolization of collaterals, as well as septal ablation. This is a voluntary registry, and a total of 57 centers (Appendix I) furnished their data on the total procedures performed during the year 2002. The data were collected by circulating a proforma.

Figure 1 shows that there has been an increase in the number of all the procedures performed during the year 2002 as compared to 1996, with the addition of a new procedure—septal ablation. The total number of noncoronary interventions performed during 2002 (9,420) increased by 59% as compared to those performed during 1996 (5,925).

Procedures and Participating Units

Percutaneous transvenous mitral commissurotomy: Percutaneous transvenous mitral commissurotomy (PTMC) still forms the bulk of noncoronary cardiac interventions in India. It accounted for 79.4% of all the noncoronary cardiac interventions performed during 2002 as compared to 80.1% during 1996. This reflects the higher prevalence of mitral stenosis in the country as well as the safety and cost-effectiveness of mitral valvotomy by the reusable Inoue balloon technique.

A total of 7,475 PTMC procedures were performed in 57 centers during the year 2002. The details of patient characteristics as well as the main outcome and complications are shown in Tables 1a and 1b. The corresponding data for the year 1996 are also incorporated in the same tables.

Inoue balloon is used most often (70.1%), while the metal commissurotome has not become popular yet, and is used only in 1.84% of cases. The number of older patients, i.e. those 40 years of age or above, has increased in 2002 (22.4%) as compared to 1996 (14%). There was not much change in the proportion of patients with calcification in the years 2002 and 1996 (17.4% v. 19%, respectively), or in the proportion of pregnant patients being taken up for PTMC (3.34% v. 3.9% in the years 2002 and 1996, respectively). The incidence of most complications remained unchanged in 2002 as compared to 1996, with the exception of severe MR, the incidence of which increased considerably in 2002 (5.17%) as compared to 1996 (1.4%). The north and south zones performed the maximum PTMCs in India in 2002 (Fig. 2).

Tricuspid valve balloon dilatation: Tricuspid stenosis often coexists with rheumatic mitral stenosis. Conventional polyethylene balloons as well as Inoue balloons have both produced excellent results for tricuspid valve balloon dilatation (TVBD). Coexisting hypertensive tricuspid regurgitation is not a contraindication for balloon dilatation of tricuspid stenosis. The number of centers doing TVBD in India increased to 16 in 2002 as compared to 8 in 1996, (Table 2); TVBD was performed concomitantly with mitral dilatation in all the cases in 2002 as was done in 1996.

Aortic valve balloon dilatation: The number of centers doing aortic valve balloon dilatation (AVBD) increased to 33 in 2002 from 23 in 1996. As in 1996, most of the patients in 2002 were young males with moderate symptoms (NYHA class II or III). The success rate was 96.5%, with the average gradient falling from 98.4 mmHg to 30.1 mmHg. The complication rate in 2002 was lower (0.9%) compared to that in 1996 (5.3% including death in 2%). There was no mortality in 2002 (Table 3).

Pulmonary valve balloon dilatation: Pulmonary valve balloon dilatation (PVBD) has gained wide acceptance, with the number of centers performing the procedure increasing to 50 in 2002 as compared to only 24 in 1996. Most centers continue to employ the single- or double-balloon technique. The national registry data are shown in Table 4.
of the patients were young with a slight female preponderance. Coil occlusion remained the most widely used technique (64% in 2002), as it is cost-effective. Rashkind devices, however, are being increasingly used compared to 1996. The registry data are presented in Table 5.

Table 1a. Patient characteristics and PTMC procedures performed during 1996 and 2002

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1996</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of centers</td>
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<td>57</td>
</tr>
<tr>
<td>Number of patients</td>
<td>4748</td>
<td>7475</td>
</tr>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38%</td>
<td>41%</td>
</tr>
<tr>
<td>Female</td>
<td>62%</td>
<td>59%</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10</td>
<td>0.6%</td>
<td>-</td>
</tr>
<tr>
<td>11–20</td>
<td>17.5%</td>
<td>-</td>
</tr>
<tr>
<td>21–40</td>
<td>59.5%</td>
<td>-</td>
</tr>
<tr>
<td>&gt;40</td>
<td>22.4%</td>
<td>-</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3%</td>
<td>5.7%</td>
</tr>
<tr>
<td>II</td>
<td>36%</td>
<td>46.8%</td>
</tr>
<tr>
<td>III</td>
<td>44%</td>
<td>40.8%</td>
</tr>
<tr>
<td>IV</td>
<td>17%</td>
<td>6.7%</td>
</tr>
<tr>
<td>BMV Procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inoue</td>
<td>-</td>
<td>70.1%</td>
</tr>
<tr>
<td>Accura</td>
<td>-</td>
<td>21.0%</td>
</tr>
<tr>
<td>Joseph</td>
<td>-</td>
<td>7.1%</td>
</tr>
<tr>
<td>Metallic commissurotome</td>
<td>-</td>
<td>1.84%</td>
</tr>
<tr>
<td>PTMC during pregnancy</td>
<td>3.9%</td>
<td>3.34%</td>
</tr>
</tbody>
</table>

PTMC: percutaneous transvenous mitral commissurotomy; BMV: balloon mitral valvotomy; NYHA: New York Heart Association

Device closure of patent ductus arteriosus: Device closure of patent ductus arteriosus (PDA) is now widely practised, with the number of centers performing it going up to 41 in 2002 as compared to 16 in 1996. The majority of the patients were young with a slight female preponderance. Coil occlusion remained the most widely used technique (64% in 2002), as it is cost-effective. Rashkind devices, however, are being increasingly used compared to 1996. The registry data are presented in Table 5.

Table 1b. Valve morphology and complications of PTMC procedures performed in 1996 and 2002

<table>
<thead>
<tr>
<th>Parameters</th>
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</thead>
<tbody>
<tr>
<td>Valve morphology</td>
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</tr>
<tr>
<td>Calcific (echocardiographic score: &gt;8)</td>
<td>19%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Severe subvalvular adhesion</td>
<td>24%</td>
<td>15.6%</td>
</tr>
<tr>
<td>Post-CMC</td>
<td>13%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Post-OMC</td>
<td>13%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Post-BMV</td>
<td>1.1%</td>
<td>-</td>
</tr>
<tr>
<td>Hemodynamic parameters</td>
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<td></td>
</tr>
<tr>
<td>MV area (cm²) (predilatation/postdilatation)</td>
<td>0.8/1.9</td>
<td>0.8/1.8</td>
</tr>
<tr>
<td>End-diastolic gradient (mmHg)</td>
<td>19/4.5</td>
<td>26.2/6.9</td>
</tr>
<tr>
<td>Success rate (%)</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>Complications of PTMC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suboptimal results</td>
<td>5.6%</td>
<td>2.72%</td>
</tr>
<tr>
<td>Technical failure</td>
<td>0.7%</td>
<td>2.17%</td>
</tr>
<tr>
<td>Severe MR</td>
<td>1.4%</td>
<td>5.17%</td>
</tr>
<tr>
<td>Need for MVR</td>
<td>0.9%</td>
<td>0.8%</td>
</tr>
<tr>
<td>ASD with L–R shunt</td>
<td>0.3%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>0.8%</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

