Background: Increased pulmonary blood flow (PBF) and shear stress may provoke irreversible vascular remodeling. Visualization of the micro-vasculature and the measurement of PBF velocity would provide insights regarding the correlation between high PBF and vascular remodeling. In this study, we aimed to establish a method for utilizing synchrotron radiation pulmonary micro-angiography (SRPA) and measure the PBF velocity in a high PBF rat model. Method: SRPA was performed at the Photon Factory of the High Energy Accelerator Research Organization (Tsukuba, Japan). Synchrotron radiation was converted to monochromatic X-rays by 13° reflection on a silicon crystal. High-sensitivity HARP (High-gain Avalanche Rushing Amorphous Photoconductor) detector camera with a fiber-optic plate provided by the NHK Science and Technology Research Laboratories and Hamamatsu Photonics was used as an image receiver. As a high PBF rat model, a fistula between the abdominal aorta and IVC was created. After 8 weeks, SRPA was performed by transvenous infusion of contrast medium. The dynamic changes of density at the pulmonary artery (PA) were measured by a density measurement software (Gray-val; Library Inc., Japan). The PBF velocity was calculated by the transit time of contrast medium in PA.

Result: The high spatial and density resolution was achieved by SRPA. The minimum identified vascular diameter was 100 μm. The velocity of PA flow in high PBF rats was significantly increased compared with control (2.3 ± 8.5 vs. 46.1 ± 4.3 mm/s).

Conclusion: These results demonstrate the effectiveness of SRPA for visualizing the flow distribution in micro-vasculature and measure PBF velocity in a high PBF rat model. This newly developed technology may help investigate the mechanism of vascular remodeling associated with high PBF and shear stress.

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Effects of closed vs. open repeated endotracheal suctioning during mechanical ventilation on the pulmonary and circulatory levels of Endothelin-1 in a lavage induced surfactant depleted Rabbit ARDS model

Hideaki Sakuramoto, Subrina Jesmin, Nobutake Shimojo, Junko Kaniyama, Majedul Islam, Tanzila Khatun, Satoshi Kawano, Taro Mizutani

Department of Cardiovascular Surgery, Faculty of Medicine, Ibaraki Clinical Education and Training Center, University of Tsukuba, Ibaraki, Japan
Department of Cardiology, Department of Internal Medicine, Triemli Hospital, Zurich, Switzerland
Molecular Internal Medicine, University of Zurich, Zurich, Switzerland
E-mail address: chiho-t@md.tsukuba.ac.jp (C. Tokunaga)

Despite the beneficial roles, endotracheal suctioning is known to accelerate lung injury during mechanical ventilation. More recently, a growing body of evidence demonstrates discrecely the difference of open endotraelect suctioning (OES) and closed endotraelect suctioning (CES) on the respiratory and hemodynamic parameters in acute respiratory distress syndrome (ARDS). Endothelin-1 (ET-1), a mediator of vascular inflammation, cell proliferation, and fibrosis in addition to being a potent vasoconstrictor has been potentially implicated in the pathogenesis of ARDS. We investigated the effects of repeated OES vs. CES during mechanical ventilation on circulatory and pulmonary levels of ET-1 in ARDS. Briefly, 18 Japanese White Rabbits were anesthetized and intubated with a 3.5-mm endotracheal tube. Normal saline was instilled into the lung and washed mildly. After instillation, rabbits were ventilated at a definite setting; OES and CES duration was for 6 h and performed every 30 min. At circulatory level, either OES or CES did not alter plasma ET-1 level compared to the ET-1 level in ARDS before the initiation of endotracheal suctioning (OES 4.7 ± 1.3 CES 4.8 ± 1.5, p = .839). In contrast, pulmonary ET-1 level was significantly higher in CS group compared to the the OES group after 6 h of repeated suctioning in lavage-induced ARDS (OES 27.2 ± 2.2 CES 29.7 ± 3.3, p = .05). This change in pulmonary ET-1 level could maintain a parallel relation with PaO2 level. The current observation for the first time reported the involvement of vasoactive peptide like ET-1 underlying the pulmonary changes of closed suctioning during mechanical ventilation in a lavage induced ARDS model.

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Localized effect of vascular aging on NADPH oxidase-mediated contractions to endothelin

Matthias R. Meyer1,5, Matthias Barton1, Eric R. Prossnitz1

1Department of Cell Biology and Physiology, University of New Mexico Health Sciences Center, Albuquerque, NM, USA
2Division of Cardiology, Department of Internal Medicine, Triemli Hospital, Zurich, Switzerland
3Molecular Internal Medicine, University of Zurich, Zurich, Switzerland
E-mail address: matthias.meyer@bluewin.ch (M.R. Meyer)

Renal hemodynamics have important effects on blood pressure. Renal arteries are highly sensitive to endothelin-1 (ET-1)-induced contractions, which partly depend on NADPH oxidase (Nox)-mediated superoxide generation. Aging is associated with increased superoxide production, but whether this affects Nox-mediated vascular reactivity to ET-1 is unknown. We studied the effect of aging on Nox-mediated contractions to ET-1 (0.1 nmol/L-100 nmol/L) in isolated rings of renal arteries and aortas from young and old C57BL/6 mice (4 and 24 months of age). Responses were obtained in the presence and absence of the Nox-selective inhibitor gp91ds-tat (3 μmol/L) and calculated relative to KCl (60 mmol/L)-induced contractions. The nitric oxide synthase inhibitor L-NAME (300 μmol/L) was used throughout the study to exclude differential effects of nitric oxide bioavailability between vascular beds. When compared to the aorta, maximal contractions to ET-1 in renal arteries were 6-fold greater in young (102 ± 4% vs. 18 ± 4%, P < 0.01) and 2.3-fold greater in old animals (92 ± 8% vs. 4 ± 1%, P < 0.01). Aging did not affect ET-1-induced contractions in renal arteries, which were inhibited by gp91ds-tat in both young and old animals (2-fold, P < 0.01). In the aorta of young animals, contractions to ET-1 were equally reduced by Nox inhibition and by vascular aging (4-fold, P < 0.05). In old aortas, Nox inhibition had no further effect on responses to ET-1. In conclusion, aging reduces contractions to ET-1 in the aorta by abolishing the contribution of Nox. In contrast, the renal artery appears to be resistant to aging-induced changes of Nox-dependent responses to ET-1. These findings indicate a specific, localized role of Nox in functional vascular aging that determines ET-1-dependent regulation of arterial tone.

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Selective endothelin (ET)-A receptor antagonist and dual ET-A/B receptor antagonist are effective in preventing the decrease in VEFG signaling and inadequate coronary collateral development in the diabetic hearts

Yumi Miyazaki1, Subrina Jesmin1, Nobutake Shimojo1, Seiji Maeda1, Satoshi Sakai1, Tomoko Yokota1, Sohel Zaedi2, Taro Mizutani1, Satoshi Homma1, Kazutaka Aonuma2, Takashi Miyazaki3

1Department of Cardiovascular Surgery, Faculty of Medicine, Ibaraki Clinical Education and Training Center, University of Tsukuba, Ibaraki, Japan
2High Energy Accelerator Research Organization, Ibaraki, Japan
3NHK Science and Technology Research Laboratories, Tokyo, Japan
4Hamamatsu Photonics K.K., Hamamatsu, Japan
5Tokyo Denki University, Tokyo, Japan
E-mail address: chiho-t@md.tsukuba.ac.jp (C. Tokunaga)