

SSRCTS



SCANDINAVIAN SOCIETY FOR RESEARCH IN
CARDIOTHORACIC SURGERY

31st Annual Meeting in SSRCTS

on Cardiac, Vascular, and Thoracic Research

8-11 February 2023

Bardøla Høyfjellshotell, Geilo, Norway



Program & Abstracts

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WELCOME

Dear colleagues and friends,

It gives us great pleasure to welcome you to the 31st Annual Meeting in SSRCTS on Cardiac, Vascular and Thoracic Research, after two years of cancellations due to COVID-19 pandemic.

As members of the organizing committee, we are excited to reunite and meet our colleagues again and engage in intellectually stimulating and fruitful scientific discussions in the relaxed atmosphere that these meetings provide.

We would have loved to welcome even more participants this year, but we also recognize the impact that the lockdowns related to the pandemic have had on society as a whole. However, our meeting remains a unique platform for both young and senior researchers in the fields of cardiac, vascular, and thoracic research, to promote and enhance the interdisciplinary collaboration. We encourage the attendees to seize opportunities for informal discussions beyond the scheduled hours, as they may provide the first step towards creating exciting new research projects and establishing strong research consortia.

We look forward to some enriching and productive few days with you in Geilo.

On behalf of the organizing committee,

Peter Johansen
President of SSRCTS



PROGRAM: DIAGNOSTICS

THURSDAY, 9 FEBRUARY

2:00 – 2:45 PM **Arrival and registration**

2:45 – 3:00 PM **Welcome**

Assoc. Prof. Peter Johansen, MSc PhD, President of SSRCTS

3:00 – 4:00 PM **Keynote Talks**

Moderator: Peter Johansen

Prof. Won Yong Kim, MD PhD DMSc

Dept. of Cardiology, Aarhus University Hospital, Denmark

MR coronary angiography

Prof. Jørgen Arendt Jensen, MSc PhD DrTechn

Dept. of Health Technology UltraSound and Biomechanics, Centre for Fast Ultrasound Imaging, Technical University of Denmark, Denmark

Estimation of flow in the human circulation using ultrasound: from the major arteries to the smallest vessels

4:00 – 4:15 PM **Refreshments**



4:15 – 5:15 PM

Podium presentations

Chairmen: Ari Mennander & Tua Gyldenholm

Zineb Chaabi et al.

Early detection of perioperative myocardial injury after cardiac surgery

Sidsel Loft Nagel et al.

Improving Forensic Autopsies by Investigating Cause of Death using Ex-vivo Cardiac Imaging

Daria Semenova et al.

In an in vitro model of aortic valve calcification, valve endothelial cells stimulate calcification by Notch-dependent mechanisms

Rasmus E. Kraghede et al.

Consequence of open versus closed tracheostomy immediately after decannulation

5:15 – 5:30 PM

Refreshments

5:30 – 6:30 PM

Keynote Talk

Moderator: Jørgen Arendt Jensen

Assist. Prof. Kaare Mikkelsen, MSc PhD

Dept. of Electrical and Computer Engineering, Aarhus University, Denmark

Machine Learning in Biomedicine

6:30 – 7:30 PM

Keynote Talk

Moderator: Won Yong Kim

Prof. Jarle Vaage, MD PhD

Dept. of Cardiothoracic Surgery, Oslo University Hospital, Norway

How to write a scientific article – and get it published

8:00 PM

Dinner



PROGRAM: INTERVENTIONS

FRIDAY, 10 FEBRUARY

2:00 – 3:00 PM

Keynote Talks

Moderator: Jarle Vaage

Prof. Anders Jeppsson, MD PhD

Dept. of Cardiothoracic Surgery, Sahlgrenska University Hospital,
Sweden

2021 EACTS/ECS guidelines on valvular disease

Assoc. Prof. Peter Johansen, MSc PhD

Dept. of Electrical and Computer Engineering, Aarhus University
*Experimental cardiovascular biomechanics in surgical and
interventional procedures*

3:00 – 3:15 PM

Refreshments



3:15 – 4:30 PM

Gudbjartsson Award Session

Chairmen: Won Yong Kim & Jørgen Arendt Jensen

Mary Rezk et al.

Associations between new-onset postoperative atrial fibrillation and long-term outcome in patients undergoing surgical aortic valve replacement

Discussant: Daria Semenova

Trina Chen et al.

