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Implantable Sensors for Heart Failure

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Why Heart Failure Monitoring

About 5 million Americans suffer from heart failure, carrying significant morbidity and mortality. It is estimated that 550,000 new cases occur each year, and the estimated cost of treatment reaches $33.2 billion, most of the cost were incurred during hospitalization for acute decompensation heart failure (ADHF).1

ADHF refers to a clinical condition of worsening heart failure with dyspnoea and often with evidence of fluid overload.2 This is often triggered by one of the four main factors: atrial fibrillation, anemia, hypertension and medication/dietary indiscretion.

In the 1991-1994 Connecticut Medicare beneficiaries review,3 ADHF that results in hospitalization carries an 8% in-hospital mortality. Importantly, of the 17,448 survivors, 44% will be re-admitted once, of which 18% were due to recurrent heart failure. Overall, 24% would die in 6 months after the first ADHF, and 53% either died or re-admitted over the same period. Thus prevention of ADHF can have significant prognostic impact for the patient, in addition to reducing the cost of heart failure management.

Limitations of Symptoms, Signs and Investigations

While dyspnea is the commonest presenting complaints for hospitalization in ADHF, it occurs relatively late in relation to hemodynamic and fluid status changes. Until the era of implantable devices, it is not possible to evaluate the hemodynamic changes leading to ADHF. Adamson et al4 implanted a right ventricular (RV) sensor to measure RV systolic and diastolic pressure during heart failure exacerbation in 32 patients. They found that at a mean of 4±2 days before admission, RV systolic pressure started to increase in 9/12 heart failure event. As a group, there was an increase in RV systolic pressure by 25±4% and heart rate by 11±2% during ADHF. This study suggests that pressure changes is the initiating mechanism responsible for heart failure exacerbation. Likewise, using an implantable intrathoracic impedance sensor to assess pulmonary fluid, fluid overloading occurs at 18.3±10.1 days before dyspnea occurred.5 Thus, dyspnea is a late event and does not allow neither the clinician nor the patient to have enough time for intervention to avert hospitalization.

The cardinal physical signs of congestive heart failure are: a third heart sound, pulmonary crackles, raised jugular venous pressure and peripheral edema. However, these signs have poor sensitivity to detect heart failure. In a study6 of 50 patients with raised pulmonary arterial wedge pressure (PAWP) ≥22 mm Hg, lung crackles were identified in 19% of patients, and a raised jugular venous pressure and peripheral edema were
present in only 50% and 20% of patients respectively. While a third heart sound was heard in most cases, it was also detected in those with a low PAWP. The combination of these signs have a sensitivity of 58% and specificity of 100% for congestive heart failure. Physical examination of jugular pressure is difficult and inaccurate.7

Body weight change is both a complaint or signs for ADHF. It has been suggested that this is an unreliable sign as body weight is not only reflective of body fluid, but may depend on amount of food/fluid intake and other causes of weight loss or weight gain. In a recent study,8 134 patients with heart failure hospitalization were compared with a case matched group without hospitalization. Body weight one week before hospitalization was associated with increasing risk of hospitalization (Relative risk: >2-5 lb=2.77; >5-10 lb= 4.46 and 5-10 lb=7.65). It is suggested that monitoring of body weight remains useful and identifies a high risk group for intervention.

Radiological evidence of ADHF tends to occur late. Brain natriuretic peptide (BNP) is proposed to improve heart failure management. In a randomized study on the N-terminal BNP to guide heart failure therapy (TIME-CHF) study,9 499 patients ≥60 years old with systolic heart failure were randomized. Titration to achieve a N-terminal BNP level of ≤2 times upper limit was compared to conventional management without BNP guidance. There was no difference in the survival rates free from all cause hospitalization between BNP-guided versus conventional therapy (41 vs 40%), and a similar degree of quality of life improvement. However, the secondary endpoint of heart failure hospitalization was significantly reduced (72 vs 62%), and outcomes were better in the 60-75 years old patients but not in those 75 years or older.

While vigilant monitoring of symptoms and signs (and BNP levels) are useful, they are not guarantee to accurately predict ADHF. On the other hand, frequent monitoring of some of these signs and symptoms, and the use of external physiological (and implantable) data are clearly superior to conventional care. In a meta-analysis of both cohort (2,354 patients) and randomized trials (6,258 patients),10 with 6-12 months of follow up, there is a significantly lower rate of deaths and hospitalization compared to conventional management.

Taken together, frequent monitoring of physiological parameters are useful for clinical management of heart failure. As many patients with LV dysfunction requires implantable cardiac implantable electronic devices (CIED) either for arrhythmia prevent or therapy (ICD), or heart failure treatment (CRT or CRT-D), this opens the possibility to add implantable sensors for heart failure monitoring in these devices. The use of implantable sensors will allow continuous monitoring of physiological parameters without intensive manpower. Furthermore, the ability of these sensors to detect earlier physiological changes before ADHF may open a window for averting heart failure hospitalization. They can also measure hemodynamics at different body positions and on an ambulatory basis, and may obviate the need of invasive monitoring when the patient is admitted for heart failure therapy.

**Monitoring of Pathophysiological Changes of Heart Failure**

There are three possible pathophysiological areas for heart failure monitoring: monitoring of electrical remodeling, mechanical remodeling and neurohormonal changes that occur with heart failure (Table 1). Electrical remodeling in either the atrium or ventricle will result in changes in normal automaticity, conduction properties, and refractory period and predispose to atrial fibrillation (AF) and ventricular tachyarrhythmias. The occurrence of arrhythmias are routinely monitored and treated by CIED, both by pacing and defibrillation. Effective refractory period (ERP) can be monitored by physician activated electrical stimulation through a programmer.

Intra and inter-chamber conduction timing in heart failure are important, as they are either a result of, or the cause of electrical remodeling in heart failure. In a post mortem series of 34 patients with pre-morbid serial ECG, progressive PR and QRS duration prolongation occurred with worsening of heart failure. Cardiac mass index was significantly correlated with V1-V6 R-wave amplitude.11 A wide LBBB QRS complex is associated with ventricular dyssynchrony
and impair left ventricular function. Optimal left side and atrio-ventricular (AV) and cross chamber sequencing are important for the proper systolic function of the heart. While relatively simple, these conduction parameters have not been examined as long term monitor of cardiac decompensation.

The initiating event of heart failure is most often systolic left ventricular dysfunction. This will affect the right and left ventricular size, and their systolic and diastolic function. There will also be an effect on the atria. Early recognition of these changes by monitoring may allow pharmacological or interventional approaches to reverse the changes before clinical heart failure develops. This opportunity may already present itself in a patient already implanted with a device such as a pacemaker in whom long term monitoring of heart failure may be possible.

However, the major immediate clinical consequence of heart failure is acute decompensated heart failure (ADHF). ADHF arises because of fluid overload (particularly in the lungs), and monitoring of pressure and volume status and appropriate therapy can prevent ADHF.

Finally, many neuro-hormonal changes result from the compensating mechanisms of heart failure. While not easily measurable directly, these changes may be reflected through heart rate variability and electrical repolarization such as the QT interval. This will be an interesting new area for monitoring and as a guide to therapy.

### Sensors for Heart Failure

Sensors for rate adaptation can be classified according to the technical instrumentation. Table 2 summarizes the sensors that have been used for or proposed to monitor the events of heart failure. The paced QRS enables QT duration to be evaluated. In addition, the QRS width, measured as the ventricular depolarization gradient, had been proposed as a marker that is sensitive to catecholamines. These sensors have long been used as surrogate markers of sympathetic level that increases with exercise, with a view to drive a rate augmentation. It is uncertain if they are also good markers of increase sympathetic tone that accompanies heart failure. These parameters are influenced by pacing rate, cardio-active medications and electrolytes that frequently occur in heart failure patients, making them unlikely to be robust sensors for heart failure. On the other hand, a high percentage of biventricular pacing is necessary to deliver a high dose of cardiac resynchronization therapy (CRT). A low percentage of biventricular pacing may herald worsening of LV

### Table 1. Monitoring for heart failure pathophysiology

<table>
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<tr>
<th>Electrical remodeling</th>
<th>Examples</th>
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<td>Atrium</td>
<td>Size, function, structure</td>
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<tr>
<td>Ventricle</td>
<td>Size, function, structure</td>
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<td>Pressure changes</td>
<td>End-diastolic pressure, pulmonary artery pressure (and wedge pressure), venous pressure</td>
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<td>Neurohormonal changes</td>
<td>Examples</td>
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<td>Sympathovagal invalence</td>
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<td>Renina-angiotensina-aldosterona-system</td>
<td>BNP</td>
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BNP=B-type natriuretic peptide; ERP=effective refractory period
function due to failure of adequate CRT, and is a good marker of heart failure decompensation. AF and ventricular tachyarrhythmias can either be a consequence or trigger event of heart failure that could be easily recognized and treated. Heart rate variability (HRV) can be measured in a non-pacing dependent patient, and is a well established prognostic marker of heart failure. Reduction of heart rate variability antedates heart failure events. While percentage of biventricular pacing and HRV are rhythm diagnose rather than implantable sensors, they provide important indications of the prevailing heart failure status.

Piezoelectric crystals are used to monitor body motion. Decrease body activity is an intuitive consequence of heart failure exacerbation.

Impedance refers to low non-cardiac tissue stimulating alternating currents injected and recorded between pacing electrode pairs. When injected between a RV and LV leads, the lead configuration will encompass part of the LV, thus allowing intraventricular volumes and contractility to be measured. When injected between an intra-cardiac lead and the CIED casing, respiratory parameters such as respiratory rate and minute ventilation can be monitored, and these parameters are affected by dyspnea that occur in ADHF. This electrode configuration can also detect pulmonary fluid status, and may be a marker of pulmonary edema.

More direct measurements are now possible with pressure sensors instrumented in the RV, pulmonary artery (PA) or in the left atrium (LA). Worsening heart failure is associated with decreasing cardiac output, which the body compensates by increasing tissue oxygen uptake leading to a widening of arterio-venous oxygen difference. This is reflected by a reduction in the mixed venous oxygen saturation, which has been measured by implantable devices. As central hemodynamic changes are the precipitating events of ADHF, pressure sensors that measure LA, PA and RV pressures, have been studied and developed. Recent development and clinical applications of some of these sensors are summarized below.

### Activity Monitoring

Kadhiresan et al\textsuperscript{15} reported the use of externally attached accelerometers at the chest wall to monitor walking distance in heart failure patients. Using an acceleration

<table>
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<th>Table 2. Sensor for monitoring heart failure</th>
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<td><strong>Sensors</strong></td>
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<td>Ventricular dysfunction or its triggers</td>
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AF=atrial fibrillation; LA=left atrial; LV=left ventricle; PA=pulmonary artery; PEA=peak endocardial acceleration
threshold of 50 mG, a walking speed of 2 mph (approximately=2.8 METS) can be detected in a group of 30 patients. The activity log index so defined was closely related to the walking distance of these patients, and was increased when patients were tested during CRT-on versus CRT-off phase. Similarly, time per day with physical activity greater than a threshold of 70 steps/minute was detected in an implanted accelerometer sensor, and the activity level trended similarly to HRV trend during ADHF, and correlates with the NYHA class at baseline. While a crude index, activity sensing is a good reflection of general well being of a heart failure patient. It is a readily available sensor in most CIEDs, and uses minimal battery energy. In addition, the absence of activity usually signifies the patient is at rest, and allows other measurements such as respiratory parameters to be determined. The use of accelerometer rather than piezoelectric crystal avoids some of the external vibration interference on measuring body activity. An activity sensor is used in conjunction with other sensors for heart failure monitoring.

Heart Rate Variability

In patients with heart failure, neurohormonal activity predicts cardiovascular outcome. HRV is an indirect measure of autonomic tone, and predicts both sudden and non-sudden cardiac death. HRV has been proposed not only to prognosticate heart failure severity, but also as a guide to treatment and perhaps predict ADHF.

In a randomized study of 50 patients with an implanted CRT, HRV was measured in the atrial sensing mode (VDD at 30 bpm) in either the CRT-on or CRT-off mode. HRV, measured as the SD of atrial cycle length of all atrial sensed beats, was significantly higher in the CRT-on versus the CRT-off arm (25% higher) and when the patients were receiving betablocker (27% higher). There was no difference in the level of catecholamines measured in the study. The authors concluded that time-domain HRV was improved with CRT, likely reflecting changes in both sympathetic and parasympathetic activities with heart failure improvement.

In the Boston Scientific device, HRV is measured by the so-called SDANN. SD of the intrinsic intervals in the 288 five-minute segments of a day is measured, and averaged over a week. If the percentage of intrinsic beats is <67% for 24 hours, the data for that day is discarded. Using the SDANN in a cohort study of 113 heart failure patients with CRT, CRT resulted in a reduction in the ventricular heart rate, mean heart rate and an increase in SDANN (from 69±23 ms to 93±27 ms) after three months. Furthermore, lack of HRV improvement predicts non-responders to CRT.

The HRV can be plotted at each heart rate over a twenty four hours period, resulting in a so-called "footprint" in the Boston Scientific CRT devices (Figure 1). The normalized size of the footprint is termed the footprint number, and the graph and number give an easy understanding of the level of HRV: "the larger the better". In another cohort study, HRV using either the SDANN or footprint predicts mortality in 842 patients implanted with CRT during a 11.8 months follow-up. A clinical score was derived based on a 2-week post implant diagnostic data: SDANN <43 ms, mean heart rate >74/bpm, foot-print number <29 and activity percent <5% from a 436 patient cohort in the CRT RENEWAL study. Using this scoring system, patients could be triaged to a low, moderate and high risk group. When applied to a separate group of CRT recipients in the HF-HRV cohorts, this scoring system accurately predicted the level of mortality risk (low 2.8%, moderate 10.1% and high 13.4%) depending on tertiles of their score.

In the Medtronic device, a long term measure of HRV, the SD of a 5-minute median AS-AS interval (SDAAM) is used. The algorithm averages the 24-hour SD of intrinsic atrial cycle length, and will exclude the day’s data if the percentage of atrial pacing exceed 80% or an atrial high rate episode (AHRE) are detected. The change in SDAAM is compared to a rolling average of the preceding 6 months. The SDAAM, night time heart rate and activity level were used to predict outcome and to detect HF hospitalization in a 397 patients cohort. A SDAAM <50 ms predicts overall mortality, and the absolute value of SDAAM remains low in those who were either hospitalized or died. SDAAM declines from 76±27 ms to 64±26 ms at the time of hospitalization,
and the change was apparent up to 3 weeks before the event. An algorithm was developed to use SDAAM to predict hospitalization. At a threshold of 200 ms days, a sensitivity rate of 70% was associated with 2.4 false-positive events per patient year of follow up, at a median of 16 days before the event. The sensitivity is not affected by the use of beta blockade. The SDAAM is significantly better than the night time heart rate and activity level change for predicting heart failure. These data suggest that autonomic surveillance such as the use of HRV is a good way to monitor both HF prognosis and to predict ADHF. HRV is limited when these are high percentage of atrial pacing and during atrial tachyarrhythmias, and medications may affect HRV measurements.

**Percentage Biventricular Pacing**

When CRT is used to treat patients with heart failure with a widened QRS complex on the ECG, it is expected that an adequate percentage of biventricular pacing will be needed to maximize the "dose" of resynchronization. In a cohort retrospective analysis of 2 heart failure trials involving CRT-D's (1,812 patients), Koplan et al\textsuperscript{13} analyzed the relationship between the percentage of biventricular pacing and the outcome of death and heart failure hospitalization. The mean age of the patients was 72±11 years, 72% were men and 67% had ischemic cardiomyopathy. When subjects were divided into quartiles, there was a lower event rate with an increasing percentage of biventricular pacing. In particular, there was a 44% reduction in event rates in those paced 100% of the time versus those paced less than 92%, and even subjects paced 93-97% had a higher event rate compared to those paced between 98-99% (22% higher mortality). The main reason for an inadequate percentage of pacing was atrial arrhythmias. Thus a high percentage of biventricular pacing of ≥98% is an important goal to achieve in patients with CRT (Figure 2).

A low percentage of biventricular pacing is particular the problem in those with AF, especially when permanent. Because of frequent intrinsic conduction and fusion beats in AF, a high percentage of biventricular pacing may still not reflect the percentage of true mechanically synchronized beats. In one study on 19 patients with permanent AF with diagnostic counters showing >90% biventricular pacing,\textsuperscript{25} 12 lead Holter System was used to monitor 'true' complete biventricular capture using a template matching system. Only 9/19 (47%) had adequate complete biventricular pacing, the remaining had either fusion or pseudo-fusion beats. Patients with 86.4±17.1% full capture had ≥1 NYHA Class

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**Figure 1.** Heart Rate Variability represented by "foot-print". In this patient, improvement of heart failure concurred with an increase in size of the foot-print after initiation of cardiac resynchronization therapy (CRT).
improvement than those fully captured at 66.8±19.1% of the time. This study suggests careful evaluation of the percentage of biventricular pacing using multiple surface ECG lead will be needed in those with AF and conducted response, and sensor to detect full biventricular capture will be an interesting development.

**Right Ventricular Pressure**

PA pressure and PAWP monitoring have been shown to be effective for tailored therapy in patients admitted with advanced heart failure. Early attempts have been made to continuously record PA pressure on an ambulatory basis. An implantable sensor that measures pressure has been incorporated into a pacing electrode with an initial application for rate adaptive pacing. This sensor is a hermetically sealed piezoelectric crystal with a diaphragm facing the blood stream. Early experiences have shown the ability to continuously record RV pressure by connecting this electrode to an implanted hemodynamic monitor.

The Medtronic Chronicle IHM (Model 9520) is a non-pacing implantable pulse generator capable of

![Figure 2. Optimization of Biventricular pacing. This patient had an initial response to cardiac resynchronization therapy (CRT), but developed heart failure associated with a reduction of left ventricular pacing to 88%. This was found to be due to frequent ventricular ectopies interfering with CRT. Prescription of amiodarone suppresses ectopies, and resulted in a 97% biventricular pacing (and 67% atrial pacing) and significant clinical improvement.](image-url)
external radiofrequency connection and integration in a web-based system. It has a 128 kb of RAM for continuous storage of sensor data. Piezoelectric activity from a passively fixed lead in the RV outflow tract is sampled up to once every 2 seconds, timed to the sensed unipolar RV electrogram. The sensor frequency is linear up to 100 Hz, and a 60 Hz high pass filter is used. The frequency and timing of RV systolic pressure sampling are programmable, and often at early morning when the subject is likely to be supine and rested. In addition, high resolution recording can be made using an external triggering device. RV pressures (systolic, diastolic and dp/dt) were recorded, and RVSP reflects PA systolic pressure. A prior work\textsuperscript{32} has assessed the ability to estimate PA diastolic pressure which occurs at the time of pulmonic valve opening. This is estimated at the time of the maximum positive RV dp/dt. Pre-implant calibration pressure is required to allow absolute pressure measurement. An external barometric pressure measurement device provides external pressure reference against which sensor data can be subtracted.

\section*{Feasibility Study}

The long term stability of the pressure sensor has been previously reported. In one study,\textsuperscript{33} serial Swan-Ganz catheterizations at 3, 6 and 12 months post implant showed a small baseline error at 12 months of <1 mm Hg from the time of implantation. Furthermore, the accuracy of pressure measured is not affected by body posture. Adamson et al\textsuperscript{4} studied 32 patients with heart failure who received a Chronicle IHM. They found that long term RV pressure was stable in most patients. However, in certain subjects, it showed significant variability despite measurements were taken at 4 am with no activity level registered. During a total of 36 volume-overloaded events, RV systolic pressure increased by 25±4\%, heart rate by 11±2\% and estimated PA diastolic pressure rose 26±4\%. In all events, pressures were increased one day before the required clinical intervention. In patients with heart failure hospitalization, increases in one of the pressures occurred in 9/12 events, whereas this occurred in 9/24 patients during a non-hospitalized episode. During a volume depleted state in 7 patients, RV pressure parameters were reduced. All patients returned to baseline levels after therapeutic intervention. The authors further proposed a sustained increase in one of the pressures (>20\% from baseline) may occur in patients subsequently admitted, at a mean of 4.2 days before admission. When the device data were available to the monitoring physician, a reduction in heart failure hospitalization was subsequently observed. This important study also documents the time sequence of RV pressure changes that occurred before heart failure exacerbation, suggesting that pressures (and very possibly also volume) build up may occur for several days and reduce the patient's "tolerable reserve", before the final increase in pressures that lead to clinical heart failure exacerbation. In a further study, Zile et al\textsuperscript{34} compared the ongoing RV hemodynamics between systolic and diastolic heart failure patients during heart failure events. They found RV diastolic pressure to be elevated in both conditions, although there was a trend for more rapid RV diastolic pressure elevation to occur in diastolic heart failure with less compliable ventricle than during systolic heart failure. Thus quite aside from monitoring heart failure for intervention, the implantable pressure device enables an understanding of heart failure pathophysiology that was not possible before.

\section*{Clinical Outcome Study}

The COMPASS − HF (Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure) Study\textsuperscript{35} prospectively randomized 274 NYHA Class III or IV heart failure patients into conventional care group or therapy guided in addition by Chronicle derived RV pressure parameters. The two safety endpoints documented no pressure sensor failure and 8% implanted system complications. During a follow up of 6 months, there was a statistically insignificant trend for reduction of either heart failure hospitalization or the need of intravenous diuretics (primary endpoint) by 21\%. A post-hoc analysis showed a 36\% prolongation in time to the final heart failure-related hospitalization in the Chronicle-guided treatment group.

As suggested by the authors, the lack of significance observed in the primary efficacy endpoint may be due to the lower than expected number of heart failure events (predicted 1.2/6 patient-month; actual
0.85/6 patient-month), thus decreasing the power of the study. The lower event rate may be due to enrollment in highly specialized centres in which there was high compliance of evidence based heart failure treatment. Importantly, Chronicle guided therapy resulted in 54% more adjustment in diuretic doses, without an increase risk in hypovolemic related heart failure events. At the time of study, patient transmitted Chronicle data at least once per week. It is arguable if a more frequent transmission such as in a remote patient monitoring system may further contribute to reduction in ADHF. As mentioned above, the study also includes 70/274 patients with diastolic heart failure patients. A subgroup analysis found a 20% non-significant reduction in heart failure events when diastolic heart failure patients were managed occurred with Chronicle-guided information. This will be of interest in future larger trials to prevent heart failure in diastolic heart failure which has few proven therapies.

Other Pressure Sensors

Left Atrial Sensor

PA diastolic pressure is an indirect assessment of the filling LV pressure, and measurement of LA pressure may reflect an earlier pressure change that triggers pulmonary congestion. This may allow a longer time window for physician intervention to avert ADHF.

The HeartPOD LA pressure monitoring device (St Jude Medical Inc) comprises an implantable sensor lead that is attached to a coil antenna for telemetry of sensor signals. The sensor is a pressure sensor with a titanium pressure sensing membrane of 3 x 7 mm. It is capable of high fidelity pressure, temperature and electrogram measurement. An external patient advisory module (PAM) sends a 125 KHz radiofrequency transmission to the antenna, which then captures a 20 second sensor data. The PAM has a 13 Mb of memory, and can store about 3 months’ data of 6 recordings per day.

In a feasibility study in a single centre, 8 patients received the LA pressure device using a transeptal approach from the femoral vein. Venous entry at 1 cm above the inguinal ligament was achieved guided by a guide wire introduced in the conventional manner in the femoral vein below the inguinal ligament. After standard transeptal puncture, an II F sheath was placed in the LA, and the sensor was deployed until the distal set of anchor was on the left side of the atrial system. The sheath was then removed, and the sensor membrane was positioned 1-2 mm on the left atrial septum. All patients received dual antiplatelet therapy for 6 months (aspirin 160 mg and clopidogrel 75 mg per day). The device was calibrated overtime using a Valsalva maneuver technique during which the expiratory pressure as measured by the PAM will equate to the LA pressure. Over a period of 6 months, the net drift was 0.2±1.9 mmHg per month, although in 1 patient the drift was much more. The authors commented on the need to maintain the sensor orthogonal to the septum to avoid distortion of LA pressure waveform.

The Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patient (HOMEOSTASIS) trial enrolled 40 patients with Class III to IV HF. All patients received LA pressure device successfully, although sensor failure occurred in 4 patients, which was subsequently replaced in 3. The study started after a 3 months run in period in which heart failure hospitalization and related events, and medication dosages were documented. Thereafter, LA pressure data were disclosed to the patients, who in conjunction with the physician, adjust the dosages of diuretics. Survival without heart failure events occurred in 61% at 3 years. Mean daily LA pressure therapy resulted in a fall of LA pressure (17.6 mmHg to 14.8 mmHg), reduction in elevated LA pressure frequency (events >25 mmHg by 67%), and better NYHA Class, LVEF, and more frequent up-titration of angiotensin converting enzyme inhibitors and reduction in diuretic dosages. This titration was effected by the patients themselves using a regimen advised by the digital assistant machine that interrogate the device on a daily basis.

The HOMEOSTASIS trial is an interesting observational study in which LA pressure parameter is treated similarly to blood glucose parameters in a diabetic patient, in which self adjustment of dosages of diuretics may maintain an euvolemic state. Thus the possibility of reduced clinical events may be due to up-
titration of angiotensin converting enzyme inhibition by reducing the dose of diuretics if LA pressure is low. Conversely, when LA pressure increases, increasing the dose of diuretics would enable a larger dose of beta blockers to be given. As a result the target doses of both drugs were achieved in 54% of patients compared to only 27% at baseline.

The LA pressure sensor is an interesting concept and will require to be confirmed in prospective randomized trials. At present, there remains the issue of sensor stability, ease of implant (subclavian implant tools are now available), and the risk of thromboembolism (which is probably low similar to occluder for closing atrial septal defect).

**Pulmonary Arterial Pressure Sensors**

A PA pressure transducer (Champion, CardioMENS, Atlanta, GA USA) has been developed. The preliminary results of a 550 Class III heart failure trial has been recently reported. Patients were either randomized to PA pressure guided therapy versus conventional care, and a 30% relative risk reduction was observed. The trial has not reported any significant safety issues.

**Intrathoracic Impedance for Pulmonary Fluid Status**

Dyspnea is the commonest presenting symptoms for ADHF, and congestion or edema are the main underlying mechanisms for dyspnea. Increase in fluid in the lungs will decrease the transthoracic impedance which can now be measured with an implantable device.

**Device Description**

The concept of impedance to monitor pulmonary congestion is based on a canine experiment by Wang et al. The Medtronic Optivol™ fluid management system uses transthoracic impedance to measure pulmonary fluid. Low voltage, non-stimulating currents are injected between RV ICD electrode (e.g. InSyn Sentry) or RV bipolar electrode (e.g. Advisa) to the ICD or pacemaker casing between noon and 5 pm, at a time when the subject is presumably ambulant and upright. A sampling over every 20 patients is made and averaged. The moving average of the impedance used to establish a baseline impedance level against which any change can be compared. The algorithm is inactive for the first 34 days after device implantation to allow time for post-implant pocket healing and electrode stabilization. When pulmonary fluid has accumulated beyond a programmable threshold, an alarm will be used to alert the patient (or the physician via remote monitoring).

**Feasibility Studies**

The feasibility of using intrathoracic impedance to monitor fluid status has been tested in 34 patients with NYHA Class III or IV heart failure in the MId-Heft Study. A defibrillation lead in the RV apex is connected to a special pacemaker capable of injecting and sourcing impedance. Three impedance current vectors were tested: RV lead ring to device case and sampled from coil to device case; RV coil to device case and sampled from RV coil to device case; RV ring electrode to device case and sampled from RV tip electrode to device case. The electrode pairs that use RV coil to device case has been found to be most suitable. An initial decrease in impedance followed by an increase to steady state is observed during pocket healing, which peaks by about 4 weeks.

**Figure 3.** Recurrent heart failure episodes in a patient with dilated cardiomyopathy, as documented by impedance recoding of pulmonary fluid index (Medtronic Optivol). A threshold of 60 Ω day was found to be unspecific to detect fluid overload. Fluid index exceeding 100 Ω day was used and correctly identified clinical (and BNP confirmed) heart failure episodes.
During a follow up of 20±8.4 months, 25 adjudicated heart failure hospitalization occurred in 10 patients. Intrathoracic impedance started to decrease before worsening symptoms at 15.3±10.6 days, whereas dyspnea was only reported at the earliest 3 days before hospitalization. During 17 hospitalizations, pulmonary capillary wedge pressure was found to significantly correlated with impedance (r=-0.61, p<0.001), and impedance increased as fluid removal occurred with diuresis.

An algorithm for heart failure detection was derived from 6.2 patient-years of monitoring from 10 patients, and tested in the remaining cohort. Depending on the set threshold for impedance crossing, a receiver operator curve was constructed. Lower detection thresholds lead to higher sensitivity to detect ADHF but also a higher false positive rate of detection. Conversely, a higher threshold will be more specific but may underdetect some ADHF events. A 60 Ω. day was suggested to give a sensitivity of 76.9% at the expense of 1.5 false-positives per patient-year of monitoring. Early warning occurred at 13.4±6.2 days of heart failure hospitalization event. This landmark study shows that intrathoracic impedance is correlated with pulmonary congestion, and changes in a predicted way as diuresis occurs, allowing its use for acute monitoring. Furthermore, the impedance changes days before ADHF and suggests its role to monitor heart failure on an ambulatory basis.

Clinical Outcome Studies

The impact of automatic Optivol alert to guide therapy was observed in 532 heart failure patients in the Italian Optivol Study.41 With the Optivol heart failure alert on, a 67% detection of heart failure that required either hospitalization or therapy adjustment were detected. Interestingly, of the remaining patients in whom Optivol alert was inactivated, heart failure hospitalization was significantly higher (20% vs 7%). The study also showed a false positive detection rate of 0.5 per patient-year of follow up.

While impedance monitoring from RV coil to device case monitors lung edema, measurement of RV and LV lead vectors (for lead integrity) may be able to assess LV volumes better. In an interesting study on 170 patients, with 43 being replacements, Maines et al.42 showed that a 12-week maturation period was required for the pocket and the leads occurred in the de-novo implants. However, a similar, albeit stabilizing earlier, adaptation was still required for replacement group, suggesting the adaptation is in part due to the leads or algorithm itself. Interestingly, using the RV-LV impedance vectors, this study suggests that there are significantly difference in impedance measured in the volume responder versus non-responder groups, with a higher biventricularly measured impedance in the responders This suggests the role of impedance to tract responders to CRT.

The ability of Optivol to reflect heart failure outcome has been examined in several cohort studies. In a multi-centre studies of 558 heart failure with In Sync Sentry from 34 Italian centres, device recorded Optivol fluid index above 60 Ω. day was associated with a 36% increased risk heart failure hospitalization over a 326±216 days of follow up.43 Multivariate analysis showed that in addition to Optivol level, a higher percentage of days with low activity, low HRV and increased night time heart rate were independent predictions of hospitalization. In 62 patients with Optivol algorithm, prospective observational measurements of NT-pro BNP, clinical heart failure status were collected over 27±2 weeks.44 There was a significant but weak relationship in all pooled change in impedance and change in NT-Pro-BNP level over all the visits (r=0.30, p<0.001). However, NT-Pro-BNP level increased significantly when an Optivol alert is associated with clinical signs of ADHF (89±25% increase) versus an insignificant increase in those without signs (25% increase). In patients with an alert, NT-Pro-BNP increase by >10% in most incidents. By the time of patient medical visit, impedance continued to fall suggesting worsening heart failure status. In 42% of cases, a device alert was not related to clinical signs of heart failure, although BNP on the whole increased significantly by 25% in these patients. Several explanations are proposed, including improvement of medication/dietary compliance by the patients due to the alert, signs of heart failure may be less sensitive than objective monitoring, or true false detection by the Optivol. Nevertheless, the higher BNP level related to Optivol alert means that heart failure prognosis will be
affected when Optivol threshold crossing occurred.

The usefulness of Optivol to prevent heart failure was reported in a single centre case control study in which 27 patients with InSyn Sentry was compared to clinically similar group of 27 patients with CRT-D without Optivol. 45 12/27 patients had Optivol alerts, resulting in intervention. Hospitalization occurred in only 1/27 over a year of follow up. In contrast, 7/27 patients had heart failure hospitalization in the controlled patients treated with conventional CRT-D without the Optivol algorithm. When coupled with remote patient monitoring (Medtronic Carelink), 46 20/28 (71%) Optivol alerts in 67 patients can be remotely managed. The temporal relationship between arrhythmias and Optivol measured fluid level has been reported. In one study, 47 Optivol threshold crossing >60 Ω. day was related to a higher risk of occurrence of AF. AT occurred in 43% before or 29% after Optivol level crossing. This relationship was not observed in another study. However, the latter study showed a higher prevalence of VT/VF at lower level of Optivol 15-45 Ω. day, suggest VT/VF occurred at a time of fluid index crossing. The ability of fluid index to predict arrhythmias required further study.

Algorithm Considerations

Small et al 49 examined in a prospective cohort of 326 patients with InSyn Sentry followed up for nearly a year. In the first 4 months (observational period), threshold crossing at the nominal 60 Ω. day occurred in 17 patients (22 ADHF episodes). The occurrence of threshold crossing predicted a 35% increase in hospitalization in the subsequent period. Furthermore, the following are predictive of hospitalization: >3 threshold crossing per year or >30 days threshold crossing per year. When a multivariate analysis was applied, only night time heart rate remained predictive of ADHF in addition to Optivol threshold crossing. Thus not only the threshold crossing but the duration in which Optivol threshold above the programmed threshold are predictive of heart failure hospitalization.

The threshold for Optivol alert has also been tested in 115 patients implanted with Medtronic InSyn Sentry CRT-D. 50 During a follow up of 9±5 months, 45 Optivol alerts occurred in 30 patients. Fifteen alerts (33%) were correlated with clinical signs and symptoms of heart failure, and the authors suggested an increase of threshold to 90 Ω. day may increase the specificity to 73%. The authors did not find any causes for false positive alerts, but patients with heart failure had significantly higher Optivol level versus those without. On the other hand, in the European InSyn Sentry Observational Study on 373 subjects, 51 the level of 60 Ω. day was associated with a 60% sensitivity and 60% positive prediction of ADHF. This study documented 9/53 (17%) events were not associated with an Optivol alert, and in an additional 11 events, an increase in Optivol level occurred but did not exceed the programmed detection threshold. These studies confirm the usefulness of intrathoracic impedance to monitor ADHF, but pointed out the need of fine tuning of detection algorithm and/or individual programming of Optivol detection level.

The SENSE-HF study is a prospective trial to assess the sensitivity and positive predictive value of implantable intrathoracic impedance to predict heart failure hospitalization. 52 The study is of 3 phases. Phase I is a double blind phase in which retrospective analysis of Optivol algorithm in predicting ADHF is evaluated. In Phase II which takes place after 6 months in Phase I, the device alarm is used to identify ADHF. When this happens, the patients enter Phase III in which the utilization of Optivol level is assessed prospectively in averting ADHF and hospital resource utilization. The recruitment has been completed in 2008.

Advantages and Limitations

Intrathoracic impedance to monitor heart failure is one of the most extensively used sensors for monitoring heart failure. The advantages of this sensor is the relative ease of instrumentation, requiring no additional leads or complexity of implantation. The battery energy expenditure is low. It has been relatively well characterized in acute setting and for long term monitoring. While sensitive, its specificity may be limited as impedance in the vector used may be liable to be affected by a number of clinical events that do not indicate pulmonary congestion, such as the occurrence of pleural effusion (Table 3). 53 However, some of the Optivol alert without clinical evidence of heart failure
might represent clinical resolution of heart failure due to delayed presentation, subclinical congestion in addition to being false positive. Nevertheless, when combined with other sensors, intrathoracic impedance is useful for long term and acute monitoring of heart failure (see below).

**Intracardiac Impedance**

Impedance signal derived from fully intracardiac electrodes gives better reflection of volume changes of the heart than transthoracic impedance. Indeed, Salo et al.\(^5^4\) reported the use of a tripolar RV lead to measure RV volume changes during cardiac cycle, from which RV volume and contractility can be derived for rate adaptive pacing. With the addition of a LV lead in CRT, more accurate measurement of LV volume is now possible for heart failure monitoring.

**Unipolar Impedance from Right Ventricle**

Unipolar impedance injected from the RV apex to the CIED casing samples a small region in the cardiac apex. This results in a signal that has been termed closed loop stimulation (CLS) sensor (see above). As the majority of the current is lost over a distance of about 1 cm from the apex, the signal reflects regional contractility of the ventricle rather than reflecting a change in stroke volume. Likewise, during acute induction of ventricular fibrillation, the fall in unipolar RV impedance reflects the fall in arterial pressure. However, the sensitivity is not enough to discriminate between hemodynamically stable ventricular tachycardia and supraventricular tachycardia.\(^5^5\) These results suggest that unipolar impedance reflects LV contractility only when the changes are significantly gross, and may not be able to detect small changes in cardiac contractility as in heart failure monitoring.

**Multipolar Impedance**

Several groups and manufacturers have investigated on the optimal electrode arrangement for detecting ventricular volumes. With currents flowing between intracardiac electrodes (RV, LV and RA) and to the CIED casing, enlargement in ventricular volumes will decrease impedance as more of the heart is encompassed. Four intrathoracic and 2 intracardiac vectors were examined in 16 dogs and 5 sheep.\(^5^6\) Cardiac function was monitored by biweekly cardiac catheterization and echocardiography, and LA pressure by an implantable LA pressure monitor. After several weeks of high rate pacing to induce heart failure, there was significant fall in ejection fraction (52 to 34%), increase in LV end diastolic volume (65 to 97 ml), RV end diastolic volume (7 to 16 mmHg) and LA pressure (7 to 26 mmHg). Impedance value measured by all vectors decreased with the onset of heart failure, with the maximum decrease occurring with LV-Can and LV-RV. Importantly, LV-Can impedance changes more with heart failure than vectors involving the right heart electrodes (RA-Can, RV-Can and RV Coil-Can), and RV-LV and LV-RA changes were intermediate. LA pressure correlated best with LV-Can impedance ($r^2=0.73$) than RV-Can ($r^2=0.43$) and RV Coil-Can ($r^2=0.52$). Circadian variation in impedance also decreased in heart failure ($5\pm2$ to $2\pm1\%$). Thus in these animals models, incorporation of a LV vector significantly improve the detection of LV volume increase that occurred in heart failure.

Biventricularly by measured impedance has been measured using a quadripolar electrode arrangement.\(^5^7,5^8\) In 9 mini-pigs with pacing induced heart failure,\(^5^8\) biphasic pulses (15 µs pulse width, 600 µA constant current amplitude) were injected between the RV ring and tip electrode, and impedance was sourced using the LV ring and tip electrode. The impedance signal (measured as voltage divided by 600 µA current) was

<p>| Table 3. Possible causes of increase in optivol fluid index in the absence of pulmonary congestions |</p>
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood viscosity</td>
<td>Anemia</td>
</tr>
<tr>
<td>Extra-pulmonary changes</td>
<td>Pleural effusion, Pneumothoracic</td>
</tr>
<tr>
<td>Right sided heart failure</td>
<td>Peripheral edema not detected</td>
</tr>
<tr>
<td>Pulmonary changes</td>
<td>Pneumonia</td>
</tr>
</tbody>
</table>
recorded using a resolution of 8 bits, and the mean impedance was calculated over the entire cardiac cycle. "Stroke impedance" was calculated by the difference between impedance values during systole and diastole. Systolic impedance was defined as the highest impedance 50-500 ms after the R-wave, whereas diastolic impedance was measured by a 20 ms window within the R-wave. After 20 days of heart failure induction by rapid pacing in these animals, the increase in LV end diastolic pressure was found to be significantly correlated with the end diastolic impedance, which decreased by 30% ($r=-0.81$, $p<0.001$). End-diastolic volume also trended in the same direction as the impedance value which decreased by 20%. The corresponding measured intrathoracic impedance decreased by 8%, which had a poorer correlation with the end diastolic pressure. The less striking change of intrathoracic impedance versus biventricularly measured impedance might be attributed to countering effect of lead device casing maturation which did not occur with biventricular impedance, and the fact that pulmonary fluid collection was relatively less in the mild heart failure model studied.

Clinical Studies

An acute study on biventricularly measured impedance in 14 heart failure patients during implantation of CRT devices was reported. The authors also tested the effect of different LV lead locations on biventricular impedance measurements, changes in stroke volume were induced with overdrive pacing. During a study of 20 overdrive pacing episodes and 6 different lead locations, the pooled data showed good correlation between measured stroke impedance with stroke volume ($r=0.82\pm0.10$) and pulse pressure ($r=0.81\pm0.16$). The authors reported no significant effect of LV lead positions but the accuracy and signal sizes tend to be the best in the mid-ventricular region compared to either the basal and apical regions. There was one outlier in the study, and lack of lead fixation was suggested.

At present, there is lack of data on long term implant. The relative merits and limitations of intrathoracic and intracardiac impedance are summarized in Table 4. In patients with a suitable device (i.e. with an LV lead), it is very likely that a combined transthoracic and biventricular impedance can be used.

Minute Ventilation

Dual sensor pacemakers encompassing activity and minute ventilation have been available for rate adaptive pacing. Heart failure leads to compensatory hyperventilation especially in the resting state. An expert system has been tested to examine the combined activity and minute ventilation (MV) to predict heart failure. The algorithm includes:- (1) mean daily resting and MV during activity; (2) mean daily activity level. A stable MV and activity level will suggest stable clinical heart failure, whereas an increase in MV especially at rest and combined with decrease in activity suggests deteriorating heart failure. Conversely, a stable MV level with increase in activity indicates recovery from heart failure. Nineteen patients with no history of heart failure receiving Talert™ (Sorin-ELA, Italy), were compared with 48 patients with Talent CRT with heart failure. Wide inter-individual and intra-individual variability occurred, and a fast Fourier transformed data allowed 7-day periodicity to be accounted for. While mean activity was similar, the resting and activity MV levels were higher in the CRT group. Overall, it was reported that the expert system allowed a sensitivity of 88%, specificity of 94.7%, positive predictive value of 71%
and negative predictive value of 98.2% for heart failure.

**ST-Segment Shift**

ST segment deviation either heralds ischemia or myocardial injury. Myocardial ischemia requires medical therapy or revascularization, especially in symptomatic individuals. Myocardial injury, on the other, is a medical emergency that calls for emergency reperfusion. Prompt treatment of a myocardial infarction will significantly reduce mortality. Delay in recognition by the patient of chest pain due to infarct (and in some instances silent infarct) is a significant contribution to delay presentation of myocardial infarction.61 As long term external ambulatory ECG recording is unlikely to be practical, intracardiac electrograms have been tested and proposed to reflect infarct and ischemia in an animal model.62 When incorporated into a CIED with patient alert and remote monitoring, ST segment monitoring becomes a possibility.

The Angel Med Guardian (now under St Jude Medical) is a single chamber device with a RV apical lead. An intracardiac electrogram (ICEG) was derived from RV apex to the device casing. The device records a 10s ICEG data once every 90s for normal sinus beat within 50 - 90 bpm. Data are amplified with a gain of 62.5 - 625 times and band passed between 0.25 to 45 Hz, followed by A/D conversion at 200 Hz. ST segment level is compared to the corresponding PQ segment level, and a baseline ST segment level is calculated as a rolling 24-hour average which are acquired hourly. The extent of the deviation is normalized by the average R-wave voltage. The "normalcy" of ST segment deviation at different heart rates is further tested during an exercise, as ST shifts tend to occur at different heart rates in the absence of ischemia. A rate adjusted spontaneous ST deviation will then be considered as an ischemic events and an alert will be triggered.

A limited number of devices have been implanted in humans.63 During angioplasty with temporary coronary artery occlusions, ST segment deviations occurred, with a negative shift during left anterior descending artery occlusion, and a positive shift in other arteries. Ten abnormal alerts occurred in 6 patients, leading to coronary artery interventions. During stress testing, the ICEG showed much cleaner signal and bigger shift than the corresponding surface ECG. Typically a 40% ST depression in ICEG corresponds to -0.8 mV on the surface ECG. As the ICEG is recorded at the RV apex closed to the left anterior descending territory, ischemia in this artery leads to ST depression, whereas ischemia in other territories results in a reciprocal ST elevation. Further work will be required to explore the ability of ST segment sensor to detect the culprit artery.

The ST segment sensor is an interesting sensor for ischemia. In addition to ischemic detection, the relationship of ST deviation and occurrence of arrhythmia such as ventricular tachycardia may shed

<table>
<thead>
<tr>
<th>Heart failure parameters</th>
<th>Intrathoracic impedance</th>
<th>Biventricular impedance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrode arrangement</td>
<td>RV lead or coil to casing (tripolar)</td>
<td>RV-LV bipoles (Quadripolar)</td>
</tr>
<tr>
<td>Lead/casing maturation</td>
<td>Takes up to 1 month</td>
<td>Less</td>
</tr>
<tr>
<td>Influence of lung disease</td>
<td>Yes</td>
<td>Less</td>
</tr>
<tr>
<td>Influence of lead location</td>
<td>Less</td>
<td>Significant</td>
</tr>
<tr>
<td>Circadian &amp; postural effect</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sensitivity &amp; specificity</td>
<td>~70% (depends on threshold)</td>
<td>N/A</td>
</tr>
<tr>
<td>Applicability</td>
<td>Pacemakers and ICD</td>
<td>CRT-P or CRT-D</td>
</tr>
<tr>
<td>Clinical evaluations</td>
<td>Relatively extensive</td>
<td>Limited</td>
</tr>
</tbody>
</table>
light on the ischemic cause of arrhythmia. Quite aside from the logistic implication of ST segment monitoring [which requires urgent intervention], ST segment monitor will be possible only for non-pacemaker dependent patient. The influence of medications, electrolytes and heart rate on ST segment needs further evaluation.

**Peak Endocardial Acceleration**

Peak Endocardial Acceleration (PEA) sensor has been used for rate adaptation. The PEA signal measures the closure sound of the mitral valve, and reflects cardiac contractility. A minimal PEA signal occurs during optimal AV interval in DDD devices, and reflects the optimal AV interval in most patients. A new CRT-P (The New Living™ CHF, Sorin-Ela, Italy) is now available to monitor heart function and to program AV interval in CRT device. The PEA is contributed by both the contractility and LV filling and an index known as PEA area is derived by measuring the PEA values at different AV interval scanning at each VV interval. The maximum PEA area will define the optimal VV and AV interval for the patient.

In 15 patients implanted with CRT with PEA sensor, cardiac catheterization with LV dp/dt was measured with PEA area determined. AV interval was scanned between 60 and 220 ms. The authors found a responder rate to CRT (defined by 10% increase in dp/dt) in 75% of patients. Concordance of PEA area versus dp/dt methods occurred in 8/12 patients. These data are interesting, although the role of AV interval programming on the long term is uncertain, and the ability of the sensor to monitor LV function remains to be tested.

**Combined Heart Failure Diagnostics**

The PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients with Heart Failure) study is an observational study on the use of diagnostics to predict heart failure. 100 sites in the US prospectively recruited 694 CRT-D patients and followed them for 11.7 + 2 months. Table 5 shows the diagnostic data considered important in an algorithm to predict ADHF. A positive algorithm was defined as the occurrence of

<table>
<thead>
<tr>
<th>HF device diagnostic parameter</th>
<th>Algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF duration</td>
<td>AF ≥6 hours on at least 1 day in patients without persistent AF (7 consecutive days with ≥23 hours AF)</td>
</tr>
<tr>
<td>Ventricular rate during AF</td>
<td>AF ≥24 hours and the average ventricular rate during AF ≥90 beats/min on at least 1 day</td>
</tr>
<tr>
<td>Fluid index (OptiVol)</td>
<td>High fluid index on at least 1 day; thresholds included ≥60, ≥80, and ≥100 Ω·day</td>
</tr>
<tr>
<td>Patient activity</td>
<td>Mean patient activity &lt;1 hour over 1 week</td>
</tr>
<tr>
<td>Night heart rate</td>
<td>Mean night heart time rate &gt;85 beats/min for 7 consecutive days</td>
</tr>
<tr>
<td>HRV</td>
<td>HRV &lt;60 ms everyday for 1 week (minimum 5 measured days)</td>
</tr>
<tr>
<td>% of biventricular pacing</td>
<td>Ventricular pacing ≤90% for 5 of 7 days</td>
</tr>
<tr>
<td>ICD shock for potentially lethal VT/VF</td>
<td>≥1 shocks during the evaluation period</td>
</tr>
</tbody>
</table>

AF=atrial fibrillation; AT/AF=atrial tachycardia/atrial fibrillation; CRT=cardiac resynchronization therapy; HF=heart failure; HRV=heart rate variability; ICD=implantable cardioverter-defibrillator; VT/VF=ventricular tachycardia/ventricular fibrillation.
22/8 variables during a 1-month period that include: Long AF duration, rapid AF rate, increase Optivol fluid index, low patient activity, abnormal autonomic tone, or device therapy. A very high Optivol fluid level (>100) is considered ADHF.

Ninety patients had 141 adjudicated heart failure events, occurring after 60 days of implantation. A positive combined diagnostic set predicts a 5.5 fold risk of hospitalization in the next month, even after adjusting for the clinical variables. The main diagnostic parameters are Optivol ≥60 Ω·day, low activity and HRV. When additional Optivol ≥100 (28% of patients), it is also predictive of ADHF. Further sub-group analysis suggests that the specificity of ADHF is improved with setting a higher level of fluid index, and using more non-fluid related indices at the expense of loss of specificity. Interestingly, in patients with a prior history of heart failure, diagnostic parameters are no longer predictive. There is an improvement of diagnostic accuracy if sampling is performed every 15 days versus less frequently. Whether closer monitoring with the use of remote web based system can further reduce ADHF remains to be tested. Using externally measured parameters such as Weight Monitoring in Heart Failure67 and/or blood pressure (SPAW CHF II),68 benefit of monitoring was not observed in the former but occurred in the later study. In the first study, patients were recruited right after a heart failure hospitalization. The authors suggest that the role of diagnostic data in repeat heart failure hospitalization may be less than inpatients without prior hospitalization.

The PARTNERS HF is an important study suggesting the role of combined heart failure diagnostics to predict ADHF. While the sensitivity and specificity of the algorithm needs to be tested in prospective randomized trials, the occurrence of positive diagnostic criteria are predictive of a group of high risk heart failure patient. Conversely, the absence of diagnostic alerts predict a stable heart failure group. This risk stratification is over and above the conventional clinical risk factors.

**Conclusion**

Sensors have been introduced to optimize pacing rate in patients with chronotropic incompetence. The art has now matured such that sensor driven rate adaptive pacing is a programmable parameter of almost all CIEDs. With the increasing use of CIED to treat and monitor heart failure, sensors have now metaphor to optimize programming of CRT devices, and to monitor heart failure progression.

**References**

biventricular pacing in patients with heart failure: is a goal of 100% biventricular pacing necessary? J Am Coll Cardiol 2009; 53:355-60.


42. Maines M, Landolina M, Lunati M, et al; Italian Clinical Service Optivol-CRT Group. Infrathoracic and ventricular impedances...


Hong Kong College of Cardiology

Nineteenth Annual Scientific Congress

April 29-May 1, 2011
Sheraton Hong Kong Hotel and Towers
Hong Kong

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Scientific Programme

Friday, 29 April, 2011

0800  Registration

0900-1100  **Free Paper Session**
Coronary Artery Disease and Cardiac Surgery
Arrhythmia, Cardiac Pacing and Heart Failure

1100-1130  Coffee Break
Visit Exhibits

1130-1300  **Free Paper Session**
Cardiac Intervention
Basic Science

1300-1430  Light Lunch

1430-1530  **Best Paper Oral Presentation**

1530-1600  Coffee Break
Visit Exhibits

1600-1830  **Joined Symposium – Cross-straits 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)

A Rare Case of Heart Failure Caused by Hypocalcemia
Fei She

A Case Presenting with Recurrent Edema and Refractory Dyspnea
Liwen Li

OCT to Assist PCI for Strategies
Mengyue Yu

Bifurcation Case Report
Zhan Gao

A Case of Integrated Therapy of Chronic Heart Failure Complicated with Atrial Fibrillation: Where is the GAP?
Hanxiong Liu

Staged Recannualization of Right Coronary Chronic Total Occlusion
I-chang Hsieh

Acute Coronary Closure
Ying-keung Lo

1830-1900  Left Main PCI by Transradial Approach
Yuejin Yang

1915-2000  **Hong Kong Heart Foundation Lecture**
Transcatheter Aortic Valve Implantation (TAVI) – The Hong Kong Experience
Chung-seung Chiang

2000-2130  **Welcome Dinner**
**Saturday, 30 April 2011**

0800  
Registration

0830-1230  
**Joined Symposium — Cross-straits 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)

A Coronary Rupture Sealed with Cover Stent in Extraordinary Difficulties  
Yuejin Yang

Transient ST-Segment Elevation after Transseptal Puncture for Atrial Fibrillation Ablation  
Ribo Tang

Transcatheter Aortic Valve Implantation: CoreValve Experience in Taiwan  
Mao-chin Lin

Two Cases Presented with Right Ventricular Failure: What Lie Behind?  
Lianfang Chang

Is Revascularization Enough after AMI?  
Yawei Xu

What Stent for STEMI?  
Kang-yin Lee

Cardiac Tamponade after Primary PCI: A New Look at Old Problem  
Yujie Zhou

Simultaneous Late Stent Thrombosis in Two Coronary Arteries  
Yan Wang

Syncope  
U-po Lam

Unexpected Catastrophy: Small Right Coronary Dissection Evolving into Extensive Aortic Dissection  
Ning Tan

A Calcified Nightmare  
Eugene Brian Wu

0930-1030  
**Allied Cardiovascular Health Professionals Symposium — Data Interpretation for CCU Patients**

Chest X-ray Interpretation  
Yu-leung Chan

ECG Interpretation  
Andy Wai-kwong Chan

1100-1200  
**Allied Cardiovascular Health Professionals Symposium — Data Interpretation for CCU Patients**

Laboratory Results Interpretation  
Kin-lam Tsui

Echocardiogram Interpretation  
Chi-chung Choy
1230-1400  Lunch

1400-1430  **Opening Ceremony**

1430-1530  **Medtronic Symposium**

- Make the Complex Simple – Real World Clinical Practice
  David Edward Kandzari

- Innovative Therapy for Unmet Clinical Needs
  David Edward Kandzari

- Transcatheter Valve Therapy with the Medtronic CoreValve in 2011
  Anita W. Asgar

1530-1630  **Boston Scientific Symposium**

- What Tools You Need in Challenging Cases – Boston CRV
  Simon Lo

- How the New Generation DES Helps on the Complicated Lesion in PCI
  Simon Lo

- How to Manage Difficult Atrial Flutter Ablation
  Chin-pang Chan

1630-1730  **Abbott Vascular Symposium**

- 2011 DES Clinical Trials Update
  Pavit Pienvichit

- Vascular Restoration Therapy: The Abbott Vascular ABSORB BVS Program
  Arlene Yang

- To Be Confirmed

1730-1900  **Plenary Lecture**

- Use of 5 French Guiding Catheters in Transradial Coronary Intervention Procedures
  Lung-ching Chen

- Bio-Engineered Stent and Reduced Anti-platelet Therapy
  Giuseppe Sangiorgi

- How Imaging Can Optimize Stent Implantation
  Giuseppe Sangiorgi

1915-2000  **Sun Chieh Yeh Heart Foundation Lecture**

- Artificial Hearts: Science Fiction or Reality?
  Steven S. L. Tsui

2000-2040  Latest Updates of Mechanical Circulatory Support as an Option for the Management of Advance Heart Failure Patients
  Andrew Boyle

2040-2200  **Dinner**

*Coffee will be served from 1030-1100 and 1600-1700 at 4/F of Sung Terrace.*
Sunday, 1 May 2011

0830  Registration

0900-1030  **Plenary Lectures**

Peripheral Intervention
Pavit Pienvichit

Potassium and Blood Pressure: What Evidence We Have
Dong Zhao

Personalized Medicine in ACS PCI Patient
Gary Yiu-kwong Mak

1030-1100  Coffee Break
Visit Exhibits

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

1300-1430  Lunch

1430-1630  **Plenary Lectures**

Challenges and Opportunities in the Management of AF – Asia Pacific Regional Perspective
Hiroshi Tamada

Gastrointestinal Disease in Patients with Ischemic Heart Disease
Fook-hong Ng

Early Intra-Aortic Balloon Pump and Extracorporeal Membrane Oxygenator-Assisted Primary PCI Improved 30-Day Clinical Outcomes in Patients with STEMI Complicated with Profound Cardiogenic Shock
Hon-kan Yip

Update on CTO Intervention
Rajneesh Kapoor

1630-1700  Coffee Break
Visit Exhibits

1700-1800  **EPS Symposium**

Management of VF Storm in Brugada Syndrome
Buncha Sunsaneewitayakul

Cardiac Resynchronization Therapy: Present & Future
Yat-sun Chan

1800-1915  **CT/MRI Symposium**

Clinical Indications for Cardiac CT and MRI: Illustrated by an Entertaining Mix of Moderated Cases
Carmen Wing-sze Chan

Radiation Hazards of Cardiac CT: Myths and Controversies
Jack Shang-jen Shu

Magnetic Resonance Imaging in Patients with MRI-compatible Pacemaker System
Benny Wing-hung Ho

1915-2100  **Farewell Dinner**
Paediatric Cardiology Programme

Saturday, 30 April 2011

0900-1040  **Paediatric Cardiology Symposium I**

- Remote Ischemic Preconditioning: From Initial Observation to Randomized Clinical Trials
  Andrew Redington

- Hydrogen Sulfide as a Novel Gasotransmitter in Cardiovascular System
  Junbao Du

- Management of Cardiac Sequelae in Kawasaki Disease
  Guoying Huang

- Comparisons of Surgical Results for Transposition of Great Arteries
  Jinghao Zheng

1040-1100  Coffee Break

1100-1200  **Free Paper Session**

- Paediatric Cardiology I

1230-1400  Lunch

1400-1430  **Opening Ceremony**

1430-1630  **Paediatric Cardiology Symposium II**

- Pulmonary Hypertension: a Biventricular Disease?
  Andrew Redington

- The Multi-Center Experience of Interventional Treatment of Ventricular Septal Defect in China
  Zhiwei Zhang

- Paediatric Transplantation in Hong Kong
  Kin-shing Lun

- Ventricular Mechanics in Congenital Heart Disease
  Yiu-fai Cheung

- To Be Confirmed
  Fang Liu

1630-1700  Coffee Break

1700-1830  **Free Paper Session**

- Paediatric Cardiology II
### ABSTRACTS

Abstracts for Free Paper Session:

#### CORONARY ARTERY DISEASE AND CARDIAC SURGERY

1. Association of lower total bilirubin level with statin usage: Results from the United States National Health and Nutrition Examination Survey 1999-2008

2. Coronary artery disease and cardiac surgery

#### 3. The impact of Lifestyle Changes on Atherosclerotic Process in 3-Gorges Territories of Yangtze River

#### 4. Coronary artery disease and cardiac surgery

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### 3. The impact of Lifestyle Changes on Atherosclerotic Process in 3-Gorges Territories of Yangtze River

**Title:** The impact of Lifestyle Changes on Atherosclerotic Process in 3-Gorges Territories of Yangtze River

**Authors:** W.G. Song, J.K. Li, Z.H. Zhang, Y.X. Guo, J.J. Wang

**Affiliations:** First Affiliated Hospital of Chongqing Medical University, Chongqing Medical Sciences, Centre for Disease Prevention and Control of Wu Shan, Kai County, Chongqing, China

**Purpose:** To evaluate the impact of such lifestyle changes on atherosclerotic process in 3-Gorges population.

**Methods:** A total of 475 subjects aged 40-65 years were recruited from 3-Gorges territories ( Wu Shan, Kai County and Fuling) and were studied for up to 3 years (2008-2010). Changes in lifestyle factors were analyzed using the chi-square test and logistic regression analysis.

**Results:** The prevalence of hypertension, diabetes mellitus, and dyslipidemia significantly decreased over the study period. The prevalence of smoking, obesity, and physical inactivity also decreased.

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### 4. Coronary artery disease and cardiac surgery

**Title:** Coronary artery disease and cardiac surgery

**Authors:** J. Lee, S. Kim, J. Park, H. Choi, et al.

**Affiliations:** Department of Cardiology, Seoul National University Hospital, Seoul, Korea

**Purpose:** To evaluate the impact of lifestyle changes on atherosclerotic process in 3-Gorges population.

**Methods:** A total of 475 subjects aged 40-65 years were recruited from 3-Gorges territories ( Wu Shan, Kai County and Fuling) and were studied for up to 3 years (2008-2010). Changes in lifestyle factors were analyzed using the chi-square test and logistic regression analysis.

**Results:** The prevalence of hypertension, diabetes mellitus, and dyslipidemia significantly decreased over the study period. The prevalence of smoking, obesity, and physical inactivity also decreased.
ABSTRACTS

Abstracts for Free Paper Session:

5. Monocyte Plant Cell Aggregates: A Novel Pathology-based Prognostic marker for acute myocardial infarctions with integrated assessment on inflammation, thrombosis and antithrombotic treatment failure

H Lam, CK Chan, WH Leung, SF Yip, PW Yam, KL Chu, YH Chan, KK Yeung, YH Wong, WF Leung, LI DP, WK Chan, WK Lai, M Wong, CS Lam, KF Tsui, YH Yeung L Chiu

Department of Medicine and Geriatrics and Department of Pathology, Tuen Mun Hospital, Tuen Mun, Hong Kong

Background: Risk stratification is important in the management of acute myocardial infarctions (AMI). During AMI, deteriorated platelets adhere to the monocytes and form monocyte-platelet aggregates (MPA). The level of MPA can therefore reflect pathological change and indicate degree of inflammation and thrombosis in AMI. Using an in vivo-platelet function assessment tool, measurement of MPA may further evaluate the effect of antithrombotic treatment resistance.

Objective: To evaluate the prognostic value of MPA in AMI patients.

Methods: In this single-center prospective observational study, we enrolled 29 consecutive AMI patients and 19 healthy controls. Blood samples in the first 24 h of AMI and Day 5 after dual antithrombotic treatment were taken with written consent from five patients. MPA is circulating blood was identified by CD14+CD41 and CD14+ CD41+ positive population and its level was analyzed using flow cytometry. In the same analysis, patients with high MPA was compared with that of low MPA, in which the grouping cut-off was set for the upper quartile limit of the healthy subjects. To assess two analysis, patients with rising trend of MPA after dual antithrombotic treatment and patients with decreasing trend of MPA after dual antithrombotic treatment were compared. The baseline characteristics and clinical endpoints between any of the two groups were one- and two analysis were compared. The endpoint is composite cardiovascular endpoints of death, recurrent ACS, cardiac shock, heart failure and venous thromboembolic events till post AMI day 30.

Results: MPA level in AMI patients (mean ± SD) were significantly higher than healthy subjects (mean ± SD) (p < 0.05). In the same analysis, high MPA group (n = 9) and low MPA group (n = 20) reaching the endpoint were 35% (n = 5) and 30% (n = 6), respectively, (p = 0.62). In the two analysis, rising MPA group (n = 12) showed 95.8% (n = 11) patients reaching endpoints. Decreasing trend MPA group (n = 9) showed 11.1% (n = 1) patients reaching endpoints. Rising MPA group showed a trend of more post MI complications compared to decreasing MPA group but statistically it was not significant (p = 0.06).

Conclusion: MPA may be a potential prognostic marker for AMI patients but a larger scale study was needed. There is a trend that high MPA and rising MPA in AMI patients will have more post MI complications.

6. Thrombolytic Therapy in Patients with ST-elevation Myocardial Infarction in a University Hospital in Hong Kong: Demographics, Intracranial Haemorrhage and Other Outcomes

Simon CC Lam, Stephen Wai Lun Lee, Michael PH Chan, Kelvin KW Chan, Joyce SH Hui, Frankie CC Tam, Michael KL Wong, Shun Ling Kong, Raymond HW Chan.

From the Division of Cardiology, Department of Medicine, the University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China.

Introduction: Thrombolytic therapy remains an important reperfusion therapy strategy for eligible patients with acute ST-elevation myocardial infarction (STEMI). Customarily used thrombolytic agents are streptokinase and fibrin-specific agents (FSA), including tirofiban (TNK-AP) and alipase.

Method: A total number of 342 Patients who received thrombolytic therapy for management of ST-elevation myocardial infarction in 2001 to 2009 were analyzed. Cases were identified through Hospital Pharmacy Record, Hospital Authority Clinical Management System (CMS) and Acute Myocardial Infarction Clinical Pathway. Clinical records were retrieved. Data were analyzed using software SPSS 16.0.

Results: 296 patients (77.78%) and 76 patients (22.22%) were given Streptokinase and Fibrin-specific agents (TNK-AP, Tirofiban) respectively. The median door-to-needle time and pain onset-to-needle time was 68 minutes and 3 hours 23 minutes respectively. The overall rate of intracranial haemorrhage was 1.46% (5 out of 342). The rate of intracranial haemorrhage of Fibrin-specific agents (TNK-AP, Tirofiban) and Streptokinase was 5.26% (4 out of 76) and 0.38% (1 of 266) respectively (p < 0.002 Odds Ratio 14.71). Rate of intracranial haemorrhage was significantly higher in patients with admission systolic blood pressure ≥ 160mmHg (p = 0.043 Odds Ratio 5.33). Higher rates of intracranial haemorrhage were observed in sub-groups of Age > 75, Female, History of Stroke/Transient Ischaemic Attack (p < 0.014, 0.266, 0.155 respectively). Streptokinase was associated with more adverse events (34.95%) at time of thrombolysis administration which included hypotension, bradycardia and allergic reactions (p = 0.000). The success rate of reperfusion was higher with TNK-AP (78.67%) compared to Streptokinase (71.57%), but not reaching statistically significant level (p = 0.246).

Conclusion: This study showed that the rate of intracranial haemorrhage was much higher statistically with FSA than streptokinase. However the rates of successful reperfusion after thrombolysis in STEMl were only marginally better by FSA (tirofiban and alipase) than by streptokinase, and the difference was statistically insignificant. These findings warrant extreme caution to be taken when selecting thrombolytic agents in Chinese patients with STEMI.

7. Evaluation of platelet inhibition with point-of-care device VerifyNow in local Chinese patients with acute coronary syndrome treated with clopidogrel and prasugrel: a single centre cohort study

CC Tam, LLT Lam, YT Wong, SY Yang, KL Wong, KW Chan, CC Lam, PH Chnn, JJ Hai, JWH Chnn, SWE Loo

Department of Medicine, Queen Mary Hospital, Hong Kong

Purpose: Clopidogrel has been used widely in the treatment of acute coronary syndrome but there is increasing evidence concerning its limited platelet activity especially in Asian population. Prasugrel has been shown to have superior efficacy in platelet inhibition compared to clopidogrel and it has been translated to improved clinical outcomes but increase bleeding risk.

Methods: From December 2010, Chinese patients admitted with acute coronary syndrome who were clopidogrel or prasugrel naive were treated with either loading dose of clopidogrel 300mg or 600mg, or prasugrel 60mg at physicians’ discretion according to usual practices. Antiplatelet effects were evaluated by VerifyNow P2Y12 at 4 hours and 24 hours post-loading. Results: 20 patients’ results are included so far, 5 patients received clopidogrel 300mg, 10 patients received clopidogrel 600mg and 5 patients received prasugrel 60mg. There is no significant difference in diagnosis, baseline clinical characteristics between all groups. Mean platelet reactivity units (PRU) at 4 hours and 24 hours in clopidogrel 300mg group are 338 and 315 respectively, in clopidogrel 600mg group 352 and 321 respectively, in prasugrel 60mg group 37 and 16 respectively. PRU in prasugrel group is significantly lower than that in clopidogrel 300mg and 600mg group (p < 0.005) while there is no difference between clopidogrel 300mg and 600mg group. The percentage of clopidogrel hypersensitivity as defined by PRU > 240 is 92.9% at 4 hours and 84.6% at 24 hours while percentage of prasugrel hypersensitivity is 0% at both 4 and 24 hours. Conclusions: A loading dose of prasugrel 60mg in local Chinese patients with acute coronary syndrome has significantly more potent antiplatelet effect than loading clopidogrel 300mg or 600mg. The proportion of clopidogrel hypersensitivity in Chinese patients is high. Further studies are necessary to delineate whether such dramatic difference will translate into superior clinical efficacy or increase bleeding risk of prasugrel and those may influence our decision on antiplatelet agents when treating our Chinese patients.

8. Endothelial Nitric Oxide Synthase Enhancer Reverses ADMA-induced Endothelial Dysfunction in Human Internal Mammary Artery

Chao Xuan1, Xiao-Yan Bai1, Xiao-Cheng Liu1, Qin Yang2 & Gai-Wei He3

1TEDA International Cardiovascular Hospital, Medical College, Nankai University, Tianjin, China; 2The Chinese University of Hong Kong, Hong Kong, China; 3Providence Heart and Vascular Institute, Starr Academic Center, and Department of Surgery, Oregon Health and Science University, Portland, Oregon, U.S.A.

Purpose Endogenous nitric oxide (NO) synthase inhibitor asymmetric dimethylarginine (ADMA) is a cardiovascular risk factor. Increased ADMA levels are associated with reduced nitric oxide synthesis. AVE3085 is a novel endothelial NO synthase (eNOS) enhancer. This study tested the hypothesis that AVE3085 may improve the endothelial function altered by ADMA in the human artery.

Methods Isolated human internal mammary artery (IMA) rings (n = 44, taken from 20 patients undergoing coronary artery bypass grafting surgery) were studied in myograph. Cumulative concentration-relaxation curves to acetylcholine (ACh, -11 to -5 log M) were established in precontraction induced by U46619 (-8 log M). Protein expressions of eNOS were also determined by Western blot.

Results: The maximal relaxation to ACh (35.3 ± 5.0% in control) was significantly attenuated by ADMA (12.7% ± 2.9%, P < 0.05). Compared to ADMA alone, ADMA+AVE3085 significantly increased the relaxation (23.4 ± 2.8%, P < 0.05). The eNOS expression (0.36 ± 0.03) was significantly decreased by ADMA (0.30 ± 0.4, P = 0.014) and markedly restored by AVE3085 (0.29 ± 0.003; P = 0.012).

Conclusion: The results demonstrate that the NO enhancer AVE3085 may restore the endothelium-dependent relaxation reduced by ADMA through up-regulation of eNOS expression in the human artery. This may provide new therapeutic insights in clinical situations with endothelial dysfunction associated with eNOS down-regulation.
9.
The Relationship Between Postoperative Pain and Arterial Endothelial Function and the Impact of Anaglytic Therapy after Non-cardiovascular Surgery.

Wu Meng Jun’, Chock Ping’, Liu Yan Jun’, Wei An Ning’, Yin Yue Hai’, Woo Kam Sang’. The Second Affiliated Hospital, Chongqing University of Medical Sciences and The Chinese University of Hong Kong.

Purpose: Perioperative cardiovascular complications occur frequently, and arterial endothelial function is a surrogate prognostic end-organ factor. The purpose of present study is to evaluate the relationship between postoperative pain and changes of endothelial function, and the impact of anaglytic therapy after non-cardiovascular surgery.

Methods: 129 patients (age 57.7±10.0 years) undergoing abdominal operation (10 laparoscopy and 110 laparotomy surgery) were randomly assigned to routine intravenous fentanyl and droperidol (drug group, n=60), or on demand anaglytic therapy (control group, n=69). Endothelium-dependent dilatation (EDD) of brachial artery (measurement by ultrasound) and pain visual analogue score (VAS) were evaluated at 1 day preoperative, 2 hours, 1 day and 5 days after anesthesia recovery.

Results: EDD of both groups at 2 hours after anesthesia recovery decreased significantly (P<0.002 & P=0.033) compared with the other three time points (figure), while VAS increased significantly (P<0.05). VAS of drug group were lower than those of control group at 2 hours (2.8±1.9 vs. 3.8±2.2, P=0.013) and 1 day postoperative (1.6±1.4 vs. 2.3±1.8, P=0.031). EDD of drug group (7.9±1.2 & 7.3±1.9) were higher than the control group (7.1±1.5 & 6.7±1.6%) at postoperative day 1 (P=0.048) and day 5 (P=0.003) respectively. VAS ≥ 5 were independently associated with postoperative EDD<7% (OR=2.7, 95%CI 1.0-5.0, P=0.041). At 2 hour after anesthesia recovery, VAS<5 of drug group were independently associated with EDD<7% (OR=2.5, 95%CI 1.0-6.0, P=0.047).

Conclusion: Reduced postoperative venous endothelial function is closely related to postoperative pain, and arterial endothelial function can be improved by routine anaglytic treatment after non-cardiovascular surgery.

10.
The Impact of Noncardiovascular Surgery on Reactive Hyperaemia and Arterial Endothelial Function

Yan Jun Hu1,2, MD; An Ning Wei1, MD; Ping Chock1, MD; Yuehai Yin1, MD; Meng Jun Wu3, MPH; Kam Sung Woo2, MD. The Second Affiliated Hospital, Chongqing University of Medical Sciences, and The Chinese University of Hong Kong.

Background: Vascular reactivity is a surrogate atherosclerosis marker predictive of cardiovascular outcome. Noncardiovascular surgery is associated with perioperative cardiovascular complications in high risk patients.

Purpose: To evaluate the impact of noncardiovascular surgery on reactive hyperaemia and arterial endothelial function, and the relationships between invasive versus minimally invasive surgery and endothelial dysfunction.

Methods: We evaluated prospectively 106 patients undergoing general anestesia abdominal surgery (71 laparoscopy, 35 laparoscopic surgery), with measurement of pain visual analogue scale (VAS), brachial endothelium-dependent flow-mediated dilatation (FMD), endothelium-independent dilatation (nitroglycerin-induced dilatation, NTG), and reactive hyperaemia were measured by high resolution 2-mode ultrasound at postoperative day 1 (baseline), postoperative 2 hours, day 1 and day 7.

Results: Blood pressure and heart rate were significantly higher at postoperative 2 hours. VAS were higher (P<0.001), reactive hyperaemia and FMD were significantly lower (P=0.001) at postoperative 2 hours and day 1 compared with baseline and postoperative day 7. FMD at postoperative day 7 recovered to baseline level. Patients undergoing laparoscopic surgery had less FMD reduction at day 1 (7.3±1.7%) and day 7 (7.9±1.5%), compared with laparotomy surgery (6.4±1.7% and 7.0±1.5% respectively) (P<0.01) (Figure 1). NTG was stable throughout. On backward multivariate linear regression analysis, FMD was independently related to age and VAS (model R^2=0.486, F-value=6.4, P=0.001).

Conclusion: Reactive hyperaemia and arterial endothelial function are significantly reduced in the early postoperative period, but recover in one week, with implication for nonperioperative cardiovascular complications.

11.
Suxiao Jiu Xin WU (巫素曉新心) Induces Potent Vasorelaxation in Human Internal Mammary Artery

Xiao Yan Bai1, Ping Zhang1, Qin Yang1, Xiao Cheng Liu1, Song Jin Xiong1, Li Huang Liu1, Lei Wang1 & Guo Wei He1
TEDA International Cardiovascular Hospital, Medical College, Nankai University, Tianjin, China; Tianjin Zhongxin Pharmaceutical Group Co., Ltd., Tianjin, China; The Chinese University of Hong Kong, Hong Kong, China; TEDA School of Biological Sciences and Biotechnology, Nankai University, TEDA, Tianjin China; Providence Heart and Vascular Institute, St. John's University, and Department of Surgery, Oregon Health and Science University, Portland, Oregon, U.S.A.

Purpose: The graft remnant is challenging in coronary artery bypass grafting (CABG) surgery. We investigated the inhibitory effect of the compound Chinese medicine - suxiao jiu xin wu, on the vasorelaxation mediated by potassium chloride (KCl) and U46619 in human internal mammary artery (IMA) segments from patients undergoing CABG.

Methods: Isolated IMA rings (n = 60, taken from 24 patients) were studied in myograph in two ways: the relaxing effect of suxiao jiu xin wu was evaluated on the aortic ring precontracted by KCl and U46619 and the relaxing effect of suxiao jiu xin wu was on the contraction. Protein expression of eNOS were also determined by Western blot.

Results: Suxiao jiu xin wu caused full relaxation in KCl (99.3 ± 10.6%, n=6) and U46619 (100.0 ± 5.9%, n=6) precontracted IMA rings with similar potency (ECS0: 0.27 ± 0.21 vs. 0.18 ± 0.21 log mm/Hg, p > 0.05). Pretreatment of IMA with plasma-concentrations of suxiao jiu xin wu (1 mg/ml), calculated from the plasma concentration of its major component borneol, significantly depressed the maximal contraction to KCl (from 35.8 ± 6.0 mm Hg to 12.6 ± 5.6 mm Hg, P = 0.03) and U46619 (from 19.4 ± 2.9 mm Hg to 5.7 ± 2.4 mm Hg, P = 0.007). Pretreatment of IMA with suxiao jiu xin wu (10 mg/ml) abolished the subsequent contraction to both KCl and U46619. The eNOS expressions in IMA had no significant differences between the control and suxiao jiu xin wu (1 mg/ml) pretreated group. However, no eNOS expression was detected in suxiao jiu xin wu (10 mg/ml) pretreated group.

Conclusion: We conclude that suxiao jiu xin wu has potent inhibitory effect on the vascular contraction mediated by a variety of vasconstrictors in human arteries such as IMA. This use of suxiao jiu xin wu is in favor of treating and preventing vasospasm in CABG and in patients with coronary artery disease.

12.
Left ventricular assist device - a surgical treatment for end-stage heart failure - a case series in Hong Kong

CKL Ho, K Fung, WK Au, LC Cheng, Department of Cardiothoracic Surgery, Queen Mary Hospital, Cardio Medical Unit, Grantham Hospital.

Purpose: To introduce an advanced non-transplant surgical treatment for patients suffering from end-stage heart failure (ESHF). Left ventricular assist device (LVAD) implantation for ESHF was accepted as an effective therapy worldwide as a bridge to transplant or even a destination therapy. Recently it has been introduced in Hong Kong as a choice of therapy for patients awaiting heart transplant.

Results: From August 2010 to March 2011, 3 patients with ESHF were selected for LVAD implant. Continuous-flow Heartmate II device was used in all 3 patients. After implantation, all 3 patients improved from NYHA class IV to class I clinically; they were all ambulatory and returned to the society readily. The selection criteria, contra-indications, peri-operative and post-operative management would be discussed.

Conclusions: Though LVAD implant is a newly introduced therapy for ESHF in Hong Kong, so far the clinical results are satisfactory. With further accumulation of clinical experiences, the outcome of patients will be improved and more patients can be benefited from this kind of therapy.
A Clinical Analysis of 40 Cases of Prosthetic Valve Endocarditis

XL Sun, J Guan, Y Sun, J Zhang, GG Wang

Department of Cardiology, Cardiovascular Institute and Fuwei Hospital, Peking Union Medical College and Chinese Academy of Medical Science, Beijing

**Purpose:** To analyze the clinical characteristics of prosthetic valve endocarditis.

**Methods:** The study population comprised 40 consecutive patients who fulfilled the modified Duke criteria for prosthetic valve endocarditis from May 2003 to May 2008 at our institution. Data were collected retrospectively on demographic characteristics, presenting signs and symptoms, results of laboratory and microbiological investigations, echocardiographic findings, treatment modality (antibiotic regimen, valve surgery), and clinical outcomes.

**Result:** The mean age at presentation was 40 ± 11 years, with a slight male preponderance. There were 38 (95%) patients with involvement of a mechanical prosthesis; the majority (65%) had late prosthetic endocarditis. General fatigue (83%), fever (64%), major vessel embolism (61%), and anemia (44%) were the most frequently manifestations. Major complications occurring during the acute infective phase were also recorded, including renal dysfunction (75%), such as renal infarction, glomerulonephritis, nephrotic syndrome, New York Heart Association class III–IV heart failure (66%), and neurological complication (22%). Twenty-three cases (58%) had positive culture results with 36 causative pathogens, including 18 Gram-negative bacilli (7 were Acinetobacter, 4 were Citrobacter rodentium, 3 were Pseudomonas aeruginosa, 3 were Enterobacter cloacae, 2 were Burkholderia cepacia), 10 coagulase-negative Staphylococcus, 3 Staphylococcus aureus, 2 fungi, 2 Enterococcus faecalis, and 1 Streptococcus. All patients underwent transthoracic echocardiography, but only 8 (20%) had further evaluations with transesophageal echocardiography. More than half of patients detected prosthetic valve vegetations. Twenty-seven prosthetic valve endocarditis (68%) developed peri-annular complications (16 leakage, 6 abscesses, 4 dehiscence, 1 perforation of cardiac valve). The overall hospital mortality was 20% (8 patients), in spite of intensive managements.

**Conclusion:** Prosthetic valve endocarditis is associated with a high mortality despite diagnostic and therapeutic improvements. The spectrum of microorganism is quite different from that of native valve endocarditis. Early diagnosis, bacterial culture and transesophageal echocardiography may be essential for prosthetic valve endocarditis.
ABSTRACTS

Abstracts for Free Paper Session:

14. The efficacy of warfarin versus aspirin for stroke prevention among local Chinese population with atrial fibrillation and CHADS2 Score 1
Dr. Lai San Wah, Caritas Medical Centre 
Dr. Cheung Ling Ling, United Christian Hospital

Background- Atrial fibrillation (AF) is the most commonly encountered cardiac arrhythmia, occurring in 1-2% of the general population. It was associated with 5-fold increase in risk of ischemic stroke/ TIA. In patients with CHADS2 score ≥ 1, warfarin or aspirin are equally recommended as a measure of stroke prophylaxis. In Asian population, it was said that warfarin use was associated with substantially higher bleeding complications. The purpose of this study is to evaluate whether aspirin has similar efficacy as compared to warfarin for stroke prophylaxis and to compare their respective bleeding complication risk.

Method- This was a retrospective cohort study. The study recruited patients diagnosed to have atrial fibrillation with CHADS2 score ≥ 1 between 2004 and 2006. The primary outcome were the occurrence of ischemic stroke or TIA, systemic embolic event and total cardiovascular mortality. The secondary outcomes were bleeding complications including hemorrhagic stroke.

Results- Totally 252 non-surgical atrial fibrillation patients with CHADS2 score ≥ 1 were recruited. There were 102 patients in the warfarin group whereas 118 patients in the aspirin group. All patients taking warfarin had INR maintained between 1.5-3.0 (mean =2.1). During the follow up period (median=57.8 months), the incidence of ischemic stroke among patients taking aspirin was significantly higher compared with patients taking warfarin using Kaplan-Meier analysis (Log rank q = 2.6, p = 0.04). Hazard ratio 3.0). The incidence of major bleeding including hemorrhagic stroke was not significantly different between the 2 groups; 6.9% (7/102) in the warfarin group, 9.9% (7/118) in the aspirin group (p=0.76). However, minor bleeding was more common among patients receiving warfarin; 17.5% (18/102) in warfarin group, 8.5% (9/108) in aspirin group (p=0.05).

Conclusion- Warfarin was better than aspirin in preventing ischemic stroke among patients with atrial fibrillation and CHADS2 score ≥ 1 without significantly increasing major bleeding complications.

15. Clinical Profile of patients having acquired Tordes of de pointes in a regional hospital
KY. Le, CS Yue, KF Leung, CK Chan, Raymond CY Fung, TS Chung, LL Cheung, KT Ho. Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong

Purpose: The acquired form of Torsades de-pointes (TDP) is a rare but potentially catastrophic emergency (in hospital setting). Acquired long QT syndrome is usually caused by drugs, electrolyte disturbance and bradyarrhythmia. Limited data are available in our community. We sought to review the clinical profile of patients diagnosed to have TDP in our hospital.

Methods: This was a single-center retrospective study. Patients with diagnosis of TDP were identified through the hospital’s computerized data base system (CODASE). TDP was defined as polymorphic VT with prolonged QTc interval (more than 470ms and 480ms in males and females respectively). Demographic and medication history, presentation, ECG features and outcomes were retrospectively analysed.

Results: Twenty-one patients (13 females, mean age 73 years, range 54-87 years) were identified from year 2004 to 2010. Structural heart disease was not uncommon in this group of patients (ischemic heart disease, history of heart failure and poor LV systolic function in 34%, 48% and 19% of patients respectively). The mean QTc on presentation was 552±60ms (range 470-720ms) with 17 patients having a QTc > 500ms. Most patients presented with cardiac arrest (29%), syncope (43%) or palpitation (24%). Contributing factors included drug-induced TDP in 67% of cases, significant bradycardia and electrolyte disturbance in 48% and ischaemia in 19% of cases. Most patients (65%) had multiple contributing factors. QTc at baseline (mean = 464ms, range 400-560ms) was prolonged in 43% of cases with 4 cases having a QTc > 500ms. Eight patients (38%) required implantation of permanent pacemaker or implantable cardioverter defibrillator eventually. After a mean follow-up period of 20±22months, cardiac death occurred in 4 cases (19%).

Conclusion: Multiple risk factors for TDP were identified in our group of patients including baseline long QTc, use of QT-prolonging drugs, heart diseases, electrolyte disturbance and bradyarrhythmia. Early recognition and correction of reversible causes may help to reduce the incidence of TDP.

16. Single Center Prospective Cohort Study of Catheter Ablation of Atrial Fibrillation
C.L. Chang, J.Y.S. Chen, H.C.K.Chan, Y.K. Koe, P.W.H. Fung, C.M. Ye. Division of Cardiology, Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong

Purpose: Anti-arrhythmic 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 and assess the efficacy of ablation procedure by using different ablation catheters.

Methods: This study evaluated 95 consecutive patients (61 men, age 58±10.2 years, LA size 44±6 mm, LVEF 0.57±0.10) with AAD refractory symptomatic AF (67 patients had paroxysmal AF, 28 patients had persistent AF) were studied. Ablation procedure was undergone by one of the following techniques: (1) Ablation Frontiers Cardiac Ablation System (n=35) or (2) Ensite NavX system in combination with irrigation ablation catheter (n=60). Patients were followed clinically for recurrence of AF at months 3, 6 and 12. Clinical recurrence of AF was defined as AF/atrial flutter >1 minute in duration.

Results: The mean duration of AF was 60±13.5 months before index procedure. During the follow-up time of 16±3 months, 70.1% of patients with paroxysmal AF and 53.6% of patients with persistent AF remained free from recurrence of AF after single procedure. Also 62.9% of patients who underwent ablation by Ablation Frontiers and 66.7% of patients who underwent ablation by using irrigation catheter were free of symptomatic AF (P=NS). About 15.7% of patients are taking AAD after single procedure. Major adverse events occurred in 3.2% 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 with paroxysmal AF after a single procedure. The clinical efficacy of using different ablation catheters was similar and the procedural risk was low.

17. Electrocardiographic effects and plasma concentrations of flecainide and propafenone in healthy Chinese subjects
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Purpose: Flecainide and propafenone are antiarrhythmic drugs for the management of supraventricular and ventricular arrhythmias mainly through their effects on sodium channel blockade but additional mechanisms might be involved. We assessed the electrocardiographic (ECG) changes in healthy Chinese subjects after taking single oral doses of flecainide and propafenone and examined the relationship of these with the plasma concentrations.

Methods: Plasma concentration-time profile and ECG changes at 3 h and 12 h after administration of a single oral dose of flecainide (100 mg) or propafenone (150 mg) in 15 or 30 healthy Chinese male subjects were evaluated.

Results: At 3 h after dosing, flecainide significantly prolonged PR (160.8±23.1 vs. 146.8±23.6 msec, P<0.05) and QRS duration (96.5±7.9 vs. 93.6±8.5 msec, P<0.05) compared to baseline. The prolongation of the PR interval persisted for 12 h after dosing (153.9±21.5 msec at 12 h, P<0.05 vs. baseline). Propafenone prolonged the PR interval at 3 h (167±28.5 vs.157.5±23.6 msec, P<0.05), but not at 12 h after dosing. Neither flecainide nor propafenone prolonged QTc, QTd and Jt/e intervals. The drug concentrations at 3 h tended to be related to the ECG effects of flecainide (r=0.387, P=0.05) and propafenone (r=0.181, P=0.05).

Conclusions: In healthy subjects, PR prolongation persisted for 12 h after a single dose of flecainide 100 mg but not for propafenone 150 mg, which may be related to the shorter half-life of propafenone. Plasma concentrations of flecainide and propafenone showed a tendency to be related to the ECG changes induced by the two drugs, but this was not significant possibly due to the small sample size.
ABSTRACTS

Abstracts for Free Paper Session:

18. 
Auxiliary Vein is a Better Access than Subclavian vein or Cephalic vein With Respect to Long-term Pacing Lead Survival

NY Chai1, YY Cheong1, NP Kwong2, TC Law2, NS Mok3, PT Tsui1, CC Choy1, CL Lau1, YK Lo1, PS Chu1, HC Yuen1, HF Chow1, ST Lau1. Department of Medicine & Geriatrics, Prince Margaret Hospital, Hong Kong1, Department of Medicine, Yan Chai Hospital, Hong Kong2

Purpose: To investigate the relationship between venous access and long-term pacemaker lead failure (PLF)

Methods: This is a retrospective cohort study. Case records of 409 patients (221 women, mean age 72.2±10.5 years) undergoing pacemaker implantation in 2 hospitals in the period between January 2000 and December 2004 were reviewed. PLF was defined as abnormal impedance and/or high pacing threshold and/or low sensing threshold leading to replacement or abandonment of the lead.

Results: A total of 66 (27.4 atrial and 40.8 ventricular) leads were implanted with contrast-guided axillary vein puncture (AP, 25%), subclavian vein puncture (SV, 212) or cephalic vein cutdown (CP, 218). Over a mean follow-up of 73.7±33.3 months, 25 PLF were documented. Three (1.2%) were in AP group, 9 (4.1%) were in CP group and 13 (6.5%) were in the SV group. Using Cox regression, only the use of AP (HR=0.25, 95% CI 0.07-0.92; p=0.037), but not the other variables (age, sex, etiology of bradyarrhythmia, cardiac chamber of lead implantation, lead size, lead material and lead fixation mechanism) was an independent predictor of PLF. With Kaplan-Meier analysis, AP results in significantly less PLF than SV or CP (p=0.013) or CP (p=0.047).

Conclusions: The use of AP is an independent predictor of PLF. AP results in less PLF than SV or CP.

19. 
Multi-Disciplinary Service for Patients Having Pacing Implantation

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Purpose: The introduction of a multi-disciplinary team approach for patients following implantation of pacemaker or implantable cardioverter defibrillator with cardiac rehabilitation model applied, the service was provided to in-patient and out-patient phase. The aims of the service were to enhance patients’ knowledge and self-management skills, as well as to improve their physical and psychosocial well-being.

Methods: The first initiative in 2006 was the out-patient pacemaker workshops launched in May 2007. Each workshop consisted of 2 sessions with various disciplines including nurses, occupational therapists, physiotherapists and social workers involved. The workshop was held at least 4 weeks post-implantation. In-patient PIS was started in May 2010. Patients requiring pacemaker implantation would be recruited into Phase I PIS. Assessment, counselling, exercise, advice on activities of daily living, stress management and precautions following implantation were provided at both phases. At the early discharge period, community nursing service was arranged for wound care, monitoring of drug compliance and reinforcing self-management at home. At present, PIS was offered to patients received implantation for the first time.

Results: Two hundred and ninety-three patients (151 males, 52%) received at least one service in PIS. Among them, 81% of patients received pacemaker implantation. One hundred and eighty-four patients with mean age of 71 years (SD=9) with 279 attendances were made to the multidisciplinary workshops. Fifty-five patients (26 males, 47%), mean age of 75 years (SD=9), were referred for Phase I PIS. Thirty-seven patients received home-based care offered by community nurses. Three patients were found with shoulder stiffness during workshop were referred to physiotherapists for further management. Phase II cardiac rehabilitation was provided to 8 patients due to their underlying heart disease.

Conclusion: PIScan be developed to support patients with pacemaker and implantable cardioverter defibrillator implantation. Outcome measures to evaluate the effectiveness and benefits of the program will be further explored.

20. 
Single Center Prospective Cohort Study of Performance of Attain StarFix Left Ventricular Lead in Patients Receiving Cardiac Resynchronization Therapy

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Purpose: Cardiac Resynchronization Therapy (CRT) is established treatment for patients with symptomatic heart failure. In spite of the advancement of implantation equipments and improved implantation technique, stability of left ventricular (LV) pacing lead is still the major obstacle to success. The aim of this study was to assess the performance of Attain StarFix LV lead (model 4195) and compared this with other passive LV leads (model 4194 and model 4193).

Methods: This study evaluated 175 consecutive patients (98 men, age 69.6±10.7 years) who had undergone CRT implantation were studied. Three different types of LV leads were implanted during index procedure (1) model 4195 (n=82), (2) model 4193 (n=61) and (3) model 4194 (n=32). Pacing threshold, impedance, sensing and number of dislodgement were analyzed at implant, 3 months, 6 months, 12 months, 18 months and 24 months.

Results: During the follow-up time of 24 months, pacing threshold of these leads were 1.4±0.5 mV (model 4193), 1.2±0.5 mV (model 4195) and 1.1±0.5 mV (model 4194) (p=NS). R wave were 14.8±mV (model 4193), 16.3±mV (model 4195) and 14.9 mV (model 4194) (p=NS). Lead impedance were 579 ohms (model 4193), 560 ohms (model 4195) and 550 ohms (model 4194) (p=NS). Numbers of lead dislodgements were: model 4193 = 34%, model 4195 = 1% and model 4194 = 3% (p=NS). No major complication was recorded during implantation.

Conclusion: Among patients who underwent CRT implantation, StarFix LV lead had an excellent performance and there was high rate of successful implantation. Its active fixation mechanism may lead to better stability when it is compared to other LV leads and it did not associated with extra-procedural complication.

21. 
Left Ventricular Remodeling After Long-term Right Ventricular Pacing Is Predicted by Electrical and Mechanical Dysynchrony, but not Pacing Site

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Purpose: Long-term right ventricular pacing (RVP) has been shown to cause adverse left ventricular (LV) remodeling and clinical outcomes. This is a retrospective cohort study on the predictors of LV remodeling after long-term RVP pacing.

Methods: One hundred and two patients (54M, mean age 71.5±13.0, 50 RV septal and 52 RVA pacing) undergoing pacemaker implantation for atriovenous block from January 2003 to June 2008 were studied. LV remodeling was assessed by echocardiography performed at least 18 months after implantation. Clinical outcomes including all-cause mortality, heart failure, ischemic stroke and atrial fibrillation were analyzed. Electrical dysynchrony (EAP) was measured by QRS duration during pacing. Mechanical dyssynchrony (MAP) was measured by standard deviation of time to peak systolic velocity of 17 LV segments from echocardiography during pacing.

Results: There was no difference in all clinical outcomes between RV septal and RVA pacing groups (Mann-Whitney U test). With multivariable stepwise regression, only EAP(p=0.002) and MAP(p=0.016) but not pacing site (RVA or RV septal), were independent predictors for LV remodeling indices, namely LV ejection fraction (LVEF), end-systolic volume (LVESV) and end-diastolic volume (LVEDV). The presence of 2 positive criteria (EAP<150ms, MAP<33ms) compared to 0 or no positive criteria, resulted in significantly less adverse LV remodeling. LVESV(20.1±7.8 vs33.7±6.9, p<0.001), LVEDV(54±12.9 vs75.5±25.9, p<0.001) and LVEF(59±0.1 vs37.6±10.9, p<0.05).

Conclusion: EAP and MAP were independent predictors for LV remodeling after long-term RV pacing. They may be targets for pacing site optimization.
ABSTRACTS

Abstracts for Free Paper Session:

22. A New Era in extracorporeal membrane oxygenation management

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Purpose: To review the results of extracorporeal membrane oxygenation (ECMO) in our center.

Method: A retrospective review of medical records of patients who received ECMO support between Nov 2009 to Nov 2010 was performed.

Results: Between Nov 2009 to Nov 2010, ten patients (5 male, 5 female) received ECMO support. The indications for ECMO support include acute myocarditis (3 patients) and post cardiac surgery low output syndrome (3 patients), post-heart transplant right ventricular failure (2 patients), restrictive or dilated cardiomyopathy (2 patients). Four patients had bleeding complications requiring re-exploration and haemostasis. One patient had intracranial haemorrhage. The average duration of ECMO support was 5.4 days. Six patients were successfully weaned off ECMO support and were discharged without neurological deficit.

Conclusions: With the recent advances in medical equipments, better ECMO circuits and intensive care support, ECMO has become increasingly employed as a method of temporary support for patients with low cardiac output due to acute myocarditis, cardiomyopathies or after cardiac surgery.

23. Fulminant Myocarditis: Uncommon Presentation of Influenza A (H1N1) 2009 Rescued by Veno-arterial Extracorporeal Membrane Oxygenation. A Case Report

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Fulminant myocarditis is an uncommon but potentially lethal complication of influenza which may require mechanical circulatory support. Case reports on Influenza A (H1N1) 2009 associated fulminant myocarditis were scarce and successful use of extracorporeal membrane oxygenation (ECMO) as the only mechanical circulatory support was not reported in the literature.

We described a 56-year-old man presented with 3 days history of fever, generalized malaise and progressive shortness of breath after recent travel to Mainland China. He was in cardiogenic shock with blood pressure 90/60mmHg, sinus tachycardia with rate up to 157 beats per minute, oliguria, cold periphery, lung field congestion and diffuse inlftrates on chest X-ray as well as left ventricular ejection fraction of around 20% on echocardiogram. Electrocardiogram showed 0.5-1mm ST elevation over inferior leads, poor R wave progression and early repolarization changes over anterior leads. Coronary angiogram showed only non-critical lesion over left anterior descending artery with TIMI 3 flow. Troponin was elevated from 0.13 to 3.35ng/ml. Nasoparyngeal aspirate was positive for RT-PCR for Influenza A (H1N1) 2009. Although endomyocardial biopsy was normal, overall clinical picture was still compatible with the diagnosis of fulminant myocarditis. Venoarterial extracorporeal membrane oxygenation (VA-ECMO) system had been set up for mechanical circulatory support via right common femoral artery and right common femoral vein using percutaneous approach. Octreoscan V, broad spectrum antibiotics and methylprednisolone was given and his cardiac function significantly improved. He had successfully weaned off all isotopes and ECMO was off after 41 hours. He then received a short course of rehabilitation and was discharged on Day 17 with echocardiogram before discharge revealed normalized left ventricular ejection fraction at 55%.

To the best of our present knowledge, this is the first case of fulminant myocarditis associated with Influenza A (H1N1) 2009 successfully supported by ECMO as the only mechanical circulatory support in the medical literature.

24. Hemodynamic effects and clinical outcome of sildenafil therapy on patients with severe pulmonary hypertension secondary to restrictive heart failure considered ineligible for cardiac transplantation

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Background: Inversely raised pulmonary vascular resistance (PVR > 2.5 Woods units) is an independent predictor of early mortality in heart transplantation. Heart failure patients (pts) with pulmonary hypertension (PH) with demonstrated reversibility of PVR with nitroglycerinic infusion have lead to a significant decrease in post-transplant mortality. Use of sildenafil, a phosphodiesterase-5 inhibitor, has been suggested for heart failure pts with PH who would have been excluded from heart transplantation.

Purpose: To assess the effect and outcome associated with sildenafil for treatment of irreversible pulmonary hypertension secondary to congestive heart failure

Methods: A retrospective case series of 6 pts with severe congestive heart failure considered ineligible for cardiac transplantation because of irreversible pulmonary hypertension were reviewed. Right heart catheterization findings and reversibility testing with nitroglycerinic infusion before and after sildenafil treatment were compared and analyzed.

Results: Six pts (mean age 67.5 ± 6.4; 5 men 75%) enrolled for heart transplantation were found to have severe PH with irreversible PVR with nitroglycerinic infusion. The mean dose of sildenafil was 75.3 ± 8.2mg/day. The duration between baseline and follow-up right heart catheterization ranged from 28 to 195 days. There was a definite trend of PVR reduction from 10.35 ± 4.05 to 5.62 ± 3.66 Woods units (p = 0.03). Reversibility of PVR could be demonstrated in 4 pts. Two pts subsequently underwent successful heart transplantation. One pt with dilated cardiomyopathy and large ASD improved which allowed successful surgical ASD closure. One pt was delisted from heart transplant list because of continuous improvement in functional class and symptoms but not yet dead while waiting for heart transplantation. None of the pts developed side effect of sildenafil therapy.

Conclusion: Sildenafil is effective in congestive heart failure pts with secondary irreversible pulmonary hypertension in who were otherwise disqualified for heart transplantation. Its beneficial effects in improving functional and hemodynamics status in heart failure pts are encouraging.
ABSTRACTS

Abstracts for Free Paper Session:

25. Evaluation of early Endothelialization of Graft (EPC Capture) Stent by Optical Coherence Tomography
Stephen Wai Luen LET, Simon CC LAM, Kelvin KW CHAN, Frankie CC TAM, Michael PH CHAN, Michael KL WONG, Anthony HY Wong, Arthur SY Yung, Shun LING KONG, David CW CHU, Hung Fat TSE, Raymond HW CHAN
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Background: While able to reduce restenosis, drug eluting stents (DES) causes poor stent healing and incomplete endothelialization (after more than 1 year), and leads to the development of late stent thrombosis which could be fatal. The Endothelial-progenitor cell (EPC) capture stents emphasize on the pre-healing concept with a bio-engineered coating of anti-G24E antibody on the inner stent surface to capture circulating EPCs. Documenting endothelialization and stent coverage in vivo have never been possible until the availability of the ultra-high resolution of the optical coherence tomography (OCT). While animal models and autopsy findings are available, in vivo documentation on the extent of neointimal coverage shortly (within one month) after stent implant in human coronary artery has not been reported. This study is the first study conducted to document neointimal stent coverage by OCT within 1 month of implantation.

Method: In this prospective, open-label study, 30 consecutive patients with acute coronary syndrome requiring PCI were treated with the Genous stents. Restudy angiograms and OCT analyses were randomised from 15 days to 30 days after the index PCI. All OCT frames and all stent struts would be analyzed, targeting on the degree of stent coverage and the neointimal hyperplasia.

Results: All patients had uneventful PCI procedure and were discharged. Good endothelialisation has already been documented by 15 days and near complete stent coverage by 28 days.

Conclusion: OCT with the ultra-high resolution represents a new novel imaging technology in evaluation of endothelialization and healing after stenting at a very early stage. The Genous stent allows for very early endothelialisation with its pre-healing EPC capturing capacity, as disclosed by OCT.

26. Two years clinical outcome for the treatment of in-stent restenosis with second generation compared to first generation drug eluting stent
RCT. Fang, CK Chan, CS Yee. 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 Dec 2010 were treated with either first generation (sirolimus or paclitaxel) or secondary generation (everolimus or zotarolimus) DES. Their clinical outcome was compared.

Methods: Patients who had bare metal ISR treated with DES in the United Christian Hospital between 1 Jan 2006 and 31 Dec 2010 were included. Those who have mixed drug DES were excluded. Demographic data was retrieved from our clinical records and percutaneous coronary intervention registry. Patients' baseline characteristics including clinical presentation, age, gender, smoking status, left ventricular ejection fraction, previous history of cardiovascular disease, previous coronary intervention, comorbidities including diabetes mellitus, hypertension, hyperlipidemia, peripheral vascular disease and renal impairment were collected. Angiographic hits including target vessel, ISR patency, 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 62 patients were included. Thirty-one patients were treated with first generation (paclitaxel and sirolimus) stents and thirty-one patients were treated with second generation (everolimus and zotarolimus) stents. Their mean follow up duration were 34.6±17.9 and 26.1±20.1 months (P = 0.152) respectively. Baseline characteristics were similar between the two groups, except mean maximal inflation pressure was significantly higher in the second generation stent group (17 ± 5.0 mmHg vs 15 ± 2.6 mmHg, P = 0.01). The mean maximal inflation pressure was no longer significantly different after adjustment in the multivariate analysis. There were two death (one cardiac and the other non-cardiac) and six nonfatal myocardial infarctions in the first generation DES group. One patient died of acute pulmonary oedema , seven patients developed non-fatal myocardial infarctions and two patients required target lesion revascularization in the second generation DES group. The incidence of MACE between both groups of patients were not significantly different (19.4% vs 12.3%, respectively, P = 0.24).

Conclusion: In this study, two years clinical outcome 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 ISR.

27. Spontaneous Coronary Dissection – A rare but serious illness hitting clean artery
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Background: Spontaneous coronary dissection (SCD) is rare. The incidence is around one or two cases out of 1000 coronary angiography. It predominantly affects otherwise healthy pre-menopausal woman with little conventional cardiovascular risk factors. Specific risk factors are female sex, pregnancy and estrogen therapy. It can be fatal with diagnosis only at post-mortem. Proximal or distal extension of dissection and thus procedural complication is common during percutaneous coronary intervention (PCI).

Methods: This was a retrospective case series study conducted in cardiac intervention center of Princess Margaret Hospital.

Results: Seven patients (7 female, 1 male) of age 45±7 were identified. Six females were pre-menopausal. Four female patients were taking various health supplements. The only male patient has congenital absence of one upper limb. All of them presented with acute myocardial infarction. Right coronary, left circumflex and left anterior descending artery was the culprit in 5, 1 and 2 patients respectively. Two patients presented with cardiac arrest due to ventricular fibrillation. Diagnosis was made by angiography and 5 cases were confirmed by intravascular ultrasonography. Presence of dissection flap, near normal unaffected segments and containment of dissection by branching points were tell-tale signs. Conventional cardiovascular risk factors were uncommon: diabetes (0%), hypertension (38%), dyslipidemia (14%), current or history of smoking (29%). PCI was attempted in 6 and extension of dissection was noted in 5. PCI was abandoned in 2 but was successful in remaining 4. Two patients had complete spontaneous healing of SCD. All patients survive without acute clinical complication. One patient suffers from sequelae of hypoxic brain damage related to cardiac arrest at presentation.

Conclusion: SCD is a serious illness and early recognition is critical before PCI. Extension of dissection is very common and it makes intervention much more difficult. Spontaneous complete recovery without intervention is possible.

28. Left Main Stenting Registry in Teaching Hospital
Dr. KH Kam, Dr. EB Wu, Dr. YS Chan, Prof. G Yip, Prof. YY Lam, Dr. KY Chan, Prof. B Yun, Dr. PW Lee, Dr. CP Chan, Dr. CY Chan, Prof. CM Yu, Division of Cardiology, Department of Medicine and Therapeutics, Prince of Wales Hospital, CUHK, Hong Kong

Purpose: The objective of this registry is to reveal the basic information, clinical outcome, complication and mortality of percutaneous coronary intervention (PCI) of left main coronary artery disease in Teaching Hospital.

Methods: From January 2007 to November 2009, 39 consecutive patients who underwent PCI for left main coronary artery disease were selected and analyzed. Retrospective demographics, procedure information, complication, clinical outcome and mortality of the procedures were retrieved from procedure book.

Results: There were a total of 39 patients undergone the procedures in the above period. The mean age was 71 year old male with female ratio of 3:1. A quarter had prior myocardial infarction (MI). The average left ventricular ejection fraction (LVEF) was 41%. More than 60% of them underwent procedure because of acute coronary syndrome. The ratio of left main body lesion to bifurcation lesion was 3:2. Drug eluting stents (DES) were used in 74% of cases. Single stent technique was used in 36 cases while T-stenting, crush and minicrush technique were employed in the remaining cases. Intravascular ultrasound was commonly employed (77%) in left main stenting. The mean procedure complication rate was 10% and one half of them were due to left main dissection. In-hospital mortality was 5% whereas all of these cases were performed on compassionate basis. In-hospital rate of non-fatal MI, target vessel revascularization (TVR) and stent thrombosis were zero. The incidence of all-cause mortality, cardiac death, non-fatal MI, TVR and stent thrombosis in one year were 15.4%, 12.8%, 0%, 8% and 2.6% respectively. Major adverse cardiac event (MACE) -free survival in 1 year was 84.6%.

Conclusion: Our local registry showed a better MACE-free survival (84.6% vs. 75.7%) and non-fatal MI rate (0% vs. 7.5%) than the DELFT (Drug Eluting Stent for Left Main) Registry in one year. The 1-year mortality rate using DES (7.7% vs 6.7%) and 1-year TVR rate (8% vs. 16%) were similar to DELFT data.
ABSTRACTS

Abstracts for Free Paper Session:

29. Optimal Timing on Re-Vascularization and Outcome in Acute Coronary Syndromes (OPTIVO-ACS) Kelvin KW Chan, Stephen Wai Lam Lee, Michael Pui Chan, Simon CC Lam, Joie SH Hui, Frankie CC Tam, Michael KL Wong, Raymond HW Chan. From the Division of Cardiology, Department of Medicine, the University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China.

Introduction: Several earlier studies have shown that early invasive intervention strategy could improve outcome in patients admitted for non-ST segment elevation myocardial infarction (NSTEMI) and acute coronary syndromes (ACS), especially in some high-risk subgroups. However, the optimal timing for arranging such intervention remains uncertain. To determine whether coronary intervention (percutaneous coronary intervention or bypass surgery) performed as early as less than 48 hours after admission for NSTEMI-ACS patients can result in a reduction of major adverse cardiac events (MACE) when compared with delayed intervention done after 48 hours.

Method: Patients admitted to Queen Mary Hospital from the period of 1st January 2004 to 30th June 2009 were identified retrospectively, all with the diagnosis of NSTEMI, unstable angina or acute coronary syndrome. Patients were then separated into 2 main time groups according to their time of receiving coronary intervention that is <48-hrs time group and >48-hrs time group, for statistical analysis. The primary endpoint was major adverse cardiovascular events (MACE) at 6 months follow-up. MACE was defined as a composite endpoint comprising of death from any cause, myocardial infarction, stroke and urgent target vessel / lesion revascularization.

Results: Totally 1,296 patients admitted for NSTEMI-ACS were identified and 164 of them received coronary angiography. Of these, 142 patients had revascularization treatment, in which 128 patients had percutaneous coronary intervention (PCI) and 14 patients had coronary artery bypass graft (CABG). At 6 months, MACE occurred in 1 patient in the <48-hrs time group and 15 patients in the >48-hrs time group (OR 0.03, 95% CI 0.01-0.65, p=0.005). Major secondary endpoints also showed that the outcome was better in patients with age≤60 years old (p=0.02) subgroup, as well as a shorter length of hospital stay in the <48-hours group (mean 4.26d vs. 8.21d, p=0.001).

Conclusion: In patients admitted for NSTEMI-ACS, a strategy of early coronary intervention by angioplasty or bypass surgery, is short as less than 48 hours after admission, when compared to delayed intervention, reduced MACE at 6 months and the average length of hospital stay for the index hospitalization.

30. A Case Series of Using Drug Eluting Balloon for In-Stent Restenosis KT Hui, CK Chan, CS Yee. Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong SAR.

Background: The management strategy for in-stent restenosis (ISR) is changing over recent years. Although Drug Eluting Stent (DES) remains the standard treatment for ISR, recurrent ISR after DES implantation is sometimes encountered. Several factors including inadequate drug coverage to the vessel wall in between areas allowing for potential cell growth and the inflammation response induced by polymers on DES were possible for raising restenosis. In addition, double or even triple vessel lesion in bifurcation lesions also make analysis difficult and increase procedure complexity. From these points of view, Drug Eluting Balloon (DEB), with multifocal coating on angioplasty balloons, provides an alternative treatment option for ISR. Presenting promising results from clinical studies in comparing DES with angioplasty (PACCICATT, BIR) and DES with DEB (PES/CRID) support the use of DEB for ISR in terms of better angiographic and clinical outcomes. Moreover, avoidance of prolonged dual anti-platelet therapy following DES implantation makes DES advantageous to patients with high bleeding risk.

Endline: Our centre has started to use DEB on selected patients with ISR since 2010. A total of 15 patients with 13 lesions were treated. Special consideration of using DEB was taken in one patient with underlying malignancy having ISR as six months after Greenstreet view of high bleeding risk, and in another patient having recurrent ISR over left main coronary artery bifurcation lesion six months after DES implantation. The mean age of patients is 72.1 years (range 57-94). Majority of them had cardiovascular risk factors including diabetes (78%), hypertension (100%), hyperlipidemia (44%) and smoking (44%). 2 patients had their ISR transferred as acute coronary syndrome and 1 patient presented with stable angina before ISR being identified. The remaining 3 patients were asymptomatic and the ISR was evaluated on elective coronary angiography. Among the 13 ISR lesions, 6 of them were recurrent ISR after second stenting with DES and 3 of them were first episode of DES ISR. Average time between DES implantation and index procedure of DEB was 6.3 months (range 2.5-12 months). The remaining 4 lesions were Bare Metal Stent (BMS) ISR with BMS implanted on average 3.5 (range 2.5-6.5) months before DES. The mean reference vessel diameter was 2.57 (range 2.01-3.54) mm. Average DES size and length were 2.0 (range 2.5-2.35) mm and 21.2 (range 15-30 mm) respectively. We have re-coated on 6 lesions by coronary angiography at 3.5 (range 3.5-6.5) months after DEB. In-stent lumen was 0.29 (range 0.12-0.64 mm). There was no target lesion recalcitrance (TLR), myocardial infarction, stoke, death or major adverse cardiac events (MACE) in all of the 9 patients during the Follow-up period of 5.4 (range 1.1-7) months after index procedure of DEB. Angiographic and clinic follow-up is being continued.

Conclusion: DEB provides an alternative treatment option for ISR with potential advantage for recurrent ISR, bifurcation lesions and patients with high bleeding risk. The early angiographic result is satisfactory and the clinical outcome is promising. Longer follow-up period and larger number of patients for study is necessary to draw long term efficacy and safety.

31. Fractional Flow Reserve assessment in Clinical Practice CL Lau, Tsui PT, YK Lo, PS Chu, HC Yuen, HF Chow, CC Choy, NY Chan, NS Mok, ST Lau Department of Medicine & Geriatrics, Princess Margaret Hospital.

Purpose: Fractional flow reserve (FFR) assessment has been proven to be a reliable functional test of coronary stenosis in DEFER and FAME study. We aimed to review the application of FFR assessment in real life clinical practice.

Methods: This is a retrospective cohort study of 101 consecutive patients with FFR assessment before angioplasty. Coronary stenosis with FFR>0.8 would be treated with optimal medical therapy.

Results: 86 males and 15 females of age=62±10/1 were recruited. Underlying coronary risk factors were history of smoking (29%), diabetes mellitus (26%), hypertension (41%) and hypercholesterolemia (50%). Prior myocardial infarction was present in 31 (31%) patients. A total of 243 lesions were assessed by measuring FFR. Intracoronary ATP was used in majority of cases to produce maximal hyperemia. Significant drop in blood pressure was documented in all cases during maximal hyperemia. Ninety-three (65%) non-significant lesions were deferred (LAD 43, LCX 13, RCA 19) and 50 (35%) significant lesions (LAD 27, LCX 12, RCA 11) were stented. This cohort was followed for 212±36 days. None of the patients developed acute myocardial infarction related to deferred lesions.

Conclusion: FFR as a form of functional test could be applied in daily clinical practice and non-ischemic angiographic moderate lesions are common. Deferring stenting non-significant lesions together with optimal medical therapy is safe.

32. Initial experiences of transarterial aortic valve implantation (TAVI) in Queen Elizabeth Hospital Dr. LK Chan, Dr. K Kwok, Dr. NL Lok, Dr. WS Kwan, Dr. SC Choi, Dr. M Cheung, Dr. SC Chan, Dr. HS Mo, Dr. CS Fu, Dr. LT Lau, Dr. CW Chan, Dr. KY Lyu, Dr. KT Chan, Dr. HK Cho, Dr. CS Chung, Dr. HH Chong, Dr. CC Ma, Dr. D Fok, Dr. Eric So, Dr. VF Choy Queen Elizabeth Hospital, Hong Kong.

Purpose: Surgical aortic valve replacement is the only and the most effective treatment for patients with symptomatic, severe aortic stenosis. However, around 30% of patients declined for surgery because of being high risk or inoperable. In the past decade, transarterial aortic valve implantation (TAVI) has been developed and used widely over the world to treat this group of patients. TAVI program has been started since December, 2010 in our hospital. The study tried to show the initial experience and outcome of the patients.

Method: A retrospective case series. All the demographic data, presenting symptoms, echocardiogram finding, outcomes were measured and recorded. Chi-square and T-test were used for analysis.

Results: There were all together four patients receiving TAVI in our hospital up till now. Details of demographic and procedure are summarized in table 1. Findings between pre-pro and post-pro TAVI in table 2. The TAVI procedures were performed under general anesthesia, with co-operation with cardiothoracic surgeons and anesthesiologist in our catheterization laboratory. We used CoreValve reveling system R in our procedure. The procedure success rate was 100%. There was no in hospital or 30-day mortality. All patients could be ambulatory on post-op day 2 and they all (100%) showed improvement in functional class for at least 1 class 1 month later. No patients suffered from stroke but 2 patients (50%) had permanent pacemaker implanted (one patient had 1st degree heart block post-OT, resulting in complete heart block after OT and the other patient had paravalvular aortic regurgitation with borderline paced QT; resolving in atrial fibrillation with 1:1 BBB). All patients showed no residual aortic stenosis 1 month after operation. The mean aortic valve area and EF were significantly different after TAVI, p<0.05. The utility of 64 slice coronary CT (MS-CT) was significantly improved on two lesions.

Table 1: 2 post-pro assessment 1 month after TAVI

<table>
<thead>
<tr>
<th>Age</th>
<th>gender</th>
<th>Symptom</th>
<th>Euro- score (angiogr. +)</th>
<th>LVEF (%)</th>
<th>aPVCa</th>
<th>aPVCb</th>
<th>annulus (mm)</th>
<th>approach</th>
<th>Correlate</th>
<th>Ø size</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>CHCA</td>
<td>9</td>
<td>62</td>
<td>26</td>
<td>Aortoly</td>
<td>29</td>
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<tr>
<td>2</td>
<td>F</td>
<td>Chronic</td>
<td>10</td>
<td>66</td>
<td>23</td>
<td>Fenestr</td>
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Conclusion: TAVI is a feasible and effective way to treat the patients who are symptomatic with severe aortic stenosis and high surgical risk. The short term results are quite promising. However, we need to observe and assess the long-term results before considering further expansion of the indication.
Abstracts for Free Paper Session:

BASIC SCIENCE

33. The Preliminary Study of Ultrasound Evaluation on Animal Experimental Model of Iliac Artery Stenosis in Youth Rabbits

J Guo, X Ji, GS Yu, YH Bai, XQ Zhai, Y Tang, P Zhang, Y Wang

Department of Cardiology, Department of ultrasonic, The Children’s Hospital of Chongqing Medical University; College of Pharmacy of Chongqing Medical University, PR China

Objective: To explore the method of establishing iliac artery stenosis experimental model through balloon injured artery on youth rabbits. And to proof the application value and significance of ultrasonic imaging technology in stenosis of animal models through the measuring of the narrow vascular blood flow parameters by ultrasonic.

Methods: 15 New Zealand rabbits of (60±15) days year-old were selected, male and female unlimited, who were divided into 3 groups roughly. In group A, the youth rabbits’ iliac artery were damaged by intra-operative balloon expansion. The parameters, including the vascular diameter (D), the thickness of endolumen (R), the thickness of middle-inner membrane (M-O), and Systolic flow velocity (Vs), the diastolic flow velocity (Vd), resistance index (RI), and Vs/Vd of the corresponding section, were measured by the ultrasound after 4 weeks of the surgery and been compared with the results of pathology testing. In group B, the youth rabbits were pretended to be damaged by ligation of the distal femoral artery. The remaining processing were consistent with group A. Group C was the normal control group.

Results: All rabbits were completed the operation and live to the end of experiment. The average operation time was (30±10) min. 2. Iliac artery stenosis experimental model on youth rabbits was established successfully. Compared with group B and group C, D was decreased in group A, while E-M-O were increased. Vs and Vd were increased obviously in the surgical artery. The diameter of the artery was decreased significantly by pathological HE dying, with the cells of endolumen, middle, and the outer membrane were hyperplasia obviously. Compared with the group C, The results of measurement by ultrasound and the Pathology testing were both had no obvious statistical significance.

Conclusion: 1. This method successfully established the iliac artery stenosis experimental model on youth rabbits which can be used for studying of the pathological mechanism of restenosis and the testing of drug intervention. 2. Ultrasonic imaging techniques can be used to evaluate the vascular stenosis noninvasively and dynamically, which has a high consistent with the result of pathology testing, so it is worth to be recommended.

34. Prednisone Attenuates Coxsackievirus B3-induced Viral Myocarditis in Mice

J Guan, XL Sun

Department of ICU, Hua Xi hospital First hospital of hainan university

Purpose: The goal of this study was to investigate the therapeutic benefits of prednisone on Coxsackievirus virus B3-induced myocarditis in mice. Discussion the difference between different time of prednisone on viral myocarditis in mice at the medication.

Methods: 175 male 4-week-old Balb/C mice were divided into eight groups randomly, including normal control group, prednisone group/infected control group/group of infected mice with prednisone treatment at early stage; group of infected mice with prednisone treatment at late stage. Prednisone was given 3 or 10days after viral challenge and treatment lasted for 14 days. The Echocardiograms were examined on days 3, 7, 10, 14, 21, and 30 after virus inoculation. Blood samples were collected for cardiac troponin I detection at the same time. Myocardial inflammation, cell apoptosis and Fas expression were detected by histology and western blot RT-PCR.

Results: The myocardial histopathological score of mice in each infected group on day 7-10 after infection were significantly higher than that in normal control group, but no significant difference in each infected group. On day 14 after infection, the myocardial histopathologic score of mice with Prednisone treatment at early stage were significantly lower than that in other infected groups, H&E staining and transmission electron microscopy revealed significant improvement of quantitative pathological features in the prednisone treatment at early stage. Immunohistochemical microscopy also showed a marked decrease in the level of cardiac cell apoptosis in the Prednisone-treated group compared to infected animals that did not receive treatment. The differences in CVd values between the virus-challenged animals and prednisone-treated virus-challenged mice achieved statistical significance, there was a trend toward a decrease in CVd in the Prednisone-treated mice RT-PCR and western blotting revealed that the virus induced marked increases in Fas mRNA and protein expression, which could be prevented by treatment with Prednisone.

Conclusion: These results demonstrate that Prednisone reduces the histological and functional severity of CVB3-induced myocarditis, and inhibits apoptosis and Fas expression in the myocardium of CVB3-infected mice especially used in early stage of the disease.

35. HTR7 inhibitor. Curcumin ameliorates the HTR7 hyperacetylation and heart development-related genes over-expression induced by alcohol in cardiac progenitor cells.

Linyi Wang, Bo Tang, Liliin Zheng, Jing Zhou (Department of Heart Centre, Pediatric Institute, Children’s Hospital of Chongqing Medical University, Chongqing, PR China)

Purpose: Our preliminary research showed that alcohol selectively increased acetylation of histone H3 at lysine 9 (H3K9) and augmented the expression of heart development-related genes in cardiac progenitor cells. This may be a mechanism by which the alcohol alters the gene expression in occurrence of CHD. Therefore, the objective of this study is to further explore the possible potential pathway by increasing the regulation of alcohol with curcumin, and to detect that whether curcumin ameliorates the H3K9 hyperacetylation and related genes over-expression induced by alcohol.

Methods: Cardiac progenitor cells were treated with alcohol at 200mM and curcumin was dissolved in the 200mM alcohol at 5,15,25,55mM respectively. Miocardial chamber assay (MCA) assay was used to assess the viability of cardiac progenitor cells. Western blot analysis was employed to detect the acetylation of histone H3K9 to select the effective concentration of curcumin. Real-time PCR was applied to measure the expressions of heart development-related genes GATA4, MeF2c and Tbx5.

Results: Alcohol at 200mM reduced cell viability by 28%; curcumin that was dissolved in 200mM alcohol at 5,15,25,35mM reduced cell viability by 30%,33%,37%,52% curcumin that was dissolved in DMSO at 25mM reduced cell viability by 26%. Alcohol at 200mM increased the acetylation of H3K9 by 2.76-fold (P<0.05) and significantly augmented the expression of GATA4 and MeF2c (P<0.05) compared to control group. Alcohol at 200mM and curcumin at 5, 15, 30mM increased the acetylation of H3K9 by 2.22- 1.58-fold, respectively (P<0.05).There are significant differences between the H3K9 acetylation and the expression of GATA4, MeF2c and Tbx5 in alcohol at 200mM and curcumin 25mM compared to the control group (P<0.05) at the point time, the HAT activity and histone acetylation were inhibited by curcumin (P<0.05).

Conclusion: curcumin can ameliorate the hyperacetylation of histone H3 at lysine 9 and the over-expression of heart development-related genes induced by alcohol in the cardiac progenitor cells, which may be one of the pathogenesis that alcohol leads to CHD

36. The effect of BMP-9 and BMP-12 in myocardioctyes differentiation of CmH12T3 stem cell in vitro

Hai Wei, Yun Chen, Hiao Shen. Medical Department of Cardiovascular System, Institute of Pediatrics of the Attached Children’s Hospital of Chongqing Medical University, Chongqing, PR China

Purpose: To investigate the effect of BMP-9 and BMP-12 on stem cell(CmH12T3) differentiating into myocardioctyes-like cells in vitro.

Methods: The cardiac specific proteins cTnT, cCx34.5, MHC, α-actin and were measured by Western Blot and immunofluorescence technique and the cardiac specific gene GATA4 and MEF2c expression were detected by Q-PCR at 1w,2w,3w,4w after the CmH12T3 stem cell transfected with pAdEasy-BMP-9, pAdEasy-BMP-12, AdGFP plasmid. The ultrastructure actin filament and intercalary disc of the cells were detected by electron microscope and masson staining technique for 4 weeks. Then electrophorogic changes of the CmH12T3 stem cells were tested by the whole - cell patch clamp technique.

Results: Cells began to stretch after transfected, the refractivity of cells enhance conspicuously, cells trend become unanimous and the connection between cells were compact. At week 3 and 4, cTnT,cCx34.5,MHC and α-actin were detected in pAdEasy-BMP-9 and pAdEasy-BMP-12 group but not found at week 1 and 2 (p<0.05). In AdGFP and control group we could not find any cardiac-specific proteins at week 1,2,3,4. The expression of GATA4 and MEF2c in BMP-9 could be detected in all groups, but more in pAdEasy - BMP-9 and pAdEasy-BMP-12 group but not found at week 1 and 2 (p<0.05). In AdGFP plasmid and control group (p<0.05) . Myocardioctyes ultramerry structure actin filament and intercalary disc could be detected by electron microscope and masson staining technique for 4 week. The super activation delayed rectifier K' current (IKs) and the inward rectifier K' current (IKir) were increased in pAdEasy-BMP-9 and pAdEasy-BMP-12 group but not found in AdGFP and control group.

Conclusion: BMP-9 and BMP-12 probably promote the differentiation of CmH12T3 stem cells into myocardioctyes.
37. BMP13 on C3H10T1/2 Cells to Improve Cardiac Function in Myocardial Infarction Rats
Y Chen
Department of Cardiology, The Children's Hospital of Chongqing Medical University, PR China

Objective: To investigate the bone morphogenetic protein 13 (BMP13) induced BMP13 expression in cardiomyocytes in microenvironment and improve the cardiac function of the rats after myocardial infarction (MI).

Methods: MI and sham operation were established Sprague Dawley (SD) male rats. Totally 56 rats were divided into 4 groups: sham operation group (8 rats), MI group (16 rats), MI + BMP13 group (16 rats), MI + BMP13 group (16 rats). Left ventricular ejection fraction assessed by echocardiography on day baseline and 4 weeks after operation. After measuring body weight once a week, 4 weeks after completion of cardiac function test, rats were sacrificed to take the heart. Masson's staining compared the differences in infarct size of heart. Cell growth observed by fluorescence microscopy in frozen sections, immunofluorescence detection cardiac-specific structural protein a-MHC and cTNT of cells were implanted in each group.

Results: Each C3H10T1/2 cells had about 80% of cells expressed green fluorescence. Cells grew well in 1.23 weeks after implantation, very few cells surviving in 4 weeks. On day 4 weeks of experiment, in addition to the sham group, the other three groups compared with baseline LVEDD significantly exceeded, but among the three groups no significant difference (P>0.05). LVEDD, MI + BMP13 group and MI + GFP group compared with MI group were reduced (P<0.05). MI + BMP13 group compared with MI + GFP reduced more significantly (P<0.05), the same as LVP/B. Implanted cells in group MI + GFP and MI + BMP13 had normal cardiomyocyte-like cells in micro-environment of myocardial infarction; it can also improve cardiac function in myocardial infarction rats. It can be strengthened by transfected BMP13. Differentiation of implanted cells and improve cardiac function in myocardial infarction rats are not necessarily consistent.

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39. ABSTRACTS
Abstracts for Free Paper Session:

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Conclusion: These data suggested that TAA enhanced the cardiac differentiation of MSCs after 5-aza induction and during co-culture with CMs through a mechanism beyond the inhibition of HDAC activity.
42. Effects of ulinastatin on injury of neurons in hippocampus CA1 area and cardiac dysfunction after cardiopulmonary resuscitation in rabbits
Xiao-Xing Liao, Chun-lin Hu, Xin Li, Hongyan Wei
Emergency Department, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

Purpose: To investigate whether ulinastatin can reduce the systemic inflammatory response, improve cardiac dysfunction and reduce injury of neurons in hippocampus CA1 area after ROSC.

Methods: Cardiac ventricular fibrillation was induced by alternating current in 24 New Zealand rabbits, which were randomly divided into Control and ulinastatin treated group after ROSC. Dynamic observation of the effects of ulinastatin on the levels of plasma inflammatory cytokines TNF-α, IL-6, cardiac function including FS, EF and E/A, and neuron injury in hippocampus CA1 area after ROSC were performed.

Results: Plasma inflammatory cytokines TNF-α and IL-6 in Control group peaked at 8h after ROSC, the levels were 441.60 ± 169.89 ng/ml and 587.00 ±102.50ng/ml at 16h. The levels of TNF-α and IL-6 at each time interval in ulinastatin group were significantly lower than the Control group (P<0.05). At 4h after ROSC, FS, EF and E/A in Control group were 26.20±3.35%, 33.00 ± 2.12% and 1.34±0.12 respectively. EF, E/A in ulinastatin treated group were higher than the Control group at 4h, 8h and 12h after ROSC. FS Values after ROSC 4h, 8h were higher than the Control group (P<0.05). At 72h after ROSC, the number of dynamic neurons in CA1 area of Control group was 13.67±1.03, fewer than the ulinastatin group 16.89±1.45, P=0.003, and the number of apoptotic neurons in hippocampus CA1 area in Control group was 15.67±1.37, while in ulinastatin group was 13.67±1.03, P=0.019.

Conclusions: Ulinastatin can decrease plasma inflammatory cytokines TNF-α and IL-6, improve cardiac dysfunction and have protective effects on neurons in hippocampus CA1 area after ROSC in New Zealand rabbits.

43. Preventive effect of inhibiting nuclear factor kappa-B activity on the aorta endothelial cells in rats with high lipid diet
Xin Li, Xiao-Xing Liao, Chun-lin Hu, Hongyan Wei
Emergency Department, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

Purpose: To examine the effect of pyrrolidine dithiocarbamate (PDTC) on the aorta endothelial cells in rats with high lipid diet.

Methods: Eighty Sprague-Dawley rats were randomly divided into three groups: high lipids group, PDTC and high lipid group (PDTC group) and normal control group. The aortas were harvested for histomorphometry and transmission electron microscope 12 weeks after the induction of high plasma lipid. The nuclear factor xB (NF-xB) activity was measured by use of electrophoretic mobility shift assays (EMSA) in aortas. The levels of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) in serum were measured by use of radio-immunometry and the level of soluble thrombomodulin (sTM) in serum was measured by use of enzyme linked immunosorbent assay (ELISA).

Results: There was obvious necrosis or apoptosis for aorta endothelial cells in high lipids group, but this phenomenon was no clear in PDTC group and normal control group. The level of sTM in the PDTC group was significantly higher than that of normal control group and was lower than that of high lipids group (P=0.05). The activity of NF-xB and the levels of IL-6, TNF-α were evidently higher in high lipids group than normal control group and PDTC group. There was a positive relation between the NF-xB activity and the levels of TNF-α, IL-6 and sTM (P<0.05).

Conclusions: These results indicate that PDTC can protect aorta endothelial cells by inhibiting the activity of NF-xB and the inflammatory response in rats with high lipid diet.
Abstracts for Free Paper Session:

45. Implantable cardioverter defibrillator (ICD) in children and young adults: experience in Hong Kong
TC Yang, K K Lun, K Fan, L C Cheng
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Introduction: ICD therapy is increasingly used in children and young adults. The purpose of this single centre study in Hong Kong is to evaluate the indications, underlying heart disease, efficacy, outcome and complications involved with ICD therapy in this group of patients.

Methods and Results: The hospital records of all patients aged ≥30 years who underwent ICD implantation were reviewed retrospectively. From 1996 to 2010, 11 patients (mean age 15.6 years, range 4 years 8 months to 29 years) underwent ICD placement. The ICD was implanted for aborted cardiac arrest (5), syncope (5) and primary prevention of sudden cardiac death (1). The underlying cardiac diseases were congenital long QT syndrome (3), idiopathic ventricular fibrillation (1), hypertrophic cardiomyopathy (3), dilated cardiomyopathy (1) and post-operative Tetralogy of Fallot (5). Ten patients had the ICD system implanted transvenously, and 1 had the ICD lead placed subcutaneously. Two youngest patients had the generator placed at the abdominal position. The mean follow-up duration was 4 years 2 months, range 7 months to 14 years. Three patients received appropriate shocks for ventricular arrhythmias at a mean duration of 6 months after ICD implant. One patient had anti-tachycardia pacing for fast ventricular tachycardia. Complications occurred in two patients. They had inappropriate shocks because of sinus tachycardia and lead fracture in one, and atrial fibrillation in the other. Three patients required reintervention: generator replacement in two, generator plus ICD lead replacement in the other. One patient died because of congestive heart failure 9 months after ICD implant, otherwise there was no ICD or arrhythmia related mortality.

Conclusions: The mid term outcome of ICD therapy for prevention of sudden cardiac death in children and young adult is good. ICD implant procedure is safe in this age group.

46. Follow Up the Arrhythmia Caret Tachycardia in Kawasaki Disease with High-Frequency Ultrasound
QZ Zhou, JXG Gu, SY Yu, YH Bai, et al.
Department of Cardiology, The Children’s Hospital of Chongqing Medical University, PR China

Purpose: To study the value of detecting the carotid intima media thickness (C-IMT) and buffering function, including cross-sectional compliance (CSC), volumetric distensibility (VD), arterial stiffness index (ASI), in children with Kawasaki disease in acute stage and long-term stage with high-frequency ultrasound.

Methods: 50 patients received ultrasound, including 15 patients with Kawasaki disease in acute stage (group 1), 18 patients with Kawasaki disease in long-term (group II) and 17 normal children (control group).

Results: C-IMT and ASI of acute stage group and long-term group were significantly higher than that of control group (P<0.05). VD of acute stage group and long-term group was significantly lower than that of control group (P<0.05). CSC of long-term group was lower than control group and acute stage, but there is no significant difference between acute stage group and control group. C-IMT negatively correlated with VD (r= -0.301, P=0.034), and positively correlated with ASI (r=0.269, P=0.042).

Conclusions: There were increased C-IMT and abnormal Buffering Function in the acute stage and long-term of Kawasaki disease. It is feasible to detect the value of carotid artery intima thickness with high-frequency ultrasound.

47. Application of Modified Blalock-Taussig Shunts in Infants with Complex Congenital Heart Malformations and Outcomes of Follow-up
WQ Tan
Children’s Hospital of Fudan University, PR China

Objective: The modified Blalock-Taussig shunt (MBTS) is believed to be a low-risk management option for palliation in patients with severely cyanotic heart anomalies in western countries. In mainland China, MBTS is considered an important procedure to save lives of baby patients with cyanotic CHD. But the morbidity and mortality associated with MBTS remains challenge in developing countries. We will estimate this procedure by retrospectively analyzing patients data and follow-up outcomes.

METHODS: 88 patients with severely cyanotic complex heart anomalies underwent modified Blalock-Taussig shunts (MBTS) in our hospital between October 2000 and December 2010. The mean age was 2.5±1.1 months (6–6.2 months). The mean weight of the babies was 5.0±2.1 kg (3.2–9.3 kg). The cardiac anatomy was as follows: pulmonary atresia with intact ventricular septum in 14, pulmonary atresia with ventricular septal defect in 34, tricuspid atresia in 9, tetralogy of Fallot In 6, complex single ventricle physiology in 14, transposition of great artery with pulmonary stenosis in 10, and transposition of great artery with left ventricular maldevelopment in 1. All patients were severely cyanotic, and preoperative prostatical end was used in all patients to ensure ducus patent and maintain oxygen saturations prior to shunt operation. The shunts were accomplished with 8.0mm polyethylene hydroxyethylene grafts in 2 patients, 5.5mm in 16, 4.0mm in 44, 3.5mm in 28 and 5mm in 8 patients. The mean follow-up duration was 1.8±2.8 days (4–5.5 days). The mean cardiac intensive care unit stay was 6.2±8.5 days (2–16 days). There were severe hypoxemia in 1 and sudden death in 1, severely arrhythmia in 1. Oxygen saturation increased by 60.2% preoperatively to 77.3% postoperatively. Four patients had shunt block, additional shunt was created successfully. There was 3 late death. Follow-up of 65 patients revealed satisfactory systemic oxygen saturation of 77±10% (63–95%). So far, 18 patients received further treatment which included 4 TEF operation, 22 Rastelli, 16 GLENN and 8 Fontan.

CONCLUSIONS: With an encouraging early shunt patent rate and oxygen saturation improvements, we do not recommend MBTS as an alternative in patients with severely cyanotic heart anomalies. Modified BT shunt is a good palliation for patients with cyanotic heart anomalies, which can increase pulmonary blood flow. Excellent surgical skills and perioperative treatment contribute to good operation results, and to low morbidity and low mortality.
49.

Hemofiltration of Blood-Primed Solution in Paediatric Cardiac Surgery

H Zhong
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Objectives: We tested the hypothesis whether hemofiltration of the blood-primed solution is sufficient for reaching a physiologic state and investigated the effects on hemodynamics and respiratory function in 40 patients undergoing cardiac surgery. Methods: The study population undergoing heart surgery were divided into two groups. The study group (n=20) used hemodiafiltrated stored blood in the CPB circuit for twenty minutes and the control group (n=20) used the non ultrafiltration blood. Data were obtained from the priming blood before and after hemodiafiltrated blood prime. Blood gas test results, C-reactive protein, interleukin (II)-8 were documented preoperatively and the cardiac function was measured by echocardiogram.

Results: The measured substrates changed to normal values after ultrafiltration of the blood prime (PH from 6.89±0.22 to 7.40±0.37; BE from -16.12±0.98 mmol/l to +0.31±2.4 mmol/l; potassium from 10.33±1.13 mmol/l to 4.27±0.93, glucose from 13.9±1.72 mmol/l to 10.61±1.89 mmol/l). Interleukin-8 (IL-8) decreased from 78.4±5.1 pg/ml to 64.3±48.1 pg/ml (P=0.038). The duration of mechanical ventilation was significantly shorter in study group than in control group (21.3±7.5 hours vs 34.0±12.6 hours, P=0.024). 4 hours after CPB, the systolic, diastolic and end systolic BP were significantly increased in the study group comparing the control group (P=0.02, 0.003; 0.001). Contractility improved greatly (-0.28±0.13 vs -0.01±0.21, P=0.002) in study group from the terminal of CPB to 4 hours after surgery, but did not change during the same period in the control group (-0.26±0.12 vs -0.26±0.16, P=0.33). Conclusion: The usefulness of hemofiltrated stored blood for CPB priming may confer an advantage in maintaining more physiological conditions and prevent lung and heart dysfunction in pediatric open heart surgery.
PAEDIATRIC CARDIOLOGY II

50. Clinical Investigation of Anthracycline-induced Cardiotoxicity in Children Cancer Survivors
HY Deng, YJ Gao, Y Gao, XC Liang, XI Ma, GY Huang. Department of Cardiology, Children’s Hospital of Fudan University. Shanghai, China.

Purpose: This study aimed to determine whether latent cardiac dysfunction is present in children who were treated with anthracycline because of leukemia or lymphoma and screen for risk factors of cardiac abnormalities.

Patients and Methods: Serial echocardiogram data of 118 children cancer survivors who received anthracycline treatment and finished all chemotherapy were retrospectively reviewed. Measurements of these patients were compared with those of normal children at the same age. Associations between age at diagnosis, cumulative dose of doxorubicine (DNR), sex, length of follow-up, and deviations from normal values in M-mode echocardiograms were evaluated using multivariate linear regression analysis.

Results: Compared to age-matched normal children, cancer survivors who received anthracycline had thinner left ventricle posterior wall (LVPW), increased left ventricular internal dimension at end-systolic (LVIDs) and heart rate (HR), decreased left ventricular internal dimension at end-diastole (LVIDd), fractional shortening (FS), ejection fraction (EF), cardiac output (CO) and ratio of mitral E velocity to mitral A velocity (MEV/MAV). Thirty-five of the patients (32%) had EF below 60%. Survivors who received DNR cumulative doses above 210 mg/m² had a 5.6-fold excess risk of reduced EF (95% CI, 1.5 to 31.2) compared with those received less than 210 mg/m². DNR cumulative dose was correlated with dilated LVID and reduced FS and EF.

Conclusions: Our data suggested that patients received anthracycline therapy had decreased heart function and DNR cumulative dose was an independent risk factor for dilated LVID and reduced FS and EF. Survivors treated with DNR doses above 210 mg/m² are at higher risk for reduced EF and dilated left ventricle who need long-term follow-up and pay more attention to prevent cardiomyopathy.

52. Hydrogen sulfide stimulates pulmonary smooth muscle cell apoptosis in rats with increased pulmonary blood flow-induced pulmonary hypertension
HongFang Jin, Wei Li, Xiaobin Li, Peijin Jia, Chaochu Tang, Junbao Du. Department of Pediatrics, Peking Union Medical College Hospital, Beijing, China.

Purpose: The present study aimed at exploring the effects of hydrogen sulfide (H_2S) on pulmonary vascular smooth muscle cell (PVMSC) apoptosis in increased pulmonary blood flow-induced pulmonary hypertension rat models.

Methods: Anesthetized rats were subjected to sham operation group or rats with increased pulmonary blood flow-induced pulmonary hypertension group. The H_2S concentration in rats was significantly increased after the operation and increased without significant differences compared with the sham operation group.

Results: There was no significant difference in the pulmonary arterial pressure between the two groups. The mPAP in rats of 4-week-shunt group was significantly higher than the sham group. However, the mPAP in 11-week-shunt group was significantly lower than the sham group. H_2S concentration in rats was significantly increased after 4-week of shunt but decreased after 11-week of shunt procedure. Administration with NaHS increased lung tissue H_2S concentration. Compared with 4-week-shunt group, the positive rate of apoptosis in PVMSCs was significantly decreased. The expression of TBP-2 protein significantly increased in 4-week-shunt group. Compared with 11-week-shunt group, the positive rate of apoptosis in PVMSCs and expression of TBP-2 protein was significantly decreased but expression of TBP-2 protein significantly increased in 11-week-shunt group. Compared with 11-week-shunt group, the positive rate of apoptosis in PVMSCs was significantly increased in 11-week-shunt group. Compared with 11-week-shunt group, the positive rate of apoptosis in PVMSCs was significantly increased in 11-week-shunt group.

Conclusion: H_2S obviously induces PVMSC apoptosis in high pulmonary blood flow induced pulmonary hypertension.

53. Extracorporeal life support in the paediatric population
Fieh Tso, KT Chiu*, LC Cheng. Department of Cardiothoracic Surgery and * Department of Paediatric Cardiology, Queen Mary Hospital, Hong Kong.

Purpose: To review the results of paediatric extracorporeal life support (ECLS) in Hong Kong.

Method: A retrospective review of medical records of patients under 18 years old who underwent ECLS between Nov 2000 to Nov 2010 was performed. The indications for ECLS support were acute myocarditis (8 patients), dilated cardiomyopathy (2) and post cardiac surgery low output syndrome (4 patients). Seven patients had cardiac arrest requiring active resuscitation before ECLS support. Nine patients had bleeding complications requiring re-exploration and haemostasis. One patient had intracranial haemorrhage. The average duration of ECMO support was 5.77 days. Eight patients were successfully weaned off ECMO support and were discharged without neurological deficit.

Conclusion: ECMO is an effective form of temporary support for patients with low cardiac output as a result of acute myocarditis, dilated cardiomyopathy or post-cardiac surgery.
Abstracts for Free Paper Session:

54. Improvement of Left Ventricular Function after Aortic Valve Repair in Pediatric Patients. Follow-up Study Using the Novel 2D Strain Method
YP Mi
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Objective: To evaluate the outcome and regional and global left ventricular (LV) function after aortic valve repair in children with congenital aortic valve disease.

Methods: 32 consecutive patients aged 1.56 years undergoing aortic valve repair due to valve stenosis (AS group, n=23) or aortic regurgitation (AR group, n=11) were prospectively studied over a follow-up period of 12 months in regard to change and adaptation of myocardial function using conventional and novel echocardiographic methods including two-dimensional (2D) strain echo. Conventional and 2D strain echo studies were performed and analysed off-line using commercially available software (EchoPac 6.1.0, GE).

Results: The peak aortic valve gradient decreased from 62.0±30.34 mmHg before surgery to 22.8±14.13 mmHg 2 weeks after surgery and 35.7±22.11 mmHg 12 months after surgery (p<0.01). The degree of AR was decreased significantly to grade 0 in 20 children and grade I in 12. There was a significant reduction of thickness of interventricular septum (IVS) and posterior wall resulting in improvement of LV mass index (p = 0.007, p = 0.043 and p = 0.001, respectively). Significant reduction of myocardial thickness was found especially in the IVS in the AS group (p=0.008) and the significant reduction of LV end-diastolic dimension (EDD) was found in the AR group (p=0.007). 2D strain analysis demonstrated that the global peak strain, global systolic strain rate and global early diastolic strain rate improved significantly for all the patients during the study period after aortic valve repair (p=0.001, P=0.037 and P=0.018, respectively). The global strain and strain rate correlated significantly to IVS thickness (r=0.02 and r=0.003), LV mass index (r=0.02 and r=0.015) and EDD (r=0.26 and r=0.005).

Conclusion: Aortic valve repair surgery in pediatric patients results in improvement of aortic valve function in the majority of the studied patients and therefore improvement of global and regional systolic and diastolic LV parameter. The improvement of systolic myocardial deformation indicates significant functional and morphological remodelling.

55. Surgical Strategy and Outcome for Transposition of Great Arteries with Intact Ventricular Septum
TT Zhang
Children's Hospital of Fudan University, PR China

Objective: To report our experience with surgical strategy, perioperative management and outcome of transposition of the great arteries with intact ventricular septum (TGA/IVS), to investigate the optimal surgical strategy with different operative ages and perioperative left ventricular functions.

Methods: Between June 2005 and October 2010, 53 patients with transposition of great arteries with intact ventricular septum who underwent arterial switch operation (ASO) in our center were included. Hospital charts, echocardiographic data and operative reports of all patients were reviewed. Demographics and perioperative variables were recorded.

Results: Of the 53 patients in our study 29 patients were younger than 3 weeks (group A) with median age of 10.7±1.3 days (range, 2-21 days), they all received primary ASO. 24 patients older than 3 weeks (group B) with median age of 153.2±34.0 days (range, 25-1469 days). 18 patients underwent primary ASO (group B1) and 6 patients received rapid two-stage ASO (group B2). There were 3 (5.67%) early deaths: coronary artery malformation was the only risk factor associated with early mortality. Two patients required postoperative extracorporeal membrane oxygenation (ECMO) support who were both older than 3 weeks and underwent primary ASO. finally they were survived to discharge. Early and mid-term Follow-up about left ventricular function and development: there are no significant differences between groups.

Conclusion: Preoperative assessment about LV function is very important. Late presenters with TGA/IVS, who have LV degeneration on echocardiography or LV/RV ratio>0.65 during surgery measure should be subjected to LVT in order to avoid low cardiac output syndrome and potential ECMO use. There are no significant differences among groups on LV function in early and mid-term Follow-up.

56. Three-Dimensional Mechanical Dysynchrony and Myocardial Deformation of the Left Ventricle in Patients with Tricuspid Atriosus after Fontan Procedure
Po-Ki Ho, Clare TM Lai, Sophia J Wong, Yiu-fai Cheung. Division of Paediatric Cardiology, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, University of Hong Kong

Objective: The contributory role of mechanical dysynchrony in ventricular dysfunction is increasingly recognized. This study tested the hypothesis that dysynchronous ventricular contraction occurs in Fontan patients with functional single ventricle and is related to indices of myocardial deformation and global ventricular function.

Methods: Twenty Fontan patients, aged 23.5±7.1 years, with tricuspid atresia and 20 age-matched controls were studied. Three-dimensional echocardiography was performed for detection of left ventricular (LV) volumes and systolic dysynchrony index (SDI), while speckle tracking was used to assess LV longitudinal, circumferential, and radial myocardial deformation. The average septal and LV posterior wall calibrated integrated backscatter (iCB) intensity was measured as an index of myocardial fibrosis.

Results: Compared with controls, patients had significantly greater SDI (p=0.001). The prevalence of LV mechanical dysynchrony (SDI > 5.74%) was patients 55% (95% CI: 32% to 77%). The LV global systolic longitudinal, radial, and circumferential strain (all p>0.001), longitudinal systolic (p=0.001) and early diastolic strain rate (p=0.001) and circumferential systolic (p=0.001) and early diastolic strain rate (p=0.009) were significantly lower, while the average iCB was higher in patients than controls (p<0.001). Patients with LV dysynchrony (n=11) had significantly lower global LV longitudinal strain (p=0.017), reduced LV ejection fraction (p=0.002), and higher average iCB (p=0.027) than those without (n=9).

Conclusion: A high proportion of patients with tricuspid atresia after Fontan operation exhibits LV mechanical dysynchrony, which may in part be related to myocardial fibrosis and has implications on myocardial deformation and global ventricular function.

57. Percutaneous balloon aortic valvuloplasty with rapid ventricular pacing in the right ventricle in managing congenital aortic stenosis in infants
YG Li
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Purpose: To evaluate the efficacy and technique of percutaneous balloon aortic valvuloplasty (PBAV) in managing congenital aortic stenosis (AS) in infant.

Methods: Two infants (14-month-old and 3-month-old respectively) underwent the procedure through the retrograde femoral route. A bipolar pacing catheter was placed in the right ventricle and rapid ventricular pacing was performed to stabilize the balloon when the midpoint of the inflated balloon was located at the level of the valvular aortic plane.

Results: The ratio of balloon diameter to annulus diameter was 0.83 and 0.8 respectively. Peak-to-peak systolic pressure gradient (PG) across aortic valve dropped from 90mmHg and 90mmHg to 20mmHg and 18mmHg respectively after balloon valvuloplasty. A follow-up of 3 months to 1 year by echocardiography showed that PG was 30mmHg and 43mmHg respectively, and aortic regurgitation was not significant.

Conclusion: PBAV was a method of choice in managing congenital AS in infants with satisfactory short and midterm results. Rapid ventricular pacing is an effective method to stabilize the balloon during aortic valvuloplasty and decrease the incidence of complications.
58. Evaluate Heart Function of Adolescent Scoliosis by Tissue Doppler
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Department of pediatric cardiology, the First Affiliated Hospital of Sun-Yat-sen University, Guangzhou, 510080

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 14 normal control. Then check the tissue doppler of heart. During the study, we measured the pulse tissue doppler of mitral annulus and tricuspid annulus, and 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. ICT/RR of the scoliosis group (1.81±1.18) was much larger than normal control (1.35±0.24). Also, IRT/RR of the scoliosis group (2.38±0.64) was much larger than normal control (1.07±0.18), and Tdi of the scoliosis group (0.40±0.05) was 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/RR of scoliosis group (1.99±0.61) VS normal control (1.09±0.4) · Tdi of scoliosis group (0.42±0.13) VS normal control (0.25±0.06) · There’s no statistical difference of Am, Sm and Em/Am between the two groups.

Conclusion The heart function of left and right ventricles decreased in adolescent scoliosis.

60. The Early Outcomes of Trans-Right Ventricle Pulmonary Valve Perforation and Balloon Valvoplasty Procedure for Pulmonary Atresia with Intact Ventricular Septum
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Children’s Hospital of Fudan University, PR China

[A]bstract Background For patients with pulmonary atresia with intact ventricular septum, percutaneous radiofrequency-assisted valvotomy and balloon dilation is the first choice for most patients. Lacking of the radiofrequency perforation equipment in China, we first report an alternative hybrid procedure: trans-right ventricle pulmonary valve perforation and balloon valvoplasty. Objective To evaluate the early outcomes of trans-right ventricle pulmonary valve perforation and balloon valvoplasty procedure for pulmonary atresia with intact ventricular septum. Methods 6 patients with pulmonary atresia with intact ventricular septum were undergoing trans-right ventricle pulmonary valve perforation and balloon valvoplasty procedure from January 2010 to December 2010. The mean body weight of the 6 patients was (3.8±1.6) kg, and the mean saturation was (71±10) %. The mean age was (56±45) days. All the 6 patients had tricuspid right ventricle and the z score of the tricuspid valve ranged from -2 to -3.2, with the mean value (-4.4±1.5). We evaluate the early outcomes of the hybrid procedure. Results There was no procedure-related death and no procedural complications. The mean size of the largest balloon was (7.3±1.2)mm, and the mean ratio of the size of the balloon and pulmonary valve ring was (1.0±0.1). The mean saturation was (89±5) % postoperatively; the mean ventilation time was (3.2±1.0) days and mean ICU stay time was (16±5) days. The mean pressure gradient between right ventricle and main pulmonary artery was (19±21.11) mm Hg. The mean ratio of forward flow from right ventricle and from the ductus in pulmonary artery was (0.35±0.06). All the 6 patients were followed up (4±2.6)months and 1 case required balloon valvoplasty reintervention 2 weeks after the hybrid procedure. The mean saturations on last follow-up was (85±5) %, higher than the saturation before procedure (76±5) %. Conclusion Our results showed that this technique was effective in selected cases of pulmonary atresia with intact ventricular septum with normal sized right ventricle. The hybrid procedure had less pulmonary regurgitation and could improve the size of the right ventricle.

59. Left Cardiac Sympathetic Denervation for Catecholaminergic Polymorphic Ventricular Tachycardia in a Chinese Child
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Catecholaminergic-polymorphic ventricular tachycardia (CPVT) is a rare but potentially lethal arrhythmia in children and it usually presented as syncope or sudden cardiac death related to exertion or emotion. The management of CPVT is difficult and beta-blockers are the cornerstone of therapy. Some patients continue to have syncope or documented exercise induced ventricular tachycardia despite on maximum dose of beta-blocker. Implantable cardioverter-defibrillator (ICD) may be necessary for those with recurrent cardiac arrest and complications of ICD are not uncommon. Few patients with CPVT have been treated successfully by left cardiac sympathetic denervation (LCSD). We would like to present a Chinese boy with this rare disease treated successfully by LCSD and the possible mechanisms of LCSD were also discussed.
Abstracts for Poster Session:

P1.

Managing Hypertension with Physical Activity Participation
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Purpose: The prevalence of hypertension has increased all over the world and it affects people in all age groups (from 9% in children to 46% in elderly). It is suggested that elevated systolic and diastolic blood pressure are associated with increased risk of coronary heart disease, heart failure and stroke. Literature supported that increase in physical activity participation level showed beneficial effects in managing hypertension. The purpose of this study is to identify how physical activity could manage the prevalence of hypertension.

Methods: A systematic search of published literature, from year 2006-2011, was conducted using the following databases: Medline, Cinahl and Embase.

Results: Clinical trials indicated that increasing physical activity was an important behavior in managing hypertension. Physical activity participation was found to be inversely associated with blood pressure and hypertension development. With young adults who were most physically active had a decreased risk of developing hypertension. As obesity is a risk factor for hypertension, regular physical activity could help with weight control, thus modified the risk of hypertension. Evidence also supported that people who perform regular physical activity had smaller blood pressure reaction to stress exposure whereas it increased among the sedentary ones.

Conclusion: To conclude, physical activity participation is of utmost importance in managing hypertension. It is recommended that regular physical activity should be performed in order to maintain a normal blood pressure.

P2.

Cardiac Rehabilitation - Patient Empowerment through Self-help and Lay leader Led Health Qigong Program at United Christian Hospital

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Occupational Therapy Department 1, Cardiology Division 2, Department of Medicine and Geriatrics 3, Health Resource Centre 4, United Christian Hospital

Introduction: Cardiac disease is a chronic disease with potentially disabling and even fatal complications and may lead to frequent re-admission. Patient active participation, forming self-help and establishing mutual support network is effective way for facilitating community reintegration, managing patients' promoted life role and encouraging active and healthy lifestyle engagement. A 12-week health qigong (BaDuanJin) program was proven effective from our previous study in improving the quality of life of patients with cardiac problems, their self-efficiency and lifestyle as well. To further enhance patient empowerment, a patient self-help and lay leader led health qigong program was therefore launched in 2006, which aimed at:
1. to facilitate cardiac patient community reintegration and resume their normal life role
2. to enhance self-efficiency in managing active and healthy lifestyle pattern of cardiac patients
3. to strengthen cardiac patient self-help and peer support network

Methodology: A patient self-help and lay leader led health qigong program was therefore launched in 2006. The program mainly focused on patient self-help and led by trained lay leader with supervision and support by Health Resource Center. Occupational therapist continued to act as consultant and advisor for the program. A health survey was adopted to assess the health status and effectiveness of the patient self-help and lay leader led health qigong program. The patient satisfactory survey consisted of 10 questions, which measured degree of patient's satisfaction towards the program content and quality of the program.

Results: Thirty-one patients were recruited in the survey, including 22 males and 8 females. Their age ranged from 56 to 80 years (mean=66 years, SD 6.7). 94.6% patients perceived an enhanced feeling of self-efficiency in maintaining active and healthy lifestyle pattern when practiced health qigong more than 3 times per week with more than 30 minutes each time. 93.3% patients perceived that they were able to relax and to build up healthy, active life style after practiced QIG. Other advantages after practicing QIG were improved physique and breathing, less pain over lower limbs and improved cardio-pulmonary fitness. 96.8% patients were not admitted in the past 1 year (due to cardiac related problem) after practicing QIG. All patients commented that the patient self-help and lay leader led program, mutual experience sharing created a sense of empowerment, mutual encouragement, peer support and competence for them to resume their normal life role. Besides, all of them were satisfied with the program format and contents. They would recommended others to join the program.

Conclusion: Through the use of culturally relevant health qigong treatment modality, recruitment and training of lay leaders, peer support and multi-disciplinary collaboration, the cardiac patient self-help and lay leader led health qigong program can facilitate community reintegration, enhance self-efficiency in maintaining active and healthy lifestyle pattern, strengthens self-help and peer support network of cardiac patients.