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Dronedarone: A New Generation of Anti-arrhythmic Drug for the Treatment of Atrial Fibrillation

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From ¹Department of Medicine & Geriatrics, Princess Margaret Hospital; ²Hong Kong Sanatorium and Hospital, Hong Kong

CHAN ET AL.: Dronedarone: A New Generation of Anti-arrhythmic Drug for the Treatment of Atrial Fibrillation. Amiodarone is currently the most effective anti-arrhythmic drug for the treatment of atrial fibrillation. Its chronic use, however, has been associated with serious extra-cardiac adverse effects. Dronedarone is a new anti-arrhythmic drug that does not possess the different organ toxicities associated with amiodarone. With the addition of a methylsulfonyl group and the removal of iodine moieties, dronedarone has lower tissue accumulation and a shorter half-life than amiodarone. Dronedarone is a potent blocker of multiple ion currents, including the rapidly activating delayed-rectifier potassium current, the slowly activating delayed-rectifier potassium current, the inward rectifier potassium current, the acetylcholine activated potassium current, peak sodium current, and L-type calcium current, and exhibits antiadrenergic and coronary vasodilatory effects. Although less effective than amiodarone as a rhythm-control agent, dronedarone has been shown to reduce ventricular rate and AF recurrence and it is the first anti-arrhythmic drug shown to reduce the combined outcome of cardiovascular mortality and hospitalization in AF patients. Dronedarone, however, is contraindicated in patients with moderate to severe heart failure. The most common side-effects associated with dronedarone are gastrointestinal including nausea, vomiting and diarrhea. This article will review the current evidence of safety and effectiveness of dronedarone in treating patients with atrial fibrillation and the position of this new drug in the currently available anti-arrhythmic armamentarium will be discussed. (J HK Coll Cardiol 2010;18:1-10)

Amiodarone, anti-arrhythmic drug, atrial fibrillation, dronedarone

摘 要
目前心房顫動的治療中，乙胺碘呋酮（胺碘酮）是最有效的抗心律失常藥。但是長期持續服用卻會導致嚴重的內外不良反應。決奈達隆是一種新型的抗心律失常藥物，不會和胺碘酮一樣對不同器官產生毒性。決奈達隆是在胺碘酮基礎上添加了甲硫鎓基團同時去除了碘，因此比胺碘酮更不易在組織中聚集並且半衰期更短。決奈達隆是多種離子泵的有效阻斷劑，包括迅速啓動延遲整流的鈉電流，緩慢啓動延遲整流的鈉電流，內向整流鈉電流，乙醚脂肪酸控制的鈉電流，峰値鈉電流，L 型鈣電流，同時也具有抗腎上腺素能及擴張冠脈的作用。儘管在控制心率方面，決奈達隆不如胺碘酮那麼有效，但在減少心室率及控制心房顫動復發方面已見成效。作爲一線抗心律失常藥，它能同時減少房顫病人心血管死亡率及住院率。但是決奈達隆不能用於中重度心衰病人。決奈達隆最常見副作用為胃腸道反應如噁心、嘔吐、腹瀉。本文將回顧決奈達隆在治療心房顫動病人心安性和有效性的現有證據，並討論這種新藥在當今已有的所有抗心律失常藥物中的地位。

關鍵詞：胺碘酮，抗心律失常藥物，心房顫動，決奈達隆

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. The prevalence of AF increases with age, from 0.7% in people aged 55-59 years to 18% in those older than 85 years. The number of patients suffering from AF in Hong Kong is expected to be on an increasing trend as the proportion of elderly continues to grow. Although not immediately life-threatening, AF does result in significant morbidity, namely a three-fold increase in the risk of congestive heart failure, a five-fold increase in the risk of stroke and a two-fold increase in mortality.

The integral components of treatment for AF include anticoagulation for stroke prevention and either one of the strategies, namely rate-control or rhythm-control. With the currently available anti-arrhythmic drugs for rhythm-control, no difference in the incidence of mortality or stroke could be found between the two strategies. On the other hand, the strategy of rhythm-control resulted in a higher incidence of hospitalizations and drug-related adverse events.

Currently available anti-arrhythmic drugs for the treatment of AF are limited by their suboptimal efficacy and safety. In the AFFIRM study, only 62.6% of patients were maintained in sinus rhythm at 5-year follow-up. 37.5% of patients crossed over from rhythm-control arm to rate-control arm because of development of persistent AF or adverse drug effects. Amiodarone is the most effective anti-arrhythmic drug for AF and is used most commonly in the AFFIRM study. However, it is associated with different organ toxicities, e.g. corneal microdeposits (>90%), hyperthyroidism (0.9-2%), hypothyroidism (6%), liver function derangement (15-30%) and pulmonary toxicity (1-17%), and its long half-life leads to drug accumulation in the body.

There is significant advancement in both non-pharmacological and pharmacological treatment for AF in recent years. Catheter ablation, with evolution over 10 years, has been put as a reasonable alternative to pharmacological therapy to prevent recurrent AF in symptomatic patients with little or no left atrial enlargement. On the other hand, dronedarone, a new generation of anti-arrhythmic drug for the treatment of AF, has been tested in different clinical trials with promising results. The present review focuses on pharmacological and electrophysiological features of dronedarone and the results of major clinical studies with this drug.

Pharmacodynamics and Electrophysiological Properties of Dronedarone

Dronedarone is a synthetic benzofuran, amiodarone derivative that is structurally modified to reduce toxicities associated with chronic amiodarone therapy. The addition of methylsulfonyl group makes dronedarone more water-soluble and less likely to accumulate in organ tissue while the removal of 2 iodine atoms prevent the accumulation of the drug in the thyroid gland and other organs, thus avoiding the organ toxicities of Amiodarone (Figure 1).

Dronedarone has a complex electrophysiological profile with multichannel-blocking properties. It delays the action potential repolarization by blocking both the rapid and slow component of the delayed rectifier potassium current. The blockade of both channels decreases the risk of early after-depolarization and thus torsades de pointes. Dronedarone has also been shown to block the slow L-type calcium current and the sodium current. In addition, dronedarone also inhibits the muscarinic acetylcholine receptor-operated

Figure 1. Chemical structures of dronedarone and amiodarone. (Reproduced from Singh BN. Amiodarone as paradigm for developing new drugs for atrial fibrillation. J Cardiovasc Pharmacol 2008;52:300-5 with the permission from Wolters Kluwer Health)
potassium current. This may contribute partly to the anti-
arrhythmic effect of dronedarone since vagal activation
may be important in the pathophysiology of AF in some
patients.\textsuperscript{12,13}

Similar to amiodarone, dronedarone has
anti-adrenergic effects by antagonizing α and β-
adrenoceptors\textsuperscript{14} and it possesses coronary vasodilating
properties.\textsuperscript{15} These pharmacological properties may lead
to favourable clinical cardiovascular outcomes.\textsuperscript{16}

**Pharmacokinetics of Dronedarone**

Dronedarone is well absorbed by oral route (70-
90\%). Absorption increases by 2 to 3-fold when it is
taken with food. Dronedarone undergoes significant
first-pass metabolism with subsequent reduction of
bioavailability to 15\%. With drug administration of
400 mg twice daily, steady state plasma concentration
was reached in 7 days. The clearance of dronedarone is
mainly non-renal with a terminal half-life of 24 hours.\textsuperscript{17}

Dronedarone is a substrate for and a moderate
inhibitor of CYP3A4.\textsuperscript{18} As a result, dronedarone should
not be given with potent CYP3A4 inhibitors like
antifungals, macrolide antibiotics or protease inhibitors
which may increase dronedarone exposure by as much
as 25-fold. When given together with moderate CYP3A4
inhibitors like verapamil and diltiazam, lower doses of
concomitant drugs should be used to avoid severe
bradycardia and conduction block.

Likely a result of P-glycoprotein-mediated
interaction in the kidney, concomitant administration
of dronedarone with digoxin results in a 1.7 to 2.5-fold
increase in serum concentration of digoxin.\textsuperscript{17} On the
other hand, serum level of simvastatin, a CYP3A4
substrate is increased 2 to 4-fold when given with
dronedarone.

Dronedarone is also a CYP2D6 inhibitor. It
causes a modest increase in bioavailability of metoprolol
in CYP2D6 extensive metabolizers.\textsuperscript{18} Like amiodarone,
dronedarone leads to partial inhibition of tubular
transport of creatinine. This leads to increase in serum
creatinine concentration which is not related to reduced
glomerular filtration or renal function.\textsuperscript{19}

**Rate-Control With Dronedarone (ERATO)**

In the ERATO (Efficacy and Safety of
Dronedarone for Control of Ventricular Rate) study, 174
elderly patients were randomized to receive 800 mg of
dronedarone daily or placebo.\textsuperscript{20} All patients had
suboptimal rate control defined by a resting heart rate
of ≥80 beats per minute despite prior rate-control
therapy with β-blockers, digoxin or calcium channel
blockers. Majority of patients had structural heart
disease but none had severe heart failure.

In the ERATO study, a satisfactory ventricular
rate reduction of 11.7 beats per minute at rest and 24.5
beats per minute during exercise was achieved in
patients taking dronedarone. However, no change in
exercise tolerance was observed in the dronedarone
group. There were no adverse interactions between
dronedarone and other rate-control drugs or
anticoagulants, apart from a 41\% increase in serum
digoxin level. While there were no occurrence of organ
toxicity or pro-arrhythmia, the general incidence of side
effects including gastrointestinal problems were
relatively higher in the dronedarone arm compared to
the placebo arm.

**Rhythm-Control With Dronedarone (DAFNE, EURIDIS and ADONIS) (Table 1)**

DAFNE (Dronedarone Atrial Fibrillation Study
After Electrical Cardioversion) was a prospective,
randomized and dose-finding study. Two hundred and
seventy patients with persistent AF were randomized
to receive dronedarone 400 mg BD, 600 mg BD,
800 mg BD or placebo.\textsuperscript{21} There was a dose-dependent
conversion to sinus rhythm in 5.8\%, 8.2\% and 14.8\% of
patients in the 3 dose groups, respectively, compared
to 3.1\% in the placebo group. Upon failure of conversion
to sinus rhythm within 5-7 days of dronedarone
treatment, patients were electrically cardioverted. One
hundred ninety-nine patients who were in sinus rhythm
were planned to take dronedarone for 6 months.

The primary endpoint in DAFNE was the time to
DRONEDARONE

Table 1. Summary of major clinical trials on dronedarone

<table>
<thead>
<tr>
<th>Trial</th>
<th>Subjects enrolled</th>
<th>Follow-up period</th>
<th>Main outcome</th>
<th>Common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAFNE</td>
<td>N=270 Persistent AF</td>
<td>6 months</td>
<td>First AF recurrence was 5.8% with 800 mg, 8.2% with 1200 mg and 14.8% with 1600 mg dronedarone vs 3.1% in placebo (p=0.0261)</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>EURIDIS and ADONIS</td>
<td>N=612 in EURIDIS N= 625 in ADONIS Paroxysmal AF</td>
<td>12 months</td>
<td>First recurrence of AF/AFL was 64.1% with dronedarone vs 75.2% with placebo (p&lt;0.001)</td>
<td>Gastrointestinal (diarrhea)</td>
</tr>
<tr>
<td>ERATO</td>
<td>N=174 Permanent AF</td>
<td>6 months</td>
<td>Reduction of 11.7 beats per minute in ventricular rate at day 14 (p&lt;0.0001) - this effect was sustained for the duration of trial (-8.8 beat/minute at 4 months) (p&lt;0.001)</td>
<td>Infections</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANDROMEDA</td>
<td>N=627 NYHA Class III/IV CHF or PND plus LVEF&lt;35%</td>
<td>13 months (including additional 6 months after premature discontinuation of study)</td>
<td>Premature termination of trial due to excess mortality related to the worsening of heart failure in dronedarone group (hazard ratio of 2.13; 85% CI 1.07 to 4.25; p=0.003)</td>
<td>Worsening heart failure Increase in serum creatinine levels</td>
</tr>
<tr>
<td>ATHENA</td>
<td>N=4628 Paroxysmal/persistent AF/atrial flutter plus at least one additional cardiovascular risk factor</td>
<td>21 months</td>
<td>First hospitalization due to cardiovascular events or death was 31.9% in dronedarone group vs 39.4% in placebo group (hazard ratio of 0.76; 95% CI 0.69 to 0.84; p&lt;0.001)</td>
<td>Gastrointestinal (diarrhea, nausea) Increase in serum creatinine levels Rash, bradycardia</td>
</tr>
</tbody>
</table>

AF=atrial fibrillation; NYHA=New York Heart Association; CHF=congestive heart failure; PND=paroxysmal nocturnal dyspnoea; LVEF=left ventricular ejection fraction.

First recurrence of AF defined as any documented episode of duration ≥10 minutes, during the 6 months of follow-up. Dronedarone 400 mg BD was found to significantly prolong the time to first AF recurrence compared to placebo (60 days vs 5.3 days, p=0.001). The ventricular rates during AF recurrence also decreased significantly and in a dose-dependent manner. After 6 months, 35% of patients taking dronedarone 400 mg BD and 10% of patients in the placebo group were in sinus rhythm respectively. The higher doses of dronedarone 600 and 800 mg BD were found to lead to higher discontinuation rates with no significant incremental effects on maintenance of sinus rhythm, suggesting a bell-shaped dose-effect curve of dronedarone on rhythm-control. DAFNE has established an optimal dose of 400 mg BD of dronedarone for subsequent clinical studies.

The results of DAFNE drove the implementation of two pivotal trials on dronedarone. They were EURIDIS (European Trial in Atrial Fibrillation or Flutter...
Patients Receiving Dronedarone for the Maintenance of Sinus Rhythm) and ADONIS (American-Australian-African Trial With Dronedarone in Atrial Fibrillation/Flutter Patients For the Maintenance of Sinus Rhythm). They were multi-center, placebo-controlled, double-blinded studies with similar designs performed in different parts of the world. The presence of at least one episode of AF within the last 3 months and the presence of sinus rhythm that persisted at least 1 hour preceding randomization were pre-requisites for recruitment. Both studies had a 1-year follow-up period. A total of 1,237 patients were randomized to receive dronedarone 400 mg BD or placebo in a ratio of 2:1. The time to first recurrence of AF or atrial flutter was the primary endpoint.

Combining EURIDIS and ADONIS, dronedarone 400 mg BD was shown to significantly prolong the median times to first AF recurrence compared to placebo (116 days vs 53 days). AF recurrence rates at 1 year was 64.1% in the dronedarone arm and 75.2% in the placebo arm (HR 0.75, 95% CI 0.65-0.87, p<0.0001). On the other hand, 37.7% and 46% of patients in the dronedarone and placebo arms, respectively suffered from symptomatic recurrences (p<0.001). Both studies demonstrated significantly lower mean ventricular rates in the dronedarone arms during AF recurrence compared to placebo arms. There was no significant difference in the percentage of patients reporting adverse events between the 2 groups (67.4% in dronedarone group vs 62.8% in placebo group). Study discontinuation rates due to adverse events were 9.5% with dronedarone and 6.1% with placebo. Gastrointestinal symptoms, primarily diarrhea, were more commonly encountered in the dronedarone group.

The results indicated that dronedarone was effective increasing the time to first AF recurrence (116 days in the dronedarone group compared with 53 days in the placebo group (HR=0.75, 95% CI, 0.65-0.87, p<0.0001) and in reducing ventricular rate. The proportion of patients who remained free of symptomatic AF or AFL after 1 year was 62.3% (25% risk reduction when compared with placebo, p<0.001) in the dronedarone group. Post-hoc analysis also revealed a 27% reduction in all cause hospitalization and death (22.8% vs 30.9%, p<0.01). Even though there was a 2.4% increase in serum creatinine in the dronedarone group, discontinuation rates due to adverse events were low (9.5% with dronedarone and 6.1% with placebo).

**Dronedarone in Heart Failure (ANDROMEDA)**

Dronedarone has been studied in patients with moderate to severe heart failure. ANDROMEDA (Antiarrhythmic Trial With Dronedarone in Moderate-to-Severe Congestive Heart Failure Evaluating Morbidity Decrease) was a mortality trial in which dronedarone was compared with placebo in patients with moderate to severe heart failure, regardless of presence of AF history. Patients hospitalized with symptomatic heart failure who had suffered at least one episode of dyspnoea on minimal exertion or at rest (NYHA Class III-IV) or paroxysmal nocturnal dyspnoea within a month before admission were randomized to receive dronedarone 400 mg BD or placebo. Left ventricular ejection fraction ≤35% was a pre-requisite for inclusion. The trial was stopped prematurely 7 months after the first patient had been randomized due to excess mortality in the dronedarone arm. Twenty-five patients (8.1%) in the dronedarone arm and 12 patients (3.8%) in the placebo arm died (hazard ratio 2.13, 95% CI 1.07-4.25, p=0.027) (Figure 2). The excess mortality in the dronedarone arm was primarily due to worsening of heart failure, with the mortality risk highest in those with the most severely reduced left ventricular systolic function. There are a few possible explanations for this observation. Firstly, the small mortality difference of 13 patients between the two arms might have occurred by chance due to early termination of the study. Secondly, potent inhibition of peak sodium current and resultant impairment of ventricular contractility by dronedarone may cause worsening of heart failure. Lastly, a retrospective analysis identified a higher death rate in patients who were withdrawn from angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers in response to a rise in creatinine level with dronedarone. However, the contribution of this to
the increased mortality in the dronedarone arm is uncertain. Regardless of the exact mechanism, ANDROMEDA study does define a subset of patients not suitable to receive dronedarone.

**Clinical Cardiovascular Outcome Study for Dronedarone (ATHENA)**

The ATHENA (A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg bid for the Prevention of Cardiovascular Hospitalization or Death from any Cause in Patients with Atrial Fibrillation/Atrial Flutter) trial was a landmark study which evaluated the impact of adding dronedarone to standard rate controlling agents and anticoagulants in the management of AF. The study was designed to compare the effect of dronedarone 400 mg BD with placebo in a randomization ratio of 1:1, on the prevention of cardiovascular hospitalization or mortality. Patients with paroxysmal or persistent AF or atrial flutter and at least one additional risk factor for cardiovascular events, including age $\geq 75$ years, hypertension, diabetes mellitus, prior stroke or transient ischaemic attack, left atrial enlargement of $\geq 5$ cm or depressed left ventricular ejection fraction of $<40\%$ were enrolled. The presence of advanced congestive heart failure was one of the exclusion criteria. The primary endpoint was first cardiovascular hospitalization or mortality from any cause and the secondary endpoints included mortality from any cause, cardiovascular mortality and first cardiovascular hospitalization.

With a mean follow-up duration of $21\pm5$ months, 32% of patients in the dronedarone arm and 39% of patients in the placebo arm reached the primary endpoint (HR 0.76, 95% CI 0.69-0.84, p<0.001) (Figure 3). Dronedarone reduced the first cardiovascular hospitalizations by 26% (p<0.001), and cardiovascular mortality and arrhythmic mortality by 29% (p=0.034) and by 45% (p=0.01) respectively. However, all-cause mortality was not significantly different between the two groups.

The rate of drug discontinuation was not significantly different between the groups (12.7% in the dronedarone group vs 8.1% in the placebo group). However, the frequency of gastrointestinal (26.2% vs 22%) and dermatologic (10.3% vs 7.6%) adverse effects and the frequency of increased creatinine levels (4.7% vs 1.3%) were significantly higher in the dronedarone
arm compared to the placebo arm. Regarding the incidence of pulmonary and thyroid adverse effects, no significant difference was observed between the two groups.

A post-hoc analysis revealed that patients who received dronedarone experienced a 34% reduction in the risk of stroke (HR=0.66, 95% CI=0.46-0.96, p=0.03) and a 30% reduction in hospitalization due to acute coronary syndrome (HR=0.70, 95% CI=0.51-0.79, p=0.03).24 Interestingly, patients who remained in AF after treatment also experienced improved outcomes with dronedarone and that the benefits of treatment were not limited to patients who were converted to sinus rhythm.25

**Dronedarone versus Amiodarone (DIONYSOS)**

Dronedarone was compared to amiodarone directly with respect to safety and efficacy for sinus rhythm maintenance in patients with AF in DIONYSOS.
DRONNEDARONE

(Dronedarone versus Amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation). The study compared dronedarone 400 mg BD with amiodarone 200 mg daily (with loading of 600 mg daily for 4 weeks) during a mean follow-up of 7 months in 504 patients with documented AF of >72 hours for whom cardioversion and anti-arrhythmic drugs were indicated. The primary endpoint was recurrence of AF or drug discontinuation as a result of drug intolerance or lack of efficacy.

In DIONYSOS, fewer amiodarone-treated patients reached the primary endpoint compared with those treated with dronedarone (55.3% vs 73.9%, p<0.001). Droneraone was less effective in maintaining sinus rhythm compared to amiodarone after cardioversion (AF recurrence post-cardioversion in the dronedarone and amiodarone arm was 36.5% and 24.3% respectively). More gastrointestinal adverse events, namely diarrhea, vomiting and nausea and fewer cardiac adverse events, namely bradycardia (2% vs 6.3%) and QTc prolongation (10.9% vs 20.5%) were noted in the dronedarone arm.

A study comparing dronedarone with other anti-arrhythmic drugs on major morbidity and mortality outcomes in the treatment of AF, using a mixed treatment comparison was recently reported. Dronedarone was compared to other anti-arrhythmic drugs, namely amiodarone, flecainide, propafenone and sotalol in terms of all-cause mortality, stroke and serious adverse events. For all-cause mortality, 8 randomized controlled trials with 8,252 patients and 349 deaths were included. There was no increase in mortality with use of dronedarone compared to placebo. There was significantly less mortality comparing dronedarone with amiodarone (p=0.032) or sotalol (p=0.009). For stroke, 5 randomized controlled trials with 7,034 patients and 138 strokes were included for analysis. Dronedarone was shown to decrease risk of stroke compared to placebo (p=0.015). No significant reduction of stroke was present with use of amiodarone or sotalol compared to placebo. However, no significant difference can be shown in the risk of stroke among different anti-arrhythmic drugs. For serious adverse events, 18 randomized controlled trials with 8,351 patients and 1,433 serious adverse events were included. Compared to placebo, no significant difference was found for all anti-arrhythmic drugs. And there was also no significant difference in serious adverse events between different anti-arrhythmic drugs.

Position of Dronedarone in the Anti-arrhythmic Armamentarium

The safety and efficacy profile of dronedarone in the treatment of AF has been well studied by different clinical trials, namely ERATO, DAFNE, EURIDIS, ADONIS, ANDROMEDA and ATHENA. It is a new anti-arrhythmic drug with acceptable safety and modest efficacy in rhythm-control for AF. It is also an effective drug for rate-control. Dronedarone is less effective than amiodarone in rhythm-control for AF, as shown by DIONYSOS. However, it has a better safety profile with absence of different types of organ toxicities associated with amiodarone. With safety considered to be a priority in the use of anti-arrhythmic drugs for AF, dronedarone has been proposed to be the first-line agent in maintenance of sinus rhythm in different subsets of patients, except in patients with NYHA Class III or IV heart failure. With the unavailability of dofetilide, an adapted form of anti-arrhythmic treatment algorithm for AF in Hong Kong is suggested in Figure 4. Dronedarone, however, has not been incorporated into contemporary practice guidelines by academic bodies or professional organizations. The evidence for choosing dronedarone over other first-line anti-arrhythmic drugs, at present, is still obscure. However, based on the favourable cardiovascular outcomes in ATHENA, dronedarone is particularly preferred in the patient subset with paroxysmal or persistent AF or atrial flutter and at least one additional risk factor for cardiovascular events.

Conclusions

Dronedarone is a new generation of anti-arrhythmic drug for the treatment of AF. It is the first anti-arrhythmic agent shown to reduce the combined
outcome of cardiovascular hospitalization or mortality in patients with AF. Dronedarone has been shown to maintain sinus rhythm with modest efficacy and control ventricular rate satisfactorily during episodes of AF. When compared with amiodarone, dronedarone is less effective in reducing AF recurrence, but possesses better safety profile. Use of dronedarone, however, should be limited to patients without severe heart failure (NYHA class III or IV) as evidenced by ANDROMEDA.

The tolerability profile of dronedarone is good with gastrointestinal symptoms like nausea, vomiting and diarrhea as the most commonly encountered side effects. There is no clinically significant interaction with warfarin. Some patients may experience prolongation of QTc interval but the occurrence of torsades de pointes is rare. The drug may also cause a reversible increase in serum creatinine level but the effect is not associated with a reduction in renal function.

On the basis of the safety and efficacy portfolio of dronedarone and the favourable cardiovascular outcomes from ATHENA, the new anti-arrhythmic drug has been approved by the United States Food and Drug Administration for use in non-permanent AF or atrial flutter to reduce the risk of cardiovascular hospitalization. In clinical practice, taking safety as the priority, dronedarone may be considered the first-line anti-arrhythmic drug for maintenance of sinus rhythm in AF except in patients with moderate to severe heart failure.

References

2. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed...


Pacing Technology: Advances in Threshold Management

CHUNG-WAH SIU¹ and CHU-PAK LAU²

From ¹Research Center of Heart, Brain, Hormone and Healthy Aging, The University of Hong Kong and ²Cardiology Division, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

SIU AND LAU: Pacing Technology: Advances in Threshold Management. Over the last 5 decades, pacemaker therapy has undergone remarkable technological advances with increasing sophistication of pacemaker features. However, device longevity has remained one of the major issues in pacemaker design ever since the first endocardial pacing lead implantation in 1958. In addition to various hardware design to enhance device longevity, software-based solutions to minimize pacing energy and yet with good safety margin have also been developed. Together with desire and need of fully automatic pacing system in increasingly busy pacemaker clinic, several manufacturers have introduced different automatic threshold management algorithm. This article summarizes the current state of art in pacing threshold management in the modern pacemakers. (J HK Coll Cardiol 2010;18: 11-16)

Capture management, pacemaker

Introduction

With the aging population, there have been an increasing trend in cardiac pacemaker implantation worldwide. In the United States, up to 2.25 million electronic pacemakers were implanted in the period from 1990 to 2002, and the annual implantation rate increased almost 3-fold. Similar trend has also been observed in Hong Kong with over 1,000 electronic pacemaker implanted in 2002. Despite pacemaker therapy has undergone remarkable technologic advances as reflected by the increase in number of circuitry components from a mere two to three transistors in early pacemakers to nearly 1 million components with RAM size up to 124,000 bytes,¹ the need and desire to lengthen device longevity have remained one of the major issues in pacemaker design ever since the first endocardial pacing lead implantation in 1958. Hardware improvements to improve device longevity including high-energy density battery and high impedance, low threshold leads have been developed. Likewise, software-based solutions to pace the cardiac chamber of interest with the lowest feasible energy with good safety margin have also been developed. This article summarizes the current state of art in pacing threshold management in the modern pacemakers.

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J HK Coll Cardiol, Vol 18 April 2010
Capture Management

The primary function of a pacemaker is to pace effectively at an efficient energy output, which in turn depends on the pacing threshold that varies significantly between individuals, and within an individual over time. The intra-individual variation of pacing threshold may occur due to spontaneous threshold rise after implantation, gross or microdislodgment of pacemaker lead, diurnal changes, and changes secondary to drugs and/or myocardial ischemia. From a clinical standpoint, variation in threshold may lead to an inadequate safety margin of stimulation, thus raising potential safety issues. Thereby, the ability to track threshold automatically will maximize patient safety, minimize battery drain for pacing, and, importantly, simplify programming. Furthermore, threshold measurement remains time consuming, and if an alternative and safe method is available, the burden of programming can be reduced. Table 1 lists the reasons necessitating automatic capture management. Several manufacturers have introduced algorithms for detecting ventricular, atrial, and left ventricular (in cardiac resynchronization therapy (CRT)) thresholds. The detection of an evoked response is based on either evoked response or impedance. The threshold data are used either on a beat-by-beat basis to ensure a paced response or intermittently to adjust output parameters.

St. Jude/Pacesetter Autocapture™

St. Jude Medical first introduced the Autocapture™ pacing system in a single chamber Microny™ pacemaker in 1995. It is designed to verify a response which represents capture or myocardial depolarization, to each pacemaker stimulation, and to automatically adjust the pacing output accordingly in a beat-to-beat basis. Specifically, after a ventricular pacing stimulus, the algorithm opens an evoked response (ER) detection window for 46 ms after a 14 ms blanking period, and the detection of an ER is used to diagnose capture (Figure 1). In the event that an ER is not detected (loss of capture), a high energy back-up pulse of 4.5 V is discharged at 100 ms after the ventricular pacing stimulus, to avoid long pauses. If two consecutive back-up pulses have been delivered, the algorithm starts a stimulation threshold search by increasing the output to effect two consecutive captures. In single chamber devices (Microny and Regency SR), a margin of 0.3 V is added. In addition, to avoid pacing at high output due to diurnal fluctuation in threshold, the device automatically performs a threshold search once every 8 hours. A safety margin of 0.3 V is added to the detected threshold. In dual chamber devices, the A-V interval is shortened to 50 ms (Ap) or 25 ms (As) to ensure overdrive of intrinsic ventricular rhythm. In the Affinity DR, automatic decrements and increments of output during threshold search are 0.25 and 0.125V, respectively. In addition, beat-to-beat capture verification has recently been extended to atrial stimulation in Zephyr pacemaker by St. Jude Medical (ACP™ confirm), as the small atrial electrical signal represents a major challenge in discrimination between ER signal and pace-induced afterpolarization.

<table>
<thead>
<tr>
<th>Table 1. Potential benefits of capture management</th>
</tr>
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<tbody>
<tr>
<td>Increase in battery drain (e.g., sensors, electrogram monitoring, and multisite pacing)</td>
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<tr>
<td>Increase in battery longevity</td>
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<tr>
<td>Two-third of patients will be alive at the time of battery replacement</td>
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<tr>
<td>Pacing for populations such as those with AF and after atrioventricular nodal ablation</td>
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<tr>
<td>Reduction in battery size</td>
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<tr>
<td>Physiologic/medical variation in threshold</td>
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<tr>
<td>Reduction in time for pacemaker programming</td>
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</table>
The efficacy as well as the safety of the capture management algorithm depends very much on accuracy of detection of ER. Table 2 lists factors that affect Autocapture detection of ER. One major challenge is the difficulty to discriminate between the ER signal and the pace-induced after potential; for instance, a large electrode polarization artifact relative to size of ER can affect ER detection. This can be reduced either with the use of low polarization electrodes (made possible by increasing the microscopic electrode-tissue interface area), or with a biphasic waveform that comprises a fast precharge followed by a negative postcharge to minimize polarization effect. The effect of a modified fast prepulse on Autocapture™ algorithm was tested in 45 patients with leads from two manufacturers (Medtronic 4024 Cap Sure, and Pacesetter 1450 K/T and 1470 T leads). Whereas the ER was independent of the type of pacing pulse, the polarization artifact was significantly less during the modified pulse compared with the conventional pacing pulse, leading to an improved efficacy of the Autocapture algorithm (94% versus 71% successful ER detection). An adequate ER amplitude of greater than 2.5 mV is recommended before activation of the autocapture algorithm, and this was present in 93% of 60 patients in one study. Neither the clinical data nor the conventional electrical parameters were effective in predicting the size of the ER signal. Body posture and exercise had relatively little effect on the ER. Recently, a new ER algorithm measuring the depolarization integral (area) instead of ER signal amplitudes (voltage) to determine ER has enhanced the accuracy of capture verification; in fact, the algorithm allows ER determination even with old high polarization bipolar leads (Figure 2). Because of the enhanced sensitivity, discrimination of small atrial ER from pace-induced after potential has become possible.

The one-year stability of the algorithm has been tested in a multicenter study involving 113 patients

<table>
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<tr>
<th>Table 2. Factors affecting capture detection</th>
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<tr>
<td>Electrode polarization</td>
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<tr>
<td>Fusion beats (false negative)</td>
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<tr>
<td>Ventricular capture, intrinsic beat</td>
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<tr>
<td>Pseudofusion beats (false positive)</td>
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<tr>
<td>Pacing spike (and failure of capture), intrinsic beat</td>
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<tr>
<td>Algorithm related: Unipolar pacing, bipolar sensing</td>
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<tr>
<td>Adequate ER</td>
</tr>
<tr>
<td>Other applications: atrial, epicardial, and left ventricle</td>
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</tbody>
</table>

Figure 1. Evoked response detection. After a ventricular pacing stimulus, the algorithm opens an evoked response (ER) detection window for 46 ms after a 14 ms blanking period, and the detection of an ER (voltage) is used to diagnose capture.
implanted with Pacesetter Microny SR+. Evoked response was satisfactory for Autocapture in 102 of 113 patients, and the evoked response was stable over time. Furthermore, both the acute and chronic pacing thresholds measured at the clinic using VARIO significantly correlated with that derived from Autocapture, despite that the Autocapture threshold was higher (0.11 ± 0.22 V) owing to the way in which threshold was derived. During Holter recordings, there was no failure of ventricular capture, and back-up pulses were used in 1.1% of all paced beats. Most were due to fusion or pseudofusion beats (87%), undersensing of either R wave or ER (4.6%), and truly due to loss of capture in only 7%. Although these did not affect pacing performance, the need for back-up pulses may negate the energy saving by the Autocapture itself. Consistently, similar positive results from the Autocapture algorithm in medium term for safety and efficacy have also been published. Compared with the factory-set pacemaker setting of 5 V, Autocapture™ algorithm reduced the energy drain in the Microny SR+ (with 0.35 Ah), which translated into an increased device longevity by 53%. For the Regency SR+ with a larger battery (0.79 Ah), the increase in device longevity was more remarkable (245%). However, when the conventional output was reduced to 2.5 V, the benefit of Autocapture on battery life was much less impressive.

**Boston Scientific Automatic Capture**

Likewise, the automatic capture algorithm from Boston Scientific provides also a beat-to-beat verification of myocardial capture based on the ventricular ER. The ventricular voltage output was automatically adjusted to 0.5 V above the measured threshold. Upon the occurrence of loss of capture, a backup pacing pulse 1.5 V higher than the measured threshold is delivered 100 ms after the primary stimulus. When loss of capture is confirmed for two cycles out of four beats, an automatic threshold test will check for the new threshold.

**Biotronik Capture Control**

The Logos pacemakers from Biotronik measure the ER signals from several successful capture beats, in order to generate a reference curve, against which failure of capture is compared. There are no back-up pacing pulses, but persistent loss of capture results in increase of pulse output in 2 V steps. After a programmable period of time, the output is reduced to the programmed value. This algorithm ensures patient safety through beat-by-beat capture verification.

**Medtronic Ventricular Capture Management**

The Kappa 700 pacemakers from Medtronic incorporate a threshold assessment based on ER: the Pacing Threshold Search (ambulatory) and Capture

Figure 2. Evoked response detection with depolarization integral (area) to determine ER.
Management Threshold Test (bedside). During the procedure, the threshold at the Rheobase is determined at 1 ms by amplitude decrement until loss of capture followed by amplitude increment until capture confirmed. The Chronaxie is then determined by doubling the programmed amplitude, and decreasing the pulse width (followed by increasing amplitude to capture). A recommended pacing setting is then determined. The physician can use the ambulatory threshold data to automatically adjust the threshold (adaptive), or to use for monitoring only, or the algorithm can be turned off. A minimal adapted output needs to be programmed. The ventricular capture management can be activated once every 15 minutes for 42 days, and is not a beat-by-beat threshold tracking algorithm. In a predictive analysis, the device longevity of Medtronic Kappa 700 series pacemakers featuring three automatic algorithm including Capture management, Sinus Preference, and Search AV was tested in 22 patients. The overall longevity with all three features programmed was estimated to be 106.3±8.4 months with 8.1±5.8 months more compared with that without Capture management and Search AV.

Summary

The increased sophistication in pacemaker technology has led to pacemaker features that average pacemaker implanters may not have the time either to understand or to program appropriately, as well as prolonged pacemaker interrogation time during regular follow-up. The automaticity of the optimization of many pacing parameters has significantly facilitated daily clinical management. In fact, programming of threshold can be simplified as the algorithm-determined threshold was significantly correlated with conventional threshold assessment. The main benefit of automatic pacing threshold algorithm is to maintain effective capture during threshold changes, to prolong device longevity and to ensure patient safety. These algorithms have been demonstrated to be safe and useful for prolonging device longevity.9,11,18

References

Hong Kong College of Cardiology

Eighteenth Annual Scientific Congress

May 14-16, 2010
Sheraton Hong Kong Hotel and Towers
Hong Kong

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Scientific Programme

Friday, May 14, 2010

0800  
Registration

0900-1030  
**Free Paper Session**  
Coronary Artery Disease I  
Cardiac Arrhythmias, Electrophysiological Studies and Cardiac Rehabilitation

1030-1100  
Coffee Break  
Visit Exhibits

1100-1230  
**Free Paper Session**  
Percutaneous Coronary Intervention and Coronary Artery Disease II  
Cardiac Imaging and Coronary Risk Factors

1230-1400  
Light Lunch

1400-1515  
**Free Paper Session**  
Cardiac Surgery  
Miscellaneous

1515-1600  
**Plenary Lecture**  
Time Delay to Treatment for Acute ST-segment Elevation Myocardial Infarction in Beijing  
Dayi Hu

1600-1630  
Coffee Break  
Visit Exhibits

1630-1730  
**Plenary Lectures**  
Long Term Clinical Outcomes of Using SKB Technique to Treat Special LAD Ostial Lesion -  
An Innovative Approach on LAD Ostial Stenosis  
Jilin Chen  
The Journey of an Ideal Stent  
Harry Suryapranata

1730-1830  
**Best Paper Oral Presentation**

1845-1900  
**Opening Ceremony**

1900-2000  
**Hong Kong Heart Foundation Lecture**  
Transradial Intervention for Left-main Bifurcation Lesion  
Yuejin Yang

2000-2130  
**Welcome Dinner**
Saturday, May 15, 2010

0745  Registration

0815-1200  Joined Symposium - Cross-strait Medicine Exchange Association of Ministry of Health / Hong Kong College of Cardiology

Guidelines and Practice: Clinical Case Based Conference (GAP-CCBC)
(Presentation in English or Putonghua)

Wellen’s Syndrome
Lianfang Chang

Retrograde CTO Intervention
Yawei Xu

Emotional Problem - Fever and Dyspnea
Shaoliang Chen

Ventricular Fibrillation and No-reflow in CTO PCI
Haojian Dong

The Practice of Compromise in CTO PCI
Jianan Wang

Coronary Perforation During PCI
Yan Wang

Fever and Short of Breath
Ligang Fang

Iatrogenic Aortocoronary Dissection During CTO PCI
Weimin Li

Acute Coronary Syndrome with Fever
Jiangli Han

Left Main Dissection
I-chang Hsieh

Recurrent Chest Pain After CABG
Chiu-lai Fu

0930-1030  Allied Cardiovascular Health Professionals Symposium
Learn the Clinically Important ECGs in 2 Hours
Wide Complex Tachycardia
Yat-sun Chan

Narrow Complex Tachycardia
Andy Wai-kwong Chan

1100-1200  Allied Cardiovascular Health Professionals Symposium
Learn the Clinically Important ECGs in 2 Hours
Bradycardia and Normal Variant
Kwok-keung Chan

Cardiac Emergency
Chi-wo Chan
1200-1330: **Lunch**

1330-1500: **Eli Lilly Symposium**
- Optimizing Antiplatelet Therapy in ACS-PCI - Challenges and Solutions
  Murtaza Qasuri
- Improving Clinical Outcomes in ACS-PCI with Optimal Antiplatelet Therapy - Evidence from TRITON TIMI 38
  Derek Peng-beng Chew

1500-1600: **Sixth Congregation of HKCC**

1600-1730: **Abbott Vascular Symposium**
- Guide Wire Selection in Chronic Total Occlusions
  Craig A. Thompson
- Vascular Restoration Therapy: The Abbott Vascular's Bioresorbable Vascular Scaffold Program
  Douglas V. Follett
- Transferability of Data Between Different Drug-eluting Stents
  Bernard Bun-lap Wong

1730-1900: **Plenary Lectures**
- Biodegradable Polymer DES in Complex Lesions
  Satoru Sumitsuji
- Statin Therapy: Optimising the Benefits
  Brian Tomlinson
- Atherosclerosis in Youth
  Dong Zhao

1915-2030: **Evening Symposium on Percutaneous Valvular Intervention**
- The New Era in Treating Aortic Stenosis - TAVI
  David Muller
- MitraClip - An Innovative Mechanical Solution to Mitral Regurgitation
  Cheung-wah Cheng
  Steven Siu-lung Li

2030-2200: **Dinner**

* Coffee will be served from 1000-1100 and 1700-1800 at 4/F of Sung Terrace.
Sunday, May 16, 2010

0800   Registration

0830-1030  **Plenary Lectures**
Intervention in STEMI Patients with Left-main Occlusion
Lefeng Wang

Clinical Evidence that Early CRT Intervention Slows Heart Failure:
MADIT-CRT and 8 Years Result of MADIT II
Yat-sun Chan

ER Niacin / Laropiprant: A Novel Approach to Comprehensive Lipid Management
Albert Wai-suen Leung

Resolving Unmet Needs with Revolutionary Technologies
   i)  Resolute All Comers Trial
   ii) Breakthrough Technology in Treating Cardiovascular Disease
David Muller

1030-1100  Coffee Break
Visit Exhibits

1100-1300  **PCI Cases Discussion**
Prize Presentation

1300-1430  Lunch

1430-1630  **Joined Symposium - Asian Pacific Society of Cardiology / Hong Kong College of Cardiology**
Management of Heart Failure in 2010
Role of Neurohormones in Guidance of Heart Failure Therapy
A. Mark Richards

Application of Biventricular Pacing System: Paradigm Shift from Heart Failure to
   Non-systolic Heart Failure Patients
Cheuk-man Yu

Advances in Echocardiographic Imaging for Heart Failure with Normal Ejection
Gabriel Wai-kwok Yip

Non-pharmacological Treatment of Heart Failure
Wing-kuk Au

1630-1700  Coffee Break
Visit Exhibits

1700-1830  **Plenary Lectures on Cardiac Arrhythmia**
New Era in CRT: A True Haemodynamic Sensor for Auto-synchronization
Gerry Kaye

Cardiac Contractility Modulation (CCM) - From Basic Concepts to Clinical Practice
Yat-sun Chan

Atrial Fibrillation Ablation: Is Now Prime Time for Routine Clinical Practice?
Jeffrey Wing-hong Fung

1830-1930  **Plenary Lectures on Cardiac CT & MRI**
The Evolving Role of Cardiac CT in the Management of Coronary Artery Disease
Chi-ming Wong

Cardiac MRI in Acute Myocardial Infarction
Shang-jen Shu

1930-2100  Farewell Dinner
Paediatric Cardiology Programme

Friday, May 14, 2010

1400-1530  Paediatric Cardiology Symposium I

Echo Determinants of One vs Two Ventricular Repair  
Gerald Ross Marx

Early and Long-term Results for Correction of Total Anomalous Pulmonary Venous Drainage  
Bing Jia

Slide Tracheoplasty  
Lik-cheung Cheng

1600-1630  Coffee Break  
Visit Exhibits

1630-1730  Free Paper Session  
Paediatric Cardiology I

Saturday, May 15, 2010

0900-1030  Paediatric Cardiology Symposium II

Recent Clinical Applications of 3D Echo in CHD  
Gerald Ross Marx

Retrospective Study on Transcatheter Closure and VSD Surgery Repair of Congenital Ventricular Septal Defect in Children Focusing on Efficacy and in Mid-term and Long-term Follow-up Result  
Zhiwei Zhang

Pulmonary Artery Hypertension Associated with Congenital Heart Disease  
Lin Wu

1030-1100  Coffee Break  
Visit Exhibits

1100-1200  Free Paper Session  
Paediatric Cardiology II
ABSTRACTS
Abstracts for Free Paper Session:

CORONARY ARTERY DISEASE I

1. Resting Echocardiography for the early detection of Acute Coronary Syndromes in Chest Pain Unit Patients
V M Parato, D DeBlasio, S Amambly, M Partemi, D Rossi, E Nardini
Chest Pain Unit, Cardiology Dept, C. and G. Mazconzi Hospital, Ascoli Piceno, ITALY

Aim: The purpose of this study is to assess the ability of resting echocardiography to detect an acute coronary syndrome (ACS) before the occurrence of ischemic ECG changes or Troponin-T elevations.

Methods: 403 patients who presented to the ER with chest pain, normal ECGs, and normal Troponin-T levels were admitted to the cardiological-run Chest Pain Unit (CPU) for further monitoring. They underwent serial resting echocardiography for monitoring of left ventricle wall-motion (LVWM), ECG telemetry monitoring, and serial Troponin-T measurements.

Results: An ACS was detected in 49 patients (12.1%). These 49 patients were then subdivided into 3 different groups based on the initial mode of detection of their ACS. In group A, 16/49 (32.6%) patients had ACS shown by echocardiographic detection of LVWM abnormalities. In group B, 24/49 (48.9%) patients had an ACS detected by ischemic ECG changes. In group C, 9/49 (18.3%) patients had an ACS detected by Troponin-T elevations. The shortest time interval between CPU-admission and ACS-detection occurred in group A (A vs.B vs.C: p<0.005; A vs.C: p<0.001). In group A, cardiac angiogram showed that the culprit coronary lesion was more frequently in the circumflex artery (11/16; 68.7%) (LCx vs.LAAD: p=0.02; LCx vs.RCA: p<0.001) and of these 11 patients with circumflex lesions, the ECG was normal in 8 (72.7%).

Conclusions: This study demonstrates the utility of LVWM monitoring by serial echocardiography as part of a diagnostic protocol that can be implemented in a CPU. Furthermore, echocardiography could become an essential tool used in the diagnosis of ACS secondary to circumflex lesions.

2. Relation of Glycated Haemoglobin to Cardiovascular Outcome in Non-diabetic Adults with Acute Coronary Syndrome
YH Cheng, MKY Lee, CK Kwok, NH Luk, WS, Kwan, SF Chui, KC Chan, LK Chan, CY Wong, HS Ma, LY Tam, CL Fu, CW Chan, KT Chan, KC Ho, CS Chiang; Division of Cardiology, Department of Medicine, Queen Elizabeth Hospital, Hong Kong

Objective: To evaluate the value of glycated haemoglobin (HbA1c) in predicting cardiovascular outcome in non-diabetic adults admitted for acute coronary syndrome.

Patients and Method: This is a prospective cohort study of the patient being treated for acute coronary syndrome (ACS) in the coronary care unit of Queen Elizabeth hospital. A total of 122 patients admitted between 1st January 2009 to 31st March 2009 were enrolled. Blood sample was taken for HbA1c on admission. Demographic and clinical characteristics of the patients were recorded and clinical outcome were analyzed at the end of thirty days.

Results: 86 out of 122 patients did not have any previous diagnosis of diabetes. Sixty-five percent were male (56 males; 30 females; mean age= 68; range 34-85). The mean HbA1c was 6.47% (+/-1.42). Patients with admission HbA1c ≥ 6.0 % had higher fasting glucose (8.5mmol/l vs 7.2mmol/l p<0.03), lower ejection fraction (41.5% +/- 11.5 vs. 54% +/- 10.3) and more common to have multi-vessel disease (53.5%). HbA1c was an independent predictor of 30-day death from cardiovascular causes with an odds ratio of 2.87 (95% CI= 1.43-6.26) after adjustment for other confounding variables.

Conclusion: Glycated haemoglobin had a role of predicting cardiovascular outcome in non-diabetic adults.

3. Impact of Bleeding Risk on Prognosis of Patients with Acute Coronary Syndrome (ACS)
Lingling Cheng, Chi-Kin Chan, Chi-Lun Yuen, Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Kowloon, Hong Kong

Background: Bleeding complication has become a major concern associated with contemporary treatment of acute coronary syndrome (ACS). However, the high bleeding risk group has not been well characterized and the impact of bleeding on clinical outcome has not been extensively studied in the local population.

Methods: The study included consecutive patients admitted to coronary care unit, United Christian Hospital from 1/2007 till 12/2007 who presented with ACS. The primary outcome was all-cause mortality. Bleeding events after the onset of ACS were documented:

Results: The study recruited a total of 135 patients including 118 ST elevation myocardial infarction (STEMI), 34 Non-ST elevation myocardial infarction (NSTEMI) and 3 unstable angina. Patients with major bleeding were older (≥70 years old), had lower body weight (<50 kg), impaired renal function (CrCl<50ml/minute) and poor left ventricular ejection fraction (<40%). At 1 year follow-up, seven patients developed major bleeding and six of them died, whereas approximately 1 in 5 patients who did not have major bleeding experienced death. Major bleeding as a time-dependent covariate was independently associated with 1-year mortality after adjusting for demographic, cardiovascular risk factors and co-interventions (hazard ratio= 6.89, 95%CI 1.81-26.30; P=0.005). The impact of bleeding on mortality was shown to be dose related and persisted throughout the follow-up period. Gastrointestinal bleeding (GIB) was a common cause of major bleeding in this study.

Conclusion: The study emphasized the adverse prognostic implication of major bleeding as a complication of ACS treatment, hence should prompt further research on reduction of bleeding, especially GIB. In order to further improve clinical outcomes, patients at high risk of bleeding should first be considered for prophylaxis against GIB.

4. Review of STEMI treatment in a regional hospital in Hong Kong: Recent cases analysis of time-delay in the treatment of ST elevation myocardial infarction (STEMI).
JF Cheung, CH Chan, CS Yuen, Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Kowloon, Hong Kong

Background: "Time is muscle", Benefit of reperfusion in time-dependent. Timely reperfusion therapy for STEMI is the target. We aim at reviewing the causes of time-delay for reperfusion therapy in STEMI patients.

Methods: All STEMI patients admitted our Coronary Care Unit (CCU) from 1st Jan 2009 to 31st Dec 2009 were selected. The time of symptoms onset and the individual time from accident and emergency department (AED) in treatment received were reviewed. The causes for the time delay were analyzed. Median treatment time was selected because "median" treatment time would be usually skewed by time falling in extreme range.

Results: There were totally 136 STEMI presented to our CCU in 2009. Seventy-two patients (52.9% STEMI) received fibrinolysis. The median door-to-needle time (DNT) was 44.5min. 25.8% of patients had door-to-needle time within 30min. Thirty-right PCI (28% STEMI) were performed in our center in 2009. The median door-to-balloon time (DBT) was 80min. 52.5% of patients had door-to-balloon time within 90min. Twenty-six patients (19% STEMI) did not receive fibrinolysis therapy. For all these STEMI patients, the median door-to-ECG time (DE) was 8 min. Fourteen patients (19.3%) had no typical ST segment changes from first ECG in AED, and 12 patients (8.5%) had diagnosis of STEMI after admission to ward. The median symptom onset to AED time was 100min. Seventy-six patients (38% STEMI) had symptom onset to AED time within 120min. For those patients received fibrinolytic, forty-nine patients had DNT time more than 30min. Eleven patients (22.4%) had vague presentation and delayed DNT. Seven patients (14.3%) started fibrinolytic in CCU and were delayed by transportation. Six patients (12.2%) did not have diagnostic ECG changes in AED and need further observation in ward. For those STEMI patients received PCI. Eighteen patients had DBT more than 90min. Their median length of stay in AED was 4min. Four patients (22.2%) had vague symptoms and delayed DE. Three patients (16.7%) did not have diagnostic ECG changes in AED and need further observation in ward. Two patients (11.1%) were delayed by further diagnostic CT scan. Three patients (16.7%) were delayed by operation while being operated.

Conclusion: Early presentation and early diagnosis is the key for timely reperfusion therapy for STEMI. High suspicion for patients with vague symptom and early ECG assessment can reduce time-delay for diagnosis. fibrinolysis should be started in AED as possible, once diagnosis is made. Suspected STEMI patients should be closely monitored in AED or in ward for new ECG or clinical changes. Public education for early attendance to AED for typical chest pain, especially present pain more than 30 min, can reduce the total ischemic time. ECG in ambulance and activation of AMI team before AED arrival may reduce length of stay in AED.
ABSTRACTS

Abstracts for Free Paper Session:

5. Mortality in real life STEMI patients receiving fibrinolitics: a local hospital experience

Ling-fong Chan, Chi-Kin Chan, Chu-an Yuen. Division of Cardiology, Department of Medicine and Genetics, United Christian Hospital, Kowloon, Hong Kong.

Background: The mortality of ST elevation myocardial infarction (STEMI) has been improving in recent studies due to the advance of pharmacotherapy and coronary angioplasty. However, there is still significant variation in different real-life patient cohorts. It is therefore essential to have a more comprehensive understanding of the outcome of STEMI patients in our local cohort of Chinese patients with a view to identifying room for improvement.

Methods: The aim of this study was to evaluate 7-day, 30-day, 180-day clinical outcome of STEMI patients in a series of unselected prospectively collected consecutive patients admitted to Coronary Care Unit, United Christian Hospital from 1/1/2007 to 2/12/2007. The study included all consecutive patients presenting with STEMI for whom fibrinolitics were administered. The primary outcome of the study was the mortality of STEMI patients within 6 months after discharge.

Results: A total of 118 patients with STEMI were included. The 30-day mortality was 7.6%. The 180-day mortality was 12.2%. The mortality rate was higher in patients with anterior myocardial infarction (15.0%) than in those with inferior myocardial infarction (5.3%). The mortality rate was also higher in patients with Killip class 3 or 4 at admission (25.0%) than in those with Killip class 1 or 2 (9.3%).

Conclusion: The mortality of STEMI patients receiving fibrinolitics in this local hospital is acceptable. However, there is still room for improvement by optimizing the management of STEMI patients.

6. Local experience: Tenecteplase (TNK) as Thrombolytics for STEMI Patients

NH Luk, WS Kwan, SF Chui, YH Cheng, LK Chan, KC Chan, HS Ma, CY Wong, CW Chan, CL Fu, KY Lee, KT Chan, KC Ho, CS Chiang
Division of Cardiology, Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR, China

Objective: The aim of this study was to evaluate the short term outcome and complication of Tenecteplase (TNK) as thrombolytics for patients with ST Elevation Myocardial Infarction (STEMI).

Methods: Hospital records of all STEMI patient treated with TNK since the introduction of TNK in Queen Elizabeth Hospital (Oct 2009) were reviewed. Demographic data, co-morbidities, outcome and complications were analyzed.

Result: Total number of 26 patients were given TNK for STEMI during the study period. There was 23 male (88.4%) and 3 female (11.6%). Their mean age was 61.1 +/- 11.1 years. The mean onset of pain to needle time was 5hrs 12mins. 13 of patients had anterior MI (50%) and 13 of them had inferior MI (50%). 19 patients (73%) were showed to have successful thrombolysis. Coronary angiogram was performed following thrombolysis in 24 of them (92%). None of them showed TIMI 0 flow. Four patients did not receive coronary angioplasty.

Conclusion: The short term outcome in local population of TNK is promising. Further prospective studies are yet needed.

7. BMP9 Promotes Cardiac Progenitor Cells Ameliorate the Heart Function in the Rat Model of Myocardial Infarction

L. Zhao, Y. Chen, B. Shen, LG Zhou, H. Wei and ZL Zhang
Department of Heart Center, Children’s Hospital of Chongqing Medical University, Chongqing, PR China

Purpose: To observe whether cardiac progenitor cells (CPCs) which induced by bone morphogenetic proteins9 (BMP9) can improve the heart function of the rat with myocardial infarction.

Methods: CPCs were infected by AdBMP9 which express green fluorescent protein. After twenty-four hours, the expression of BMP9 mRNA of infected CPCs were examined by semi-quantitative RT-PCR. Then, infected CPCs by AdBMP9 were injected into the infracted heart. The hearts were collected, after postoperative four weeks. The change of CPCs morphology was observed by HE staining and immunofluorescent analysis to investigate the expression of cardiac-specific structural proteins alpha myosin heavy chain (α-MHC) and α-Actin of the implanted CPCs. The cardiac infarct size was detected by Masson staining. Heart function was examined by echocardiography, in preoperative and postoperative four weeks.

Result: After twenty-four hours, the expression of BMP9 mRNA of infected CPCs were examined by semi-quantitative RT-PCR. Then, infected CPCs by AdBMP9 were injected into the infracted heart. The hearts were collected, after postoperative four weeks. The change of CPCs morphology was observed by HE staining and immunofluorescent analysis to investigate the expression of cardiac-specific structural proteins α-MHC and α-Actin of the implanted CPCs. The cardiac infarct size was detected by Masson staining. Heart function was examined by echocardiography, in preoperative and postoperative four weeks. The change of CPCs morphology was observed by HE staining and immunofluorescent analysis to investigate the expression of cardiac-specific structural proteins α-MHC and α-Actin of the implanted CPCs. The cardiac infarct size was detected by Masson staining. Heart function was examined by echocardiography, in preoperative and postoperative four weeks.

Conclusion: CPCs induced by BMP9 can improve the heart function of the rat with myocardial infarction.

8. Secondary Prevention of Coronary Heart Disease – How closely are we answering our targets?

Yip TWC, Mun SY, Kong CM, Tam KM, Kwong NP, Yuen CM, Law TC, Kwan WK, Woo KS
Department of Medicine, Van Chai Hospital, HKSAI, China

Background: The question of “How successful is our secondary preventions being practiced at the clinics” substantially helps to improve patient outcome as well as cost saving, while repeated revascularization procedures are costly and risky.

Methods: To evaluate the patients after percutaneous coronary intervention (PCI), 143 YCH patients undergoing 173 PCI procedures in the year 2005 were recruited and followed up for a mean period of 5 years. There were a total of 5 new coronary death(3.5%) - 2 carcinomas, 1 chronic lung disease and 2 pneumonias, while 11(7.7%) were referred to other hospitals or defaulter during the follow-up period. There were 11(7.7%) cardiovascular deaths, and 106(68.1%) patients are currently being followed up at our clinic.

Results: All except one patient received aspirin (99%), clopidogrel in 19(16%), beta-blocker in 70(60%) while 19(15%) patients received statins. No patient suffered from clinical myasthenia nor hepatitis, but 2 patients stopped statins for ALT increase and 3 patients had dose reduction for CPK elevation. The table listed the blood pressure, glycaemic and lipid controls.

<table>
<thead>
<tr>
<th>5 years follow up</th>
<th>patients (n=120)</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>140 +/- 90</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>80 +/- 8</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>25.5 +/- 3.5</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>60%</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>45 +/- 10</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>130 +/- 30</td>
</tr>
<tr>
<td>TC (mmol/l)</td>
<td>5.5 +/- 1.0</td>
</tr>
<tr>
<td>TG (mmol/l)</td>
<td>2.0 +/- 0.8</td>
</tr>
</tbody>
</table>

Conclusion: The standard of our clinical practice is only fair – with suboptimal blood pressure, glycaemic and lipid controls, and room for improvement in secondary prevention.
Abstracts for Free Paper Session:

9. Radiofrequency Catheter Ablation of Symptomatic Atrial Fibrillation
CP Chan; J Y S Chan; J WH Fung; C M Yu. Division of Cardiology, Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong

Purpose: Antiarrhythmic drugs (AAD) are commonly used for prevention of recurrent atrial fibrillation (AF) but effectiveness of AAD remains inconsistent. In the advent of catheter ablation, radiofrequency ablation in the left and right atrium becomes an established therapy for patients with symptomatic AF. The purpose of this study was to assess the efficacy of catheter ablation for symptomatic paroxysmal and persistent AF in our center.

Methods: A total of 60 patients (43 men, age 55.7±11.6 years) with AAD refractory symptomatic AF (44 patients had paroxysmal AF, 16 patients had persistent AF) were studied. Ablation procedure was undertaken by one of the following techniques: (1) Ablation Procedures Cardiac Ablation System (n=30) or (2) B alte NoVX system in combination with irradiation ablation catheter (n=30). Patients were followed clinically for recurrence of AF at months 3, 6 and 12. Clinical recurrence of AF was defined as AF/sustained flutter >1 minute in duration.

Results: The mean duration of AF was 55.2±13.3 months before index procedure. During the follow-up: 22 patients (37%) with paroxysmal AF and 11 patients with persistent AF remained free from recurrence of AF after single procedure. At 6 months, 74% of patients who underwent ablation and 74.4% of patients who underwent ablation by using ablation catheter were free of symptomatic AF (p>NS). Major adverse events occurred in 5% of patients. No procedure related mortality was recorded.

Conclusion: Among patients with symptomatic AAD refractory AF, a clinically satisfactory result can be achieved in >70% of patients. The clinical efficacy of using different ablation catheters was similar and the procedural risk was low.

CP Chan, F Modady, F Bogun. University of Michigan, Ann Arbor, MI

Purpose: Post infection VT often originates from myocardial scar tissue. The arrhythmogenic substrate has not been characterized by intracardiac echocardiography. The purpose of this study was to evaluate the value of real-time intracardiac echocardiography to guide ablation of ventricular tachycardia in patients with ischemic cardiomyopathy.

Methods: In series of 20 consecutive patients (19 men, age: 65±10 years, left ventricular ejection fraction: 0.25±0.13) referred for ablation of post-infection VT, intracardiac echocardiography (CARTOSOUND) was used with a 3-D electroanatomic mapping system, to characterize critical VT isthmus areas as being located within a dyssynchronous segment, a segment with hypokinesia/s akinesia or normal contraction.

Results: 187 VTs could be induced (cycle length 385±95 ms) during the index procedure. For 90 VTs, critical isthmus areas could be identified. Critical areas for 51/90 (57%) VTs were located in a dyssynchronous segment, 33/90 (37%) VTs were located in an area of akinesia and 69/90 (77%) in an area of hypokinesia; none were located in normal contracting myocardium. The area of dyssynchrony was smaller than the area of dense scar (33±14 cm2 vs 54±25 cm2; p=0.05). Post ablation 15/20 patients were non-inducible. During a follow-up time of 1046±2 patients 2 patients had recurrent VT.

Conclusion: The majority of critical areas for post-infection VT were identified within dyssynchronous segments rather than other parts of the scar. Dyssynchronous segments identified by ICE have a localizing value in identifying the arrhythmogenic substrate.

11. Review of Electrophysiological Study as Day Case in a Local Regional Hospital
CK Kwok, NH Lui, WS Kwok, YH Cheng, SF Chai, LK Chan, CT Wong, HS Ma, LK Chan, CT Fu, LV Tam, CW Chan, KV Lee, KT Chan, KC Hiu and Dr C S Chiang
Department of Medicine, Queen Elizabeth Hospital, HK SAR

Background: Electrophysiological study (EPS) is an invasive investigation to analyze the pathophysiology of cardiac arrhythmias. Although the procedure related complication and mortality rate are negligible, there is still potential risk of vascular injury, local or systemic thromboembolism, infection, cardiac perforation, myocardial infarction, arrhythmias and stroke. As a result, patients undergoing EPS usually hospitalize overnight for close observation before discharge.

Objective: To evaluate the feasibility and safety of EPS as day cases in a local regional hospital.

Patient and methods: Day case EPS approach was introduced in our hospital since October 2005. Patients with symptomatic arrhythmias were arranged for EPS first and subsequently decided if ablative intervention was required. For those whom further intervention was not indicated or refused, transvenous catheters were removed immediately after procedure and haemostasis was achieved by manual compression. Patients were observed in cardiac dayward for few hours and were discharged home on the same admission day if no immediate complication was noted. Ward care management was educated by nurse. They were phone contacted the next day for follow up of symptoms, wound status and any complication.

Results: From October 2005 to March 2010, 23 patients underwent EPS as day cases. Mean age was 47 years old. Male to female ratio was 3:7. Supraventricular arrhythmias (52%), ventricular arrhythmias (39%) and unexplained palpation (8%) were the indications of EPS. Among them, 70% had no inducible arrhythmias or abnormal accessory pathway, while the remaining 30% had inducible arrhythmias yet radiofrequency ablation was not proceeded either because of patient’s choice or unfavorable anatomy. Average length of stay in hospital was 9 hours. Among all patients there were no reported complication including bleeding and haematoma formation.

Conclusion: Day case EPS is a feasible and safe approach provided that proper patient education is offered and close follow-up is provided. Overnight hospitalization can be avoided.

12. Monitoring and comparative analysis of remote real-time electrocardiogram monitoring system and routine 12-leads electrocardiogram in patients with cardiovascular disease
XL Sun, GJ Wang
Department of Cardiology, Fawc Cardiovascular Hospital, Peking Union Medical College and Chinese Academy of Medical Science, Beijing

Purpose: A remote real-time wireless electrocardiography monitoring system based on GPRS was tested in order to contrast the accuracy and stability of electrocardiogram with the 12 leads electrocardiogram (ECG), and then evaluated this device’s clinical practicable value, security and validity.

Methods: The data were collected from 194 in-patients from April 2008 to December 2008 in Fawc hospital. All subjects were received the remote real-time ECG monitoring and the 12 leads ECG, and those patients were divided into two groups. The aspects of ECGs were compared between 2 systems including the general waves, clinical diagnosis, time and voltage parameters.

Results: In remote ECG groups, the baseline stability of proceudial leads is better than limb leads. Compare to 12 leads ECG, detectable rate of arrhythmia is higher in remote ECG groups, and it identified 266 cases of arrhythmia, including 135 cases of tachycardia and 131 cases of bradycardia. The most common arrhythmia is ventricular premature beat(18.7%), one degree atrioventricular block is second(13.9%) and atrial fibrillation is third(13.3%) in turn. There were no significant difference found in the time parameters between 2 systems, and was significant correlation. The voltage parameter of the 2 systems was no significant difference.

Conclusion: The accuracy and stability of the remote real-time ECG monitoring system based on GPRS is in accordance with the standard ECG instrument. The remote real-time electrocardiogram monitoring system may be a helpful tool in assisting physicians in the diagnosis of common arrhythmia and malignant ventricular arrhythmia disorders, and shown high safety in data recording.
13. Effects of Aerobic Exercise Training on Exercise Capacity, Cardiac Function and Quality of Life in Chronic Heart Failure Patients with Cardiac Resynchronization Therapy - A Pilot Study

BKLYunk,1 AYM Jones,3 K Fan,2 WH Chow2
1Physiotherapy Department and 2Cardiac Medical Unit, Grantham Hospital & 3Department of Rehabilitation Sciences, Hong Kong Polytechnic University

Purpose: The objective of this study was to investigate the exercise capacity, cardiac function and quality of life in patients with chronic heart failure prior to cardiac resynchronization therapy (CRT), after one month of implantation and after an eight weeks aerobic exercise training programme.

Methods: From April 2008 to November 2009, 7 chronic heart failure patients with ambulatory NYHA functional class IV (5 men and 2 female) underwent CRT implantation and were randomized to either the aerobic exercise group or control group. The aerobic exercise group performed 8-week aerobic exercise training program under close supervision and the control group remained physically inactive.

Results: Four subjects (two of them being heart transplant candidates) were allocated to the aerobic exercise group and three patients were allocated to the control group. Two subjects in aerobic exercise group were withdrawn due to heart transplantation and repeated gouty attacks on lower limbs respectively. After one month of CRT implantation, the peak oxygen consumption (VO2max), 6-minutes walk test distance and quality of life score for all subjects were similar to baseline but left ventricular ejection fraction has improved from 29.5 \(\pm\) 6.6 to 36.0 \(\pm\) 7.2 %. After eight weeks of aerobic exercise training, the two remaining subjects in the aerobic exercise group showed an increase in VO2max (Exercise: 26.5%, control: 11.8%), peak heart rate (Exercise: 15.1%, control: 3.6%), decrease in left ventricular end diastolic diameter (Exercise: -2%, control: 0.9%), left ventricular end systolic diameter (Exercise: -7% control: 0%); mitral regurgitation score (Exercise: -100%, control: 28%). One female subject in aerobic exercise group was successfully removed from heart transplantation list during exercise phase.

Conclusion: Aerobic exercise training is safe and feasible for chronic heart failure patients with CRT. On-going collection of data is required to show the improvement on physical, quality of life and other parameters of cardiac function such as mitral regurgitation, left ventricular end diastolic and end systolic diameter.
Clinical Attributes of Patients Participated in Phase II Cardiac Rehabilitation Program over the Past 10 Years

YMW Mak, CS Yau, KF Leung. Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong

**Purpose:** The aim of the study was to examine the clinical profile of patients entering phase II cardiac rehabilitation program (CRP) from 2000 to 2009.

**Methods:** Patients were classified into 5 groups according to their period of recruitment into phase II CRP. Clinical profile of those patients was analyzed.

**Results:** A total of 1391 patients were classified into period 1 (2000-2001, n=248), period 2 (2002-2003, n=100), period 3 (2004-2005, n=277), period 4 (2006-2007, n=288), and period 5 (2008-2009, n=278). There were 1034 males (74%) and 357 females (26%). Across the period, there was no significant change in the gender distribution (male 71.5% - 78.1% vs. female 21.9% - 28.5%). The mean age was 63.9 (SD=10.1, range 28-86) years. There was no significant change in mean age and range from period 1 to period 5. However, male patients were younger than their counterpart (male vs. female = 63.2 vs. 65.8 years) when they enrolled in the program. In addition, the proportion of patients aged 75 or above was increased by 7% from period 1 to period 5. Patients with hypertension and obesity were increased by 19% and 19%, respectively, whereas, patients with hyperlipidaemia was decreased by 32%. Patients that were on welfare assistance and waived for the service were increased by 35%.

**Conclusions:** There were more elderly patients aged 75 or above having cardiac rehabilitation program. More patients that participated in Phase II cardiac rehabilitation program suffered from hypertension and obesity. On the other hand, more patients that received cardiac rehabilitation service were receivers of welfare assistance.
ABSTRACTS

Abstracts for Free Paper Session:

PERCUTANEOUS CORONARY INTERVENTION AND CORONARY ARTERY DISEASE II

18. Long term survival of Percutaneous Coronary Intervention (PCI) Patients in a local hospital Yip TWC, Kong CM, Mau SY, Tam KM, Law TC, Kwong NF, Yue CM, Kwan WK, Woe KS. Department of Medicine, Yan Chai Hospital, HDKSA, China.

Background: Revascularization therapy is not without risk and long term survival data is lacking in our local population, as tremendous effort is spent to compare and contrast PCI and by-pass surgery. As we are closely following up and prospectively treating a subset of PCI patients according to the guidelines, the demographic data of those who died can be readily compared with those survived.

Methods: To evaluate the patients after percutaneous coronary intervention (PCI), 143 YCH patients undergoing 173 PCI procedures at FMBH in the year 2005 were studied and followed up over 5 years. 2 groups of patients (survival and death) were compared.

Results: There was a total of 5 non-cardiac deaths (3.5%) while 11(7.7%) were referred to other hospitals or declared. There were 117(7.7%) cardioclausal (CV) deaths, while 116 patients are being regularly followed up at our clinics.

CV Death (n=11) Survivors (n=116)
Baseline Age (range) 72(15-79) 64(10-89)
Sex (male) 7(63.6%) 57(49.6%)
Indications (MCA/CAFCAS) (%) 23(95%) 60(51.7%)
BMI (kg/m²) 9(81.8%) 26(22.4%)
CVA (%) 7(63.6%) 30(25.9%)
SCOR (unadjusted) 111.5(59.1) 96.3(45.1)
CCF (cardiac failure) (%) 62(54.5) 72(62.1)
CCO < 60/min [70.7%] 55 26
Drop in CCl (10 to 10) 68* 28
Contraindication for PCI 18(16.4) 64.8
LAD Type or 3 lesions (%) 18(16.4) 21(18.1)
CCT > 1 lesions or lesions >11 lesions stents 86(74.6) 64.8
Stent length/mm (range) 2.9(0.0-8.0) 2.7(0.0-6.0)
Stent length/mm per vessel<2.0 mm 1.7(0.0-7.0) 1.6(0.0-8.0)
Stent Length>20.0 mm (%) 48 64
DSS (%) 64

*p<0.05, **p<0.01 as compared with the other groups

Conclusion: The elderly with higher prevalence of co-morbidities and in particular chronic kidney diseases were associated with cardiovascular death. They presented acutely with higher prevalence of congestive heart failure and a significant deterioration in renal function after the PCI procedures.

19. Improvement of Door to Balloon Time in Primary Percutaneous Coronary Intervention After Introduction of Cardiac Rapid Response (CRR) Team KC Chan, CK Kwok, NH Lui, WS Kwun, YF Cheng, SF Chiu, LC Chan, CY Wong, HS Ma, CL Fung, SY Tam, CW Chan, KY Lee, KT Chan, KC Ho, CS Chiang Department of Medicine, Queen Elizabeth Hospital, HKSA.

Background: Door to balloon time (DTBT) during primary PCI for STEMI has been extensively studied during the past several years. They are correlated with patient mortality, and numerous efforts have been made to improve this parameter. National guidelines recommend DTBT within 90 minutes.

Objective: To study the impact of the DTBT for STEMI undergoing primary PCI in a local regional hospital after the introduction of cardiac rapid response (CRR) team.

Patient and methods: CRR team was introduced in our hospital since March 2009. Patient presenting with STEMI during office hour from Monday to Friday will be assessed by our cardiologist and nurse together in the emergency department. Suitable patients will be transferred directly to the catheterization lab for primary PCI. 45 patients were screened and 26 patients had primary PCI done from 3/2009 to 2/2010. 32 patients underwent primary PCI during office hour from 3/2008 to 2/2009 were used as a control sample. Baseline clinical characteristics and door to balloon time will be analyzed and compared between 2 groups.

Result: Mean age of these 58 patients were 64. There was no difference between the age, presence of diabetes mellitus, hypertension and smoking status. They had similar occurrence of cardiogenic shocks, congestive heart failure, and had similar number of disease vessels. They used similar type of stent (bare metal vs drug eluted stents). More patients had hyperlipidemia in the study group (88.5% vs 62.5% p<0.035). There was an improvement of DTBT from 190 minutes to 81 minutes after the introduction of CRR team (p<0.000).

Conclusion: The implementation of the cardiac rapid response team result in a statistically significant improvement of door to balloon time in primary PCI setting.

20. Clinical outcomes and angiographic follow-up after stenting of unprotected left main coronary artery stenosis in a regional hospital John T Wong, CK Chan, CS Yue. Division of Cardiology United Christian Hospital, Kowloon, Hong Kong

Introduction: Stented unprotected left main coronary artery (ULMCA) disease treated medically have a 3-year mortality of 50%, and coronary artery bypass grafting (CABG) is the cornerstone of treatment for these patients. Increasing data have demonstrated the safety and feasibility of ULMCA using percutaneous coronary intervention (PCI) in fact, Acute European guidelines had upgraded the indication of PCI to ULMCA from Class III to IIb. This study aims to evaluate the clinical outcome of patients undergoing PCI to ULMCA disease in a regional hospital.

Methods: All patients who had undergone PCI to ULMCA in United Christian Hospital (UCH) during Jan 2007 - Dec 2009 were included for analysis.

Results: A total of 128 cases of PCI were performed in UCH during the above period. In 65 (51.2%) of these cases the target lesion involved ULMCA. The majority of patients whom had PCI to ULMCA was males (63.2 vs 3.8 years and most of them (74%) were males. Most patients (63%) had normal left ventricular systolic function (LVFS) (defined as LVEF >55%), 35% had poor LVFS (LVEF <55%) and 2% had poor LVESF (LVEF <35%).

Most ULMCA was affected in 84% of cases, while the rest affected either the ostium or the shaft. Immediate procedural success rate was 100%. The majority of cases had utilised drug eluting stents (DELS) (78%), the rest had non-DES for those ULMCA PCI. All ELCMA PCI performed were to the de novo ULMCA lesions except 8 insulin metastasis (ISM) cases. Intravascular ultrasound and prophylactic intracoronary balloon pump was used in 85% and 31% of patients respectively. One patient required rotational atherectomy. In distal ULMCA disease group, 75% had single stent and the rest had 2 stents implanted mainly using T-stenting strategy, and kissing balloon was performed in 36.7% for single stent and 94% for 2 stents strategy. Mean ULMCA stent size was 3.5+-0.24 mm in diameter and 19.1+-8.6 mm in length. At a mean follow-up time of 145+/-120 days, there were 2 deaths (3%); one due to chest infection and the other due to sudden cardiac death, 3 patients had recurrent Q-wave myocardial infarction (4.6%) and 3 patients required target lesion revascularization (7.9%) all due to non-DES ISR. There was no occurrence of restenosis but liaison of possible stent thrombosis in this study population.

Conclusion: ULMCA stenting provided excellent immediate procedural success rate and mid term results in this selected population. These findings suggested that PCI may be considered as a safe and effective alternative to surgery for relatively low risk patients with ULMCA disease in our hospital.

21. Two-month clinical outcome for the treatment of in-stent restenosis with second generation compared to first generation drug-eluting stents RKC Pang, CS Yue, CEC Chan. Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong

Purpose: The safety and efficacy of first generation drug-eluting stents (DES) in the treatment of in-stent restenosis (ISR) has been verified. In this study, patients with bare metal ISR diagnosed angiographically between 1 Jan 2006 and 1 Aug 2009 were treated with either first generation (sirolimus or paclitaxel) or second generation (everolimus or zotarolimus) DES. Their immediate clinical outcomes after 9 months was compared.

Method: Patients who had bare metal ISR treated with DES in the United Christian Hospital between 1 Jan 2006 and 31 July 2009 were included. Those who had mixed drug DES were excluded. Demographic data was retrieved from our clinical records and percutaneous coronary intervention registry. Patients' baseline parameters including clinical presentation, age, gender, smoking status, left ventricular ejection fraction, previous history of cardiovascular disease, previous coronary interventions, co-morbidities (including diabetes mellitus, hypertension, hyperlipidaemia, peripheral vascular disease and renal impairment were collected. Angiographic data including target vessel, ISR patients, total stent length, maximal inflation pressure were compared. Data regarding their clinical outcomes were retrieved from the computer based clinical record. Major adverse cardiac events were defined as mortality, target lesion revascularization (TLR) and myocardial infarction. Results: A total of 48 patients were included. Twenty-seven patients were treated with first generation (paclitaxel and sirolimus) stents and twenty-one patients were treated with second generation (everolimus and zotarolimus) stents. Baseline characteristics were similar between the two groups, except mean maximal inflation pressure was significantly higher in the second generation stent group (17±3 mmHg vs. 14±2 mmHg, p<0.002). During the 9-month follow up, there was no stent thrombosis and target lesion revascularization. These patients had no endoluminal myocardial infarction in the first generation DES group. One patient died of acute pulmonary edema and 4 patients developed non-fatal myocardial infarction in the second generation DES group. There was no significant difference in incidence of MACE between patients treated with first and second generation DES (11.1% vs 23.6%, respectively, p=0.679).

Conclusion: In this study, two-month clinical outcomes of the treatment of ISR with second generation DES was comparable to that of the first generation DES. Second generation DES may be a promising option for the treatment of bare metal DES.
22. Clinical Outcome of Patients Undergoing Percutaneous Coronary Intervention with Endothelial Progenitor Cell Capture Stent (Genous Stent)

SE Chui, NH Luk, WS Kwan, YH Cheng, LC Chan, KC Chan, HS Ma, CY Wong, CW Chan, CL Fu, KY Lee, KT Chan, KC Ho, CS Chiang
Division of Cardiology, Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR, China

Objective: The aim of this study was to evaluate the midterm outcome of patient undergoing PCI with Genous stent.

Method: Hospital records of all patients who received PCI with Genous stent from August 2007 to Sept 2009 were reviewed. The baseline demographic data, indication of PCI, duration of dual-antiplatelet therapy, procedure details, major adverse cardiovascular events were analyzed.

Result: A total of 33 patients were recruited between the study periods. Their mean age was 70 years (45-93 years). There were 19 females (57.6%) and 24 males (72.7%). 75.8% of patients had more than 1 cardiovascular risk factors (i.e., smoking history, DM, HT, hyperlipidemia, previous CVA/PVD). The mean LV EF was 50.0% (9.3-93%). 8 patients (24.2%) were in stable angina while 13 (39.4%) and 12 (36.4%) patients presented with NSTE-MI or STEMI respectively. 67.9% of patients had multi-vessel disease. The mean duration of dual-antiplatelet therapy was 2.03 (±0.2) months. At 6 months post-PCI, none of our patients suffered from sudden death/cardiac death, 5 patients (15%) suffered from non-cardiac death (3 died of pneumonia, 1 died of COPD exacerbation, 1 died of CVA). The cumulative rate of recurrent myocardial infarction was 12% (4 out of 33 patients) at 6 months and 2 of these patients underwent repeat revascularization.

Conclusion: The use of endothelial progenitor cell capture stent in patient with high risk of bleeding undergoing PCI is safe and appears promising. Long-term outcome remains to be evaluated.

24. Role of N-Terminal Pro-B-Type Natriuretic Peptide in Diagnosis and Prognosis of Chinese Patients with Stable Coronary Artery Disease

DQ Wang, MD BY Wong, MD SY Ng, MD MC Chan 1, MD YP Tu 2, Dr AO Kong Chan 1, Dr KY Lee, MD CC Shek 1, Dr CS Cheng 1
1 Department of Medicine and 2 Department of Pathology, Queen Elizabeth Hospital

Objective: N-terminal pro-B-type natriuretic peptide (NT-proBNP), synthesized in response to vaso-motor wall stress, cardiac ischemia and atheroma burden, has been well recognized for its clinical utility in diagnosis and prognosis of heart failure. Recently, evidences are emerging with regard to its value in patients with coronary artery disease (CAD). This study aimed to determine the diagnostic value of NT-proBNP in angiographically proven disease, as well as its prognostic implication in Chinese patients with stable CAD. The performance of NT-proBNP in comparison to measure cardiac biomarker high-sensitivity C-reactive protein (hs-CRP) was also assessed.

Methods: 260 patients were referred for coronary angiography from 1st July 2008 to 30th September 2008 were enrolled. Blood samples were taken for NT-proBNP assays before angiography. Demographic and clinical characteristics of patients, pre-operative non-invasive investigations and angiographic results were recorded and analyzed. All patients were followed up for 1 year for any major adverse cardiovascular events (MACCE).

Results: The patients were categorized according to the recommended cutoff values of the biomarkers (125 pg/ml for NT-proBNP and 5 mg/l for hs-CRP). Patients with NT-proBNP value above the cutoff point (n = 89) were older, more likely to have past history of myocardial infarction and heart failure, renal function impairment and left ventricular hypertrophy. They had more significant CAD when compared to patients with NT-proBNP level below 125 pg/ml (71.8% vs 56.0%, p = 0.006).

Using multiple logistic regression analysis, NT-proBNP was found to be an independent predictor of significant coronary artery disease with odds ratio 2.73 (95% CI 1.43 - 5.21, p = 0.002) after adjustment for confounders, although the dosing strategy was fairly low as indicated by an area under receiver operating characteristic curve of 0.624 (95% CI 0.51 - 0.73, p = 0.004). At 1 year follow up period, there were no significant differences between high and low NT-proBNP groups in terms of all-cause mortality, cardiovascular (CV) mortality, myocardial infarction (MI), heart failure (HF) and stroke. The overall MACCE (CV mortality, MI, HF and stroke combined) rate, however, was higher in high NT-proBNP group (12.5% vs 3.4%, p = 0.032). Moreover, there were significantly more patients in this group presenting with A total of 33 patients hospital admissions (10.0% vs 0%, p = 0.001).

On the other hand, the level of hs-CRP did not show correlation with angiographic severity, has no value in predicting significant coronary artery disease, and was not associated with major adverse cardiovascular events at 1 year follow up.

Conclusion: Higher NT-proBNP level in stable patient was associated with more severe angiographic disease, and was shown to be an independent predictor with fair discriminating power. More adverse events as particular severe angina were observed in higher NT-proBNP group at 1 year follow up period. Longer follow up would be indicated to further assess the prognostic value of this biomarker.

23. Genous Experience - A Local and Global Perspective on ACS and Special Indication Patients

SWL Lee
Department of Medicine, Queen Mary Hospital, Hong Kong

The Genous™ Endothelial Progenitor Cell (EPC) capturing stent has been clinically demonstrated to be a safe stent that helps reduce thrombosis and restenosis despite only a 4-week duration of dual anti-platelet therapy (DAPT) as according to on-label use. In consistency with recent publications and clinical releases on STEMI patients treated with the EPC stents, a total of 174 patients (including 29.9% STEMI patients and 26.4% NSTE-ACS patients) at Queen Mary Hospital (QMH) implanted with the stent also showed comparable findings. In addition, a small number of patients with special indications (e.g. drug intolerance, inability to withstand prolonged DAPT, bleeding issues and peri-operative etc.) also benefited from the EPC stent with favorable results.

Enrollment and Method: ACS and special indication patients with post-procedural DAPT of 4 weeks as according to on-label use.

Results/Outcomes: MACE at 30 days was 5.7% (10); Cumulative MACE at 3 months was 6.8% (12); Cumulative MACE at 1 year was 11.5% (20); Cardiovascular mortality at 1 year was 5.2% (10); Clinically-driven TLR at 1 year was 5.7% (10); Subacute Stent Thrombosis: 0.6% (1); Late Stent Thrombosis: 0.6% (1). Clinical follow-up data (overall and ACS subgroup) from QMH appears consistent with data from the worldwide 5,000-patient e-Healing Registry (primary outcome of MACE: 7.7%; SAT: 0.2%; LST: 0.3%). To further address the issue of restenosis, a multi-center randomized in-human trial called REMEDEE has been initiated to demonstrate the safety and efficacy of a combo stent that both promotes accelerated healing whilst reducing cell proliferation.

25. The Effects of Vitamin B12 and C Supplementation on Carotid Atherosclerosis in Subjects Exposed to High Environmental Tobacco Smoke

TWY Ng, P Chiu, ML Chu, HD Peng, ME Evack, KY Kooi, TYR Chu, XM Zheng, CL Chiu, HC Long, KK Woo, HC Long, CE Woo, Hospital Central Conde de S. Janssen, Macao, Kang Wu Hospital, Macao, Macau Heart Foundation, "The Chinese University of Hong Kong"

Introduction: Atherosclerosis is the most important medical problem of modern society. High environmental tobacco smoke in casino is associated with accelerated atherosclerotic process. They have previously shown vitamin B12 or C supplementation improves vascular reactivity and may be beneficial in vascular protection.

Methods: 78 passive smoking casino employees (19.2% males, mean age 45.0±8.2 years) were randomized to receive vitamin B12 (500ug daily), vitamin C (200mg daily), vitamin B12+C, or double image-match placebo capsules in double-blind 2 x 2 factorial design funding for 1 year. Carotid intima-media thickness (intagrate atherosclerosis marker, IMT) was measured by ultrasound (automated edge detection and measurement) at baseline and 12 months.

Results: Of the 78 passive smokers, 90% had hyperlipidemia, 64% had diabetes mellitus and 19% hypercholesterolemia. There were no significant changes in their blood pressure, lipid (LDL, HDL-C and TG) profile, glucose, creatinine and body mass index (BMI) during supplementation for 1 year, but a significant increase in blood B12 during vitamin B12 (p=0.05) and vitamin B12+C supplementation (p<0.01). Carotid IMT improved during 3 active treatment periods, but not during placebo, and was worse significant during vitamin B12+C combination (p=0.006) than either vitamin B12 or C period (p<0.001).

Conclusion: Vitamin B12 or C supplementation improves carotid IMT and may contribute to atherosclerosis prevention in high environmental tobacco smoke.
Abstracts for Free Paper Session:

26. Coronary Artery Disease and Visceral Fat - A Hospital Based Case Control Study
Yengar SS, Blesson V, Smitha S, Srirakshmi MA, Saranthosh MJ, Shetty GS, Kiron V, and Patil CB, St. John's Medical College Hospital, Bangalore, India

Purpose: Coronary artery disease (CAD) is assuming an epidemic proportion amongst young Indians. Central adiposity through its visceral fat is known to be associated with an increased cardio-metabolic risk. This hospital based case control study attempts to assess the correlation of visceral fat with anthropometric measurements, metabolic parameters and presence of CAD in young Indians.

Methods: Male subjects aged 55 years or less and female subjects aged 65 years or less formed the study population. 20 patients with confirmed CAD were compared with 30 age and gender matched controls. Body mass index (BMI), waist circumference and waist hip ratio (WHR) were measured. Blood samples were collected for sugar, lipids and C reactive protein (CRP). CT scan of the abdomen was done for visceral and subcutaneous fat in all subjects.

Results: There was no significant difference in BMI between controls and cases. (23.92 ± 3.00 vs. 25.47 ± 2.65, p = 0.067). Waist (88.17 ± 8.17 cms vs. 94.90 ± 6.68 cm p = 0.004), Waist Hip Ratio (WHR) (0.92 ± 0.05 vs 1.06 ± 0.05 p < 0.001), visceral fat area (VFA) (38.40 ± 24.91 cm² vs. 122.58 ± 77.59 cm², p < 0.001), visceral fat by subcutaneous fat ratio (VFA/SAF) (0.04 ± 0.06 vs. 0.06 ± 0.06 p = 0.001), fasting blood sugar (FBS) (97.77 ± 13.04 mg/dl vs 145.23 ± 57.08 mg/dl p < 0.001), triglycerides (128.60 ± 50.86 mg/dl vs 176.10 ± 73.17 mg/dl p < 0.001) and CRP (0.28 ± 0.26 mg/dl vs 0.58 ± 0.37 mg/dl p = 0.002) were significantly higher in cases compared to controls. Visceral fat area was an excellent predictor of cardio metabolic risk in young CAD patients as seen by Arest under ROC curve and also correlated well with BMI, WHR, FBS, triglycerides and CRP.

Conclusion: Visceral fat was associated with an increased risk of CAD in young Indian population and it also correlated with BMI, waist, waist hip ratio, increased serum triglyceride levels and raised C-Reactive Protein.

27. Central Aortic Pressure and Assessment of End Organ Function
A. Avolio, M. Butlin, M. Kim, A. Quadir, S. Graham. Australian School of Advanced Medicine, Macquarie University, Sydney, Australia

Purpose: Arterial blood pressure (BP) is conventionally measured in the upper arm with cuff sphygmomanometry. However, due to elastic and geometric characteristics of the arterial tree, brachial pulse pressure (PP) is usually higher than in the central aorta. Aortic pressure (ABP) determines cardiac load and stress on arteries in central organs and vascular bed (kidney and brain). Recent studies [1,2] have shown that central aortic pressure PP is independently associated with cardiovascular risk and can better differentiate anti-hypertensive agents compared to brachial PP. Aim of this study was (i) to associate aBP indices with presence of glaucoma and (ii) to use ABP for non-invasive estimation of critical closing pressure (CCP) in the cerebral circulation.

Glaucoma: 107 glaucoma subjects were compared with age matched controls (66±12 years). Brachial systolic/diastolic pressures and noninvasive radial pulse waveforms were measured and the ABP waveform calculated using a validated transfer function (SphygmoCor, AtCor Medical). Central PP was lower in the glaucoma group (41±1 vs 47±1 mmHg, p=0.001). However, pulse pressure amplification between aortic and brachial site was higher (1.24±0.01 vs 1.36±0.01, p<0.001).

Cerebral critical closing pressure. Central aortic pressure (similar to the glaucoma study) and flow velocity (FV) signals were measured in 19 healthy subjects (22-54 years, 9 females). FV signals from the right middle cerebral artery and radial ABP were recorded simultaneously using transcranial Doppler and applanation tonometry. Cerebral CCP was computed by linear regression between FV and radial and central ABP waveforms. Estimates of central CCP (mmHg, mean ± SD) were: Radial Pressure: 23.5±8.8; Aortic Pressure: 31.1±7.6 (P<0.01). The estimate using aortic waveform was closer to the values of 32.9±11 from a previous study [3] using long diameter in patients in ventricular fibrillation. While FV waveforms and radial artery pressure can be used to estimate CCP, aortic pressure gives an estimate closer to the true value.

Conclusions: Findings from these two studies have shown that central aortic pressure derived from non-invasive recordings of the radial pulse can be used, to obtain better characterization of vascular changes associated with glaucoma and improved evaluation of cerebral CCP.

ABSTRACTS

Abstracts for Free Paper Session:

28. Cardiac Imaging and Coronary Risk Factors

Clinical and Echocardiographic Characteristics of Patients with Bicuspid Aortic Valve
KF Leung, KY Lo, KT Ho, CS Yue. Division of Cardiology, United Christian Hospital, Hong Kong SAR, P.R. China

Purpose: Bicuspid aortic valve (BAV) is the commonest congenital heart abnormalities affecting 0.5 to 2% of the population. It is a serious condition with notable valvular and ascending aortic risk. Limited data are available in local community. We sought to describe the clinical and echocardiographic features of patients with BAV in a single centre serving about eight hundred thousand of population.

Method: All patients with the diagnosis of BAV were identified through hospital computerized data base (CDASE) and manually in the cardiac out-patient’s clinic. Operative records from patients with aortic valve replacement (AVR) were also traced to identify those patients with operative finding of BAV (without pre-operative diagnosis of BAV). Patient’s demographic including family history, baseline echocardiographic features including aortic root assessment and associated cardiovascular abnormalities, and clinical outcome were retrospectively analyzed.

Results: Thirty patients with the diagnosis of BAV were identified (age, 46 +/- 18 years, range 13 - 85; 67% male, 33% were < 18 years). Five patients were diagnosed at time of AVR. The mean age at diagnosis was 43 +/- 13 years. 43% of patients were asymptomatic. No patient had known family history of heart disease. Nineteen patients (63%) had heart murmur (systolic murmur in 11, diastolic murmur 4, both in 2). Associated congenital cardiac abnormalities were found in 4 patients (13%). A typical BAV (R.L. fistula) was present in 25 patients; an atypical BAV was present in 4 patients (one is not identifiable). At diagnosis, aortic aneurysm was present in 20 patients (67%), aortic regurgitation in 19 patients (60%); aortic root to ascending aorta dilatation in 18 patients (60%); of them only had mid ascending aortic dilatation. The median follow up time was 3.7 years. The incidence of total medical events (cardiac death, congestive heart failure, new cardiac symptoms/stroke and endocarditis) was 27%; and new cardiac symptoms (dyspnoea, cardiac chest pain, and syncope) 10%. The incidence of total surgical events (aortic valve, ascending aort and aortic aneurysm) was 50. Only 30% of patients were managed medically. The aortic valve surgery (AVR or valve surgery) was 50%; ascending aortic surgery 20%. One patient had aortic dissection.

Conclusion: Our cohort of patients exemplified that BAV can incur frequent cardiovascular events. Vigilant identification of BAV and associated abnormalities and comprehensive follow up are warranted.


VM Parato, S Amabili, E Nardini, M Partemi, D Delfino. Cardiology Dept., C. and G. Mazzoni Hospital, Ascoli Piceno, ITALY

A 20 year old woman, with an history of reoccurred cardiac arrest and ICD implant came to our out-patient clinic for HCM. The first clinical presentation of HCM had been ventricular fibrillation successfully resuscitated some months before our observation. Patient’s history was otherwise unremarkable in that she did not refered symptoms. The electrocardiogram revealed normal sinus rhythm, with 107 ms QRS duration and Q waves in the inferior leads; there were no ventricular depolarization abnormality. Echocardiography showed severe maximal wall thickness (28 mm at mid septal level) and absence of significant left ventricular tract obstruction (LVOTG) at rest. The right ventricle was of normal dimensions (EDD: 29 mm; RV/LV EDD ratio: 0.6); hypertrophied (free wall thickness: 12 mm) with normal systolic function (RV fractional area change: 48%; TAPSE: 14 mm). The right ventricular outflow tract was obstructed at the level of the crișa supraventricularis, and there was a septal systolic contact with the right ventricular free wall. Doppler interrogation revealed severe RVOTG, i.e. peak gradient 70 mmHg. Symptoms-limited exercise showed a flat blood pressure response, normal exercise tolerance (exercise time 11 minutes) in the absence of significant arrhythmias and STT wave modifications. Therapy with beta-blockers was instituted. At yearly intervals patient was followed-up performing electrocardiogram, echocardiogram and symptoms-limited exercise. There were no changes within the follow-up until the fifth year when electrocardiogram showed RBBB, RVOTG lesser to 40 mmHg which remained stable after 6 months. Right ventricular dimensions and function did not change.

30. Unusual Non-Compaction Cardiomyopathies. A Case Report

V M Parato, D Rossi, M Partemi, D Delfino. Cardiology Dept. C. and G. Mazzoni Hospital, Ascoli Piceno, ITALY

A young man, 35 years old, presented to our institution for palpitations. He had frequent ventricular premature beats on ECG. He had a history of hypertension and tobacco abuse. On physical examination there was a significant ejection murmur on the apex, but no clinical signs of heart failure. His ECG treadmill test was normal. The resting echocardiogram showed a typical picture of non-compaction cardiomyopathy through the following echo-criteria for the diagnosis:

1) two distinct layers of myocardium; 2) a ratio (R) of maximal thickness of noncompacted myocardium (NCM)/compacted myocardium (CMC) > 2 in end-systole; 3) prominent, deep intertrabecular recesses communicating with the LV cavity (at color Doppler).

There can be several pitfalls in the diagnosis of left ventricular hypertrophic cardiomyopathy. Non-compaction cardiomyopathy is frequently associated with congenital heart diseases, abnormal origin of coronary arteries, patient formen ovale. It may be associated also with Ebbstein’s anomaly, Wolf-Parkinson-White’s Syndrome, Tako-Tsubo like cardiomyopathy and ARVD. We found also an association with bicuspid aortic valve. Our case is quit unusual because the cardiomyopathy was associated with:

1) a monosystolic mitral valve,
2) a bicuspid aortic valve,
causing a double severe regurgitation.

To the best of our present knowledge, this is the first case with similar features in the medical literature.
ABSTRACTS

Abstracts for Free Paper Session:

31. Untwisting Rate Determines Filling Pressure Response in Dobutamine Stress Echocardiography

With C W Lam, T Marwick, University of Queensland, Brisbane, Australia

Background: Left ventricular untwisting rate (UTR) is a determinant of diastolic suction and early LV filling. Reduced UTR is associated with increased LV filling pressure (E/e') during exercise in patients with diastolic heart failure. In this study, we sought association between time course of UTR and E/e' response during dobutamine stress echocardiography (DSE).

Methods: Routine DSE was combined with measurement of transmitral pulse-wave Doppler, myocardial tissue Doppler and speckle tracking echocardiography at baseline and peak dose in 110 patients (51 women, 62±12y). Untwisting rate (proto-diastolic and isovolumic IVRT) was measured by speckle tracking imaging. Filling pressures were represented by E/e'; E/e' > 15 defined raised filling pressure. ANOVA and post-hoc analysis were used to evaluate association of filling pressure response and UTR.

Results: Patients were sub-categorized into 3 groups – Group 1 (n=44), normal resting and peak E/e'; Group 2 (n=33), normal resting E/e' but raised peak E/e'; Group 3 (n=33), abnormal resting E/e'. Risk factors and resting EF were similar in each group. Proto-diastolic untwisting rate was an independent predictor of raised filling pressure at peak stress (p=0.03, p<0.001). An abnormal filling response during DSE was independently predicted by resting UTRmax (p=0.003), and resting E/e' (p<0.0001) (model pseudo-r² = 0.76).

Conclusion: Patients with abnormal E/e' response during DSE have reduced resting LV untwisting rate during IVRT. This phenomenon supports the contribution of impaired LV suction to the filling pressure response to stress.

32. Abnormal Left Ventricular Untwist Links Ischemia with Raised Filling Pressure at Dobutamine Stress Echocardiography (DSE)

With C W Lam, T Marwick, University of Queensland, Brisbane, Australia

Background: Abnormal diastolic responses to stress are linked to myocardial ischemia. We sought whether this was associated with abnormal LV untwist.

Methods: Routine DSE was combined with measurement of transmitral pulse-wave Doppler, myocardial tissue Doppler and speckle tracking imaging at baseline and peak dose in 110 pts (51 women, 62 ± 12y). Peak diastolic untwisting rate (UTR-PD) was computed by GE EchoPac software. Ischemic responses and other echo parameters were read separately by readers blinded to the other measurement. An ischemic DSE response was defined by any new regional wall motion defect at peak dose. ANOVA was used to analyze association between LV untwisting rate and various DSE responses.

Results: Patients were categorized into 3 groups, normal DSE (n=69), ischemic DSE (n=33) and scar DSE (n=12). The ischemic and scar DSE groups had a higher proportion of pts with prior myocardial Infarction and lower resting EF. Patients in ischemic and scar DSE groups are significantly older. However, UTR – which was not different at rest – was lower in the ischemic and scar groups at peak.

Conclusion: Ischemic and scar dobutamine stress echo response is associated with raised filling pressures at rest and peak stress, and reduced diastolic untwisting velocities at peak. UTR may link ischemia to increased filling pressure.
Abstracts for Free Paper Session:

33. Gamma-glutamyl transpeptidase level predicts the development of hypertension
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1Department of Medicine, 2Research Centre of Heart, Brain, Hormone and Healthy Aging,
3Department of Psychiatry, 4The State Key Laboratory of Brain and Cognitive Sciences,
5Genome Research Centre, and 6Department of Community Medicine, University of Hong Kong

Introduction: Liver enzymes are elevated in cardiometabolic diseases, particularly when there is non-alcoholic fatty liver disease. We therefore investigated if this hypertonisation is associated with elevated levels of alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase, and γ-glutamyl transpeptidase (GGT).

Methods: We included 235 hypertensive and 708 normotensive subjects from the Hong Kong Cardiovascular Risk Factor Prevalence Study-2 (CRIPS-2) in 2000-2004 who had fewer than one alcoholic drink a week. In the follow-up study in 2005-8 (CRIPS-3), 126 out of the 708 subjects had developed hypertension.

Results: In CRIPS-2, after adjusting for age, sex, body mass index, plasma ALT (OR=1.31 per SD of log-transformed level, P<0.005) and GGT (OR=1.52 per SD of log-transformed level, P=0.001) were significantly associated with prevalent hypertension. Among subjects not on anti-hypertensive medication, plasma GGT was associated with systolic (β=0.096, P=0.004) and diastolic blood pressure (β=0.102, P=0.004). In the forward stepwise logistic regression analysis of subjects normotensive at CRIPS-2, the highest tertile of plasma GGT level was an independent predictor of the development of hypertension in CRIPS-3 (OR=2.34, 95% CI=0.010, together with age, BMI, systolic blood pressure, and plasma CRP at baseline, and change in BMI. The other liver enzymes were not significantly predictors of new-onset hypertension.

Conclusions: Among the four liver enzymes, elevated GGT level is the strongest risk factor for hypertension in Hong Kong Chinese.

34. Using glycosylated hemoglobin to define the metabolic syndrome in United States adults
BYMY Cheung, KL Ong, AWK Tao2,2 SS Cherry1,2 PC Shan1,3
1Department of Medicine, 2Research Centre of Heart, Brain, Hormone and Healthy Aging,
3Department of Psychiatry, 4The State Key Laboratory of Brain and Cognitive Sciences,
5Genome Research Centre, University of Hong Kong, Hong Kong

Introduction: Recently, the American Diabetes Association has proposed the use of glycosylated hemoglobin (GHB) in the definition of diabetes and the category of increased diabetes risk. We therefore investigated whether GHB can be used instead of fasting plasma glucose in identifying individuals with the metabolic syndrome, which is associated with increased risk of cardiovascular disease.

Methods: Participants of the US National Health and Nutrition Examination Survey (NHANES) 1999-2006 who had fasting blood glucose were included (n=3551 in 1999-2002 and n=3412 in 2003-2006). The metabolic syndrome was defined using International Diabetes Federation criteria in 2009. Raised blood glucose was defined either as fasting glucose ≥100 mg/dl (5.6 mmol/l), or as Glucose ≥5.7%.

Results: In 2003-2006, there was 91.3% agreement between GHB and fasting glucose when either is used to define the metabolic syndrome, although the use of GHB slightly lowered the syndrome’s prevalence (34.8% vs 33.4%, P=0.012). The agreement was good (κ=0.87%) irrespective of age, sex, race/ethnicity, and BMI. Only 23% of the sample population had the metabolic syndrome defined using GHB but not using fasting glucose. The syndrome, defined using GHB alone, was associated with cardiovascular diseases (ischemic heart disease, heart failure or stroke) (OR=1.95, P=0.002). Similar results were found in 1999-2002.

Conclusions: Using GHB instead of fasting glucose to define the metabolic syndrome is feasible. The syndrome defined this way also identifies individuals with increased cardiovascular risk.

35. Serum uric acid, a cardiovascular risk, is associated with common clinical variables and the SLCAI9 polymorphism in Chinese patients
Migil Ha, Valiant WL Mak & Brian Tomlinson. Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR.

Purpose: Serum uric acid levels have been associated with increased risk of cardiovascular and renal disease in epidemiological studies. Recently, genome-wide association studies have identified new loci associated with serum uric acid levels including membrane transporters SLCAI9 and ABCG2. We examined whether these and other genetic factors were associated with uric acid levels in Chinese patients.

Methods: Eight single nucleotide polymorphisms (SNPs) in SLCAI9 (rs1014290, rs1251549), SLCAI9 (rs93006, rs1231825), CCL-2 (rs1866188), GCR (rs1260326) and ABCG2 (rs23114, rs231137) were genotyped in Chinese patients with increased cardiovascular risk and relationships with uric acid were examined.

Results: In 349 patients (including 137 with familial hypercholesterolemia, 105 with diabetes, 186 with hypertension) mean (± SEM) uric acid was 0.35 ± 0.09 mmol/L. Male gender, high creatinine levels, having hypertension, high waist circumference and high levels of triglycerides were significantly related to higher uric acid levels. The SLCAI9 rs1014290 T>C polymorphism was the only SNP independently associated with uric acid levels before and after adjustment for those clinical variables (CC vs. TC + CT = 0.38 ± 0.08 mmol/L, 0.34 ± 0.09 mmol/L; 0.31 ± 0.10 mmol/L, P=1.01 × 10^-5) and the association was more pronounced in women than in men, with consistent findings in multivariable analysis. All these genotypic and phenotypic factors totally explained 36.6% of the variance in uric acid levels.

Conclusions: Uric acid levels were related to common clinical variables and the SLCAI9 rs1014290 polymorphism in these Chinese patients.

36. Influence of Genomic Variants and Other Cardiovascular Risk Factors on High-Sensitivity Wil C-Reactive Protein in Chinese Patients on Statin Therapy
Valiant WL Mak1, Michael HK Lee2, Miao Ha3 & Brian Tomlinson3
1Department of Medicine & Therapeutics, 2Department of Chemical Pathology, The Chinese University of Hong Kong, Shatin, Hong Kong SAR.

Introduction: High sensitivity CRP (hsCRP) is a marker of inflammation and cardiovascular risk and is modulated by genetic variations and other cardiovascular risk factors. Statins reduce hsCRP and achievement of lower hsCRP levels appears to be associated with better outcomes. We examined the relationships of hsCRP levels with genetic and phenotypic factors in patients on statin treatment.

Method: Lipid parameters and plasma hsCRP were measured in Chinese patients treated with simvastatin 40 mg daily for at least 6 weeks. Phenotypic factors and single nucleotide polymorphisms (SNPs). IL1b -5117L, CRP -3872G >4 and CRP -5237A >G, were analysed for relationships with on-treatment hsCRP.

Results: In 271 patients with good adherence to therapy, reductions in plasma total cholesterol and LDL-cholesterol were -35.7±8.4% and -47.3±12.7%, respectively. Higher levels of hsCRP were associated (p<0.05) with having diabetes, higher waist circumference, higher plasma triglycerides, and lower plasma HDL-cholesterol. Multivariate logistic regression analysis showed that the odds ratio of having CRP>1mg/L was 2.4 (95%CI: 1.1-5.5; p<0.05) in subjects with wild-type CRP -3872GG variant compared to patients with 3872AA alleles after adjustment for waist circumference and plasma HDL-cholesterol level. There were no significant relationships with other candidate SNPs.

Discussion: A common SNP in CRP and other risk factors related to the metabolic syndrome influence hsCRP levels in Chinese patients on treatment with simvastatin.
Role of eNOS Enhancer in Prevention of Coronary Endothelial Dysfunction Induced by Homocysteine

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Purposes: Elevation of blood homocysteine levels (hyperhomocysteinemia) is a risk factor for cardiovascular disorders that has been demonstrated to be associated with endothelial dysfunction. In this study, we investigated the effect of a newly developed transcription enhancer of endothelial NOS (eNOS), AVE3085, on homocysteine-induced coronary endothelial dysfunction.

Methods: Isometric force study was performed in a myograph with both endothelial-dependent and -independent relaxation examined in porcine coronary small arteries (diameter 600-800 μm) that were incubated for 24 hours with homocysteine (50 μM), AVE3085 (10 μM), or homocysteine plus AVE3085. Protein expression of eNOS and the phosphorylation of eNOS at serine-1177 (p-eNOS1177(Ser)) were determined by Western blot.

Results: Incubation with homocysteine for 24 hours did not alter the endothelium-independent relaxation to sodium nitroprusside in coronary arteries but significantly decreased the vasorelaxation to endothelium-dependent vasodilator, bradykinin (69.9±5.4% vs. 93.1±2.0% in control, p<0.0001). CVD, -6.4±0.39% vs. -7.73±0.26% in control, p=0.05). Protein expressions of eNOS and p-eNOS1177(Ser) were markedly inhibited by homocysteine. Cotreatment with AVE3085 restored bradykinin-induced relaxation (90.5±1.6% vs. 60.9±5.4% p<0.0001) and enhanced eNOS and p-eNOS1177(Ser) expression. Pretreatment with either protein kinase Akt inhibitor or inhibitors of phosphatidylinositol 3-kinase (PD-3-kinase; wortmannin and LY294002, attenuated the protective effect of AVE3085 on vasorelaxation. Inhibition of PD-3-kinase/Akt also decreased eNOS phosphorylation at serine-1177 that was enhanced by AVE3085.

Conclusions: AVE3085 attenuates homocysteine-induced coronary endothelial dysfunction with PI3-kinase/Akt pathway involved. This study suggests that eNOS enhancers may have potential clinical applications in controlling homocysteine-associated vascular injury and cardiovascular disease.
ABSTRACTS

Abstracts for Free Paper Session:

CARDIAC SURGERY

38. Surgical Treatment of Tricuspid Regurgitation After Mitral Valve Surgery
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1Department of Cardiovascular Surgery, TEDA International Cardiovascular Hospital, Tianjin, China; 2Providence Heart & Vascular Institute, Stav Avery Academic Center, Department of Surgery, Oregon Health & Science University, Portland, Oregon, 97223, USA

Purpose: Functional tricuspid regurgitation (TR) occurs in patients with rheumatic mitral valve disease even in those who had mitral valve surgery. The aim of this study was to analyze TR in a group of patients who underwent successful mitral valve surgery.

Methods: From September 2003 to September 2008, 45 patients with TR after mitral valve replacement and underwent second operation for TR were enrolled in this study. In these, 43 patients (95.6%) had left heart failure symptoms (adenos of lower extensions, ascites, hepatic congestion, etc.) and 40 patients (88.9%) had mitral fibrillation. Twenty-six patients (57.8%) were New York Heart Association (NYHA) functional class II and 19 (42.9%) in class IV. Previous operations included 41 for mechanical mitral valve replacement (91.1%), 4 for bioprosthetic mitral valve replacement (8.9%), and 7 for tricuspid annuloplasty (15.6%).

Results: All patients received medications to improve the heart function. The tricuspid valve were repaired with Kay’s (7 cases, 15.6%) or De Vega technique (4 cases, 8.9%). Tricuspid valve replacement was performed in 34 cases (75.6%). One patient (2.2%) died. Postoperative low cardiac output (LCO) occurred in 5 patients and treated successfully. Postoperative echocardiography showed obvious reduction of right atrium and ventricle. Comparing with the preoperative data (33.7±2.2mm), the interatrial diameter of right ventricle decreased to 23–41mm (25.5±7.1mm; P<0.05).

Conclusion: TR after mitral valve replacement in rheumatic heart disease is a serious clinical problem. If occurs or progresses late after mitral valve surgery, tricuspid valve annuloplasty or replacement may be indicated with satisfactory.

39. Inhibition of Vasocostriction by Amiodarone in Human Internal Mammary Arteries Used as Bypass Grafts
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1TEDA International Cardiovascular Hospital, Medical College, Nanai University; 2The Chinese University of Hong Kong; 3Shari Academic Center, Providence Heart & Vascular Institute, Department of Surgery, Oregon Health & Science University, Portland, Oregon, 97223, USA

Purpose: Graft spasm remains challenging in coronary artery bypass grafting (CABG) surgery. We investigated the inhibitory effect of a clinically used dihydroxyindene calcium antagonist amiodarone on the vasocostriction mediated by a number of important spasmogens potassium chloride (KCI), human urinary-III, and thromboxane mimetic U46619 in human internal mammary artery (IMA) from patients undergoing CABG.

Methods: Isolated IMA rings (n = 78, taken from 42 patients) were studied in organ baths in two ways: the relaxing effect of amiodarone on vasocostriction-induced precontraction by KCI, HU-III, and U46619 and the depressing effect of amiodarone on the contraction.

Results: Amiodarone caused full relaxation in KCI (98.0±2.1%), HU-III (98.5±2.4%) and in U46619 (99.3±1.3%) IMA rings (n = 8) with 15.5-fold higher potency to KCI than to HU-III (EC50 = 8.17 ± 0.28 vs. 6.58 ± 0.01 log M, p < 0.001) and 19.5-fold that to U46619 (EC50 = 8.17 ± 0.28 vs. 6.88 ± 0.08 log M, p < 0.001). Pretreatment of IMA with plasma-concentrations of amiodarone (0.5 log M) significantly depressed subsequent contraction to KCI (from 20.8 ± 2.8 mN to 7.6 ± 3.0 mN, P = 0.004), HU-III (from 14.1 ± 4.2 mN to 3.8 ± 2.0 mN, P = 0.025), but did not affect the contraction to U46619.

Conclusion: We conclude that in human IMA, amiodarone has a selective inhibitory effect on the vasocostriction mediated by a variety of vasocostricators. Thus, amiodarone may be useful in patients undergoing CABG for treatment and prevention of graft spasm.

40. Outcome of Thoracic Organ Transplantation for Adults with Congenital Heart Disease
KS Looi1, K Fan1, CF Wong1, TC Yong1, PC Chow1, KT Wong1, YF Cheung1, WH Chow1, AKT Chau1, SW Chiu1, LC Cheng2
1Department of Pediatric Cardiology, Queen Mary Hospital, Department of Cardiology & Department of Tuberculosis & Chest Medicine, Grantham Hospital, Department of Cardiothoracic Surgery, Queen Mary Hospital, Hong Kong

Background: Transplantation can be an option of treatment in adult patients with congenital heart disease (CHD) who develop severe cardiopulmonary dysfunctions. We describe the outcome of patients who had undergone heart (HTx) or heart-lung transplantation (HLTx) in Hong Kong.

Methods: We performed a retrospective review of seven adults (4 males) with CHD who had HTx or HLTx between 1995-2005, and compared the two groups.

Results: Median age at transplantation was 30 years (range 23-47 years) with a median follow-up of 3.3 years (range 1-8 years). There were four HTx which constituted 4% of all HTx recipients in Hong Kong. The diagnoses were: Tetralogy of Fallot (n=2), pulmonary atresia and ventricular septal defect (n=1), transposition of great arteries after Mustard operation (n=1). There were three HLTx which accounted for all HLTx in this locality. All three patients had Eisenmenger syndrome (two ventricular septal defects, one atrial septal defect). There was one early mortality (4 weeks) after HTx due to graft versus host disease complicated with febrile sepsis. All patients after HTx survive and are in NYHA class I-II except one who has neurological sequelae after reanuinated cardiac arrest before HTx. Complications of HTx patients included bleeding, antibody mediated rejection, moderate to severe acute cellular rejection, right ventricular dysfunction which resolved after appropriate therapies. One patient after HLTx had refractory chronic lung rejection and was in NYHA class III. She died 6 years 11 months after HLTx while waiting for lung retransplantation. The other surviving HLTx patient is in NYHA class I with persistent bilateral pleural effusion treated with diuretic.

Conclusion: HTx or HLTx can be considered in selected adult patients with CHD with reasonable outcome. From our observation, HTx patients appear to have better survival compared to HLTx patients, which conurs with the experiences of other centers.

41. Surgical Results of Pulmonary Valve Replacement after Repair of Tetralogy of Fallot
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Department of Cardiothoracic Surgery, Queen Mary Hospital; Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, the University of Hong Kong; and Department of Paediatric Cardiology, Queen Mary Hospital

Purpose: To evaluate the results of pulmonary valve replacement (PVR) in patients with severe pulmonary regurgitation (PR) after repair of Tetralogy of Fallot (TOF) repair in Hong Kong.

Methods: Medical records of patients requiring PVR after repair of TOF in our center between January, 2002 and December, 2008 were reviewed.

Results: Over a six years period, 17 patients (10 male, 7 female) required PVR for severe PR after previous complete repair of TOF. The mean age of PVR was 23.72 ± 13.03 years and the mean time interval between the initial repair for TOF and PVR was 18.48 years ± 9.15 years. Indications for PVR were symptomatic severe PR in these patients and asymptomatic progressive right ventricular dilatation in the remaining 14 patients. There was no in-hospital mortality. The mean post-operative duration of stay in the intensive care unit was 1 day. The mean hospital stay was 12.33 ± 7.74 days.

Conclusion: With the advances of surgical techniques and peri-operative care, the early mortality of TOF repair in patients beyond infancy has become very low and many patients survive to adulthood. Many of these patients develop chronic PR requiring PVR. Our results showed that PVR for severe PR after previous complete repair of TOF is a safe procedure and patients may benefit from PVR with improved right ventricular function.
ABSTRACTS

Abstracts for Free Paper Session:

42. Aortic dissection, Intramural hematoma and Penetrating atherosclerotic ulcer: A 10 years’ experience from a regional hospital
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Purpose: Aortic dissection carries high morbidity and mortality. Variants of aortic dissection include intramural hematomas and penetrating atherosclerotic ulcer which share similar clinical presentation and management. The aim of this study is to investigate the difference in clinical characteristics between aortic dissection, intramural hematomas (IMH) and penetrating atherosclerotic ulcer (PAU).

Methods: Retrospective review was performed to the 153 patients admitted to our hospital with the Clinical Management System (CMS) diagnosis of "dissecting aortic aneurysm" from the year 2000 to 2009. All computer tomography (CT) and transoesophageal echocardiography (TEE) reports were reviewed to differentiate between aortic dissection, intramural hematomas (IMH) and penetrating atherosclerotic ulcer (PAU).

Results: The disease was male predominant (66%) with the mean age of 68.4 years old. 141 (92.2%) patients had hypertension. There were 88 (57.5%) cases of aortic dissection, 62 (40.5%) cases of IMH, and 3 cases of PAU. Analysis was mainly performed on aortic dissection and IMH. In aortic dissection, 40 cases (53.9%) were type A and 43 cases (67.7%) were type B. In IMH, 25 cases (48.3%) were type A and 27 cases (55.7%) were type B. 30 cases (54.1%) proceeded to surgery in aortic dissections and 10 cases (16.3%) proceeded to surgery in IMH. The difference in the rate of surgical treatment was significant (P=0.04). Complications including in-hospital mortality occurred in 41 cases (46.6%) of aortic dissection, compared with 56 cases (35.8%) of IMH (P=0.03). The most common complications were hemorrhagicstroke, acute renal failure and cerebrovascular accident. The rate of in-hospital mortality was also significant more in aortic dissection (24 cases, 27.3%), compared with IMH (7 cases, 11.2%) (P=0.07).

Conclusion: The rate of complications, in hospital mortality and surgery were significantly more in aortic dissection when compared to intramural hematomas. Prompt recognition for the type of aortic dissection is essential for risk stratification and outcome improvement.

43. Predicting surgical outcome with computed tomography of right ventricle (CTRV) in patients with late tricuspid regurgitation
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Objective: Isolated tricuspid regurgitation can progressively worsen years after left sided heart valve surgery. Surgical repair or replacement became inevitable when severe symptoms appeared. Prognostic factors are lacking in the literature, especially relating right heart function to this right sided heart valve surgery. This study aimed to predict surgical outcome by using right ventricular function obtained from computed tomography.

Methods: Patients underwent isolated tricuspid surgery were enrolled. All of them had routine workup and CTRV assessment before operation. Primary end-point was survival and symptomatic improvement at 1 year follow up.

Results: From Jan 2005 to June 2008, 24 patients had either isolated tricuspid repair or replacement done. There were 12 patients in the favorable group (survivor with at least 1 NYHA class improvement) and 12 in the unfavorable group (non-survivor or survivor with no symptomatic improvement). All the baseline characteristics, echocardiogram data and surgical details were comparable between the 2 groups. Only CTRV parameters including end-systolic volume (ESV), indexed end-systolic volume (IESV), end-diastolic volume (EDV) and indexed end-diastolic volume (IEDV) were significantly different between the 2 groups. Patients had iESV > 88ml/m² or iEDV > 188ml/m² pre-operatively likely to have unfavorable surgical outcome.

Conclusions: Right ventricular function from CT can predict surgical outcome in patient underwent isolated late tricuspid regurgitation. Operation should not be delayed until severely dilated right ventricle in order to have favorable surgical outcome.
**ABSTRACTS**

Abstracts for Free Paper Session:

**MISCELLANEOUS**

44. **Pulmonary Arterial Hypertension: Characteristics of Patients**

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**Purpose:** Pulmonary arterial hypertension (PAH) is characterized by increased pulmonary vascular resistance and arterial pressure that can lead to right heart failure and death. Recently, there were significant changes in diagnosis and management of PAH. However, the treatment results were still unsatisfactory. Before further trials to study different combination of drugs, we need to have better understanding of the characteristics of the patients with PAH.

**Methods:** Retrospective study. All patients who were admitted to Queen Elizabeth Hospital with the diagnosis of World Health Organization group 1 PAH or with confirmation of group 1 PAH by cardiac catheterization during the period from 01/01/2008 to 01/03/2010 were included. Queen Elizabeth Hospital was one of the territory referral centre in Hong Kong. All the pediatric patients with age <18 were excluded.

**Results:** A total of 15 patients were admitted to our hospital with the diagnosis of Group 1 PAH in the study period. 4 of them were newly diagnosed. 93% (14/15) patients were female. The mean age was 44 years old, ranged from 27 years old to 77 years old. 2 cases were idiopathic PAH, 2 cases were associated with drugs (ex-TYVA, history of use of metamphetamine), 2 cases were associated with connective tissue disease (scleroderma, SLE), 6 cases associated with congenital systemic-to-pulmonary shunts and 3 cases with unknown association (patients refused further workup), 9 cases had right heart catheterization with mean PA pressure ranged from 27 to 70 mmHg, mean PA pressure of all 9 cases was 48mmHg. Drugs related PAH seemed to have higher mean PA pressure (58,70mmHg) and lower cardiac index (1.74,1.29L/min/m2 vs 2.84L/min/m2 in other associations).

**Conclusion:** No cases showed vasoreactivity. 5 patients were in NYHA functional class (FC) II on diagnosis, 5 patients in FC III and 2 patients in FC IV. Only 1 patient received Ca blocker but not in the therapeutic high dose. 6 patients received one of the PAH targeted therapy and 1 patient received more than 1 PAH targeted therapy, 4 patients with home C2 therapy, 7 patients received warfarin and 6 cases had diuretic. 1 patient had history of atrial septectomy and 1 patient was waiting for lung transplant. There were 3 patients died in the study period, 1 died of right heart failure with confluence, 1 because of pulmonary artery dissection and the cause of the remaining one was unknown.

45. **Profile Of Pulmonary Thromboembolism - A Retrospective Study**

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**Purpose:** Pulmonary Thromboembolism (PTE) is a potentially fatal condition, but an eminently identifiable and treatable medical emergency. This retrospective analysis was undertaken to study the profile of PTE patients in risk factors, clinical picture and its hospital outcomes.

**Methods:** From June 2002 to August 2009, 81 patients of PTE hospitalized formed the study population.

**Results:** The mean age was 49.02 ± 14.71 years and 41% were females. Diagnosis of PTE was based on clinical findings, ECG, Echocardiography, Chest x-ray, D-dimer and CT chest. Risk factors were hypertension 28.39%, Diabetes mellitus 28.39%, Smoking 19.75%, DVT 18.75%, post operative state 13.58%. Cardiopulmonary diseases 12.34%, prior PTE 8.64%, Malignancy 6.17%, fracture / trauma 4.93%. Most common symptoms were dyspnoea 96.20% followed by lower limb swelling 38.27%, chest pain 37.03%, cough 25.92%. Signs were tachycrhythmia 87.65%, raised JVP 64.19%, tachycardia 54.32% and plexus 41.97%.

**Conclusion:** Wells score was useful in assessing the probability of PTE. The mortality rate was high which highlights the importance of prevention and early detection of PTE.

46. **Effect of Hypoxia-Reoxygenation on Endothelial Canonical Transient Receptor Potential Channels**

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1Department of Surgery & 2School of Biomedical Sciences, The Chinese University of Hong Kong, Hong Kong 2TEDA International Cardiovascular Hospital, Medical College, NanKai University, Tianjin, China

**Purpose:** The importance of canonical transient receptor potential channels (TRPCs) has been revealed in endothelial ionotropic Ca2+ (iCa2+) regulation and therefore in vascular endothelial physiology. Whether TRPCs are affected by ischemia-reperfusion / hypoxia-reoxygenation has been poorly studied. Therefore, in this study, we investigated the role of endothelial TRPCs in vasoconstriction and the effect of hypoxia-reoxygenation (H-R) on these channels.

**Methods:** Primary cultured porcine coronary endothelial cells (PECs) were used for patch-clamp study. Endothelin-1-dependent relaxation to bradykinin (40–65 LogM) was studied in porcine coronary small arteries (diameter 600 to 800 μm) in a myograph. Results: Bradykinin-induced vasodilation in coronary arteries was attenuated by pre-incubation with TRPC3 inhibitor SKPL603 (10 μM) (86.5 ± 1.1% vs 94.4 ± 2.8%, p < 0.05). Similar reduction (p < 0.05) was also observed in the vessels pre-incubated with the specific TRPC3 inhibitor, PyrC (3 μM). H-R (60–90min, PO2=10 mmHg) constantly induced the vasoconstriction to bradykinin (75.3±4.4% vs 88.3±3.5% in normoxia, p < 0.05) and such reduction was restored (96.4±1.3%) by pre-incubation with TRPC3/6/7 activator 1-deoxy-1-acetylvegoto- glycoside (100 μM). In primary cultured PECs, the current density elicited by bradykinin was inhibited by exposure to H-R (8.0±0.4 vs 14.0±1.3 pA/pF at control, p<0.01). PyrC-sensitive TRPC3 current was reduced from 6.3±0.4 to 6.0±0.4 pA/pF at 3.0±0.3 pA/pF under H-R exposure (p<0.01)

**Conclusion:** TRPCs, including TRPC3, play an important role in endothelium-dependent relaxation in porcine coronary arteries. H-R inhibits the channel activity of TRPCs and the associated endothelial function. These results suggest that TRPCs may become an important and novel pharmacological target for endothelial protection in ischemic coronary disease.
ABSTRACTS

Abstracts for Free Paper Session:

49.

Measurement of errors associated with using Pulmonary Artery Thermocardiography Catheters.

**Purpose:** Thermocardiography cardiac output lacks precision, and has a quoted error (95% confidence interval for mean values) of ±20%. This lack of precision, and uncertainty about its true value, makes difficult when thermocardiography is used to validate new cardiac output technology. Our aim was to recognize the precision error of thermocardiography.

**Methods:** A test rig consisting of 1.5cm diameter plastic tubing, a water reservoir (18-litre), a high volume water pump with flow regulator and pump to insert thermocardiography catheters into a flow chamber was assembled. Flow in the test rig was measured using a commercially available flow probe and flow meter. The pump was first calibrated by timing the filling of a glass cylinder. Circulating water temperature was 36.5°C. Five Sykes (Edwards Lifesciences, USA) 8 Fr thermocardiography catheters, accustomed to a Siemens SC2000 cardiac output monitor, were then tested. Thermocardiogram cardiac output readings were made by injecting 5ml of ice cold water. The calibration of each catheter was completed by plotting the test rig reading against the thermocardiogram reading. Flow rates from 0 to 8 L/min were used and a calibration (regression) line drawn for each catheter.

**Results:** The calibration of the catheters varied from an offset of -9.5% to +45.2%. At a flow rate of 5 L/min the thermocardiogram reading ranged from 4.8 to 5.2 L/min. The estimated precision error at this flow rate was 8.0% (Figure).

**Conclusion:** The controlling variability (coefficient of variation) was 4.8%, with an estimated precision error of 8.0% (Figure).

48.

The effect of retinoid acid signaling on the embryonic cardiac development and regulation of cardiac related thsl and thbs20 expression.

**Objective:** To explore the effect of sufficient retinoid acid (RA) signaling on the early embryonic cardiac development, especially on the regulation of cardiac related transcriptional factors thsl and thbs20.

**Methods:** We designed morpholinoo antisense oligodeoxynucleotides (MO) targeting zebrinful retad2 gene to knock-down its expression and constructed rudad2-ZEOZP plasmid to verify the effectiveness and specificity of rudad2-MO. The embryonic cardiac phenotype and cardiac function were analyzed and compared between wild-type and rudad2-MO group. Then, we described the expression pattern of thsl and thbs20 in zebrinful embryos, and the regulation of their expression when retad2 gene was knocked down.

**Results:** Rudad2-MO microinjection could effectively knock-down retad2 gene expression, the mortality and abnormal embryo rate rose with the increase of rudad2-MO dosage. Rudad2-MO embryo exhibited abnormal cardiac phenotypes, including swollen pericardial cavity, tubular heart, incompletely D-loop, abnormal atria and ventricle development, blood stagnation, slow blood flow and weak heart beat. The results of whole-mount in situ hybridization of thsl and thbs20 proved that these genes had distinct expression patterns, thsl expressed in cardiac outflow tract, atrio ventricular junctional, branchio cardiomyocyte, and thbs20 expressed in the embryonic heart. In retad2 knock-down embryos, thsl and thbs20 expression were down-regulated in the heart to some extent.

**Conclusion:** RA signaling plays a critical role in several key stages of cardiac development. The expression of thsl and thbs20, which play important roles during embryogenesis, can be regulated by RA signaling during cardiac development, and the underlying mechanism still needs further investigation.

49.

Ethanol and its metabolites induce cytotoxicity and H3 lysine9 epitaposition in cardiac progenitor cells.

**Purpose:** This study was to investigate the effect of ethanol and its metabolites on acetylation of H3 lysine9 and the mRNA expression of heart development-related genes Gata4, Mef2c, Tbx5 in cardiac progenitor cells.

**Methods:** We used cardiac progenitor cells as our study object and apply MTT assay to select the intervention concentrations, Western blotting to acetylation of histone H3 lysine9, Real-time PCR to expression of genes.

**Results:** MTT assay show that low concentration groups of 50 mmol/L ethanol, 4 mmol/L acetaldehyde, 4 mmol/L acetate didn’t affect the proliferation of cells compared with control (P>0.05). But high concentration groups of 200mmol/L ethanol, 120mmol/L acetaldehyde, 16mmol/L acetate affected the proliferation about 30% (P<0.05). We reveal that low concentration groups of ethanol, acetate respectively increased 2.4 fold of acetylation of H3 lysine9 (P<0.05). The heart development-related genes had no significant change (P>0.05). High concentration groups of ethanol, acetate respectively increased 5.3, 3.6 fold of acetylation of H3 lysine9 and the expression of heart development-related genes GATA4, Mef2c increased as compared with control or the corresponding low concentration groups (P<0.05) whether low or high concentrations acetaldehyde and but had a negligible effect on the acetylation of H3 lysine9 and the expression of heart development-related genes (P>0.05).

**Conclusions:** High concentrations of ethanol and its metabolites all have a cytotoxic effect to cardiac progenitor cells. Ethanol and acetate induce H3 lysine9 epitaposition which may one of the pathogenesis of CHD caused by alcohol.
Abstracts for Free Paper Session:

51.  
Effects of Hydrogen Sulfide on the Expressions of bax and bcl-2 in Hippocampi of Rats after Cardiopulmonary Resuscitation.  
Ji-yan Lin, Hong-yan Wei, Hui Li, Xin Li, Rong Liu, Chun-lin Hu, Guo-qing Huang, Gang Dai, Xiao-xing Liao on behalf of Department of Emergency, the First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China  
Purpose: To examine the expression of bax and bcl-2 in the hippocampi of rats and investigate the effects of hydrogen sulfide (H\textsubscript{2}S) on neurons apoptosis after cardiopulmonary resuscitation (CPR).  
Methods: There were 160 male SD rats, the 108 rats were initially selected and randomly divided into 3 groups equally. Model of cardiac arrest were induced by transcutaneous electrical epicardium stimulation and standard CPR were offered in all the subjects. After ROSC, the First group were given sodium bisulfide, the second group were given hydroxylamine, and the third group were only given routine CPR. Above-mentioned the three groups were further divided three sub-groups based on the observed end point (1, 3 or 7 days), then each sub-group were divided into two groups equally and given them relevant examination such as Immunohistochemistry or RT-PCR of bax and bcl-2.  
Results: (1) Numbers of substitutes and mortality rate after ROSC were no significant difference among the three groups (\(P>0.05\)). (2) There were significant differences in the serum levels of H\textsubscript{2}S among the three groups on 1, 3 and 7 days after ROSC (\(P=0.000\)). (3) On 1, 3 and 7 days after ROSC, the sum of integrated optical density (IOD) of bax and bcl-2 in the hippocampi CA1 area among the three groups had statistic significance (\(P<0.05\)). And in every group, there were significant differences in the sum of IOD of bax and bcl-2 in the hippocampi CA1 area among the three observed end points (\(P<0.01\)). (4) On 1, 3, and 7 days after ROSC, the expressions of bax mRNA and bcl-2 mRNA in the hippocampi among the three groups had statistic significance (\(P=0.000\)).  
Conclusion: H\textsubscript{2}S may be take part in neurons apoptosis by imbalance of bcl-2/bax.

52.  
Change of Hydrogen Sulfide Content in Serum of Rats After Cardiopulmonary Resuscitation.  
Xiao-xing Liao, B-yan Lin, Hong-yan Wei, Hui Li, Xin Li, Rong Liu, Chun-lin Hu, Guo-qing Huang, Gang Dai on behalf of Department of Emergency, the First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China  
Purpose: To investigate variation of hydrogen sulfide (H\textsubscript{2}S) in serum of rats after cardiopulmonary resuscitation (CPR) and explore its pathophysiological role in CPR.  
Methods: The 30 male SD rats were randomly divided into control groups (n=6) and experimental group (n=24), then models of cardiac arrest (CA) were established in rats of experimental group by transcutaneous electrical epicardium stimulation. Blood samples were collected before CA, at 2, 4, 6, 8, 10 and 12h after restoration of spontaneous circulation (ROSC) for testing the serum levels of H\textsubscript{2}S, at the same time rectal temperature (Tr), mean arterial pressure (MAP), heart rate (HR) and respiration rate (R) were record. Next to analyze the dynamic variation of H\textsubscript{2}S content in serum of the rats after CPR and its correlation of the above-mentioned signs of life.  
Results: (1) In experimental group, all of the 24 rats were successfully induced CA and resuscitation; at end points (12h after ROSC) there were 14 rats were alive and their vital signs were stable. There was no death in the control group. (2) The variation trend of H\textsubscript{2}S content in serum was different between experimental group and the control (\(F=12.226, P=0.003\)). In experimental group, H\textsubscript{2}S content in serum increased dramatically after CPR and reached peak at 6h after ROSC, then return to the similar level of the control group. (3) H\textsubscript{2}S content in serum was negatively correlated with Tr (\(partial \ r=-0.556, P=0.000\)) and MAP (\(partial \ r=-0.240, P=0.002\)). But it wasn't correlated with HR and R (\(P=0.05\)).  
Conclusion: Change of H\textsubscript{2}S content in serum of rats after CPR may be a manifestation of compensatory responses after ROSC and participate in physiological processes such as body temperature and blood pressure regulation. But as for its precisely mechanisms, it still needs to be studied further.

53.  
Long-term enhanced external counterpulsation repairs platelet membrane fluidity and alleviates lipid peroxidation in patients with stable angina pectoris.  
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Purpose: To explore the effect of long-term enhanced external counterpulsation (EECP) on platelet membrane fluidity (PMF) and lipid peroxidation in patients with stable angina pectoris.  
Methods: Long-term EECP was performed on 106 patients with stable angina pectoris, 1 hour once a day for 36 days. Platelets were harvested from all patients pre-EECP (before EECP), during EECP (EECP for 18 hours) and post-EECP (EECP for 36 hours). Fluorescence polarizability \(P\) was measured by fluorescence spectrophotometer. Meanwhile, the levels of lipid peroxidation and plasma lipids including total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C), were measured.  
Results: Compared with pre-EECP, PMF was repaired significantly in patients with stable angina pectoris, no matter EECP performed for 18 hours or for 36 hours (\((0.337\pm0.053), (0.257\pm0.042)\) vs. \((0.543\pm0.066), (0.543\pm0.066)\), respectively, \(P<0.05\)). Similarly, lipid peroxidation levels were also alleviated obviously \((0.427\pm0.053) \ \mu\text{mol/L}, (0.302\pm0.046) \ \mu\text{mol/L} vs. (0.712\pm0.126) \ \mu\text{mol/L}, (0.712\pm0.126) \ \mu\text{mol/L}, respectively, \(P<0.05\)). Moreover, it seems a more significant change in both PMF and lipid peroxidation when EECP performed for 36 hours than for 18 hours. On the contrary, there was no significant change in the levels of plasma lipids (TC, TG, LDL-C, HDL-C). A direct negative correlation was observed between PMF and the levels of lipid peroxidation.  
Conclusion: This result demonstrates that Long-term EECP can alleviate lipid peroxidation and restore or repair PMF in patients with stable angina pectoris, contributing to postponing atherosclerosis.
Abstracts for Free Paper Session:

**PAEDIATRIC CARDIOLOGY I**

55. Outcomes in Patients with One-stage Repair of Aortic Coarctation

**MY Cheng, B Jia and ZG Chen**
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**Objective**: Review and analyse the clinical applications and follow-up results in the patients of Aortic Coarctation, who underwent one-stage total repair, in order to investigate the optimal surgical approaches and optimal operative age for Aortic Coarctation, and reduce the complication of early and median time and elevate survival rate after repair.

**Methods**: Review the information for patients since admission, who underwent one-stage total operation in our Center, collect the historical information form and follow-up results combine right statistical method, to measure the correlation factor with survival rate, reoperation and late follow-up results.

**Results**: From November 1999 to November 2009, 121 patients with Aortic Coarctation associated with heart defects underwent one-stage surgical repair in our institution. The age at operation was ranged 5 days to 12 years, the weight was ranged 2.2 kg to 44 kg. Follow-up period was ranged 3 months to 9 years. Aortic Coarctation was associated with patent ductus arteriosus and isolated in 37 patients, Ventricular septal defect was found in 53 patients, of which 27 cases were associated with patent ductus arteriosus. Aortic Coarctation was associated with other complex intra cardiac anomalies in 21 cases. Surgical techniques were as follows: 33 had patch enlargement, 77 had resection with extend end-to-end anastomosis, 11 had subclavian flap aortoplasty. Late survival rate is 94.2%. Reoperations were in 17 patients, the rate is 14.0%. Multivariate analysis revealed that early instantaneous peak velocity across the aortic and dysplasia of aorta also the diameter of anastomosis were independent risk factors for recurrent coarctation. No single operation appeared to have a clear superiority

**Conclusion**: One-stage total repair for Aortic Coarctation is feasible. Late survival rate is deviated remarkable. But improving late outcomes remains a surgical challenge.


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**Objective**: To determine the incidence, risk factors, prevention and treatment of AVB associated with ASD transcatheter closure using ASO in children.

**Methods**: A total of 450 patients underwent transcatheter ASDs closure using ASO from March 1998 to December 2005 in our institution. The median age was 6.3 years (range, 2.3 to 14 years) and median weight was 17.4 kg (range, 9 to 44 kg). Electrocardiographic tracings before procedure and at follow-up visits were reviewed. The risk factors, prevention and treatments of the AVB were analyzed.

**Results**: 14 patients developed various AVB (3.1%), including first degree AVB in 6, second degree AVB in 4 and third degree AVB in 4 patients. All AVBs occurred one to two days after transcatheter occlusion of the ASD. Among 14 patients, new-onset AVBs were found in 12 patients and aggravation of preexisting AVBs were noted in 2 patients. The larger device (24.2± 9.1 vs. 17.6±9.1 mm, P<0.001) and smaller age (4.3±1.4 vs 7.6±3.3 years, P=0.03) were two risk factors for AVB. Continuousd flow was routinely used for all patients with AVB and removal of the device was implemented for 4 patients with third-degree AVB. A vast majority of cases resolved or improved spontaneously, with no recurrence at short-term follow-up.

**Conclusions**: AVB remains the severe complication after interventional catheterization for ASDs using ASO. The larger device and smaller age can be associated with the development of AVB. Selection of the proper ASO may be the most effective measures to prevent AVB after transcatheter closure of ASDs for small children. Most of all AVBs can resolve within a short time by giving medical or surgery intervenes as soon as possible.

57. Transcatheter Embolization of Intralobar Pulmonary Sequestration in Infants

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**Purpose**: To describe experience with the safety and efficacy of transcatheter embolization technique for the treatment of pulmonary sequestration (PS) on infants.

**Methods**: Between 2008 and 2009, 3 infants (3 males, aged 6-18 months) received the treatment. All had presented with shortness of breath and repeated respiratory infections. The diagnosis of pulmonary sequestration was confirmed by Doppler ultrasonography, contrast-enhanced computed tomography and angiogram. Selective angiography revealed vascular conglomeratation and the origin, the diameter and the number of hypertrophic feeding arteries, as well as concomitant various vessel. AMPLATZER® Vascular Plug, which was 30% - 40% larger in diameter than the vessel was implanted to close the aberrant artery supplying the pulmonary sequestration using a 5F cathether via the right femoral artery.

**Results**: Two infants were considered cured by embolization alone. Two patients implanted one plug for complete closure. Another patient implanted two coils and one plug for complete closure the PS. No residual flow in the pulmonary sequestration was noted after the procedure by ultrasonography and CT. Initial follow-up was performed 1 - 2 months after the procedure by chest ultrasonography and CT and, thereafter, follow-up was performed after 6 months and then annually. Complete regression was defined as the total disappearance of abnormal lung tissue on CT image.

**Conclusion**: Our experience indicated that pulmonary sequestration in infants can be cured by transcatheter embolization alone with an AMPLATZER® Vascular Plug.

58. Evaluate Heart Function of Adolescent Scoliosis by Tissue Doppler

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**Purpose**: To evaluate heart function of adolescent scoliosis by tissue doppler.

**Methods**: Choose 11 adolescent patients with scoliosis diagnosed in our hospital from July 2009 to August 2009, and 16 normal control. Then check the tissue doppler of heart. During the study, we measured the pulse tissue doppler of mitral annulus and tricuspid annulus, then compared the data between the patients and normal control. Statistical analysis was done by SPSS11.5.

**Results**: First, mitral annulus. Em of the scoliosis group (0.18±0.03) m/s was less than normal control (0.21±0.03) m/s significantly, P<0.038. IRT/IR of the scoliosis group (1.83±0.18) was much larger than normal control (1.35±0.24). Also, IRT/IR of the scoliosis group (2.38±0.64) much larger than normal control (1.07±0.18), and Tsi index of the scoliosis (0.40±0.09) much larger than normal control (0.23±0.03), P<0.05. The results of tricuspid annulus were similar with mitral annulus. Em of scoliosis group (1.99±0.22) VS normal control (1.56±0.3). IRT/IR of scoliosis group (1.99±0.61) VS normal control (1.09±0.4). Tsi index of scoliosis group (0.2±0.13) VS normal control (0.25±0.06), P<0.05. There’s no statistical difference of Am, Sm and Et/Am between the two groups.

**Conclusion**: The heart function of left and right ventricles decreased in adolescent scoliosis.
59. Research of N-terminal Pro-brain Nitric Peptide for Congenital Heart Disease with Pulmonary Hypertension
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Objective: To investigate whether serum N-terminal Pro-Brain Nitric Peptide (NTpro-BNP) levels could reflect the severity of pulmonary arterial hypertension in children with congenital heart disease (CHD).

Methods: We performed a retrospective study to determine if serum NTpro-BNP levels varies by pulmonary artery systolic pressure (PASP) by catheterization. The population included a group of 27 pediatric patients from 2006 to 2009. All patients were diagnosed with CHD of left to right and had serum NTpro-BNP and catheterization. Exclusion criteria were impaired renal function (serum creatinine level >115 µmol/L), decreased left heart function (LVEF <50%), and stenosis of outlet of right ventricle. Serum NT-proBNP were measured using the electrochemiluminescence immunoassay. Statistical analysis of the linear correlation of NT-pro BNP and PASP were carried out.

Results: The NT-proBNP concentration can reflect the degree of PASP (r=0.58, AP=0.001). Using serum NT-proBNP concentration ≥134pg/ml as the cut point for diagnosing slight and medium PAH, the sensitivity was 90%, the specificity 86%, and ≥499.0pg/ml as the cut point for diagnosing serious PAH, the sensitivity and specificity was 64% and 82% respectively.

Conclusion: We concluded that serum NT-proBNP levels parallel changes with PASP. Serum NT-proBNP could be a useful marker to monitor disease severity in pediatric pulmonary hypertension.
64. Cited2 mutation associated with congenital heart disease

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 Purpose: To explore gene mutation of Cited2 coding strand in Chinese patients with congenital heart disease (CHD).

 Methods: DNA was abstracted from the blood samples of 120 nonhomologous and various CHD patients and 100 healthy children. The coding regions of Cited2 was amplified by PCR and compared to the Gene Bank after sequencing to identify the mutations. The families of the samples who have Cited2 mutations were investigated as well. ClustalW software was amplified for conservative analysis of the altered amino acids.

 Result: 3 new mutations of Cited2 coding strand were found in 4 CHD patients. 2 point mutations were first identified respectively in two patients, one patient with mirror image dextrocardia and tetralogy of Fallot (c.550>A), another with aortic stenosis (c.574 A>G). Apart from this, the same deletion (c.573-578del6) was first detected in other two patients, one patient with ventricular septal defect and atrial septal defect, another with aortic stenosis and pulmonary stenosis. All the mutations resulted the protein changes (p.Gly184Ser; p. Ser192Gly; p. Ser192fs). All the changes were not detected in the control group.

 Conclusion: This study show for the first time that there are 3 brand-new gene mutations of Cited2 in Chinese CHD patients with a broad phenotype spectrum. Serine-glycine rich junction (SGJ) is considered as the mutation hot spot. Cited2 mutations may be one of the causative impact in development of CHD in human.
66. Outcome of Surgical Repair of Coronary Artery Fistulas in Children
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Purpose: Coronary artery fistulas (CAF) are rare congenital malformations that can be seen in 0.06% of children undergoing echocardiography and 0.13%-0.22% of adults undergoing coronary angiography. There are no good large, complete, long-term comparative studies of a significant number of patients. Our aim of this article is to attempt to review the limited information and the outcome of surgical repair of the rare malformations in our center.

Methods: we review the clinical characteristics and surgical outcome of thirteen patients with CAF in our center from 1993-2009. The median age was 26 months (2 months, 150 months). Six patients were male and seven were female. All patients were first diagnosed with CAF by echocardiography, eight of them were undergoing angiography. Surgical repair include ligation, stitch and patch repair, ten patients had cardiopulmonary bypass. Four patient with aneurysm underwent coronary artery plasty at the same time. No anticoagulant drugs were used.

Result: The longest follow up was 16 years, median was 5 years. NO surgical death and late death, TEE showed no residual fistulas right after operation. Two patients were found fistulas in different site by echocardiography in CCU, and both had successful second operation. No recurrent fistulas, no progressive dilation of coronary arteries, no AMI in follow up.

Conclusion: we suggested that all patients with CAF should be treated. Surgical repair is a safe and effective treatment for children. According to our current follow up, patients can live an event-free life in a long time after surgery.