Aortic wall tissue analysis adds to follow-up after surgery for acute ascending aortic type A dissection

Discussant: Alexander Emil Kaspersen

Jonatan Gerard Nirmalan et al.

Measurement of the Left Atrial Appendage with an Emphasis on Optimal Device-Sizing in Percutaneous Left Atrial Appendage Occlusion

Discussant: Arsenii Zahirnyk

Sebastian Sartipy et al.

Long-term outcome after surgery for constrictive pericarditis

Discussant: Henrik Mulbjerg

Johannes H. Jedrzejczyk et al.

Reconstruction of the Entire Posterior Mitral Valve Leaflet Using 2-ply Vacuum Pressed Porcine Small Intestinal Extracellular Matrix: Acute in vivo Evaluation

Discussant: Zineb Chaabi

4:30 – 4:45 PM

Refreshments



4:45 – 5:30 PM

Podium Presentations

Chairmen: Anders Jeppsson & Alexander Emil Kaspersen

Arsenii Zabinnyk et al.

Pharmacological inhibition of aortic valve calcification in vitro

Tran Bao Ha et al.

Adaptability of left atrial appendage occluders to fixed landing zone geometries with varying degree of ovality

Tua Gyldenholm et al.

Perioperative Platelet Aggregation in Oesophageal Cancer Patients

5:30 – 6:00 PM

Poster Presentations

Chairmen: Kaare Mikkelsen & Rasmus E. Kraghede

Mette Wørmer Poulsen et al.

Effects of oxygen therapy on pulmonary perfusion and ventilation in a porcine model of acute pulmonary embolism

Henrik Mulbjerg et al.

Early detection of chronic heart failure by visualizing the pH of the heart with MR-hyperpolarization

Frederik Thørholm Andersen et al.

A Novel Method for on-line Intraoperative Visualization of Blood vessels and Tissue Perfusion

Alexander Emil Kaspersen et al.

Current practices and long-term outcome of myocardial revascularization

Caroline Damsgaard Jensen et al.

The effects of Bone Morphogenetic Protein 10 in pressure overload induced right ventricular failure - A preclinical study

6:00 – 7:30 PM

Wet Lab with Multiple Themes

8:00 PM

Dinner and Entertainment



PROGRAM: FOLLOW-UP

SATURDAY, 11 FEBRUARY

- 2:30 – 3:00 PM **Keynote Talk**
Moderator: Won Yong Kim
Assoc. Prof. Ari Mennander, MD PhD
Dept. of Cardiothoracic Surgery, Tampere University Hospital,
Finland
Ascending aortic dissection- thoughts on follow-up
- 3:00 – 3:15 PM **Refreshments**
- 3:15 – 4:00 PM **Open Discussion**
Moderator: Peter Johansen
Assist. Prof. Kaare Mikkelsen, MSc PhD
Dept. of Electrical and Computer Engineering, Aarhus University,
Denmark
AI chatbots – what to consider?
- 4:00 – 4:30 PM **Award Committee Meeting**
Chairman: Peter Johansen
Award committee:
Won Yong Kim
Jørgen Arendt Jensen
Ari Mennander
Anders Jeppsson
Jarle Vaage
- 4:30 – 4:45 PM **Award Ceremony**
- 6:30 – 7:00 PM **Evaluation**
- 8:00 PM **Presidential Dinner**



ABSTRACTS

GUDBJARTSSON AWARD SESSION

- G1 *Associations between new-onset postoperative atrial fibrillation and long-term outcome in patients undergoing surgical aortic valve replacement*
Mary Rezk et al.
- G2 *Aortic wall tissue analysis adds to follow-up after surgery for acute ascending aortic type A dissection*
Trina Chen et al.
- G3 *Measurement of the Left Atrial Appendage with an Emphasis on Optimal Device-Sizing in Percutaneous Left Atrial Appendage Occlusion*
Jonatan Gerard Nirmalan et al.
- G4 *Long-term outcome after surgery for constrictive pericarditis*
Sebastian Sartipy et al.
- G5 *Reconstruction of the Entire Posterior Mitral Valve Leaflet Using 2-ply Vacuum Pressed Porcine Small Intestinal Extracellular Matrix: Acute in vivo Evaluation*
Johannes H. Jedrzejczyk et al.