PTMC: percutaneous transvenous mitral commissurotomy; ASD: atrial septal defect; CMC: closed mitral commissurotomy; OMC: open mitral commissurotomy; BMV: balloon mitral valvotomy; MR: mitral regurgitation; MVR: mitral valve repair

Fig. 1. A comparison of the number of procedures performed during 1996 and 2002. PTMC: percutaneous transvenous mitral commissurotomy; PVBD: pulmonary valve balloon dilatation; AVBD: aortic valve balloon dilatation; ASD: atrial septal defect; VSD: ventricular septal defect; PDA: patent ductus arteriosus; CO-AO: coarctation of the aorta; TVBD: tricuspid valve balloon dilatation; PTSMA: percutaneous trans-septal myocardial ablation

Fig. 2. Zonal distribution of percutaneous transvenous mitral commissurotomy procedures performed in 2002.
Table 2. Details of tricuspid valve balloon dilatation undertaken in the years 1996 and 2002

<table>
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<tr>
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</tr>
<tr>
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<td>62</td>
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<tr>
<td>Sex</td>
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<td>Male</td>
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<td>27.7%</td>
</tr>
<tr>
<td>Female</td>
<td>72%</td>
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<tr>
<td>Age in years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
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<tr>
<td>10-20</td>
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</tr>
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<td>21-40</td>
<td>-</td>
<td>83.3%</td>
</tr>
<tr>
<td>&gt;40</td>
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<tr>
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<td>I</td>
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<td>0%</td>
</tr>
<tr>
<td>II</td>
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<td>III</td>
<td>64%</td>
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<td>IV</td>
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<td>Associated MVBD</td>
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<tr>
<td>Success rate</td>
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<td>100%</td>
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<tr>
<td>End-diastolic gradient (mmHg)</td>
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<tr>
<td>Predilatation</td>
<td>10</td>
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<td>Postdilatation</td>
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<tr>
<td>Complications</td>
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<td>Nil</td>
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MVBD: mitral valve balloon dilatation

Table 3. Details of aortic valve balloon dilatation undertaken in the years 1996 and 2002

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<tr>
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<td>75%</td>
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<tr>
<td>Female</td>
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<tr>
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<td>&lt;1</td>
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<td>1-10</td>
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<td>11-20</td>
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<tr>
<td>III</td>
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</tr>
<tr>
<td>IV</td>
<td>14%</td>
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<tr>
<td>Calcified valves</td>
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<td>Average procedure time (min)</td>
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<td>Peak systolic gradient (mmHg)</td>
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<tr>
<td>Death</td>
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<td>0%</td>
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</table>

Table 4. Details of pulmonary valve balloon dilatation performed during the years 1996 and 2002

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<td>Female</td>
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<tr>
<td>II</td>
<td>42%</td>
<td>56.4%</td>
</tr>
<tr>
<td>III</td>
<td>27%</td>
<td>11.6%</td>
</tr>
<tr>
<td>IV</td>
<td>7%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Average procedure time (min)</td>
<td>50</td>
<td>41.3</td>
</tr>
<tr>
<td>Peak systolic gradient (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predilatation</td>
<td>110</td>
<td>93.3</td>
</tr>
<tr>
<td>Postdilatation</td>
<td>26</td>
<td>28.4</td>
</tr>
<tr>
<td>Success rate</td>
<td>96%</td>
<td>98.8%</td>
</tr>
<tr>
<td>Complications</td>
<td>2.7%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

Atrial septal defect closure: There is a considerable increase in the number of centers practising ASD closure—from only 5 in 1996 to as many as 34 in 2002. The success rate was 99.1% in 2002 compared to 83% in 1996. The complication rate in 2002 fell to 4.3% compared to 8% in
Table 6. Details of atrial septal defect device closure undertaken in the year 1996 and 2002

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1996</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of centers</td>
<td>5</td>
<td>34</td>
</tr>
<tr>
<td>Number of patients</td>
<td>14</td>
<td>403</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>50%</td>
<td>44.8%</td>
</tr>
<tr>
<td>Female</td>
<td>50%</td>
<td>55.2%</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>-</td>
<td>0.7%</td>
</tr>
<tr>
<td>1–10</td>
<td>-</td>
<td>37.9%</td>
</tr>
<tr>
<td>11–20</td>
<td>-</td>
<td>32.2%</td>
</tr>
<tr>
<td>21–40</td>
<td>-</td>
<td>34.1%</td>
</tr>
<tr>
<td>41–60</td>
<td>-</td>
<td>4.5%</td>
</tr>
<tr>
<td>&gt;61</td>
<td>-</td>
<td>0.6%</td>
</tr>
<tr>
<td>Average procedure time (min)</td>
<td>70</td>
<td>49.2</td>
</tr>
<tr>
<td>Success rate</td>
<td>83%</td>
<td>99.1%</td>
</tr>
<tr>
<td>Complications</td>
<td>8%</td>
<td>4.3%</td>
</tr>
<tr>
<td>Mean size (mm)</td>
<td></td>
<td>24.9</td>
</tr>
<tr>
<td>Commonest device: Amplatzer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Details of dilatation of coarctation of the aorta undertaken in the years 1996 and 2002

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1996</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of centers</td>
<td>19</td>
<td>36</td>
</tr>
<tr>
<td>Number of patients</td>
<td>82</td>
<td>277</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>71%</td>
<td>69%</td>
</tr>
<tr>
<td>Female</td>
<td>29%</td>
<td>31%</td>
</tr>
<tr>
<td>Age in years (percentage)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>74%</td>
<td>70%</td>
</tr>
<tr>
<td>20–30</td>
<td>19%</td>
<td>21%</td>
</tr>
<tr>
<td>30–40</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>&gt;40</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>NYHA class (percentage)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>II</td>
<td>72%</td>
<td>70%</td>
</tr>
<tr>
<td>III</td>
<td>12%</td>
<td>16%</td>
</tr>
<tr>
<td>IV</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Average procedure time (min)</td>
<td>42</td>
<td>40</td>
</tr>
<tr>
<td>Success rate</td>
<td>97%</td>
<td>98%</td>
</tr>
<tr>
<td>Complications</td>
<td>0%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Hypertension controlled on follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With drugs</td>
<td>44%</td>
<td>40%</td>
</tr>
<tr>
<td>Without drugs</td>
<td>56%</td>
<td>60%</td>
</tr>
</tbody>
</table>

1996. The mean size of the defect was 24.9 mm. The commonest device used is the Amplatzer device (Table 6).

Dilatation of coarctation of the aorta: The number of centers performing balloon dilatation of the coarctation of aorta increased from 19 in 1996 to 36 in 2002. Most of the patients were young males. The mean procedure time in 2002 was similar to that in 1996. The procedure had a high success rate, and resulted in good control of hypertension (Table 7).

Table 8. Details of miscellaneous procedures undertaken in the years 1996 and 2002

<table>
<thead>
<tr>
<th>Procedure</th>
<th>1996</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon atrial septostomy</td>
<td></td>
<td>41</td>
</tr>
<tr>
<td>Major aortopulmonary collateral embolization</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>Ventricular septal defect closure (Sideris/Rashkind)</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>Blalock-Taussig shunt dilatation</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Ruptured sinus of Valsalva aneurysm closure</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Percutaneous trans-septal myocardial ablation</td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>

Table 9. Details of percutaneous trans-septal myocardial ablation undertaken in 2002

<table>
<thead>
<tr>
<th>Parameters</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total centers:</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Total no. of patients:</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Male: female:</td>
<td>9:6</td>
<td></td>
</tr>
<tr>
<td>Mean age (years):</td>
<td>34.6</td>
<td></td>
</tr>
<tr>
<td>Mean procedure time (min):</td>
<td>36.1</td>
<td></td>
</tr>
<tr>
<td>Average duration of hospital stay (days):</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Success rate:</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>Complications:</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

Miscellaneous procedures

Balloon atrial septostomy: Balloon atrial septostomy (BAS) is being performed at many Indian centers, and the results are very encouraging in terms of its life-saving rate, especially as a bridge to surgery in many congenital heart diseases. The total number of BAS performed per year increased to 66 in 2002 compared to 41 in 1996 (Table 8).

Ventricular septal defect closure: VSD closure with the Sideris or Rashkind device is being performed at many centers in India with encouraging results. The total number of VSD closures performed increased to 35 in 2002 compared to 11 in 1996 (Table 8).

Coil embolization of collaterals/shunts: Coil embolization of major aortopulmonary collaterals in cyanotic congenital heart disease is required in selected patients, in whom the postoperative period could be stormy due to uncontrolled hemoptysis. The number of coil embolizations was the same in 2002 as in 1996 (Table 8).

Percutaneous trans-septal myocardial ablation: Percutaneous trans-septal myocardial ablation (PTSMA) is a new procedure for treating patients with hypertrophic obstructive cardiomyopathy with a significant gradient, unresponsive to medical treatment. In 2002, a total of 15
patients underwent PTSMA in 4 centers. The mean procedure time was 36.1 min with a success rate of 98%. One death was reported (Table 9).

Others: Data furnished by many centers reveal that Blalock-Taussig shunt dilatation, and ruptured sinus of Valsalva aneurysm closure with a device were also successfully performed.

Limitations of the data: These data are not free from the limitations inherent to any pooled data. There was no response from some important high-output centers. The documentation of patient characteristics and hemodynamic data, and patient follow-up were often inadequate. From 1996 till date, no data have been published from the Non-Coronary Cardiac Intervention Registry of India. Thus, it is difficult to comment on the pace of growth of various procedures.

Future plan: Our future aim is to set up a computerized database, which can easily be accessed by individual centers. They can enter their data on the website, which can then be analyzed by the members of the Registry. The members of the Registry can also interact via the Internet with individual centers, so that data collection and recording become impeccable. The indications, contraindications, and success criteria of different procedures also need to be standardized.

Acknowledgments

We take this opportunity to sincerely thank the members of the executive committee of the CSI for entrusting us with the responsibility of collecting these data. The compilation of these data was made possible by the contribution of individual centers, and the active cooperation of zonal members. We will be failing in our duty if we do not acknowledge the contributions made by Manoranjan Mondal and Debabrata Roy, consultant cardiologists, who have compiled the entire data, and helped us to give it the present shape. We also thank PC Rath, Convenor, Interventional Council, CSI, for his active help, and day-to-day guidance regarding the collection of data.

Appendix 1 (Participating Centers)

I. NORTH ZONE
1. GB Pant Hospital, New Delhi
2. All India Institute of Medical Sciences (AIIMS), New Delhi
3. Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGI), Lucknow
4. Escorts Heart Institute and Research Centre, New Delhi
5. Batra Cardiac Care Centre, New Delhi
6. Upgraded King George's Medical College, Lucknow
7. Saroj Hospital and Heart Institute, New Delhi
8. Regency Hospital, Kanpur
9. Indraprastha Apollo Hospitals, New Delhi

II. CENTRAL ZONE
1. Apollo Hospital, Hyderabad
2. Nizam's Institute of Medical Sciences, Hyderabad
3. Medical Centres, Bhopal and Indore
4. Care Hospital, Hyderabad
5. SCB Medical College, Orissa
6. Osmania Medical College and Hospital, Hyderabad
7. Mahavir CV Centre, Hyderabad
8. Apollo Hospital, Visakhapatnam
9. Image Hospital, Hyderabad

III. WEST ZONE
1. KEM Hospital, Mumbai
2. Bombay Hospital, Mumbai
3. Spandon Heart Institute and Ekvita Heart Institute, Nagpur
4. Krishna Heart Institute, Ahmedabad
5. UN Mehta Institute of Cardiology, Ahmedabad
6. Dr Balabhai N Hospital, Mumbai
7. Military Hospital, Pune
8. Holy Family Heart Institute, Mumbai
9. Ruby Hall Clinic, Pune
10. Nanavati Hospital, Mumbai
11. Sir JJ Group of Hospitals and Grant Medical College, Mumbai

IV. EAST ZONE
1. GNRC Heart Institute, Dispur, Assam
2. Rabindranath Tagore International Institute of Cardiac Sciences (RTICS), Kolkata
3. BM Birla Heart Research Centre, Kolkata
4. Suraksha Hospital, Kolkata
5. SSKM Hospital, Kolkata

V. SOUTH ZONE
1. Trichur Heart Hospital, Kerala
2. Fathima Hospital, Calicut, Kerala
3. Madras Medical Mission, Chennai
4. Vijaya Heart Foundation, Chennai
5. Sri Ramchandra Medical College, Chennai
6. Sri Satyasai Institute of Higher Medical Sciences, Bangalore
7. G Kapuswamy Naidu Memorial Hospital, Coimbatore
8. Medical College, Calicut
9. St John's Medical College Hospital, Bangalore
10. Trinity Hospital Heart Foundation, Bangalore
11. KLE Society Hospital and MRC, Bangalore
12. KG Hospital, Coimbatore
13. Wockhardt Hospital and Heart Institute, Bangalore
14. Sri Jayadeva Institute of Cardiology, Bangalore
15. Amrita Institute of Medical Sciences, Cochin
16. Omega Hospitals, Mangalore
17. Christian Medical College (CMC), Vellore
18. AJ Hospital and Research Centre, Mangalore
19. Narayana Hrudayalaya, Bangalore
20. Perambur Railway Hospital, Chennai
21. Vikram Heart Centre and Hospital, Mysore
Anomalous Right Coronary Artery From the Left Sinus of Valsalva Diagnosed by Multislice Computed Tomography

Gurpreet S. Gulati, Nitish Naik, Sanjiv Sharma, AK Bisoi
Departments of Cardiovascular Radiology, Cardiology, and Cardiothoracic Surgery, Cardiothoracic Centre, All India Institute of Medical Sciences, New Delhi

A 45-year-old man presented with a history of gradually progressive exertional angina of 5 months’ duration. He also had an episode of unstable angina requiring hospitalization. Electrocardiogram (ECG) showed T wave inversion in precordial leads V1-3. Echocardiography showed mild anteroseptal hypokinesia, and a left ventricular ejection fraction of 45%. A coronary angiogram demonstrated a thrombus in the mid left anterior...

Correspondence: Dr Sanjiv Sharma, Department of Cardiovascular Radiology, Cardiothoracic Centre, All India Institute of Medical Sciences, New Delhi 110029. e-mail: meetisv@vsnl.com
descending (LAD) artery with evidence of myocardial bridging immediately distal to this segment. The left main and circumflex arteries were normal. Repeated attempts to cannulate the right coronary artery (RCA) were not successful. A semiselective injection into the left coronary sinus with a left Amplatz catheter demonstrated an anomalous RCA arising from the left coronary sinus (Fig. 1). Although no significant obstructive disease was seen, multiple views to confirm its course could not be taken as the catheter kept getting unhooked repeatedly. Transesophageal echocardiography suggested an interarterial course of the vessel. A stress thallium study also demonstrated ischemia in the inferior wall, in addition to ischemia in the LAD territory.

To confirm the anomalous origin and course of the RCA, a multislice computed tomography (MSCT) of the heart was performed on a 16-slice machine (Somatom Sensation 16, Siemens, Germany). A volume data set was acquired (12 x 0.75 mm collimation, gantry rotation time 420 ms, table feed 2.8 mm per rotation, and tube voltage 120 kV), covering the distance from the carina to the diaphragm, with retrospective ECG gating. Nonionic contrast (iohexol; 100 ml) was injected at 4.5 ml/s. Images were reconstructed with a slice thickness of 1.0 mm in 0.5 mm increments, using an ECG-gated half-scan reconstruction algorithm to obtain an image acquisition window of 210 ms. Multiple datasets were reconstructed at varying points along the R–R interval, and the dataset with the fewest motion artifacts was used for further evaluation of the coronary arteries. Axial images (Fig. 2) showed the RCA originating from the left coronary sinus, anterior to the origin of the left coronary artery, and then taking an acute bend to course between the aorta and pulmonary trunk. Three-dimensional displays generated by the volume-rendering technique (Fig. 3) clearly depicted the origin of the RCA and its interarterial course. Based on these observations, the patient underwent surgery. The RCA was found to be compressed between the aorta and pulmonary artery. It was dissected out, and the ostium was reimplanted into the ascending aorta. The patient also received an internal mammary graft to the LAD. The postoperative course was uneventful.

Coronary artery anomalies affect approximately 1% of the general population.1 In adults referred for coronary angiography, the incidence of these anomalies is 0.6%–0.2%.2,3 An anomalous origin of the right coronary artery from the left aortic sinus was first described in 1948 by White and Edwards.4 There are 3 subtypes based on the anatomic course of the artery. The aberrant vessel may course posterior to the aorta (retroaortic), between the ascending aorta and pulmonary trunk (interarterial), or anterior to the pulmonary trunk. The interarterial subtype has been reported to be associated with angina pectoris, myocardial infarction, or sudden death in the absence of atherosclerosis.5 Several theories have been proposed to explain the “malignant” characteristics of this anomaly: (i) compression of the RCA between the aorta and pulmonary trunk, which may occur during exercise-induced dilatation of the great arteries in response to increased cardiac output, coupled with increased coronary blood flow to the myocardium; (ii) a sharp turn or bend at the origin; or (iii) an ostial stenosis of the artery.

Coronary anomalies are usually diagnosed during coronary angiography. However, X-ray angiography is limited by its inability to provide information regarding the spatial orientation of the anomalous artery with regard to the surrounding cardiovascular structures.6,7 Besides, the anomalous vessel may be erroneously overlooked or assumed to be occluded if not selectively catheterized.7 Transesophageal echocardiography has been utilized to detect coronary anomalies; however, the operator may miss the diagnosis.1 Electron beam computed tomography (EBCT) has been reported to be very useful in imaging coronary anomalies.2 It has the advantage of nonmechanical generation of the X-ray beam, thus achieving a high temporal resolution of 50–100 ms.8 The disadvantages of EBCT include the fact that the tube current cannot be changed, which means that the radiation dose can be reduced only by decreasing the acquisition time, which results in a pronounced image noise.8 MSCT is superior to EBCT in providing a higher signal-to-noiseratio, and a higher spatial resolution (0.6 x 0.6 x 1.0 mm3 in MSCT v. 0.8 x 0.8 x 2.5 mm3 in EBCT).9 The temporal resolution of MSCT, although inferior to EBCT, can be improved by retrospective ECG gating. Magnetic resonance imaging (MRI) angiography has also been shown to be accurate in the identification of the origin and course of aberrant coronary arteries.10 Its limitations include a significantly long acquisition time, and certain patient characteristics, such as claustrophobia, and the presence of metallic implants, which are contraindications for the techniqu11. MSCT has the potential to accurately visualize the coronary arteries, as has been illustrated in various recent reports.9,12 However, only anecdotal reports showing its utility in detecting anomalous coronary arteries have been published.13,14 In the present case, the MSCT images clearly demonstrated the anomalous origin with a sharp bend, and the interarterial course of the RCA. These findings were confirmed at surgery. This report emphasizes the potential use of the MSCT technique in identifying anomalous coronary arteries.

References
1. Angelini P, Velasco JA, Flamm S. Coronary anomalies: incidence,
External Reference Point for Estimating Jugular Venous Pressure: Sternal Angle or Clavicle?

Central venous pressure (CVP) is commonly estimated by measuring the height of the jugular venous pressure (JVP) relative to the sternal angle (SA).

Utility of calculating CVP in routine practice: The criteria given by Sir Thomas Lewis in 1930, that CVP equals the vertical distance between a point 5 cm below the SA and the top of the neck veins is still widely used. However, recent studies on the measurement of CVP have found a discrepancy between the clinician’s estimate of CVP from the physical diagnosis, and direct supine measurement with a catheter. The reason for this is that the vertical distance between the patient’s zero point (centre of the right atrium [RA]), and the conventional reference point (SA) is not constant. Hence, extrapolation of JVP to CVP by adding a constant figure of 5 cm introduces an error, and does not serve any useful clinical purpose. Other authorities also feel that the clinician should avoid taking decisions about the degree of elevation of CVP because it is imprecise, and often difficult to reproduce. Once we find that the JVP is raised, its exact measurement is needed only for evaluation of the results of therapy in the given patient during follow-up. Repeated examination of the jugular veins is enough to provide this information, and extrapolation to the CVP provides no extra advantage. The first priority for a clinician during physical examination should be to determine whether the JVP is raised or not. This is vital for the triage of a critically ill patient.

Limitation of the SA as an external reference point: There is no justification for retaining the SA as an external reference point for measuring JVP at the bedside for several reasons: (i) the SA does not have a constant relationship with the center of the RA. Median SA–RA distance with the patient lying supine is 5.4 cm, and at 30°, 45°, and 60° elevation it is 8 cm, 9.7 cm, and 9.8 cm, respectively. Smoking, age, and anteroposterior diameter of the chest are also known to independently affect this figure; (ii) this relationship is further distorted in patients with chest deformities, a displaced mediastinum, and selective enlargement of certain cardiac chambers; (iii) anatomical sexual differences in the thoracic cage and sternum introduce another potential variable. The female thorax is shorter and wider than that of the male, and the sternal body is less than twice the length of the manubrium in females, while it is more than twice the length of the manubrium in males.

Utility of the clavicle as an external reference point: The clavicle is a more convenient and more correctly reproducible bedside external reference point for the clinical evaluation of JVP than the SA for several reasons: (i) the clavicle is more easy to locate, even in obese individuals with thick chests; (ii) the clavicle lies in proximity to the pulsating veins, and is in the same coronal plane as the jugular veins as compared to the SA; (iii) the upper limit of normal pressure in the upright position is at the level of the suprasternal notch. Thus, normal JVP is not visible above the clavicle in the sitting position. Therefore, one can easily decide whether the JVP is normal or raised; (iv) the vertical height of the pulsating column above the clavicle can easily be measured with an ordinary centimeter scale, and does not require a carpenter level or tongue blade or two scales, which are usually not carried by clinicians. Further, the results obtained by using the carpenter level or two scales could be fallacious if the ruler is not held exactly vertical, and if the straight edge is not exactly horizontal. Moreover, if the JVP is normal or only slightly raised, the clavicle often comes in the way of the straight edge, making the measurement somewhat difficult; (v) the patient need not be tilted to a precise degree, which is usually not possible without a protractor, and such protractors are available only in well furnished hospitals, that too for indoor patients. Examining a patient in the sitting position does not require a special table, and can be performed anywhere. The results are exactly reproducible for follow-up even by different examiners.

It is therefore suggested that to evaluate the JVP, the patient should be clinically examined in the sitting position and the clavicle be used as a reference point.

References


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JLN Medical College, Ajmer
Prevalence of Chlamydia pneumoniae IgG Antibodies in Patients With Coronary Artery Disease: A Report From an Indian Population

Several studies have shown a positive association between Chlamydia pneumoniae (C. pneumoniae) seropositivity and coronary artery disease (CAD).\(^1,2\) Demonstration of C. pneumoniae in atheroma from various arteries\(^3\) adds strength to the theory that the organism is a potential agent for initiating or modulating plaque development and progression. Preliminary clinical trials using antibiotics in patients with CAD suggest that this mode of management may be useful.\(^4,6\) There is a paucity of information on the prevalence of C. pneumoniae antibodies in developing countries, and the association of infections with CAD.

Patients undergoing coronary angiography for the evaluation of chest pain in the Department of Cardiology, Christian Medical College and Hospital, Vellore, during the period April–September 1999 were included in the study. A lesion was considered significant if the degree of stenosis was more than 50% in two views. Patients with myocardial infarction within the past 1 month, evidence of CAD with poor left ventricular ejection fraction (<25%) or patients who had undergone coronary artery bypass graft surgery during the past 4 weeks were excluded from the study. Sera were tested at 1/64 dilution by the microimmunofluorescent antibody (MIF) test (MRL Diagnostics, California, USA). Sera from apparently healthy blood donors were included as controls. The investigators reading the MIF test were blinded to the status of the subjects.

A total of 152 patients and 60 apparently healthy blood donors were included in the study. Three patients were excluded from further analysis since the MIF test was invalid. Of the remaining 149 patients, 122 (82%) were positive for C. pneumoniae antibodies. Only 27 of the 60 blood donors (45%) were similarly positive (p<0.001; OR 5.57 [2.7–11.3]). Only 99 of the 149 patients showed antibodies. Only 99 of the 149 patients showed antibodies. Of these 99 patients, antibodies to C. pneumoniae were seen in 82 (83%). Antibodies were also seen in 40 of the 50 patients (80%) without significant stenosis. There was a significant difference in antibody prevalence between blood donors and those with stenosis (p<0.001).

Among blood donors, only 5 of the 16 individuals (31%) in the younger age group had C. pneumoniae antibodies compared to 16 of the 19 individuals (84%) with angina in the similar age group. This difference was statistically significant (p<0.01). In patients above 40 years of age, the prevalence of C. pneumoniae antibodies increased with age.

Univariate and multivariate analyses of risk factors, such as age, sex, smoking, hypertension, family history of myocardial infarction, abnormal lipids and diabetes mellitus, were performed using the SPSS statistical package. The prevalence of C. pneumoniae antibodies was significantly associated with hypertension (p<0.05).

The prevalence of C. pneumoniae antibodies in titers of 64 or above is 45% in a normal Indian adult population. However, antibodies were significantly more common in those clinically suspected to have angina, and in those with coronary artery stenosis as compared to apparently healthy blood donors. The association was more marked in the younger age groups.

These preliminary data show that there is an association between antibodies to C. pneumoniae and CAD in the Indian population. The prevalence of C. pneumoniae IgG antibodies was significantly higher in young Indians with coronary stenosis compared to healthy individuals. Further studies on various infectious agents are required to draw more definite conclusions on the role of infections in CAD in developing countries.

Acknowledgment

We thank MRL Diagnostics, Cypress, California USA for providing a free kit for the study.

References

1. Gupta S. Chronic infection, Chlamydia and coronary heart disease—the story evolves. Indian Cardiology Rounds 2002; 6: 2

Vivekanandan Perumal, Elizabeth Mathai, Jacob Jose, Sandeep Gupta

Christian Medical College and Hospital, Vellore, India, and Whipps Cross and St Bartholomew’s University Hospitals, London, UK
Prudent Diet and Preventive Nutrition

I read with great interest the exhaustive article on the subject of prudent diet by Enas et al. The US Department of Agriculture (USDA) database release 16 says that sunflower oil contains 60% or more of linoleic acid, and one tablespoon of sunflower oil contains 3 g of MUFA and 9 g of PUFA. This contradicts the facts stated in Table 3.

Reference

1. Enas EA, Senthilkumar A, Chennikkara H, Bjurlin MA. Prudent diet and preventive nutrition from pediatrics to geriatrics: current knowledge and practical recommendations. Indian Heart J 2003; 55: 310-338

IM Ahuja
Consultant Cardiologist
4, Sahni Sujan Park
Pune

Reply

We agree with Dr Ahuja that naturally occurring safflower and sunflower oils are high in polyunsaturated fatty acids (PUFA) and low in monounsaturated fatty acids (MUFA). The predominant PUFA and MUFA in these oils are linoleic and oleic acids, respectively. However, both safflower and sunflower oils can be blended with oils containing high amounts of oleic acid to yield high MUFA varieties. This is done to take advantage of the marked beneficial effects of MUFA. For example, substitution of the high oleic acid content of sunflower oil for butter was associated with a significant 10%-20% reduction in total cholesterol, low-density lipoprotein, triglycerides, and apolipoprotein B-100, without any reduction in the high-density lipoprotein levels. This was achieved in a relatively short span of 5 weeks without any decrease in the total fat intake.

There are 4 types of sunflower oil represented in the US Department of Agriculture (USDA) database, namely, high oleic (>70%), linoleic (>60%), linoleic (<60%), and hydrogenated varieties. Three of these are represented in Table 3 of the article. The high oleic (>-70%) variety has the highest MUFA content, even higher than olive oil. The linoleic (>-60%) variety has more PUFA than MUFA. The linoleic (<-60%) variety has equal amounts of MUFA and PUFA.

In short, both the high PUFA- and MUFA-containing varieties of safflower and sunflower oils are available. To the best of my knowledge, high MUFA (high oleic) varieties are not available in India.

References


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Summary

The VALIANT trial was a multicenter, double-blind, randomized, parallel-group study that assessed the efficacy and safety of long-term treatment with valsartan, captopril, and their combination in high-risk patients after myocardial infarction (MI). It is the largest trial conducted in post-MI patients till date, enrolling 14,703 patients in 24 countries from 931 centers. The inclusion criteria were post-acute MI (AMI) patients with LV dysfunction, with documented ejection fraction (EF) <35%, signs and symptoms of acute heart failure, or both, presenting within 10 days of the index event. Patients with hypotension, serum creatinine >2.5 mg%, or prior intolerance to either drug were excluded. Patients were randomized within 12 hours–10 days after AMI to one of the 3 regimens, with the dose being up-titrated over 3 months: (i) valsartan 20 mg b.d. daily, up-titrated to 160 mg b.d. daily (n=4090); (ii) captopril 6.25 mg t.i.d., titrated to captopril 50 mg t.i.d. daily (n=4090); and (iii) valsartan 20 mg b.d. daily titrated to 80 mg b.d. + captopril 6.25 mg t.i.d. daily, up-titrated to 50 mg t.i.d. (n=4885). At the time of randomization, 70.4% of patients were on beta-blockers, 91.3% on aspirin, and 24.8% on other antithrombotic agents. After a median follow-up of 24.7 months, the all-cause mortality—the primary end-point of the trial—was 19.9% in the valsartan group, 19.5% in the captopril group, and 19.3% in the combination group. Since valsartan could not be considered superior or inferior to captopril alone, the prespecified analysis of noninferiority was carried out, and showed valsartan to be noninferior to captopril both intention-to-treat, and per-protocol analyses (valsartan was estimated to have 99.6% of the effect of captopril, p<0.002 for both). Secondary end-points of cardiovascular death, MI, heart failure, and hospitalization for heart failure were also similar in the 3 treatment groups, with the p-value for noninferiority being <0.001 for all. Furthermore, the relative efficacy of the treatment in all the subgroups of patients (including those on beta-blockers) was also similar. About 55% of patients in each monotherapy group reached target medication, but fewer patients in the combination arm did so. Discontinuation due to adverse events (primarily hypotension and renal dysfunction) was lowest in the valsartan group (5.8%). Medication was discontinued in 7.7% of the captopril group (mainly due to cough, rash, taste disturbance). However, discontinuation was commonest in the combination arm (9%), mostly due to hypotension and renal causes. Thus, valsartan and captopril were found to be equally effective, while their combination was found to increase the rate of adverse events without improving survival.

Comments

Patients with AMI complicated by heart failure and/or LV dysfunction are at a high risk for subsequent death, and major nonfatal cardiovascular events. At least 3 major trials have consistently shown the long-term benefits of angiotensin-converting enzyme inhibition (ACEI). The SAVE trial with captopril, the AIRE trial with ramipril, and the TRACE trial with trandolapril have all shown a mortality reduction of at least 20%. A meta-analysis of these 3 trials revealed that ACEI was associated with a 26% risk reduction for death, 27% risk reduction for re-admission for heart failure, 20% risk reduction for re-infarction, and 25% risk reduction for death/MI or re-admission for heart failure. Till date, 4 trials have compared angiotensin receptor blockers (ARBs) with ACEI head-to-head in different subsets of patients. In the OPTIMAAL trial, losartan 50 mg o.d. was compared with captopril 50 mg t.i.d. in post-MI patients with heart failure. The trial favored the use of captopril but had several limitations. The number of patients was small (a little more than 5000), and the dose of losartan used was low (50 mg daily rather than an optimal dose of 200 mg). The VALIANT trial, being a larger study (14,808 vs. 5477 patients), has a higher statistical power, and enrolled even sicker patients. The second trial in post-MI patients, ELITE II, was a comprehensive study, carried out on 3182 patients. This trial showed no difference in outcome between losartan and captopril. The CHARM-Added and Val-HeFT studies also showed that ARBs were equivalent to ACEIs, but in addition showed benefits due to their combination, unlike the VALIANT trial. There may be several reasons for the difference. First, they were trials of chronic heart failure (unlike VALIANT, which evaluated post-MI acute heart failure), with a greater role played by neurohormones. Second, the regimen of therapy was different in the CHARM-Added and Val-HeFT studies; ARBs were added to a pre-existing therapy with ACEIs, whereas in the VALIANT trial, they were used simultaneously. Furthermore in these 2 trials, a suboptimal dose of ARB was used vis-a-vis the VALIANT trial, in which a full prespecified dose was used. The CHARM-Added and Val-HeFT studies also showed that ARBs were equivalent to ACEIs, but in addition showed benefits due to their combination, unlike the VALIANT trial. There may be several reasons for the difference. First, they were trials of chronic heart failure (unlike VALIANT, which evaluated post-MI acute heart failure), with a greater role played by neurohormones. Second, the regimen of therapy was different in the CHARM-Added and Val-HeFT studies; ARBs were added to a pre-existing therapy with ACEIs, whereas in the VALIANT trial, they were used simultaneously. Furthermore in these 2 trials, a suboptimal dose of ARB was used vis-a-vis the VALIANT trial, in which a full prespecified dose was used. Finally, the use of valsartan may not be equitable with the use of other ARBs. Many of these differences will probably be resolved by the results of other ongoing trials with ARBs, in various subsets of patients, of which the ONTARGET trial compares telmisartan with ramipril in the kind of patients who were the subjects for the HOPE trial.
Cardiovascular Risk Factors in Childhood and Carotid Artery Intima-Media Thickness in Adulthood: The Cardiovascular Risk in Young Finns Study

Summary
The Cardiovascular Risk in Young Finns Study is a population-based, prospective, cohort study conducted in Finland among white adults, who were first examined in childhood and adolescence, and then 21 years later. It is increasingly being recognized that exposure to cardiovascular risk factors during childhood and adolescence may be associated with the development of atherosclerosis that is silent initially, before the occurrence of clinical events such as myocardial infarction (MI) or stroke later in life. However, there is only limited direct evidence of this relationship. Studies using ultrasound imaging have demonstrated atherosclerotic wall thickening in the arteries of children and adults with risk factors. The intima-media thickness (IMT) of the common carotid artery measured by ultrasound imaging has been shown to be a reliable marker of preclinical atherosclerosis. IMT can be related to the severity and extent of coronary artery disease, and can predict the likelihood of cardiovascular events in population groups. In the Young Finns Study, common carotid IMT was measured in a large cohort of adult men and women in whom the risk factor data were available from their childhood and adolescence. The first cross-sectional survey was conducted in Finnish children at 5 centers in 1980, with 3596 participants. Follow-up studies were conducted 3 years apart in 1983 and 1986. The common carotid IMT was subsequently measured 21 years later in 2229 adults between September 2001 and January 2002. The left common carotid artery was studied with the posterior wall in focus. Both current risk factors (lipid profile, blood pressure [BP], body-mass index [BMI], smoking habits) as well as risk factors measured in childhood were analyzed. In the multivariate analysis for current risk variables, systolic BP, BMI, and smoking were significantly associated with IMT. The effect of low-density lipoprotein cholesterol (LDL-c) was, however, not found to be significant. In a model adjusted for age and sex, the analysis of childhood risk variables with the current IMT showed that childhood LDL-c level, systolic BP, BMI, and smoking were significantly associated with adult IMT. When adjusted for current risk variables, the effects of childhood LDL-c levels and systolic BP remained independently associated with carotid IMT. However, the effects of childhood smoking status and BMI were not significant, when the current status and BMI were adjusted. In both men and women, carotid IMT was significantly related with multiple risk factors measured at 12–18 years of age (p<0.001). The risk factors measured at 3–9 years of age showed only a weak association with carotid IMT in men (p=0.02) but not in women (p=0.63). The Young Finns Study found that the risk factors measured during adolescence were significantly associated with common carotid artery IMT measured in adulthood. The association remained strong and significant even when the adulthood risk factors were taken into account. The onset of adolescence may indicate a point in development after which childhood exposure to risk factors begins to be associated with increased risk for atherosclerosis in adulthood.

Comments
In the 1970s, researchers from Muscatine, Iowa, Bogalusa, Louisiana, Finland, and elsewhere began to survey children and adolescents for physiologic variables that had been established as risk factors for coronary heart disease (CHD) in adults. In members of the Bogalusa cohort who died of accidents, homicides or suicides, CHD risk factors measured years earlier were found to be associated with atherosclerotic lesions. In 1985, the Pathological Determinants of Atherosclerosis in Young (POAY) Study Group assessed risk factors during autopsy in 3000 persons who died of external causes. They analyzed postmortem blood samples, and atherosclerosis was evaluated in the coronary arteries and aortas. There was a high prevalence of advanced atherosclerotic lesions in adolescents and young adults, with recognized coronary risk factors. The Muscatine study showed that the risk variables measured in children were associated with coronary artery calcifications in young adults. An association between childhood risk variables and adult carotid IMT was also found. The data from the Young Finns study indicate that childhood risk variables are strongly associated with adult IMT, which is an accepted noninvasive method to assess the extent of atherosclerosis. Importantly this association was found to be independent of current risk variables. Another prospective study by Hodin et al. has suggested that every 0.1 mm increase in carotid IMT may increase the subsequent risk of coronary events by approximately 30%. The Atheroscleroma Risk in Communities (ARIC) study suggested that the risk of subsequent CHD may increase faster at lower levels of mean IMT (<1 mm). In the Young Finns Study, IMT was measured in the common carotid artery. The prognostic value of IMT measurements for predicting future cardiovascular events may increase when data from all the 3 segments (common carotid artery/bifurcation/internal carotid artery) are considered. Despite minor differences, the trend of results from the various studies is clear. Risk factors begin to matter during adolescence—the age range during which the fatty streaks start being converted into raised lesions. The age at which the measurement of cholesterol levels should be performed may now be reconsidered. The Adult Treatment Panel III recommends 20 years as the age for screening for dyslipidemia. The screening for cardiovascular risk factors in adolescence, and noninvasive techniques of measuring the extent of atherosclerosis may select a population at high risk. There is little doubt regarding the safety of lifestyle modification for young individuals; these include maintaining recommended serum lipoprotein levels, avoiding smoking, and maintaining a healthy body weight, but the safety of pharmacologic therapy at a young age has not been established. The available evidence indicates that it is time to move forward to start preventing CHD at an earlier age. It is essential to promote a culture where young persons are encouraged to maintain safe and healthy lifestyles.
Summary

The ALKK study a multicenter, open, randomized, German study is the first one conducted to systematically evaluate the long-term benefits of percutaneous coronary intervention (PCI) on an infarct-related artery (IRA) in stable survivors of acute myocardial infarction (AMI), with mild/no symptoms or residual ischemia. The inclusion criteria were (i) stable patients, 8-42 days after AMI with single-vessel disease in the IRA (a significant stenosis or total occlusion); (ii) mild or no angina pectoris (CCS class I or II); and (iii) in whom PCI appeared technically feasible. Patients with severe angina (CCS class III and IV), significant stenosis in another artery, coronary artery bypass graft (CABG) as the infarct vessel, and those with an indication for CABG (left main coronary artery disease, left ventricular aneurysm, or marked valvular lesions) were excluded from the study. The primary end-point of the study was the combined end-point of survival free from reinfarction, ischemia-driven PCI/ CABG, or rehospitalization for severe angina at 1 year. Over a period of 3 years (August 1994 to September 1997), 300 patients were randomized to either the PCI or medical groups. The mean time interval between the index MI and randomization was 18 days (range 14-28 days). PCI was successful in 86% of patients with a success rate of 92.5% in patients with stenosed, and 72.7% in patients with an occluded IRA. However, stents were implanted in only 17% of the cases. At 1 year, the primary end-point (without revascularization) occurred in 6.7% of patients in the PCI group versus 14.5% in the medically treated group (p=0.04). Furthermore, the use of nitrates was also significantly lower in the PCI group (38% vs. 67%, p=0.001). More importantly, the hard end-point of death (although not statistically significant) was also lower in the PCI group (0.7% vs. 3.3%, p=0.21). On long-term follow-up (mean 56 months, range 0-72 months) mortality was significantly lower in the PCI group (4% vs. 11%, p=0.02). There was a higher rate of revascularization procedures in the conservative arm (24% vs.17%, p=0.17). More patients were free from symptoms in the angioplasty arm (77% vs. 61%), and fewer patients were receiving nitrates (36% vs. 56%, p=0.006). An interesting finding seen on subgroup analysis was that the benefit of PCI was not apparent in patients with an occluded IRA (~30% of the patients). However, there was no effect of thrombolysis on study end-points.

Comments

Primary percutaneous transluminal coronary angioplasty (PTCA) has become the treatment of choice for patients with AMI. The value of post-acute intervention is still controversial. Patients with recurrent angina, inducible ischemia in a large territory, or severe multivessel disease with left ventricular dysfunction after MI are likely to benefit from invasive revascularization strategies, but stable patients with no/mild angina, and those with single-vessel disease are a very low-risk subset, and generally not considered appropriate for revascularization strategy. In the TIMI-II trial, patients with AMI receiving tissue plasminogen activator (tPA) were randomized to early invasive therapy (18-48 hours) versus conservative strategy. The combined end-point of death or reinfarction within 42 days was higher in the invasive arm (10.9% vs. 9.7%, p=NS), and no significant benefit was seen in the rest or exercise EF at the end of 6 weeks. The SWIFT trial, enrolling 800 patients, also could not demonstrate any benefit with invasive therapy, the mortality being 5.8% vs. 5%, and reinfarction rates 15.1% vs. 12.9% at the end of 1 year. However, these studies had several limitations. First, these studies were relatively old and, since then, both interventional and medical therapy have evolved a great deal. Second and more importantly, none of these studies have really evaluated the long-term effect of revascularization procedures. The issue of subacute angioplasty after AMI is well addressed in the current study, which has demonstrated a mortality benefit at 1 year that becomes even more pronounced at about 5 years’ follow-up. Similarly, event-free survival is also significantly better after 5 years in the interventional arm. Several mechanisms may be operative for these long-term benefits. An open vessel may be beneficial in case of further progression, and as a conduit to provide collaterals to other diseased vessels. Second, an open artery has been shown to have a favorable effect on ventricular remodeling post-MI. Finally, it may improve electrical stability by altering any arrhythmogenic substrate. The DANAMI trial with 1008 patients, has shown that while short-term outcomes were poorer, at longer-term follow-up (2.4 years), there was lesser mortality (3.6% vs. 4.4%, p=NS), lower incidence of recurrent MI (5.6% vs. 10.5%, p<0.005), and fewer admissions for unstable angina (17.9% vs. 29.5%, p<0.001) in the PCI arm. The present study is also not without several limitations. First, it is a small study. Second, since it is an open study, there is always a chance of operator bias. Finally, there was underuse of stents (17% only).
Calendar of Conferences

February 13–15, 2004, 9th Annual Conference of Indian Academy of Echocardiography and International Conference on Advances in Cardiology, Bhubaneswar, India
Contact: Dr SN Routray & Dr M Behera
Department of Cardiology
SCB Medical College
Cuttack 753007, India
e-mail: drsroutray@yahoo.co.in

March 19–21, 2004, Annual Conference of Indian Society of Electrocardiology, New Delhi, India
Contact: Dr R Juneja, Organizing Secretary
Department of Cardiology
All India Institute of Medical Sciences
New Delhi, India
Fax: 91 11 2658 8663
e-mail: isecon2004@rediffmail.com

February 18–20, 2005, International Summit on CAD and Cardiovascular Interventions, Mumbai, India
Contact: Dr Satyavan Sharma
Bombay Hospital and MRC
Room No. 104, 1st Floor MRC
12, New Marine Lines
Mumbai 400 020, Maharashtra, India
Tel: 91 22 2205 4532
e-mail: drsharma@bom3.vsnl.net.in and
drsatyavan@vsnl.net

April 6–9, 2004, 4th Congress of the Asian Pacific Society of Atherosclerosis, Bali, Indonesia
Contact: Dr Slamet Suyono
Lagoon Tower, Level B-1
Jakarta 10270, Indonesia
Fax: 62 21 5705798
e-mail: pactoltd@idola.net.in

May 7–10, 2004, 77th Scientific Session, American Heart Association (AHA), New Orleans, Louisiana, USA
Contact: American Heart Association
7320 Greenville Avenue
Dallas TX 75231, USA
Tel: 1 214 373 6300
Fax: 1 214 373 3406

November 26–28, 2004, 3rd International Congress on Cardiovascular Disease, Taipei, Taiwan
Contact: Dr CE Chiang
Taiwan Society of Cardiology
7F, Min-Chuan West Road
Taipei 104, Taiwan
Fax: 886 2 25976180
e-mail: tsoc@tsoc.org.tw

November 26–28, 2004, 3rd International Congress on Cardiovascular Disease, Taipei, Taiwan
Contact: Dr CE Chiang
Taiwan Society of Cardiology
7F, Min-Chuan West Road
Taipei 104, Taiwan
Fax: 886 2 25976180
e-mail: tsoc@tsoc.org.tw

May 21–25, 2005, 6th International Conference on Preventive Cardiology, Iguassu, Brazil
Contact: Dr Mario Maranhao
Congress Internacionales
PO Box 83005,
1080, Amsterdam, The Netherlands
Fax: 31 20 6758236
e-mail: prcardio2005@congressOsint.com