PULSUS
WWW.PULSUS.COM

International Conference on

# HEART CONGRESS, VASCULAR BIOLOGY AND SURGEON'S MEETING

December 04-05, 2017 Dallas, USA

## Poster Presentations

## Bilateral internal iliac artery aneurysm submitted to endovascular treatment: Case report

**André Luís Foroni Casas[1]*, Daniela Vieira, Letícia Moreira** and **Edwaldo Edner Joviliano**
[1]University of Franca, Brazil

Isolated internal iliac artery aneurysms affected 0.1% of the population and account for approximately 1% of aortoiliac aneurysms. They are bilateral in half the cases. Fusiform aneurysms are the most common presentation and they are frequently associated with atherosclerotic disease. Internal iliac aneurysms are usually asymptomatic, except when there is rupture, with a related high risk of mortality. They can be diagnosed by ultrasound, computed tomography, angioresonance and angiotomography (the gold standard exam). Surgical repair of iliac artery aneurysms is indicated for those that had significant expansion, diameter higher than 3 centimeters and for symptomatic cases. We report the case of a 69-year-old hypertensive patient with an incidental finding in abdominal ultrasound exam of bilateral aneurysm in the internal iliac arteries, both with surgical indication. Was performed endovascular treatment in two successive stages, first with preservation of the right internal iliac artery followed by embolization of the left internal iliac artery.

### Biography

André Luís Foroni Casas has completed his Medical Degree from the University of Ribeirão Preto, Medical Residency in General Surgery from the Federal University of Amazonas, Medical Residency in Vascular Surgery from the School of Medicine of São José do Rio Preto, Medical Residency in Angioradiology and Endovascular Surgery from the School of Medicine of São José do Rio Preto and a Masters in Health Promotion from the University of Franca. He is a Vascular and Endovascular Surgeon who practices at Santa Casa de Franca, Unimed - Franca and Franca's prefecture. He holds a Specialist Degree in Vascular Surgery from the Brazilian Society of Angiology and Vascular Surgery. He is a Professor of Vascular Surgery at the Medical School of the University of Franca (UNIFRAN). He has experience in Medicine, with emphasis in Angiology, Vascular Surgery and Angioradiology and Endovascular Surgery.

vascular@andrecasas.com

**Notes:**

## Fluvastatin inhibits AGE-induced cell proliferation, migration, and ECM accumulation in VSMC by targeting CTGF

**Young Jin Kang**
Yeungnam University, South Korea

Connective tissue growth factor (CTGF) is a novel fibrotic mediator, which is implicated in fibroblast proliferation, cellular adhesion, angiogenesis and extracellular matrix (ECM) synthesis. Recent studies have demonstrated that advanced glycation end products (AGE) and their receptor-ligand interactions play a key role in neointimal formation and renal fibrosis after vascular injury. However, the potential link between CTGF and AGE has not been investigated. Based on this, we aimed to examine whether Fluvastatin could protect AGE induced vascular smooth muscle cell (VSMC) fibrosis and its putative transduction signals. In the present study, we have shown that AGE stimulated CTGF mRNA and protein expression time-dependent manners. The CTGF induction signal mediated by AGE was demonstrated via ERK1/2, JNK, and Egr-1 but not p38, consequently cell proliferation, migration, and ECM accumulation were regulated by CTGF signal pathway. And AGE also stimulated VSMC proliferation, migration, and ECM accumulations were blocked by Fluvastatin. In addition, the inhibitory effect of Fluvastatin was restored by administration of CTGF recombinant protein. Furthermore, AGE-induced VSMC proliferation was dependent on cell cycle arrest, increasing G1/G0 phase. Fluvastatin repressed cell cycle regulatory genes, cyclin D1 and CDK4 and augmented cyclin-dependent kinase inhibitors, p27 and p21 in AGE-induced VSMC. Taken together, Fluvastatin suppressed AGE-induced VSMC proliferation, migration, and ECM accumulation in by targeting CTGF signaling mechanism. Therefore, it might be recent evidence for CTGF as a potential therapeutic target in diabetic vasculature complication.