G1

Associations between new-onset postoperative atrial fibrillation and long-term outcome in patients undergoing surgical aortic valve replacement

Mary Rezk^{1,2}, Amar Taha^{1,3}, Susanne J. Nielsen^{1,2}, Andreas Martinsson^{1,3}, Lennart Bergfeldt^{1,3}, Tomas Gudbjartsson^{4,5}, Anders Jøppsson^{1,2}

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BACKGROUND

Data on prognostic implications of new-onset postoperative atrial fibrillation (POAF) and the role of oral anticoagulation in patients with recent surgical aortic valve replacement (SAVR) is limited. The aim of this study was therefore to explore potential associations between POAF, early-initiated oral anticoagulation (OAC) and long-term outcome after SAVR and combined SAVR+CABG.

MATERIALS AND METHODS

This is a retrospective, population-based study including all isolated SAVR patients (n=7038) and combined SAVR and CABG patients (n=3854) without a history of preoperative atrial fibrillation in Sweden 2007-2017. Information about comorbidities, medications, and long-term complications was collected from the SWEDEHEART registry, National Patient Registry, Cause of Death Registry, and Dispensed Drug Registry. Inverse Probability Treatment Weighting (IPTW) adjusted Cox regression models were used to examine associations between POAF, early-initiated OAC, and long-term outcome. Median follow-up time was 4.7 years (range 0-10 years).

RESULTS

POAF occurred in 3131/7038 (44.5%) and 1954/3854 (50.7%) of SAVR and SAVR+CABG patients, respectively. In SAVR patients, POAF was associated with increased long-term risk of death [adjusted hazard ratio (aHR) 1.21 (95% confidence interval 1.06-1.37)], ischemic stroke [aHR 1.32 (1.08-1.59)], any thromboembolism [aHR 1.35 (1.15-1.58)], heart failure hospitalization [aHR 1.46 (1.23-1.72)], and recurrent atrial fibrillation [aHR 6.81 (6.06-7.65)]. In SAVR+CABG, POAF was associated with death [aHR 1.31 (1.14-1.51)], recurrent atrial fibrillation [aHR 5.97 (5.13-6.95)], and heart failure [aHR 1.4 (1.21-1.73)], but not with ischemic stroke [aHR 1.04 (0.84-1.29)] or thromboembolism [aHR 1.17 (0.98-1.41)]. OAC was dispensed within 30 days after discharge to 67.0% and 65.9% respectively of SAVR and SAVR+CABG patients with POAF. Early initiated OAC was not associated with reduced risk of death, ischemic stroke or thromboembolism in any group of patients.

CONCLUSION

POAF after SAVR was associated with an increased risk for long-term mortality and morbidity. Further studies are warranted to clarify the role of OAC in SAVR patients with POAF.



G2

Aortic wall tissue analysis adds to follow-up after surgery for acute ascending aortic type A dissection

Trina Chen^{1,2}, Ivana Kholova², Timo Paavonen², Ari Mennander¹

1. Tampere University Heart Hospital and Tampere University Medical School, Tampere, Finland; 2. Department of Pathology, Fimlab Laboratories, Tampere University Hospital and Tampere University Medical School, Tampere, Finland

BACKGROUND

The extent of aortic resection during surgery for acute ascending type A aortic dissection (ATAAD) is debatable. While patient safety determines surgical management during ATAAD, the need for subsequent aortic reoperation after surgery may be dependent on aortic tissue frailty. We investigated whether aortic tissue analysis would reveal susceptibility for ongoing aortic event after surgery for ATAAD.

MATERIALS AND METHODS

During 2008-2022, 141 consecutive patients undergoing surgery for ATAAD at Tampere were analyzed and followed. The resected ascending aortic wall at surgery was processed for 42 degenerative, atherosclerotic and inflammatory histological variables. Patients undergoing aortic reoperations (Redos) during follow-up were identified and compared with those without aortic reoperations (Controls).

RESULTS

Altogether, there were 93 male patients. Redos were younger than Controls (56±14 and 66±13, years, respectively, $P<0.001$), and had less frequently previous aortic valve, coronary artery bypass or aortic surgery prior to ATAAD. Initial surgery encompassed replacement of the ascending aorta in the majority. Median follow-up was 4.3 years (interquartile range 2.7- 11.6). There were 21 Redos, of which one patient died during follow-up as compared with 48 deaths in Controls (log Rank $P=0.002$). Histology of the aortic wall revealed increased elastic fiber fragmentation, loss, and disorganization in Redos as compared with Controls (2.2±0.5 vs 1.9±0.5, Point score unit (PSU), $P=0.043$ and 1.7±0.8 vs 1.3±0.8, PSU, $P=0.016$, respectively). Moderate atherosclerosis was less present in Redos vs Controls (0.1±0.3 vs 0.3±0.5, PSU, $P=0.028$, respectively).

