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CARDIOLOGY



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Occupational Awareness of Quality Assurance Program to Lead Aprons Used by Cardiologists: Defect Analysis and Dose Measurement

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LAW ET AL.: Occupational Awareness of Quality Assurance Program to Lead Aprons Used by Cardiologists: Defect Analysis and Dose Measurement. By visual inspection and fluoroscopic examination lead aprons, the procedures of a quality assurance program to ensure occupational safety can be accurately performed in a cardiology unit with in-house fluoroscopic apparatus by trained radiation personnel. (*J HK Coll Cardiol* 2014;22:35-37)

Cardiologist, lead apron, occupational dose, quality assurance

摘要

通過外觀檢查和螢光檢測鉛保護衣，以確保職業操作安全的品質保證程式可以在具備螢光檢測儀器設備的心臟病單元病房內，由訓練有素的放射科人員準確地執行。

關鍵詞：心臟病學專家、鉛保護衣、職業劑量、品質保證

Introduction

Cardiologists are among the most intensive users of radiation fluoroscopy in the medical profession. While occupational protection in catheterization laboratory is important, lead aprons are used for staff protective apparel against ionizing radiation.¹ An accurate and reliable quality assurance (QA) program is recommended to maintain a high level of good practice.² In order to promote a practical QA program for lead aprons in cardiology units in Hong Kong, results are presented on defect analysis and dose measurement

for a batch of lead aprons used by a group of cardiologists. The program can be extended to perform acceptance test to new lead aprons, from which lead equivalent thickness deficiency is occasionally detected. Therefore the important steps to start up a regular QA program with associated resource are introduced. We also share our experience to upcycle defective lead aprons into clinical use to make the QA program environmental friendly.

Methodology

Twenty-six lead aprons, estimated age between 3 years and 8 years old since their first use, were assigned into different groups by their shapes (vest, skirt and standard). We followed the annual QA program in our institute,³ based on which apron with defect dimension $\geq 3 \text{ mm}^2$ or the length of a fault line $\geq 2 \text{ cm}$ would be regarded as failure and then removed from

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occupational protection against ionization radiation. Any visible defects, namely holes, cracks and tears, were firstly evaluated and documented. The aprons were then screened under X-ray fluoroscopy and sizes of defect were measured.

A defective skirt apron, with crack length and opening of about 12 cm wide, was chosen to measure the radiation dose received at the defective site as if this defective apron was used during interventional procedure. A pelvis phantom, to simulate the lower body of a cardiologist, was draped with this defective apron. By placing three direct readout bleeper type pocket dosimeters (Vertec, United Kingdom) at different regions (defective, semi-defective and no-defect) underneath the lead apron, radiation dose to the pelvis phantom was measured to simulate a cardiologist performing interventional procedure. As we would compare between the dose underneath the defective sites and that underneath properly shielded area of the apron, the phantom draped with the defective apron was placed on the X-ray tube side with routine fluoroscopy irradiation.

Results

Five aprons (19%) were visually observed to have different sizes of holes and/or tears associated with fabric material of adhesive magic tape design.

One lead apron of skirt (4%) was observed to have a crack with largest portion at about 12 cm width observed under fluoroscopic screening. However there was no visual defect on the fabric material for this skirt.

The radiation doses, as received by the cardiologist performing interventional procedure with the use of the defective apron, were measured with the dosimeters underneath the defective, semi-defective and no-defect regions. The measured doses were 18 $\mu\text{Sv}/\text{min}$ and 12 $\mu\text{Sv}/\text{min}$ underneath the defective and semi-defective region respectively and underneath the no-defective region of 1 $\mu\text{Sv}/\text{min}$. It implied that the regions with defective and semi-defective protection would receive more than 10 times higher radiation exposure than that of well protected region.

By visual inspection of this batch of aprons, it was common to have exterior damages on the surface

of the fabric material. Torn fabrics were found at the vicinity of the magic tapes. It was believed that the textiles of the lead aprons could not withstand long-term tearing which might cause holes and tears. By vigorously repeated pulling type force of the aprons, holes and tears on the aprons were increasingly formed in size. However defects within the lead lining enclosed by the fabric material were difficult to detect visually but could be examined with readily available X-ray fluoroscopy method because of the high spatial resolution for the fluoroscopic machine to detect defects localization and size determination.

Discussion

In order to set up a long term tracking system for the aprons, it is essential to have a systematic management system and to train up operators for the use of fluoroscopic machine. Information of the age since its first use of aprons, date of previous QA test and other updated status are usually not clearly labeled and documented, all of which were experienced in the batch of lead aprons as presented here. This situation is more obvious when new aprons are regularly purchased for replacement to be used along with those existing ones, in addition to the situation of not easy to access to privately owned lead aprons. A complete management system with documentation for lead aprons is important. There should be a person responsible for the management of the lead aprons with reference to some international criteria for rejecting defective aprons after the QA testing.⁴

Trained operators in radiation machine play an important role in the QA program. They should be familiar with the fluoroscopy machine and have the license to operate the radiation apparatus. If there are defects on the lead aprons, operators should be experienced to report the size and location. It is believed that radiographers from radiology unit fulfill the above requirements. They have much experience in using the radiation machine including those in cardiology units. The QA service of using fluoroscopic machine can be arranged when the facility is not for patient service and the radiographers still remain on duty in catheterization laboratory.

Conclusion

Despite regular check for existing lead aprons, it is equally important to have the same program on new aprons. From our experience, it cannot assume that new lead aprons are perfect enough for radiation protection. Not only tiny defects on lead aprons are found, but also deficiency in the lead equivalence is occasionally observed in new aprons. Wearing a defective or insufficient lead equivalence lead apron violates the code of practice in hospitals.⁵ Therefore, lead equivalent test is essential before the occupational use of new aprons. Physicist team in hospital is with experience and knowledge in this area and in our institute, new apron acceptance test is performed by physicist. Experience can be shared to centres without the support of physicist.

The defective lead aprons should be disposed in a proper way as the lead lining is composed of rubber layers uniformly mixed with lead powder, both of which are materials not friendly to our environmental disposal. There are some programs in the radiology unit in our institute studying the upcycle process for defective lead aprons, in which the usable portions are cut into different sizes of blankets to be clinically used as radiation shielding during radiological imaging. An example of this is to cover nuclear medicine patient pelvis region with such blanket in order to reduce the radiation exposure to staff during positioning the patient undergoing imaging. Cardiology unit is suggested to work with the radiology unit to upcycle the defective aprons.

A defective lead apron may cause unnecessary occupational exposure because of inappropriate protection. Occupational dose would be accumulated when defective aprons are regularly used. Therefore, QA program for lead aprons should be established in cardiology unit with available in-house equipment and expertise to assure occupational safety. It is recommended that the integrity of all new protective aprons be verified upon receipt as well as at yearly intervals. Upcycle of defective aprons is also suggested.

References

1. Chambers CE, Fetterly KA, Holzer R, et al. Radiation safety program for the cardiac catheterization laboratory. *Catheter Cardiovasc Interv* 2011;77:546-56.
2. Durán A, Hian SK, Miller DL, et al. Recommendations for occupational radiation protection in interventional cardiology. *Catheter Cardiovasc Interv* 2013;82:29-42.
3. Lead Equivalent Personal Protective Equipment Annual QA Procedure. Quality & Safety Service Internal Report. Hong Kong: Queen Mary Hospital, 2013.
4. Testing lead aprons used in diagnostic radiology departments, Department of Health, Melbourne, Australia, 2011. [http://docs.health.vic.gov.au/docs/doc/8735C062151DCE47CA25796E001E4DD9/\\$FILE/Testing%20of%20lead%20aprons.pdf](http://docs.health.vic.gov.au/docs/doc/8735C062151DCE47CA25796E001E4DD9/$FILE/Testing%20of%20lead%20aprons.pdf) (accessed on 10/July/2014 11:30 hr)
5. Chapter 3 of Code of Practice on Radiation Safety. Hong Kong: Hospital Authority of Hong Kong, 2011.

Accordion Phenomenon: A Rare Cause of Acute Total Occlusion During Percutaneous Coronary Intervention

DANNY HOI-FAN CHOW, CHUN-LEUNG LAU, PUI-SHAN CHU, HO-CHUEN YUEN, YING-KEUNG LO, CHI-CHUNG CHOY, NGAI-YIN CHAN, PING-TIM TSUI, NGAI-SHING MOK

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CHOW ET AL.: *Accordion Phenomenon: A Rare Cause of Acute Total Occlusion During Percutaneous Coronary Intervention.* Placement of stiff guidewires through tortuous coronary arteries allows smooth advancement of stents during coronary intervention. However, the straightening of coronary vessels leads to a mechanical alteration and induces vessel wall shortening. The transient effect of such coronary pseudo-stenosis is referred as "accordion phenomenon". This case described the accordion phenomenon after placement of a stiff guidewire through a tortuous right coronary artery leading to acute total occlusion with ST elevation during coronary intervention. (*J HK Coll Cardiol* 2014;22:38-41)

Accordion phenomenon, pseudo-stenosis, stiff guidewire, ST-segment elevation

摘要

經皮冠狀動脈介入治療時在彎曲的冠狀動脈處放置剛性導絲有助於支架的順利安置。然而，冠狀動脈的被動伸直會導致機械性改變，致使血管牆縮短。此類冠狀動脈假性狹窄的短暫效應被稱為「手風琴現象」。本案例記錄了經皮冠狀動脈介入治療時在彎曲的冠狀動脈處放置剛性導絲後導致冠狀動脈急性完全性梗阻並伴有ST段上抬的手風琴現象。

關鍵詞：手風琴現象、假性狹窄、剛性導絲、T段上抬

Case Report

A 63-year-old gentleman who was an ex-smoker had history of diabetes mellitus, hyperlipidemia, and hypertension. He was admitted for inferior ST elevation myocardial infarction (STEMI) treated with tenecteplase (TNK). Peak Troponin I was 90.67 ug/L. He initially refused coronary intervention and was treated medically. He presented again with inferior STEMI a year later and was complicated with heart failure. He was treated with TNK within 3 hours. Peak

Troponin I was 87.52 ug/L. The gentleman finally agreed for early invasive procedure in view of repeated myocardial infarctions.

During diagnostic angiogram through the right radial approach, there was difficulty in advancing a 5 French Tiger II catheter. Angiogram confirmed high radial artery remnant. Coronary angiogram showed normal left main artery, proximal left anterior descending artery (LAD) 90% stenosis, middle LAD 90% stenosis, distal LAD 70% stenosis, and the left circumflex artery was small in calibre. The right coronary artery (RCA) ran a very tortuous course with middle RCA 90% stenosis and posterior left ventricular branch (PLV) 80% stenosis (Figure 1).

