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Tissue factor expressed by aortic valve interstitial cells is able to generate thrombin in vitro

Joke Breyn [Orateur] (1), Emmanuelle Jeanpierre (1), Delphine Courtaux (1), Alexia Jadot (1), Francis Juthier (1), Carlo Banti (1), Christophe Zawadzki (1), André Vincentelli (1), Thierry Le Tourneau (2), Brigitte Jude (1), Eric Van Belle (1), Sophie Susen (1)

(1) Université Lille Nord de France, UFR114, EA-2693, Faculté de Médecine, Lille, France (2) Inserm UMR915, Université de Nantes, CHU Nantes, Institut du Thorax, Nantes, France

Objectives: We recently demonstrated the presence of tissue factor (TF), the main contributor to atherosclerotic plaque thrombogenicity, and thrombin in diseased valve leaflets. TF may be involved in the mineralization process of aortic valves by enhancing the generation of the pro-inflammatory osteopontin (OSP) N-half through thrombin induction. To strengthen our hypothesis, we evaluated TF expression by cultured valve interstitial cells (VICS) and studied their ability to generate thrombin in vitro.

Methods: VICS were obtained from explanted aortic valves after collagenase digestion. TF activity was measured with a chromogenic assay under basal conditions and after stimulation with TFN-α (10-50 ng/ml; 16 h). Thrombin generation capacities of VICS were analyzed using a Calibrated Automated Thrombogram assay. A dedicated software program enabled the calculation of thrombin generation over time. The area under the curve (ETP) represents the total amount of thrombin generated. The lag time is the time needed to achieve an explosive burst of thrombin.

Results: The isolated VICS express active TF. Basal TF antigen and activity varied among valves and were dose-dependently increased after stimulation with TFN-α. VICS were able to generate thrombin in vitro, proportional to the amount of cells used for the experiments. TFN-α stimulation led to a shorter lag time (12.6 min vs 10.8 min basal vs stimulated conditions) and increased both the maximal and total concentration of generated thrombin (peak: 141 nM vs 116 nM; ETP: 1034 nM/min vs 1179 nM/min; stimulated vs unstimulated).

Conclusion: We showed here for the first time that VICS express active TF and are able to generate thrombin in vitro. TF expression by VICS can be induced by TFN-α stimulation. The concentration of thrombin generated is proportional to the amount of cells and TF activity. These results strengthen our hypothesis that TF may play a role in aortic valve mineralization through thrombin generation.

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Exercise pulmonary hypertension in asymptomatic severe aortic stenosis: determinant and impact on outcome

Julien Magne [Orateur] (1), Erwan Donal (2), Kim O’Connor (1), Luc A. Piérard (1), Patrizio Lancellotti (1)

(1) CHU Sart Tilman, Cardiologie, Liège, Belgique (2) CHU de Rennes, Rennes, France

Background: Pulmonary hypertension (PHT) in patients with severe aortic stenosis (AS) is associated with increased morbidity and mortality. In asymptomatic patients, the additive value of exercise (Ex) PHT is unexplored. We aimed to identify the determinants and impact on outcome of ExPHT in asymptomatic patients with severe AS.

Method and results: Asymptomatic patients with severe AS (n=106) and preserved left ventricular (LV) function were prospectively referred to exercise stress echo. Resting and ExPHT were defined as a systolic pulmonary arterial pressure (SPAP) >50 mmHg and >60 mmHg, respectively. Ex PHT was more frequent than resting PHT (55% vs. 6%, p<0.0001). Patients with ExPHT were more frequently male (p=0.035), had significant higher mean aortic gradient (p=0.04) and longer diastolic filling time (p=0.015) than those without ExPHT. ExSPAP was correlated with resting aortic mean pressure gradient and peak aortic velocity (r=0.49 and r=0.48, both p<0.01), with LV diastolic filling time (r=0.54, p=0.003) and the Ex-induced changes in E/Ea ratio (r=0.53, p=0.007). Multivariate logistic regression analysis showed that only Ex-induced changes in E/Ea ratio (p=0.02) and resting peak aortic velocity (p=0.007) were independently associated with ExSPAP. The results were similar when the analysis was repeated using ExSPAP (peak: 141 nM vs 116 nM; ETP: 1034 nM/min vs 1179 nM/min; stimulated vs unstimulated).

Conclusion: We showed here for the first time that VICS express active TF and are able to generate thrombin in vitro. TF expression by VICS can be induced by TFN-α stimulation. The concentration of thrombin generated is proportional to the amount of cells and TF activity. These results strengthen our hypothesis that TF may play a role in aortic valve mineralization through thrombin generation.

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Evaluation of the radiation dose received by the medical team during transcatheter aortic valve implantation

Paul Luporsi [Orateur] (1), Nicolas Menneveau (1), Vincent Descotes-Genon (1), Romain Chopard (1), Sebastien Janin (1), Kais Mrabet (1), Sidney Chocron (2), Francois Schiele (1)

(1) CHU Besançon, Cardiologie, Besançon, France (2) CHU de Rennes, Car- diologie, Rennes, France

Background: Transcatheter aortic valve implantation (TAVI) is a growing cardiac intervention, using ionising radiation with deterministic and stochastic effects for the patient as well as for the medical heart team. Operator radiation depends on numerous factors, such as distance to the source, fluoroscopy time, and X ray tube angulation. Lead protection is routinely used for coronary angiography, but is less suitable for use during TAVI, and areas such as the hands and eyes are not systematically protected. We aimed to quantify the radiation dose received by the heart team members during TAVI and evaluate the role of the position of each member.

Methods: Operator radiation was evaluated by means of small dosimeters located on the outside of the lead protection at shoulder, knee and hip. We also measured radiation at the level of the eyes and hands, using small dosimeters that could be mounted on glasses and rings. The whole team was equipped (3 surgeons, 2 interventional cardiologists, 1 nurse and 1 echocardiographer).

Results: 12 TAVI were performed between February and May 2010 (4 apical and 8 femoral access). The most exposed area was the knee for all areas measured. During a difficult implantation procedure, we observed an alarmingly high dose at the level of the hand (4 apical and 8 femoral access). The most exposed area was the knee for all areas measured. During a difficult implantation procedure, we observed an alarmingly high dose at the level of the hand (4 apical and 8 femoral access).

Conclusion: A higher radiation dose was received by the surgeon closest to the X-ray tube during TAVI. Further to this study, we modified our procedure to reduce the radiation dose as much as possible for the medical team, with systematic use of lead protection and glasses, and identification of the fluoroscopy period.