CONCLUSION

Identifying patients in need of aortic reoperations adds to patient safety after surgery for ATAAD. In contrast with presence of moderate aortic atherosclerosis, presence of ascending aortic wall elastic fiber fragmentation, loss and disorganization during ATAAD is suggestive for ongoing aortic event necessitating vigilant follow-up for need of aortic reoperations.



G3

Measurement of the Left Atrial Appendage with an Emphasis on Optimal Device-Sizing in Percutaneous Left Atrial Appendage Occlusion

Jonatan Gerard Nirmalan¹, Jens Erik Nielsen-Kudsk², Anders Kramer³, Kasper Korsholm⁴

1. Faculty of Health, Aarhus University, Denmark; 2. Dept of Cardiology, Aarhus University Hospital, Denmark; 3. Dept of Cardiology, Aarhus University Hospital, Denmark; 4. Dept of Cardiology, Aarhus University Hospital, Denmark

BACKGROUND

Left atrial appendage occlusion (LAAO) has advanced as an alternative strategy to lifelong anticoagulation in patients with atrial fibrillation- especially among those intolerant to anticoagulation. At this time, Amplatzer AMULET and WATCHMAN-FLX are the most frequently utilized devices in LAAO. Each manufacturer has proposed distinct sizing protocols based on the diameter of the landing zone in the left atrial appendage (LAA). However, for both devices, it remains uncertain if the maximum diameter of the landing zone is the optimal measure in accurate device sizing.

MATERIAL AND METHODS

In this retrospective single-center cohort study, we investigated four different measures of the landing zone diameter and their ability to accurately predict the implanted device size. 120 patients implanted with Watchman FLX device and 104 patients with the Amulet device were included. Maximum, mean, area-derived and perimeter-derived diameter of the landing zone were estimated from pre-procedural cardiac CT scans. Based on the manufacturers' sizing algorithms predicted device size was determined from these diameters.

RESULTS

When comparing mean difference between predicted and implanted device size across the four parameters, our results suggest the maximum diameter to be least accurate in device sizing for Watchman FLX and Amulet with mean (SD) difference of -1.29mm (± 2.84) and -2.42mm (± 2.60) respectively. Whereas mean, area-derived, and perimeter-derived diameter seemed equally valid for both devices. In oval landing zones max diameter demonstrated poor performance in both the devices, whereas the three additional parameters performed equally well.

CONCLUSION

Our results indicate manufacturer proposed maximum diameter of the LAA landing zone to be the least accurate in predicting implanted device size. Mean, area- and perimeter-derived diameter perform better and seem equally accurate.

PERSPECTIVE

Prospective studies, preferably introducing a new sizing algorithm based on either mean, area-derived or perimeter-derived diameter are warranted. This is necessary to examine the consequences of utilizing other parameters than max diameter in device-sizing.



G4

Long-term outcome after surgery for constrictive pericarditis

Sebastian Sartipy¹, Anders Jeppsson¹, Göran Dellgren¹, Emma C Hansson¹

1. Dept. of Cardiothoracic Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden

BACKGROUND

Constrictive pericarditis is a rare and severe condition characterized by fibrotic and constrictive changes to the pericardium which leads to restriction of diastolic relaxation. The only definitive treatment is pericardiectomy. This study provides additional knowledge regarding long-term outcomes after surgical pericardiectomy due to constrictive pericarditis.

METHODS

This retrospective single-center study included all pericardiectomy procedures (n=22, 17 male, 5 female, mean age 59 ± 11.4 years) at Sahlgrenska University Hospital between March 2008 and November 2020. Data was obtained by extracting information from existing electronic medical records and from the Swedish cardiac surgery registry. Baseline demographics as well as pre-, peri- and postoperative variables were analyzed. Patients were mainly diagnosed based on symptoms in combination with echocardiography.

RESULTS

Median duration of symptoms before surgery was 12 (IQR 6.3-16.5) months. Fourteen (64%) of the patients had a subtotal pericardiectomy and the remaining 8 (36%) patients had a total pericardiectomy. Other concomitant surgery was performed in 6 patients (27%). CPB was utilized in 13 operations (59%). NYHA-class was improved after the procedure (see figure 1). There was a significant decrease in central venous pressure (CVP) both when we compared preoperative data with 2 months postop and at latest follow-up (see figure 2). One patient died in-hospital. Cumulative 5-year survival rate was 80% and 10-year survival rate was 62%.

CONCLUSIONS

Pericardiectomy for constrictive pericarditis is associated with favourable short- and long-term outcome with patients experiencing significant improvement of heart failure-like symptoms and improvement in CVP. This is consistent with previously published studies.

PROSPECTS

Studies have shown better outcome for patients having a total pericardiectomy compared to patients undergoing a subtotal pericardiectomy. We observed no difference in our study, mainly due to the small sample size. Thus, we aim to investigate the difference in outcome, comparing total versus a subtotal approach, in a larger Swedish cohort. We expect to receive the data by the end of December 2022.



FIGURE 1

Illustration of changes in NYHA-class among patients after pericardiectomy. Results show significant improvement of symptoms after pericardiectomy, at both one year and at latest follow-up, as compared to preoperative symptoms.

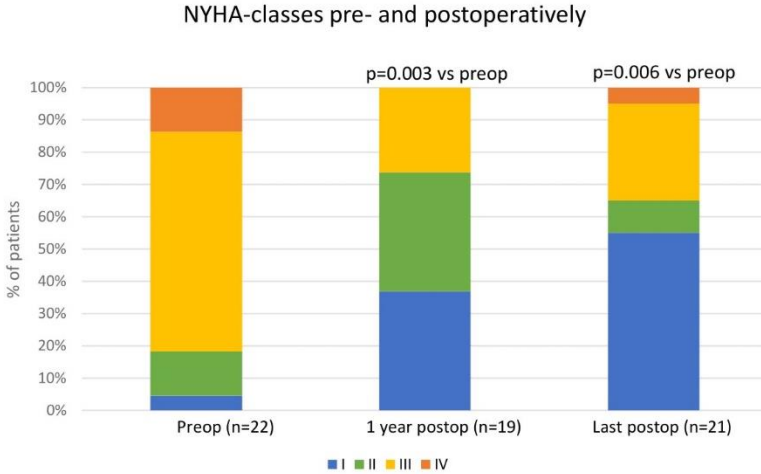
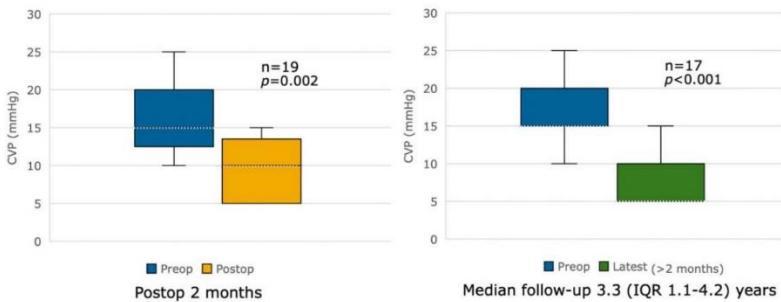


FIGURE 2

Illustration of changes in central venous pressure (CVP) among patients after pericardiectomy. Results show significant decrease in CVP both when comparing preoperative data with 2 months postop and at latest follow-up.





G5

Reconstruction of the Entire Posterior Mitral Valve Leaflet Using 2-ply Vacuum Pressed Porcine Small Intestinal Extracellular Matrix: Acute in vivo Evaluation

Johannes H. Jedrzejczyk^{1,2}, Marcell J. Tjørnild^{1,2}, Alexander Emil Kaspersen^{1,2}, Jens T. Væsel^{1,2}, Dennis Ammitzskov^{1,2}, Stine Krogh^{1,2}, Søren Nielsen Skov^{1,2}, J. Michael Hasenkam^{1,2,3}

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OBJECTIVE

To create a standardized patch design using MRI scans of healthy pigs and use it to investigate reconstruction of the entire posterior mitral valve with 2-ply vacuum pressed porcine small intestinal submucosa extracellular matrix.

MATERIALS AND METHODS

Five healthy pigs underwent MRI scans. