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Almanac 2012: Interventional Cardiology

PASCAL MEIER¹ AND ADAM TIMMIS²

From ¹The Heart Hospital, University College London Hospitals UCLH; ²London Chest Hospital, Barts and the London School of Medicine and Dentistry, London, UK

MEIER AND TIMMIS.: *Almanac 2012: Interventional cardiology.* The field of interventional cardiology continues to progress quickly. The efficacy of percutaneous interventions with newer generation drug-eluting stents has advanced a lot over the last decade. This improvement in stent performance has broadened the level of indication towards more complex interventions such as left main and multi- vessel PCI. Major improvements continue in the field of medical co-therapy such as antiplatelet therapies (bivalirudin, prasugrel, ticagrelor) and this will further improve outcomes of PCI. The same is true for intravascular imaging such as ultrasound IVUS and optical coherence tomography OCT. However, interventional cardiology has become a rather broad field, also including alcohol septal ablation for hypertrophic obstructive cardiomyopathy, etc. At the moment, the fastest growing area is the structural interventions, especially for aortic valve stenosis (transcatheter aortic valve implantation TAVI) and for mitral regurgitation (mitral clipping). This review covers recent advances in all these different fields of interventional cardiology. (*J HK Coll Cardiol 2013;21:1-14*)

摘要

介入心臟病學領域持續飛速發展。在過去的10年，經皮介入新一代藥物洗脫支架的療效取得長足的進步。這種支架性能的改善擴展了介入干預的適應症，使其應用於更複雜的干預，如左主幹和多支血管經皮冠狀動脈介入治療（PCI）。藥物聯合治療的不斷優化，如抗血小板治療（比伐盧定，普拉格雷，替卡格雷），將進一步改善PCI的預後。同樣血管內成像技術也取得了顯著發展，如超聲血管內顯像和光學相干斷層成像術等。然而，介入性心臟病學已發展為一個相當廣泛的領域，包括酒精室間隔消融術治療肥厚型梗阻性心肌病等。目前發展最快的是結構性干預領域，尤其是主動脈瓣狹窄（經導管主動脈瓣植入術TAVI）和二尖瓣關閉不全（二尖瓣剪裁）。本文涵蓋了介入性心臟病學所有不同領域的最新進展。

Address for reprints: Dr. Pascal Meier
The Heart Hospital, University College London Hospitals UCLH,
16-18 Westmoreland Street, London, United Kingdom

Email: pascalmeier74@gmail.com

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Percutaneous Coronary Intervention Versus Medical Treatment

Percutaneous coronary intervention (PCI) has guideline recommendations for treatment of ST elevation and non-ST elevation myocardial infarction (MI).¹ However, its role in stable coronary disease has been the subject of reappraisal following publication of the COURAGE trial, which showed that, in patients

receiving optimal medical therapy, PCI does not improve cardiovascular outcomes, while incremental benefits for quality of life disappear by 36 months.^{2,3} A more recent meta-analysis of eight trials of optimal medical therapy versus PCI involving 7229 patients bears out the COURAGE conclusions by showing no significant differences between the groups with regard to death (9.1% vs 8.9%), non-fatal MI (8.1% vs 8.9%), unplanned revascularisation (30.7% vs 21.4%) and persistent angina (33% vs 29%).⁴ Drug-eluting stents (DESs) were used in only a minority of these patients and may have reduced the need for further revascularisation while improving symptomatic responses. Nevertheless, the meta-analysis reinforces contemporary guideline advice for optimal medical treatment as the initial treatment for stable angina.⁵ Whether this will change current practice remains to be seen, but early signs are not encouraging. Thus a US registry analysis of patients undergoing PCI before (n=173 416) and after (n=293 795) the COURAGE report showed no change in the proportions receiving optimal medical treatment (43.5% vs 44.7%).⁶

PCI Versus Coronary Bypass Surgery

The safety of PCI at hospitals without on-site cardiac surgery has been confirmed in two recent reports.^{7,8} Add to this the feasibility of PCI in increasingly complex disease and we need look no further to explain the substantial reductions in rates of coronary bypass surgery (CABG) in recent years. A recent US study of revascularisation procedures during 2001-2008 showed a 38% decline in rates of CABG, while PCI decreased by only 4%.⁹ Some have questioned whether patients are being appropriately advised according to contemporary guidelines,¹⁰ a US analysis of 500 154 PCIs reporting that, among the 28.9% of cases performed for non-acute indications, only 50.4% were appropriate and that angina was not present in many of the inappropriate cases.¹¹ In the absence of any evidence of prognostic benefit, there can be no indication for PCI in stable patients without angina. In patients with angina, on the other hand, PCI is as effective as CABG in providing symptom relief at 12 months, judging by a recent report from the SYNTAX

investigators.¹² However, CABG may have the advantage of providing prognostic benefit, recent US registry data showing a lower 4-year mortality compared with PCI (16.4% vs 20.8%) in an analysis that adjusted for selection bias.¹³ Of course, being a registry study, treatment allocation was not random and any conclusions about relative prognostic benefits require caution. Nevertheless, guideline recommendations are for surgery in complex three-vessel and left main stem disease, although many patients continue to express a preference for PCI, particularly now we have reports of the feasibility and safety of same-day discharge. This is particularly applicable with radial access (or post-procedural deployment of a femoral closure device), and, in a US registry study, 1339 patients discharged on the same day as their procedure had similar 30-day readmission rates to 105 679 patients who stayed overnight.¹⁴ This is important because it is now recognised that readmission within 30 days after PCI is associated with a significant increase in 1-year mortality.¹⁵

Left Main Stem Disease

The trespass of PCI on to territory that was formerly surgical is best illustrated by its increasing application in unprotected left main stem disease. Registry data from the USA for 131 004 patients with unprotected left main stem disease show the proportion treated with PCI increasing from 3.8% to 4.9% between 2004 and 2008. PCI recipients were older with more comorbidities, probably accounting for their higher hospital mortality compared with the overall cohort (13% vs 5%).¹⁶ Technical improvements since 2008 have seen further increases in rates of PCI in unprotected left main stem disease, and we now have randomised trial data confirming its safety and efficacy in selected patients. Thus in the Korean PRECOMBAT trial of drug-eluting stenting versus CABG in 600 patients, 8.7% of patients in the stent group and 6.7% in the CABG group met the primary end point (a composite of death, MI, stroke and ischaemia-driven revascularisation at 12 months), a difference significant for the non-inferiority of stenting.¹⁷ As in previous randomised comparisons, the difference was driven largely by a higher rate of

repeat revascularisation in stent recipients (9.0% vs 4.2% after 2 years, $p=0.02$).

Selection for revascularisation in left main stem disease has traditionally been based on angiographic assessment, but a recent study suggests that measurement of minimum lumen area by intravascular ultrasound (IVUS) might be a better means of selection in patients with 'intermediate' angiographic stenoses in the range 25-60%.¹⁸ Correlation between minimum lumen area and angiographic stenosis was poor, but a 6 mm² area measurement provided a safe threshold for determining revascularisation, the event-free survival being no worse in the patients with an area measurement >6 mm² who did not undergo revascularisation compared with the patients with an area measurement <6 mm² who did. These were non-randomised data, but point to a useful role for IVUS in the management of left main coronary artery disease.

DESs and Stent Thrombosis

The introduction of bare metal stents (BMSs) towards the end of the last decade dramatically improved the performance and safety of PCI, but it required drug-eluting technology to make a significant impact on restenosis rates. Concerns about an increased risk of stent thrombosis with DESs¹⁹ appear to have been exaggerated, particularly with the current generation of DESs, but the beneficial effects on restenosis have been borne out. Thus a recent meta-analysis comparing sirolimus-eluting and bare metal stents in patients with diabetes reported dramatic reductions in the need for repeat revascularisation with the DES (HR 0.27, 95% CI 0.18 to 0.41) without any increase in the risk of stent thrombosis.²⁰ However, it has been the everolimus-eluting stent that has emerged as the interventionists' favourite, a meta-analysis of 13 randomised trials including 17 101 patients reporting thrombosis rates of only 0.7% during 21.7 months' follow-up, compared with 1.5% in patients treated with any other type of DES.²¹ A further meta-analysis pooled data from 49 randomised trials including 50 844 patients and came to similar conclusions by showing that everolimus-eluting stents had the lowest risk of stent thrombosis at 30 days and 1

year compared with other stents approved for use in the USA, including BMSs.²² The difference in favour of everolimus-eluting stents remained significant at 2 years when the odds of stent thrombosis was 0.34 (95% CI 0.19 to 0.62) compared with paclitaxel-eluting stents and 0.35 (95% CI 0.17 to 0.69) compared with BMSs.

Data on DESs in saphenous vein grafts are somewhat less clear, but the limited available randomised trials do suggest superiority compared with BMSs.²³ For primary PCI, concerns that the thrombotic environment might predispose to DES thrombosis have not been fully realised, a pooled analysis of 15 STEMI trials comparing first-generation DESs with BMSs reporting a lower requirement for target vessel revascularisation with DESs (RR 0.51, 95% CI 0.43 to 0.61), with no difference in the rate of stent thrombosis compared with BMSs.²⁴ Indeed, the risk of stent thrombosis during the first year was reduced for DESs (RR 0.80, 95% CI 0.58 to 1.12) but increased thereafter (RR 2.10, 95% CI 1.20 to 3.69), suggesting that the early benefit of first-generation DESs in primary PCI is offset by a later increase in the risk of stent thrombosis. Newer-generation DESs may overcome this drawback, but, until we have sufficient data, operators should carefully weigh the differential risk of restenosis and stent thrombosis between the two stent types.

Interest in bioresorbable stents has been enhanced by reports from a phase II evaluation of imaging data 12 months after implantation in 56 patients.²⁵ The restenosis rate was only 3.5%, and >95% of the stent struts were endothelialised. Moreover, variable coronary dilatation in response to acetylcholine was observed, indicating some return of normal vasomotor responses. The results of randomised trials now in the planning stage are eagerly awaited.

Optimal Arterial Access

Radial access for coronary angiography has now achieved widespread application.^{26,27} One reason is the accumulating evidence that it reduces bleeding risk and, perhaps because of this, may reduce mortality in primary PCI.²⁸ Thus a comprehensive meta-analysis pooling all the data from randomised primary PCI trials comparing

femoral with radial access showed a nearly 50% mortality reduction in the radial group.²⁹ Whether this beneficial effect is generalisable to everyday clinical practice is unclear, but observational data support the trial results and indicate benefit of radial access for primary PCI.^{30,31} Another potentially important advantage of radial access is its association with a reduced risk of kidney injury, as reported in a large Canadian study of 69 214 patients undergoing cardiac catheterisation.³² The mechanism is unclear and the largest trial comparing radial and femoral access, the RIVAL trial, did not show a clear advantage for either access route, although radial access appeared preferable in the subgroup undergoing primary PCI.³³ On the basis of current evidence, the choice between radial and femoral access should be individualised taking into account operator experience, bleeding risk and patient preference.

Antiplatelet Therapies – What's New?

In patients undergoing PCI, dual antiplatelet therapy with aspirin and clopidogrel remain central to guideline recommendations. For clopidogrel, a pooled analysis of available data favoured a loading dose of 600 mg, which was associated with a 34% reduction in the rate of major adverse cardiac events (MACE) without any increase in the risk of major bleeding compared with a 300 mg loading dose.³⁴ Now we have randomised trial evidence confirming that, compared with the 300 mg loading dose, the 600 mg dose in primary PCI is associated with significant reductions in infarct size, measured by median CKMB mass over 72 h (2070 vs 3029 ng/ml).³⁵ Continuing therapy with aspirin and clopidogrel is usually recommended after PCI in both stable and patients with acute coronary syndromes (ACS), but the antiplatelet effect of clopidogrel is variable, and high on-treatment platelet reactivity can be demonstrated in 14.7-26.9% of patients, depending on the test used.³⁶ Part of this variability in antiplatelet responsiveness is explained by the fact that clopidogrel is a prodrug, and the enzymes that form its active metabolites exhibit functionally distinct polymorphisms. However, a study from the Netherlands

of 1069 clopidogrel-pretreated patients undergoing elective PCI found that loss-of-function CYP2C19 carrier status explained only part of the variability in platelet reactivity (13.0-20.6%), depending on the test used.³⁷ One approach to modifying high on-treatment platelet reactivity in carriers of loss-of-function CYP2C19 variants is to use antiplatelet drugs metabolised by different pathways, and this was confirmed by investigators from Korea in a substudy of the CILON-T randomised trial.³⁸ In patients with loss-of-function CYP2C19 variants who were randomised to dual antiplatelet therapy plus cilostazol, a selective phosphodiesterase-3 inhibitor, on-treatment platelet reactivity was significantly reduced compared with patients who received only aspirin and clopidogrel. This effect of cilostazol was not seen in non-carriers of the loss-of-function polymorphism. An alternative approach for modifying high on-treatment platelet reactivity after PCI is to increase the dose of clopidogrel. However, this was found ineffective in the GRAVITAS trial, the 6-month rate of the composite of cardiovascular death, MI and stent thrombosis being identical for groups randomised to high-dose (150 mg daily) or standard-dose (75 mg daily) clopidogrel.³⁹

Current guideline recommendations are for clopidogrel to be stopped 12 months after DES deployment when endothelialisation is complete, reducing the risk of thrombosis. Worryingly, a clustering of late clinical events has been associated with this policy, perhaps because of an increase in arachidonic acid-induced platelet activation as reported in a recent UK study,⁴⁰ lending support to the accumulating evidence that clopidogrel exerts some of its antiplatelet effects via this pathway, independently of aspirin. Indeed, it has been suggested that discontinuation of aspirin instead of clopidogrel might be more rational 1 year after stenting.⁴¹ This question will soon be tested in the large GLOBAL-LEADERS randomised trial. The limitations of dual antiplatelet therapy with aspirin and clopidogrel have been further illustrated by the on-TIME-2 trial, in which patients undergoing primary PCI were randomised to additional prehospital tirofiban or placebo.⁴² The addition of tirofiban produced more effective platelet inhibition than aspirin and clopidogrel alone, and this was associated with a reduction in MACE

and early stent thrombosis. On-TIME-2 lends further support to guideline recommendations for early glycoprotein IIb/IIIa inhibition together with dual antiplatelet therapy in patients undergoing primary PCI.

Newer P2Y₁₂ Receptor Inhibitors

These include prasugrel and ticagrelor, which now have guideline indications in ACS⁴³ based on the TRITON and PLATO randomised trials, which were the subject of recent review.⁴⁴ TRITON randomised patients undergoing PCI for ACS to either clopidogrel or prasugrel therapy for 12 months after the procedure.⁴⁵ Prasugrel showed superiority over clopidogrel for the composite primary end point, driven mainly by periprocedural MI. It also showed significant risk reduction for stent thrombosis. However, these benefits came with an increased risk of major and minor bleeding. In the PLATO trial of ticagrelor versus clopidogrel in patients with ACS managed medically or with PCI,⁴⁶ ticagrelor was superior with regard to the primary composite end point of MACE, but, while minor bleeding was more common with ticagrelor, the major bleeding risk was comparable to that with clopidogrel. These randomised trials have confirmed that more intensive platelet inhibition with prasugrel or ticagrelor delivers better clinical outcomes in ACS, although there is a bleeding penalty, particularly it seems for prasugrel. The clinical outcome advantage for both drugs is small in absolute terms, raising important questions about cost-effectiveness. A US evaluation for prasugrel concluded it was 'an economically attractive treatment strategy',⁴⁷ but a more recent National Institute for Health and Clinical Excellence (NICE) technology assessment was more guarded, recommending prasugrel as an option in patients with STEMI if immediate primary PCI is necessary (based on its rapid onset of action compared with clopidogrel), or if diabetes is present or if stent thrombosis has occurred during clopidogrel treatment.⁴³ However, concern was expressed about its likely cost-effectiveness in other situations. A recent health-economic analysis based on the PLATO study concluded that treating patients with ACS with ticagrelor for 12 months is associated with a cost per QALY (quality-adjusted life year) below generally accepted thresholds for cost-effectiveness.⁴⁸

Bivalirudin and Heparin

Bivalirudin is now available for treatment of ACS and has rapidly gained a central role in primary PCI.⁴⁹ It is a direct thrombin inhibitor with additional activity against thrombin-mediated platelet activation that showed superiority over a combined regimen of heparin plus a glycoprotein IIb/IIIa inhibitor in HORIZONS-AMI, due largely to a lower rate of major bleeding (4.9% vs 8.3%). All-cause mortality was lower at 30 days, and we now have 3-year follow-up data confirming persistent mortality benefit (5.9% vs 7.7%), ensuring a guideline recommendation for bivalirudin in primary PCI.⁵⁰ The clinical benefits of bivalirudin have also been associated with cost-effectiveness, patient lifetime costs in the UK being £267 lower than for glycoprotein IIb/IIIa inhibitors.⁵¹ A small increase in rates of stent thrombosis with bivalirudin was not seen in patients pretreated with heparin, and the mortality benefits of combining bivalirudin with heparin pretreatment have since been reported from the SCAAR registry,⁵² leading the editorialist to recommend dual therapy in patients undergoing primary PCI.⁵³

Unfractionated heparin retains a class 1 recommendation for use during PCI, but a recent meta-analysis of pooled data from 23 studies has shown that enoxaparin is associated with significant reductions in the composite of death and MI and in major bleeding rates compared with unfractionated heparin.⁵⁴ These benefits were greatest for primary PCI, but were also seen in PCI for non-ST elevation MI and stable angina. The time may be right for a change of policy in favour of low-molecular-weight heparin during PCI.

Intravascular Imaging – Clinical Benefit?

The clinical benefit of using IVUS to guide PCI remains controversial, although a pooled analysis of seven randomised BMS trials has concluded that IVUS-guided PCI is associated with a reduced risk of in-stent restenosis.⁵⁵ IVUS is also finding a role in assessing left main stem lesions for revascularisation.¹⁸ As a research tool, however, and for validation of non-invasive imaging of coronary stenosis, IVUS has proved particularly valuable.⁵⁶ Thus, in a recent study

comparing coronary CT angiography and IVUS for plaque volume measurements, there was only modest agreement between the two methods (Bland-Altman limits of agreement -67 to +65 mm³), reflecting the limitations of coronary CT for assessing the extent of coronary disease.⁵⁷ While the ability to image across the coronary arterial wall is a particular strength of IVUS, the technology is limited by image resolution, which is considerably inferior to optical coherence tomography (OCT). In a substudy of ODESSA, for example, suboptimal stent deployment was identified by OCT at the level of individual stent struts, a detail that could never be reproduced by IVUS.⁵⁸ Increasingly, OCT is being used to assess stent strut endothelialisation, a recent Japanese study of everolimus-eluting stent implantation showing that, of 5931 struts assessed, 98.4% were endothelialised 8 months after implantation, an observation reflected in the low thrombotic risk for these second-generation DESs.⁵⁹

Intravascular imaging has also been used to assess plaque stability, the PROSPECT trial confirming that IVUS can differentiate stable from unstable plaque and predict adverse events.⁶⁰ A key feature of unstable plaque is thin-cap atherosclerosis, and recent data remind us that the inflammatory environment is an important determinant of instability, an OCT study showing a clear association between the cap thickness of plaques and inflammatory plasma markers such as high-sensitivity C-reactive protein.⁶¹

Technical Aspects of Stenting – What Have We Learnt?

Overlapping Stents

Re-endothelialisation of overlapping stent segments is slower, and most operators prefer single stent deployment for that reason.⁵⁸ However, in the real world, overlapping stent deployment is often unavoidable, and, for DESs, the conventional wisdom has been that homogeneous stents should be used to avoid elution of different pharmacological compounds within the overlapping segment. This has now been challenged by a Korean study of 1080 patients who received overlapping DESs.⁶² The study showed that

cardiac death, MI or target lesion revascularisation occurred with similar frequency regardless of whether the DESs were homogeneous or heterogeneous.

Bifurcation Stenting

Several studies have shown that a single, main vessel stent deployment provides outcomes that are comparable-and often superior-to two-stent deployment. Thus a combined analysis of the NORDIC Bifurcation Study and the British Bifurcation Coronary Study showed that, in patients randomised to 'simple' main vessel stenting, the composite MACE end point at 9 months occurred in 10.1% of patients compared with 17.3% of patients who underwent complex two-vessel stenting (p=0.001).⁶³ However, questions remain, particularly concerning the value of final kissing balloon inflations across the bifurcation following main-vessel stenting. This was addressed in a large observational study of 1055 patients undergoing bifurcation stenting.⁶⁴ A comparative propensity analysis of patients who did and did not have final kissing balloon inflations showed a higher incidence of MACE and target lesion revascularisation, mostly in the main vessel, for patients who had final kissing balloon inflations. The pendulum therefore has now swung away from final kissing balloon inflation, which may cause more harm than good.

Myocardial Infarction – High-Sensitivity Troponin Assays

Central to the diagnosis of acute MI is the demonstration of a raised and changing troponin concentration in the first 24 h after symptom onset. The availability of high-sensitivity troponin (hsTn) assays is likely to see diagnostic thresholds fall, with important implications for clinical management and cardiac outcomes. Thus, in a recent study in which hsTn-I was measured in 1038 patients with suspected ACS, values below the previous limit of detection (0.20 ng/ml) showed graded association with death or non-fatal MI.⁶⁵ In a further 1054 patients, the diagnostic threshold was lowered to 0.05 ng/ml, and attending physicians were invited to modify their management accordingly. Rates

of death and recurrent MI fell from 39% to 12% among patients with troponin concentrations 0.05-0.19 ng/ml, levels that would have been undetectable with conventional troponin assays. The investigators concluded that lowering the diagnostic threshold using hsTn assays has the potential to identify many high-risk individuals with suspected ACS and produce major improvements in their prognosis.

It has always been the recommendation that the diagnostic threshold level chosen for troponin should be based on a coefficient of variation of #10%, but new guidance is for the 99th centile value to be adopted regardless of assay imprecision.⁶⁶ The potential clinical impact of this change in guidance was evaluated in the same cohort as reported previously,⁶⁵ this time using a diagnostic threshold of 0.012 µg/l (coefficient of variation 20.8%)⁶⁷ At 1 year, patients with troponin concentrations of 0.012-0.049 µg/l, who previously would have escaped a diagnosis of MI, were more likely to be dead or readmitted with recurrent MI than those with troponin concentrations <0.012 µg/l (13% vs 3%, $p<0.001$). The authors concluded that lowering the diagnostic threshold to the 99th centile and accepting greater assay imprecision would identify more patients at high-risk of recurrent MI and death, but increase the diagnosis of MI by 46%. It remains to be established whether reclassification of these patients and treating them according to conventional MI guidelines will improve their outcomes.

hsTn assays will not only cause diagnostic thresholds for acute MI to fall, but may also allow identification of patients with apparently stable coronary disease who have vulnerable coronary lesions.⁶⁸ Thus a recent study has shown a strong correlation between hsTn-T and non-calcified plaque burden ($r=0.79$, $p<0.001$) in 124 patients with stable angina undergoing CT angiography, patients with remodelled non-calcified plaque having the highest hsTn-T values.⁶⁹ hsTn assays have already found clinical application for the early diagnosis of MI in patients with chest pain attending the emergency department. In the Randomised Assessment of Treatment using Panel Assay of Cardiac Markers (RATPAC) trial, the use of hsTn-I within a panel of biomarkers allowed successful discharge of 32% of patients compared with 13% of patients

receiving standard diagnostic procedures.⁷⁰ Beyond their central role for diagnosis, troponins also provide a measure of the severity of MI, and, in a report from the GRACE registry,⁷¹ incorporating 16 318 patients with non-ST elevation MI, each 10-fold increase in the troponin ratio was associated with stepwise increments in ventricular arrhythmias, heart failure, cardiogenic shock and death.⁷²

Non-Culprit Lesions in ACS

The importance of myocardial salvage during the acute phase of infarction is emphasised by the fact that prognosis is driven largely by ultimate infarct size. We could therefore hypothesise that treating all significant lesions is beneficial. One of the first primary PCI randomised trials testing this hypothesis was reported last year. Among 214 patients with multivessel disease, adverse event rates during a mean follow-up of 2.5 years were higher with culprit-only PCI compared with multivessel PCI, whether performed during the index procedure or as a staged procedure afterwards.⁷³ However, the trial was small and not definitive, a more recent meta-analysis finding in favour of culprit-only primary PCI with a staged strategy for non-culprit lesions.⁷⁴ This has become the guideline recommendation and was further supported by analysis of observational data from the HORIZONS-AMI trial in which outcomes for 275 patients treated with single-procedure stenting were compared with outcomes for 393 patients treated with staged procedures.⁷⁵ The single-procedure group received significantly more stents yet had a significantly higher 12 month mortality (9.2% vs 2.3%) than the staged procedure group. The weight of evidence is now firmly in favour of culprit-only stenting during primary PCI.

Infarct Size and Myocardial Salvage

Circadian rhythms in the onset of MI are well established, the morning hours being the period of greatest risk. Intriguingly, infarct size appears to show similar circadian variation, a retrospective analysis of 811 patients with STEMI showing that creatine kinase (CK) and troponin I curves peak between 06:00 h and

noon.⁷⁶ Myocardial salvage in response to reperfusion therapy with PCI is the major strategy for limiting infarct size therapeutically and can now be quantified by cardiovascular magnetic resonance (CMR). A study of 208 patients presenting with STEMI confirmed that the extent of salvage measured by CMR is closely related to long-term prognosis, patients with a myocardial salvage index (MSI) above the median level having a lower number of adverse cardiovascular events (7 vs 26) and deaths (2 vs 12) after 18.5 months than patients with MSI below the median level.⁷⁷ Myocardial reperfusion, however, can itself exacerbate injury, by a variety of mechanisms which include interstitial haemorrhage. This can be detected by CMR and was reported in 25% of patients with STEMI treated successfully by primary PCI.⁷⁸ The presence of haemorrhage was an independent predictor of adverse remodelling, as reflected by increased left ventricular (LV) end-systolic volume at 3 months. The importance of interstitial haemorrhage as a predictor of LV remodelling was emphasised by the improvement in the area under the receiver operating characteristic curves from 0.699 to 0.826 when it was added to LV ejection fraction and infarct size in the predictive model. Microvascular obstruction after primary PCI is also predictive of remodelling, and in another CMR study was found to correlate significantly with reperfusion haemorrhage ($r^2=0.87$, $p<0.001$).⁷⁹

Strategies to protect against reperfusion injury remain high on the research agenda and have been the subject of recent review.⁸⁰ In one study the effect of erythropoietin was tested based on beneficial experimental effects for reducing infarct size.⁸¹ However, the study was negative, with patients randomised to erythropoietin (50 000 IU) before primary PCI showing an increased incidence of microvascular obstruction and LV dilatation without reduction in infarct size compared with patients randomised to placebo. Another study using forearm plethysmography tested a bradykinin B2 receptor antagonist, based on the hypothesis that endogenous bradykinin is a mediator of reperfusion injury.⁸² The investigators found that remote ischaemic preconditioning abolished the impairment of endothelium-dependent vasomotor function induced by plethysmography, but bradykinin

receptor blockade had no effect. Nevertheless, the finding that conditioning stimuli provide a clinically applicable means of protection against reperfusion injury was not new and has been replicated in other more recent clinical trials. A comparative primary PCI study of post-conditioning by staccato reversus abrupt reperfusion, for example, showed that the staccato protocol was associated with better preservation of microvascular function and LV dimensions 12 months later.⁸³ Staccato reperfusion was also partially effective in another primary PCI study in which patients were randomised to staccato reperfusion versus control. Infarct size was unaffected, except in patients with large areas at risk in whom it was significantly reduced by post-conditioning.⁸⁴

The benefits of intra-aortic balloon counterpulsation (IABC) when cardiogenic shock complicates acute MI are generally accepted. Recently, the role of IABC for reducing infarct size in haemodynamically stable patients with anterior MI was tested in a randomised trial of 337 patients.⁸⁵ Infarct size at 3-5 days determined by MRI showed no significant difference between the groups, but those patients randomised to IABC showed a trend towards more vascular complications. The authors concluded that IABC produces no clinical benefit in this group of patients.

Contrast-Induced Acute Kidney Injury (CI-AKI)

Whether newer contrast agents, such as iso-osmolar contrast, have an impact on the CI-AKI risk is controversial.⁸⁶ Risk of CI-AKI is particularly high in patients presenting with an ACS, and recent data confirm it has a significant impact on clinical outcomes, including length of hospital stay and mortality.^{87,88} The ACS setting offers little time to apply reno-protective measures, and strategies requiring up to 12 h of prehydration are clearly impractical. The need for a change in practice was emphasised by Wi et al,⁸⁷ who concluded that renal function should be measured at baseline and after primary PCI, to refine risk stratification. Meanwhile consideration should be given to reno-protection with bicarbonate, which has

been reported to be more effective than normal saline using short-infusion or singlebolus protocols.⁸⁹ In certain subgroups, such as patients requiring urgent surgery for infective endocarditis, preoperative coronary angiography does not appear to increase the risk of acute kidney injury,⁹⁰ but, in general, contrast exposure should be kept at as low a level as possible during primary PCI. Meanwhile, randomised trials testing short-duration prehydration protocols or bolus applications of potentially reno-protective substances are needed.

Carotid Artery Stenosis – Is Stenting Still an Option?

Life style adjustment and secondary prevention drugs may not always be effective in protecting against progression of carotid atherosclerosis. A recent trial of weight reduction with rimonabant, for example, reported that a 5% reduction in body weight over 30 months failed to influence the progression of carotid disease compared with patients who received placebo.⁹¹ Many patients therefore require an interventional solution to their carotid disease, but whether this should be surgical or percutaneous remains contentious.⁹² A large randomised trial of 2502 patients with symptomatic or asymptomatic carotid stenosis showed no significant difference in the estimated rates of the primary composite end point (periprocedural stroke, MI, or death or any ipsilateral stroke within 4 years) and no differential treatment effect by symptomatic status.⁹³ However, a recent meta-analysis pooling data from 11 randomised trials comparing carotid endarterectomy (CEA) with carotid artery stenting (CAS) showed that the periprocedural risk of mortality or stroke was lower for CEA (OR 0.67, 95% CI 0.47 to 0.95), mainly driven by a decreased risk of minor stroke, whereas the risk of death or disabling stroke was similar between the two groups. The odds of periprocedural MI or cranial nerve injury were significantly higher in the CEA group.⁹⁴ Current NICE guidelines recognise CAS as a treatment option for patients with symptomatic carotid artery stenosis, but emphasise that patients need to understand the risk of stroke and other complications associated with this procedure. Patient selection should be carried out by a

multidisciplinary team.⁹⁵

For asymptomatic carotid artery disease, the situation is even less clear. We know that patients with carotid stenosis undergoing cardiac surgery for their coronary artery disease have an increased periprocedural stroke risk and probably should be considered for treatment even if asymptomatic. The American guidelines recommend CEA if the stenosis is $\geq 80\%$, either before or combined with CABG. CAS before CABG is an alternative option with good results in patients who are considered 'high risk' for CEA.⁹⁶ Attempts to refine risk prediction in such patients have been the subject of considerable research, a recent carotid ultrasound study reporting that the total plaque area (HR 1.29, 95% CI 1.08 to 1.55), the number of plaques (HR 1.14, 95% CI 1.02 to 1.27) and the number of segments with plaque (HR 1.45, 95% CI 1.09 to 1.93) were all significantly associated with the 5-year risk of cerebrovascular events.⁹⁷

Transcatheter Aortic Valve Implantation

Transcatheter aortic valve implantation (TAVI) in older high-risk patients has yielded excellent results in most centres, the 2-year follow-up of patients in the PARTNER trial supporting the procedure as an alternative to surgery in high-risk patients.⁹⁸ Thus improvement in valve areas was similar for TAVI and for surgery, with comparable rates of death and stroke during follow-up. However, paravalvular regurgitation was more common after TAVI and has been associated with significantly worse outcomes, the German registry reporting higher in-hospital mortality, even after multivariate adjustments for potential confounders (OR 2.50, 95% CI 1.37 to 4.55).⁹⁹ Another cause for concern is the potential for myocardial injury during TAVI, as evidenced by elevations of CK-MB in 77% of 101 patients undergoing uncomplicated procedures.¹⁰⁰ Median maximal CK-MB levels were higher for transapical than transfemoral access (22.6 ml vs 9.9 ml), but were unaffected by the presence of coronary artery disease. Elevations of cardiac troponin T were also observed and were predictive of cardiac death at 9 months. Clearly, therefore, TAVI, like surgery, is

commonly associated with some degree of myocardial injury that is not benign. In most other respects, however, TAVI appears safe and has been associated with important symptomatic benefits, as reflected in the improvement in health-related quality of life reported by the PARTNER investigators.¹⁰¹ Smaller studies have reinforced these findings by reporting improvement in the 6 min walk distance and quality of life scores, while brain natriuretic peptide (BNP) levels decline substantially.¹⁰² Add to this the cost-effectiveness of TAVI in US and UK analyses, and it seems certain that indications will continue to expand.^{103,104} Indeed, off-label TAVI is commonplace, with reported outcomes that are comparable to on-label procedures.¹⁰⁵ Paradoxically, increasing TAVI activity appears to have led to a significant increase in referrals for surgical aortic valve replacement,¹⁰⁶ with Manchester, for example, seeing a 37% increase in surgical AVR activity within the 2 years of starting a TAVI programme.¹⁰⁷

Percutaneous Mitral Valve Repair

The development of percutaneous systems for mitral valve repair in patients with severe mitral regurgitation has proved more challenging than TAVI. NICE gave a guarded verdict on the MitraClip device in 2010, recommending it only be used with 'special arrangements for clinical governance, consent and research for patients who are well enough for surgical mitral valve leaflet repair'.¹⁰⁸ This was based on the findings of the Endovascular Valve Edge-to-Edge REpair Study (EVEREST) investigators in an observational study of 107 patients with moderate or severe mitral regurgitation, which reported a successful MitraClip implant in 74% of patients, of whom 66% achieved freedom from death, mitral valve surgery and severe mitral regurgitation ($\geq 3+$).¹⁰⁹ Since then the EVEREST investigators have undertaken a further observational study in 78 older patients at high risk of conventional surgery, which showed that the MitraClip device reduced mitral regurgitation in the majority of patients, with improvement in symptoms associated with significant LV reverse remodelling over 12 months.¹¹⁰ The benefits of the MitraClip appear closely related to its efficacy in

reducing mitral regurgitation, the midterm outcomes showing significant association with the acute haemodynamic response.¹¹¹

Alcohol Septal Ablation in Hypertrophic Cardiomyopathy

Three studies have recently reported longer-term outcomes after alcohol septal ablation in symptomatic patients with hypertrophic cardiomyopathy (HCM). The results have been encouraging. Among 874 patients with class III or IV symptoms in a US study, six (0.7%) died in relation to the procedure, and survival estimates at 1, 5 and 9 years were 97%, 86% and 74%, respectively.¹¹² Symptoms improved to class I or II in all but 5% of cases, although 13% required repeat ablation and 3% required surgical myomectomy. In a Canadian study of 649 patients with HCM, 38% were managed conservatively, and 62% underwent invasive therapy with alcohol septal ablation (21%), surgical myomectomy (71%) or dual chamber pacing (8%).¹¹³ In multivariate analysis, invasive therapy was independently associated with better overall survival (HR 0.6; 95% CI 0.4 to 0.97, $p=0.04$), but not with HCM-related survival. Among the invasive group, the pacemaker-treated group fared less well than patients treated with septal ablation or myomectomy, questioning the call for a reappraisal of pacemaker therapy in a recent Spanish study that reported favourable long-term results in a group of 50 patients.¹¹⁴ Finally, a Scandinavian study reported marked reductions in outflow tract gradients in response to 313 ablation procedures in 279 patients with HCM, of whom 94% had class III/IV symptoms.¹¹⁵ Only 21% had class II/IV symptoms at 1 year, with little change thereafter. Estimated survival rates at 1, 5 and 10 years were 97%, 87% and 67%, respectively, and were comparable to survival rates in an age- and gender-matched population. Taken together, these studies testify to the long-term benefits of alcohol septal ablation in HCM, which appears to be a valid alternative to surgery in symptomatic HCM that does not respond to medical therapy.

Competing Interests

None.

Provenance and Peer Review

Not commissioned; internally peer reviewed.

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Dabigatran as Alternative Anticoagulant for Intra-Aortic Balloon Pump in a Patient with Suspected Heparin-Induced Thrombocytopenia

JOE KIN-TONG LEE,¹ KIN-LAM TSUI,¹ HO-NAM WONG,² BONNIE CHI-SHAN KHO,² HERMAN SUNG-YU LIU,² KWOK-KEUNG CHAN,¹ SHU-KIN LI¹

From ¹Division of Cardiology; ²Division of Haematology, Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong

LEE ET AL.: Dabigatran as Alternative Anticoagulant for Intra-Aortic Balloon Pump in a Patient with Suspected Heparin-Induced Thrombocytopenia. Heparin induced thrombocytopenia (HIT) is an uncommon condition but can result in devastating outcomes. Alternative anticoagulants are recommended for HIT patients with on-going needs of anticoagulation. We report a case of cardiogenic shock treated with intra-aortic balloon pump. The patient was complicated with isolated HIT after administration of low-molecular-weight heparin, and was successfully managed with dabigatran, an oral direct thrombin inhibitor, as an alternative anticoagulant. (*J HK Coll Cardiol* 2013;21:15-20)

Anticoagulation, Dabigatran, Heparin, Heparin-induced thrombocytopenia, Intra-aortic balloon pump

摘要

肝素誘導的血小板減少症（HIT）是一種罕見的疾病，但可能會導致毀滅性的後果。為滿足HIT患者持續抗凝的需求，我們推薦替代抗凝劑。我們報導了一例採用主動脈內球囊反搏治療心源性休克的案例。低分子量肝素給藥後，該患者併發單純性HIT，然而，選擇一種口服直接凝血酶抑制劑—達比加群酯（替代抗凝劑），成功逆轉了HIT。

關鍵詞：抗凝作用主，達比加群酯，肝素，肝素誘導的血小板減少症，動脈內球囊反搏

Introduction

Two types of heparin-induced thrombocytopenia (HIT) have been described. Type 1 HIT is a non-immunogenic form of HIT and occurs more commonly. It usually occurs within the first 2 days after heparin administration and platelet counts often return to normal despite continuation of heparin. The

immune-mediated (type 2) HIT is of clinical importance. In the rest of the article, the term HIT refers to immune-mediated HIT unless otherwise specified. In susceptible patients receiving heparin, HIT antibodies are formed and bind to heparin-platelet factor 4 (PF4) complexes. Such an interaction triggers platelets activation and aggregation, and therefore leads to thrombocytopenia and thrombotic phenomenon in HIT. Patients who are using unfractionated heparin have an absolute risk of 2.6% to develop HIT, although the use of low-molecular-weight heparin may reduce the risk by ten-fold.¹ Among patients with acute coronary syndrome using heparin, a similar incidence rate of 1.6% is reported.² The occurrence is uncommon but the clinical consequence can be severe. Therefore heparin, being a substrate to cause HIT, should be discontinued in these

Address for reprints: Dr. Joe Kin-Tong Lee
Department of Medicine, Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chai Wan, Hong Kong

Email: jklee@gmail.com

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patients. However it is frequently compelling to continue anticoagulation for the initial indications of heparinization, for examples, in patients requiring haemodynamic support from intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation. Anticoagulation should also be continued in patients with HIT, as thrombosis prophylaxis or as treatment of established thrombosis if any. Different classes of anticoagulants other than heparin, including direct thrombin inhibitors (lepirudin, bivalirudin, argatroban), synthetic pentasaccharide (fondaparinux), and direct factor-Xa inhibitor (danaparoid) have been shown to be useful alternatives in such patients who are contraindicated to heparin.³⁻⁸ Unfortunately, these agents are not readily available in some parts of the world, including in our locality. We report the use of dabigatran, an oral direct thrombin inhibitor (DTI), as an alternative anticoagulant in a patient on IABP who developed isolated HIT after administration of low-molecular-weight heparin. To our knowledge, the clinical evidence describing the use of dabigatran in patients with HIT is scarce. Dabigatran may have both advantages and disadvantages over other anticoagulants in managing patients with HIT.

Case Report

A 70-year-old man was admitted to the hospital for anterior ST elevation myocardial infarction, with the presenting symptom of chest pain. He developed an episode of witnessed cardiac arrest due to ventricular fibrillation in the Emergency Department and the arrhythmia was promptly aborted by external defibrillation. The patient developed shock with blood pressure of 77/62 mmHg. He was also intubated and mechanically ventilated for respiratory failure. Electrocardiogram showed sinus rhythm and 2 mm ST segment elevation over the anterior chest leads. Severe pulmonary congestion was noted on chest X-ray. The patient was started on dopamine and an IABP was inserted for haemodynamic support. An urgent coronary angiogram showed a total thrombotic occlusion at the left main coronary artery. Primary PCI was performed, with a drug-eluting stent implanted to

the left main artery. In view of the high thrombus load, a bolus dose of intra-coronary eptifibatide was given, followed by intravenous infusion over the next 24 hours. The patient was started on double antiplatelet agents, by loading aspirin 320 mg and clopidogrel 600 mg, followed by regular doses of aspirin 80 mg daily and clopidogrel 75 mg daily. He was also started on intravenous furosemide for diuresis, intravenous amoxicillin-clavulanate for possible secondary chest infection, intravenous ranitidine as prophylaxis for stress peptic ulcer, and subcutaneous tinzaparin 12,000 anti-Xa units every 24 hours (based on the patient's body weight 63 kg) as anticoagulant for the IABP. Subsequent blood tests showed a sudden and remarkable drop of platelet counts, from $166 \times 10^9/L$ on admission, to a trough level of $59 \times 10^9/L$ on the fifth day of hospitalization (Figure 1). The red and white cell counts, prothrombin time and activated partial thromboplastin time (aPTT) were unremarkable. His renal function was normal, with creatinine level of 63 $\mu\text{mol/L}$ (estimated creatinine clearance 85.8 mL/min). Such a late drop of platelet counts was considered unlikely due to IABP-related thrombocytopenia or the use of glycoprotein IIb/IIIa inhibitor. Because of the timing (on day 5 after the administration of low-molecular-weight heparin) and the degree of drop in platelet counts (more than 50% drop than baseline level) with no obvious alternative explanation, a diagnosis of isolated HIT was suspected. Clinically there was no overt bleeding, skin necrosis or thromboembolic event, although doppler ultrasound had not been performed to detect any clinically silent deep vein thrombosis. The 4T's score for HIT was 5 (2 points for **thrombocytopenia**, 2 points for **timing of platelet count fall**, 0 points for **thrombosis or other sequelae**, 1 point for **other causes for thrombocytopenia present**, as the use of IABP and eptifibatide may cause thrombocytopenia but less likely in this case), indicating the intermediate probability of HIT.⁹ Functional assay for platelet activation, or immunoassay for heparin-PF4 antibodies were not performed as confirmatory tests because they were not readily available in our hospital. Therefore tinzaparin was taken off and dabigatran (PRADAXA®, Boehringer Ingelheim, Germany) 110 mg was given every 12 hours via the feeding tube

as an alternative anticoagulant for the IABP. Clotting profile was checked 4.5 hours after initiation of dabigatran and the aPTT prolonged from the baseline 24 seconds to 42 seconds (reference: 24-38 seconds), which was believed due to the anticoagulation effect from dabigatran. The aPTT remained prolonged in the

following few days when the patient was still on dabigatran. The continuous heparin saline flush through the IABP was also switched to normal saline. The platelet counts gradually improved and normalized on the fifty day after putting on dabigatran. The patient showed clinical improvement and was able to wean off

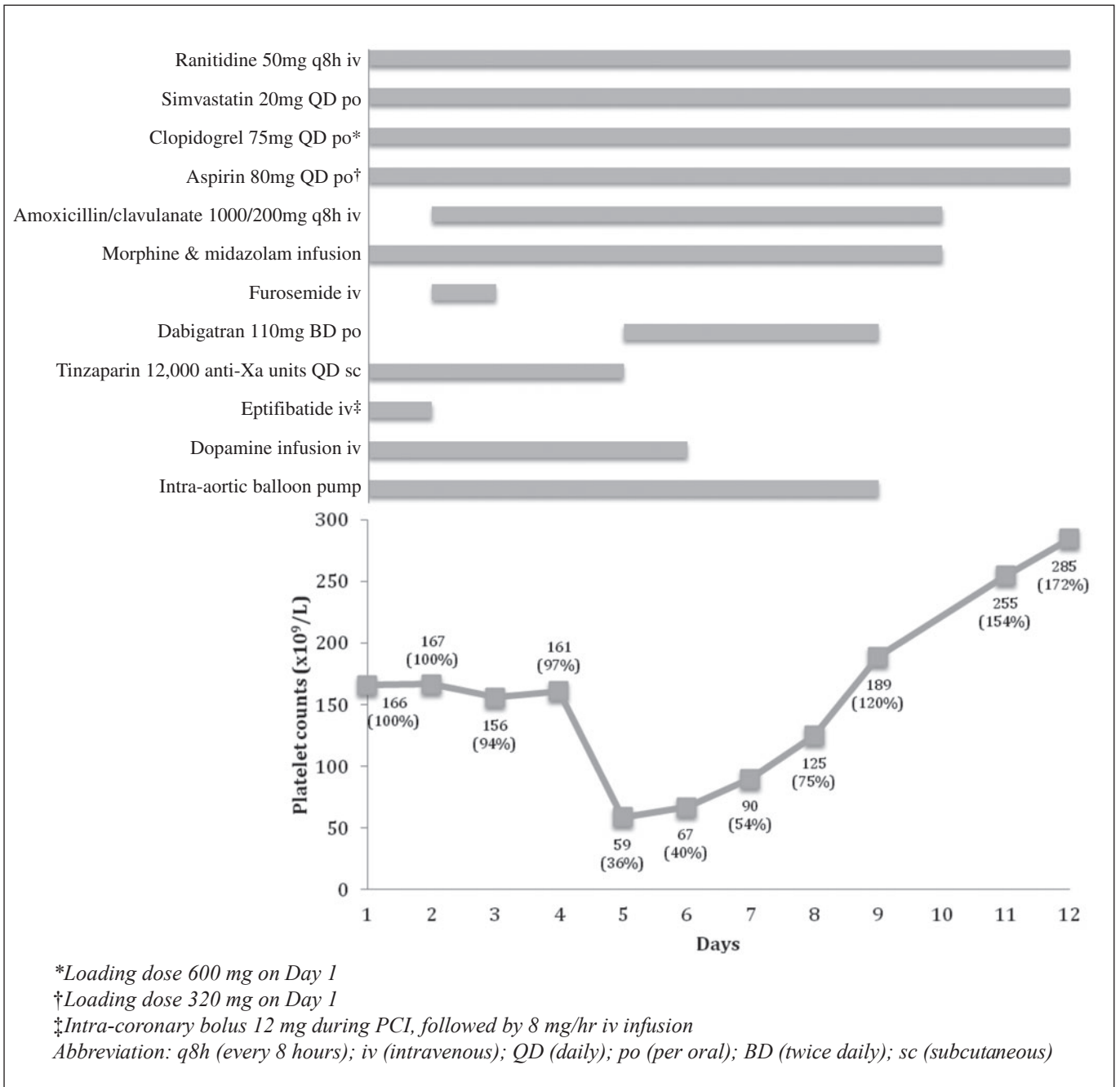


Figure 1. The list of medications administered, in conjoint with the trend of platelet counts in the first 12 days of hospitalization.

the IABP on day 9. Dabigatran was stopped once the IABP was taken off. Further anticoagulation was not contemplated, in view of absence of clinical thrombotic event and the bleeding risk associated with the concomitant use of double antiplatelet agents after implantation of a drug eluting stent. He was wean off the mechanical ventilation soon afterwards. He made good progress in rehabilitation and was discharged after 32 days of hospitalization. No clinical thrombotic event was noted during the disease course and recovery period.

Discussion

Non-heparin anticoagulants, including lepirudin, bivalirudin, argatroban, fondaparinux, and danaparoid, are used to treat HIT. However there is not much clinical evidence describing the use of novel oral anticoagulants for this indication. Fieland and Taylor have reported the use of dabigatran for stroke prevention in a patient with non-valvular atrial fibrillation who developed thrombocytopenia after coronary artery bypass graft surgery. The patient was subsequently found to have heparin-PF4 antibodies.¹⁰ However the clinical diagnosis of HIT in this case was not established, in view of the absence of thrombotic event, low probability of HIT as defined by the 4T's score, and the possible confounding effects on thrombocytopenia and heparin-PF4 antibodies by cardiopulmonary bypass.¹¹ In our case report, we describe the use of dabigatran as an alternative anticoagulation regimen in a patient with clinically diagnosed isolated HIT and yet required ongoing anticoagulation for the IABP. We endorsed the 110 mg twice daily dosage as we took reference from the RELY trial that this dosage was non-inferior to warfarin for stroke prevention in patients with non-valvular atrial fibrillation.¹² We avoided the 150mg twice daily dose in view of the bleeding risk associated with the concomitant use of double antiplatelet agents. Another reason to use the 110 mg, instead of 150 mg, twice daily dose is that administration of crushed dabigatran pellets without the capsule shell increases the oral bioavailability by 75%, which can precipitate bleeding complication.¹³ For this reason the manufacturer advises against taking the drug with the capsule broken, chewed

or opened. We still decided to give crushed dabigatran pellets via the feeding tube in this patient because we were left with no treatment option, as those non-heparin parental anticoagulants were not available in our unit.

Dabigatran has the properties of reversible, rapid and selective inhibition of thrombin. It is rapidly absorbed from oral route and once absorbed, the pro-drug dabigatran etexilate is converted to the biologically active form dabigatran. Dabigatran is approved for the use of stroke prevention in non-valvular atrial fibrillation, and deep vein thrombosis prophylaxis after orthopaedic surgery.^{12,14} We believe that dabigatran, being an univalent DTI, can act like other parenteral DTIs to exert an anticoagulation effect, and at the same time not precipitating or aggravating the pathological process of HIT. It is supported by the fact that the molecular structures of dabigatran and other parenteral DTIs are dissimilar to that of heparin, making the DTI unlikely to form complexes with PF4 and then to trigger platelet activation. The parenteral DTIs have not been shown to cause the pathological processes of HIT.¹⁵ Similarly, a recent in-vitro study also demonstrated that dabigatran does not potentiate the interactions of PF4 or anti-heparin-PF4 antibodies with platelets, supporting its practical use in patients with acute or history of HIT.¹⁶

Compared with other non-heparin anticoagulants which have established roles in HIT, dabigatran has several potential advantages: dabigatran has predictable pharmacokinetic and pharmacodynamic profiles, and at the same time it provides therapeutic anticoagulation effect with large safety margin.¹⁷ Therefore it can be taken with a fixed dosage, and blood tests for the purpose of drug titration is non-essential for approved indications. The property of reversible binding to thrombin may also provide a better side effect profile when compared with other DTIs with irreversible thrombin binding, such as lepirudin. DTI with reversible thrombin binding leaves a small amount of free, enzymatically active thrombin available for control of haemostasis.^{17,18} The better risk-benefit ratio is seen in an experimental model, in which melagatran, also a reversible thrombin binder, provides a lower bleeding risk than irreversible thrombin binder hirudin.¹⁹ Nevertheless, an effective antidote of dabigatran has not yet been established. On-going anticoagulation for

certain duration is usually required after the initial thrombocytopenic phase in HIT, and these patients are usually managed by switching the parental anticoagulants to warfarin. The use of dabigatran can omit this medication transition, and at the same time offering benefit over warfarin by not requiring drug titration.

For dabigatran being a drug in oral preparation, the alterations of pharmacokinetics in critically ill patients may make it less effective. Reduced gut motility and diminished gastrointestinal tract perfusion due to blood shunting occur in patients who are critically ill, in shock or using inotropes. In general, such physiological responses impede drugs absorption from the gastrointestinal tract, and therefore lead to a delay in achieving peak serum concentration, and possibly lower total drugs exposure, i.e. smaller area under curve for time and drugs concentration.²⁰ As dabigatran is administered twice daily, the trough plasma drug level and therefore its anticoagulation effect are particularly vulnerable to reach the subtherapeutic range when drug absorption is impeded. In contrast, such a phenomenon is less likely to occur in most of the parental anticoagulants used for HIT treatment, which are administered by continuous infusion with titration of dosage according to the clotting profile. Acute kidney injury is not uncommon in these critically ill patients and can lead to diminished renal clearance of dabigatran, which in turn increases the risk of adverse drug effects such as bleeding. Although there is a lack of study working specifically on the dabigatran pharmacokinetics in critically ill patients, we may have some clues from studies investigated on subjects who have undergone orthopaedic surgery and have received dabigatran as prophylaxis for deep vein thrombosis. The postoperative physiological changes may resemble that of a critically ill patient to some extent: Lower peak plasma dabigatran level and a delay in reaching the plasma peak level are found during the early postoperative period, when compared with the healthy control subjects.^{21,22} Such findings are considered due to reduced gastric motility and gastric pH following surgery. We had not checked the plasma dabigatran level or the ecarin clotting time in our case to confirm adequate drug absorption and therapeutic anticoagulation effect during the critically

ill status. Having acknowledged the limitation of non-linear relationship between aPTT and plasma dabigatran level, we believe certain anticoagulation effect had been exerted as suggested by the prolonged aPTT.

Eptifibatide can also cause thrombocytopenia. The incidence of eptifibatide-induced moderate thrombocytopenia ($<100 \times 10^9/L$) is 3.8%, while severe thrombocytopenia ($<50 \times 10^9/L$) occurs uncommonly, with an incidence of 0.6%.²³ In the presented case, eptifibatide had been used on day 1 and 2, and the onset of thrombocytopenia was on day 5. The use of eptifibatide was unlikely the cause of thrombocytopenia, as glycoprotein IIb/IIIa inhibitors-induced thrombocytopenia occurs early, typically within 24 hours from the initiation of treatment. The use of IABP is commonly associated with thrombocytopenia. It appears that the occurrence of thrombocytopenia is independent of the use of heparin, but instead the mechanical force of IABP takes into account.²⁴ IABP-related thrombocytopenia usually takes place right after the administration of IABP and the platelet counts drop gradually to a nadir on day 3 to day 4.²⁴⁻²⁶ In our reported patient, the pattern of stable platelet counts initially with a sudden drop on day 5 was more compatible with HIT instead of IABP-related thrombocytopenia. Although the use of beta-lactam antibiotic can also cause thrombocytopenia, the normalized platelet counts despite continuation of amoxicillin-clavulanate rejected the diagnosis of antibiotic-induced thrombocytopenia. We did not performed any functional or antibodies assay to ascertain the immune-mediated mechanism of HIT, as patients having non-immune-mediated HIT (type 1) usually do well when heparin is continued and need not to have alternative anticoagulant. Nevertheless, the molecular dissimilarity of dabigatran with heparin, and the results of in-vitro molecular studies make dabigatran a potential option in patients with HIT.^{15,16} More clinical studies are required to prove its efficacy and safety in HIT.

Conclusion

Several alternative anticoagulants have established their roles in treating patients with HIT, but

the drug supplies are not always available. The novel oral DTI dabigatran has structural dissimilarity to heparin. Its lack of interaction in the pathological process of HIT make it a feasible option in treating patients with HIT and a need of ongoing anticoagulation. Because of its pharmacokinetic and pharmacodynamic properties, dabigatran has both potential advantages and disadvantages to the other anticoagulants.

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Hong Kong College of Cardiology



Twenty-first Annual Scientific Congress

June 7-June 9, 2013

**Sheraton Hong Kong Hotel and Towers
Hong Kong**

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Scientific Programme

Friday, 7 June 2013

0800	4/F	Registration	
0900-1100	Ching Room	Free Paper Session Percutaneous Coronary Intervention Ischemic Heart Disease and Atherosclerosis	
	Ming Room II	EPS, Cardiac Arrhythmia and Pacing + Cardiac Surgery	
1100-1130	Terrace of Sung Room	Coffee Break & Visit Exhibits	
1130-1300	Ching Room	Free Paper Session Structural and Congenital Heart Diseases Cardiac Imaging, Heart Failure and Cardiac Rehabilitation	
	Ming Room II	Miscellaneous	
1300-1430	Terrace of Sung Room	Light Lunch	
1430-1530	Ballroom C	Best Paper Oral Presentation	
1530-1600	Ballroom C	Plenary Lecture Engineering a Bioresorbable Vascular Scaffold	Ashleigh Z Sheehy (USA)
1600-1630	Terrace of Sung Room	Coffee Break & Visit Exhibits	
1630-1815	Ballroom C	Cross-straits PCI Symposium 1. Contrast Induced Nephropathy 2012 Updated 2. Overview of Retrograde CTO Technique 3. Research Status and Perspective of CT-FFR 4. RCA is Totally Occluded, and I Cannot Engage It - Case Discussion	Ben He (China) Jason Ko (HK) Ya-wei Xu (China) Hung-taw Yi (Taiwan)
1830-1845	Ballroom C	Opening Ceremony	
1845-1945	Ballroom C	Hong Kong Heart Foundation Lectures 1. Trends of Serum Lipid Levels in Shanghai Population, China 2. China CVD Prevention and Rehabilitation: Status and Challenges	Hao-zhu Chen (China) Dayi Hu (China)
1945-2115	Ballroom A&B	Welcome Dinner	

Saturday, 8 June 2013

0800 3/F Registration

0830-1230 **Ballroom C** **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)

1. Alcohol Septal Myocardial Ablation For Hypertrophic Obstructive Cardiomyopathy: A Case Report and Experience from Fuwai Hospital
Fuwai Hospital CAMS & PUMC 阜外心血管病醫院 Jian-song Yuen
袁建松
2. Successful TAVI in a Lady with Radiation-induced Aortic Stenosis and Porcelain Aorta
Cheng Hsin General Hospital 臺灣振興醫院 Wei-hsian Yin
殷偉賢
3. A Patients with Benign Metastasizing Leiomyomatosis
Guangdong General Hospital 廣東省人民醫院 An-ping Cai
蔡安平
4. A Weird Left Main Disease
Zhongshan Hospital Xiamen University 廈門中山醫院 Yan Wang
王焱
5. Double Dislodged Stents
Queen Elizabeth Hospital 伊利沙伯醫院 Kam-tim Chan
陳鑑添
6. A Patients with Pericardial Effusion
Shanghai Tenth People's Hospital 上海市第十人民醫院 Ya-wei Xu
徐亞偉
7. Neurocognitive Improvement after Endovascular Recanalization in a Patient with Carotid CTO and Repeated TIA
National Taiwan University Hospital 台大醫院 Mao-hsin Lin
林茂欣
8. The ECG, Coronary Picture and Management in Protamine induced Anaphylactic Shock: A Case Report
Fuwai Hospital CAMS & PUMC 阜外心血管病醫院 James SM Yeh
葉學明
9. The Disturbance of the SVG
The First Affiliated Hospital of Harbin Medical University
哈爾濱醫科大學第一附屬醫院 Wei-min Lin
李為民
10. A Patient with Heart Failure and Frequent Premature Ventricular Contractions
Peking University Third Hospital 北京大學第三醫院 Fei She
佘飛
11. Revascularization Strategies of Multivessel Coronary Artery Disease
Conde S. Januario General Hospital 澳門山頂醫院 Jie Zhao
周傑
12. A Case with Intramural Hematoma after PCI
Guangdong General Hospital 廣東省人民醫院 Wen-hui Huang
黃文輝

0930-1200	Ballroom A&B	Allied Cardiovascular Health Professionals Symposium Cardiopulmonary Resuscitation 2013	
		1. Update and Overview of Advanced Cardiac Life Support (ACLS)	Andy WK Chan (HK)
		2. Common Misconceptions of Airway Management	Ming-chi Chu (HK)
		3. Resuscitation Pharmacology that You Must Know	Man-chun Choi (HK)
		4. Resuscitation Procedures (Emergency Pericardiocentesis, Chest Tapping.....etc)	Kwok-tung Ho (HK)
1230-1415	Ballroom C	HKCC Live in China (Shanghai - Nanjing - Hangzhou) Interactive Live Transmission Session (Sponsored by AstraZeneca Hong Kong Ltd) Lunch will be provided	
		1. ACS Treatment Status	Ji-yan Chen (China)
		2. Case Sharing 1 from Shanghai - Clopidogrel Resistance	Min Fan (China)
		3. Case Sharing 2 from Nanjing - Primary PCI	Jianbing Gong (China)
		4. Case Sharing 3 from Zhengjiang - ACS High Risk Patient	Cheng Zong (China)
		5. Update of ACS Management from International Guidelines to Clinical Practices	Vincent OH Kwok (HK)
1430-1530	Ballroom	7th Congregation of HKCC Guest-of-Honour: Dr. Wing-man Ko Secretary for Food and Health, HKSAR	
1530-1630	Ballroom C	Medtronic Symposium	
		1. Renal Denervation: The Latest or the Safest	Tony Walton (Australia)
		2. Simplified the Challenge of Unplanned DAPT Interruption	
1630-1730	Ballroom C	Takeda Pharmaceuticals Symposium	
		1. High Blood Pressure, Towards Optimal Control: What are the Current Opportunities?	Alan Gradman (USA)
		2. Diabetes Close to Our Heart: Cardiovascular Diseases in Diabetic Patients	Norman Chan (HK)
1730-1800	Ballroom C	Plenary Lecture Management of Hyponatraemia in Acute Heart Failure	Gordon Moe (Canada)
1800-1830	Terrace of Sung Room	Coffee Break & Visit Exhibits	
1830-1930	Ballroom C	Evening symposium	
		1. The History of Cardiac Pacing: The Australian Contribution	Harry Mond (Australia)
		2. Transradial VS Transfemoral Approach for Rotablation	Wei-hsian Yin (Taiwan)
1930-2100	Ballroom A&B	Dinner	

**Coffee break will be served from at 10:30 - 11:10 & 18:00 - 18:30 at 4/F of Sung Terrace.*

Sunday, 9 June 2013

0800	3/F	Registration	
0900-1100	Ballroom C	PCI Cases Discussion Prize Presentation	
1100-1130	Terrace of Sung Room	Coffee Break & Visit Exhibits	
1130-1400	Ballroom C	Plenary Lectures	
		1. Experience of Antiplatelet for ACS-PCI Patients in Korea (Interactive Live Transmission)	Joo-yong Hahn (Korea)
		2. Dual Therapy Stent: Why is There a Need	Rosli Mohd Ali (Malaysia)
		3. The Beacon II Registry-4 Year Outcomes in an Asian Patient Population	Tian-Hai Koh (Singapore)
		4. Stroke Prevention for Non-valvular AF 2013	Yat-yin Lam (HK)
		5. DPP-4 Inhibition: Similarities & Differences	Peter CY Tong (HK)
1400-1530	Ballroom A&B	Lunch	
1530-1700	Ballroom C	Transcatheter Valvular Intervention Symposium	
		1. Difficult TAVI Cases and Complications	Tony Walton (Australia)
		2. TAVI - QEH Experience	Michael KY Lee (HK)
		3. From EVEREST to the Real World	Phil Wray (Australia)
1700-1730	Terrace of Sung Room	Coffee Break & Visit Exhibits	
1730-1910	Ming II	EP Symposium: Sudden Cardiac Death	
		1. Introduction to The HK Jockey Club "Heart-safe School" Project	Chris KY Wong (HK)
		2. Sudden Cardiac Death in Hong Kong - An Overview	Kathy LF Lee (HK)
		3. Diagnostic Workup for Sudden Cardiac Death	Andy WK Chan (HK)
		4. Treatment Update for Sudden Cardiac Death	Gary CP Chan (HK)
1910-2045	Sung Room	Farewell Dinner	

Paediatric Cardiology Programme

0845-1040	Ching Room	Paediatric Cardiology Symposium I	
		1. Arrhythmias in Repaired TOF	Mei-hwan Wu (Taiwan)
		2. The Follow Up Study on Patients with Eisenmenger Syndrome	Hong Gu (China)
		3. Difficult Points about Interventional Therapy for ASD	Hui-shen Wang (China)
		4. Echocardiographic Assessment of Right Ventricular Function in Congenital Heart Disease: A Practical Approach	Yiu-fai Cheung (HK)
		5. Outcome Evaluation and Database Registration for Congenital Heart Surgery in Hong Kong	Xin Li (HK)
		6. Intrauterine Fetal Cardiac Intervention on Near-term Fetal Goat Model	Kai-yu Zhou (China)
1040-1110	Terrace of Sung Room	Coffee Break & Visit Exhibits	
1110-1215	Ching Room	Free Paper Session Paediatric Cardiology I	
1230-1415	Ballroom	HKCC Live in China <i>Lunch will be provided</i>	
1430-1530	Ballroom	7th Congregation of HKCC Guest-of-Honour: Dr. Wing-man Ko Secretary for Food and Health, HKSAR	
1530-1725	Ching Room	Paediatric Cardiology Symposium II	
		1. Paediatric Tachyarrhythmias: Treatment Strategy	Mei-hwan Wu (Taiwan)
		2. The Percutaneous Intervention of Non-PDA Congenital Heart Disease Using New Amplatzer Duct Occluder (ADO 2)	Fen Li (China)
		3. Strategy and Technique of Transcatheter closure of Ventricular Septal Defect in Young Children	Zhi-wei Zhang (China)
		4. Pediatric Acute Fulminant Myocarditis Supported by Extracorporeal Membrane Oxygenation	Kin-shing Lun (HK)
		5. Chronic Pulmonary Regurgitation - When Should We Intervene?	Flora Tsang (HK)
		6. Device Closure of Coronary Artery Fistula: Outcome and Review	Fang Liu (China)
1725-1800	Ching Room	Free Paper Session Paediatric Cardiology II	
1800-1830	Terrace of Sung Room	Coffee Break & Visit Exhibits	
1830-1900	Ching Room	Free Paper Session (Con't) Paediatric Cardiology II	

ABSTRACTS

Abstracts for Free Paper Session:

PERCUTANEOUS CORONARY INTERVENTION

Adiponectin Profile in Asian Patients Undergoing Coronary Revascularization and Its Association With Culprit Lesion Necrotic Core Content: Results From the IDEAS-ADIPO Study

Chi-Hang Lee,^{*,†} William K.T. Hau,^{*,#} Bee-Choo Tai,[‡] Mark Y Chan,^{*,‡} Betty Saw,[‡] Qian-Hui Phua,^{*} Adrian F Low,^{*,‡} Tiong-Cheng Yeo,[‡] A Mark Richards,^{*,‡} Huay-Cheem Tan[‡]
^{*}Department of Medicine, National University of Singapore, Singapore; [‡]Cardiac Department, National University Heart Centre, Singapore; [‡]Department of Epidemiology and Public Health, National University of Singapore, Singapore; [†]Department of Laboratory Medicine, National University Health System, Singapore; [#]Institute of Cardiovascular Medicine and Research, LiKaShing Faculty of Medicine, The University of Hong Kong, Hong Kong

Purpose: Adipose tissue is an active endocrine system, and it plays a pivotal role in regulating metabolic and vascular homeostasis through secretion of several biological mediators, collectively known as adipokines. Adiponectin is an adipokine with potent insulin-sensitizing, anti-inflammatory, and antiatherogenic effects demonstrated in animals. Yet the relations between serum adiponectin levels and coronary artery disease in patients remain unclear.

Methods: Ninety-four Asian patients (Chinese, 61; Malay, 18; Indians, 12; other, 3; body mass index, 25.3±3.7 kg/m²) undergoing percutaneous coronary intervention were recruited. The serum adiponectin level was measured, and the baseline virtual histology intravascular ultrasound (VH-IVUS) examination was performed.

Results: The median level of adiponectin was 3.7 µg/mL (interquartile range, 2.8 to 4.5 µg/mL). The serum adiponectin level was below 10 µg/mL in 90 patients (95.7%) and below 6µg/mL in 80 patients (85.1%). There was a significant association between ethnicity and serum adiponectin level (P=0.048). The median adiponectin level was highest among the Chinese, followed by the Malay and the Indians. Serum adiponectin levels were positively associated with culprit lesion necrotic core content. A per µg/mL increase in log adiponectin was associated with a 3.04% (95% CI: 0.33-5.44) increase in culprit lesion necrotic core content. This association remains significant after adjusting for age, sex, ethnicity, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and procedural indication.

Conclusion: We found a low serum level of adiponectin in Asian patients and a significant ethnic effect on serum adiponectin level. Increased serum adiponectin levels were independently associated with increased culprit lesion necrotic core burden, suggesting a role for adiponectin in modulating coronary plaque vulnerability.

Outcome of Radial Approach in Primary PCI - A Local Centre Experience

Sunny CF Tsang; YW Cheng; CK Kwok; WS Kwan; NH Luk; SF Chui; CY Wong; LK Chan; YH Cheng; HS Ma; LY Tam; CL FU; CW Chan; KY Lee; KC Ho; KT Chan; CS Chiang.

Queen Elizabeth Hospital, Hong Kong SAR, China.

ABSTRACT: Background. Transradial primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI) has been shown by various studies to be effective when compared with transfemoral approach. **Aim and Methods.** This is a retrospective analysis of clinical outcomes in a registry of STEMI patients treated by PPCI through the transradial approach from January 2011 to February 2013 in a regional hospital. **Results.** 44% (n = 37) of patients treated by PPCI were performed by transradial route, of which 92% (n = 34) were male. 6 patient treated with PPCI were in shock at the time of procedure (16%). 3 of the transradial approach failed and had to switch to transfemoral route (8%). 3 cases required IABP support (3%). Mortality in 30 days was 3% (n = 1). The average door-to-balloon time was 82.2 minutes. Average length of hospital stay was 6.5 days. Bleeding occurred in 5% (n = 2), none of which were related to access site. **Conclusion.** Transradial approach is a feasible, safe and effective means in primary PCI in the management of STEMI.

Role of platelet reactivity test in management of stent thrombosis related to target lesion after percutaneous coronary intervention (PCI)

Y.W. Cheng, C.F. Tsang, C.K. Kwok, N.H. Luk, S.F. Chui, W.S. Kwan, Y.H. Cheng, K.C. Chan, L.K. Chan, H.S. Ma, C.Y. Wong, L.Y. Tam, C.L. Fu, C.W. Chan, K.Y. Lee, K.C. Ho, K.T. Chan, C.S. Chiang
 Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR, China

Purpose:

Many factors can result in stent thrombosis. High on-treatment platelet reactivity (OTR) after percutaneous coronary intervention, defined as OTR ≥230 P2Y12 reaction units with the VerifyNow P2Y12 platelet function test, had been identified as one of the important factors. Routine platelet reactivity test is not yet recommended for all patients undergoing PCI. This study aims to analyze the prevalence of High on-clopidogrel platelet reactivity in patients with clinical syndromes or angiographic feature compatible with stent thrombosis and assess the outcome of management.

Methods:

A retrospective review of all patients undergoing Platelet reactivity test with the VerifyNow test between January 2011 and April 2013 in Queen Elizabeth Hospital was performed. Patients with clinical syndromes or angiographic feature compatible with stent thrombosis were identified. Repeat coronary intervention and management outcome was analyzed.

Result:

A total of 27 patients, 20 male (74.1%) and 7 (25.9%) female, with a mean age of 59.9 ± 9.9 were identified. The majority (48.1%) presented as STEMI and 33.3% presented with NSTEMI/UA. 17 (63%) of them were having stent thrombosis in LAD. For LM, LCx and RCA stent, it involved 1 (3.7%), 3 (11.1%) and 6 (22.2%) patients respectively. 22 (81.5%) were having drug eluting stent (DES) implanted and 5 (18.5%) for bare metal stent (BMS). The stent thromboses were of subacute, late and very late type in 18.5%, 29.6% and 51.9% respectively. 17 of them (63%) were identified as high OTR with mean PRU value of 297 ± 54.2. Of those who had high OTR, 1 of them was treated with increased dose of aspirin and clopidogrel, 3 of them had cilastazol added. 11 of them finally received either Prasugrel or Ticagrelor. The majority of them had another DES implanted (58.8%), 2 had Drug eluting balloon (DEB) (11.8%) and 2 received CABG (11.8%) as revascularization strategy for the target lesion. There was no major bleeding. Only 1 had minor bleeding from hemorrhoid. 2 of these patients had developed major adverse cardiac event (MACE) and 1 of them died.

Conclusion:

There were a high percentage of patients having clopidogrel resistance in this cohort of stent thrombosis patients. Point-of-care testing of clopidogrel response in highly selected patients could be useful to help us optimize their clinical management with alternative anti-platelet agent or escalate dose of anti-platelet agent.

Characteristics and outcomes of patients with percutaneous coronary intervention for unprotected left main coronary artery disease

Ka-Yip Lo, Tsz-Ki Lau, Chun-Yue Mui, Chi-Kin Chan

Aims: Unprotected left main coronary artery (ULMCA) percutaneous coronary intervention (PCI) is increasingly performed nowadays. And yet, limited local data is available on the medium-term outcomes.

Methods and Results: In this single-center registry evaluating outcomes among patients with ULMCA disease undergoing stenting with bare-metal stents (BMS) or drug-eluting stents (DES) between January 2008 and September 2011, 111 patients were included. 86 patients received DES (77.5%) and 25 cases BMS (22.5%). Procedural success was achieved in 98.1% of cases. Angiographic follow-up was available in 83.8% and restenosis was significantly lower with DES (14% versus 40%; P=0.004). After a mean clinical follow-up of 26.1±12.6 months, the incidence of cardiac death (5.8% versus 16%; p=0.191) or nonfatal myocardial infarction (MI) (3.5% versus 8%; p=0.262) was similar between DES and BMS. However the risk of target lesion revascularization (TLR) (9.3 versus 32%; p=0.001) and major adverse cardiac and cerebrovascular events (MACCE) (19.8% versus 44%; p=0.004) were significantly lower with the use of DES than BMS.

Conclusions: Performing PCI to ULMCA disease was safe and feasible in selected patients with high procedural success. The incidence of MACCE in patients receiving DES remains low after a medium follow-up. Compared with BMS, DES was associated with a reduction in the need for repeat revascularization without increasing the risk of death or MI for patients with ULMCA disease.

ABSTRACTS

Abstracts for Free Paper Session:

PERCUTANEOUS CORONARY INTERVENTION

Analysis of Patient Characteristics and Door-to-Balloon Time for Primary Percutaneous Coronary Intervention in an Acute District Hospital in Hong Kong

YK Lau, Danielle Lee, KK Keung, KL Lee, Jaeky Chan, Thomas Tunggal, Andrew Li, C Y Yung, Jessica Poon, F H Ng, Ruttonjee Hospital, Hong Kong.

Purpose: Primary percutaneous coronary intervention (PCI) with a door-to-balloon (DTB) time of ≤ 90 minutes (min) significantly reduces mortality and morbidity of ST-elevation myocardial infarction (STEMI). We aimed to evaluate local patient characteristics and our performance in Primary PCI to strive for improvement.

Methods: We conducted a retrospective review for all patients with STEMI who underwent Primary PCI between 1 January 2011 and 30 April 2013. Patients' initial presentations, DTB times and relevant time intervals were obtained and analyzed.

Results: During this period, 76 emergency PCI (defined as immediate PCI for STEMI, failed lytic or ACS with refractory ischemia & shock) were performed. 43 patients received primary PCI for STEMI. Among those, the majority was male (86%). Mean age was 62 (range 44-83). 53% (23) of patients were brought in by ambulance, 35% (15) by self-transportation. 12% (5) developed STEMI while in hospital. Chief complaints were chest pain/discomfort in 77% of patients (33), syncope and dizziness in 14% (6), abdominal or back pain in 7% (3), and anemic symptom in 2.3% (1). Cardiac arrest/ventricular fibrillation occurred in 8 patients (19%) prior to PCI, with 2 occurring prior to arrival to A&E. Another 9 patients (21%) presented with cardiogenic shock or profound hypotension. The DTB time was within 90 min in 72% (31) & within 120 min in 93% (40) of patients. Mean DTB time was 86.3 min. Three patients had DTB time over 120 min (related to atypical presentation, subtle ECG change, and tortuous coronary anatomy respectively). In-hospital MACE was 4.7% as two patients died within a few hours from presentations despite successful PCI. 41 of 43 patients (95%) were well and discharged home shortly. Patients assigned into lower priority categories at A&E had a progressively longer mean DTB time. Compared to those with DTB time ≤ 90 min, those exceeded 90 min had significantly longer A&E arrival to ECG time [median (interquartile range) 4.5 (8.5) min vs 10.5 (7) min, $p=0.011$], ECG to cardiac consult time [10 (8.5) min vs 27 (17) min, $p<0.001$], and local anesthesia (LA) to balloon time [17 (6) min vs 22.5 (12) min, $p=0.049$]. When comparing an earlier cohort (January 2011 to April 2012, 22 patients) to a later cohort (May 2012 to April 2013, 21 patients), mean DTB time decreased from 91 min to 81 min, with a significant reduction in ECG to cardiac consult time [17 (18) min vs 8 (11) min, $p=0.017$] and start of LA to balloon time [19.5 (8.5) min vs 15 (7) min, $p=0.008$].

Conclusion: Our Primary PCI program achieved DTB time ≤ 90 min in 72% of patients, and a mean DTB time of 86.3 min, with a temporal trend of improvement. Identification of the local characteristics of patient presentations and factors in delay may help further shorten our DTB time.

ABSTRACTS

Abstracts for Free Paper Session:

ISCHEMIC HEART DISEASES & ATHEROSCLEROSIS

Trends of Serum Lipid Levels in Shanghai Population, China

Chen Haozhu, Jin Xuejuan, Chen Yunqin, Zhou Jun
Shanghai Institute of Cardiovascular Disease, Zhongshan Hospital, Fudan University, Shanghai, China

Purpose: This study assessed 36-year trends in serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG) and TC/HDL-c ratio in Shanghai healthy resident aged from newborn to 80 years old.

Methods: Five independent, cross-sectional, population-based surveys of all age groups were conducted in the Shanghai, 1973-1974 (n=1385), 1982 (n=3302), 1983 (n=2399), 1997-1999 (n=3205), and 2008-2009 (n=2397).

Results: Mean total cholesterol concentrations increased significantly between 1982-1983 to 1997-1999. Fortunately, the upward trend stopped between 1997-1999 to 2008-2009, and small but significant declines in the prevalence of hypercholesterolemia in both men and women. The mean prevalence of hypercholesterolemia in 2008-2009 was 11.2% for women and 8.6% for men in age >40 groups, while in 1997-1999 were 16.02% and 11.57%, respectively. As for LDL-c and TC/HDL-c ratio, the majority trends were similar to those of total cholesterol. On the other hand, both women and men aged more than 20 years have shown significant linear upward trends in mean serum triglyceride concentrations across the whole study period, especially in the most recent period (all P value for linear trend<0.0001). Age-adjusted mean serum triglyceride among adults aged≥20 years old in 1973-1974, 1982-1983, 1997-1999 and 2008-2009 were 75, 80, 82, 101 mg/dl respectively in women, while in men, were 74, 83, 99, 139 mg/dl, respectively. Greater and significant decreases were observed in both men and women for the mean HDL-c concentrations during the period from 1982-1983, 1997-1999, however, these favorable trends did not continue in the most recent period, significant decreases in HDL-c concentrations in most age groups in both women and men were observed during the period from 1997-1999 to 2008-2009 (P<0.05).

Conclusions: Between 1990s and 2000s, favorable trends in total cholesterol levels have occurred among both women and men in China, while the significant upward trends were observed in triglyceride levels.

Serum Uric Acid correlates with Extracellular Superoxide Dismutase in early atherosclerosis

Wong Chun Kit Arthur, Chen Yan, Zhen Zhe, Tse Hung Fat, Yiu Kai Hang
Division of Cardiology, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR

Aim: Serum uric acid (UA) is related with vascular dysfunction. Its production by xanthine oxidase is increased during ischemia, along with increased superoxide free radicals generated. Superoxide reacts with nitric oxide to form peroxynitrite – a powerful oxidizing agent that mediates atherosclerosis. Extracellular superoxide dismutase (ecSOD), an enzyme produced predominantly by vascular smooth muscle cells, catalyses the removal of superoxide and reduces oxidative stress. Clinical evidence regarding how UA and ecSOD interact with each other is scarce. Our study investigates whether UA and ecSOD contribute to the underlying mechanism that leads to vascular dysfunction.

Methods: Study subjects were recruited through a local community health screening program. Cardiovascular (CVS) risk profile of each individual was carefully determined by collecting information regarding hypertension, diabetes, coronary artery disease (CAD), hyperlipidemia, obesity, smoking, age, gender and family history of CAD. Furthermore, all subjects received blood tests for UA, ecSOD, and renal function. Tests for vascular surrogate markers of atherosclerosis, including brachial flow mediated dilatation (FMD), GTN-induced dilatation (GTND), brachial ankle pulse wave velocity (ba-PWV), central-PWV and carotid intima media thickness (IMT) were also performed.

Results: A total of 631 patients (age=65.2±0.5, male=68.1%) with at least one CVS risk factor were recruited into the study. The number of subjects with ≤2 CVS risk factors (lower risk group) was 209 (33.1%). Comparing with subjects in the higher risk group (≥2 CVS risk factors), subjects in the lower risk group had a significantly higher FMD% (p<0.05) and GTND% (p<0.05). The arterial stiffness of the lower risk group was significantly less (p<0.001). The IMT was significantly greater in the higher risk group (p<0.05). In the lower risk group, serum UA level was shown to be significantly lower (p<0.001), while ecSOD level was shown to be significantly higher (p<0.001). Serum UA was inversely correlated with FMD% (r=-0.093, p=0.033) and GTND% (r=-0.241, p=0.001). Moreover, serum UA was positively related with ba-PWV (r=0.095, p=0.043) and IMT (r=0.147, p=0.001). Serum UA was also demonstrated to be inversely correlated with ecSOD in the group of subjects with the most preserved vascular function: (a) the tertile with highest FMD% (r=-0.233, p=0.017), (b) the tertile with lowest ba-PWV (r=-0.259, p=0.04), (c) the tertile with lowest central-PWV (r=-0.329, p=0.005)

Conclusion: The vascular function and arterial stiffness can reflect the CVS risk burden of an individual. Serum UA and extracellular SOD may serve as additional biomarkers for CVS risk profiling in this study population, reflecting the degree of oxidative stress. UA and extracellular SOD were significantly correlated in subjects with early stage of atherosclerosis or lower CVS risk profile, suggesting that the underlying mechanism for early atherosclerotic changes in vasculature may be mediated by UA and extracellular SOD, and have implications with oxidative stress-mediated cellular damage. More studies are required to further understand the pathogenesis of vascular dysfunction.

Comparing the prognosis of type B acute aortic intramural hematoma (IMH) and type B aortic dissection in a local Chinese population

Chui Ka Lung
Prince of Wales Hospital, Hong Kong

Methods: All patients with age >18, admitted for type B acute aortic syndrome during the period of Jan 2000 to Dec 2009 were included.

Results: There were total 86 cases of type B aortic dissection and 29 cases of type B intramural hematoma. All type B IMH and dissection were managed by medical therapy initially. The in-patient, 1 month, 3 months, 1 year, 3 years and 5 years survival for acute type B IMH were 100%, 100%, 100%, 94%, 86% and 77% respectively. Whereas in type B aortic dissection, the in-patient, 1 month, 3 months, 1 year, 3 years and 5 years survival were 87%, 85%, 81%, 61%, and 56%. A trend towards better outcome was observed in type B intramural hematoma, although the P value is not significant by Log-rank test (P=0.0889). Moreover, there are significantly more acute complications in type B aortic dissection when compared to IMH. In type B aortic dissection, there are 8 cases (9.3%) of rupture, 1 case (1.16%) of stroke, 1 case (1.16%) of lower limb ischemia, 5 cases (5.81%) of renal infarct, 1 case (1.16%) of bowel ischemia, 1 case (1.16%) of spinal cord ischemia and 1 case (1.16%) of splenic rupture. In type B IMH, there is only 1 case (3.44%) of spinal cord ischemia during that period of time. The P value is significant at 0.0398.

Conclusion: Acute type B IMH had a trend towards better survival than type B aortic dissection (P=0.0899 by Log-rank test). There is significant less acute complications related to end organ ischemia or rupture (P=0.0398).

High-frequency QRS Analysis is More Specific and Accurate Than Conventional ST-segment Analysis in Diagnosing Coronary Ischaemia

Ngai-Yin Chan, Hoi-Fan Chow, Ho-Chuen Yuen, Pui-Shan Chu, Suet-Ting Lau, Ping-Tim Tsui, Chi-Chung Choy, Chun-Leung Lau, Ying-Keung Lo, Ngai-Shing Mok
Department of Medicine & Geriatrics, Princess Margaret Hospital, Hong Kong

Purpose: High-frequency QRS analysis (HFQRS) is a new tool for detecting stress-induced coronary ischaemia. This study aims to compare HFQRS with conventional ST-segment analysis (STA) in the diagnostic performance in patients with chest pain and no history of coronary artery disease, which has not been investigated before.

Methods: One hundred and seventy-five patients (120 men; mean age 58.2±7.5) with chest pain referred for diagnostic workup of coronary ischaemia were recruited. They underwent symptom-limited exercise treadmill test with both HFQRS and STA, followed by myocardial perfusion imaging (MPI) to confirm presence or absence of ischaemia.

Results: Coronary ischaemia was present in 20 (11.4%) patients by MPI. HFQRS was more specific (85.8 vs 68.4%; p=0.002) and similarly sensitive (45 vs 60%; p=0.371) compared with STA. HFQRS had a higher positive predictive value (29 vs 19.7%; p=0.01) and similar negative predictive value (92.4 vs 93%; p=0.61) compared with STA. The diagnostic accuracy for coronary ischaemia by HFQRS was significantly higher than STA (81.1 vs 67.4%; p=0.001).

Conclusions: HFQRS is more specific and accurate than STA in diagnosing coronary ischaemia in patients with chest pain and no prior history of coronary artery disease.

ABSTRACTS

Abstracts for Free Paper Session:

ISCHEMIC HEART DISEASES & ATHEROSCLEROSIS

Evaluation of Mobile Phone-based Telemedicine System for Real-time Transmission of ECG in Patients with Acute ST-segment Elevation Myocardial Infarction in Coronary Care Unit Patients: An Observational Study

Xiao-lu Sun

Department of Cardiology, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, China

Objective: The aim was to investigate the clinical value of remote real-time electrocardiography monitoring system based on GPRS in patients with Acute ST-elevation myocardial infarction (STEMI).

Methods: All subjects were received the remote real-time ECG monitoring and the 12 leads ECG. The remote monitoring device collects electrocardiosignal to imitate V1, V3, and V5 lead and I lead. These electrocardiograms, which were printed during the monitoring and measured by an independent cardiovascular doctor to survey heart rate, the ECG profile uniformity, and ST segment, change amplitude and arrhythmic detection rate.

Results: Patients completed 88% of all practicable remote ECGs transmissions by themselves. A total of 658 remote ECGs were transmitted to telemonitoring system. In STEMI group, the electrocardiographic of the two groups has no statistical difference ($P>0.05$). The arrhythmic diagnose accordance rate show no difference ($P>0.05$). The ST segment elevates amplitude also show no difference ($P>0.05$) in V1, V3, V5 lead and I lead. Except for V1 lead, elevate ST segment diagnose accordance rate show no difference ($P>0.05$).

Conclusions: The portable remote real-time electrocardiogram monitoring system may be a helpful tool in assisting physicians in the diagnosis of common arrhythmia and malignant ventricular arrhythmia disorders. The sensitivity of the change of ST segment of the two groups is similar, and the remote monitoring device can help to the location of myocardial ischemia.

Arterial Reactivity and Atherosclerosis Burden in Subjects with Chronic Obstructive Pulmonary Disease (COPD)

Wu Meng Jun^{1,3}, Chook Ping², Wei An Ning^{3,4}, Hu Yan Jun^{3,5}, Woo Kam Sang²

¹The Chengdu Women and Children Affiliated Hospital of Chongqing University of Medical Sciences; ²The Chinese University of Hong Kong; ³Second Affiliated Hospital of Chongqing University of Medical Sciences; ⁴The Xuefu Hospital of Chongqing; ⁵The Ninth People's Hospital of Chongqing, China

Introduction: Patients with COPD are associated with cardiovascular diseases. Arterial reactivity and carotid intima-media thickening are surrogates of atherosclerosis burden predictive of cardiovascular outcomes.

Subjects and Methods: We enrolled 60 patients (43 males, 70.7%) aged 60-80 years (mean 57.1±11.5 years) 1 day before undergoing laparoscopic abdominal surgery. 30 patients had COPD (CMA Respiratory Society 2007 Diagnostic Criteria) and 30 were gender and age-matched non COPD patients (Control). None had any cardiovascular disorder. Brachial flow-mediated dilation (FMD), nitroglycerin induced dilation (endothelium-independent, NTG), and carotid intima-media thickness (IMT) were measured by high resolution ultrasound.

Results: Their smoking status, body mass index, blood creatinine, fasting glucose, and lipid profiles, heart rate and blood pressures were similar between the 2 groups. Compared with control group, COPD group had lower brachial FMD (4.3±1.0% vs 6.2±1.2%, $p=0.005$) and greater carotid IMT (1.13±0.43mm vs 0.74±0.12mm, $p=0.014$), but there was no significant difference in their NTG-induced dilation, and extent of reactive hyperaemia and shear rate. Carotid plaque was present in 18 COPD (60%) compared with 10 Control patients (33.3%), $p=0.038$.

	COPD	CONTROL	P-VALUE
Blood Flow (ml/min)	21.6±12.3	26.7±9.83	0.397
Hyperaemia (%)	355.7±101.6	417.5±193.3	0.463
Shear Rate	81.2±20.8	86.0±21.9	0.545
Brachial FMD (%)	4.3±1.0	6.2±1.2	0.005
NTG (%)	16.2±3.2	14.8±2.3	0.354
Carotid IMT (mm)	1.13±0.43	0.74±0.12	0.014

Statistical significance: $p<0.017$ (after Bonferroni adjustment)

Conclusions: Brachial arterial reactivity (FMD) is reduced and carotid IMT is increased in COPD compared with control patients, proposing a greater atherosclerosis burden in COPD.

ABSTRACTS

Abstracts for Free Paper Session:

STRUCTURAL & CONGENITAL HEART DISEASES

Transcatheter aortic valve implantation (TAVI) in patients with bicuspid aortic valve

Dr. Jason Leung Kwai, Chan on behalf of the Heart Team of Queen Elizabeth Hospital Department of Medicine, Queen Elizabeth Hospital, Hong Kong

Introduction: TAVI has been approved as an alternative treatment in symptomatic severe aortic stenosis patients who are high risk for conventional surgery. The patients usually have tricuspid aortic valve that received TAVI. Success had been reported in patients with bicuspid valve in small case series.

Purpose: Report our experience of TAVI in patients with bicuspid aortic valve

Method: Retrospective study, from Jan 2011 to March 2013, all patients with bicuspid aortic valve received TAVI in our hospital had been reviewed.

Results: There were three patients with bicuspid aortic valve and severe aortic stenosis received TAVI during study period. Table 1 showed baseline characteristics and parameters in echocardiogram. All procedures were performed under general anesthesia and with Trans-esophageal echocardiogram guidance. All patients received CoreValve Revalving system™ (Medtronic) via femoral artery. Table 2 showed procedures details and outcomes at 30 days. Oversize of the devices ranged from 14% to 26%.

Conclusion: TAVI with Corevalve Revalving system™ in patients with bicuspid aortic valve and severe aortic stenosis is feasible and safe. The procedural and clinical outcomes are similar to TAVI in patients with tricuspid aortic valve. Further large-scale studies are needed to confirm the long-term effectiveness.

No.	Age	Sex	Diabetic	IHD	Peripheral vascular disease	FC NYHA	Logistic Euroscore	EF %	AVA cm2	Mean AV grad mmHg	Aortic Annulus mm
1	75	M	N	N	Y	3	12.2a	60	0.43	89	21
2	81	M	N	N	N	3	13.2b	70	0.85	84	27
3	83	F	Y	N	N	2	13.7	65	0.53	84	20.6

Table 1. Baseline characteristics and parameters in echocardiogram

No.	Corvalve size	Procedure success	Complications (any)	30day Mortality	30day PACE	30day NYHA	30day EF %	30day AVA cm2	30day Mean AV grad mmHg	30day Paravalvular leak
1	26mm	Y	No	N	N	2	60	1.7	15	Mild
2	31mm	Y	No	N	N	1	70	1.7	10	Mild
3	26mm	Y	GHF with pacing done	N	N	1	80	1.63	8.9	N

Table 2. Procedures details and outcomes at 30 days

Clinical outcome and Quality of Life in High-Risk Patients after TAVI

Chan MC1, Lee MKY1, Lam CB3, Leung KW2, 1 SF Chu1, WS Kwan1, Chan JKT1, Chan KC1, Wong CY3, Ma H51, Chan KT1, Chiong CS1, Li P1, Yu TW2, Chung Y52
 1. Division of Cardiology, Department of Medicine, Queen Elizabeth Hospital.
 2. Department of Physiotherapy, Queen Elizabeth Hospital

Introduction:

Aortic stenosis (AS) is the most prevalent native valve disease in the elderly. Symptomatic AS will cause serious disability, restrictions in daily living and high mortality. Surgical aortic valve replacement (AVR) is regarded as gold standard for symptomatic severe AS. However, AVR is often declined for old age or high-risk patients because of underlying co-morbidities. With the advancement of technology, an alternative therapeutic option- TAVI is currently available. TAVI seems to be an effective procedure with high success and improved mortality rate. Nevertheless, better Quality of Life (QoL) is a major expectation by this group of patients. Other than the success rate and mortality figures, QoL is crucial to assess the efficacy of this novel procedure. In Hong Kong, Queen Elizabeth Hospital is the first hospital to perform TAVI. Since December 2010, 25 patients were recruited to our TAVI program.

Objectives:

To evaluate the Clinical outcome and QoL in High Risk patients after TAVI

Methodology:

From December 2010 to April 2013, 25 patients have undergone TAVI in QEH. All of them were declined for AVR. The SF-12, ejection fraction (EF), New York Heart Association (NYHA) functional class, 6-minute walk test and 30-days mortality were measured at 1 and 6 months after TAVI.

Results:

25 patients with mean age 82 (SD 4.83), 9 female and 16 male were recruited. The mean logistic Euro Score (25.4 +/- 10.67) and mean gradient across the aortic valve (57.56 +/- 10.48) were high. All of them were old age patients with high surgical risk that not fit for surgical valvular replacement. Mean pressure gradient decreased from 52 to 9.11mmHg. Aortic valve area increased from 0.73 to 1.95. The in-patient and 30 days mortality was 0%. One patient died at 3 month after TAVI for coronary stent thrombosis. EF (p < 0.05) and 6-minute walk test (p < 0.05) were significantly improved at 1 and 6 month. Similar results were shown in New York Heart Association (NYHA) functional class, 75% improved 1 class, 20% with 2 classes and 4% with no changes at 6 month. The quality of life using the most extensively validated generic health status tool, SF-12 also shows profound results in both the mental and physical component (p < 0.05).

Conclusions: QoL is the major concern for this group of high risk, old age patients. TAVI has shown promising results in improving the quality of life and clinical outcomes. With more accumulating data in the future, TAVI might prove to be a more viable and appropriate treatment modality for this group of high-risk patients. A multi-disciplinary team approach should be established at TAVI centers.

22q11.21 Deletion Associated with Sporadic Tetralogy of Fallot in Han Chinese

Guo-Wei He^{1,2}, Cheryl L. Maslen³, Ge Gao¹, Xiao-Cheng Liu¹, Zhi-Gang Liu¹, Qin Yang^{1,4}
¹TEDA International Cardiovascular Hospital, Medical College, Nankai University, Tianjin, 300457, China; ²Department of Surgery & Heart Research Center, Oregon Health & Science University, Portland, Oregon, 97239, USA; ³Division of Cardiovascular Medicine & Heart Research Center, Oregon Health & Science University, Portland, Oregon, 97239, USA; ⁴Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR.

Purpose: Tetralogy of Fallot (TOF) is a congenital cardiac malformation that consists of an interventricular communication, also known as a ventricular septal defect, obstruction of the right ventricular outflow tract, override of the ventricular septum by the aortic root, and right ventricular hypertrophy. Overall it is the most common cause of cyanotic cardiac disease in infants. In the United States TOF occurs in approximately one in 3,000 live births and accounts for 10% of all serious congenital heart disease. However, studies suggest that the incidence in TOF is substantially higher in China. This study was designed to investigate the genetic basis of TOF in Han Chinese.

Methods: Genomic DNA was extracted from peripheral blood for each index patient and control subject. Affymetrix genome-wide human SNP array 6.0 was used. Each array has 1,800,000 genetic markers, including more than 906,600 single nucleotide polymorphisms (SNPs) and more than 946,000 probes for the detecting copy number variations (CNVs). DNA was extracted, amplified and hybridized to an Affymetrix Genome-Wide Human SNP array 6.0. Copy number was calculated based on probe hybridization signal intensity data relative to the signal of disease-free normal controls. To determine CNV status on each sample we performed real-time PCR. TaqMan™ probes designed by the manufacturer (Applied Biosystems, Foster City, CA) were used to target each of the specific regions. The *RNase P* was chosen as the reference gene.

Results: Deletion of 22q11.21 was seen in 8/60 (13.3%) cases. However, the deletion was seen in different patterns in those patients, shown by different starting and ending loci and involving genes. Parents of TOF probands with a disease-associated CNV provided with ability to determine if any of the CNVs were inherited or *de novo*. The CNVs were *de novo* mutations for all these cases.

Conclusions: 22q11.21 deletion is associated with sporadic tetralogy of Fallot in Han Chinese involving a large number of genes and the related individual genes warrant further detailed investigations.

Relationship of Mutation and Methylation in CITED2 with Congenital Heart Disease

Min Xu, Xiaoyun Wu, Jie Tian
 Chongqing Medical University, China

Objective: Explore CITED2 mutations that how to impact the expression of the transcription factor HIF-1alpha and to determine the role of methylation of CITED2 promoter in congenital heart disease.

Methods: CITED2 (c.573-578del6) mutant recombinant plasmid and wild recombinant plasmid were successfully constructed in our early study. Transfecting them into HepG2 and H9C2 respectively. Expression differences of HIF-1alpha mRNA were compared among groups by Q-PCR, and protein expression differences were detected by western-blotting. Myocardial tissues from 31 children with congenital heart disease was collected during surgery in department of cardiothoracic surgery, and tissues samples of 2 health children were harvested after accidental death. Bisulfite-sequencing PCR (BSP) and methylation-specific PCR (MSP) were used to detecting methylation in CITED2 promoter. And then expression differences of CITED2 mRNA were compared between methylated and control group.

Results: Comparing with the empty vector group, Expression of HIF-1alpha mRNA and protein was down in wild group (P<0.05), but it was higher in mutation group than that of wild group (P<0.05). Empty vector group and no transcription group showed no significant difference (P>0.05). CITED2 methylation was found in 10 of 12 congenital heart disease by BSP and 16 of 19 congenital heart disease by MSP. Positive rate of CITED2 methylation was 83.3% (10/12) and 84.2% (16/19) respectively. We did not find methylation in control group. Compared with the control group, CITED2 mRNA expression was significantly reduced in methylated group. There is a significantly statistical difference (P<0.05).

Conclusion: HIF-1alpha can be Negative feedback inhibited by CITED2, the negative feedback inhibition was broken by CITED2 mutation. The CITED2 mutation leads to overexpression of HIF-1alpha, which maybe one of factors of the incidence of congenital heart disease. Abnormal methylation of CITED2 promoter is found in congenital heart disease. The abnormal methylation leads to decrease in mRNA expression of CITED2, which might be involved in the incidence and development of congenital heart disease.

ABSTRACTS

Abstracts for Free Paper Session:

CARDIC IMAGING

Role of Multi-modality Imaging Techniques in Selecting Size of Prosthesis for Transcatheter Aortic Valve Implantation
 CY Wong¹, SF Chui¹, LK Chan¹, KC Chan¹, KY Lee¹, KT Chan¹, CS Chiang¹, P Li¹, MC Chan¹, KW Leung², MK Chan³, W Chan³, S Chan³, Department of Medicine¹, Department of Radiology & Imaging², Queen Elizabeth Hospital.

Introduction
 Transcatheter Aortic Valve Implantation (TAVI) has become a well established alternative treatment for severe aortic stenosis in patients who are considered inoperable or high risk for conventional open heart surgery. Appropriate prosthesis selection is of paramount importance in succeeding the procedure and avoiding the complications. Oversizing may increase the risk of aortic rupture and atrio-ventricular block necessitating pacemaker implantation. On the other hand, undersizing may result in significant peri-prosthetic aortic regurgitation or increase the chance of device dislodgement. Unlike surgical aortic valve replacement where sizing of the aortic annulus could be done under direct vision, TAVI procedures rely heavily on different cardiac imaging techniques to provide information on aortic annulus dimension. We report our experience on multi-modality imaging techniques on procedural preparation and peri-operative outcomes.

Method
 From December 2010 to April 2012, 25 patients (15 male, 10 female) with symptomatic severe aortic stenosis underwent TAVI procedures. Severity of aortic stenosis is assessed by both transthoracic (TTE) and transesophageal echocardiogram (TEE). Aortic annulus diameter measurement is required for determining the size of prosthesis (CoreValve) to be used. Currently three different sizes of CoreValve are available (26mm, 29 mm and 31 mm) and guideline on size selection is provided by the manufacturer. All patients had TTE, TEE and cardiac computerized tomography (CT) for determination of aortic annulus diameter. The relationships of these measurements with the final size of CoreValve selected, and the peri-operative complications are analyzed.

Result
 Table 1 shows the relationship between predicted and actual CoreValve size implanted using different aortic annulus measurement method. TTE and TEE aortic annulus measurements were available for all patients while CT measurements were not available in 2 patients prior to the procedure. The agreement rate of predicted versus actual CoreValve size were 84%, and 88% for TTE and TEE respectively. For CT measurements, agreement rate were 39.1% and 26.1% for CT minor diameter and CT major diameter alone, respectively. This was improved to 73.9% when CT mean diameter was used. In 10 patients with CT aortic annulus perimeter reported (in more recent period of TAVI program) prior to the procedure, 8 (80%) were in agreement with actual CoreValve size implanted while the remaining 2 was considered undersized. 16 out of 23 (69.6%) patients had TEE and CT mean diameter predicted CoreValve size agreed with each other.

There was no aortic rupture or device dislodgement in all patients. 4 patient (17.4%) developed conduction disturbance (3 atrioventricular block, and 1 paroxysmal atrial fibrillation with new onset left bundle branch block) requiring permanent pacemaker implantation. None of these CoreValve implanted were considered oversized by both TEE and CT mean diameter measurement. On the other hand, 2 patients (10.5%) developed peri-prosthetic aortic regurgitation of more than mild degree prior to discharge; in whom one of the prosthesis was considered undersized by CT mean diameter, whereas the other prosthesis was considered appropriate size by both TEE and CT mean diameter.

Conclusion
 The performances of TEE and CT in appropriate CoreValve size selection are comparable. In addition, each of these imaging provides unique and yet complementary information in overall management of patient undergoing TAVI procedure. Collaboration between cardiac imaging specialists from different departments is the key to achieve optimal results.

	Aortic Annular Diameter				
	TTE	TEE	CT Minor	CT Major	CT Mean
Actual CoreValve Size agrees with Predicted Size	84%	88%	39.1%	26.1%	73.9%
Actual CoreValve Size LARGER than Predicted Size	12%	12%	52.2%	0%	4.4%
Actual CoreValve Size SMALLER than Predicted Size	4%	0%	8.7%	73.9%	21.7%

Table 1. Relationship between different aortic annular measurements and agreement between predicted and actual CoreValve size implanted.

Assessment of carotid intima-media thickness in patients with Spondyloarthritis: relationship with disease severity

Chen Yan¹, Chung Ho-Yin², Wong Arthur¹, Zhen Zhe¹, Tsang Helen Tsang Hoi-Lun², Lau Chak-Sing², Tse Hung-Fat³, Yiu Kai-Hang^{1,3}
¹Cardiology Division, Department of Medicine, Queen Mary Hospital, the University of Hong Kong; ²Division of Rheumatology, Department of Medicine, Queen Mary Hospital, the University of Hong Kong; ³Research Centre of Heart, Brain, Hormone and Healthy Aging, Li Ka Shing Faculty of Medicine, the University of Hong Kong, Hong Kong SAR

Objective: Spondyloarthritis (SpA) is a chronic rheumatic disease characterized by inflammation of the spine, sacroiliac and peripheral joints, causing pain and functional disabilities. As the disease advances, syndesmophytes will form in axial joints leading to further functional loss. Carotid intima-media thickness (CIMT) is widely used as a surrogate marker for subclinical atherosclerosis. It is proposed that persistent systemic inflammation in SpA is associated with early carotid atherosclerosis. The aim of this study was to evaluate the changes of CIMT in patients with SpA and their relationship with the underlying disease severity.

Methods: A total of 104 SpA patients (mean age 45.5 ± 13.3 years, 69.2% male) and 52 age and gender-matched healthy controls were enrolled into the study. All patients underwent clinical examination, laboratory blood tests and spine radiographs. High-resolution ultrasonography was used to measure far-wall CIMT at the common carotid artery. Bilateral maximum CIMT measurements were performed offline using automated imaging processing software and the mean CIMT was calculated for evaluating atherosclerosis. The disease duration, ESR and CRP levels, BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and BASFI (Bath Ankylosing Spondylitis Functional Index) scores were recorded. And the disease severity of the SpA patients was assessed by mSASSS (modified Stoke Ankylosing Spondylitis Spine Score).

Results: CIMT was significantly increased in patients with SpA compared to controls (0.78 ± 0.19 mm vs. 0.69 ± 0.10 mm; *P*<0.001). In SpA patients, BASDAI (*r*=0.22, *P*=0.03), BASFI (*r*=0.45, *P*<0.001), and mSASSS (*r*=0.60, *P*<0.001) correlated significantly with CIMT. Multivariate analysis adjusting for potential confounding factors demonstrated that mSASSS was independently associated with CIMT (*β*=0.23, 95% confidence interval 0.00-0.01, *P*=0.03). In SpA patients with mSASSS score above the median value (14.75), CIMT was significantly higher compared with patients below the median value (0.85 ± 0.18 mm vs. 0.71 ± 0.16 mm; *P*<0.001).

Conclusion: Our study demonstrated that patients with SpA had early carotid atherosclerosis. mSASSS remained independently associated with CIMT after adjusting for the confounding factors. Importantly, the SpA group with mSASSS score above the median value had a significantly higher CIMT. In conclusion, this study shows that patients with SpA have a tendency to develop subclinical atherosclerosis which correlates significantly with the disease severity. Whether effective disease control could prevent the development of atherosclerosis remains to be investigated.

ABSTRACTS

Abstracts for Free Paper Session:

HEART FAILURE

Refractory heart failure in infective endocarditis: characteristics and outcomes

Guo-gan Wang, Jian Zhang

Department of Cardiology, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, China

Purpose: Despite improvements in medical and surgical therapies, infective endocarditis (IE) is associated with a poor prognosis and a considerably high risk of mortality and morbidity. This study was designed to explore the general characteristics, treatment patterns, and outcomes of patients with IE complicated by refractory heart failure.

Methods: A case report form was used to collect the following data: demographic information, predisposing factors for IE, possible source of infection, echocardiographical and microbiological data and treatment received during the course of hospitalization. Heart failure during the initial hospitalization was diagnosed according to Framingham criteria.

Results: One hundred forty-three consecutive IE patients complicated by refractory heart failure (NYHA class III and IV) were admitted to Fuwai hospital. The mean age was 43 years old and 69.2% were men. The average in hospital time was 30.5 days. Of these patients, 129 (90.2%) patients had native infective endocarditis (NVE), 13 (9%) patients had prosthetic infective endocarditis (PVE) and 1 (0.7%) cardiac device-related infective endocarditis (CDRIE). Twenty-four patients (16.8%) were older than 60 years. Vegetations were visualized in 75.6% of cases and perivalvular complication was identified in 18.9% of cases. Major complications occurring during the acute infective phase were also recorded, including renal dysfunction were in 88 patients (61.5%), embolic events in 77 patients (53.8%), neurological events in 25 patients (17.5%), and uncontrolled infection in patients (36.4%). Fifty-six patients (39.2%) underwent valve replacement during hospitalization. The overall hospital mortality rate was 24.5%. Mortality was higher in patients with PVE (4 of 13 cases, 30.7%) than in patients with NVE (31 of 129 patients, 21.7%). A better outcome was observed in patients treated with a combined medical and surgical therapy.

Conclusion: IE patients complicated by refractory heart failure are associated with a high mortality rate. Surgery performed in selected cases may improve the outcomes.

Correlation between systolic dysfunction and diabetic retinopathy

Z Zhen, ACK Wong, CT Zhao, Y Chen, CW Siu, HF Tse, KH Yiu
Queen Mary Hospital, Hong Kong

Background: Diabetic mellitus (DM) patients may have cardiac structure and functional changes or microvascular disease in the absence of cardiovascular disease. While the relationship between the occurrence of microvascular disease and cardiac changes in DM patients without history of heart disease are unclear. The present study sought the correlation between diabetic retinopathy and cardiac functional changes by A) ophthalmological assessment and B) detailed echocardiography for assessment of heart function.

Methods: 257 patients with type 2 DM without history of cardiovascular disease were recruited. Transthoracic echocardiography was performed and results were analyzed in detail with the following parameters: (i) LV systolic function was assessed by Simpson's method derived ejection fraction and speckle tracking derived longitudinal strain (LS), (ii) myocardial structural alteration by calibrated integrated backscatter (cIBS) and (iii) diastolic function by tissue Doppler derived E/e' ratio. Furthermore, all patients undertook ophthalmological assessment.

Result: Of all the 257 subjects (mean age 62.90±8.82, 45.91% male), there were 77.43% who had retinopathy. Patients with and without retinopathy (as a categorical variable) had similar LV ejection fraction and cIBS. However, retinopathy had a significant correlation with LV global strain ($r=-0.241$, $P<0.01$) and E/e' ($r=-0.215$, $P<0.01$). In multivariate analysis, after adjusted for age, sex, BMI, smoking, hypertension, and medications (anti-hyperglycemic and anti-hypertensive), LV global strain significantly correlated with diabetic retinopathy ($p<0.05$).

Conclusion: This study indicated that the occurrence of diabetic retinopathy significantly correlated with LV global strain and E/e'. Above all, the correlation with LV global strain still existed after adjusted for potential confounding factors, suggestive of an independent relationship between diabetic retinopathy and systolic function. The link between these two parameters highlighted the importance of the need for more detailed cardiac assessment for subtle changes in systolic function for DM patients with retinopathy but without history of cardiac disease and relevant symptoms.

ABSTRACTS

Abstracts for Free Paper Session:

CARDIC REHABILITATION

How Can Empowerment Program Attenuate Patient Barriers for Joining Formal Phase II Cardiac Rehabilitation Program in a Regional Hospital

YMW Mak¹, CS Yue¹, CW Wong², SW Wong², SWN Wu³, MWP Chan³, M Wan³, ¹Division of Cardiology, ²Physiotherapy Department, ³Occupational Therapy Department, United Christian Hospital, Hong Kong

Purpose: Work and time constraints were common barriers to low participation rate in phase II cardiac rehabilitation program (CRP). Empowerment program was piloted with a total of 3 sessions of hospital-based training and 4-telephone counselling in order to accommodate more eligible cardiac rehabilitation patients to receive rehabilitation service in secondary prevention of coronary artery disease. The aim of this study was to evaluate the outcomes of the program.

Method: Exercise stress test was a pre-requisite to the empowerment program. Eligible patients would be recruited. Exercise, education and motivational interviewing in lifestyle modification were provided. Outcome measures were evaluated by exercise stress test, International Physical Activity Questionnaire (IPAQ), Short Form 36 (SF-36), Exercise and Cardiac Self-efficacy Questionnaires and Hospital Anxiety and Depression Scale before and after program. Paired T-test was used for analysis.

Results: A total of 39 patients (36 males), with mean age was 55 ± 10 years, were recruited into the Empowerment Program during the period from September 2012 to March 2013. Among them, 27 patients (69%) were recruited following acute coronary syndrome, 11 patients (28%) following percutaneous coronary intervention and 1 patients (3%) following ASD repair. All patients refused a formal 12-session Phase II CRP due to work or time constraints (33 patients, 84%), financial hardship (3 patients, 8%), preference for self-exercise (2 patients, 5%) and no escort (1 patient, 3%). By time of analysis, 13 patients (33%) completed the course of empowerment program with outcome evaluated. There were statistically significant improvement in exercise capacity (+1.5 METs) and increase in physical activity after program (p<0.05). Stress test results showed that patients with poor or impaired exercise capacity for their age and sex were decreased from 4 to 1. Patients showed improvement in their self-efficacy in exercise (score from 60.00 to 64.98, p=0.05). With respect to quality of life, patients showed statistically significant improvement in vitality after program in SF-36 (P<0.05).

Conclusion: The study showed improvement in exercise capacity and physical activity level after training. However, further study would be required to assess the benefits to patients after the program and identify the suitable group of patients to receive the service.

Cardiac Rehabilitation in Private Practice is Workable in Hong Kong

Albert WS Leung, Gary YK Mak, Cyrus TH Chow, Sylvia SW Lam, Tracy MF Liu, Dominic WH Lui, Andrew WF Tam
PRO-CARDIO Heart Disease & Stroke Prevention Centre, Hong Kong

Introduction: In Hong Kong, structured cardiac rehabilitation (CR) programs have been developed since the 1990's. Surveys on the CR service in HK were conducted in 2002 and 2005, showing that phases I and II services were provided mainly in the public hospital system, while the community-based phases III and IV services were provided by non-government organizations or patient self-help groups. There was CR program in one of the private hospitals, and most private cardiologists had considered it useful.

Objective: To set up a clinic-based structured CR program in private sector in HK, to analyze the similarities to and differences from those of public sector, and to evaluate on the current status.

Results: The program was fully implemented in November 2011, as a clinic-based phase II service. It is recommended for patients with heart attack (post-AMI), heart failure, or after interventional procedures. Service providers include a nurse, a dietitian and a physical trainer, with cardiologists as organizers and supporters. Participants can choose an either 4-weeks or 8-weeks program, which is either individual- or group-based. Each participant attends 1 session per week. A 30-minutes consultation is given in every session, which covers drug knowledge, nutrition therapy, psycho-social counseling, and smoke cessation. Exercise capacity is assessed through treadmill test, and exercise therapy is prescribed by a cardiologist according to the result. Exercise training is carried out for 45-60 minutes in each session by the physical trainer. Program extension for an extra 4-8 weeks will be considered if appropriate. Progress on participants was monitored by evaluating improvement in quality of life (QOL). From November 2011 to October 2012, 25 participants had been recruited (19 males and 6 females). 23 were post-PCI (including 4 AMI) cases, 1 heart failure and 1 valve replacement. 10 patients attended 8-week program, while 15 attended 4-weeks program. QOL evaluation was done for 10 participants, and 7 of them showed improvement.

Conclusion: This study illustrated the implementation of a structured phase II cardiac rehabilitation program in a private clinic in Hong Kong. Owing to the fundamental differences from the public setting, there are diversities from the public counterpart in the logistic, design and workflow of the program. Twenty-five participants had joined the program, and their responses were positive and encouraging. Further program review and evaluation will be accomplished.

ABSTRACTS

Abstracts for Free Paper Session:

MISCELLANEOUS

E64d deteriorates post-myocardial infarction left ventricular remodeling by inhibiting cathepsin s-mediated fibroblast trans-differentiation

Jian-An Wang
2nd Affiliated Hospital, Zhejiang University School of Medicine, China

Background: Extracellular matrix (ECM) turnover is a major process of left ventricular (LV) remodeling following myocardial infarction (MI). Cysteinyln cathepsins participate in ECM catabolism in human arterial diseases, but their functions in cardiac remodeling remains unknown.

Materials and Methods: Mouse MI model was induced by left anterior descending (LAD) artery ligation. Both infarct and remote myocardium from post-MI 1, 2, 3, 7 and 28 days were collected to evaluate mRNA expressions and activities of different cysteinyl cathepsins comparing to sham operated ones. To further investigate the role of cathepsins in post-MI LV remodeling process, a non-selective cysteinyl cathepsin inhibitor E64d was administrated within the first 7 days of post-MI. Cardiac functions were analyzed by echocardiography at baseline, 7 and 28 days post-MI. Mice were sacrifice at 7 and 28 days post MI for further studies.

Results: CatS expression and activity were increased in infarcted mouse myocardium. E64d administration deteriorated cardiac functions at 7 and 28 days post-MI, although did not change significantly infarct size. This cathepsin inhibitor increased post-MI inflammatory cell infiltration and cytokine expression, altered collagen type-I and type-III deposition, and suppressed the expressions of myofibroblast trans-differentiation-essential protein fibronectin extra domain A (ED-A) and myofibroblast marker alpha-smooth muscle actin, but did not affect myocardium apoptosis or angiogenesis. Further mechanistic studies demonstrated that inhibition or deficiency of CatS reduced myocardium expression of ED-A fibronectin, thus suppressed TGF-beta1-induced fibroblast trans-differentiation and alpha-SMA expression, thereby leading to adverse collagen turnover, enlarged LV dilation, and deteriorated cardiac functions, similar to those from E64d-treated mice.

Conclusion: E64d deteriorates LV remodeling and cardiac functions after experimental MI by affecting myofibroblast trans-differentiation via inhibition of CatS activity and suppression of fibronectin ED-A production.

Adrenomedullin level is influenced by a single nucleotide polymorphism in adiponectin gene

Wong HK¹, Ong KL², Leung RYH¹, Cheung TT¹, Xu A¹, Lam KSL¹, Cheung BMY¹
¹Department of Medicine, University of Hong Kong, Hong Kong; ²Centre of Vascular Research, University of New South Wales, Sydney, NSW 2052, Australia

Purposes: Adrenomedullin (ADM) and adiponectin are both biomarkers for cardiovascular diseases. Plasma ADM levels is elevated in hypertension and heart failure while adiponectin level is lowered in metabolic syndrome. Plasma levels of these peptides are influenced by single nucleotide polymorphisms (SNPs) in their respective genes. Recently there has been evidence suggesting that ADM can regulate adiponectin gene expression, but whether adiponectin can regulate ADM expression is not clear, and therefore it is investigated in this study.

Methods: Plasma ADM levels were obtained in 476 subjects recruited in the Hong Kong Cardiovascular Risk Factor Prevalence Study-2 (CRISPS2). We genotyped them for 2 adiponectin tagging SNPs that are associated with plasma adiponectin levels.

Results: The minor allele frequencies of adiponectin SNPs rs182052 and rs12495941 were 40.6% and 42.2% respectively. Plasma ADM levels were significantly associated with rs182052 but not with rs12495941 ($\beta=0.104$, $P=0.023$ for rs182052 adjusting for age and sex). The association remained significant after full adjustment ($P=0.026$). In multivariate analysis, plasma ADM levels increased with the number of minor allele A carried in rs182052 ($P=0.013$). Compared to subjects with GG genotype, those with AA genotype had 17.7% higher plasma ADM levels (95% CI: 3.6%-33.7%).

Conclusion: Plasma ADM level is related to the SNP rs182052 but not rs12495941 in adiponectin gene. This provides new evidence of the interaction between these two important peptides in cardiovascular diseases. Knowing the genotype may help to refine the interpretation of the levels of these biomarkers in these pathologies.

Increase of SUMO-1 expression in response to hypoxia: direct interaction with HIF-1 α in hypoxic pulmonary hypertension

Yongliang Jiang^a, Jing Wang^a, Hua Tian^a, Guang Li, Hao Zhu, Lei Liu, Ruicheng Hu, Aiguo Dai
Institute of Respiratory Medicine, Hunan Province Geriatric Hospital, Changsha 410016, China

#These authors contributed to equally to this work

Purpose: The present study investigates the regulation of small ubiquitin-related modifier-1 (SUMO-1) expression in response to hypoxia in rat pulmonary arterial smooth muscle cells (PASMCs), and rat hypoxic pulmonary hypertension (HPH) models and COPD patients(with or without PH).

Method: We observed a significant increase in SUMO-1 mRNAs and proteins after hypoxic stimulation in vivo and vitro. Because SUMO-1 interacts with various transcription factors, including hypoxia-inducible factor-1 α (HIF-1 α) in vitro, we not only demonstrated that the HIF-1 α and target gene (Vascular endothelial growth factor (VEGF)) expression is increased by hypoxia in HPH, but also provided evidence that SUMO-1 regulates HIF-1 α in response to hypoxia by gene silence and over-expression. The specific interaction between SUMO-1 and HIF-1 α was additionally demonstrated with co-immunoprecipitation.

Result: In the present study, we have demonstrated that SUMO-1 gene expression is enhanced by hypoxic stimulation in rat PASMCs, rat HPH models and COPD patients(with or without PH). Furthermore, SUMO-1 physically interacts with HIF-1 α in response to hypoxic stimulation in vivo and vitro. We discovered that HIF-1 α and VEGF mRNA and protein were distinctly decreased after SUMO-1 gene intervened by siRNA, whereas obviously increased at SUMO-1-LV group.

Conclusion: These results indicate that the increased levels of SUMO-1 participate in the modulation of HIF-1 α function through sumoylation in HPH.

Study the cytokines balance of Th1\Th2 at the course of using recombinant interleukin -12 to treat the mice with viral myocarditis

Yu Xia, Sun Jinghui
The First Hospital of Jilin University, China

Objective: Through detecting the level of interleukin -6 and interleukin -10, and studying the cytokines balance of Th1 and Th2, to study the treatment mechanism of recombinant interleukin-12.

Method: A total of 240 BALB/C mice were randomly divided into six groups, 40 mice in each group: blank control group, the virus control group, drug control group, rmlL-12 small-dose treatment group, medium-dose treatment group, high dose treatment group. Each mouse was injected Coxsackie B₃ 0.2 ml/d for 3 consecutive days by intraperitoneal injection, except the mouse in blank control group. After inoculating 4 h, in the blank control group and the virus control group, each mouse was inoculated 0.9% saline 0.1 ml/d by intraperitoneal injection, in the drug control group, each mouse was inoculated interferon- γ 400 IU/d, rmlL-12 small-dose, medium-dose and high-dose treatment group, the mouse in each group were injected recombinant interleukin-12 respectively 1 ng/d, 10 ng/d, 100 ng/d for 5 consecutive days. At 5 days, 10 days and 15 days of the experiment. Taking 8 mice from each group, and getting blood from eyeballs for detecting cytokine and heart specimens for detecting myocardial pathology. ELISA was used to detect the serum interleukin-6 and IL-10 level, and HE staining was used to detect myocardial pathological changes.

Result: There was significant differences in different groups and on different time of interleukin-6 and interleukin-10. Interleukin-6 belong to the Th1 cytokines, and interleukin-to Th2 cytokines. Compare the levels of Interleukin-6 between the groups, $F=72.28$, $P<0.01$, 10 statistically significant, the different time after treatment, $F=183.82$, $P<0.01$, statistically significant. At 5 days and 10 days of the experiment, the serum levels of interleukin-6 increased with the amount of recombinant interleukin-12. At 5 days the level of interleukin-6 reached the peak, and at 15 days reduced to the level of the blank control group level. Compare the levels of Interleukin-10 between the groups, $F=50.16$, $P<0.01$, statistically significant. Different time after treatment, $F=28.52$, $P<0.01$, statistically significant. At 10 days the level of interleukin-10 reached the peak, and at 15 days the serum levels of each group reduced, but not reached to the level of the blank control group. Myocardial pathological change is lighter in medium-dose treatment group than the other treatment groups, in addition to the blank control group.

Conclusions: Cytokines of Th2 can prevent Th1 excessive response through inhibiting the cytokine of Th1. Appropriate amount of recombinant IL-12 can reduce the myocardial pathological changes and treat viral myocarditis, through the adjustment of Th1 and Th2 cytokine balance.

ABSTRACTS

Abstracts for Free Paper Session:

MISCELLANEOUS

The roles of ulinastatin (UTI) in cerebral cortex injury after cardiopulmonary resuscitation

Dai Xuan¹, Hu Chun-lin¹, Li Xin¹, Wei Hong-yan¹, Li Ying-qing¹, Liu Rong¹, Zhan Hong¹, Liu Xiao-xing¹
 Department of Emergency, The First Affiliated Hospital of Sun Yat-Sen University, China

Objective: The roles of ulinastatin (UTI) in cerebral cortex injury after cardiopulmonary resuscitation (CPR) haven't been elucidated. The present study was designed to evaluate effects of ulinastatin (UTI) on inflammation, oxidation and neuronal survival in the injured cerebral cortex after CPR.

Methods: Ventricular fibrillation (VF) was induced in seventy-six adult male Wistar rats by an external transthoracic alternating current; Six minutes after VF, manual chest compression and mechanical ventilation were initiated. The rats were randomly divided into two groups: (1) VF + phosphate buffered saline (PBS) group or (2) VF+UTI group depending on whether they received co-treatment with medication after return of spontaneous circulation (ROSC). Before CPR and at 2, 4, and 8 h after ROSC, blood samples (n = 6 at each time point) were collected to quantified the plasma levels of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and levels of TNF- α , IL-6 by enzyme-linked immunosorbent assay, myeloperoxidase (MPO) and malondialdehyde (MDA) in the cerebral cortex were measured by spectrophotometry. Quantitative real-time polymerase chain reaction (RT-PCR) was applied for detection of TNF- α and IL-6 mRNA. A Western blot assay was used to analyze the ratio of translocation of nuclear factor- κ B (NF- κ B) p65 from the cytoplasm to the nucleus. Nissl and TUNEL staining of brain sections were performed at 72 hours after ROSC.

Results: UTI decreased plasma levels of TNF- α and IL-6, expression of mRNA, and levels of TNF- α IL-6, MDA and MPO in the cerebral cortex as well as attenuated the translocation of NF- κ B p65 from the cytoplasm to the nucleus at 2, 4 and 8 hours after ROSC. In addition, UTI increased the number of living neurons and decreased the number of TUNEL-positive neurons in the cortex 72 h after ROSC.

Conclusions: This study demonstrated that UTI preserved neuronal survival and inhibited neuron apoptosis after ROSC in Wistar rats via attenuating the oxidative stress and translocation of NF- κ B p65 from the cytoplasm to the nucleus in the cortex, and subsequently decreased the production of TNF- α , IL-6, MDA and MPO. Our study will provide scientific basis for UTI in treatment of neuronal injury after ROSC.

Postmarketing Surveillance Study with Iodixanol in 20185 Chinese Patients from Routine Clinical Practices

Bu-Chun Zhang¹; Lei Hou¹; Wei-Ming Li¹; Wei Chen¹; Yun-Lan Lu¹; Neng Dai¹; Yi-Dong Wei¹; Bin Lv²; and Ya-Wei Xu¹
¹Department of Cardiology, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai 200072, China; ²Department of Radiology, Beijing Fuwai Cardiovascular Hospital, Beijing 100037, China

Background: Iodinated radiographic contrast media are considered safe diagnostic drugs with a low incidence of adverse drug reactions (ADRs). However, ADRs may still occur, ranging in severity from minor disturbances to severe and potentially fatal complications.

Material and Methods: A total of 20,185 patients were enrolled in a prospective postmarketing surveillance registry with iodixanol. A standardized questionnaire was used to collect the following patient information from 95 centers in the mainland of China: baseline demographics, risk factors, type of examination, route of injection, volume and selected concentration of iodixanol, and overall tolerance to iodixanol (utilizing specific criteria and descriptors).

Results: Male patients account for 63.1%. The mean age of the patients was 60.4 years. Overall incidence of ADR was 1.52% (307/20,185 patients), of which 0.58% was immediate, and 0.97% was delayed onset. Five patients experienced both immediate and delayed ADR. The most common immediate ADRs were nausea, vomiting, and other gastrointestinal disorders with an incidence of 0.22% (45/20,185 patients). The most common delayed ADRs were rash, pruritus, mucocutaneous rash and subcutaneous tissue disorders with a total incidence of 0.68% (138/20,185 patients). Serious ADRs (defined as acute anaphylactic shock) occurred in two patients (0.01%). Sub-group analysis shows ADR rate was significantly higher in the following groups: (1) patients with prior contrast media reaction versus patients without prior reaction (P=0.024); (2) patients with age \leq 65 years versus patients with age $>$ 65 years (P<0.001); (3) patients with "poor" punctured vein status versus patients with "moderate" (P=0.023); (4) patients with intravenous injection versus intra-arterial injection (P<0.001); (5) patients receiving pre-heated iodixanol versus those injected with non pre-heated product (P<0.001); (6) patients without hypertension versus those with hypertension (P=0.031); (7) ADRs rate in coronary angiography/contrast-enhanced CT was significantly higher than rate in other procedures (P<0.001). 73.3% (14,791/20,185) of patients in this study had no pain after injection of iodixanol, and 21.5% (4,338) reported a composite score of 1-3, 5.2% of 4-15, 2 reported over 15.

Conclusions: The safety of iodixanol in routine clinical practice was shown to be comparable to the published safety profiles of other nonionic iodinated contrast agents. ADRs rate was affected by age, examination type, contrast medium temperature, status of vein, administration route, and risk factors. Patient discomfort during administration was mild or absent in most patients.

Development of Software for Cardiac Auscultation Cardiac Auscultation - A Audible and Visible Tutorial

Zhang Shuiwang, Guo Wenling, Feng Qiaoi
 The First Hospital, Shanxi Medical University, P.R. China

Objective: The stethoscope remains a valuable and cost-effective clinical tool that often enables many well-trained and experienced cardiac auscultators to make a rapid and accurate cardiac diagnosis. However, sophisticated high technology is not a substitute for a solid foundation in clinical cardiology including cardiac auscultation. But to master cardiac auscultation is more difficult. Cardiac auscultation is rapidly becoming a lost art. For more easily learning cardiac auscultation, software for learning cardiac auscultation is developed.

Method: Audio data of heart sound and its changes, extra heart sound, and all kind of heart murmur were recorded or collected. All audio data were played and video data were recorded at same times. The audio data and video data were synthesized by Authorware.

Result: When the program plays, audio data and video data (Phonocardiogram) were played simultaneously. The content included:

1. Overview: Cardiac cycle; stethoscope; auscultation; auscultation content.
2. The heart sounds: S1; S2; S3; S4.
3. Changes of the heart sounds: Changes of first heart sound; changes of the second heart sound.
4. The extra heart sound: Diastolic extra heart sound; systolic extra heart sounds.
5. Heart murmur: Systolic murmur; diastolic murmur; continuous murmur; innocent murmur; pericardial friction rub.
6. Test.

Conclusion: To learn cardiac auscultation is an intelligent technique and to master it is more difficult. This skill is difficult to grasp by self-study. To learn it needs a long-term repeated practice. But there are few opportunities for advanced studies in primary care doctors and medical students. Therefore, the development of an easy-to-use tutorial is imperative. The development of this tutorial provides a new means and methods for learning cardiac auscultation.

A review of earlier Warfarin Titration: Better or worse in thromboembolic prevention or bleeding?

Leung YW, Leung KF, Yue CS, Chan CK, Chow KS, Law KF, Tang SK
 Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong

Introduction: Warfarin is an effective oral anti-coagulant commonly used in prevention of thrombosis. The higher percentage of time in target range (TTR) of international normalized ratio (INR); the more optimal is the therapeutic effect and less risk for bleeding. But when to titrate will be more appropriate in balancing the benefit and risk?

Objectives: To evaluate whether patient outcome can be improved if warfarin is titrated earlier than usual Methodology: Cardiac nurse performed phone warfarin titration (if no signs of bleeding) under principles as below in two identical four-month periods: Period 1: (usual practice) Titration when INR is out of target range \geq 0.5, or repeat INR and review if only out range $<$ 0.5 Period 2: Direct titration when INR is out of target range \geq 0.3 A retrospective review was performed to 102 randomly selected patients, including 72 male and 30 female; aged from 31 to 83 with mean age 60. Their indications for warfarin were: atrial fibrillation (AF) for prophylactic stroke prevention (n=42); for post-mechanical valve replacement (n=54); and for pulmonary embolism (PE) (n=6).

Results: During period 1, the average TTR was 65%. There was no major bleeding event but one minor haematuria event and one ischemic stroke. During period 2, the average TTR was 68%. Two major bleeding events including one intracranial bleeding and one massive gynecological bleeding were recorded. There were also four thromboembolic events including two ischemic strokes and two recurrent PE. Besides, total number of phone titrations performed by Cardiac Nurse and investigations done by laboratory staff also increased 40% in period 2.

Conclusion: In balancing the benefit in thromboembolism prevention and risk for bleeding, titrating warfarin dosage too early is not recommended. In addition, Cardiac Nurse phone warfarin titration also demonstrated its effectiveness although will be safer if coupled with nurse clinic assessment.

ABSTRACTS

Abstracts for Free Paper Session:

EPS, CARDIAC ARRHYTHMIA AND PACING

Catheter Ablation of atrial fibrillation in patients with structural heart disease: long term follow up results

Li Li Cheung, Chin Pang Chan, Yiu Kwan Ko, Joseph Yat Sun Chan
Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

Background: Catheter ablation of atrial fibrillation (AF) has become an established therapeutic modality for the treatment of patients with symptomatic AF. Patients with structural heart disease (SHD) are believed to differ from those with normal hearts in the underlying pathophysiology of their AF. This notion has deterred the ablative therapy in this group of patients. The aim of this study was to review the long-term outcomes and safety of AF ablation in patients with underlying structural heart disease.

Method: Data from consecutive patients with AF and SHD who underwent catheter AF ablation between June 2010 and November 2012 in Prince of Wales Hospital were analyzed retrospectively for outcome and complications.

Results: The study consisted of 13 patients who are highly symptomatic and drug refractory (amiodarone=5, dronedarone=4, felcainide=1, carvedilol=1, bisoprolol=1) AF. The cohort consisted of 11 paroxysmal and 2 persistent AF; hypertrophic cardiomyopathy (n=4); had atrial septal defect with surgical repair (n=3) and with Amplatzer occluder implanted (n=1); ischemic cardiomyopathy (n=1); chronic rheumatic mitral stenosis with (n=1) and without (n=1) prosthetic valve surgery; and partial anomaly pulmonary venous drainage to superior vena cava (n=1). Patient demographic data were shown in table 1. Acute successful ablation was achieved in all patients. Four patients need external cardioversion to sinus rhythm as part of the procedure. The mean fluoroscopy time was 77.40±18.71 minutes. There was no peri-procedure complication. Two patients with very early recurrence defined as within 48 hours and 2 patients had early recurrence of AF defined as recurrence within 3 months of ablation. One patient underwent redo AF ablation and all patients was maintained on antiarrhythmic agents and 9 (69.24%) patients with no recurrence of AF on a mean of 431.23±363.17 days of follow up.

Conclusion: For patient with structural heart disease and symptomatic atrial fibrillation, catheter AF ablation is a feasible and viable option.

Patient demographic:

Patient number	13 (8 male, 5 female)
Age (year)	60.38±9.82
AF duration before ablation (year)	4.54±3.26
CHAD-VASc score	1.15±1.14
Left atrial size (cm)	4.22±0.81
Left ventricular ejection fraction (%)	57.15±12.51
Post AF Ablation EHRA score	1.38±0.87

Molecular Autopsy Unmasked a Novel Mutation in CACNA1C Underlying Brugada Syndrome in a Young Victim of Sudden Nocturnal Death

NS Mok¹, Chloe Mak², Hencher Lee², Carol Siu², CY Tsang³, Albert Chan², KC Lee²
¹Dept of Medicine & Geriatrics, PMH; ²Dept. of Pathology, PMH; ³Forensic Pathology Service, DH

Background – Brugada syndrome (BrS) is an inherited cardiac ion channelopathy with genetic heterogeneity that can result in sudden cardiac death (SCD) in the young healthy population. Mutations in *SCN5A* and much less commonly in *CACNA1C* and *CACNB2b* may be implicated in BrS.

Purpose – To conduct molecular autopsy (postmortem genetic testing) to look for mutations implicated in BrS in a young Chinese male victim of sudden unexplained nocturnal death whose autopsy findings and toxicology screening were negative and ECGs suspicious of BrS on lead V1 recorded during exercise stress test.

Methods & Results – Formalin-fixed postmortem heart tissues from the victim were retrieved for genetic testing for BrS. We targeted at *SCN5A* first. There was presence of significant inhibitors and damaged DNA in the prolonged formalin-fixed heart tissues. Only five out of 27 coding exons of *SCN5A* were amplified and no known disease-causing mutations were detected by direct sequencing. As BrS is a familial disease, we then changed our strategy by testing his parents' *SCN5A* but again no mutation was found. Then, we tested the L-type calcium channel genes *CACNA1C* and *CACNB2b* and a heterozygous 12-nucleotide deletion in *CACNA1C* was detected in one of his parents. This mutation was predicted to cause deletion of four amino acids in the carboxyl terminus of the L-type calcium channel alpha 1c subunit. This 12-nucleotide deletion is novel and is predicted to be deleterious by *in silico* analysis. Mutation-specific genetic testing on victim's extracted DNA found the same mutation, thus confirming BrS underlying his SCD.

Novel Role of the CHADS2 Scores Combined with PR Prolongation to Predict Adverse Vascular Function, Ischemic Stroke and Cardiovascular Death in High-Risk Patients without Atrial Fibrillation

YH Chan, KH Yiu, KK Lau, YF Yiu, SW Li, TH Lam, CP Lau, CW Siu, HF Tse
Division of Cardiology, Queen Mary Hospital, The University of Hong Kong, Hong Kong

Background: Whether the CHADS2 and CHA2DS2-VASc scores have clinical utility for prediction of vascular dysfunction-mediated cardiovascular (CV) events in patients without atrial fibrillation (AF) was unknown. PR prolongation as a novel precursor to AF may further enhance risk prediction of CV patients without clinical AF.

Methods: We analyzed 579 high-risk CV outpatients without clinical AF in a prospective cohort for new-onset ischemic stroke, myocardial infarction (MI), congestive heart failure (CHF), and CV death. Brachial flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NMD), carotid intima-media thickness (IMT) and Pulse Wave Velocity (PWV) were determined.

Results: Baseline CHADS2 score was associated with lower FMD (Pearson R= -0.16, P<0.001) and NMD (R= -0.17, P<0.001), higher carotid IMT (R=0.30, P<0.001) and PWV (R=0.35, P<0.001; similar for CHA2DS2-VASc score: All <0.05). After follow-up of 63±11 months, 82 patients (14.2%) developed combined CV endpoint. ROC Curves showed that both CHADS2 and CHA2DS2-VASc scores were predictors for ischemic stroke (C-Statistic: CHADS2 0.70, P=0.004; CHA2DS2-VASc 0.68, P=0.010), MI (CHADS2 0.63, P=0.030; CHA2DS2-VASc 0.70, P=0.001), and CV death (CHADS2 0.63, P=0.022; CHA2DS2-VASc 0.65, P=0.011). Higher CHADS2 score was associated with reduced event-free survival from combined CV endpoints (Log-Rank=16.7, P<0.001; with differences potentiated if stratified by CHA2DS2-VASc score (Log-Rank=29.2, P<0.001). Incorporating PR prolongation, the CHA2DS2-VASc-PR score achieved the highest C-Statistic for CV death prediction (0.70, P<0.001) superior to the CHADS2 score (Chi-Square: 12.1, P=0.0005).

Conclusions: The CHADS2 and CHA2DS2-VASc predict vascular dysfunction and cardiovascular events in high-risk CV patients without clinical AF, with novel enhanced performance incorporating PR prolongation.

Conclusions – We reported the first local experience of using molecular autopsy to unveil BrS underlying an autopsy-negative SCD and that BrS due to *CACNA1C* mutation can be identified in the local Chinese population. While molecular autopsy may be used in elucidating the cause of unexplained SCD in young victims, genetic testing of parents may be considered as an alternative in case quality of victim's DNA is unsatisfactory.

ABSTRACTS

Abstracts for Free Paper Session:

EPS, CARDIAC ARRHYTHMIA AND PACING

Predictors of Mortality and Implantation of Permanent Pacemaker in Patients with Bradyarrhythmia.

Tan GM, Chan JYS

Division of Cardiology, Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong.

Purpose:

Bradyarrhythmia is one the common cause of admission to a coronary care unit (CCU). The outcomes of these patients during their inpatient stay, and the factors influencing these outcomes however have not been elucidated. We have conducted a retrospective single-center hospital-based cohort study to determine the predictors for inpatient mortality and implantation of permanent pacemakers (PPM).

Method:

Patients with the diagnosis of bradyarrhythmia admitted to CCU in Prince of Wales Hospital (PWH) during January 2012 to February 2013 were identified. Information on background clinical information, drug history, physical finding on admission, ECG diagnosis on admission and initial laboratory result were extracted from computerized clinical record (CMS). The primary outcome variable measured was death during the index admission, and the secondary outcome was implantation of PPM. The associations of primary outcomes with different variables were first established with Chi-square test for categorical variables, and Student t-Test for continuous variables. Variables with significant association (ie. with p value of <0.05) were extracted and used in the stepwise forward logistic regression analysis to determine the relationships with the primary and secondary outcomes.

Result:

In this retrospective cohort, a total of 101 patients were identified. Mean age was 75.9 years (SD +/-10.8). A total of 11 primary events were recorded, presenting a mortality rate of 10.9% for patients with bradyarrhythmia. 73.3% of patients had PPM implanted. The association analysis had identified age, history of CVA, hypotension on admission, left bundle branch block on ECG, elevated TnT, anaemia and renal failure as significantly associated with the mortality. Forward logistic regression analysis of these variables showed that age, history of CVA and anaemia significantly predicted mortality, with an odd ratio (OR) of 1.2 (CI 1.03-1.39), 8.5 (CI 1.228-58.956) and 26.8 (CI 3.883-184.796) respectively. Rate/rhythm control drug usage, hypotension on admission, Mobitz type I ECG, elevated TnT, renal failure, hyperkalemia, hypocalcaemia and anaemia were identified as significantly related with the secondary outcome of implantation of PPM. In the forward logistic analysis, elevated TnT, hyperkalemia and anaemia were found to be significantly less likely to be associated with implantation of PPM, with an OR of 0.284 (CI 0.085-0.952), 0.166 (CI 0.041-0.678) and 0.126 (CI 0.035-0.454) respectively.

Conclusion:

Patients admitted to CCU for bradyarrhythmia had a high mortality. Advanced age, history of CVA and anaemia significantly increase the in-hospital mortality of patient admitted for bradyarrhythmia, while patients with elevated TnT, anaemia and hyperkalemia were less likely to have PPM implanted during their index admission.

An evaluation of modified Pacemaker rate sensor optimization with conventional method

Leung YW,¹ Yue CS,¹ Leung KF,¹ Mak YMW,¹ Wong E,² Chow KS,¹ Law KF,¹ Tang SK¹

¹Division of Cardiology, Department of Medicine and Geriatrics, ²Physiotherapy Department, United Christian Hospital, Hong Kong

Introduction: Rate sensor optimization is crucial for those with chronotropic incompetence. However, it was generally underutilized due to limited clinic time; limited resources for treadmill exercise test (TET); also the rapidly growing patient volume.

Objectives: To evaluate different sensor optimization methods, that may best fit the patients also Hong Kong clinic setting.

Methodology: An eighteen months pilot study was conducted in our Cardiac Nurse Pacemaker clinic from April 2011 to September 2012. Twenty ambulatory patients with symptoms of exercise intolerance were recruited; sensor optimization was performed using 3 different methods.

Method: (1) Using conventional TET with supervision by Cardiologist and collaboration with physiotherapist. (2) Perform pre and post 6-10 minutes walk in clinic with heart rate histogram data collected, adjust based on the result. (3) Adjust only by experience and review in clinic every 1-2 months.

Results: All patients recruited in method 1 (n=2) and method 2 (n=6) shown similar improvement in all monitored parameters: average HR histogram; exercise tolerance (floor of stairs); patient satisfaction and quality of life (QoL). Two of them (one in each group) could even resume their previous job. For patients recruited in method 3 (n=12), only 50% showed improvement in the average HR histogram, although 67% claimed with subjective improvement in their exercise tolerance and QoL. Repeated clinic follow-up and re-adjustment were needed in most of them, four of them without any improvement were thus terminated.

Conclusion: Rate sensor optimization of pacemaker under TET or 6-10 minutes walks are both shown to be effective, and the latter one seems to be more cost effective and time-saving which fits Hong Kong clinic setting more. On the other hand, it also demonstrated that Cardiac Nurse Pacemaker Clinic can offer quality specialized care and continued support for pacemaker patients including those with exercise intolerance after implant.

ABSTRACTS

Abstracts for Free Paper Session:

CARDIAC SURGERY

Surgical treatment for infective endocarditis

Herman HM Chan, Nicholson Yam, MF Lin, KY Sit, Barnabe A Rocha, Daniel TL Chan, Cally KL Ho, Flora HF Tsang, Xin Li, Alan Sihoe, Alan WS Suen, Timmy WK Au
Department of Cardiothoracic Surgery, Queen Mary Hospital, Hong Kong

Purpose: To evaluate our experience of surgical treatment in patients with infective endocarditis.

Methods: We reviewed all patients who have undergone surgical treatment for infective endocarditis between Jan 2008 and Dec 2012. The demographics and relevant clinical data of studied patients were retrieved via CDARS and hospital record.

Results: Fifty patients (19 women and 31 men) who had undergone valvular operations for infective endocarditis within the study period were evaluated. The mean age of patients was 44 (39.8 for female and 46.4 for men). Of the blood culture criteria for endocarditis, there were two cases of culture negative endocarditis and two cases of fungal endocarditis. Isolated aortic valve or mitral valve involvement occurred in 18 and 24 patients respectively. Dual valve endocarditis occurred in 5 patients. There were two patients who had isolated tricuspid endocarditis and one patient who had pulmonary valve involvement. The 30-day mortality was 4%. Postoperative morbidities including bleeding, arrhythmia, renal and liver impairment, thromboembolic events, prolonged intubation, groin seroma, hemothorax, empyema and wound infection were encountered.

Conclusions: The surgical treatment for infective endocarditis can be safely performed. The associated morbidity warrants further investigation and study.

Redo-cardiac surgery with repeated sternotomies in Hong Kong population

N Yam, TWK Au
Division of Cardiothoracic Surgery, Department of Surgery, Queen Mary Hospital, The University of Hong Kong, Hong Kong

Background: Redo-cardiac surgery with previous sternotomy is known to be an important risk factor for post-operative morbidity/mortality. With increasing longevity of patients following cardiac surgery, redo operations with increasing technical complexity were performed routinely nowadays.

Purpose: To evaluate the surgical experience of managing redo-cardiac surgery with repeated sternotomies in a cardiothoracic surgery centre in Hong Kong.

Methods: We retrospectively collected demographics, pre-operative, operative and post-operative data in all consecutive patients with redo operations in our operative record registry between 2008-2012.

Results: 257 repeated sternotomies were performed for cardiac re-operations from Jan 2008 to Dec 2012. Isolated valve surgery or valve-and-other surgery for accounted for the majority (up to 90%) of re-sternotomies over the years. Redo-aortic surgery and redo-coronary artery surgery were less commonly performed, possibly related to development of endovascular therapies and percutaneous coronary interventions. Redo-cardiac surgery after previous congenital heart operations was an expanding entity, accounting for 30% of the total re-sternotomies in recent years. Our overall mortality (30-days mortality) for re-operations is 6.2%, increasing mortality risk with increasing number of previous sternotomies: 5% in 1st redo, 9% in 2nd redo, and 25% in 3rd redo and above.

Conclusion: Redo-cardiac surgery with previous sternotomies has accounted for an significant proportion of operations performed nowadays. Unlike Western populations, cardiac re-operations is mostly related to valvular pathologies instead of vascular pathologies in Asian population.

10 years experience of coronary bypass grafting using radial arterial graft: clinical outcome and comparison between endoscopic and open graft harvesting

MF Lin, WK Au, KL Ho, TL Chan, BA Rocha
Department of Cardiothoracic surgery, Queen Mary Hospital, Hong Kong

Purpose: Radial graft was known to improve survival in CABG. We reviewed our clinical outcome of using radial arterial grafting. Endoscopic graft harvesting was started in our centre since 2007. Result of using endoscopic graft harvesting was compared with open method.

Method: From January 2002 to April 2012, 126 patients underwent CABG using radial arterial graft. We changed the method of graft harvesting from open to endoscopic since 2007

The data of major adverse cardiac and cerebrovascular event (MACCE) was reviewed retrospectively. Statistical analysis was performed using SPSS 17.0 for window. Cumulative event rates were estimated by Kaplan-Meier method.

Results: The overall 10 years survival rate was 91%. The cumulative event rate of MACCE was 28.5%. Rate of myocardial infarction or re-intervention was 15.2%. The 5 years result of patient underwent endoscopic radial arterial graft harvesting was compared to open group. There was no difference in survival (95.8% vs 90%, p=0.40), rate of MACCE (23.8% vs 25%, p=0.31) and rate MI or re-intervention (12.7 vs 13.7%, p=0.52) at 5 year follow up.

Conclusions: Radial arterial grafting gives excellent result in long term. Endoscopic graft harvest gives similar survival and MACCE when comparing to open method.

Mitral Repair Surgery – Mini-thoracotomy versus Median sternotomy:

Case matched study

Daniel TL Chan, Cally KL Ho
Department of Cardiothoracic Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong

Purpose: The aim of this study is to compare minimally invasive approach mitral repair surgery (MIS) with conventional median sternotomy (MS) approach in a tertiary referral university teaching hospital.

Methods: From January 2008 to June 2012, out of the total 131 open mitral repair surgery, 60 patients were retrospectively analysed. 31 patients (52%) had mini-thoracotomy, 29 patients (48%) had median sternotomy. Isolated mitral repair surgery was performed in 73% of patients, 19% had additional tricuspid annuloplasty, 5% with radiofrequency ablation surgery and 4% with ASD closure. Post-operative hospital and ICU stay, complications, 30 day mortality and early post-op mitral regurgitation (MR) status were studied.

Results: There were no difference in peri-operative risk factors and casemix between the MIS and MS group except the MS group had more diabetic mellitus. There was no hospital mortality in both groups. Complexity of mitral repair techniques and concomitant cardiac surgery performed in both groups were statistically similar. There were significantly longer bypass and aortic cross clamp time in the MIS group. However, the MIS group showed tendency to have a shorter ICU stay and hospital stay and together with significant fewer blood transfusion. There were no significant differences between the 2 groups in post-operative complications, mortality and early follow up mitral regurgitation status. Follow up completion was 100%.

Conclusions: MIS required longer bypass and cross clamp time but it appeared to have no significant difference in terms of quality of surgery, post-operative complications and mortality when compares to MS approach; while offering advantages of few blood transfusion and tendency of shorter ICU and hospital stay. Further evaluation is required to study different approaches in minimal invasive cardiac surgery.

ABSTRACTS

Abstracts for Free Paper Session:

CARDIAC SURGERY

Determinants of Adverse outcome in Patients with Combined Aortic and Mitral Valve Replacement: Implication of Left Ventricular Dimension

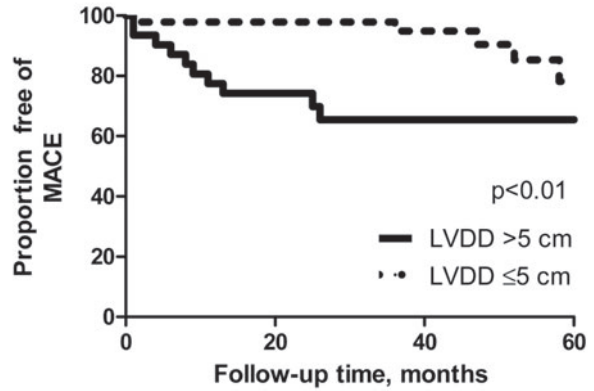
Wong Chun Kit Arthur¹, Chen Yan¹, Zhen Zhe¹, Sit Ko Yung², Au Wing Kok², Lam Yui Ming¹, Siu Chung Wah¹, Tse Hung Fat¹, Yiu Kai Hang¹
¹The University of Hong Kong, Queen Mary Hospital, Department of Medicine, Division of Cardiology, Hong Kong, HKSAR, People's Republic of China.
²Queen Mary Hospital, Department of Surgery, Division of Cardiothoracic Surgery, HKSAR, People's Republic of China.

Introduction: Because of advancement in cardiac surgical techniques over the past decade, the number of patients undergoing combined aortic and mitral valve replacement increases significantly. Apart from a low left ventricular ejection fraction (LVEF), other possible determinants of adverse outcome, such as left ventricular (LV) dilatation, in these patients is however unknown. As a result, the implication of LV dimension has not been considered in the current guideline. The aim of the present study was to examine whether LV dilatation may affect the outcome of patients undergoing this type of surgery.

Methods: A total of 79 patients (52 males and 27 females, age=56.6±10.1 years) who underwent surgery for combined aortic and mitral valvular disease between 2007 and 2011 were followed up for an average of 40.3 months. Detailed echocardiography and clinical parameters were collected. A left ventricular diastolic diameter (LVDD) >5.0cm was considered as LV dilatation. Major adverse cardiovascular event (MACE) was defined as heart failure (HF) requiring admission, thromboembolic events and cardiovascular (CVS) mortality.

Results: The mean LVEF was 60±10% and 30 (38%) patients had LV dilatation. There were 14 MACE (10 HF, 3 thromboembolic events and 1 CVS death) with an annualized event rate of 5.9%. Patients with MACE were more likely to have diabetes mellitus (DM), a lower LVEF and LV dilatation (all P<0.05). Further, Kaplan Meier curve (Figure) demonstrated that patients with LV dilatation experienced more MACE than those with no LV dilatation. Importantly, multivariate analysis determined that DM (Hazard ratio [HR] 13.5, Confidence interval [CI] 3.3-55.5), impaired LVEF (HR=6.3, CI=1.4-27.6) and LV dilatation (HR 4.3, CI 1.1-16.7) (all P<0.05) were independent predictors of MACE.

Conclusion: Patients who underwent surgery for combined aortic and mitral valvular disease have good clinical outcome. Besides a low LVEF, the present result firstly demonstrated that a LVDD >5.0 cm was independently predictive of MACE. Therefore patients should be considered to undergo such surgery before the development of LV dilatation. This finding should be implemented in the current guideline for better surgical risk stratification in this group of patients.



ABSTRACTS

Abstracts for Free Paper Session:

PAEDIATRIC CARDIOLOGY I

Impact of fetal echocardiography on parents' decisions in China.

A preliminary report from a single center in Shanghai

Lin Wu¹, Qi Sun², Luming Sun²

¹Children's Hospital of Fudan University, Shanghai First Maternity and ²Infant Hospital, Tongji University School of Medicine, China

Purpose: Fetal echocardiography allows for prenatal diagnosis of congenital heart disease or severe arrhythmia, and now serves as a routine screening tool for fetal cardiac anomalies in Shanghai. The aim of this retrospective study was to evaluate the impact of prenatal echocardiography diagnosis on parents' decisions.

Methods: A total of 53 fetuses were confirmed by fetal echocardiography to have cardiac anomalies in prenatal counseling clinic of Shanghai First Maternity and Infant Hospital from Jan 2011 to Dec 2012. The serial echocardiographic assessment was performed by experienced fetal sonographer with paediatric cardiologist together. Based on the simplified grading scale of fetal echocardiography, paediatric cardiologist, obstetrician and geneticists will provide the prenatal counseling for the couples, to outline the treatment options and to provide a true and clear picture of prognosis.

Results: All of these 53 fetuses were divided into four categories as follows: Class I, minor anomalies probably without treatment needed; Class II, simple defects with normal life quality after interventional or surgical therapy; Class III, complex anomalies with reasonable life quality after the definitive surgical repair, possibly further re-intervention needed; Class IV, severe malformation or arrhythmia with multiple staged surgical repair needed or very poor prognosis. The abortion rate was 21.4% (3/14), 30% (3/10), 40% (4/10) and 84.2% (16/19) in class I, II, III and IV, respectively and the difference among these groups was statistically significant ($p < 0.05$).

Conclusions: It is of note that we are able to provide a comprehensive prenatal counseling by using of simplified grading scale of fetal echocardiography. In China, most parents are not willing to accept multiple staged surgical repair and possible long-term complication. And the medical cost and ultimate quality of life play important roles on parents' prenatal decisions.

OUTCOME OF PREGNANCY IN WOMEN WITH CONGENITAL HEART DISEASES (CHD) OF A TERTIARY CENTRE IN HONG KONG

Pak-cheung CHOW¹, Kelvin Ki-wan CHAN², Kin-shing LUN¹, Tak-cheung YUNG¹, Yiu-fai CHEUNG¹, Kai-tung CHAU¹

¹Department of Paediatric Cardiology, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital¹; ²Division of Cardiology, Department of Medicine, Queen Mary Hospital²

BACKGROUND: Advance in congenital heart disease management allows female patients to reach reproductive age. Congenital heart diseases, either native or operated, were known to complicate the pregnancy course. Appropriate assessment is important to anticipate and manage adverse events during pregnancy, which may be facilitated by the recently published modified World Health Organization (WHO) risk classification. We reported our experiences of the outcome of pregnancy in women with CHD and the usefulness of WHO risk classification.

METHODS: Women who were followed up in Department of Paediatric Cardiology Queen Mary Hospital and with history of pregnancy during the period January 2000 to January 2013 were identified. Clinical information was retrieved from the records and electronic patient record system (ePR). WHO risk class 1 – 4 was assigned according to their cardiac conditions. Maternal events, obstetric events and foetal outcome were retrieved and comparison was made among different WHO risk class.

RESULTS: Fifty women with 80 pregnancies were identified. There was one twin pregnancy, while the others were singleton. Sixty-three pregnancies (78.8%) had cardiac assessment with the mean age and gestation at first assessment being 28.8±5.0 years and 14.9 weeks (range 4.9-36.6weeks) respectively. Forty-five pregnancies were assigned to be WHO class 1, while 28 pregnancies as class 2 and 7 pregnancies as class 3. There was no maternal death. Maternal cardiac events complicated 6 pregnancies (7.4% of total pregnancies), including heart failure (n=2), right ventricular functional impairment (n=1), streptococcal viridians endocarditis during second trimester (n=1), post-partum hypotension required resuscitation (n=1), and post-partum pulmonary oedema (n=1). Thirteen pregnancies were terminated (16%) and miscarriages developed in 13 pregnancies (16%). There was one stillbirth. The remaining 53 successful pregnancies were delivered at 39.0±1.3 weeks. Labour was spontaneous in 33 pregnancies (62.2%) and induced in 11 pregnancies (20.8%). Vaginal delivery occurred in 34 pregnancies (64.2%), 11 of them were assisted by forceps (n=2) or vacuum extraction (n=9) to shorten second stage. Caesarean section was performed in 20 pregnancies, 9 of which were emergency due to obstetric reasons. There were 54 babies born including one pair of twins. Mean birth weight was 3.13±0.42kg among 45 babies with data available. Three babies (5.5% of the livebirths) were found to have heart lesions including perimembranous ventricular septal defect (n=1), bicuspid aortic valve (n=1), and supravalvular aortic stenosis (n=1). Occurrence of maternal cardiac events was associated with higher WHO risk class ($p=0.04$). Greater proportion of pregnancies within WHO risk class 1 (69%) and 2 (72%) resulted in livebirth when compared to that of class 3 (28.5%) ($p=0.07$). Mode of labour and delivery were not related to cardiac risk class. Babies born to class 1 mother tended to have heavier birth weight than those born to class 2 mother (3.30±0.27kg vs 2.93±0.52kg, $p=0.06$).

CONCLUSIONS: Women with congenital heart diseases of WHO class 2 or 3 tended to have higher incidence of maternal event and foetal compromise. They should be carefully assessed and monitored during pregnancy.

Relationship of Mutation and Methylation in CITED2 with congenital Heart Disease

Min Xu, Xiaoyun Wu, Jie Tian

Children's Hospital of Chongqing Medical College, China

Objective: Explore CITED2 mutations that how to impact the expression of the transcription factor HIF-1 α , and to determine the role of methylation of CITED2 promoter in congenital heart disease, so that help us to understand the pathological mechanisms of congenital heart disease.

Methods: CITED2(c.573-578del6) mutant recombinant plasmid and wild recombinant plasmid were successfully constructed in our early study. Transfecting them into HepG2 and H9C2 respectively. The cells were cultured in hypoxia. RNA was extracted and transcribed into cDNA after 24h. Expression differences of HIF-1 α mRNA were compared among groups by Q-PCR. And the expression of HIF-1 α protein were detected by Western-blotting after 48h. Myocardial tissues from 31 children with congenital heart disease was collected during surgery in department of cardiothoracic surgery from March 2011 to March 2012, and tissues samples of 2 health children were harvested after accidental death. Bisulfite-sequencing PCR (BSP) and methylation-specific PCR (MSP) were used to detect methylation in CITED2 promoter. And then expression differences of CITED2 mRNA were compared between the methylate and control group.

Results:

1. Expression of HIF-1 α mRNA was down in wild group comparing with the empty vector group ($P < 0.05$), but it was higher in mutant group than that of wild group ($P < 0.05$), empty vector group and no transcription group showed no significant difference.
2. Expression of HIF-1 α protein was down in wild group comparing with the empty vector group ($P < 0.05$), but it was higher in mutant group than that of wild group ($P < 0.05$), empty vector group and no transcription group showed no significant difference.
3. CITED2 methylation was found in 10 of 12 congenital heart disease by BSP, positive rate of CITED2 methylation was 83.3% (10/12).
4. CITED2 methylation was found in 16 of 19 congenital heart disease by MSP, positive rate of CITED2 methylation was 84.2% (16/19).
5. Abnormal methylation was not found in the control group.
6. Compared with the control group, CITED2 mRNA expression was significantly reduced ($P < 0.05$).

Conclusion:

1. HIF-1 α can be negative feedback inhibited by CITED2.
2. The negative feedback inhibition was broken by CITED2 mutation.
3. The CITED2 mutation leads to overexpression of HIF-1 α , which maybe one of factors of the incidence of congenital heart disease.
4. Abnormal methylation of CITED2 promoter (CpG island) is found in congenital heart disease.
5. The abnormal methylation leads to decrease mRNA expression of CITED2, which might be involved in the incidence and development of congenital heart disease.

Comparison of transthoracic echocardiography and angiography guided transcatheter occlusion in patent ductus arteriosus

Zhu Ling, Li Xuan-di, Lin Yue-se, Li Yun-quan, Li Shu-juan, Qin You-zhen,

Wang Hui-shen

Department of Pediatric Cardiology, The First Affiliated Hospital, SUN Yat-sen University, Guangzhou 510080, China

Objective To investigate the feasibility of transthoracic echocardiography(TTE) guided transcatheter occlusion for patent ductus arteriosus (PDA).

Methods Totally 58 cases of patients of simple funnel shape(Type A)PDA were studied retrospectively, which were divided into the angiography group(n=21) and echocardiography groups(n=37). The angiography group used traditional transcatheter occlusion technique, and the echocardiography group received TTE guided transcatheter occlusion.

Results Successful occlusion was performed in all patients. Both of the TTE and angiogram group showed that good position of the occlusion devices. Moreover, the velocities of blood flow in left pulmonary artery and the descending aorta were in normal range. Compare with angiography group, echocardiography group showed shorter operation time($P < 0.05$), shorter X-ray time($P < 0.05$), lower radiation dose, less Length of hospital stay($P < 0.05$) and less expense for the medication ($P < 0.05$).

Conclusions TTE guided transcatheter occlusion for simple funnel shape PDA(Type A) is a simplified occlusion method, which is effective and preferential treatment than the method of traditional angiography guidance in clinical trials.

ABSTRACTS

Abstracts for Free Paper Session:

PAEDIATRIC CARDIOLOGY I

Analysis of Arrhythmia and Follow-up After Transcatheter Closure of Secundum Atrial Septal Defect in Children

ZHANG Li, WANG Zhou-ping, XIA Shu-liang, YU Ming-hua, GUO Yan, HUANG Xiao-ming, XIE Jia-er, ZHOU Hui-ming
Department of Pediatrics Cardiology, Guangzhou Women and Children's Center, China

Purposes: To analyze the information and outcome of the transcatheter closure of secundum atrial septal defect (ASD) in children from January 2006 to November 2011.

Methods: One hundred thirty-three patients (male 56, female 77) with the secundum atrial septal defect were treated successfully with occluder device through percutaneous procedure. The patients were assessed with echocardiograph, twelve-lead electrocardiography and chest X-ray before and after transcatheter closure and during follow-up. Analyze the information and outcome of successful closure.

Results: 8 (male 5, female 3) patients occurred arrhythmia after ASD occlusion. They were aged from 5.1 to 7.8 (average, 6.5) years, weight from 16.5 to 24 (average, 18.7) kg, the diameter of device from 20 to 28 (average, 23) mm. Arrhythmia occurred in three day after occlusion. Five of eight patients used the devices whose diameter were 4 mm more than the big size of defect measured by echocardiography. First-degree atrioventricular block (AVB), second-wenckebach, third-degree AVB, and junctional tachycardia were seen in 5, 1, 1 and 1 case, respectively. One patient had First-degree AVB after the first day of occlusion. During intervention. This patient transiently occurred second-wenckebach. We injected a bonus of dexamethasone, then return to sinus rhythm. In another patient, she was 5.2 years old. The size of the defect measured by echocardiography were 12-14 mm. Interatrial septum were 37 mm, we implanted 20 mm occluder. Third-degree AVB was found in the first day. She had supportive treatment. But it had little effect on AVB. So she was removed occluder and made ASD repair after six day of intervention. But she was still third-degree AVB after surgery and during a two-year follow-up. Other patients were recovered well and had no new arrhythmia in one to two years follow-up.

Conclusions: Transcatheter closure of atrial septal defect in children is satisfactory in a whole. Transcatheter occlusion of ASD has a likelihood of happening arrhythmia. Arrhythmia are mostly happened in implanting bigger size of occluder and in a week of closure. Most of arrhythmia are reversible after routine treatment. The prognosis is good.

Postoperative mortality and respiratory complications in heterotaxy patients with congenital heart disease and their relationship with ciliary dysfunction

Weicheng Chen¹, Yuan Yuan¹, Xiaojing Ma¹, Fang Liu¹, Bing Jia¹, Duan Ma², Guoying Huang^{1,2}
¹ Pediatric Heart Center, Children's Hospital of Fudan University, Shanghai, China
² Institute of Biomedical Science, Fudan University, Shanghai, China

Background and Objective: CHD patients with heterotaxy show high postsurgical morbidity/mortality, with some developing respiratory complications. While this is often attributed to the CHD, airway clearance and left-right patterning both require motile cilia function. Recent studies have revealed an association among heterotaxy, congenital heart disease, and primary ciliary dyskinesia (PCD). Thus airway ciliary dysfunction (CD) similar to that of PCD may have relevance for increased respiratory complications in heterotaxy patients. Thus we explore the mortality and respiratory complications in heterotaxy patients as compared to CHD patients without heterotaxy in china, and then we investigate the effects of CD on increased respiratory complications in heterotaxy patients.

Methods: A retrospective review of patients undergoing cardiac surgery was undertaken at our hospital between Jan, 1st, 2000 and Dec, 31st, 2011, which was performed on postsurgical outcomes of 107 patients with heterotaxy and congenital heart disease exhibiting the full spectrum of situs abnormalities associated with heterotaxy. As controls patients, 867 cardiac surgical patients with congenital heart disease, but without laterality defects, were selected, and surgical complexities were similar with a median Risk Adjustment in Congenital Heart Surgery-1 score of 3.0 for both groups. For prospective CD study, 37 CHD patients with heterotaxy were recruited, and 51 CHD patients without heterotaxy and 100 healthy persons were also recruited as controls. Videomicroscopy was used to examine ciliary motion in nasal tissue, and nasal nitric oxide (nNO) was measured by NO analyser.

Results: We found the postsurgical deaths (16.8% vs 4.7%; OR, 3.0), mean length of postoperative hospital stay (12.7 vs 9.1 days) and mechanical ventilation (57 vs 42 hours) were significantly increased in the heterotaxy patients. Also elevated were rates of prolonged ventilatory courses (6.5% vs 2.1%; OR, 3.1), critically ill notice (13.1% vs 5.8%; OR, 2.4), salvage (11.2% vs 5.1%; OR, 2.3), fever (66.4% vs 34.9%; OR, 3.7) and rales (30.0% vs 18.9%; OR, 1.8). For prospective study, 16 patients (43.2%) exhibited CD characterized by abnormal ciliary motion among total 37 heterotaxy patients, compared with 4 patients with CD among total 51 CHD controls (7.8%) and 1 subject with CD among 100 health controls (1%). Among 16 heterotaxy patients with CD, 10 patients' appeared below or near the PCD cutoff values, compared with all normal nNO levels in CHD controls and health controls.

Conclusions: Our findings show heterotaxy patients had more postsurgical events with increased postsurgical mortality and risk for respiratory complications as compared to control patients with similar Risk Adjustment in Congenital Heart Surgery-1 surgical complexity scores. Prospective CD study show that CHD patients with heterotaxy have substantial risk for CD with low nNO. We speculate that CD contribute to the increased mortality and respiratory complications in heterotaxy patients.

Vascular Mechanics at Rest and During Exercise after Arterial Switch Operation for Complete Transposition of the Great Arteries

Robin HS Chen, Wilfred HS Wong, YF Cheung
Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

Background: Progressive neo-aortic root dilatation and regurgitation after arterial switch operation (ASO) for complete transposition of the great arteries (TGA) are well documented. We tested the hypothesis that neo-aortic stiffness is increased and is associated with neo-aortic dilatation in patients after ASO. We further explored the changes in mechanics of the neo-aorta during exercise stress.

Methods: Thirty patients (22 males) aged 16.2±2.1 years and 22 healthy controls (15 males) were studied. Central and peripheral arterial pulse wave velocity (PWV), carotid (c-AI) and radial (r-AI) augmentation indices and central systolic blood pressure (cSBP) were assessed by applanation tonometry. Dimensions of the aortic annulus, sinus, sinotubular junction, ascending aorta, and right carotid artery dimensions were determined at rest and during exercise by 2-dimensional echocardiography. Aortic strain, distensibility, aortic and carotid stiffness indices were calculated.

Results: At rest, patients compared with controls had higher c-AI, heart-carotid PWV, CsBP, and r-AI (all p<0.05), while brachial-ankle arterial PWV were similar. During at rest and exercise, patients had significantly lower aortic strain and distensibility, and significantly greater systolic blood pressure, and aortic and carotid stiffness (p<0.05). Aortic root dimensions at all levels were significantly greater in patients compared with controls (all p<0.05). Patients with aortic dilatation had higher cSBP and aortic stiffness at rest, and lower aortic strain and distensibility at rest and at submaximal exercise (all p<0.05). Linear regression model identified resting aortic stiffness (β=0.464, p=0.003) and age at operation (β=0.40, p=0.005) as significant determinants of aortic sinus z score. Significant aortic regurgitation was identified in 20% (6/30) of patients, in whom significant higher z scores for aortic annulus and sinotubular junction were found (both p<0.05).

Conclusions: In adolescents late after ASO for TGA, aortic root dilatation and regurgitation is prevalent and is associated with stiffening of central arteries at rest and during exercise.

Genome-wide expression profile of pediatric patients with Vasovagal Syncope

Yu-Juan Huang, Zai-wei Zhou, Miao Xu, Qing-wen Ma, Jing-bin Yan, Jian-yi Wang, Quo-qin zhang, Yan-feng Lu, Qin Lu, Hong Tian, Li-Ming Bao, Min Huang
Department of Pediatrics, Shanghai Children's Hospital, Shanghai Jiao Tong University, Shanghai 200040, China

Vasovagal syncope (VVS) is easy to cause accident harm of teenagers and getting a lot of attention lately. A novel insight into the pathophysiology of VVS obtained by studying gene expression should help to discover novel biomarkers of VVS and to suggest novel strategies of therapy. The aim of our study was to establish gene expression patterns in leukocytes from syncope patients.

Ten patients with head-up tilt test (HUT) induced syncope were included. The blood was collected on the time of positive reaction during the HUT. Control group comprised 10 children without history of syncope and had a negative HUT. The blood was collected on the time of the HUT was finished. Gene expression analysis was performed with Affymetrix Human Gene 1.0 ST microarrays and GCS3000 TG system. Lists of genes showing altered expression levels (fold change>1.2, p<0.05) were submitted to Ingenuity Pathway Analysis. Gene lists were examined for canonical pathways and molecular and cellular functions. Comparing syncope with positive HUT and control group we found 103 genes with changed expression (100 were up- and 3 down-regulated). Comparing VVS genes with control group, dozens of genes from several pathways linked with apoptosis, B cell receptor signaling pathway, G protein-coupled signal transduction pathway show altered expression. Up-regulation of GNG2 and GPR174 genes in vasovagal syncope is observed in the vast majority of patients.

This is the first genome-wide expression study for Syncope patients which provides a new insight into the molecular mechanism of VVS.

ABSTRACTS

Abstracts for Free Paper Session:

PAEDIATRIC CARDIOLOGY II

Use of Sertraline in the Treatment of Vasovagal Syncope in Children

SHI Lin, LIN Yao, WANG Yun, ZHENG Tong, CONG Xiao-hui, MA Li-juan, LIANG Lu, PAN Yan
Cardiology Department, Children's Hospital affiliated to Capital Institute of Pediatrics, Beijing 100020, China

Objective: Role of the serotonergic system in the genesis of vasovagal syncope has been concerned increasingly. It was reported that as a kind of selected serotonin re-uptake inhibitor, sertraline could be used for the treatment of vasovagal syncope. However, there are few researches focusing on this drug treatment in children currently. The purpose of this study was to investigate the treatment effect of sertraline to vasovagal syncope in children.

Method: Eighty-nine children with unexplained syncope or pre-syncope were enrolled, who were diagnosed as vasovagal syncope (VVS) with positive head-up tilt test (HUTT) in Children's Hospital affiliated to Capital Institute of Pediatrics from Jan 2007 to Jun 2010, with the mean age of (10±3) years old. These children were divided into 3 groups, including health education group (n=20), oral rehydration salt (ORS) treatment group (n=31), and sertraline treatment group (n=38). All children underwent HUTT, which helped to identify responses to different treatment protocols and regulate drug dose. Then according to the result of HUTT, treatment effects were evaluated. After 6-month's follow-up, if there was no syncope episode or pre-syncope occurred, drug treatment should be stopped, and then follow-up should still be continued. The recurrence rates of syncope and pre-syncope, drug side effects and hemodynamic changes after treatments were evaluated. Data were analyzed by soft SPSS 11.5.

Result: (1) Respectively, 20.0% (4/20), 61.3% (19/31) and 73.7% (28/38) of patients became HUTT-negative in health education group, ORS treatment group and sertraline treatment group. Rates were significantly higher in the latter two groups than the former one ($P<0.05$). However, there was no significant difference between ORS treatment group and sertraline treatment group ($P>0.05$). (2) Over a follow-up period of 6 to 12 months, recurrence rates of syncope and pre-syncope in health education group, ORS treatment group and sertraline treatment group were 80.0% (16/20), 71.0% (22/31), and 26.3% (10/38) respectively. The rate in sertraline treatment group was significantly lower than the other two groups ($P<0.05$). The difference was not statistically significant between the other two groups ($P>0.05$). (3) Differences of baseline blood pressure and heart rate before and after treatments were not statistically significant in all groups ($P>0.05$). Blood pressure and heart rate difference between supine position and initial upright tilt after treatment (Δ BP and Δ HR) were significantly decreased in sertraline group ($P<0.05$).

Conclusion: Health education and ORS treatment are basic therapeutic measures of vasovagal syncope in children, and sertraline which is safe and effective can enhance the treatment effectiveness.

Clinical study of percutaneous balloon angioplasty of coarctation of the aorta in 37 children

Lan He, Lin Wu, Fang Liu, Ying Lu, Danyan Zhang, Guoying Huang
Heart center of Children's Hospital of Fudan University Department, Shanghai, China 201102

Objective: To evaluate the immediate efficiency and midterm outcomes of percutaneous balloon angioplasty of coarctation of the aorta in children

Methods: A retrospective study was done in 37 COA patients in whom percutaneous balloon angioplasty was attempted between 2006 and 2012 at Children's Hospital of Fudan University. The inclusion criteria was excluded sever hypoplastic aortic arch and complex congenital heart malformation. All the patients underwent percutaneous balloon angioplasty, some of them with simple heart disease underwent one stage complete repair operation after angioplasty. We divided into two groups to analyze the hemodynamics and outcomes of follow-up.

Results: A total of 37 patients were included in this study, 26 males and 11 females. 13 of 37 (35%) had associated cardiovascular defects. The mean age at catheterization was 10.87±19 months (7 days to 6 years old), and the mean body weight was 6.5±4.78kg. Thirteen patients underwent the hybrid technique (Group B) which was a combination of balloon dilation and surgically repairing. Five patients received balloon angioplasty twice, one patients died after the operation because of left ventricular dysfunction. Successful reduction in the post angioplasty gradient, 40.65±17.48mmHg versus 13.04±7.63mmHg, and the post coarctation diameters was (4.26±1.53)mm versus pre (2.05±1.01) mm. The size of the balloon ranged from 4mm to 12mm. In group B, less time (59.38±20.69 minutes) was on the aortic clamp cardiopulmonary bypass, mechanical support and the mean ventilation time was 8.07±6.18 days and the mean ICU stay was 14.38±10.67 days. Small pseudoaneurysm were found in 4 patients, but all disappeared during follow-up.

Conclusion: Percutaneous balloon angioplasty is an effective treatment alternative to surgery in most patients with recurrent postoperative or native membranous coarctation of the aorta. The early outcome of the hybrid procedure (balloon dilation of the coarctation of the aorta and surgical repair of simple heart defect) for children was satisfying which could avoid from circulatory arrest. It is a relatively safe procedure which could be the optional method for one—stage surgical repair.

Catecholaminergic polymorphic ventricular tachycardia in Chinese children

TC Yung, TC Yu
Department of paediatric cardiology, Queen Mary Hospital, Hong Kong

Background: Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare inheritable and potentially lethal arrhythmia syndrome characterized by bidirectional polymorphic ventricular tachyarrhythmia in patients with normal heart structure and normal QT interval. It is inducible by increased sympathetic activity such as physical exercise and emotional distress.

Method and Results: Retrospective chart review of all patients with the diagnosis of CPVT was performed in the only tertiary cardiac referral centre in HKSAR. Demographic data, clinical presentations, diagnostic methods, genetic mutation, treatment modalities and severe arrhythmic events were recorded. Ten patients (4 males, 2 of them brothers) were identified. The mean age of presentation, mean age of diagnosis and mean duration of follow-up were 11.7 ± 2.8 years, 12.7 ± 3.1 years and 3.3 ± 2.1 years respectively. The mean duration from first presentation to diagnosis was 1.0 ± 1.5 years. All presented with recurrent syncope. Three out of 10 had cardiac arrest and ventricular fibrillation requiring cardiopulmonary resuscitation and defibrillation. For the above 3 patients, one was initially treated as epilepsy with anticonvulsant until the patient presented with the near fatal arrhythmic event. Diagnosis was mainly confirmed by adrenaline / isoprenaline infusion test (5/10) or treadmill (3/10). Of the 9 patients who underwent genetic test, mutations of RyR2 gene were confirmed in 4. One patient refused any treatment. All other patients were initially treated with beta-blocker, 4 were added on Flecainide in view of recurrent syncope or persistent exercise induced arrhythmia. Cardiac sympathectomy was performed in 2 patients. Implantable cardioverter-defibrillator (ICD) was implanted in 2 patients as indicated by near fatal cardiac events despite optimizing medical treatment with or without cardiac sympathectomy. No ICD shock was delivered in the 2 patients so far. No mortality was observed so far.

Conclusion: CPVT must be considered in children or adolescents with sudden loss of consciousness, especially when it occurs during exercise or emotional stress, and with normal heart structure and resting ECG. To minimize risk of fatal arrhythmic events, a stepwise approach in medical and further intervention options including cardiac sympathetic denervation and implantable cardioverter-defibrillators is the current standard treatment.

H2S attenuates CoCl2-induced proliferation through the upregulation of COX-2/PGI2 pathway in HPASMC

LI Yun-quan, WANG Hui-shen
Department of Pediatrics, the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, 510080, China

Purpose: To observe the effect of hydrogen sulfide (H2S) on the proliferation of human pulmonary artery smooth muscle cells (HPASMC) induced by chemical hypoxia and to dissect the role of cyclooxygenase-2 (COX)-2 in this process.

Methods: HPASMC were treated with CoCl2, a hypoxia-mimicking agent, to set up a cellular model of hypoxic pulmonary arterial hypertension (PAH). Prior to the treatment with CoCl2, HPASMC were preconditioned with NaHS (a donor of H2S). Cell viability, intracellular expression of COX-2 and PGI2 level in culture medium were detected, respectively.

Results: Exposure of HPASMC to CoCl2 at 25, 50 or 100 µmol/L for 24 h markedly induced cellular proliferation, and the ratio of proliferation is (112.7±4.6)%, (116.2±3.3)% or (113.3±4.7)%, when comparing with the control group the P value is <0.05, <0.01 or <0.05, respectively. Treatment of HPASMC with 50 µmol/L CoCl2 for 18 to 24 h time-dependently enhanced cellular proliferation (R=0.99). Treatment with 50 µmol/L CoCl2 for 24 h significantly attenuated intracellular COX-2 expression (P<0.05) and PGI2 secretion from HPASMC (P<0.05), and exogenous administration of PGI2 statistically reduced CoCl2-induced cellular proliferation by nine percent (P<0.05). Before treatment with CoCl2, pretreatment of HPASMC with 400 µmol/L NaHS obviously suppressed the cellular proliferation (P<0.05). In addition, pretreatment with 400 µmol/L NaHS partially rescued the decreased expression of COX-2 from 0.17±0.08 to 0.59 ± 0.21, and increased the secretion of PGI2 about 2-fold.

Conclusion: H2S could improve hypoxia-induced cellular proliferation, and its molecular mechanisms might underlie the upregulation COX-2/PGI2 pathway.

ABSTRACTS

Abstracts for Free Paper Session:

PAEDIATRIC CARDIOLOGY II

Morphological characteristics of major aortopulmonary collateral arteries in complex congenital heart disease

Ping Huang; Li Zhang; Wei Li; Jie-min Zeng; Xin-xin Chen; Hu-jun Cui; Jia Yuan;

Fang Gong; Li-ling Jin

From the Heart center, Affiliated Guangzhou women and children's Medical Center of Guangzhou Medical College, Guangzhou 510623, China

Purpose: To assess the values of multidetector-row computed tomography (MDCT) on the morphological characteristics of major aortopulmonary collateral arteries (MAPCAs) in complex congenital heart disease (CHD).

Method: We retrospectively analyzed the imaging data of patients with CHD and MAPCAs. The distribution, number, and morphological characteristics of MAPCAs were summarized.

Results: This patient cohort consisted of 34 males and 17 females. Their ages ranged from 12 days to 13 years, median age 1 year old. Among them, 33 patients (64.71%) were pulmonary atrial/ventricular septal defect, 11 (21.57%) were tetralogy of Fallot, 2 (3.92%) were double outlet right ventricle, 1 (1.96%) was complete transposition of the great arteries, 1 (1.96%) was complete atrioventricular septal defect, 1 (1.96%) was pulmonary stenosis, 1 (1.96%) was pulmonary artery sling, 1 (1.96%) was absence of pulmonary artery. Besides, 16 patients (31.37%) had patent ductus arteriosus. In this group, central pulmonary arteries and confluent were present in 43 patients (84.31%). Totally, 117 MAPCAs were founded in 51 patients, 1-6 per patients, mean 2.29 per patients. Their opening diameter were 2.0-18.0 mm, mean 4.3 mm. There were 16 MAPCAs (13.68%) from aortic arch, 75 (64.10%) from thoracic descending aorta, 2 (1.71%) from brachiocephalic artery, 11 (9.40%) from right subclavian artery, 12 (10.26%) from left subclavian artery, and 1 (0.85%) from other rare arteries. Three MAPCAs (2.56%) had narrowed in opening and followed by dilation, and 57 MAPCAs (48.72%) had squirm twist before turned into lungs. MAPCAs were the only supply of relative lung lobes in 8 patients (15.96%). Besides, 13 MAPCAs (11 patients with pulmonary arterial/ventricular septal defect) had their branches, with larger opening diameter. The number of MAPCAs branches were 2-4, usually 2.

Conclusions: Assisted with MDCT, it was more easily and accurately to know about their origins, numbers, sizes, courses and arborizations. It mainly conducted to the choice of operations.

Atrial Deformation and Electromechanical Coupling after Surgical Repair of Tetralogy of Fallot

Jia Hou^{1,2}, Hong-kui Yu¹, Sophia J Wong¹, Yiu-fai Cheung^{1*}.

¹Division of Paediatric Cardiology, Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong, China

²Cardiovascular Center, Children's Hospital of Fudan University, Shanghai, China

Background and aims: Ventricular diastolic dysfunction in patients with repaired tetralogy of Fallot (TOF) may potentially affect atrial mechanics. This study aimed to explore the right (RA) and left atrial (LA) deformation and electromechanical coupling and their relationships with ventricular diastolic function in repaired TOF patients.

Methods: Fifty-four patients aged 17.8±8.3 years and 40 healthy subjects aged 16.9±6.3 years (p=0.57) were studied. Global RA and LA strain and strain rate at ventricular systole (SRs), early diastole (SRed) and atrial contraction (SRac), and electromechanical delay were determined using speckle tracking echocardiography (STE). Ventricular diastolic function was assessed by tissue Doppler imaging and STE. Ventricular volumes and pulmonary regurgitant volume were derived from 3D echocardiography.

Results: Compared with controls, patients had significantly lower RA and LA peak positive and total strain, SRs, SRed and SRac (all p<0.001). The timing of RA (178±33ms vs 152±17ms, p<0.001) and LA (170±32ms vs 152±24ms, p=0.006). electromechanical coupling was significantly longer in patients than in controls. The corresponding RA and LA strain, strain rate, and electromechanical coupling parameters correlated significantly with each other (all p<0.001). The RA and LA total strain and SRed were associated with diastolic annular velocities and early and late diastolic strain rates of the respective ventricles (all p<0.05). The LA SRed correlated further with pulmonary regurgitant volume (r=-0.33, p=0.016) and RV end-diastolic volume (r=-0.33, p=0.015).

Conclusions: Impaired mechanics of the two atria, atrial electromechanical delay, and atrial-atrial interaction are evident in patients with repaired TOF. Furthermore, our data suggest an association between atrial mechanics and ventricular diastolic function.

Alcohol consumption during gestation induced Histone3 lysine9 hyperacetylation and an alternation of expression of heart development-related genes in mice

Bo Pan

Jie Tian Heart Centre, Children's Hospital of Chongqing Medical University, Chongqing, PR China.

Purpose: Alcohol abuse during gestation may cause congenital heart diseases (CHD). The underlying mechanisms of alcohol induced cardiac deformities are still not clear and definite. In our study, we investigated the effect of alcohol consumption during gestation on the imbalance of H3AcK9 acetylation and the alternation of expression of heart development-related genes during cardiogenesis.

Methods: The pregnant mice were exposed to a single dose of alcohol (10ul/g/d, 56% alcohol) by gavage between E7.5 to E15.5. H&E staining was applied for observing the general structure of embryonic hearts before term. Western-Blot and quantitative real-time PCR were used for detecting the level of H3AcK9 acetylation and genes expression.

Results: Alcohol consumption caused low density of muscular ventricular septum without ventricular septal defect. The level of H3AcK9 acetylation reached peak at E17.5 and decreased sharply to a significantly low level at birth and maintained in a subside state afterward. And total histone3 acetylation level decrease abruptly from E17.5 to newborn also. Alcohol exposure increased H3AcK9 acetylation at E11.5, E14.5, E17.5 and E18.5 respectively (p<0.05), and enhanced the expression of Gata4 at E14.5 and E17.5 and Mef2c at E14.5 each (p<0.05).

Conclusion: These data showed the sequential level of H3AcK9 acetylation during heart development and demonstrated alcohol exposure in utero induced H3AcK9 hyperacetylation and increased the expression of heart development-related genes. These findings indicate a new mechanism that stands behind alcohol induced congenital heart diseases.

Study on the diagnosis and treatment of childhood supraventricular tachycardia with intracardiac electrophysiology attached with reports of 50 cases

Chunhua Qi, Lin Wu, Ying Lu, Lan He

Pediatric Heart Center, Children's Hospital of Fudan University, China

Background: The aim of this study was to clarify the electrocardiographic characteristics of supraventricular tachycardia (SVT) in children and improve the technique of intracardiac electrophysiologic study (EPS) and radio-frequency catheter ablation (RFCA) in children.

Methods: 50 patients with SVT were enrolled in the study from December 2007 to July 2012. The data of ECG and the results of RFCA (ablation success, complications and recurrence) were studied retrospectively.

Results: Among the 50 patients, 29 cases (58%) with atrial ventricular reentrant tachycardia (AVRT); 10 cases (20%) with atrial ventricular node reentrant tachycardia (AVNRT); 6 cases (12%) with atrial tachycardia (AT). Two cases with AVRT accompanying with AVNRT. One case with AVRT and AT at the same time. The procedure was abandoned in 2 patients because of considering the risk in one case (AVRT and accessory pathway (AP) location near His bundle), and 1 case not induced by EPS. No recurrent tachycardia and complication was found in all 50 cases by now.

Conclusions: RFCA is a safe procedure with high success rate and low complication for tachycardia management, but the indications for RFCA should be carefully considered in patients with small age.

ABSTRACTS

Abstracts for Poster Session:

Transcatheter closure of patent ductus arteriosus with severe pulmonary hypertension in children: Immediate and mid-term results

ZHANG Li, YU Ming-hua, WANG Zhou-ping, LI Wei, TONG Min, ZHANG Ming-jie, HUANG Xiao-ming
Guangzhou Women and Children Medical Center, China

Objectives: To explore the immediate and mid-term results of patent ductus arteriosus(PDA) with severe pulmonary hypertension in children after the interventional occlusion.

Methods: We retrospectively analyzed the clinical data of the forty-one children who were with PDA and severe pulmonary hypertension, focused on therapeutic results, complications and follow-up results.

Results: Forty devices (97.5%) were implanted successfully, including thirty-seven domestic ductal occluders were used, two muscular ventricular septal defect devices and one membrane symmetric ventricular septal defect device were also used. Echocardiogram in 72 hours after procedure were checked up: residual shunt were found in 2 cases (5%), left ventricle end-diastolic dimension (LVEDd), left atrial diameter(LA), Left ventricular ejection fraction (LVEF), pulmonary artery systolic pressure (PASP), mitral flow velocity, aortic flow velocity and mitral regurgitation (MR) decreased or alleviated in contrast with those before operation, the differences was statically significant ($P<0.05$). Systolic aortic pressure (AOP) and aortic regurgitation (AR) increased or aggravated, the differences was statically significant ($P<0.01$). Follow-up was conducted in 40patients with the follow-up rate of 100%, median follow up time was 4 months (0.25-56 months). Residual shunt all disappeared in one month after device occlusion. Follow-up in one year: LVEDd and LA significantly reduced from those before operation ($P=0.000$), further reduced compared with those in 3 days. LVEF in 1-12 months after procedure significantly improved more than that in 3 days after procedure ($P<0.05$). MR in one year after procedure alleviated compare to that before procedure ($P=0.035$, AR and TR in one year after procedure unchanged compare to those before procedure ($P>0.05$).

Conclusions: Transeatheter closure of patent ductus arteriosus with severe pulmonary hypertension in children is safe and feasible, but long-term follow-up need to make further study on narrowing of left pulmonary artery and descending aorta related to occluder device.

The AMPLATZER Cribriform Occluder for Porous-type Atrial Septal Defect

Yu Minghua, Li Wei, Tong Ming, Guo Yan, Xia Shuliang, Wang Zhouping, Huang Xiaoming
Department of Pediatric Cardiology, Guangzhou Children and Women's Medical Center, China

Purpose: To know about the feasibility and security of the AMPLATZER Cribriform occluder in the treatment of Porous-type Atrial Septal Defect.

Method: The AMPLATZER Cribriform occluder were implanted in 2 patients with Porous-type Atrial Septal Defect under the guidance of X-ray. They were assessed by echocardiography after the procedures.

Result: Both of 2 patients were successfully implanted the AMPLATZER Cribriform occluder. One patient was trivial residual shunt observed by echocardiography after the procedure, the other had no trivial residual shunt.

Conclusion: The AMPLATZER Cribriform occluder for Porous-type Atrial Septal Defect was feasible. And the security and complications were needed to be proved by large samples and accumulated experiences.

The clinical analysis of peripheral vascular complications after the intervention in infant and children with congenital heart disease

Xia Shuliang, Li Wei, Tong Ming, Yu Minghua, Guo Yan, Wang Zhouping, Huang Xiaoming
Department of Pediatric cardiology, Guang Zhou Women and Children's Medical Hospital, China

Purpose: Analyzing peripheral vascular complications of infant cardiac intervention to investigate the causes and treatment of peripheral vascular complications.

Method: We retrospectively analyzed clinical data of 7 cases of peripheral vascular complications occurred in 609 cases of congenital heart defects intervention.

Result: 609 cases in children were done cardiac intervention. Seven cases had peripheral vascular complications, including 2 cases of femoral arteriovenous fistula, pseudoaneurysm in 1 case, the femoral vein thrombosis in 1 case and the femoral artery thrombosis 3 cases.

Conclusion: Infant peripheral anatomical characteristics, unskilled the puncture technique, and incorrect hemostasis mainly caused infant peripheral vascular complications. skilled puncture technique, correct hemostasis, close observation after intervention, and timely dealing with complications can greatly increase the success rate of interventional treatment.

1:1 matched case-control study on risk factors of congenital heart disease

Tian Jie, Lv Tiewei
Department of Cardiology, the Children's Hospital of Chongqing Medical University, China

Objective: To explore the risk factors of congenital heart disease and to provide references for research in the etiology of congenital heart disease and its scientific precautions.

Methods: A hospital-based congenital heart disease 1:1 matched case-control study was conducted. Patients were diagnosed by echocardiogram, cardiac catheterization or surgery and controls with no congenital disease were selected at the corresponding period. Children's parents were interviewed with a unified face-to-face questionnaire. All factors were analyzed by univariate and multivariate conditional Logistic regression; risk factors associated with congenital heart disease were screened out.

Results: Information of 260 pairs of children with congenital heart disease and controls were analyzed. All factors were analyzed by univariate Logistic regression at $\alpha = 0.05$ level and 21 suspected risk factors were initially screened out then multivariate conditional Logistic regression was used to do multivariate comprehensive analysis. Results indicated that maternal age (>35 years: $P=0.010$, $OR=3.075$; <20 years: $P=0.012$, $OR=5.084$), passive smoking (small amount: $P=0.040$, $OR=1.728$; large amount: $P=0.000$, $OR=3.903$) and cold in early pregnancy ($P=0.023$, $OR=1.787$) were the risk factors of congenital heart disease; taking folic acid regularly ($P=0.004$, $OR=0.447$) and eating meat (≥ 4 times/week: $P=0.001$, $OR=0.293$; 1-3 times/week: $P=0.008$, $OR=0.372$) were significantly associated with a reduced risk for congenital heart disease.

Conclusions: The first trimester is a critical period of fetal heart development. Mother old or young, exposing to tobacco and getting cold in early pregnancy are at increased risk for giving birth to a child with congenital heart disease; taking folic acid regularly and eating more meat are associated with a reduced risk for congenital heart disease.

ABSTRACTS

Abstracts for Poster Session:

Morphological characteristics of major aortopulmonary collateral arteries

Li Zhang, Wei Li, Jie-min Zeng, Xin-xin Chen, Hu-jun Cui, Jia Yuan, Fang Gong, Li-ling Jin
The Heart Center, Affiliated Guangzhou Women and Children's Medical Center of Guangzhou
Medical College, China

Background: To assess the values of multidetector-row computed tomography (MDCT) on the morphological characteristics of major aortopulmonary collateral arteries (MAPCAs) in complex congenital heart disease (CHD).

Study Design: We retrospectively analyzed the imaging data of patients with CHD and MAPCAs. The distribution, number, and morphological characteristics of MAPCAs were summarized.

Results: This patient cohort consisted of 34 males and 17 females. Their ages ranged from 12 days to 13 years, median age 1 year old. Among them, 33 patients (64.71%) were pulmonary atria/ventricular septal defect, 11 (21.57%) were tetralogy of Fallot, 2 (3.92%) were double outlet right ventricle, 1 (1.96%) was complete transposition of the great arteries, 1 (1.96%) was complete atrioventricular septal defect, 1 (1.96%) was pulmonary stenosis, 1 (1.96%) was pulmonary artery sling, 1 (1.96%) was absence of pulmonary artery. Besides, 16 patients (31.37%) had patent ductus arteriosus. In this group, central pulmonary arteries and confluent were present in 43 patients (84.31%). Totally, 117 MAPCAs were founded in 51 patients, 1-6 per patients, mean 2.29 per patients. Their opening diameter were 2.0~18.0 mm, mean 4.3 mm. There were 16 MAPCAs (13.68%) from aortic arch, 75 (64.10%) from thoracic descending aorta, 2 (1.71%) from brachiocephalic artery, 11 (9.40%) from right subclavian artery, 12 (10.26%) from left subclavian artery, and 1 (0.85%) from other rare arteries. Three MAPCAs (2.56%) had narrowed in opening and followed by dilation, and 57 MAPCAs (48.72%) had squirm twist before turned into lungs. MAPCAs were the only supply of relative lung lobes in 8 patients (15.96%).

Conclusions: Assisted with MDCT, it was more easily and accurately to know about their origins, numbers, sizes, courses and arborizations. It mainly conducted to the choice of operations.

The effect of alcohol on biological characteristics and cardiomyocyte-like cells differentiation of mesenchymal stem cells C3H10T1/2

Tian Jie, Liu Zhenguo
Department of Cardiology, the Children's Hospital of Chongqing Medical University, China

Objective: Mesenchymal stem cells C3H10T1/2 were treated with different concentrations of alcohol, observe the biological characteristics and the effect on C3H10T1/2 cells differentiation into cardiomyocyte-like cells.

Methods: MTT assay was used to observe the cytotoxicity of alcohol and filter out appropriate intervention concentrations, counted cells at different culture times and drew the growth curve. After treated with the different concentrations of alcohol for 48h, we used flow cytometry to detect cell cycle, Q-PCR and Western blot to detect Oct-4 expression levels. BMP2 was used as the inducer to investigate the effect on differentiation after the intervention of alcohol for 24h, cells were divided into four groups: BMP2 induced group, 200mM/L alcohol+BMP2 induced group, C3H10T1/2 group and positive control group. Cardiac-specific genes and proteins were detected by Q-PCR and Western blot at 1, 2, 3, 4 weeks.

Results: MTT assay showed that 50mM/L alcohol does not affect cell proliferation, while 200mM/L cell inhibition rate was about 20%. We selected 50, 100, 200mM/L as intervention concentrations of alcohol, cell cycle among the groups showed no significant difference; Oct-4 expression levels also showed no significant difference. In the process of differentiation, there were no significant difference between the BMP2 induced group and alcohol+ BMP2 induced group on the expression levels of GATA4 and MEF2C, but they were still significantly lower than the positive control group, C3H10T1/2 cells sustained low expression levels. The results of cTnT and Cx43 were similar to genes, while no related proteins were detected in C3H10T1/2 cells.

Conclusion: The high concentration of alcohol had cytotoxicity on C3H10T1/2 cells, but no significant differences were detected on the cell cycle and stem cell marker Oct-4 expression levels. Alcohol also did not affect the process of C3H10T1/2 cells differentiation into cardiomyocyte-like cells.

RALDH2 IS ESSENTIAL FOR CARDIOMYOGENESIS DURING P19 STEM CELL DIFFERENTIATION

Lifeng Zhang, Yonghao Gui, Wei Wang
Cardiovascular Center, Children's Hospital of Fudan University, Shanghai, P.R. China

Background: Retinoic acid (RA), a bioactive derivative of vitamin A, plays a crucial role in multiple steps of cardiovascular development. The retinaldehyde dehydrogenase 2 (RALDH2) catalyzes the second oxidative step in RA biosynthesis. RA deficiency is involved in impaired cardiomyogenesis. However, the interaction of RA signaling with other signaling pathways that stimulate or inhibit cardiomyogenesis is not fully elucidated. To investigate the mechanism(s) underlying RA signaling in controlling cardiomyogenesis, we determined the role RALDH2 in regulating cardiomyogenic differentiation of murine P19 pluripotent embryonal carcinoma cells.

Methods: Murine P19 embryonal carcinoma stem cells were utilized to differentiate into cardiomyocytes. The RALDH2 siRNA was used to knock down the expression RALDH2 in P19 cells. The expression levels of cardiomyogenic related genes (Nkx2.5, WT-1, N-myc, GATA4, a-MHC and CTnT) were profiled using quantitative RT-PCR in a time-dependent manner of differentiation.

Results: Endogenous RALDH2 levels were decreased from day 0, indicating that down-expression of RALDH2 in the transfected cells was confirmed. RALDH2 knock-down alters the gene expression files. The data from quantitative real-time RT-PCR reveals changed expression levels of cardiac muscle-specific molecular markers in RALDH2 knock-down cell lines when compared to that in control cells during differentiation. The progenitor specific gene expression of Nkx2.5 was significantly up-regulated during the cardiomyogenic differentiation of P19 cells, whereas the differentiation related gene expression levels of GATA4, TEF-1, a-MHC and CTnT were markedly decreased. The WT-1 were increased in the early stage of differentiation but decreased in the late stage of differentiation.

Conclusion: These finding suggest that RA signaling is critical for cardiac progenitor differentiation through regulation of cardiomyogenic related gene expression. Reduction of RA signaling may restrict cardiac progenitor differentiation through up-regulation of progenitor cell specific transcription factor Nkx2.5.

The Genotype and Expression of TGFβ2 Gene in Children with Congenital Conotruncal Defects

Yingying Meng¹, Xiaojing Ma¹, Jing Zhang¹, Huijun Wang¹, Duan Ma², Guoying Huang¹
¹Cardiac Center, Children's Hospital of Fudan University, Shanghai, China
²Key Laboratory of Molecular Medicine, Ministry of Education, Department of Biochemistry and Molecular Biology, Institute of Medical Sciences, Shanghai Medical College, Fudan University, Shanghai, China

Objectives: Animal studies have shown that knockout of the transforming growth factor beta 2 (TGFβ2) gene results in diverse cardiovascular malformations and its dysregulated expression is involved in the pathogenesis of heart defects. However, little information is available on the genetic and expression alternations of TGFβ2 gene in children with congenital heart disease. Herein, we investigated the genotype and expression of TGFβ2 gene in children with congenital conotruncal defects (CTD).

Methods: We sequenced the whole coding region of TGFβ2 gene in 400 children with CTD. We further analyzed the mRNA and protein expression of the TGFβ2 gene in the myocardial tissues in 37 children with CTD and 5 age-matched healthy children with real-time PCR and immunohistochemistry.

Results: DNA sequencing showed no pathogenic mutations in the coding region of TGFβ2 gene except for a silent mutation (1250T>C) in the exon 4 in one patient. There were no significant differences for the TGFβ2 expression at either mRNA or protein level in the myocardial tissues between children with CTD and children without heart defects.

Conclusion: The results indicate that germline mutation of the TGFβ2 gene is not a common cause of CTD in human and the TGFβ2 expression level may be less critical in humans than in animals for the pathogenesis of CTD.

ABSTRACTS

Abstracts for Poster Session:

Aberrant methylation of the RXRA promoter region may be responsible for its aberrant expression in patients with TOFZHANG Jing¹, MA Xiao-jing¹, WANG Hui-jun¹, MA Duan^{2,3}, HUANG Guo-ying^{1,3}¹Children's Hospital, Fudan University, Shanghai, China, 201102; ²Key Laboratory of Molecular Medicine, Ministry of Education, Shanghai Medical College, Fudan University, China, 200032; ³Research Center for Birth Defects, Fudan University, Shanghai, China, 200032

Background: Conotruncal defects (CTD), induced by abnormal development of the outflow tract (OFT), can be categorized as TGA, DORV, tetralogy of Fallot, and PTA. It has been clearly clarified that RA (retinoid acid) signaling is essential for cardiogenesis including the development of OFT. As an important component of RA signaling pathway, the retinoid X receptor alpha (RXRA) is considered to play important role in pathogenesis of CTD. Indeed, deficiency of RXRA or germline mutation of this receptor in mice results in conotruncal defects and ventricular abnormality. Taken together, *RXRA* may be a potential candidate gene of tetralogy of Fallot (TOF) which involves ventricular defects and conotruncal abnormalities.

Objective: The aim of the study was first to investigate the expression level of RXRA in the right ventricular outflow tract (RVOT) myocardium tissue of TOF patients compared with controls and then to preliminarily clarify the possible regulation mechanism of RXRA in TOF patients.

Methods: The expression level of *RXRA* mRNA and RXRA protein in TOF patients and controls were detected by real-time PCR and immunohistochemistry respectively. To clarify the cause of the expression difference of *RXRA*, methylation status of the *RXRA* promoter region in TOF patients and controls were detected by BSP cloning-based sequencing. Dual-luciferase assay combined with methylation assay in vitro were performed to determine the transcription activity of unmethylated and methylated CpG region in *RXRA* promoter.

Results: Real-time PCR analysis and immunohistochemistry revealed that both the mRNA and protein expression of *RXRA* in the RVOT myocardium were significantly decreased in TOF patients compared to the controls ($p < 0.0001$). The methylation status of CpG region containing CpG sites 1-23 (-1000~-1453, relative to the TSS) in the *RXRA* promoter region was statistically higher in TOF patients than the controls. By searching the web site <http://www.cbrc.jp/research/db/TFSEARCH.html> we found that this CpG region contained several transcription factor sites including SP1. In addition, dual-luciferase assays combined with methylation assay in vitro showed that this CpG region had transcriptional regulate activity and methylation of this region can depress its transcriptional regulate activity.

Conclusion: To our knowledge, this is the first report that there is down-regulation of *RXRA* expression and aberrant promoter methylation status in the RVOT myocardium of TOF patients compared with the controls. The aberrant methylation at *RXRA* promoter may be responsible for the aberrant gene expression in RVOT myocardium of TOF patients. These findings suggest that TOF may also be an epigenetic disease.

Genetic analysis of the RXRA gene promoter in tetralogy of Fallot patientsZHANG Jing¹, MA Xiao-jing¹, WANG Hui-jun¹, MA Duan^{2,3}, HUANG Guo-ying^{1,3}¹Children's Hospital, Fudan University, Shanghai, China, 201102; ²Key Laboratory of Molecular Medicine, Ministry of Education, Shanghai Medical College, Fudan University, China, 200032; ³Research Center for Birth Defects, Fudan University, Shanghai, China, 200032

Objective: Congenital heart disease (CHD) is the most common birth defects in humans. The genetic causes for CHD remain largely unknown. Tetralogy of Fallot (TOF) is one major component of conotruncal defects (CTD), a complex CHD consisted by abnormal development of the outflow tract. Retinoid X receptor alpha (RXRA), a ligand-dependent transcript factor, plays a critical role in multiple aspects of cardiogenesis including the development of outflow tract (OFT). Taken together, *RXRA* may be a potential candidate gene of TOF. To date, *RXRA* gene promoter region has not been analyzed and reported in TOF patients. We hypothesized that the sequence variants within *RXRA* gene promoter region may change RXRA levels and mediate TOF development. In this study, the promoter regions of *RXRA* gene were genetically analyzed.

Methods: Case group included 213 DNA samples from patients with TOF, which had been confirmed by cardiac catheterization and surgery. Control group consisted of 500 DNA samples from randomly selected healthy children. Genomic DNA was extracted from peripheral blood. PCR was used to amplify the 1417bp promoter region from genomic DNA. PCR products were sequenced by ABI Prism BigDye system.

Results: The promoter regions of *RXRA* gene were genetically analyzed in 213 TOF patients and 500 healthy controls. One novel heterozygous mutation, A-1191G (according to the transcription start site), was found in one TOF patients, but in none of controls. Three novel single-nucleotide polymorphisms, C-1287T, C-800A and C-760T were found in both TOF patients and controls. There were no statistically significant change in the genotype and allele frequencies of the three SNPs between TOF patients and control group ($p > 0.05$). We found several transcription factor binding sites within the region containing these single-nucleotide variations by searching <http://www.cbrc.jp/research/db/TFSEARCH.html>. What's more, the A at position -1191 follows C, and C at position -800 is followed by G, thus these single-nucleotide variations provide additional candidate cytosines (CpG) for methylation that may influence the level of gene expression.

Conclusion: The sequence variants within *RXRA* gene promoter may contribute to the TOF etiology by altering the expression levels of RXRA gene.

The Collection and Preliminary Analysis of Familial Congenital Heart DefectsYUAN Yuan¹, CHEN Wei-cheng¹, MA Xiao-jing¹, JIA Bing¹, LIU Fang¹, WU Lin¹, Huang Guo-ying^{1,2}¹Children's Hospital of Fudan University, Shanghai, China, 201102; ²Research Center for Birth Defects, Fudan University, Shanghai, China, 200032

Background: Theoretical studies have suggested that pedigree approach may be the most effective method for identifying quantitative trait loci underlying disease phenotype, and moreover, new methods available can compute linkage statistics efficiently and accurately in extended pedigree. Therefore, we expect to find new susceptible gene of congenital heart defects in a number of recognized pedigrees of congenital heart defects. First of all, we conduct the preliminary study of the collected 17 pedigrees.

Method: Firstly, by browsing the medical records, we screen out the patients of congenital heart disease (CHD) who have family histories. Secondly, we get them contacted and recruit the probands and the other related family members to our study. Thirdly, after we obtain consent from adult subjects and from parents on behalf of their children, the phenotype of each member in the recruited pedigrees is confirmed by physical examination, medical history collection, electrocardiography, chest X-ray, echocardiography and abdominal B ultrasound. At last, their whole blood samples are collected, and genealogical trees are drawn by Cyrillic. Data of each family is kept in both separate paper document and electronic sample library system.

Result: (1) The top three phenotypes among the probands and the other CHD patients are ventricular septal defect (VSD), atrial septal defect (ASD) and tetralogy of Fallot (ToF). (2) There are 8 pedigrees which the affected share the same phenotype-cardiac septal defect. (3) We find among both father's and mother's relatives of two affected family members, there are CHD sufferers. (4) In one consanguineous marriage family, the children of the third generation present CHD: one suffers VSD, the other ToF. In another sib mating family, their three children all died: the first son died of multiple congenital malformations, the third son CHD. (5) Two adults are first diagnosed as VSD and patent ductus arteriosus respectively.

Conclusion: (1) According to our study, the more frequent types are quite consistent in familial and sporadic congenital heart diseases. (2) The children whose both father and mother have CHD family histories are supposed to accept more risk factors and liable to suffer CHD. (3) Consanguineous marriage increases the risk of CHD. (4) The applying of echocardiography and other inspections are of great importance to identify phenotype and lay a solid foundation for subsequent genetic analysis.

Right-sided Heart Thrombus and Protein-Losing Enteropathy in Two Children Due to Constrictive Pericarditis

Wei Li, Ping Huang, Li Zhang, Jie-min Zeng, Xin-xin Chen, Hu-jun Cui, Jia Yuan, Fang Gong, Li-ling Jin

From the Heart center, Affiliated Guangzhou women and children's Medical Center of Guangzhou Medical College, Guangzhou 510623, China

Constrictive pericarditis represents a rare cause of right-sided heart thrombus and protein-losing enteropathy. We report two pediatric patients with atypical clinical presentation of constrictive pericarditis. Both cases were successfully treated with pericardiectomy. We conclude that constrictive pericarditis should be considered in the presence of thrombus and protein-losing enteropathy.

ABSTRACTS

Abstracts for Poster Session:

P38MAPK signaling pathway is involved in BMP-13-induced cardiomyocyte-like differentiation from C3H10T1/2 cells

SUN Wen-jing, CHEN Yuan
Department of Cardiology, Children's Hospital, Chongqing Medical University, China

Purpose: To investigate the role of p38MAPK in BMP-13-induced differentiation of C3H10T1/2 cells into cardiomyocyte-like cells.

Methods: The four parts of experiment are grouped as follows: (1) BMP-13 adenovirus (Ad-BMP-13) on the role of p38MAPK:Ad-BMP-13 transfection group, Ad - GFP transfection group and C3H10 blank group. The phosphorylated p38MAPK (p-p38MAPK) and total p38MAPK (t-p38MAPK) were detected by Western blot. The positioning of p-p38MAPK was detected by immunofluorescence technique. (2) p38 MAPK interference adenovirus (Ad-si-p38) on the role of p38MAPK:si-p38 interference group, si-NC control interference group and C3H10 blank group. The t-p38MAPK was detected by Western blot. (3) The influence of BMP-13 induced differentiation after Ad-si-p38 blocking p38MAPK signal pathway:si-p38+Ad-BMP-13 transfection group, si-NC+Ad-BMP-13 transfection group, si-NC+Ad-GFP transfection group and C3H10 blank group. The cTnT and Cx43 were detected by Western blot and the *GATA-4* and *MEF-2C* were detected by fluorescent quantitative PCR. (4) The influence of BMP-13 induced differentiation after SB203580 blocking p38MAPK signal pathway: DMSO+Ad-BMP-13 transfection group, SB203580 (2,5 and 10 μ mol/l)+ Ad-BMP-13 transfection group. The *GATA-4* and *MEF-2C* were detected by fluorescent quantitative PCR.

Results: BMP-13 promoted the p38MAPK phosphorylation. Ad-si-p38 can effectively lower the p38MAPK expression. Ad-si-p38 which can block p38MAPK signal pathway significantly inhibited the BMP-13-induced expression of cTnT, Cx43 ($P<0.05$) and *GATA4*,*MEF-2C* ($P<0.05$). With the increased concentration of p38MAPK specific inhibitor SB203580, expression of *GATA-4*, *MEF-2C* was reduced significantly ($P<0.05$).

Conclusions p38MAPK signal pathway can be activated by Ad-BMP-13 to promote cardiomyocyte-like cells differentiation from C3H10T1/2 cells.

Bone morphogenetic proteins-9 induces C3H10T1/2 stem cell differentiation to cardiomyocyte-like cells in vitro

Lu Chen, Yuan Chen
Department of Cardiology, Children's Hospital of Chongqing Medical University

Purpose: This study aims to determine the effect of BMP9 on mesenchymal stem cells (C3H10T1/2) differentiating into cardiomyocyte-like cells in vitro.

Methods: C3H10T1/2 cells were transfected with recombinant adenovirus plasmids pAdEasy-BMP-9. Cells without transfection or transfected with GFP control vector served as controls, neonatal mouse cardiac myocytes as positive control. The expressions of cardiac isoform of troponin T (cTnT) and connexin 43 (Cx43) were measured by Western blotting and immunofluorescence staining. Cardiac-specific genes *GATA4* and *MEF2C* were detected by quantitative RT-PCR. The ultrastructure of the cells was observed by electron microscopy and masson stain. cell-membrane electric were detected by patch clamping technique.

Results: cTnT and Cx43 were found in BMP9 groups and positive control group. Neither was found in GFP group and non-transfected group. *GATA4* and *MEF2C* were detected in all groups, higher in BMP9 group than GFP group and non-transfected group ($P>0.05$), and lower than positive control group ($P>0.05$). In BMP9 group, myocardial leap dish and myofilament-like structure were found, but not in GFP and non-transfected group. Some currents were found in BMP9 group including some outward currents (IKur), some inward currents (IKir, IT-Ca2+), and a small amount of sodium current (INa+), none were found in GFP group and non-transfected group.

Conclusion: BMP9 probably promote the differentiation of the C3H10T1/2 stem cells into cardiomyocytes-like cells with ultrastructures and ion channel currents similar to cardiomyocytes.

Transforming growth factor beta2 increases heart development-related transcription factors through histone H3 hyperacetylation in H9C2 cells

Wenwen Wang^{1,2}, Jie Tian¹, Min Zheng^{1,2}, Huichao Sun¹, Chen Guozhen²
¹Heart Centre, Children's Hospital of Chongqing Medical University, ²Key Laboratory of Developmental Disease in Childhood, China

Objective: Transforming growth factor beta2 (TGF- β 2) plays an important role during heart development, however, the underlying mechanism is not clear. The present study was to investigate the effect of TGF- β 2 on histone3 acetylation and its role in regulating the expression of heart development-related transcription factors and related mechanism.

Methods: Myocardial cell H9C2 were cultured in vitro and treated with TGF- β 2 at concentrations of 1.25 μ g/L, 2.5 μ g/L, 5 μ g/L, 10 μ g/L, 20 μ g/L. Inverted phase contrast microscope (IPC) was applied to observe cell morphology and cell-counting at different timepoints (post-intervention 12h, 24h, 48h and 72h) and draw the cell-growth curve. Quantitative real-time PCR assay was used to select suitable intervention concentration of TGF- β 2 by comparing the mRNA expressions of Mef2c and GATA4. The acetylation levels of histone H3 were detected using western blot. HATs Activity Colorimetric Assay Kit was used to measure the level of HATs activities. And, levels of H3 acetylation in promoter regions of Mef2c and GATA4 were measured by chromatin immunoprecipitation (CHIP) Real-time PCR assays.

Results: The proliferation activity of myocardial cell H9C2 was improved after treating with TGF- β 2 at concentration of 5 μ g/L ($p<0.05$). The up-regulation of mRNA expressions of Mef2c and GATA4 by TGF- β 2 was in a dose dependant manner, and reached peak at the dose of 5 μ g/L, and increased by 1.8 folds and 2.3 folds, respectively ($p<0.05$). The treatment of TGF- β 2 increased acetylation level of histone H3 by 4-fold, as well as the HATs activities by 1.34-fold ($p<0.05$). The intervention of TGF- β 2 enhanced the levels of acetylation of histone H3 in the promoter regions of Mef2c and GATA4 by 2.56- and 2.16-fold, each ($p<0.05$).

Conclusion: TGF- β 2 could promote proliferative abilities of myocardial cell H9C2 at the concentration of 5 μ g/L in vitro, and improve the levels of histone H3 acetylation and then up-regulated the expressions of Mef2c and GATA4. These findings reveal that the effect of TGF- β 2 on heart development-related genes may be mediated by histone acetylation, suggesting a new mechanisms during cardiogenesis.

Comparison on Three Procedures for Treating Ventricular Septal Defects in Children

Yuan Chen
Heart Center, the Children's Hospital, Chongqing Medical University, China

Purpose: To compare three different procedures, including percutaneous transcatheter closure, open-heart surgery and transthoracic minimally invasive surgery and to analyze which procedure is possibly the best option in treatment of ventricular septal defect (VSD) in children.

Methods: The study involved 250 children with VSD in our hospital during the period from January 1, 2011 to December 31, 2011. One hundred and twenty-three children were treated by percutaneous transcatheter closure (transcatheter group), 104 by traditional open-heart surgery (open-heart group) and 23 by transthoracic minimally invasive surgery (minimally invasive surgery group).

Results: Operation time, volume of blood transfusion, postoperative ventilation duration, intensive care unit(ICU) care duration, hospitalized duration were significantly longer in open-heart group than in transcatheter group and minimally invasive surgery group ($P<0.001$). Blood transfusion, mechanical ventilation and ICU care were unneeded in transcatheter group. Operation time and postoperative hospitalized duration in minimally invasive surgery group were significantly longer than those in transcatheter group ($P<0.001$). There was no statistical difference in operation success rate and major complication incidences among three groups ($P>0.05$).

Conclusions: Three procedures are all safe and effective in treating VSDs. Condition should be fully assessed and right procedure should be chosen according to different indications.

ABSTRACTS

Abstracts for Poster Session:

Practical Utility of Special Continuous Scan in Suprasternal View for Diagnosing Double Aortic Arch in Children by Transthoracic Echocardiogram

ZHU Ling¹, GUO Yan², YU Ming-hua², LIU Te-chang², ZHANG Ming-jie², WANG Hui-shen¹ (1. Department of Pediatric Cardiology, The First Affiliated Hospital, SUN Yat-sen University, Guangzhou 510080, China; 2. The Guangzhou women and childrens medical center, Guangzhou 510623, China)

Objective: To assess the practical utility of the special continuous scan from suprasternal special view by transthoracic echocardiogram(TTE) in the diagnosis of double aortic arch(DDA), in order to improve the accuracy of diagnosis for DDA by TTE.

Methods: Echocardiogram was performed in every patient, with a continuous scan in sequence of several planes of section, which included subcostal view, apical four chamber view, apical five chamber view, long axis view, short axis view, parasternal view and suprasternal view, to observe the viscerotracheal situs, atrium and ventricular, great artery relationships.

Results: One case of vascular ring caused by DAA was found by echocardiogram. Cardiac CT scan was performed to confirm the vascular anomaly and the relationship between the great vessels and the trachea. A DAA total correction was performed under general anesthesia ultimately.

Conclusion: DAA could be diagnosed accurately by TTE in children. The key point was the continuous and careful scan in suprasternal special view.

Study on rabbit model of abdominal aortic stenosis induced by balloon-injury with different size balloon

GENG Huaxiao¹, JI Xiaojuan¹, YU Gengsheng¹, GUO Jun², et al
¹Department of Cardiology the Children's Hospital of Chongqing Medical University, Key Laboratory of Child Development and Disorders Co-founded by Provincial Government and Ministry of Education Key Laboratory of Pediatrics in Chongqing, Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Chongqing 400014, China; ²Pediatrics Department of Mianyang Central Hospital in Sichuan, Sichuan 621000, China

Purpose: To estimate the effect on rabbit model of abdominal aortic stenosis induced by balloon-injury with different size balloon.

Methods: Twenty five New Zealand White rabbits, aged 80 plus 10 days, were randomly divided into normal control group (5 rabbits) and operated groups (20 rabbits), operated groups were averagely divided into (group A, group B, group C, group D), matching to four types of balloon diameters, such as 2.5mm, 3.0mm, 3.5mm, 4.0mm. Intima-media ratio and neointimal hyperplasia were observed to evaluate the degree of stenosis at 28 days after balloon-injury with high-frequency ultrasonography and pathology examination.

Results: Stenosis ratio of group A, group B and group C were higher than the normal control group and group D. Intimal thickness, neointimal area and intimal-media ratio increased in the operated groups at 4 weeks after injury compared with the normal control group. A significant positive correlation was noted between the degree of vessel expansion and the neointimal area and intima-media ratio in group A, group B and group C. The degree of vessel expansion in group D was the highest, but neointimal area and intimal-media ratio of this group were smaller than those of group C.

Conclusion: Rabbit model of abdominal aortic stenosis could be founded successfully with suitable size of balloon with balloon catheter technique.

Prediction of Clinical Outcomes in Chinese Patients with XIENCE V Everolimus-Eluting Stent with Baseline and Residual SYNTAX Score: One Year Outcomes From the SEEDS study

Yelin Zhao¹, Bo Xu¹, Yuejin Yang¹, Yaling Han², Bao Li³, Qiang Liu⁴, Guoying Zhu⁵, Junyu Cui⁶, Lang Li⁷, Shuzheng Lu⁸

¹Fu Wai Hospital, National Center for Cardiovascular Diseases, China, Beijing, China, ²Shenyang Norther Hospital, Shenyang City, China, Shenyang, China, ³Shanxi Provincial Cardiovascular Institute, Taiyuan, China, ⁴Shenzhen Sun Yat-Sen Cardiovascular Hospital, Shenzhen, China, ⁵Wuhan Asia Heart Hospital, Wuhan, China, ⁶Beijing Military General Hospital, Beijing, China, ⁷First Affiliated Hospital of Guangxi Medical University, Nanning, China, ⁸Affiliated Anzhen Hospital of Capital Medical University, Beijing, China

Purpose: SPIRIT II and III study demonstrated the safety and efficacy of everolimus-eluting stent (XIENCE V, EES) in patients with high-risk complex disease. The Syntax score has been proposed recently as a valuable tool to characterize the coronary prospectively with respect to the complexity. However, the safety and efficacy of XIENCE V in patients with small vessel, long lesion and multivessel diseases stratified by Syntax score in Chinese population has not been addressed yet.

Methods: This was a prospective, multicenter registry designed to enroll up to 1900 patients with small vessel (target vessel diameter ≤ 2.75 mm), long lesion (length ≥ 25 mm), or multivessel diseases (≥ 2 target vessels) suitable for treatment with XIENCE V at 48 centers in China mainland, Macao and Taiwan. The primary outcome was the ischemia-driven target vessel failure (ID-TVF, composite of cardiac death, MI (Q and non-Q wave) and ID-TVR) at 12 months. The baseline Syntax score (bSS_{low} ≤ 6 , 6 < bSS_{mid} ≤ 12 , bSS_{high} > 12) and residual Syntax score (rSS_{low} ≤ 0 , 0 < rSS_{mid} ≤ 4 , rSS_{high} > 4) were applied in all enrolled patients.

Results: A total of 368(19.37%) small vessel patients, 807(42.47%) long lesion patients, and 725(38.16%) multivessel patients with 2849 lesions were treated. The primary outcome ID-TVF at 1 year was 5.57% in all patients, and 2.89%, 4.59% and 8.00% in patients with small vessel, long lesion and multivessel disease, respectively. ARC defined definite and probable stent thrombosis in all patients through 1 year was 0.58%. ID-TVR and each component were all significant higher in patients in the highest bSS or rSS tertile. The cumulative ID-TVF at 1 year was 9.16% in bSS_{high} patients, 4.02% in bSS_{mid} patients and 2.61% in bSS_{low} patients (p < 0.0001). When patients stratified by rSS, the primary endpoint was 8.67% in bSS_{high} patients, 6.10% in bSS_{mid} patients and 4.05% in bSS_{low} patients (p = 0.0008).

Conclusions: Low rates of ID-TVF and stent thrombosis were observed in this large, multi-center, real-world study of XIENCE V on Chinese population, which demonstrated its safety and effectiveness in high risk cohorts with small vessel, long lesion and multivessel diseases. A significant higher rate of 1 year ID-TVF was observed in the highest baseline and residual Syntax Score groups, indicating that baseline and residual Syntax Score may be used to predict clinical outcomes in patients of complex lesion subsets.

A Review on the Rare Complications of Percutaneous Coronary Intervention

SY Yau¹, YL Cheung²
¹Open University of Hong Kong; ²Tuen Mun Hospital, Hong Kong

Purpose: Percutaneous coronary intervention (PCI) is a life-saving procedure widely applied as the primary reperfusion treatment for acute heart attack that improves the blood flow to the narrowed coronary arteries. The major complications of PCI such as death, heart attack, stroke, emergency bypass surgery are studied extensively. However, special attention is needed to be taken on the rare complications for PCI which are life-threatening to individuals. The purpose of the present study is to review the rare complications of PCI from case reports.

Methods: Case reports on the rare complications of PCI were retrieved from recent studies through multiple databases. The reports were reviewed and summarized.

Results: The review of studies suggested that there were rare complications caused by PCI with high morbidity and mortality rate. The rare complications included entrapment of catheter components like coronary stent and balloon catheter; infectious complications such as coronary artery aneurysms, coronary abscess, mycotic aneurysms, septic arthritis, sterna osteomyelitis; fistula between coronary artery vein graft and cardiac chamber; acute aortic dissection; sinus of Valsalva dissection; and spinal cord embolism.

Conclusion: Although the complications were rare, they happened in reported cases during PCI. These emergent conditions were fatal and the managements of these rare complications were challenging.