Percutaneous coronary intervention (PCI) to RCA was performed. Because of the tortuosity of the RCA and high radial remnant, an ASAHI 6.5 French sheathless Amplatz 1 guiding catheter and a Finecross

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MG microcatheter (Terumo, Japan) were used for supporting the 0.014-in. Runthrough guidewire. (Terumo, Japan). The distal RCA was wired with difficulty and was later exchanged to a 0.014-in. ASAHI GRAND SLAM (Abbott Vascular, USA) through the finecross catheter for better support.

Electrocardiogram suddenly showed ST elevation over lead II and patient complained of severe chest pain. Angiogram showed acute total occlusion of flow in middle RCA (Figure 2). The Grand Slam guidewire was withdrawn half way with the floppy part of the guidewire in middle RCA and the flow was improved to TIMI III with improvement of symptoms (Figure 3). A 3.0*15 mm stent (Energy®, Biotronik, Germany) was deployed at middle RCA lesion at 14 atm after predilatation with 2.0*10 compliance balloon (Tazuna®, Terumo, Japan) at 14 atm. The PLV branch was rewired with the Runthrough guidewire with finecross support and later exchanged with 0.014-in. Sion Blue guidewire (Asahi, Japan). However, a 2.5*18 stent (Energy®, Biotronik, Germany) failed to advance through the first bend of RCA through the Sion blue guidewire. There was frequent backing of the guidewire due to the vessel tortuosity during exchange of guidewires through the Finecross catheter. Therefore, a Crusade catheter

(Kaneka, Japan), a double-lumen multifunctional probing microcatheter, was used to exchange for the Grand Slam guidewire. Not only did the Crusade catheter allow the exchange of guidewires, the catheter also allowed both the Grand Slam guidewire and Runthrough guidewire to act as buddy wires. The Grand Slam guidewire was withdrawn partially prior the delivery of the stent to the PLV branch to avoid the accordion effect, so an accurate road map can be recorded for the location and size of the PLV stent. The 2.5*18 stent (Energy®, Biotronik, Germany) was finally advanced to PLV and was deployed at 14 atm. Post dilatations with to middle RCA stent and PLV stent were done with 3.5*10 non-compliant balloon (Hiryu®, Terumo, Japan) up to 14 atm and 2.5*8 non-compliant balloon (Pentera Leo®, Biotronik, Germany) up to 14 atm respectively.

PCI to middle LAD was done with ASAHI 6.5 French sheathless Judkins Left 3.5 guiding catheter. Distal LAD was wired with Sion Blue guidewire. A 3.0*15 (Multilink®, Medtronic, USA) was deployed at 16 atm to middle LAD lesion through buddy wire technique with Grand Slam guidewire. A 3.5*12 stent (Multilink®, Medtronic, USA) was deployed at 14 atm at the proximal LAD lesion.

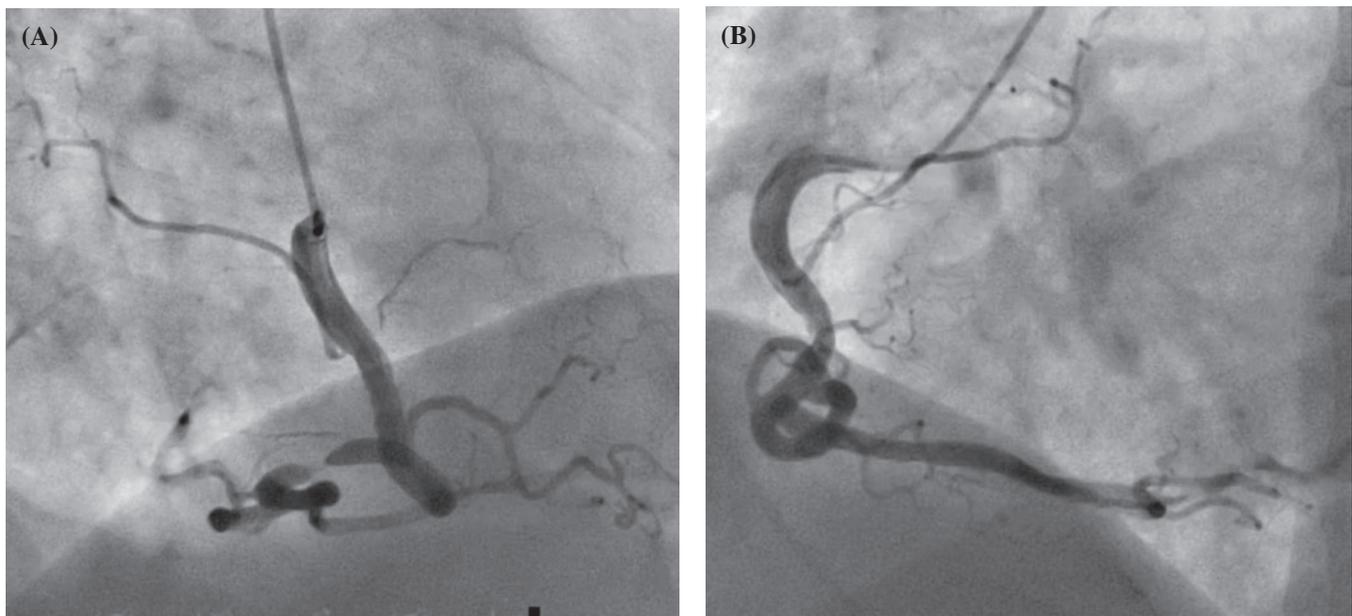


Figure 1. Angiogram of right coronary artery (RCA) showed a tortuous RCA anatomy. (A) Right Anterior Oblique (RAO) view of RCA; (B) Left Anterior Oblique (LAO) of RCA.

ACCORDION PHENOMENON

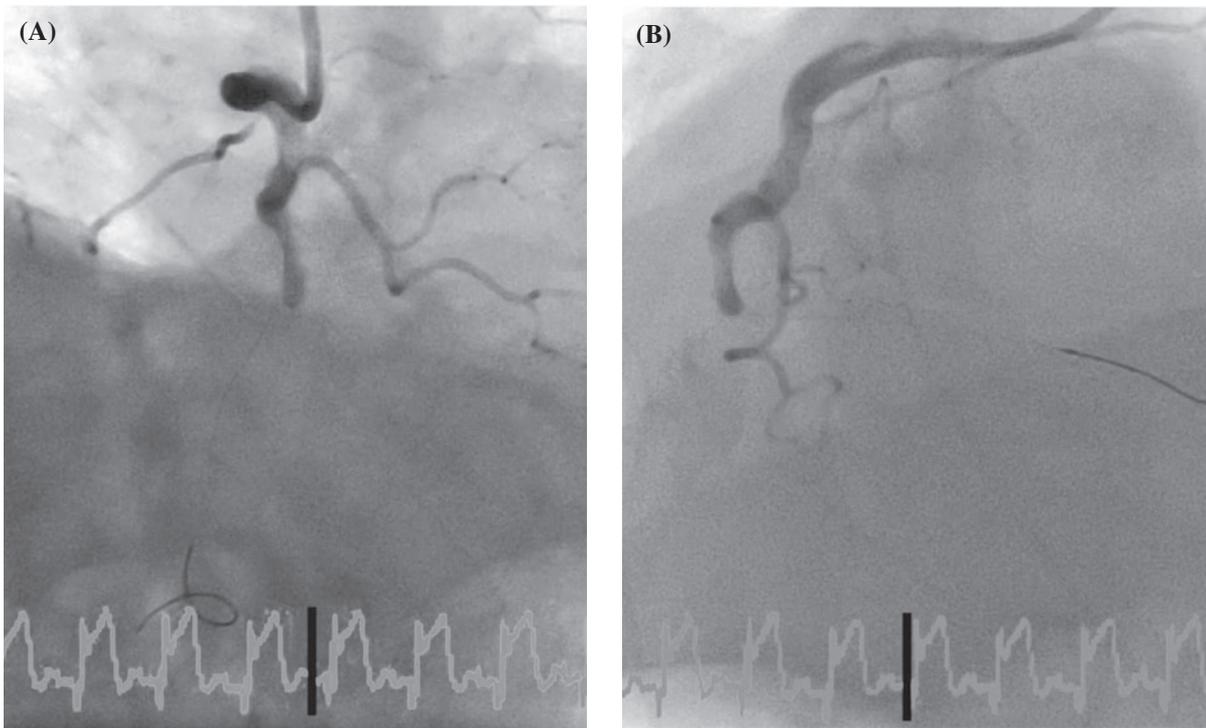


Figure 2. Angiogram of right coronary artery (RCA) after wiring with GRAND SLAM guidewire showing acute total occlusion of middle RCA. Underlying electrocardiogram showed ST elevation. (A) Right Anterior Oblique view of RCA with GRAND SLAM guidewire; (B) Angiogram of Left Anterior Oblique view of RCA with GRAND SLAM guidewire.

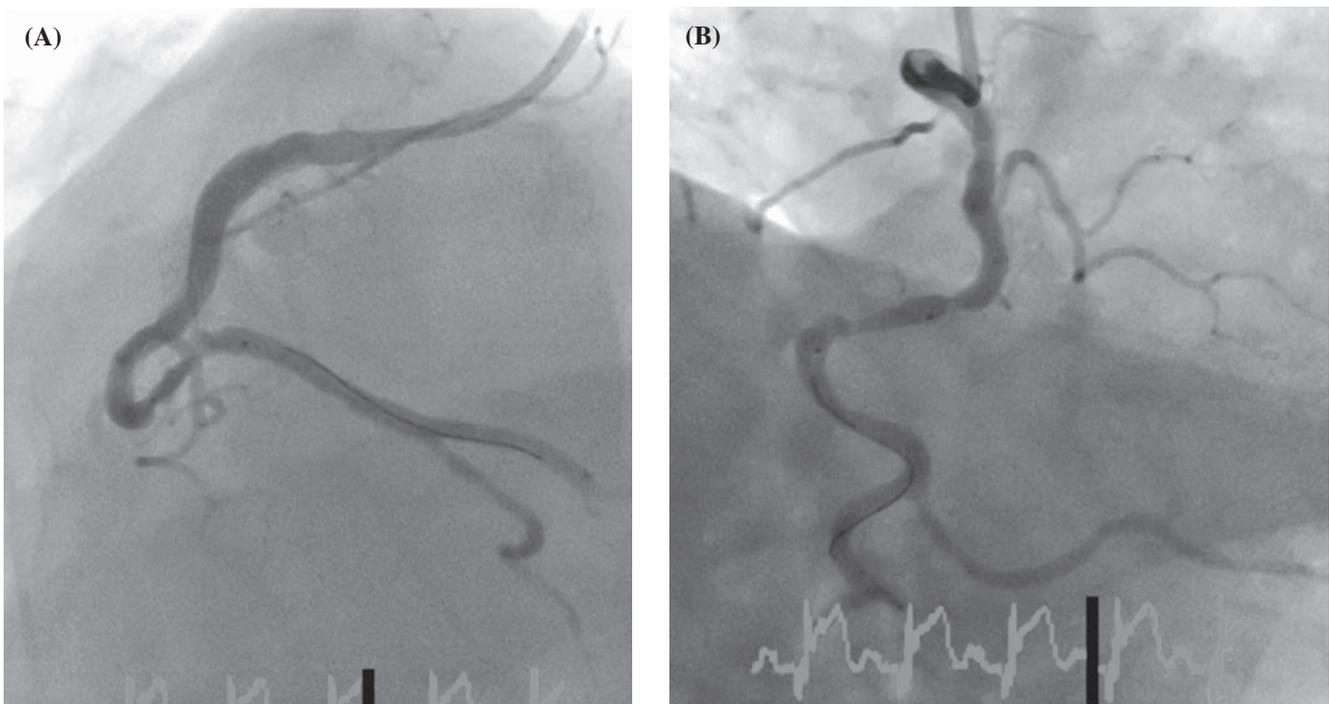


Figure 3. (A) Left Anterior Oblique and (B) Right Anterior Oblique view of right coronary artery after withdrawal of GRAND SLAM wire showed recovery of TIMI III flow.

Discussion

This case demonstrates the importance to recognize the effect of "accordion" or "concertina" phenomenon. The use of sheathless guiding catheter allows its advancement a small, high radial remnant artery without perforation. With the use of an extra support guidewire, the angiographic geometry was altered, resulting in straightening of the curvature of a tortuous RCA (Figure 4). Previous case reports¹⁻³ demonstrated invagination of vessel wall during angiogram. If the phenomenon is not recognized early, unnecessary stent deployment may occur. Accordion causing ST elevation with acute total occlusion is rare. Differential diagnosis of acute vessel closure during PCI include dissection, spasm, and embolization. Despite the fact that accordion phenomenon is a well-recognized effect of stiff guidewires, the use of stiff wires to gain support through tortuous vessels to allow smooth advancement of stents is sometimes inevitable. Delivery of stent to PLV branch would be extremely difficult in this case without a good guiding catheter support, strong guidewire, and a well-prepared proximal passage. This is supported in the case when the stent failed to advance through the bend through non-stiff guidewires (Sion Blue) during the PCI to PLV branch. Therefore, the middle RCA lesion was stented prior the delivery of the stent to the PLV branch. A special point of note is that the accordion effect did not recur despite the use of

a stiff guidewire during the delivery of the PLV stent, illustrating slight anatomical change can alter the accordion outcome.

To differentiate the accordion phenomenon from other differential diagnosis, it is recommended to withdraw the guide wire while keeping the floppy part of the wire in vessel.⁴ Withdrawal of the guidewire will allow coronary blood flow to improve. However, one must document clearly the desired stent placement location upon withdrawal of the guidewire as the accordion effect will recur once the stiff guidewire is advanced for the stent deployment. Totally removing the guidewire is discouraged because the operator may not be able to rewire the lesion if the cause of the acute vessel closure is due to dissection or distal embolism.

References

1. Olivier M, Michalis H, Ntalianis A, et al. The accordion phenomenon lesion from a movie. *Circulation* 2008;118:e677-e678.
2. Kim W, Jeong M, Lee S, et al. An accordion phenomenon developed after stenting in a patient with acute myocardial infarction. *Int J Cardiol* 2007;114:E60-2.
3. Davidavicius G, Manoharan G, De Bruyne B. The accordion phenomenon. *Heart* 2005;91:471.
4. Chalet Y, Chevalier B, Hadad S, et al. "Pseudo-narrowing" during right coronary angioplasty: how to diagnose correctly without withdrawing the guidewire. *Cathet Cardiovasc Diagn* 1994;31:37-40.

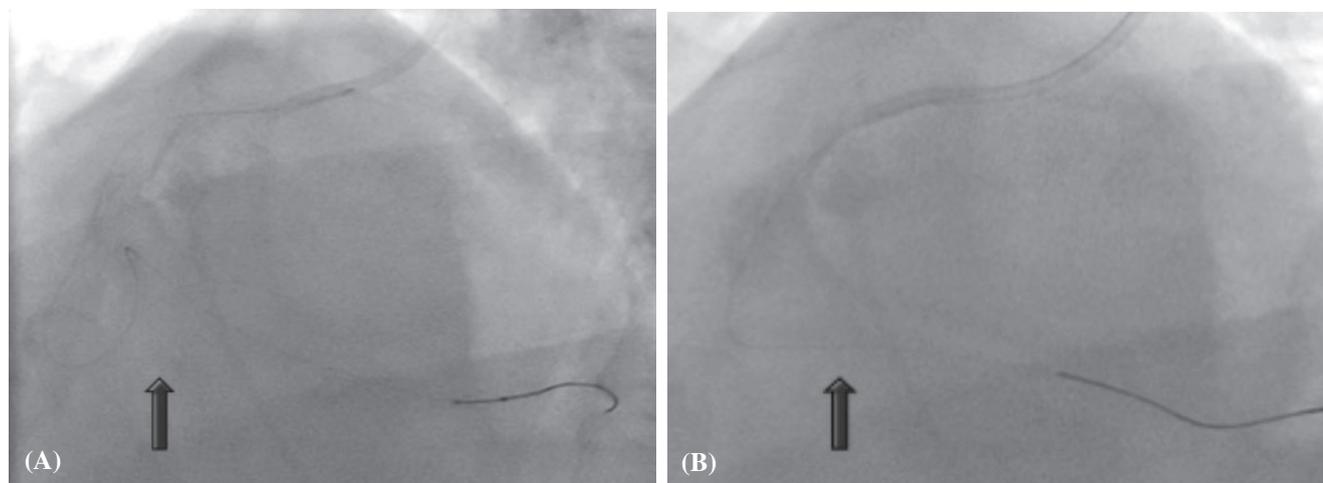


Figure 4. (A) The anatomy and tortuosity of right coronary artery (RCA) is preserved with non-stiff Sion Blue guidewire. (B) Use of GRAND SLAM stiff guidewire straightened tortuosity of the RCA. The arrow highlighted the straightened bend of the original RCA anatomy.

Endovascular Closure of a Subclavian Artery Pseudoaneurysm

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SINGH AND KUMAR: Endovascular Closure of a Subclavian Artery Pseudoaneurysm. Accurate diagnosis and anatomical delineation of pseudoaneurysm is important for the precise management of the patient. A number of techniques like ultrasonography, Doppler imaging, computed tomography angiography, magnetic resonance angiography as well as conventional angiography are currently available. The image submitted shows the sequential steps in the endovascular management of one such pseudoaneurysm. (*J HK Coll Cardiol* 2014;22:42-43)

Covered stent, endovascular closure, pseudoaneurysm, subclavian artery

摘要

假性動脈瘤的迅速診斷和解剖結構特點描述對患者的正確處理至關重要。多項技術應用於此，如超聲檢查、多普勒成像、C T 血管成像、M R 血管成像及傳統血管造影術等。本文中的影像展示了介入技術處理假性動脈瘤的連續過程。

關鍵詞：覆蓋支架、介入夾閉、假性動脈瘤、鎖骨下動脈

Introduction

Pseudoaneurysms are encapsulated hematomas that communicate with an artery because of an incomplete seal by the media. Due to their non-compressibility, relative proximity to vital structures, likelihood of distal thromboembolism and the unpredictable risk of rupture, they pose unique challenges in the management. Accurate delineation of the aneurysm is very important for efficient management whether planned percutaneously or by open technique. Endovascular closure has its own advantages because shorter operative time, less bleeding and a shorter

hospital stay. Open technique is more likely to give problems like injury to nerve trunks in vicinity and difficulty handling branches particularly in presence of active bleed/hematoma.

Case

This 40-year-old male had a history of gunshot injury over left shoulder region a month prior to presentation; and was being managed conservatively with intercostal tube drainage for left hemothorax when he started noticing weakness of left upper limb. Left brachial plexus injury was suspected. Ultrasonography of the neck was done for brachial plexus evaluation which showed that infraclavicular part of brachial plexus trunk was severed. In addition, there was a mass in distal part of subclavian artery. Computed tomography (CT)-angiography was done which showed it to be a pseudoaneurysm in distal part

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of left subclavian artery. Diagnostic peripheral angiography of left upper limb was done which showed a wide neck aneurysm, in the distal part of left subclavian artery directed posteriorly and superiorly (Figure 1a).

Endovascular procedure was performed via access through the right femoral artery. Using 8F multipurpose guiding catheter, pseudoaneurysm was crossed with a floppy wire (Figure 1b) and then 0.035" exchange wire was crossed (Figure 1c).

Endovascular exclusion of the pseudoaneurysm was achieved with the deployment of a 6x22 mm balloon expandable peripheral stent-graft (Advanta, ATRIUM MEDICAL CORPORATION; Hudson, NH, USA) within the lumen of left subclavian artery (Figures 1d & 1e). The process was done under the cover of unfractionated heparin 5000 U, the ACT was maintained above 220 seconds. Completion angiography showed complete closure and exclusion of the pseudoaneurysm (Figure 1f).