### Biography

Young Jin Kang has completed her PhD degree from Gyeongsang National University in 2000 and she is working at Yeongnam University since 2005 as a Professor. Her major subject is what kind of signal gene regulates vascular fibrosis and how to modulate vascular smooth muscle cell proliferation in diabetes or hypertension?

yjkang@med.yu.ac.kr

**Notes:**

## Right foot replantation after trauma: Case report

**André Luís Foroni Casas**
University of Franca, Brazil

The purpose of this study is to present a case about right foot replantation in a young woman with severe ankle and foot trauma. The patient suffered a motorcycle accident which resulted in an ankle and right foot fracture with bone loss, total section of the neurovascular pedicles and total avulsion of the right foot. She had a grade 3 shock at hospital admission, about 30 minutes after the trauma. During the procedure, a proximal and distal catheter was inserted into the sectioned right dorsal artery attempting to perfuse the amputated foot while an orthopedic team repaired the fractures using the external fixator. After the fixation, an end-to-end anastomosis of the dorsal artery was performed. The patient satisfactorily progressed after surgery and could return to work, to physical and habitual activities without vascular or neurological damage. We realize that in some cases of traumatic amputation the replantation may be totally appropriate to avoid functional damage.

### Biography

André Luís Foroni Casas has completed his Medical Degree from the University of Ribeirão Preto, Medical Residency in General Surgery from the Federal University of Amazonas, Medical Residency in Vascular Surgery from the School of Medicine of São José do Rio Preto, Medical Residency in Angioradiology and Endovascular Surgery from the School of Medicine of São José do Rio Preto and a Masters in Health Promotion from the University of Franca. He is a Vascular and Endovascular Surgeon who practices at Santa Casa de Franca, Unimed - Franca and Franca's prefecture. He holds a Specialist Degree in Vascular Surgery from the Brazilian Society of Angiology and Vascular Surgery. He is a Professor of Vascular Surgery at the Medical School of the University of Franca (UNIFRAN). He has experience in Medicine, with emphasis in Angiology, Vascular Surgery and Angioradiology and Endovascular Surgery.

vascular@andrecasas.com

**Notes:**

PULSUS
WWW.PULSUS.COM

International Conference on

# HEART CONGRESS, VASCULAR BIOLOGY AND SURGEON'S MEETING

December 04-05, 2017 Dallas, USA

## Accepted Abstracts

## Operations in the internal carotid artery in patients with atrial fibrillation with using dabigatran etexilate

**Alexandr Korotkikh**
Regional clinical hospital & Far Eastern State Medical University Russian Federation

**Objective:** To evaluate the effectiveness of dabigatran etexilate in patients with atrial fibrillation who underwent operative treatment at the ICA.

**Materials and Methods:** From Sept 1, 2015 to Dec 27, 2016, in the Department of Vascular Surgery and Cardiology was performed 694 operations on the ICA. Of these 94 (13,5%), surgery patients with atrial fibrillation. The average age of patients in the main group 68,5 ± 8,5 years, the control group - 65,0 ± 10,2 years. The comparison groups significantly differed in the following characteristics: postinfarction cardiosclerosis in the anamnesis of the main group 25,5%, control – 15,0% (P-value – 0,015); NYHA functional class I, main group 16,0%, control – 31,0 % (P-value 0,002); NYHA functional class III, 18.1%, control 4.8% (P-value 0.00028); diabetes mellitus main group 28.7%, controls 18,2% (P-value 0,024). All patients with atrial fibrillation for 5-7 days before surgery, warfarin was canceled and dabigatran etexilate was administered at a dose of 150 mg 2 times a day. When optimal numbers of INRs were reached, surgery was performed. Operational criteria and the results were evaluated in the endpoint - "stroke + lethality."

**Results and Discussion:** Total completed 84 CEA and CAS 10. The average time of operations of the main group 44,5 ± 17,1 min, control group - 40,7 ± 9,5 min, P-value <0,05. The average time of occlusion of ICA at CEA in the main group was 13,7 ± 6,1 min, in the control group 13,1 ± 1,8 min, P-value> 0,05. In patients with atrial fibrillation surgery performed significantly longer, but the time of the main stage - clamping ICA, were not significantly different. Consequently, an increase in the time of surgery is associated with a longer hemostasis at the stage of allotment of the ICA and/or after removal of the clamps off the arteries. In the early postoperative period, extensive hematomas in the postoperative areas and sites of arterial puncture were not noted. Indicator "stroke + lethality" inobservation group was 0%.

**Conclusions:** CEA and CAS in patients with atrial fibrillation receiving dabigatran etexilate are effective and safe. When performing CEA, additional time is required for more thorough hemostasis.

ssemioo@rambler.ru

## *HDAC1* depletion in human cardiac mesenchymal stromal cells facilitates paracrine-mediated endothelial cell growth and tube formation through a mechanism involving enhanced bFGF production and secretion

**David Hagan**
University of Louisville, USA

**Introduction:** Cardiac mesenchymal stromal cell (CMC) administration has been documented to improve cardiac function in pre-clinical animal models of heart failure. While the precise mechanism(s) underlying their therapeutic benefits remain unclear, both transdifferentiation (contributing to formation of new cardiac parenchyma) and secretion of paracrine signaling molecules (promoting neovascularization, cell survival, etc.) have been implicated as major modes by which transplanted cells exert their cardiac reparative effects. Thus, many laboratories have focused on novel methods to improve donor cell cardiogenic differentiation and/or cytokine secretion to enhance their therapeutic potential. We have previously shown either pharmacologic inhibition or genetic depletion of *HDAC1* to promote CMC lineage commitment towards a cardiomyogenic/endothelial cell-like fate. Further, in a pilot study, human CMCs pre-treated with the benzamide *HDAC1* inhibitor, entinostat (MS-275), exhibited superior ability to attenuate adverse left ventricular remodeling and yielded greater improvement in ventricular function relative to untreated CMCs when transplanted into a rat infarct model. While cardiogenic differentiation of *HDAC1*-inhibited CMCs may account for these functional improvements, we have previously shown inhibition of *HDAC* activity to alter CMC cytokine secretion – an effect that may have profound consequences on endogenous repair mechanisms (including cell proliferation and neovascularization). To this end, in the current study, we sought to investigate the influence of *HDAC1*-depletion on CMC cytokine secretion and associated paracrine-mediated activities on endothelial cell function *in vitro*.

**Methods:** Patient-derived CMCs were transduced with shRNA constructs targeting human *HDAC1* (sh*HDAC1*) or non-target (shNT) controls. Conditioned media (CM) was collected from shHDAC1 or shNT transduced CMCs cultured in F12 media in the absence of FBS for 24 h. Cytokine protein arrays were employed to comprehensively assess and compare/contrast the expression of >100 secreted proteins in CM from sh*HDAC1* or shNT-transduced CMCs. *In vitro* functional assays for cell proliferation, protection from oxidative stress, cell migration, and tube formation were performed on human endothelial cells incubated with CM from untransduced, shNT, or sh*HDAC1* human CMCs to compare/contrast paracrine signaling activity.

**Results:** Cytokine protein arrays revealed a pronounced increase in the secretion of a number of cytokines involved in cell growth, migration, and differentiation in CM from sh*HDAC1*-transduced CMCs. Consistent with these observations, sh*HDAC1* CM more efficiently promoted endothelial cell proliferation and tube formation compared to that of CM from shNT or untransduced CMCs. In an effort to narrow down which secreted factors may be responsible for these affects, key cytokines previously implicated in cell therapy-mediated cardiac repair were interrogated in shHDAC1, shNT, and untransduced CMCs. We revealed bFGF to be significantly upregulated at both the mRNA and protein levels in sh*HDAC1*-transduced CMCs vis-à-vis shNT and untransduced CMCs. Furthermore, shRNA-mediated depletion of *bFGF* in *HDAC1*-depleted CMCs was able to inhibit the effects of sh*HDAC1* CM in promoting both endothelial proliferation and tube formation. Thus, our results demonstrate that *HDAC1* depletion activates CMC proangiogenic paracrine signaling through a mechanism involving the enhanced secretion of bFGF. Conclusion: These results reveal a hitherto unknown role for *HDAC1* in the modulation of CMC cytokine secretion and implicate the targeted inhibition of *HDAC1* in CMCs as a means to enhance paracrine-mediated neovascularization in cardiac cell therapy applications.

dphaga01@louisville.edu

PULSUS
WWW.PULSUS.COM

International Conference on

HEART CONGRESS, VASCULAR BIOLOGY AND SURGEON'S MEETING

December 04-05, 2017 Dallas, USA

## Small vessel disease in ARVD and HCM

**Guy Hugues Fontaine**
Hôpital de la Salpêtrière, France

Small vessels in the heart are distal coronary arteries with a diameter between 50 and 200 microns. The same histologic pattern is found in two inherited cardiomyopathies ARVD and HCM. The typical pattern is an increase in the thickness of the leiomyocytes in the media of these vessels. There is also a reorientation of these leiomyocytes which are no longer parallel to the vessel but perpendicular. In addition, this anomaly seems independent of the surrounding tissue which can be dysplastic or not in ARVD. This histological structure is the basis of "atypical" chest pain which is the main clinical sign of the small vessel disease. Atypical means that they are not effort related as in common coronary artery disease. Their occurrence is unpredictable and duration variable from seconds to hours as well as their intensity. They occur more frequently in middle age women triggering multiple investigations to assess coronary vessels which are all negative. The histological structure of the distal coronary vessel may explain chest pain by spasm produced by the contraction of leiomyocytes leading to ischemia. An impressive case of ARVD was a 30 years old woman with frequent atypical chest pain even awaking her at night. Standard coronarography was normal. However, an ergonovine test triggered her typical episode of chest pain and a spasm of 1.5 cm was observed on the middle of the main descending artery. Pain and spasm disappeared after vasodilator injection. In her case ARVD was diagnosed by atrial arrhythmias (flutter) and extrasystoles with a left bundle branch block. ARVD was confirmed by ventriculography of the right ventricle. However, a systematic histologic study of the right ventricle of 82 patients who died of a non-cardiac cause in a general hospital of Paris showed that a quiescent form of ARVD (no arrhythmias) was observed in 3,7% of cases (Fontaine Editorial AJC 2014). Therefore, it can be that atypical chest pain commonly observed in middle age women are in fact the expression of a concealed form of ARVD. The presence of a similar histologic pattern and atypical chest pain in ARVD and HCM suggests a genetic mechanism which is presently unknown. This new concept needs further studies.

guy.fontaine2@numericable.fr

## The management of aortic graft infection

**Nicholas M Price**
Guy's & St Thomas' NHS Foundation Trust, UK

Aortic graft and endograft infection (AGI) complicates approximately 1-4% of deployments. At present, no universally accepted case definition exists and clinical guidelines that are underpinned by high-quality published evidence are severely lacking. There is general consensus that AGI is diagnosed by a combination of clinical, radiological and laboratory findings. However, in the current literature, microbiological details are brief and in a substantial number of cases there is no positive microbiology available to base targeted antimicrobial treatment upon. Published radiological data are mainly descriptive and the utility of various new diagnostic imaging modalities remains unclear. The fundamental tenets of management involve removal of the infected device, revascularization and antimicrobial therapy. However, surgical explanation carries a mortality of 18-30% and if an infected device is left in situ, mortality approaches 100% within 2 years. The best published surgical studies are mostly large case series but there are there are no randomised controlled trials evaluating the optimum surgical strategies. In addition, no well-designed trails of the ideal antimicrobial agents, administration route and treatment duration have been conducted. As a consequence, diagnosis and treatment is both extremely challenging and inconsistent, with highly variable and often poor outcomes. A multidisciplinary model of care is essential and this seminar is aimed at vascular surgeons, microbiologists and infectious diseases physicians. With reference to the limited published evidence, approaches to diagnosis and treatment of AGI will be discussed. Towards the development of evidence-based clinical guidelines, a proposed formal case definition will be presented, providing a consistent diagnostic standard that is essential for clinical trial design and meaningful comparison between various management strategies. In addition to highlighting areas for future research, a recently launched an international, multicentre AGI service evaluation database will be introduced.

Nicholas.Price@gstt.nhs.uk

## What can we learn from vascular differentiation in plants?

**Roni Aloni**
Tel Aviv University, Israel

Vascular tissues connect the leaves with the roots and enable a long distance transport of water and nutrition between the organs. The signals which induce vascular differentiation originate at the tips of young growing organs: leaves and roots, promoting early patterns of vascular differentiation, first in these peripheral organs. The vascular-inducing signal of leaves is auxin, which starts to flow from cell to cell by diffusion, induces a polar auxin transport process, which leads to the canalization of the auxin flow along a narrow file of cells. These cells become more polarized and more efficient transporters of auxin. The continuous polar transport of auxin through the canalized cells results in the formation of a vessel. Gradients of auxin along the plant body induce gradients of vessel sizes; the fast differentiating cells result in the narrowest vessels. This information allows the physically replacement of an injured vessel by an auxin-induced-regenerated vessel around a wound. Tumor development in plants demands de novo vascularization. Growing tumors produce the hormonal signal ethylene, which substantially decreases vessel width in neighboring healthy tissues, giving priority of water and nutrient supply to the growing tumor. By using plants that are insensitive to ethylene, tumor development can be eradicated. In this lecture, I will illustrate how the differentiation, regeneration and pattern formation of vascular tissues are controlled in plants. This general information will likely contribute to better understanding and practice in vascular tissues of humans.

alonir2@gmail.comuk

PULSUS
WWW.PULSUS.COM

International Conference on

HEART CONGRESS, VASCULAR BIOLOGY AND SURGEON'S MEETING

December 04-05, 2017 Dallas, USA

## Ascorbate prevents cigarette smoke-induced lung alveolar damage and vascular remodeling

**Souradipta Ganguly**
University of Calcutta, India

Cigarette smoke (CS) not only causes emphysema, a fatal disease involving progressive destruction of the lung alveoli but also induces right ventricular dysfunction due to pulmonary hypertension in chronic smokers. Here we show that guinea pigs exposed to sustained CS exposure over 10 weeks, undergo extensive emphysematous alveolar damage accompanied by pulmonary vascular remodeling that is implicated to the pulmonary hypertension. While the observed alveolar damage is characterized by an enlargement of pulmonary air spaces due to proteolytic degradation of the extracellular matrix proteins constituting the alveolar wall and extensive cellular apoptosis, the pulmonary vessel remodeling shows increased adventitia, peri-vascular fibrosis and thickening of the vessel wall. We demonstrate that such diverse pathological fates of the lung tissue are not only triggered by CS-induced oxidative stress but are also mobilized through distinct immunological pathways defined by diverse cytokine involvement. Besides directly oxidizing lung proteins, tobacco smoke induces release of the cytokines TNFα and IL-8 along with the pro-inflammatory factor, Rtp801 which in turn causes overproduction of nitric-oxide (NO) by inducible NOS (iNOS) as well as superoxide, which combine to produce, peroxynitrite, a potent oxido-nitrosative species that contributes to extensive lung protein nitration. Such nitrated lung proteins along with those oxidized directly by tobacco smoke oxidants become susceptible to proteolysis by lung proteases causing extensive destruction of the lung alveoli. Lung-specific administration of an anti-inflammatory glucocorticoid to the CS-exposed guinea pigs revealed that tobacco smoke oxidants and not the oxido-nitrosative species generated in the lung are predominantly responsible for the observed cigarette smoke-induced lung alveolar damage marked by the increased expression of TNFα and IL8. However, sustained tobacco smoke exposure was found to induce the release of increased levels of TGF-$\beta$, the major pro-fibrotic cytokine, which predisposed the lung vasculature to remodelling. Such different cytokine(s) involvement is also responsible for mobilizing diverse enzymatic pathways, which results in the concurrent occurrence of two contrasting pathological events within the lung tissue during smoking - alveolar destruction and vascular remodeling. Interestingly inhibition of the inflammatory enzyme inducible nitric oxide synthase (iNOS) by an iNOS-specifc inhibitor, L-NIL despite preventing protein nitration, could not forestall CS induced protein oxidation or alveolar damage. Our results indicate that iNOS inhibition actually enhanced CS induced vascular remodeling. The dietary antioxidant ascorbate on the other hand, substantially prevented both alveolar destruction as well as vascular remodeling presumably by inhibiting the initiating tobacco smoke and ROS induced lung protein oxidation and the consequent generation of the responsible cytokines. Taken together, our results indicate the major role of tobacco-smoke oxidant(s) as the primary etiopathogenic factor behind lung alveolar damage and as a significant contributor to pulmonary vascular remodelling witnessed during cigarette smoke-induced lung damage along with the endogenous oxidants generated by inflammation. Our results also highlight the versatile capability of the inexpensive antioxidant, vitamin C in the prevention of both forms of damage through the abrogation of the causal tobacco smoke induced oxidative damage.

alonir2@gmail.com