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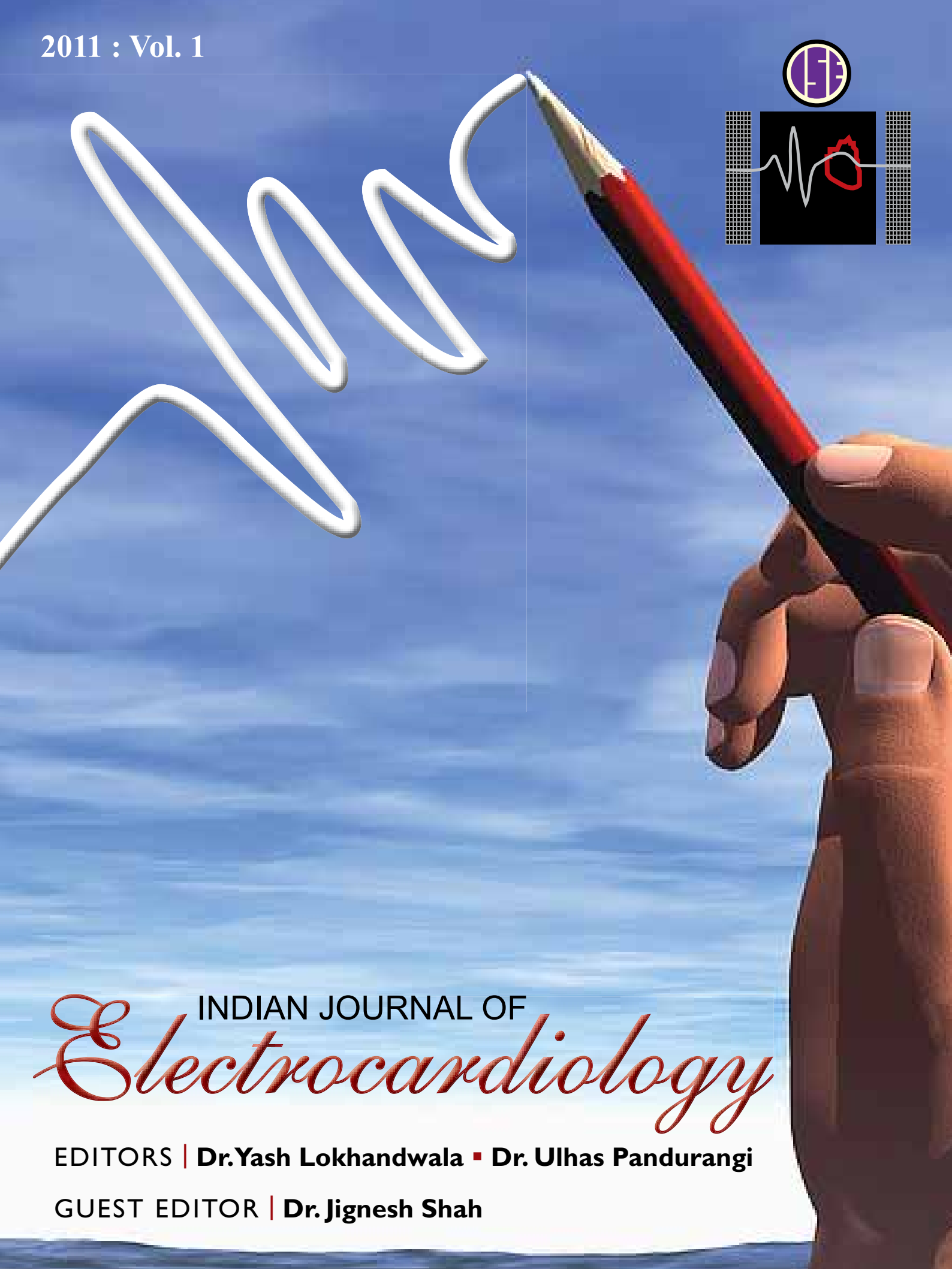

INDIAN JOURNAL OF Electrocardiology

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Editorial

Dear Friends,

As we release this issue of the IJE, we are at the threshold of ISE Kochi. The scientific committee has prepared an exciting academic program. I am sure their teachings and your interest will once again create the right mix for a very good learning experience.

The current issue of the IJE carries a wide range of interesting articles. Dr. Raju and Dr. Ranjan Thakur have written a comprehensive review on cardiac arrest management. The article provides an overview of cardiac arrest epidemiology, the principles behind each link in the "Chain of Survival," an overview of the core components of CPR while emphasizing the recent changes in the American Heart Association (AHA) guidelines. They have reviewed critical role of hypothermia in the management of cardiac arrest in this article. We have noticed a recent increase in interest among cardiologists in implanting RV lead at sites other than the RV apex. Dr. Darrat et al. have reviewed the ill effects of RV apical pacing and the current data on alternate site pacing in a fairly comprehensive review article. Dr. Kabde and colleagues have presented a unique case of wide complex tachycardia with rare 2:1 block. Dr. Bindra has presenting interesting ECGs demonstrating AF in a patient with multiple accessory pathways.

Dr. Thomas and colleague have presented an excellent review of the role of MRI in making the diagnosis of ARVD. Considering the increased availability of cardiac MRI in India, we need to keep up to date regarding its utility. Hence this article has been re-printed with permission from the web-based Indian Pacing and Electrophysiology journal. As always, the ECG Quiz is one of the highlights of the IJE.

Happy reading and we hope to have more contributions from you for future issues.

We acknowledge the untiring efforts of Dr Gopi Krishna Panicker in assistance with this issue.

Jignesh Shah
Guest Editor

Yash Lokhandwala
Editor

Ulhas Pandurangi
Editor

From Vice President's Desk

Dear Members,

It is our great pleasure in bringing out the latest issue of Indian Journal of Electrocardiology on the eve of ISECON 2011 – The Annual Conference of Indian Society of Electrocardiology.

We organized ISECON-2010 at Mumbai from 19th to 21st February 2010. I am sure every one enjoyed the great scientific bonanza.

Indian Society of Electrocardiology also organized many programs during the year :

a. "ECG Learning Course" for postgraduate students at Mumbai on 1st and 2nd May 2010, at New Delhi on 22nd and 23rd May 2010, at Chennai on 10th July and 11th July 2010, at Kolkata on 4th and 5th September 2010, at Bangalore on 25th and 26th September 2010 and at Navi Mumbai on 5th and 6th March 2011. About 80-100 delegates participated in each course and successful candidates were awarded the Certificate of Competence for ECG reading

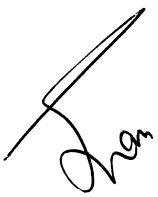
Patna Arrhythmia Course 2010 (PAC-2010) was organized by Dr Ajay Sinha and his team and needs congratulations for organizing the event.

A CME was organized under the banner of ISE at Amritsar on 18th December 2010 by Dr Rajinder Singh and his team – a very successful program.

A CME on Recent Guidelines on the Management of AF and Heart Failure at Mumbai on 16th January 2011.

My sincere thanks to Dr Yash Lokhandwala, Dr Ulhas Pandurangi, Dr Jignesh Shah, Dr Gopi Panicker and the Editorial Team for bringing out the ISE Journal – 2011, 1st Volume.

Long Live Indian Society of Electrocardiology



Dr. S.B. Gupta
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Alternate Site Pacing

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Introduction

Cardiac pacing was utilized clinically for the first time in 1959.[1] Over the past 5 decades, the technology of cardiac pacing has seen major changes from surgically placed epicardial leads and large generator size for single chamber devices to transvenous endocardial leads and small battery size for complex physiologically tuned dual chamber pacemaker generators. This has made implant procedures easier and has led to expansion in the indications for pacemaker implant. This continuing expansion of indications along with the aging population will lead to increased utilization of artificial cardiac pacing in the years to come.

Over the years it has been a standard practice to position the ventricular lead in the apex of the right ventricle (RV) because of the ease of implantation and the stability of passive-fixation leads in the apical trabeculae. In recent years, the optimal ventricular pacing site has been abundantly debated. Several early studies have demonstrated that right ventricular apical (RVA) pacing has adverse effects on cardiac function.[2-6] During RVA pacing, the conduction of the electrical wave front propagates through the myocardium, rather than through the His-Purkinje conduction system resulting in abnormal electrical and mechanical activation pattern of the ventricles.[7] In 1925, several years before the use of the first transvenous pacer, Carl Wiggers showed that RVA pacing was associated with a diminished dP/dt and an asynchronous left ventricular (LV) contraction pattern.[8] RVA pacing results in iatrogenic intraventricular conduction delay and a left bundle branch block (LBBB) pattern. Such LBBB morphology results in abnormal ventricular activation sequence resulting in regional wall motion abnormalities and LV systolic dysfunction. Moreover, myocardial perfusion is decreased at site of ventricular stimulation leading to regional wall motion abnormalities.[9] These functional abnormalities during RVA pacing were associated with impairment of LV diastolic function and progressive deterioration of left ventricular ejection fraction (LVEF) over time.[9] Furthermore, myofibrils at a ventricular pacing site exhibited reduced systolic shortening and external work. Such detrimental effect was also more pronounced with RVA pacing than with RV basal pacing.[10]

Clinically, RVA pacing is known to higher incidence of LV dysfunction, mitral regurgitation, atrial fibrillation and congestive heart failure.[4,11-15] In the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial, implantable cardioverter defibrillator (ICD) patients with already depressed cardiac function were randomized to DDDR pacing at a relatively short AV interval versus ventricular backup pacing at 40/min; increased RVA pacing observed in the former group was associated with a significantly higher incidence of new or worsened CHF.[11] Further analysis demonstrated that the percent right ventricular pacing was predictive of the outcome of death or CHF hospitalization in this trial.[11] Likewise, the Mode Selection Trial (MOST) randomized 2,010 sinus node dysfunction patients and a preserved LV ejection fraction to DDDR mode vs VVIR mode and found a reduction in signs and symptoms of CHF in DDDR mode patients.[12] However, when Sweeney et al.[15] subsequently examined a subset of 1,339 MOST study patients with normal baseline QRS duration, they found that a higher cumulative percent RVA *paced* rhythm was strongly predictive of CHF hospitalization regardless of whether these patients were programmed to DDDR or VVIR pacing. Thambo et al showed that after a mean of 10-year cardiac pacing, 23 young patients, in comparison with 30 matched healthy control individuals, had significantly higher values of intraventricular dyssynchrony, LV remodeling, dilatation, and hypertrophy, with lower cardiac output and exercise performance.[16] In addition, histopathologic studies have shown long term RVA pacing leads to cellular and intracellular alterations, cellular disarray, heterogenous extracellular matrix remodeling as well as degenerative fibrosis.[17,18]

The multiple significant adverse effects (Table 1) of RVA pacing have fueled interests in seeking alternative sites for ventricular pacing that may mimic the normal physiological pacing system. Wiggers[8] has proposed that the shorter the distance for the impulse to travel to reach the Purkinje system, the more effective the contraction. Therefore it may be expected that pacing in or near the His-Purkinje system will lead to a more physiological ventricular activation with a corresponding reduction in QRS duration and a more favorable hemodynamic response. Multiple sites were considered including RVOT, RV septal (RVS), free wall, His-bundle and bifocal RV pacing.[19] We will review literature regarding the effects of RVOT, RVS and His-bundle pacing sites compared to RVA pacing.

RVOT pacing

Most of the studies that compared the two most commonly reported nonapical pacing sites, RVOT and RVS, include small patient population, investigated short term outcomes and acute hemodynamic changes rather than long term clinical outcomes. A meta-analysis conducted by De Cock et al.[20] included studies from 1984 to 2000 comparing these RVOT and RVA pacing sites. A total of 9 studies having a study population of 6 to 89

Table 1 : Adverse Effects of RVA pacing

Iatrogenically accentuated intraventricular conduction delay
Left ventricular electrical and mechanical dyssynchrony
Abnormalities in myocardial histopathology
Left ventricular remodeling
Systolic and diastolic left ventricular dysfunction
Congestive heart failure
Myocardial perfusion defects and regional wall motion abnormalities
Functional mitral regurgitation
Increased risk of atrial fibrillation

patients for a total of 217 patients were assessed in the meta-analysis. Varied parameters of hemodynamics such as LV EF by echocardiography, radionuclide measurements, dP/dT or cardiac output by thermodilution methods were used by the various studies. Overall, the meta-analysis noted a positive impact of RVOT pacing on acute hemodynamics compared to RVA pacing. Of the 9 studies, 6 noted no acute hemodynamic benefit of RVOT pacing over RVA pacing. The largest study included in the meta-analysis by Giudici et al.[21] involving 89 patients was primarily responsible for the positive results and removal of this study from the meta-analysis left the study equivocal on the benefits of RVOT pacing. But, the study by Giudici et al. did demonstrate that cardiac output improved at the time of implant from 6.6 ± 2.4 L/min at the apex to 7.8 ± 2.9 L/min at the outflow tract. Patients with preexisting LV dysfunction had a greater improvement in their hemodynamics. However, in direct contradiction to this study is a more recent ROVA trial[22] (not a part of the meta-analysis). This randomized study assessed quality of life after 3 months of apical or outflow tract pacing among 103 patients with heart failure, chronic atrial fibrillation, and LVEF <40%. QRS duration was shorter during RVOT (167 +/- 45 ms) than RVA pacing (180 +/- 58 ms, P < 0.0001). At 6 months, the RVOT group had higher (P = 0.01) QOL scores than the RVA group. After 9 months of follow-up, LVEF was higher (P = 0.04) in those assigned to RVA rather than RVOT pacing and there were no significant differences in QOL scores between RVOT and RVA groups. Comparing RVOT to RVA pacing within the same patient, mental health subscale scores were better (P = 0.03) during RVOT pacing. Overall, throughout the study duration there were no other significant differences between RVA and RVOT in QOL scores, NYHA class, distance walked in 6 minutes, LV ejection fraction, or mitral regurgitation.

More recent studies comparing RVOT to RVA pacing have been similarly equivocal and disappointing. In a study among 96 consecutive patients with high or third-degree atrial ventricular block, the LV dysynchrony was more severe in the RVA pacing group of 48 patients compared to that in the RVOT pacing group of 48 patients (P < 0.05), while diastolic synchrony was similar in the 2 groups. However, there were no significant differences with respect to the mean LVEF, LV end-diastolic and systolic volume in the 2 groups at 12 months of follow-up.[23] Similarly, in the single largest study of 122 consecutive patients (70 men, 69 +/-11 years), randomized to RVA (66 patients) or RVOT (56 patients) pacing, mortality was assessed after the 10-year follow-up period. During the long-term follow-up, 31 patients from the RVA group died versus 24 patients in the RVOT group (hazard ratio (HR), 0.96; 95% confidence interval (CI), 0.57-1.65; P=0.89). There were 10 cardiovascular deaths in the RVA and 12 in the RVOT group (HR, 1.04; 95%CI, 0.45-2.41; P=0.93). There were no differences in the all-cause or cardiovascular mortality between the pacing sites after adjustment for various co-morbidities.[24] Even the most basic assumption about improved synchrony by RVOT pacing has recently been challenged. In an echocardiographic study among 36 patients with sick sinus syndrome (SSS) and intact AV conduction, RVOT pacing decreased the LVEF (51.4 +/- 6.2% with RVOT pacing vs 55.9 +/- 7.1% without RVOT pacing, P = .001), worsened intraventricular dyssynchrony of the LV while increasing the systolic and diastolic dyssynchrony as assessed by tissue doppler echocardiography.[25]

Interestingly, though clinical data on the benefits of RVOT pacing over RVA pacing is sparse, larger studies involving 460 patients over a longer duration of 9 years have been published regarding the feasibility and safety of RVOT pacing over RVA pacing.[26] The stability of the leads, pacing thresholds and impedance has been well documented in the literature.[27-29]

Thus based on these studies, it is feasible and safe to pace the RVOT. However, it is unclear as to whether RVOT provides any acute hemodynamic benefits over RVA pacing in any subgroup of patients. Furthermore, it is not clear if whatever hemodynamic benefit is derived translates into clinical improvement in the short, mid or long term. Also, widely discussed in the literature is the fact that there is no standard definition of RVOT pacing and optimal RVOT site to achieve whatever marginal benefit is likely from this pacing site.

RV septal pacing

The short term studies (Table 2) that investigated RVS pacing have included a relatively fewer patients although they have shown favorable outcomes. One of these studies, conducted by Victor et al, compared the effects of RVS to RVA pacing in 28 patients. Patients were randomly assigned to RVS or RVA pacing for 3 months and then crossed over for 3 more months. At 3 months, among patients with baseline LVEF < or = 45%, LVEF was 42 +/- 5% after RVS pacing versus 37 +/- 4% after RVA pacing (P < 0.001). However, there was no significant difference in mean NYHA class, exercise duration or peak VO2 between both groups.[30]

There are two long term studies among patients with structurally normal hearts with preserved LVEF that showed favorable outcomes with RVS pacing. Takemoto et al[31] assessed LV synchrony and LVEF measured by echocardiography among 55

patients (40 assigned to RVS pacing and 15 to RVA pacing). . The study demonstrated that RVS pacing guided by paced QRS morphology preserves LV function by minimizing pacing-induced electrical and mechanical LV dyssynchrony after a mean follow up duration of 4 years. Critical decrease in LVEF was seen in 45.5% of patient with full RV A pacing, but only in 7.4% with full RVS pacing. Tse et al[32] conducted a randomized trial of 24 patients with atrial fibrillation and assessed clinical outcomes. At 6 months, 6 minute hall walk and LVEF were comparable in patients with RVA and RVS pacing (P > 0.05). At 24 months, patients with RVA pacing had significant decreases in LVEF and 6 minute hall walk (P < 0.05), whereas RVS pacing preserved LVEF and improved 6 minute hall walk (P < 0.05).

RVS pacing also had a positive outcome with regard to LVEF in two mid-term studies. Thirty six patients were randomly assigned to RVS or RVA pacing.[33] RVS pacing improved LV systolic performance (from 52% +/- 3.3% to 59% +/-3.0%, P<0.05) and preserved LV volume compared to RVA pacing. However, these changes were not the result of improved LV dysynchrony or interventricular dysynchrony. The improvement in LV systolic function among those with RVS pacing did not translate into improved functional class. A study by Muto et t al.[34] included 273 patients with atrial fibrillation and LVEF <30% undergoing RV septal or RVA pacing. The results showed an improved LVEF in the RVS group (from 28 +/- 2% to 33 +/- 1%, P = 0.0125) and there was also a statistically significant improvement in NYHA class (form 2.9 +/- 0.4 to 1.7 +/- 0.3, P = 0.01) after 18 months. No change was observed in the RVA group with respect to in LVEF and NYHA class. Both studies confirm the favorable influence of RV septal pacing on LVEF and the later study has shown an improved functional status.

Two randomized studies have shown that RVS pacing is not superior to RVA pacing. A recent study[35] randomly assigned 93 patients with no structural heart disease to RVS pacing, RVA pacing and a control group (< 10% ventricular pacing). The RVA pacing group had more interventricular dyssynchrony at 12 months compared to RVS pacing. The maximal delay to peak systolic velocity between any of the 6 left ventricular basal segments (measure of LV synchrony) was similar in the RVS group (35.5 +/- 20.6 ms) and control group (36.5 +/- 17.8 ms). Meanwhile, although LVEF was lower in patients with RVA pacing there was no statistically significant difference (p=0.14) among the groups.. Another study by Kypta et al,[36] among 98 patients showed that there was no statistically significant difference in clinical outcomes (LVEF, exercise tolerance and pro-BNP levels) between RV mid to high septal pacing and RVA pacing after 18 months.

Conversely, Ng et al,[37] studied 55 patients who underwent RVS pacing. Median pacing durations were 436 days for RVS pacing and 2,398 days for RVA pacing. Mean QRS duration for RVA pacing was longest, followed by septal pacing and control (p <0.001). LV mass index, end-systolic volume index, and LVEF were more impaired in RVS than in RVA pacing (all p values <0.05). Septal pacing was associated with more impaired circumferential strain (p <0.001) and worse LV dyssynchrony than apical pacing and control. Although RV septal pacing in this study was performed by a single experienced operator under electrocardiographic and fluoroscopic guidance it consisted of a heterogenous group of difference pacing sites, ranging from the RV free wall to the midseptal segment and even in the free wall of the true outflow tract. There was a modest agreement on anatomic location of the leads between echocardiography, EKG and Chest X ray.

The feasibility and safety of RVS pacing has been established. Burri et al[38] studied the thresholds of RV septal and RV pacing in 362 patients over 24 months. The results showed similar sensing thresholds between both groups. Risk of lead dislodgement was low in the RV septal group. The investigators recommended using multiple fluoroscopic views to ensure obtaining the desired pacing site and to avoid the anterior free wall. Another study in 371 patients demonstrated that RV Septal lead pacing and sensing thresholds remained stable over a period of 3 months although lead impedance decreased.[39] In addition, a recent review article demonstrated that RV septal pacing can be reliably achieved using conventional active fixation technique and is associated with a low lead complication rate.[40]

Thus, it appears that initial smaller studies had demonstrated improved QRS duration, LV synchrony and LVEF and functional status with RVS pacing over the short, mid and long term, more recent studies with larger patient population have questioned these findings by producing contradicting results. Even the definition of RVS pacing has been questioned since there is no uniformity in definition between studies and lack of agreement in the lead position as assessed by various imaging and electrocardiographic methods. However, the feasibility and safety has been clearly documented in the literature.

His-Bundle pacing

From a physiological standpoint His-bundle may represent an optimal pacing site with potential hemodynamic benefits by mimicking activation over the normal conduction system. The attempt was made by Narula et al[41] in 1970 during an EP study to prove the feasibility of pacing the His bundle and demonstrating paced EKG similar to that during sinus rhythm. In the first attempt at using His bundle as a pacing site for permanent pacemaker, Deshmukh et al[42] successfully implanted it in 12 out of 14 patients with chronic AF and dilated cardiomopathy. Acute pacing thresholds were 2.4+/-1.0 V at a pulse duration of 0.5 ms. Lead complications included exit block requiring re-operative adjustment and gross lead dislodgment. They demonstrated decrease in LV end-diastolic dimension from 59+/-8 to 52+/-6 mm (P</=0.01) and in the end-systolic dimension from 51+/-10 to 43+/-8 mm (P<0.01), with an accompanying increase in LVEF from 20+/-9% to 31+/-11% (P<0.01). However, 10 out of 12 patients also underwent AV node ablation. Also, the

procedure time was 3.7±1.6 hours, significantly greater than would be expected from a standard implant procedure. The same investigators in 2004 were successful again in applying this pacing technique in 39 of 54 similar patients with chronic AF, QRS <120ms and a mean LVEF of 23%. Twelve patients also underwent RVA pacing. After a mean follow-up of 42 months, 29 patients survived and their LVEF improved from 0.23 + 0.11 to 0.33 +0.15. Functional class improved from 3.5 to 2.2. Cardiopulmonary testing revealed longer exercise time (RVA 255 + 110 s, His 280 + 104 s, $P < 0.05$), higher O2 uptake (RVA 15 + 4 mL/kg per minute, His 16 + 4 mL/kg minute, $P < 0.05$) with His bundle pacing compared to RVA pacing. Therefore, long-term His-bundle pacing is safe and effective in humans.[43] A recent case report[44] of a patient with LBBB and congestive heart failure showed significant improvement of functional class, LVEF (from 28 to 50%), LV diameter and mitral regurgitation after 27 months of His bundle pacing.

However, the approach is technically difficult due to anatomic location and size of His-bundle. Furthermore, lead stability is a considerable issue. The long fluoroscopy time during His bundle pacing and compromised pacing and sensing performance has been well documented even in "expert" hands. In a study[45] among 37 patients, permanent His pacing was achieved in only 35.5% of possible cases.. High capture thresholds and issues with lead stability have contributed to the low success rate. Subsequently, in another study of 91 patients the same investigators had a success rate of 44% in all possible cases and 65% in all attempts.[46]

Discussion

This review stimulates many unanswered questions such as: *RV APEX IS BAD BUT ARE ALTERNATE SITES BETTER? IS THERE A BETTER ALTERNATE SITE? IS THERE A CLINICALLY IMPORTANT MEASURABLE DIFFERENCE BETWEEN THE CONVENTIONAL (RV APICAL) and ALTERNATE SITES?*

Prolonged RV pacing has been conclusively shown to result in progressive LV systolic dysfunction. The current review highlights absence of equivocal proof that alternate site pacing is physiologically superior to RV apical pacing. The various studies available have heterogeneous designs with inconsistent expermimental methods, heterogeneous definitions of alternate sites, lack of quality control and varied study endpoints. Many studies, especially the earlier studies are methodologically flawed since many leads were placed in the mid RV or RVOT and not necessarily in the RV septum. RVOT is a complex structure which includes the RV free wall, anterior wall and septum. Also, a radiographic study confirmed that 61 % of leads placed using a simple curved stylet were shown to lie on the septum (LAO) while the remainder on the anterior and free walls.[47] The septal regions are the initial zone to depolarize. Hence initiating pacing and hence initiating pacing from the RV septum would achieve as normal a contraction pattern as possible. In contrast the RV free wall is the last zone to depolarize. Hence it is not logical to select RVOT with a heterogenous mix of both septal (potentially good sites) and free wall pacing (potentially poor sites).[48]

Although in theory, pacing the His bundle may preserve ventricular synchrony with native ventricular activation and narrow QRS, the implant technique is complicated with both acute (dislodgement) complications and long term (increase in threshold) difficulties. The technique also cannot be utilized in patients with distal conduction disease and AV block and is likely an overkill in patients not needing frequent RV pacing. For ablate and pace strategy among AF patients, the acute lead complications and long term increased stimulation threshold may result in poor device longevity and hence may not be suitable.

Conclusion

RV apical pacing has been used extensively for decades in patients requiring ventricular pacing mainly because of its easy accessibility. Chronic RV apical pacing however carries potentially significant long-term complications such as dyssynchronous ventricular activation with decrease of left ventricular function and congestive heart failure. The use of more physiologic alternative pacing sites in the close vicinity to the His bundle is safe and feasible in many patients. Stability of RVOT and RV septal leads has been well proven. Unlike the RV apex, the muscular RVOT avoids risks of pericardial tamponade, diaphragmatic pacing, or pericardial pain. However, large, long term, randomized clinical trials with convincing evidence of superior clinical outcomes are needed before recommending these alternatives in all or a subgroup of patients requiring permanent cardiac pacing.

Currently two prospective, long term, non-cross over trials (Right Ventricular Apical and High Septal Pacing to Preserve Left Ventricular Function (Protect Pace), and Right Ventricular Apical versus Septal Pacing (RASP), currently enrolling patients should clarify the optimal RV pacing site (especially in the long term preservation of LV function in patients that require ventricular pacing) and help answer the many questions.

However, for patients with high grade AV block and LV dysfunction in need for frequent ventricular pacing, who do not have a clear indication for resynchronization, alternate site pacing (RV septal) with modified tools in experienced hands represents a viable alternative to conventional RV apical pacing, till these long term properly conducted studies provide more definitive answers.

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Sudden Cardiac Arrest and Post-Resuscitation Hypothermia Management

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Introduction

Sudden cardiac arrest (SCA) and sudden cardiac death (SCD) refer to the sudden cessation of cardiac activity with hemodynamic collapse, typically due to sustained ventricular tachycardia (VT) or ventricular fibrillation (VF). These events mostly occur in patients with structural heart disease, particularly coronary heart disease (CHD). It is not unusual for SCA to be the first manifestation of CHD. Maximizing survival from SCA requires early recognition, followed by initiation of cardiopulmonary resuscitation (CPR), early defibrillation and advanced care.[1] This article provides an overview of cardiac arrest epidemiology, the principles behind each link in the "Chain of Survival," an overview of the core components of CPR and emphasize the recent changes in the American Heart Association (AHA) guidelines.

Epidemiology

Important advances in prevention and treatment of cardiovascular diseases (CVD) over the last three decades have lead to a decrease in cardiovascular mortality in Western countries. In spite of this, SCA remains a substantial public health problem and the leading cause of death.[2] SCA occurs both in and out of the hospital. In the US, approximately 350 000 individuals per year (approximately half of them in-hospital) suffer a cardiac arrest and undergo resuscitation.[3–7]

The estimated incidence of Emergency Medical Services (EMS) -treated out-of-hospital SCA in the US and Canada is about 50 to 55/100 000 persons/year and the estimated incidence of in-hospital SCA is 3 to 6/1000 admissions.[3-8] SCA victims who present with VF or pulseless VT have a substantially better outcome compared with those who present with asystole or pulseless electric activity (PEA).[1,7,9] The vast majority of cardiac arrest victims are adults, but thousands of infants and children also suffer either an in-hospital or out-of-hospital cardiac arrest each year in the US and Canada.[7,10]

The Indian Scenario

Over 80 per cent of deaths and 85 per cent of disability from CVD occur in low- and middle-income countries.[11-13] The Indian subcontinent (including India, Pakistan, Bangladesh, Sri Lanka, and Nepal) is home to 20 per cent of the world's population and may be one of the regions with the highest burden of CVD in the world.

Coronary artery disease (CAD) is, by far, the largest causative factor for SCD. In addition to the high rate of CAD mortality in the Indian subcontinent, CAD manifests almost 10 yr earlier on average in this region compared with the rest of the world resulting in a substantial number of CAD deaths occurring in the working age group.[14,15] The annual incidence of SCD is three to four times higher in men than in women, resulting in approximately 75% of SCD in men. The reason for this difference is attributed to the gender difference in the incidence of CAD and the protection from atherosclerosis in women before menopause.[16]

The time from symptom onset to emergency department arrival for patients with acute ST elevation myocardial infarction

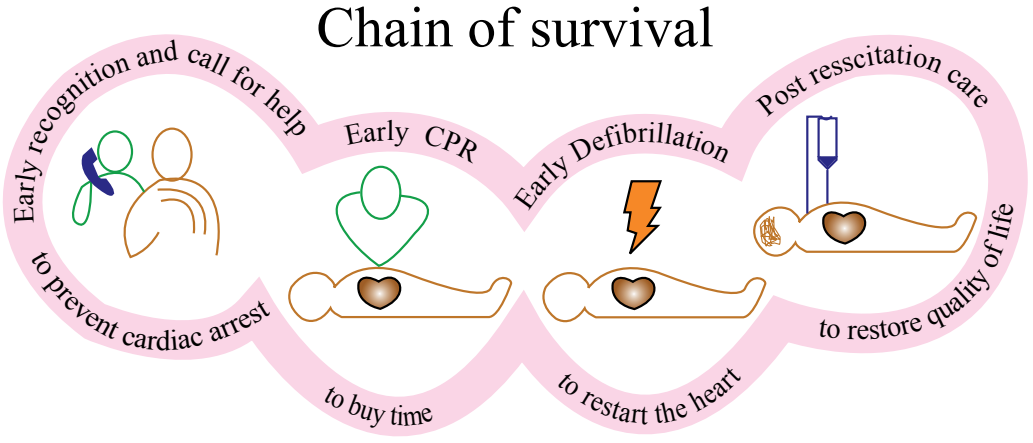

Figure 1 : American Heart Association's "Chain of Survival" to maximize survival. From Resuscitation Council (UK) 2010.

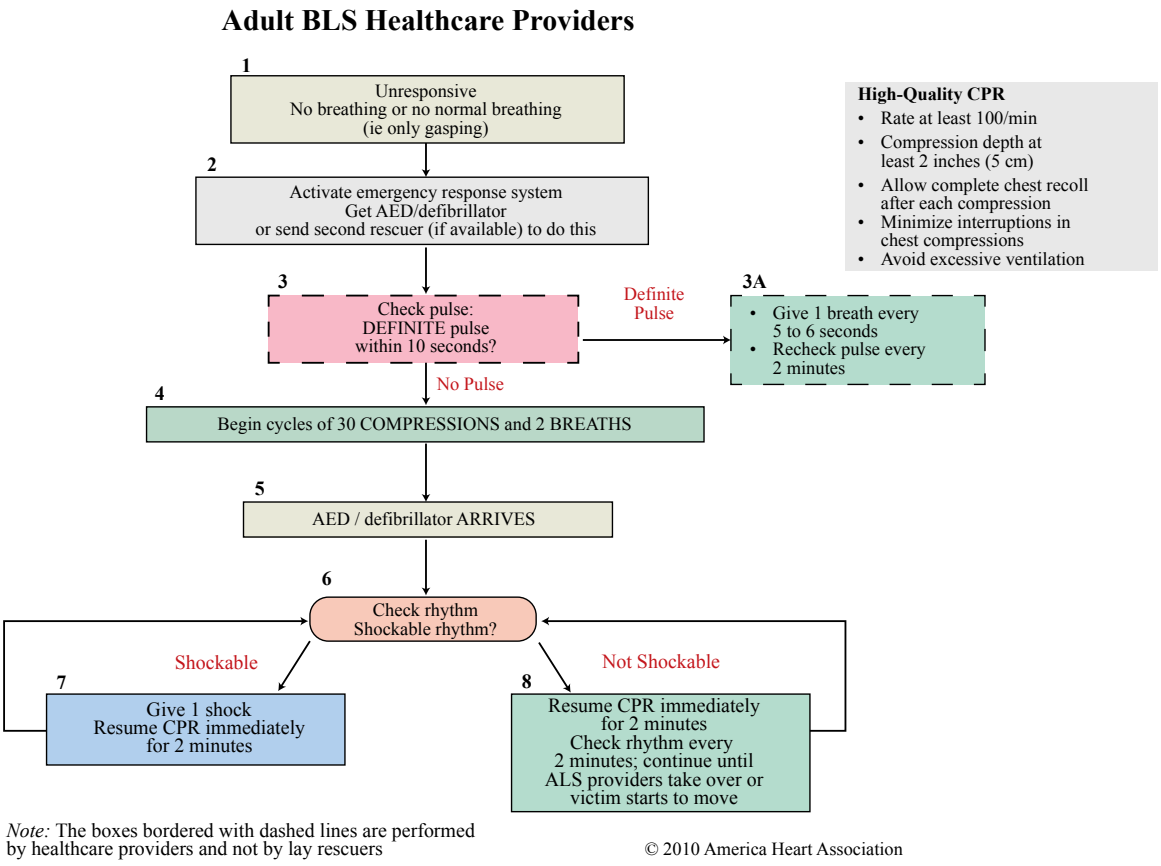

Figure 2 : Basic Life Support (BLS) healthcare provider algorithm. From 2010 American Heart Association Guidelines.

(STEMI) ranges between 110 and 140 minutes in North America, while in India, it is 180–330 minutes.[17-20] This delay in presentation is due to several factors such as lack of symptom awareness, longer distances travelled to reach hospital, poor EMS systems to facilitate transportation to a health care facility and traffic/road conditions. On the Indian subcontinent, only a small fraction of patients are brought to hospital in an ambulance, with the large majority using public transport (buses) and hired vehicles.[21] This implies an inability to offer early CPR, early defibrillation and advance cardiac life support, resulting in poor chances of surviving a cardiac arrest.

Strengthening the Links in the Chain of Survival

Successful resuscitation following SCA requires an integrated set of coordinated actions represented by the links in the Chain of Survival (Figure 1). The links include the following:

- Early recognition - If possible, recognition of illness before the patient develops a cardiac arrest will allow the rescuer to prevent its occurrence. Early recognition that a cardiac arrest has occurred is key to survival - for every minute a patient remains in cardiac arrest, chances of survival drop by roughly 10%.[22]
- Early CPR - improves blood and oxygen flow to vital organs and is an essential component of treating cardiac arrest. In particular, by keeping the brain supplied with oxygenated blood, chances of neurological damage are decreased.
- Early defibrillation - is effective for the management of ventricular fibrillation and pulseless ventricular tachycardia.[22] If defibrillation is delayed, the rhythm is likely to degenerate into asystole, for which outcomes are worse.
- Early advanced care - Early Advanced Cardiac Life Support (ACLS) is the final link in the chain of survival.
- Integrated post– cardiac arrest care.

Emergency systems that can effectively implement these links can achieve witnessed VF cardiac arrest survival of almost 50%.[23-26] In most emergency systems, however, survival is lower, indicating that there is an opportunity for improvement by carefully examining the links and strengthening those that are weak.[3] The individual links are interdependent, and the success of each link is dependent on the effectiveness of those that precede it. The challenge is how to encourage early, effective CPR for as many victims as possible, taking into account the wide range of rescuers, victims, and available resources. This task is particularly challenging in emerging economies that lack the infrastructure of EMS, absence of public access defibrillation,

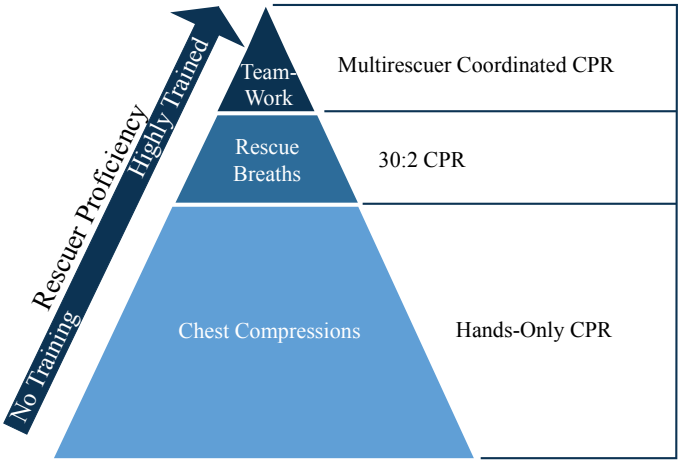

Figure 3 : Building Blocks of CPR. From 2010 American Heart Association.

societal awa reness and poor road/traffic conditions.

Adult BLS Skills

The Universal Adult Basic Life Support (BLS) Algorithm is a conceptual framework for all levels of rescuers in all settings (Figure 2).

Conceptual Framework for CPR - Interaction of Rescuers and Victims:

CPR traditionally has integrated chest compressions and rescue breathing with the goal of optimizing circulation and oxygenation. Rescuer and victim characteristics may influence the optimal application of the components of CPR.

Rescuer

CPR skills and their application depend on the rescuer's training, experience, and confidence. Chest compressions are the foundation of CPR (see Figure 3). ***All rescuers, regardless of training, should provide chest compressions to all cardiac arrest victims***. Because of their importance, chest compressions should be the initial CPR action for all victims regardless of age. Rescuers who are able, should add ventilations to chest compressions.

Victim

Most cardiac arrests in adults are sudden, resulting from a primary cardiac cause; circulation produced by chest compressions is therefore paramount.[27] In contrast, cardiac arrest in children is most often asphyxial, which requires both ventilations and chest compressions for optimal results.[28] Thus, rescue breathing may be more important for children than for adults in cardiac arrest.[28]

Early Action: Integrating the Critical Components of CPR

Modified Adult Basic Life Support emphasizes the key components that any rescuer can and should perform (Figure 4).

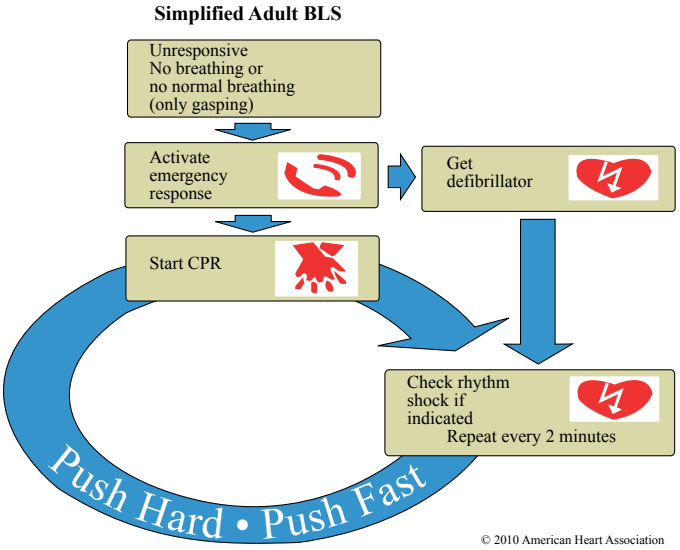

Figure 4 : Simplified Adult BLS Algorithm. From 2010 American Heart Association.

Recognition and Activation of Emergency Response

Prompt emergency activation and initiation of CPR requires rapid recognition of cardiac arrest. A cardiac arrest victim is not responsive. Breathing is absent or is not normal.[29,30] Agonal gasps are common early after sudden cardiac arrest and can be confused with normal breathing.[31-34] Pulse detection alone is often unreliable, even when performed by trained rescuers, and it may require additional time.[35- 38] Consequently, rescuers should start CPR immediately if the adult victim is unresponsive and not breathing or not breathing normally (ie, only gasping). Since time is of the essence, the prior directive to "look, listen, and feel for breathing" to confirm the presence of a cardiac arrest is no longer recommended.

Chest Compressions

The Change From "A-B-C" to "C-A-B" The newest development in the *2010 AHA Guidelines for CPR and ECC* is a change in the basic life support (BLS) sequence of steps from "A-B-C" (Airway, Breathing, Chest compressions) to "C-A-B" (Chest compressions, Airway, Breathing) for adults and pediatric patients (children and infants, excluding newborns). CPR improves the victim's chance of survival by providing heart and brain circulation. Rescuers should perform chest compressions for all victims in cardiac arrest, regardless of rescuer skill level, victim characteristics, or available resources. Rescuers should focus on delivering high-quality CPR (Figure 2):

Airway and Ventilations

Opening the airway (with a head tilt– chin lift or jaw thrust) followed by rescue breaths can improve oxygenation and ventilation. However, these maneuvers can be technically challenging and require interruptions of chest compressions, particularly for a lone rescuer who has not been trained. Thus, the

untrained rescuer should provide **Hands-Only (compression-only) CPR** (ie, compressions without ventilations), and the lone rescuer who is able, should open the airway and give rescue breaths with chest compressions. Ventilations should be provided if the victim has a high likelihood of an asphyxial cause of arrest (eg, infant, child, or drowning victim).

Compression-only CPR

Studies have shown that compression-only CPR may be as effective as combined ventilation and compression in the first few minutes after non-asphyxial arrest. A prospective, randomized study showed no significant difference with respect to survival at 30 days between instructions given by an emergency medical dispatcher, before the arrival of EMS personnel, for compression-only CPR and instructions for standard CPR in patients with suspected, witnessed, out-of-hospital cardiac arrest.[40] Lay rescuers who are unable or unwilling to provide rescue breaths, should be encouraged to give chest compressions alone.[39,40]

Early Defibrillation

The victim's chance of survival decreases with an increasing interval between the arrest and defibrillation.[41,42] Thus, early defibrillation remains the cornerstone therapy for ventricular fibrillation and pulseless ventricular tachycardia. One of the determinants of successful defibrillation is the effectiveness of previous chest compressions.

Integrated post-resuscitation care

Post–resuscitation care after return of spontaneous circulation (ROSC) has significant potential to reduce early mortality caused by hemodynamic instability and later morbidity and mortality from multi-organ failure and brain injury.[43,44] In this section, we would like to highlight the 2010 *AHA Guidelines for* hypothermia induction for comatose patients.

Therapeutic Hypothermia

Therapeutic hypothermia should be part of a standardized treatment strategy for comatose survivors of cardiac arrest. [45-47] Two randomized clinical trials and a meta-analysis showed improved outcome in adults who remained comatose after initial resuscitation from out-of-hospital VF arrest and who were cooled within minutes to hours after ROSC.[48-50] Patients in these studies were cooled to 33°C or the range of 32°C to 34°C for 12 to 24 hours.

The practical approach of therapeutic hypothermia can be divided into 3 phases: induction, maintenance, and rewarming. Induction can be instituted easily and inexpensively with intravenous ice-cold fluids (saline 0.9% or Ringer's lactate, 30 mL/kg) or traditional ice packs placed on the groin and armpits and around the neck and head.[51-55] Initial cooling is facilitated by concomitant neuromuscular blockade with sedation to prevent shivering. The maintenance phase is best achieved with external or internal cooling devices that include continuous temperature feedback to achieve a target temperature. The rewarming phase can be regulated with the external or internal devices used for cooling or by other heating systems. The optimal rate of rewarming is not known, but current consensus is to rewarm at approximately 0.25°C to 0.5°C per hour.[56] Particular care should be taken during the cooling and rewarming phases, because metabolic rate, plasma electrolyte concentrations, and hemodynamic conditions may change rapidly.

A number of potential complications are associated with cooling, including shivering which is common in the induction phase,[57] bradycardia, coagulopathy, arrhythmias, and hyperglycemia, particularly with an unintended drop below target temperature.[58,59]

If therapeutic hypothermia is not feasible or contraindicated, then, at a minimum, pyrexia must be prevented. Pyrexia is common in the first 48 hours after cardiac arrest and the risk of a poor neurological outcome increases for each degree of body temperature above 37°C.[60-62]

In summary the *2010 AHA Guidelines for CPR and ECC* recommend that comatose (ie, lack of meaningful response to verbal commands) adult patients with ROSC after out-of-hospital VF arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours (Class IB indication). Induced hypothermia may also be considered for comatose adult patients with ROSC after in-hospital cardiac arrest of any initial rhythm or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electric activity or asystole (Class IIB indication). Active rewarming should be avoided in comatose patients who spontaneously develop a mild degree of hypothermia (32°C [89.6°F]) after resuscitation from cardiac arrest during the first 48 hours after ROSC. (Class IIIC indication).

Conclusions

There is a striking disparity in survival across systems of care for cardiac arrest victims. Although future discoveries will offer opportunities to improve survival, we currently possess the knowledge and tools, represented by the "Chain of Survival," to address many of these care gaps. Each system, whether in the hospital or in the community, must assess its performance and implement a strategy for improving resuscitation outcomes. SCA continues to be an all-too-common cause of premature death, and small incremental improvements in survival can translate into thousands of lives saved every year. The challenge is daunting enough in developed economies with adequate infrastructure, but ironically, it's the emerging economies, such as South East Asia, that has the highest burden of cardiac arrest and yet, very few resources mobilized to deal with it.

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The Role of Cardiac Magnetic Resonance Imaging in the Evaluation of Arrhythmogenic Right Ventricular Dysplasia

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Key words: magnetic resonance imaging, arrhythmogenic right ventricular dysplasia

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a cardiac muscle disorder characterized pathologically by fibrofatty replacement of the right ventricular (RV) myocardium [1]. In the early stage of the disease, structural changes may be confined to, the so called "triangle of dysplasia" in the RV. Clinical expression ranges from an asymptomatic phenotype, arrhythmias or even ventricular systolic dysfunction (right or left or both). Although the word 'right' has remained prominent in the description of the disease, left ventricular involvement is now acknowledged at a stage earlier than conventionally acknowledged [2].

ARVC/D is now recognized to be a genetic disease affecting the desmosomes that are responsible for cell-to-cell binding with mutations eventually affecting gap junction functioning [2]. Other mutations in non-desmosomal genes have been described as well. The link between ARVC/D and myocarditis is controversial and unclear despite recent reports that indicate a similar clinical presentation [3,4].

The original 1994 International Task Force criteria (ITFC) for the clinical diagnosis of ARVC/D focused primarily on RV disease manifestations and mandated the absence of or only mild LV involvement to prevent confounding with commoner diseases such as ischemic heart disease and dilated cardiomyopathy, that may also have an arrhythmogenic substrate.

The 1994 ITFC were derived from clinical experience gained from cases with extreme phenotypic manifestations and survivors of SCD and represented what we know today to be the extreme end of the spectrum of a disease [5]. As a result of this bias, criteria were highly specific (identified the unaffected well because of the need to satisfy rigorous criteria), but they lacked sensitivity for early and familial disease (where the manifestations are less remarkable).

The 1994 ITFC mentioned morphological changes in the RV including alteration in systolic function, dilatation and aneurysmal changes as major criteria if these were severe in nature and relegated them to a minor status if less accentuated. Tissue characterization of the wall to demonstrate fibrofatty replacement of the myocardium on endomyocardial biopsy was also indicated as a major criterion. In the morphological evaluation of the RV, no mention was specifically made about the imaging modality to be used and cardiac MRI was in its infancy at that stage in the evaluation of ARVC. As it became clear that MRI was preferable to evaluate the RV compared to echocardiography, namely transthoracic echocardiography (TTE) and because of the fact that a high signal on some sequences could indicate fatty tissue, MRI began to be adopted for the evaluation of ARVC at a rapid rate despite the unresolved status of the technique in the evaluation of the disease. Some referral centers accumulated large cohorts of patients, studying them rigorously and applying CMR also in the evaluation of these patients [6]. As these centers published their experience and images often from patients with advanced stages of the disease, numerous other centres with MRI units began evaluating patients without fully understanding many of the caveats related to the technique itself. The border between what was normal and clearly abnormal was rather blurred in many situations.

The rather dramatic presentation of SCD or malignant ventricular arrhythmias that may accompany the disease, especially in young individuals, was of most concern to many clinicians and the threshold for clinical suspicion was therefore lowered. The fear of the consequences of a missed diagnosis, also medicolegal, led many clinicians to order a cardiac MRI, considered by some to be a definitive test while often ignoring to perform many other indicated tests to fulfil ITFC. The ability to assess for major criteria and minor criteria made MRI a promising technique despite the subjectivity inherent in the interpretation of wall thinning, wall motion, and intramyocardial fat. Despite lacking standardized CMR protocols and studies systematically comparing it with other imaging techniques, a problematic practice pattern emerged which was highlighted in a report from the highly experienced group at Johns Hopkins on the misdiagnosis of ARVC/D [7] (Figures 1, 2). A few salient findings of this landmark study merit emphasis. 92% of the patients who underwent a MRI study previously in centers around the US prior to the reevaluation at the Hopkins center were reported to have an abnormal study. In 76% of these patients (the ones with an abnormal study), the only findings were intramyocardial fat/wall thinning. None of these findings were confirmed on re-evaluation and none of these patients eventually were diagnosed with ARVC based on the 1994 ITFC. Remarkably on re-evaluation, only 27% of the 89 patients were confirmed to have ARVC whereas all had been advised to undergo placement of an ICD and 34% had already done so.

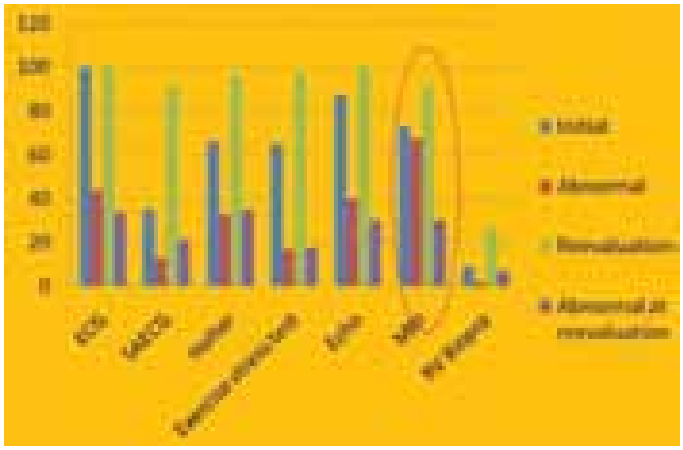

Figure 1 : Shows that MRI was one of the most commonly ordered in various centres to rule out ARVC and a larger percentage of MRI studies were considered abnormal in comparison to other tests like signal averaged ECG and RV biopsy. [Reproduced with permission from the publisher John Wiley and Sons. Bomma C, Rutberg J, Tandri H, Nasir K, Roguin A, Tichnell C, Rodriguez R, James C, Kasper E, Spevak P, Bluemke DA, Calkins H: Misdiagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. J Cardiovasc Electrophysiol 2004,15(3):300-306].

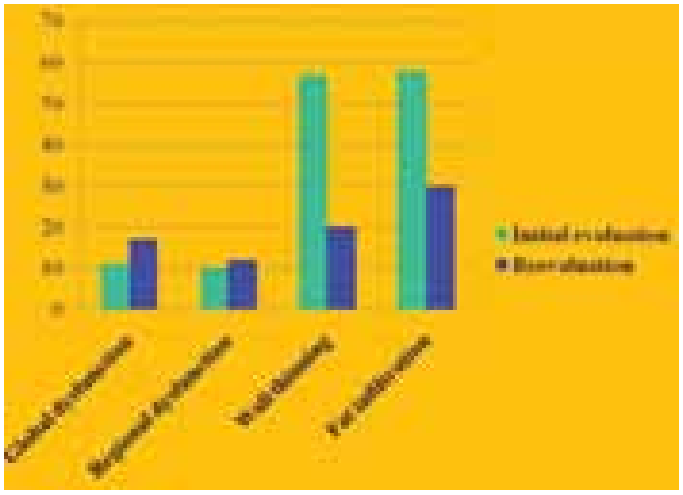

Figure 2 : In the initial evaluation a large number of studies reported wall thinning and fat infiltration on the CMR study that was not subsequently confirmed at the more experienced referral centre where these subjects sought a second opinion. [Adapted from Bomma C, Rutberg J, Tandri H, Nasir K, Roguin A, Tichnell C, Rodriguez R, James C, Kasper E, Spevak P, Bluemke DA, Calkins H: Misdiagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. J Cardiovasc Electrophysiol 2004 , 15(3):300-306].

The ECG and a TTE were the only exams that were performed more frequently than a cardiac MRI.

The purpose of this review is to critically evaluate the role of

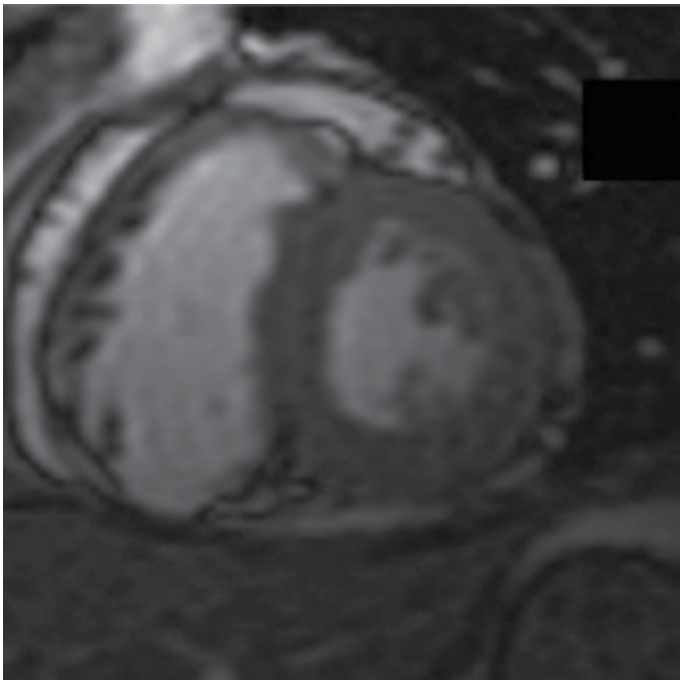

Figure 3 : The inferior RV wall shows obvious bulging in a patient who was diagnosed with ARVC after satisfying ITFC.

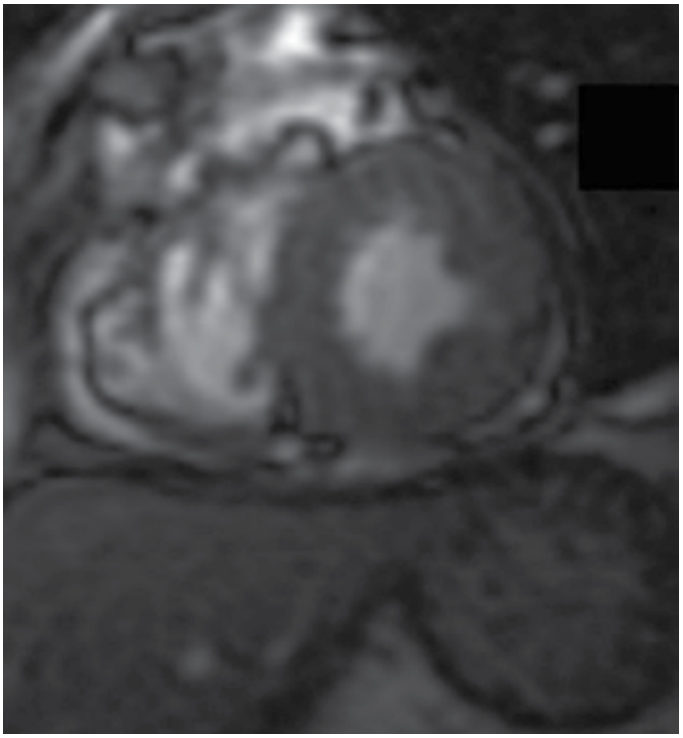

Figure 4 : The RV free wall shows various areas of aneurysmatic changes in the same patient in the short-axis view.

MRI in ARVC and to emphasize the redefined role of MRI as proposed in the revision of the original ITFC, which was published recently [2]. In an era of surfeit of information, the authors believe that numerous comprehensive reviews about

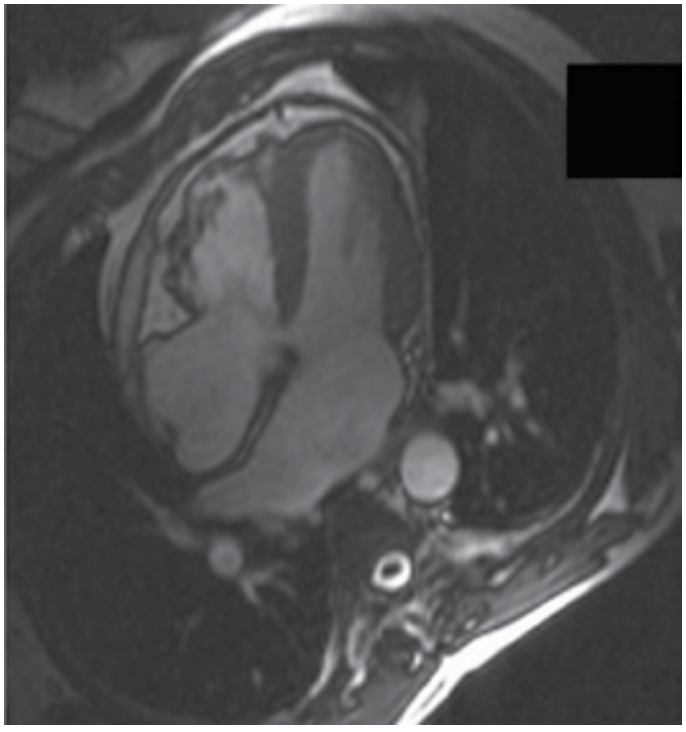

Figure 5 : The aneurysmatic changes are more obvious on the four-chamber view.

ARVC exist in the literature and a few specific ones regarding the role of CMR [8]. This is not meant to be a complete review of ARVC but one that provides some practical advice for a practitioner (often in nonreferral centers) who encounters a probable clinical diagnosis of ARVC and is considering the use of CMR to evaluate the patient as part of a comprehensive work-up.

What is the added value that CMR adds in the evaluation of ARVC?

Morphological and functional evaluation of the RV is greatly facilitated by currently available MR techniques. Cine sequences help in the assessment of wall motion abnormalities if present and in the volumetric quantification of RV function. A major departure from the 1994 ITFC in the revision published recently has been the provision of specific numbers for both ejection fraction and end-diastolic volume indexed to body surface area [2]. The current criteria require the presence of a WMA (Figures 3-5) and an increased RVEDV or decreased EF for one major or minor criterion to be fulfilled (distinguished by the severity of the quantitative parameters). A qualitative parameter (WMA) and one quantitative (either EF or indexed EDV) is therefore required together.

The current revision therefore clearly defines the following MRI parameters to be considered to fulfil a major or minor criteria:

MAJOR: Regional RV akinesia or dyskinesia or dyssynchronous RV contraction ***and*** 1 of the following:

- Ratio of RV end-diastolic volume to BSA ≥110 mL/m2 (male) or ≥100 mL/m2 (female)
- ***or*** RV ejection fraction ≤40%

MINOR: Regional RV akinesia or dyskinesia or dyssynchronous RV contraction ***and*** 1 of the following:

- Ratio of RV end-diastolic volume to BSA ≥100 to <110 mL/m2 (male) or ≥90 to <100 mL/m2 (female)
- ***or*** RV ejection fraction >40% to ≤45%

There is no mention of fatty infiltration, trabercular disarray, wall thinning or delayed enhancement suggestive of fibrosis and current data are incomplete and rather preliminary to consider mentioning LV involvement but subsequent revisions, which hopefully will be more regular may take note of this changed paradigm.

Because ARVC is a progressive disease that spans the spectrum from being completely asymptomatic to presenting as SCD, morphological abnormalities begin to appear and worsen over time and it is unclear which is the first abnormality to appear - e.g ECG vs CMR vs

SAECG vs Holter. It is intuitive that as phenotypic manifestations appear abnormalities on various tests appear either sequentially or concomitantly. It is our experience and that of others [8] that it is unlikely to have an abnormal CMR scan with other tests reported as normal. Therefore in the frankly manifested cases CMR and other tests will show abnormalities and a diagnosis may sometimes be clinched without a CMR study. This was confirmed recently in the the Multidisciplinary study of Right Ventricular Cardiomyopathy/Dysplasia which established the North American ARVC/D Registry [9].

There are some situations where a CMR study provides additional information that may be unique. Although ARVC has traditionally been designated a disorder affecting the RV and the original criteria specified the absence of LV involvement, recently this paradigm has been challenged by the publication of a report of patients with predominantly mutations in the desmoplakin gene and marked LV involvement with relative sparing of the RV [10]. The group emphasized the differentiation from dilated cardiomyopathy based on a clinical presentation dominated by arrhythmias and fewer symptoms suggestive of congestive heart failure. Moreover a very specific type of delayed enhancement was seen after administration of gadolinium which involved the midmyocardial or subepicardial regions. There are changes in the ECG which may suggest this variant of ARVC designated as left-dominant arrhythmogenic cardiomyopathy. Another situation where CMR may provide additional value may be in the screening of relatives of patients with diagnosed ARVC. The Johns Hopkins group carefully selected asymptomatic relatives of patients from their registry and were able to demonstrate that carriers of mutations in some genes (mainly plakophilin - 2)

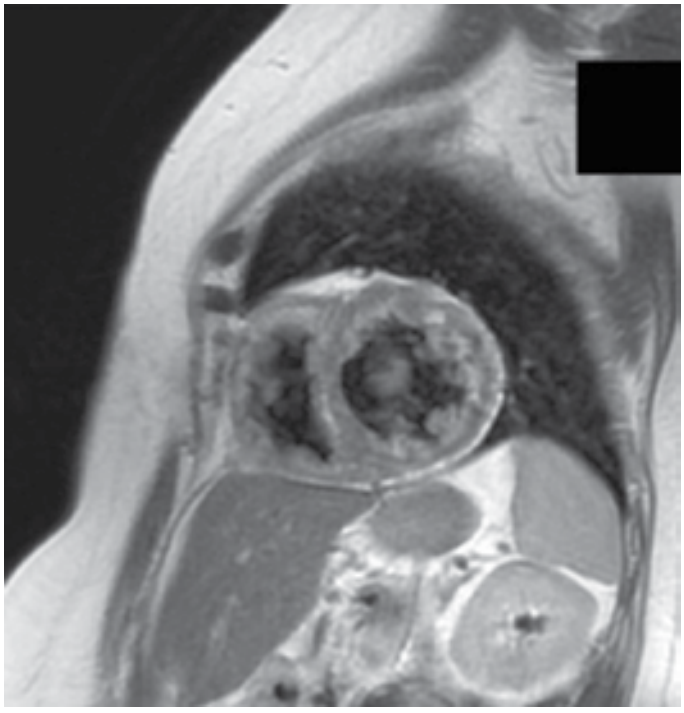

Figure 6 : The normal LV has a grayish appearance on this sequence often labeled a black-blood sequence (the blood filled cavities have no signal) and fat gives off a high signal appearing white (the subcutaneous fat has a very high signal). In this patient the grayish LV wall is interspersed in various areas with high signal most likely to be fat in this patient who presented with ventricular tachycardia.

were likely to have a very specific WMA in the subtricuspid region that they designated the ***accordion sign*** attributable to a crinkling effect that accentuated in systole [11]. However, they could not find prominent LV involvement in PKP2 in their cohort unlike the group that eventually described the LDAC variant. Remarkably all four of the patients with a mutation for DSP demonstrated fatty infiltration of the LV **(Figures 6,7).** It is possible that LV involvement may be more prominent or confined to those with a mutation in the DSP gene and the accordion sign may be more common among carriers with the PKP2 mutation. Targeting asymptomatic family members of index cases with mutations in either DSP or PKP2 for screening using CMR may therefore be a reasonable strategy. It must be emphasized that the study which demonstrated the utility of the accordion sign included subjects who were truly asymptomatic and did not seek medical attention but were family members of probands who were offered genotyping and a CMR study.

Although the RVOT is well evaluated by CMR, and even though one group has suggested early involvement of the RVOT as a forme-fruste of ARVC, in some cases labelled clinically as idiopathic RVOT VT [12], recent work has suggested that the RVOT involvement and dilatation seems to accompany generalized RV involvement especially when investigated by CMR [9,11]. Therefore currently available CMR data indicate concurrent dilatation and involvement of the RVOT and the main body of the RV. Isolated RVOT involvement is not detected by CMR.

What is the role of CMR in patients with an initial clinical presentation suspicious for ARVC?

Most robust studies have come out of referral centers including patients with established disease according to the 1994 TFC and CMR studies were usually performed in these probands and often offered to family members if they met what was designated as modified TF criteria for familial ARVC [6,10,11,13]. The inclusion of a mixture of patients who fulfilled original or 'modified' TF criteria for familial disease where a family member with 200 ventricular ectopics could qualify for a diagnosis of ARVD/C may be rather liberal as it does not exclude the possibility of inclusion of patients with other cardiomyopathies [10,13] (the possibility of a family member having another cardiomyopathy is not totally excluded obviously in such circumstances).

As patients with ARVC may present at virtually any clinical practice it is important to properly identify these patients and do a comprehensive work up. These de novo patients have often presented some of the most difficult situations and misdiagnosis was not an unusual phenomenon as previously reported. One culprit in misdiagnosis was the inaccurate interpretation of CMR studies, the overuse of CMR compared to other diagnostic modalities and even ignorance regarding the TFC [7]. The Multidisciplinary study of Right Ventricular Cardiomyopathy/ Dysplasia established the North American ARVC/D Registry (North American Multidisciplinary study, NAMS) which consisted of 18 enrolling centers to address this problem partially because some of these centers were experienced referral centers and may not represent general cardiology practices where patients may present with symptoms suggestive of ARVC/D [9]. The fact that only three centers enrolled more than ten patients underscores the relative rarity of the disease. The commonest symptoms were palpitations, syncope, dizziness or chest pain and 38 had sustained clinical VT.

The role of MRI in the newly defined criteria in 2010 was determined from the study [2]. To exclude a bias in the determination of the sensitivity and specificity of any test in the diagnosis of ARVC, proband data were excluded if that test was crucial for the diagnosis of the individual patient because while establishing diagnostic criteria and in determining the sensitivity and specificity of a new screening test, it is recommended that the primary diagnosis should have been arrived at without the particular test being evaluated. Compared to the MRI studies of 462 normal subjects there was a clear decrease in RVEDV indexed to BSA and RVEF in both males and female probands (n= 44). This was the basis for the inclusion of volumetric criteria by MRI in the Revised TFC of 2010. Post hoc application of this Revised version showed an increase in sensitivity compared to

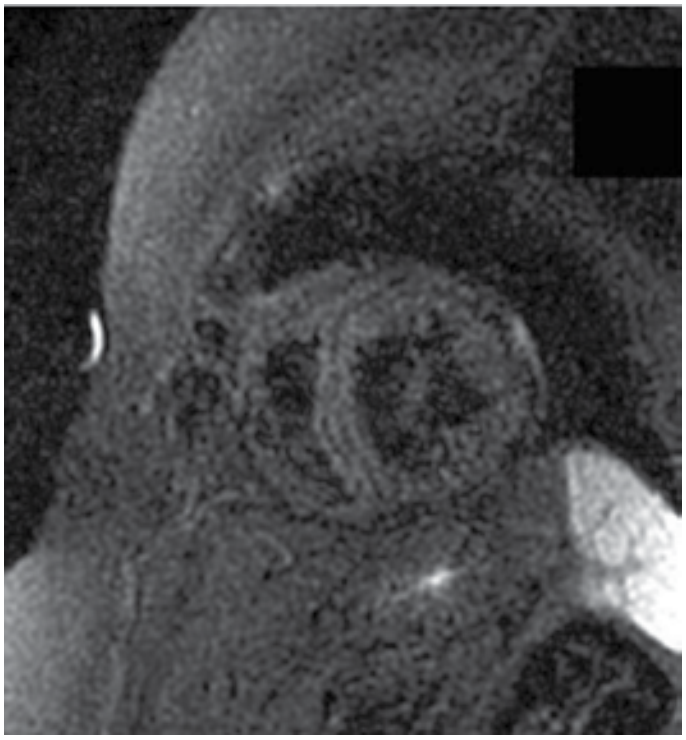

Figure 7 : Using a sequence that suppresses the high fat signal, the white patches in the LV (also noted as a linear streak in the septum) in figure 6 are confirmed to be fat. There is also no signal from the subcutaneous fat. This patient was found to have a desmoplakin mutation.

the original ITFC. A panoply of tests are often used in these patients ranging from echocardiography, electrocardiography, angiography, SAECG, Holter, RV biopsy and MRI. A sequential analysis revealed that evaluating the RV echocardiogram, RV angiogram, SAECG complemented by the ECG and the Holter provided the best diagnostic approach even excluding MRI and biopsy. Indeed when a 7-variable model (which included all the tests applied) was compared to a best 6-variable model (where one test was excluded one and a time and the effect of this approach on diagnostic capability re-evaluated), the exclusion of MRI seemed to cause the least effect on the diagnostic capability of the 6-variable model [9]. This contradicted the general practice pattern that revealed a misdiagnosis of ARVC with overreliance on MRI [7]. However, MRI is noninvasive compared to a biopsy and the angiogram and therefore has a clear role in the evaluation of these patients.

What is the relationship between myocarditis and ARVC?

There is one school of thought that suggests that acute episodes of inflammation or myocarditis may be a stage in the evolution of ARVC [3]. Both myocarditis and ARVC can be studied by CMR and recently a very specific set of criteria for myocarditis with a dominant role for MRI was described [14]. One group has even suggested that myocarditis may even mimic ARVC upto the point of even fully satisfying the original ITFC [3]. However, the findings of this study were hotly contested [4]. Clinical difficulties may arise if a patient presents with symptoms and signs suggestive of myocarditis but there is a family history of ARVC. The morphological abnormalities detected on CMR should be reported whether they suggest myocarditis or ARVC. Delayed enhancement may be present in both and some patterns may be similar (the subepicardial involvement in both) when they involve the LV. What is important is that the diagnosis of ARVC should be made by the clinical cardiologist or the electrophysiologist who makes the therapeutic decisions and not by the physician who interprets the CMR study. At this point the controversy regarding the link between the two entities has not been settled.

Practical difficulties in studying patients with ARVC

It must be emphasized that the evaluation and detection of fat or signal suggestive of fat is completely excluded from the MRI evaluation of ARVC. While advanced cases of ARVC may show extensive fat deposition, early stage disease even with microscopic infiltration cannot be detected by MRI based on a high signal [15,16]. A high signal on some sequences should not be assumed to be fat except in the most extraordinary situations (for e.g. in the same region where there is a WMA). Numerous technical factors elucidated by others have emphasized why a high signal in the region of the RV is not unusual and it may be difficult to clearly separate the epicardial fat from the myocardium. What confounds it further is that in ARVC fibrofatty infiltration commences from the epicardium and is directed inwards. Moreover fat can be found in the myocardium of patients without ARVC. It is therefore appropriate that the search for fatty infiltration is not recommended. Even experienced groups have demonstrated that although qualitative assessment of RV structure and function is highly reproducible, fat infiltration is less reproducible and lacked specificity compared with RV kinetic abnormalities [16].

Standard protocols have been published but each center will have to optimize their protocols to include one state-of-the art cine sequence which will usually be a steady state free precession sequence (SSFP) with a conventional gradient echo type sequence as a back-up in case of the SSFP sequence failing in some patients with frequents ectopics. The optimization of a cine sequence is fundamental because volumetric and kinetic analysis forms the backbone of a CMR study for ARVC/D. However, contouring RV volumes is a more difficult task compared to the LV as the difficulty is most obvious in the most basal slices where the atrioventricular junction moving in and out of the imaging plane can cause some confusion. There are also the slices where the RVOT ending in the pulmonary valve have to be contoured meticulously. The propensity for a bias to over or underestimate the volumes can occur if the history is known. While volume analysis is inherently more objective, WMA can be more challenging. The RV has a complex shape and movement and based on the internal trabecular structure a

subject can have some untethered regions that lag behind and may look dyskinetic. To the inexperienced some of these areas may look aneurysmal. It is not only the inexperienced that may have some difficulty in interpreting WMA or just wall motion. Even experienced observers may be deceived into classifying some movements in an unaffected RV as abnormal [17]. While the emphasis on the need to also document quantitative dysfunction (increased RVEDV indexed to BSA or decreased EF) may provide some cushion from errors, this is no guarantee. According to the current modification ***a patient with quantitative dysfunction (even if both RVEDV and EF) will not satisfy one parameter in the Revised TFC if there are no WMA detected.***

A tomographic black blood sequence is also helpful to elucidate fat in the LV in those with DSP mutations. A sequence to study fibrosis after gadolinium using the standard delayed enhancement technique [18] is included in all cardiac packets sold by vendors and optimization has been made easier by software modifications that help select the optimal inversion time to null the myocardium. In practice we have not found any exceptional advantage to this modification which is sometimes offered at considerable additional cost and a good understanding of the architecture of the sequence is all that is required to acquire excellent images. Currently vendors offer these sequences in pre-packaged formats for most machines often excluding the capability to manipulate sequence parameters in some cases, which was possible previously. Although it is intuitive that most CMR practitioners need to have a reasonable understanding of the physics and the architectural composition of the common sequences, it is not always the case. For optimal image acquisition it is important to be able to manipulate some sequence parameters to adapt to each subject. As cine sequences in CMR are currently not real-time but an average of approximately 8-16 cardiac cycles in most cases, the occurrence of ectopics during some loops as the images are acquired from the base to the apex may cause some of the loops to be out of phase with the others. While contouring for ventricular volumes it should be confirmed that the right phases are added together to calculate systolic and diastolic volumes. Some commercial software may have some limitations when this happens and a tedious manual approach may have to be resorted to. In the sequence to elucidate any potential delayed enhancement after gadolinium, it is important to realize that a high signal may mean either fat or fibrosis [18] and a black blood sequence optimized for fat detection should be done to clarify this. Although a lot has been written about delayed enhancement in the RV, at this moment it is still not as reliable in comparison to detection of a high signal in the LV due to various technical reasons. What is important is that high signal from epicardial fat should not be confounded with fibrofatty replacement of the RV free wall.

In the interpretation of studies the presence of mimics of ARVC/D should be considered. Sarcoidosis is an oft-quoted mimic demonstrating WMA very similar to ARVC/D. Structural changes in the RV have also been reported recently in patients with the Brugada syndrome [19]. A complete or partial absence of the pericardium can give images that may resemble ARVC. These examples demonstrate that CMR is not a stand-alone technique in the evaluation of ARVC/D and certainly not a gold-standard.

Despite these difficulties the results of a study from the Brompton group revealed that intraobserver concordance was very high and fidelity of readings was maintained even after a year in a blinded analysis [20]. High interobserver concordance was noted with a reader who progressively gained experience alongside a more established reader and the lowest concordance was confirmed for the least experienced reader. This indicated that CMR patterns, especially WMA in ARVC can be learned over a period of time.

For those patients with numerous extrasystoles ECG gating may be problematic with some image degradation but hardware and software improvements have mitigated some of these problems. In some patients with frequent extrasystoles, a beta blocker prior to the study may help. Finally for all practical purposes, patients with ICDs implanted should not undergo a CMR study as there are other alternatives and although it may be done in highly experienced centers, it may be prudent to avoid CMR studies in these patients.

Conclusion

Cardiac MRI is a valuable imaging modality in the evaluation of patients with ARVC/D. It can be used currently to evaluate for criteria specific to MR evaluation of these patients as stated in the Revised TFC published recently in order to reach a diagnosis [2]. It may also provide morphological information of some variants of the disease that may initially and primarily involve the left ventricle [10]. It may also be used to evaluate asymptomatic family members who may potentially be carriers of some well characterized mutations in components of the desmosome [11]. It may also provide an alternative diagnosis in some cases excluding the disease given some of the unique advantages that MRI offers. Finally a negative CMR study does not exclude ARVC.

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Bradycardia-induced Torsade de Pointes – An arrhythmia Less Understood

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Key words: Torsades de Pointes; Bradycardia; Atrioventricular block

Torsade de pointes (TdP) denotes a polymorphic ventricular tachycardia that is associated with prolonged QT interval at baseline, and is potentially life-threatening. Though it is well established that the genesis of TdP is closely linked to the transmural dispersion of repolarisation (TDR), the cellular and electrophysiological milieu predisposing to torsadogenesis in many conditions is not completely understood [1].

Significantly increased TDR at contiguous myocardial sites functions as a re-entrant substrate to initiate and maintain a TdP episode. Increased TDR in myocardium is represented by the electrocardiographic finding of prolonged QT interval. More specifically, the descending limb of the T wave represents TDR and this phase is considered to be a vulnerable period for torsadogenesis [2]. When a premature beat occurs in this period, the arrhythmia is initiated and perpetuated due to phase 2 re-entry or phase 2 early after depolarization.

Bradycardia is known to be one of the major factors predisposing to TdP. The inverse relationship between heart rate and repolarization time primarily accounts for bradycardia-induced QT prolongation. In addition, bradycardia increases the torsadogenicity of drugs that block IKr because these drugs block K+ channels in a reverse-use-dependent manner [3]. TdP has been described in many conditions with bradycardia like atrioventricular (AV) block, drugs, vagotonia, hypothyroidism etc [4-7]. However, patients with chronic AV block may have mechanisms other than the magnitude of bradycardia. Pause-dependent TdP has been recognised as an important complication of chronic AV block for long [8]. Studies have noted that patients with heart block have a significantly longer QT interval than those with sinus bradycardia even at comparable heart rates [9]. This relative QT prolongation may be one of the major reasons why TdP is more commonly observed in chronic AV block than in sinus bradycardia. However, the cellular mechanisms accounting for prolongation of repolarisation in them may be varied. Early afterdepolarisations may develop in these patients through prolongation of the action potential duration secondary to both bradycardia-dependent depression of electrogenic Na+ pumping and more complete inactivation of IK [10]. In addition, low ventricular rates are associated with submaximal activation of ITO, which shifts plateau of the action potential to a voltage levels in which the Ca2+ window current availability is increased [11]. Fast heart rates tend to oppose these actions, preventing early after-depolarisations and TdP.

In this issue of the journal, Yiginer G et al report a retrospective analysis of 64 patients with chronic AV block for occurrence of TdP and its predictors [12]. The three patients who developed TdP in this group were females, had more advanced age, and were in bradycardia for longer duration. The gender-specific preponderance in females to develop drug-induced TdP when treated with antiarrhythmic drugs or during spontaneous bradyarrhythmias is already known [13]. Elderly persons are more likely to have more co-morbid conditions like hypertension, coronary artery disease and heart failure, and these co-morbidities are known to cause down regulation of potassium channels [14]. Duration of exposure to bradycardia is another factor predisposing to TdP according to the authors. Concomitant to the duration of AV block, the likelihood of slower and irregular ventricular rhythms, which can result in 'long-short' sequence, may also increase. Chronicity of bradycardia might result in many alterations in myocardial channel functions also [15]. These alternate mechanisms also may contribute to an increase in the degree of the dispersion of refractory periods and facilitate the development of extrasystoles, thus playing a major role in producing TdP, apart from the magnitude of bradycardia, in patients with chronic AV block.

The authors identified that T wave notching on ECG having a predictive value for TdP, besides QT prolongation. All 3 cases who developed TdP had notched T waves in the ECG on the occurrence day of TdP, and in them, Tpeak-Tend were longer than 85 ms. This is concordant with the previous observations in similar group of patients. Bozkaya et al noted the presence of prolonged QTc/JTc intervals, pathologic U wave and T-U complex, prolonged Tpeak-Tend interval, and LQT2-like QT morphology as the predictors of ventricular arrhythmias during chronic AV block [16]. In another retrospective case-control study, where genetic testing was done in patients with TdP in the setting of complete AV block, the terminal phase of repolarization (Tpeak to Tend) was identified as a marker of an underlying cardiac ion channel abnormality. In this study, 4/11 (36%) patients with complete AV block and TdP had a genetic mutation identified involving ion channels responsible for cardiac repolarization involving hERG (n=3) and SCN5A (n=1). Authors proposed TdP in the setting of complete AV block to represent

the subset of patients with underlying genetic predisposition to reduced repolarization reserve [17].

This study conveys a message that a subgroup of patients with chronic AV block are at higher risk to develop life-threatening ventricular arrhythmias. Presently, any of the predisposing factors identified by the authors - age, gender or duration of heart block- are not given added importance while recommending pacemaker implantation in patients with chronic AV block. In real world scenario, large prospective randomised studies in patients with chronic AV block to assess the unintervened natural history of varying subgroups may not be possible because of multitude of reasons. Hence the recommendations are often supported only by evidence from retrospective observations. It is interesting to note that not a single recommendation (Class I-III) in the current ACC/AHA guidelines for pacing in bradycardia is backed up by level of evidence A [18]. In contrast, for both biventricular pacing and cardioverter-defebrillators, the benefits of implantation are overwhelmingly evidence-based. The reasons for this apparent paradox could be multifactorial. Pacemaker is clearly life saving at least in a selected population and may not need further evidence. Furthermore, only a few patients with unintervened natural history may be available to assess the long term outcome. These limitations leave a few clinical scenarios like asymptomatic chronic AV block with narrow QRS escape rhythm, especially while noted for the first time in adults, with limited evidence in favour of clear benefit with pacemaker implantation. Still, the present guidelines favour implantation as reasonable for persistent third-degree AV block with an escape rate greater than 40 bpm in asymptomatic adult patients without cardiomegaly (Indication: Class IIA, Level of Evidence: C). Interestingly, the recommendations do not consider QT prolongation as an indication for pacemaker implantation in these patients. Indeed, subsequent studies would be required to establish the incremental role of the high-risk predictors identified by Yiginer et al in further risk stratification of chronic AV block.

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Case Report

2:1 VA Block in Wide QRS Complex Tachycardia

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Introduction

The differentiation of ventricular ectopics from supraventricular impulses conducted with aberrancy constitutes perennial challenge. The problem in diagnosis of VT is establishment of its ventricular origin. SVT with aberrancy can also give rise to bizarre QRS complexes which can mimic VT. Confirmation is possible by EPS alone. ECG, in addition to clinical findings, can be of considerable value in establishing the diagnosis of VT. In this report we are presenting a case of wide complex tachycardia with a rare 2:1 VA block.

Case Report

A 28 year old male patient presented to ICCU with complaints of palpitation, anxiety and chest discomfort for 6 hours. This episode was acute in onset. Patient gave past history of acute onset retrosternal chest pain with sweating about 2 months back. Previous medical reports showed that he had suffered from anteroseptal myocardial infarction. He was not thrombolysed then due to late presentation to ICCU.

At presentation, he was anxious, uncomfortable and hemodynamically unstable. His pulse was barely perceptible with unrecordable blood pressure. Physical examination revealed tachypnoea and cold clammy extremities. His 12 lead ECG was recorded which revealed a wide complex tachycardia at the rate of 172bpm with 2:1 VA conduction. A synchronised DC shock of 200 J was given after which wide complex tachycardia reverted to sinus rhythm. After cardioversion his pulse rate was 100/min with few premature beats. BP was 104/80 mmHg. His post cardioversion ECG revealed sinus rhythm with left anterior fascicular block with old anteroseptal myocardial infarction. Routine investigations were normal (Hb 11.1g/dl, TLC 6,400/mm³, N65%, L30%, E2%, M3%, Serum bilirubin 1.0mg/dl, Blood urea 24mg/dl, serum creatinine 1.1mg/dl, Na+ 131.30 mEq/L, K+ 3.86 mEq/L). Colour Doppler echocardiography revealed regional wall motion abnormality in LAD territory and moderate mitral regurgitation with LVEF of 20%. He subsequently underwent coronary angiography (carried out elsewhere) which revealed 100% block in LAD.

The first ECG (Fig. 1) reveals a regular ventricular rate of 172/min. The QRS duration is 160 msec with an axis of -70°. The QRS morphology does not fit in any bundle branch block pattern. Lead V1 shows P wave alternately after each QRS complex (2:1 block). This confirms the diagnosis of VT and suggests retrograde conduction through the AV node. The RP' interval is 220 msec.

Discusion

The site of origin in ventricular tachycardia is usually distal to the bundle of His.[1] SVT can mimic the criteria established for VT due to preexisting BBB, aberrant conduction or due to conduction over accessory pathway.[2] Conversely, ectopic beats

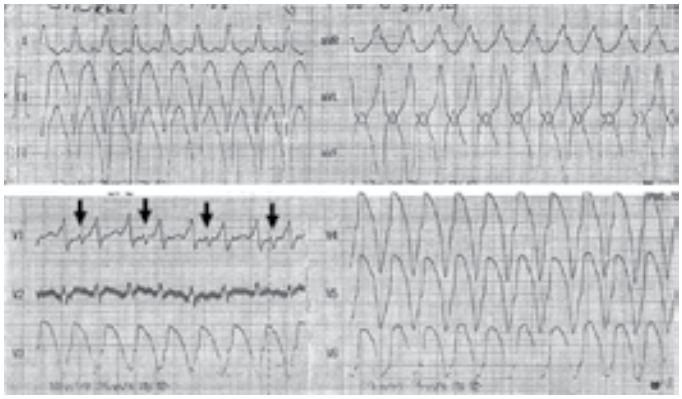

Figure 1 : ECG shows wide complex tachycardia with retrograde atrial activation (shown by arrow) best seen in lead V1.

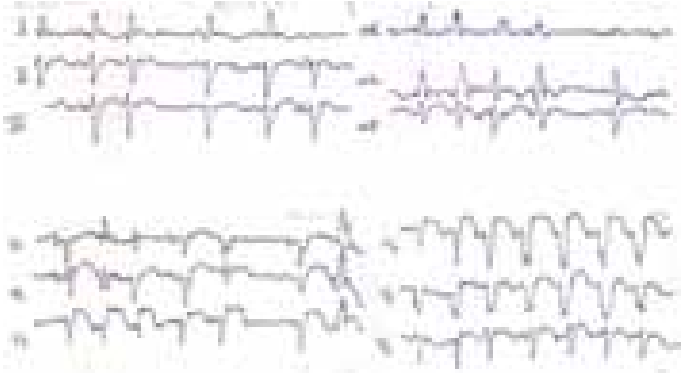

Figure 2 : Post DC shock ECG shows LAFB (left anterior fascicular block) with an anterior wall MI of some duration . There are also a few premature complexes.

originating from ventricle can uncommonly have normal shape and duration.[1]

Usually the ECG diagnosis of VT is based on following findings[3]

1. P:QRS relationship
2. Recognition of capture and fusion beats
3. QRS configuration

1 *P:QRS Relationship*: AV dissociation, when present, is diagnostic of VT.[1] So is variable VA conduction as seen in this patient. This occurs in about 25% of patients with VT.[1]

VA block has been described to be of 3 types.[4]

First degree VA block- It is characterized by a delay in retrograde conduction (R-P' interval exceeding 0.20 sec.).

Second degree VA block- Here there is intermittent interruption of ventricular impulses to atria. This occurs most commonly in 2:1 ratio. Rarely Wenckebach's type VA block may be seen in form of increasing VA intervals terminating in block.

Third degree VA block- In this instance there is AV dissociation.

2. *Recognition of capture and fusion beats* **:** Such beats momentarily capture the ventricle. They provide maximum confidence in favour of VT.[1] In the present case this phenomenon is not seen since there is VA conduction.

3. *QRS Configuration* **:** Classical features in favour of VT are **-** Bizzare frontal plane QRS axis (northwest region), QRS complexes not resembling classic bundle branch block pattern, negative concordant precordial pattern, ventricular extrasystoles observed during normal sinus rhythm resembling VT and presence of initial slurring in lead V1 with LBBB-like morphology.[5]

This ECG exemplifies importance of giving a close look to P: QRS relationship, ventricular rate and QRS pattern to make a certain diagnosis of ventricular tachycardia.

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Clinical Vignette: Irregularly Irregular Wide Complex Tachycardia

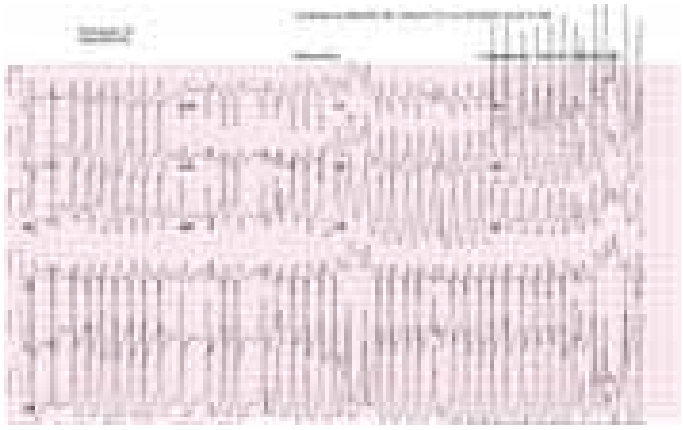

Figure 1 : Preexcited Atrial fibrillation with rapid ventricular response

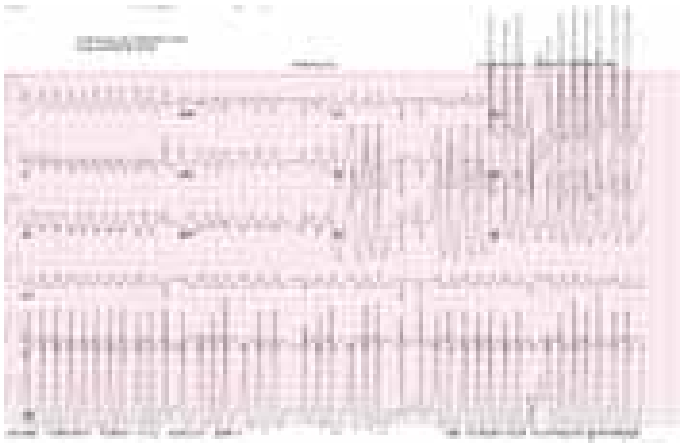

Figure 2 : Preexcited Atrial fibrillation with rapid ventricular response.

Figure 1 and 2, EKGs reveal

A. Irregularly irregular, wide-QRS complex tachycardia with R-R intervals varying from 0.20 to 0.48 second, representing a rate range of 125 to 300/minute.

B. Three types of different QRS complexes are seen :

    1. One narrow, normal QRS complex marked with " normal conduction through the AV node.

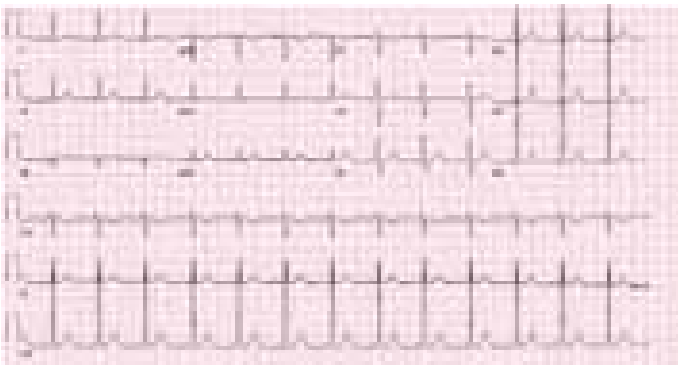

Figure 2 : EKG post cardioversion (subtle delta waves in V4,V5)

    2. Few broad bizarre QRS complexes marked with fusion complexes formed due to conduction over both AV nodal and bypass tract.

    3. Rest of the QRS complexes are wide and of similar shape, due to antegrade conduction through the bypass tract, theraby producing delta wave.

C. Two different morphologies of broad bizarre QRS (figure 1: inferiorly directed axis of delta waves ; figure 2: superiorly directed axis of delta waves).

Since the patient was haemodynamically unstable, he was managed with DC cardioversion at 200 Joules.

The arrhythmia terminated, and subsequent 12-lead electrocardiogram revealed features suggestive of WPW type of pre-excitation syndrome (Figure 2):

1. A slurred, initial upstroke of the QRS complex, which is termed as the delta wave. Delta wave seen in V4, V5.

2. A relatively normal, narrow ensuing terminal QRS

3. PR interval (not short since left sided pathway).

RF ablation was performed to ablate two distinct accessory pathways,

Left lateral and Left posterior.

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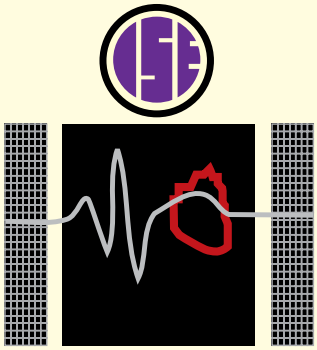

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