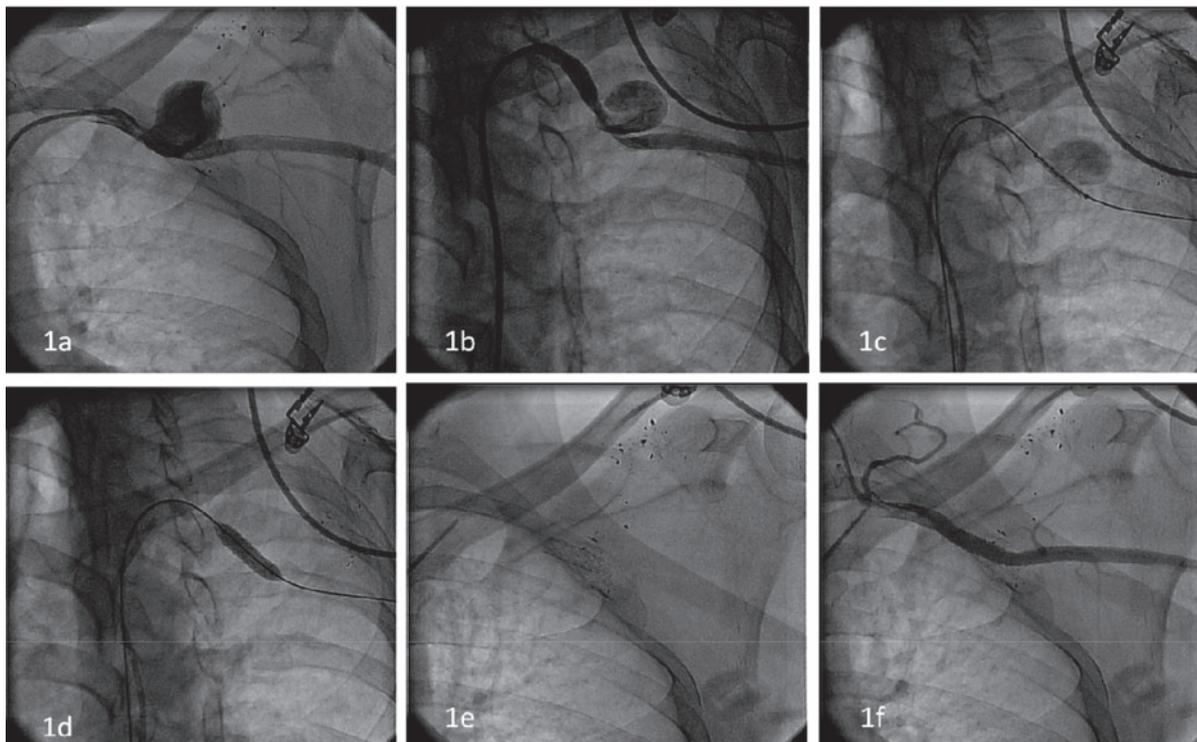


Figure 1. (a) Diagnostic peripheral angiography of left upper limb showing a wide neck aneurysm, in the distal part of left subclavian artery directed posteriorly and superiorly. (b) Using 8F multipurpose guiding catheter, pseudoaneurysm was crossed with a floppy wire. (c) The floppy wire has been exchanged with a 0.035" exchange. A 6 x 22 mm balloon expandable peripheral stent-graft (Advanta, Atrium Medical Corporation) placed within the lumen of left subclavian artery covering both the edges of the neck. (d) The balloon expandable stent deployed in the artery. (e) The deployed stent can be visualised under fluoroscopy. (f) Post-deployment peripheral angiography showing exclusion of the pseudoaneurysm, and no extravasation of the dye.

SCIENTIFIC PROGRAMME

1 NOVEMBER 2014 (SATURDAY)

08:30-09:00 **Registration**

09:00-09:45 **Institute of Vascular Medicine Keynote Lecture I**

Chairman: Prof. Paul Vanhoutte, The University of Hong Kong

Stroke in Asia

Prof. Lawrence Wong, Chinese University of Hong Kong

09:45-10:45 **Oral Presentations for Young Investigator Award
Sponsored by Sun Chieh Yeh Heart Foundation**

Chairmen: Dr. Heather Ballard, The University of Hong Kong

Dr. Qing Yang, Chinese University of Hong Kong

10:45-11:45 Coffee Break, Booth Visit, **Poster Presentations for Young Investigator Award
Sponsored by Sun Chieh Yeh Heart Foundation**

Chairman: Dr. George Leung, The University of Hong Kong

11:45-12:45 **Morning Symposium**

Chairmen: Prof. Yu Huang, Chinese University of Hong Kong

Dr. Man-Lung Fung, The University of Hong Kong

Overcoming Barriers to the Use of Human Pluripotent Stem Cells
Derived Cardiomyocytes for Experimental and Therapeutic Applications

Prof. Ken Boheler, The University of Hong Kong

Non-Ending Search for the Best Pharmacological Vasodilator for Coronary Artery Bypass Grafts

Prof. Guo-Wei He, TEDA International Cardiovascular Hospital & The Affiliated Hospital of Hangzhou Normal University, China

12:45-14:00 **Lunch**

14:00-14:15 **Opening Ceremony**

Prof. Gabriel Leung, Dean, Li Ka Shing Faculty of Medicine, The University of Hong Kong

Dr. Kam-Tim Chan, President, Hong Kong College of Cardiology

14:15-15:45 **Afternoon Symposium I**
Chairmen: Prof. Ronald A. Li, The University of Hong Kong
Dr. Kam-Tim Chan, President, Hong Kong College of Cardiology

Pfizer Keynote Lecture

Electrical Remodeling of the Failing Heart and the Risk of Sudden Cardiac Death
Prof. Gordon Tomaselli, Johns Hopkins University, USA

Takeda Keynote Lecture

Advances in PCI : Novel Imaging and Novel Devices
Prof. Stephen Lee, Queen Mary Hospital, HKSAR

15:45-16:15 Coffee Break, Poster Viewing and Booth Visit

16:15-17:45 **Afternoon Symposium II**
Chairmen: Dr. Carmen Chan, Queen Mary Hospital, Hong Kong
Prof. Richard Yu, Hong Kong College of Physicians

Institute of Vascular Medicine Keynote Lecture II

GLP-1-Elevating Agents Benefit Endothelial Function
Prof. Yu Huang, Chinese University of Hong Kong

AstraZeneca Keynote Lecture

Recent Advance in Clinical Management of Acute Coronary Syndrome and Lipid Disorders
Dr. Michael Chan, The University of Hong Kong

Recent Advance in Imaging
Dr. Kelvin Yiu, The University of Hong Kong

17:45-18:00 **Closing Remarks and Young Investigator Award Ceremony**
Prof. Bernard Cheung, The University of Hong Kong
Prof. Chu-Pak Lau, Sun Chieh Yeh Heart Foundation

18:00 **Annual General Meeting**

Institute of Cardiovascular Science and Medicine

Faculty of Medicine

The University of Hong Kong

The Eighteenth Annual Scientific Meeting

1 November 2014
Hong Kong Convention and Exhibition Centre
Hong Kong

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ABSTRACTS

Abstracts for Invited Lectures:

IL2.**OVERCOMING BARRIERS TO THE USE OF HUMAN PLURIPOTENT STEM CELLS DERIVED CARDIOMYOCYTES FOR EXPERIMENTAL AND THERAPEUTIC APPLICATIONS**

K Boheler

The University of Hong Kong, Hong Kong

Knowledge of cell-surface proteins for isolating well-defined populations of human pluripotent stem cells (hPSCs) and their progeny will significantly enhance the characterization and translational potential of these cells. Using a chemoproteomic approach, we have developed a cell surface proteome repository containing 500 N-linked glycoproteins on human embryonic (hESCs) and induced PSCs (hiPSCs) and >600 glycoproteins from hPSC-cardiomyocytes (CMs). When compared with human fibroblasts and 50 other cell types, >100 surface proteins of interest for hPSCs and human PSC-CMs were revealed. The >30 positive and negative markers for the human PSCs verified by orthogonal approaches provide experimental justification for the rational selection of pluripotency and lineage markers, epitopes for cell isolation, and reagents for the characterization of putative hiPSC lines. Quantitative differences between the chemoproteomic-defined surfaceome and the transcriptome-predicted surfaceome directly led to the discovery of two novel metabolic inhibitors specifically toxic to hPSCs and efficient for selective elimination of hPSCs from mixed cultures, without significantly toxicity on more differentiated cell types. From the human PSC-derived CMs, we have been able to identify several surface proteins that appear apt for the selection of subpopulations of cardiomyocytes from mixed cultures. Once

characterised, these subpopulations, corresponding to different stages of in vitro differentiation should permit more robust disease modelling and pharmacotoxicology studies; and in the long-term, may help identify suitable cells for therapeutic applications. In summary, cell surface-centric research strategies are useful for the identification of markers for drug repurposing, positive or negative selection, as well as functional characterizations of better defined populations of hPSCs and hPSC-derived progeny.

IL3.**NON-ENDING SEARCH FOR THE BEST PHARMACOLOGICAL VASODILATOR FOR CORONARY ARTERY BYPASS GRAFTS**

GW He

TEDA International Cardiovascular Hospital, Tianjin & The Affiliated Hospital of Hangzhou Normal University & Zhejiang University, Hangzhou, China; and Department of Surgery, Oregon Health and Science University, Portland, Oregon, U.S.A.

In comparison with standard saphenous vein grafts, use of the internal mammary artery (IMA) as a coronary artery bypass graft has achieved superior long-term results. This is obviously related to the differences in biological characteristics between the venous and arterial grafts. However, even arterial grafts are not uniform in their biological characteristics. The variation in the perioperative behavior of the grafts and in their long-term patency may be related to different characteristics. These factors should be taken into account in the use of arterial grafts, some of which are subjected to more active pharmacological intervention during and after the operation to obtain satisfactory results. To better understand the biological behavior of the grafts, their common features and their differences, a clinical classification may be useful for a practicing surgeon. Based on experimental studies of their vasoreactivity combined with anatomical, physiological, and embryological considerations, we have proposed a functional classification for arterial grafts that may be useful clinically. Our classification suggests that there are three types of arterial grafts: **Type I**- somatic arteries; **Type II**- splanchnic arteries; and **Type III**- limb arteries. The Type I arteries have better endothelial function and release more nitric oxide and other relaxing factors; the Type II arteries, such as the gastro-epiploic artery, and the Type III arteries, such as the radial artery, have higher pharmacological reactivity

to vasoconstrictors. This classification explains why the IMA has the best long-term patency. Because Type II and III arteries are prone to spasms due to higher contractility, they require more active pharmacological interventions. Furthermore, the harvesting technique of the conduits, including saphenous vein and IMA, are described and discussed in this article. Prevention of spasms using two cocktails of medications (verapamil+nitroglycerin and nicardipine+ nitroglycerin) during harvesting of the conduits is described. Those solutions have been demonstrated to be clinically effective. With development of new vasodilator substances, such as third-generation calcium channel blockers, more effective and safer anti-spasm drugs for CABG may become feasible in the future.

ABSTRACTS

Abstracts for Oral Presentation:

OPI.

KNOCKDOWN OF REPRESSOR ACTIVATOR PROTEIN 1 FACILITATED FOAM CELL FORMATION BY AUGMENTING CHOLESTEROL UPTAKE

HK Wong,¹ Y Cai,¹ EHC Tang^{1,2}

¹Department of Pharmacology and Pharmacy; ²Department of Physiology, The University of Hong Kong, Hong Kong

Objectives: Repressor activator protein 1 (Rap1) is a telomere-associated protein with telomeric-regulating functions, but it also displays non-telomeric functions and regulates metabolism. The expression of Rap1 is enhanced in atherosclerotic plaques. Presence of foam cells is an indicator of plaque build-up. This study aims to investigate if Rap1 knockdown has an effect on foam cell formation and cholesterol transport.

Methods: Knockdown of Rap1 was established in macrophage cells derived from the human monocytic leukemia cell line (THP-1) using small interfering ribonucleic acid (RNA). Knockdown and wild-type cells were transformed into foam cells by incubating with 50 µg/mL acetylated low-density lipoprotein for 72 hours. Then the cells were stained with oil red O to assess the efficiency of foam cell formation, or subjected to RNA extraction to study the expression of key genes involved in cholesterol transport by quantitative polymerase chain reaction.

Results: Rap1 knockdown cells accumulated 40.9%±14.7% more intracellular lipids (P<0.05). The mRNA expression of peroxisome proliferator-activated receptors alpha (PPARα) increased by 3.04-fold (P<0.05), while peroxisome proliferator-activated receptor-gamma coactivator (PGC1α) was significantly reduced by 89%±2.2% (P<0.03) in Rap1 knockdown cells as compared with wild-type cells. The mRNA expression of scavenger receptor A (SR-A) in Rap1 knockdown increased by 4.79-fold (P<0.02), while there is no significant change in the expression of another cholesterol uptake receptor – cluster of differentiation 36 (CD36), and other efflux-associated genes – including ATP binding cassettes A1 and G1 (ABCA1 and ABCG1) and scavenger receptor B1 (SR-B1) was observed. **Conclusions:** Rap1 knockdown enhanced foam cell formation and significantly affected the mRNA expression of master transcriptional regulators – PPARα and PGC1α. Effective foam cell formation is accounted by increased SR-A expression and hence enhanced cholesterol uptake, which warrants further studies to confirm such postulation.

OP2.

AMELIORATION OF CIGARETTE SMOKE-INDUCED CARDIAC DYSFUNCTION AND INFLAMMATION BY MESENCHYMAL STEM CELLS

YM Liang,¹ X Li,¹ YL Zhang,¹ Z Zhen,¹ SC Yeung,¹ MSM Ip,^{1,4} HF Tse,¹ QZ Lian,^{1,2,4} JCW Mak^{1,3,4}

Departments of ¹Medicine; ²Ophthalmology; ³Pharmacology & Pharmacy; ⁴Research Centre of Heart, Brain, Hormone and Healthy Aging, The University of Hong Kong, Hong Kong

Objectives: Cigarette smoke (CS) is recognized as a major cause of cardiovascular disease (CVD). Inflammatory responses play important roles in the pathophysiological processes of CS-induced cardiac damage. Mesenchymal stem cells (MSCs) are regarded as a promising candidate for cell-based therapy in CVD. We aimed to compare the effects of bone marrow-derived MSCs (BM-MSCs) and induced pluripotent stem cell-derived MSC (iPSC-MSCs) on cardiac function and inflammation in CS-exposed rat model.

Methods: Male Sprague-Dawley rats were exposed to 4% CS for one hour daily for 56 days. On day 29 and day 43, human iPSC-MSCs or adult bone marrow-MSCs (BM-MSCs) were administered intravenously to CS-exposed rats. Echocardiography was conducted 24h after the last exposure and animals were sacrificed. Heart tissues were collected for paraffin sectioning and protein extraction to determine levels of pro-/anti-inflammatory cytokines.

Results: iPSC-MSC-treated group had a greater effect in the improvement of CS-induced cardiac dysfunction, myocardial hypertrophy and interstitial fibrosis than BM-MSC-treated group. The CS-induced elevation of cardiac pro-inflammatory cytokines, tumor necrosis factor-alpha (TNF-α), cytokine-

induced neutrophil chemoattractant-1 (CINC-1, resemble to human IL-8) and monocyte chemoattractant protein-1 (MCP-1) was attenuated by either iPSC-MSCs or BM-MSCs administration. However, CS-induced reduction of cardiac anti-inflammatory cytokines, interleukin-10 (IL-10) and adiponectin, was restored only by iPSC-MSCs administration. Both treatments reversed CS-induced reduction of cytoplasmic IκBα expression and nuclear translocation of nuclear factor-κB (NF-κB) p65 subunit.

Conclusions: Our findings demonstrate a higher capacity of iPSC-MSCs than BM-MSCs to ameliorate CS-induced cardiac dysfunction and cardiac remodeling via NF-κB signaling pathway by inhibiting pro-inflammatory cytokines and restoring anti-inflammatory cytokines in CS-exposed rat model. iPSC-MSCs may thus hold promise for the development of cell-based therapy in cardiac protection.

This work is supported by the Hong Kong Research Grant Council General Research Fund (RGC GRF) 2010-2011 [HKU 774410M] and National Natural Science Foundation of China [No 81370140].

ABSTRACTS

Abstracts for Oral Presentation:

OP3.

ENDOTHELIUM-, SOLUBLE GUANYLYL CYCLASE-DEPENDENT CONTRACTIONS IN ISOLATED ARTERIESCM Detremmerie,¹ SWS Leung,¹ A Xu,¹ Y Gao,² PM Vanhoutte¹¹Department of Pharmacology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong; ²Department of Physiology and Pathophysiology, Peking University, Health Science Center, Beijing, China

Objectives: This study focuses on the effects of thymoquinone on isolated arteries, by determining the mechanisms underlying the endothelium- and soluble guanylyl cyclase (sGC)-dependent augmentation of contraction that this natural compound causes, comparable to the augmentation described under hypoxic conditions.

Methods: Experiments were designed to study the effect of thymoquinone *ex vivo* in isolated porcine coronary and rat arteries. Rings, with or without endothelium, were suspended in conventional organ chambers for isometric tension recording. Certain rings were incubated with inhibitors of nitric oxide (NO) synthase (L-NG-nitroarginine methyl ester, LNAME), sGC (1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one, ODQ), rho-associated protein kinases (Y-27632) or L-type voltage-gated calcium channels (nifedipine). Some of the control experiments were done under depleted calcium conditions. The rings were contracted with phenylephrine (rat arteries) or prostaglandin F_{2α} (porcine coronaries) and exposed to increasing concentrations of thymoquinone. Selected rings were used to measure cyclic nucleotide levels by HPLC-MS/MS.

Results: Thymoquinone caused a sustained further increase in tension in rings with endothelium. This augmentation was prevented by endothelium removal, L-NAME and ODQ. Incubation with the NO-donor DETA NONOate in L-NAME-treated rings restored and even increased the contractile response to thymoquinone. Treatment with 8-bromo guanosine 3':5' cyclic monophosphate (cyclic GMP) or pyrophosphate did not restore the augmentation by thymoquinone. HPLC-MS/MS measurements revealed that the compound increased the production of inosine 3':5' cyclic monophosphate (cyclic IMP). Y-27632, nifedipine and calcium depletion inhibited the thymoquinone-induced contraction in porcine coronary arteries, but not in rat aortae.

Conclusions: The endothelium-dependent augmentation caused by thymoquinone requires endothelium-derived NO and activation of sGC, as described under hypoxic conditions. In addition, both thymoquinone- and hypoxia-induced augmentations require production of cyclic IMP but not the presence of either pyrophosphate or cyclic GMP. The data suggest that cyclic IMP causes vasoconstriction through calcium sensitization, although the underlying mechanism seems to differ in rat and porcine arteries. Taken into conjunction, thymoquinone can serve as a pharmacological tool to study/mimic the endothelium-dependent vasoconstrictor effects of intermittent hypoxia, as seen in the clinical setting of sleep apnea patients.

OP4.

ENDOTHELIAL DYSFUNCTION CAUSED BY INCREASED PRESSURE IN ADULT MOUSE CAROTID ARTERIES IS MEDIATED BY LOCAL ANGIOTENSIN SIGNALINGYZ Zhao,^{1,2} S Flavahan,¹ SWS Leung,² A Xu,² PM Vanhoutte,² NA Flavahan¹¹Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, MD, USA; ²Department of Pharmacology and Pharmacy and State Key Laboratory of Pharmaceutical Biotechnology, The University of Hong Kong, Hong Kong

Objectives: Experiments were performed to determine whether acute elevation of pressure in isolated arteries would impair endothelium-dependent dilatation by increasing angiotensin II signaling or by directly activating AT₁ receptors.

Methods: Dilatation of adult mouse isolated carotid arteries was analyzed in a myograph at 80 mmHg. Western blotting was used to detect the expression of angiotensinogen in arteries.

Results: Acetylcholine caused dilatation that was significantly reduced by endothelial denudation or by inhibition of NO synthase (L-NAME, 10⁻⁴ M). Transient exposure of arteries to increased pressure (150 mmHg, 3 hours) inhibited responses to acetylcholine, but did not affect dilatation to the NO donor DEA-NONOate. Inhibition of angiotensin II signaling, by blocking AT₁ receptors with the competitive antagonist losartan (3×10⁻⁶ M) or the inverse agonist valsartan (10⁻⁶ M) or by inhibiting angiotensin converting enzyme with perindoprilat (10⁻⁶ M) or captopril (10⁻⁵ M) prevented the impairment of endothelium-dependent dilatation by elevated pressure, but

did not affect dilatation to the agonist in arteries maintained at 80 mmHg. Elevated pressure caused a marked expression of angiotensinogen. Exogenous angiotensin II (3×10⁻⁷ M, 3 hours) inhibited responses to acetylcholine in arteries transiently exposed to increased pressure, but had no effect in arteries maintained at 80 mmHg.

Conclusions and implications: Exposure of adult arteries to elevated pressure rapidly impairs endothelium-dependent dilatation by causing expression of angiotensinogen and enabling angiotensin II-dependent activation of AT₁ receptors. Elevated pressure also amplified the response to exogenous angiotensin II. These processes likely contribute to the pathogenesis of hypertension-induced vascular dysfunction and organ injury.

ABSTRACTS

Abstracts for Oral Presentation:

OP5.**REPRESSOR ACTIVATOR PROTEIN 1 INDUCES PRO-INFLAMMATORY CYTOKINES PRODUCTION IN MACROPHAGES THROUGH NFκB SIGNALING**

Y Cai, PM Vanhoutte, EHC Tang

Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong

Objectives: Repressor activator protein 1 (Rap1), an established telomere-associated protein migrates to the cytoplasm and activates nuclear factor kappa B (NFκB) in human carcinoma cell lines. The present study tested the hypothesis that Rap1 induces production of pro-inflammatory cytokines via NFκB signaling in macrophages, a cell type involved in the development and progression of atherosclerotic lesions.

Methods: Small interfering RNA technology was used to knockdown Rap1 in THP-1 monocytic cells. The expression of lipopolysaccharide-(LPS) induced NFκB dependent genes and proteins in wild type (Rap1^{WT}) and Rap1 knockdown (Rap1^{KD}) cells were measured using real-time PCR and enzyme-linked immunosorbent assays. Co-immunoprecipitation assay was used to identify the protein-protein interaction. Western blotting was applied to determine the expression of Rap1 and proteins involved NFκB signaling pathway (including IKKα, IKKβ, IκBα, p65 and their phosphorylation forms) in Rap1^{WT} and Rap1^{KD} THP-1 cells. The expression of Rap1 and macrophages in human atherosclerotic lesions was detected by immunohistochemistry.

Results: Rap1 was present in the cytoplasm of differentiated THP-1 cells and associated with IKK. Knockdown of Rap1 suppressed LPS-mediated activation of NFκB, and phosphorylation of IκBα and p65 in THP-1. The reduction of NFκB activity was paralleled by a decreased production of NFκB-dependent pro-inflammatory cytokines [including interleukin (IL)-8, IL-1α, IL-6 and monocyte chemoattractant protein-1], and an increased expression of IL-10, an NFκB-dependent anti-inflammatory cytokine. Immunostaining revealed that Rap1 localized to macrophage-rich areas in human atherosclerotic plaques and that the presence of Rap1 was positively correlated to the advancement of the disease process.

Conclusions: In macrophages, Rap1 promotes cytokine production via NFκB activation favoring a pro-inflammatory environment which may aggravate the development and progression of atherosclerosis.

OP6.**ROLE OF IP RECEPTORS IN RENAL BASAL ARTERIAL TONE AND ENDOTHELIUM-DEPENDENT CONTRACTIONS**

O Baretella, A Xu, PM Vanhoutte

State Key Laboratory for Pharmaceutical Biotechnology, The University of Hong Kong, Hong Kong

Objectives: Endothelium-dependent contractions are augmented in human hypertension and in isolated preparations – including renal arteries – from hypertensive animals. Renal vasomotor tone is essential in the regulation of arterial blood pressure and renal arteries are highly sensitive to vasoconstrictor prostanoids including prostacyclin, identified as endothelium-derived contracting factor (EDCF) activating thromboxane prostanoid (TP) receptors. However, the mechanisms underlying increased EDCF responses in hypertension are not completely resolved.

Methods: Isometric tension was measured, in wire myographs at an optimal resting tension, in renal arterial rings from spontaneously hypertensive (SHR) and age (37-52 weeks)-matched Wistar Kyoto (WKY) rats. Responses were compared under control conditions and after incubation with indomethacin (cyclooxygenase inhibitor), ketanserin (5-HT₂ receptor antagonist), CAY10441 (prostaglandin I₂ [IP] receptor antagonist), and S18886 (TP receptor antagonist). All experiments were performed in the presence of L-NAME to exclude effects of endothelium-derived NO.

Results: Exposure to high potassium (High K⁺) depolarizing solution evoked significantly larger contractions in SHR (16.7±0.7 mN) compared to WKY (13.5±0.6 mN) preparations (36 rings each, *P*<0.01). CAY10441 (1 μmol/L) contracted renal arterial rings from both strains. This contraction was also significantly larger in SHR than in WKY renal arteries in absolute values, but similar between the two groups when expressed relatively to High K⁺ reference contractions (92±5% vs 80±8%, *n*=6). The phenomenon was curtailed by indomethacin, ketanserin, but not S18886. After washout and re-incubation, EDCF-mediated responses to acetylcholine were similar between SHR and WKY preparations in the presence of CAY10441 (*E*_{max} 72.6±5.3% and 67.4±3.8% High K⁺, *n*=8), but significantly larger than under control conditions (*n*=4-8, *P*<0.05). S18886 prevented EDCF-mediated responses in the absence but not in the presence of CAY10441. Contractions to prostacyclin [in the presence of indomethacin] were facilitated by CAY10441 in rings from both strains and no longer prevented by S18886, although the TP receptor antagonist abolished contractions to U46619.

Conclusions: These data suggest that: a) functional IP receptors are essential for renal basal arterial vasomotor tone; b) these receptors are also critical in the response to the endothelium-derived contracting factor prostacyclin; and c) TP blockade loses efficacy during concomitant IP receptor antagonism.

ABSTRACTS

Abstracts for Chaired Posters:

CP1.

DIFFERENTIAL MECHANISMS FOR INSULIN-INDUCED RELAXATIONS IN MOUSE POSTERIOR TIBIAL ARTERIES AND MAIN MESENTERIC ARTERIES

D Qu, J Liu, CW Lau, Y Huang

School of Biomedical Sciences, The Chinese University of Hong Kong, Hong Kong

The characteristics of endothelium-dependent relaxations in response to insulin and acetylcholine (ACh) in the mouse posterior tibial artery (PTA) were studied on wire myograph, and compared to those in the mouse main mesenteric artery (MMA). Insulin-induced relaxation in PTA was reversed by PI₃K and Akt inhibitors, LY294002 and triciribine, but not by nitric oxide synthase inhibitor, N^G-nitro-L-arginine methyl ester (L-NAME) or guanylate cyclase inhibitor, ODQ. The relaxation in PTA was also inhibited by apamin (small-conductance Ca²⁺-activated K⁺ channel blocker) plus charybdotoxin (intermediate-conductance Ca²⁺-activated K⁺ channel blocker), elevated KCl or ouabaine (Na⁺-K⁺ ATPase inhibitor) plus BaCl₂ [inwardly rectifying K⁺ (K_{IR}) channel inhibitor]; whereas L-NAME but not triciribine inhibited ACh-induced relaxation in PTA. On the other hand, nitric oxide and endothelium-derived hyperpolarizing factor albeit to a less extent mediated both insulin- and ACh-induced relaxations in MMA. The present study is for the first time dissecting out the components of endothelium-dependent relaxation in mouse PTA and suggesting differential responses to different agonists in distinctive blood vessels.

CP2.

BLACK TEA AMELIORATES ENDOTHELIAL FUNCTION BY INHIBITING ENDOPLASMIC RETICULUM STRESS IN HYPERTENSIVE RATS

WS Cheang,¹ CY Ngai,¹ Z Chen,² FP Leung,³ Y Huang¹

¹School of Biomedical Sciences, The Chinese University of Hong Kong; ²School of Life Sciences, The Chinese University of Hong Kong; ³Clinical Division, School of Chinese Medicine, Hong Kong Baptist University, Hong Kong

Hypertensive patients have elevated levels of homocysteine, known as hyperhomocysteinemia. Homocysteine (Hcy) can induce endoplasmic reticulum (ER) stress in endothelial cells. This study aims to investigate whether black tea protects against hypertension-associated endothelial dysfunction through alleviation of ER stress. Rat aortae and primary cultured rat aortic endothelial cells were treated with Hcy, black tea extract (a mixture of theaflavins), and theaflavin-3,3'-digallate (TF3). Male Sprague Dawley rats were infused with angiotensin II (Ang II) to induce hypertension, and orally administrated with black tea extract at 15 mg · kg⁻¹ · day⁻¹ for 2 weeks. Blood pressure was measured. Vasoreactivities of different arteries were examined on organ bath, wire myograph and pressure myograph. ER stress markers and reactive oxygen species (ROS) production were assessed by Western blotting and dihydroethidium fluorescence staining respectively. Hcy impaired endothelium-dependent relaxations of rat aortae in a concentration-dependent manner and led to ER stress in endothelial cells, which were ameliorated by co-incubation of black tea extract and TF3. The blood pressure

of Ang II-infused rats was normalized by black tea consumption. Impaired endothelium-dependent relaxations in renal arteries, carotid arteries and aortae, and flow-mediated dilatations in second-order mesenteric resistance arteries were significantly improved in Ang II-infused rat treated with black tea. Elevations of ER stress markers and ROS level in aortae from Ang II-infused rats were prevented by black tea treatment. The present study reveals the novel cardiovascular benefits of black tea in ameliorating vascular dysfunctions, and provides insights into developing black tea into beneficial dietary supplements in hypertensive patients (supported by GRF).

ABSTRACTS

Abstracts for Chaired Posters:

CP3.

ROLE OF ER STRESS IN VASCULAR BK_{Ca} DYSFUNCTION CAUSED BY HOMOCYSTEINE

WT Sun, XC Wang, CM Yu, Q Yang

Division of Cardiology, Department of Medicine and Therapeutics, Institute of Vascular Medicine, Li Ka Shing Institute of Health Sciences, Institute of Innovative Medicine, Faculty of Medicine, Chinese University of Hong Kong; The Chinese University of Hong Kong Shenzhen Research Institute, Hong Kong

Objectives: Large conductance Ca²⁺-activated K⁺ channels (BK_{Ca}) channels play an essential role in the regulation of vascular tone. Although previous studies suggested that inhibition of BK_{Ca} channels may contribute to vascular dysfunction caused by homocysteine, by what mechanisms homocysteine impairs BK_{Ca} channel function remains poorly understood. In this study, we investigated the role of endoplasmic reticulum (ER) stress in homocysteine-induced BK_{Ca} dysfunction in coronary arteries with a further attempt to understand the signaling involved.

Methods: Isometric force studies were performed in endothelium-denuded porcine small coronary arteries (<500 μm in diameter) in a myograph. Primary cultured porcine coronary arterial smooth muscle cells (PCASMCs) were used for western-blot analysis and whole-cell patch-clamp recording of BK_{Ca} current.

Results: Exposure to homocysteine for 24 h significantly increased the protein levels of ER stress molecules including GRP78, p-PERK and p-eIF_{2α}. The vasorelaxant response to the BK_{Ca} opener NS1619 was significantly attenuated in arteries pre-incubated with homocysteine (62.2±3.0% vs. 85.4±2.9%, p<0.01). Co-incubation of the arteries with homocysteine and the ER stress inhibitor, either TUDCA or 4-PBA restored the relaxation (76.6±3.5% and

85.4±1.7%, respectively). Preservation of NS1619-induced relaxation was also achieved by co-incubation with GSK2606414, a selective inhibitor of PERK (77.0±2.8%). The protein level of β1 but not α subunit of BK_{Ca} was lowered in PCASMCs after exposure to homocysteine, which was elevated by the co-incubation with TUDCA, 4-PBA, or GSK2606414. The upregulation of BK_{Ca} β1 protein expression was accompanied by the downregulation of p-PERK and p-eIF_{2α}. Inhibition of PERK enhanced the iberiotoxin-sensitive BK_{Ca} current (55.5±4.3 pA/pF) that was suppressed by homocysteine (42.8±5.5 vs. 70.1±8.7 pA/pF in control) in PCASMCs.

Conclusions: ER stress mediates homocysteine-induced smooth muscle BK_{Ca} dysfunction in coronary arteries. Downregulation of BK_{Ca} β1 subunit by PERK activation plays a key role in the loss of channel function.

Supported by RGC/GRF CUHK4774/12M; NSFC 81200123; and CUHK Direct Grant 4054015, 4054104.

CP4.

ROLE OF TRPC3 IN ENDOTHELIAL K_{Ca} ACTIVITY: EFFECT OF HYPOXIA-REOXYGENATION

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Objectives: We previously demonstrated the role of TRPC3 channels in EDHF-mediated relaxation and the susceptibility of TRPC3 and EDHF to hypoxia-reoxygenation (H-R) in coronary arteries. In this study, we further investigated the significance of TRPC3 in endothelial IK_{Ca} and SK_{Ca} channel activity under both normoxic and H-R conditions with exploration of the association between TRPC3 and K_{Ca} in endothelial cells.

Methods: Primary cultured porcine coronary arterial endothelial cells (PCAECs) were used. Whole cell K⁺ currents in response to bradykinin were recorded by patch-clamping with further differentiation of IK_{Ca} and SK_{Ca} components. Coimmunoprecipitation experiments using antibodies against TRPC3 and IK_{Ca}, or TRPC3 and SK_{Ca} were conducted.

Results: Pretreatment of PCAECs with the specific TRPC3 inhibitor Pyr3 significantly inhibited the IK_{Ca} (6.71±0.85 vs. 16.89±0.93 pA/pF, p<0.01) and SK_{Ca} (5.51±1.17 vs. 10.63±1.69 pA/pF, p<0.05) currents in response to bradykinin. In PCAECs exposed to H-R (60-30 min), bradykinin-induced IK_{Ca} (10.24±1.96 pA/pF) and SK_{Ca} (4.62±0.43 pA/pF) currents were markedly suppressed (p<0.05) and Pyr3 exhibited less inhibition on both components when compared with the cells without H-R exposure. The IK_{Ca} and SK_{Ca}

currents inhibited by Pyr3 were 10.18±0.73 and 5.12±1.22 pA/pF respectively in normoxic PCAECs and 5.15±1.21 pA/pF and 3.14±0.49 in cells underwent H-R (p<0.05). Coimmunoprecipitation experiments showed no physical interactions between either TRPC3 and IK_{Ca} or TRPC3 and SK_{Ca}.

Conclusions: TRPC3 is involved in the activation of IK_{Ca} and SK_{Ca} channels in coronary arterial endothelial cells. The functional association between endothelial TRPC3 and K_{Ca} does not involve physical interaction. Inhibition of TRPC3 contributes to H-R-induced suppression of channel activity of IK_{Ca} and SK_{Ca}, which serves as a mechanism underlying endothelial dysfunction under H-R condition.

Supported by RGC/GRF CUHK4774/12M; NSFC 81200123; and CUHK Direct Grant 4054015, 4054104.

ABSTRACTS

Abstracts for Chaired Posters:

CP5.

EFFECTS OF WY14643 AND FENOFIBRATE ON ACETYLCHOLINE-INDUCED CONTRACTIONS IN AORTIC RINGS FROM SPONTANEOUSLY HYPERTENSIVE RATS

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Introduction and objective: Oxidative stress is implicated in the release of endothelium-derived contracting factors, the release of which is associated with endothelial dysfunction. Peroxisome proliferator-activated receptor (PPAR) –alpha agonists, Wy14643 (WY) and fenofibrate (FF) have been found improving endothelial function in cardiovascular diseases. The present study was designed to examine whether or not WY and FF inhibit endothelium-dependent contractions through reduction of free radicals in aortae of spontaneously hypertensive rats (SHR).

Method: Male SHRs of 40-44 weeks old were used. Thoracic aortic rings with and without endothelium were suspended in organ chambers for isometric tension recording.

Results: Acetylcholine caused contractions in aortic rings with endothelium in the presence of N^ω-nitro-L-arginine methyl ester (an inhibitor of nitric oxide synthase). Tiron (a scavenger of intracellular superoxide anion) plus DETCA (an inhibitor of superoxide dismutase) significantly reduced the responses, suggesting that oxygen-derived free radicals are involved in the contractions. Both WY and FF significantly decreased the acetylcholine-induced contractions, suggesting that they may inhibit the production of hydrogen peroxide or its downstream signaling mediators. Exogenous hydrogen peroxide evoked contractions in aortic rings with and without

endothelium. Both WY and FF partially inhibited the contractions in rings with endothelium, but not in rings without endothelium, indicating that WY and FF act on the endothelium to produce their inhibitory effects.

Conclusion: Both WY and FF reduce contractions evoked by acetylcholine in aortic rings of SHR, which may result from their effects on decreasing the production of reactive oxygen species.

CP6.

INTERMITTENT HYPOXIA AGGRAVATES EARLY PATHOGENESIS OF NON-ALCOHOLIC FATTY LIVER DISEASE IN RATS

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Background/Aims: Chronic intermittent hypoxia (CIH) is associated with recurrent episodes of oxygen desaturation and reoxygenation in obstructive sleep apnea (OSA) patients. The prevalence of OSA is high in patients with non-alcoholic fatty liver disease (NAFLD). The mechanistic effect of CIH on the early pathogenesis of NAFLD remains elusive. Here we tested the hypothesis that IH aggravates oxidative stress and inflammation induced by high fat diet at an initial stage of pathogenesis of NAFLD in the rat liver.

Materials and Methods: Female Adult Sprague-Dawley rats were fed with a diet comprising of high fat (30% fish oil) or normal diet for 4 weeks with air (normoxic control) or CIH treatment (8 hours/day) which mimics obstructive sleep apnea condition during the last 2 weeks. Liver injury was detected by serum ALT and AST assay. Liver histology was evaluated by H&E staining. Lipid peroxidation was examined by malondialdehyde (MDA) assay and the expressions of pro-inflammatory cytokines (IL-1β, TNF-α, IL-6) were determined by real-time PCR and ELISA.

Results: Results showed that high fat diet (HFD) or CIH treatment increased liver injury with significant elevated levels of ALT and AST and deteriorated histological features of lipid accumulation in the liver. The effect of HFD was more prominent in the group co-treated with hypoxia. In addition, levels of MDA and the expressions of IL-1β, TNF-α and IL-6 were significantly increased in the HFD- or hypoxia-treated group and were substantially elevated in the co-treated group.

Conclusion: Intermittent hypoxia exacerbates oxidative stress and inflammation induced by high fat diet in the rat liver, suggesting a significant effect of CIH on aggravating the early pathogenesis of NAFLD.

ABSTRACTS

Abstracts for Chaired Posters:

CP7.**PREVENTION OF GLYCERYL TRINITRATE TOLERANCE BY FLAVONOIDS**

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Glyceryl trinitrate (GTN) is one of the most widely used anti-ischemic. However, the development of tolerance after continuous application for 24 to 72 hours limits its clinical utility. Tolerance appears to be associated with the oxidative stress induced by GTN in blood vessels. Flavonoids are important components in herbal medicine. They have antioxidative effect and potentiate vascular relaxation. In this study, the potential of nine flavonoids to prevent GTN tolerance were examined. Changes in isometric tension in thoracic aorta of Sprague Dawley rats were studied using organ chamber technique. Aortic rings were treated with GTN (30 μ M) for one hour to induce GTN tolerance. They were incubated with or without flavonoids for 30 minutes before GTN treatment. Afterwards, rings were contracted with phenylephrine (1 μ M) and relaxed with GTN (0.1 nM to 30 μ M). GTN-induced relaxation was reduced by prior incubation with GTN; this reduction was prevented by apigenin (10 μ M), which did not affect the relaxations in the control group (without prior treatment with GTN). On the other hand, luteolin (10 μ M) potentiated relaxations to GTN in both the control and GTN-pre-treated groups. Therefore, apigenin may have the potential to prevent the development of GTN tolerance.

CP8.**CHRONIC INTERMITTENT HYPOXIA INDUCES DEPRESSIVE-LIKE BEHAVIOR IN RATS**CS Lam,¹ YY Liu,² GL Tipoe,³ ML Fung¹Departments of ¹Physiology and ³Anatomy, The University of Hong Kong, Hong Kong; ²Institute of Neurosciences, The Fourth Military Medical University, Xi'an, China

Obstructive sleep apnea (OSA) causes recurrent oxygen desaturation (chronic intermittent hypoxia, CIH) and is associated with depression in patients. However, the relationship between OSA and depression is unclear. Synaptic degeneration, microtubule instability and monoamine deficiency are the common pathological features exhibited in both patients and depression animal models. We hypothesized that CIH induces depressive-like behavior by triggering synaptic degeneration, microtubule instability, and reducing monoamine downstream signaling deficits in the hippocampus. Adult male SD rats were exposed to air (normoxic) control or CIH treatment (8 hours/day) for 7 days. Hippocampus was harvested for the measurement of markers for synaptic vesicle protein (Synapsin I), microtubule stabilizing protein (MAP-2), and monoamine downstream signaling (protein kinase C (PKC), PKC substrate) using Western blot and immunohistochemical staining. Depressive-like behavior was assessed by forced swimming test and sucrose preference test. Immobility time was significantly elevated in the CIH-treated group when comparing to the normoxic control. In addition, sucrose solution consumption was remarkably reduced in the hypoxic group. Protein expression levels of synapsin I and synaptophysin were much less in CIH-treated group

than the control. However, MAP-2 protein level was not significantly different between hypoxic and normoxic groups. Furthermore, the number of PKC and PKC substrate positive-labeled cells were significantly reduced by the CIH treatment. In conclusion, CIH induces depressive-like behavior mediated by synaptic degeneration and reduced monoamine downstream signaling.

ABSTRACTS

Abstracts for Invited Lectures:

IL4.

ELECTRICAL REMODELING OF THE FAILING HEART AND THE RISK OF SUDDEN CARDIAC DEATH

GF Tomaselli

Johns Hopkins University, USA

Heart failure with dyssynchronous ventricular contraction is associated with genetically driven regional electrical remodeling of the ventricle which includes down regulation of K currents, increase in late Na current and altered Ca²⁺ handling as well as remodeled connexin43 with reduced conduction velocity. Cardiac resynchronization therapy (CRT) has the capacity to in part reverse cellular structural, electrical and metabolic remodeling of the failing heart.

IL6.

GLP-1-ELEVATING AGENTS BENEFIT ENDOTHELIAL FUNCTION

Y Huang

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Dipeptidyl peptidase-4 inhibition by sitagliptin stimulates insulin secretion by preventing glucagon like peptide-1 (GLP-1) degradation. However, the role of GLP-1 in hypertension is little studied. Our recent results show that sitagliptin improves endothelial function in hypertension through both GLP-1-dependent and -independent pathways by restoring NO bioavailability, suggesting that GLP-1 and related agents can be a therapeutic target in hypertension-related vascular events. Further examination shows that uncoupling protein-2 (UCP2) is the downstream target of sitagliptin and GLP-1 receptor agonist. Angiotensin II evoked endothelium-dependent contractions (EDCs) in C57BL/6 and UCP2 knockout (*UCP2KO*) mouse aortae. Chronic sitagliptin administration attenuated EDCs in SHR arteries and Ang II-infused C57BL/6 mouse aortae, and eliminated ROS overproduction in SHR arteries, which were reversed by GLP-1 receptor (GLP-1R) antagonist exendin 9-39, AMPK α inhibitor compound C, and UCP2 inhibitor genipin. By contrast, sitagliptin did not EDCs in Ang II-infused *UCP2KO* mice. Exendin-4 also improved endothelial function of renal arteries from SHR and hypertensive patients. UCP2 may serve as an important signal molecule in endothelial protection conferred by GLP-1-related agents. UCP2 could be a useful target in treating hypertension-related vascular events. (Supported by Hong Kong CRF grant)

IL7.

RECENT ADVANCE IN CLINICAL MANAGEMENT OF ACUTE CORONARY SYNDROME AND LIPID DISORDERS

MPH Chan

The University of Hong Kong, Hong Kong

Coronary artery disease remains one of the most important causes of morbidities and mortalities despite improvements in coronary risk factor management. The use of biomarkers and various non-invasive imaging techniques help to risk-stratify patients who present with acute chest pain. Randomized studies on anti-platelet and anti-thrombotic therapies further refine our management of acute coronary syndromes. Lastly, the recently published guideline on cholesterol management also made a great impact on our daily practice. All these advances help to improve our clinical management of acute coronary syndrome and lipid disorders.

IL8.

RECENT ADVANCE IN IMAGING

KY Yiu

The University of Hong Kong, Hong Kong

Speckle-tracking echocardiography has recently emerged as a quantitative ultrasound technique for accurately evaluating myocardial function by analyzing the motion of speckles identified on routine 2-dimensional sonograms. It provides non-Doppler, angle-independent, and objective quantification of myocardial deformation and left ventricular systolic and diastolic dynamics. By tracking the displacement of the speckles during the cardiac cycle, strain and the strain rate can be rapidly measured offline after adequate image acquisition. Data regarding the feasibility, accuracy, and clinical applications of speckle-tracking echocardiography are rapidly accumulating. The talk will therefore focus on the use of this technique in application for clinical research.

ABSTRACTS

Abstracts for Posters:

P01.

FLUOXETINE-INDUCED CARDIAC DEPRESSION IS ASSOCIATED WITH THE TOTAL MAGNESIUM EFFLUX IN RATS

MY Lee

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Introduction: Fluoxetine was chosen as a prototypic serotoninselective reuptake inhibitor (SSRI) without anticholinergic effects, while pemoline is a stimulant that appears to act as an indirect dopamine agonist. Although fluoxetine has been used in the field of anesthetic medicine, the cardiovascular effects of fluoxetine is still controversial. This study investigated the relation of magnesium (Mg) for fluoxetine-induced cardiac depression in rat.

Materials and Methods: The left ventricular development pressure (LVDP) accompanied with the total magnesium efflux ([Mg]e) were measured simultaneously in perfused hearts. The isolated heart was retrograde-perfused with an oxygenated modified Krebs–Henseleit buffer. We attempted to determine the values of total Mg, using atomic absorption spectrophotometer. (Analab 9200)

Results: Fluoxetine produced reversible decreases in the LVDP by increases in the [Mg]e. The effect of fluoxetine was completely blocked by the pretreatment of nifedipine, verapamil, imipramine or lidocaine and accompanied with the total magnesium efflux ([Mg]e) were blocked too.

Conclusions: These results suggest that fluoxetine-induced cardiac depression can be partly responsible to the increase in [Mg]e, but this reactions are inhibited calcium and sodium ion channel blockers.

P02.

IMPAIRED COLD TOLERANCE IN EP4 KNOCKOUT MICE IS NOT DUE TO COMPROMISED RECRUITMENT OF UCP1

F Ying,¹ Y Cai,¹ EHC Tang^{1,2}

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Objective: Uncoupling protein 1 (UCP1) is the key component of beta-adrenergically controlled non-shivering thermogenesis in brown adipose tissue (BAT). Certain white adipose tissue (WAT), upon exposition to cold, can undergo a process knowing as browning where it takes on characteristics of BAT, notably induction of UCP1 and the presence of multilocular lipid droplets and multiple mitochondria. Our preliminary data indicated that mice deficient in EP4 (one subtype of PGE₂ receptor) are cold-intolerant, suggesting that EP4 influence thermogenesis capacity. The aim of this project was to investigate whether or not the impaired thermogenesis in EP4 knockout mice is due to reduced recruitment of UCP1 in fat.

Methods: Male EP4 wild-type and knockout mice (12-15 weeks old) were treated with CL316243 (a highly selective beta 3-adrenergic agonist, 1 mg/kg/day *i.p.*) or saline for 10 days. Expression of UCP1, as well as other thermogenesis-related genes in subcutaneous white adipose tissues (sWAT), epididymal white adipose tissue (eWAT) and BAT of experimental mice were compared. In addition, isolated fat from the experimental mice were stained with hematoxylin and eosin and their morphology were compared.

Results: After chronic CL316243 treatment, eWAT of EP4 knockout were morphologically indistinguishable from that of wild-type mice. However, sWAT and BAT of EP4 knockout have smaller multilocular lipid droplets than wild-type mice. The expression of UCP1 and other thermogenesis-related genes (including epithelial V like antigen 1, type II thyroxine deiodinase, cell death inducing DFFA like effector A) in eWAT, sWAT and BAT did not differ between EP4 knockout and wild-type mice. Interestingly, after CL316243 treatment, there is a substantial increase in UCP3 mRNA in sWAT of EP4 knockout as compared to wild-type mice. An enhanced level of UCP3 was also observed in BAT of EP4 knockout as compared to wild-type mice under saline treatment.

Conclusions: Impaired cold tolerance in EP4 knockout mice is not due to compromised recruitment of UCP1 in WAT and BAT. The enhanced level of UCP3 in sWAT (after CL316243 treatment) and BAT (under basal conditions) in EP4 knockout mice may possibly serve as a compensatory mechanism to counteract the impaired thermogenesis observed in these mice.

ABSTRACTS

Abstracts for Posters:

P03.

ROLE OF EXTRACELLULAR SIGNAL-REGULATED KINASE IN THE REGULATION OF ENDOTHELIUM-DEPENDENT RELAXATIONS IN PORCINE CORONARY ARTERIES

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Objectives: Previous studies demonstrate that extracellular signal-regulated kinase (ERK) contributes to vascular contraction. The present study examined whether or not ERK modulated the different signaling pathways involved in endothelium-dependent relaxation.

Methods: Isolated porcine coronary arteries, with and without endothelium, were incubated in organ chamber for the measurement of isometric tension. They were contracted with U46619 (thromboxane A₂ analogue, 30 to 100 nM) followed by cumulative additions of different relaxing agents, in the presence or absence of the ERK inhibitor, U0126.

Results: In the presence of indomethacin (cyclooxygenase inhibitor; 10 μM), the endothelium-dependent relaxing agent bradykinin (0.1 nM to 1 μM) induced full relaxation, in a concentration-dependent manner, in arteries, with endothelium, contracted with U46619. With addition of indomethacin plus L-NAME [nitric oxide (NO) synthase inhibitor; 100 μM], bradykinin-induced relaxation cannot be mediated via cyclooxygenase and NO pathways. In this condition, U0126 (10 μM) enhanced relaxation thus suggesting that ERK activation leads to inhibition of endothelium-dependent hyperpolarization (EDH) type-mediated relaxations. When EDH pathway

was inhibited with TRAM-34 [intermediate conductance calcium-activated potassium channel (IK_{Ca}) blocker; 1 μM] and UCL1684 [small conductance calcium-activated potassium channel (SK_{Ca}) blocker; 1 μM], bradykinin-induced relaxations in the presence of indomethacin were also potentiated by U0126, thus suggesting a possible inhibitory action of ERK on the NO pathway. On the other hand, U0126 did not significantly affect relaxations to SKA-31 (IK_{Ca} and SK_{Ca} activator; 0.1 nM to 10 μM) in arteries with endothelium. As such, the inhibitory action of ERK on EDH type-mediated relaxation appears to be upstream of IK_{Ca} and SK_{Ca} activation. In arteries without endothelium, relaxations to Deta NONOate (nitric oxide donor; 0.1 nM to 10 μM) and forskolin (adenylyl cyclase activator, 0.1 nM to 10 μM) were not affected by U0126.

Conclusions: Our data suggest that ERK inhibits the generation of NO and EDH in the endothelium without affecting the signaling cascades downstream of these relaxing signals in the smooth muscle. Moreover, it does not play a role in the signaling cascade downstream of adenylyl cyclase activation in the smooth muscle.

P04.

PROTEOMIC STUDY REVEALS CHANGES OF ACUTE PHASE PROTEINS IN THE PLASMA OF PATIENTS WITH CONGENITAL HEART DISEASEX Zhang,¹ K Wang,² Q Yang,^{1,3} J Wang,¹ C Xuan,¹ GW He^{1,4}

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Objective: Ventricular septal defect (VSD), the most common congenital heart disease, has intracardiac left-to-right shunt and increased pulmonary flow that may affect the acute phase response. We examined the hypothesis that plasma proteins of the VSD patients may be altered and related to the pathogenesis of the disease.

Methods: In the plasma of VSD patients (n=55) and normal controls (n=55), two-dimensional electrophoresis and mass spectrometry were used to detect the differential protein profile and candidate proteins referred to acute phase response were further confirmed by enzyme-linked immunosorbent assay in new samples.

Results: A total of 322 protein spots were detected among which 3 acute phase proteins haptoglobin, serum amyloid P-component (SAP), and orosomuroid 2 were differentially expressed. The level of haptoglobin (0.4±0.04 vs. 0.6±0.07 mg/ml; p=0.016) and SAP (3.8±0.2 vs. 6.3±0.8 ng/ml; p=0.003) in VSD patients were significantly lower than that in normal controls. The level of orosomuroid 2 in VSD patients (3.1±0.1 mg/ml) was significantly higher than that in normal controls (2.3±0.1 mg/ml; p<0.000).

Conclusions: We have found that the plasma concentration of three acute phase proteins, haptoglobin, SAP, and orosomuroid 2 are altered that may reflect inflammation, be associated with decreased innate immune system function, and predispose the VSD patients to vulnerability to infections and pulmonary disease. These three proteins in plasma may also be developed as biomarkers for the function of innate immune system in patients with congenital heart disease.

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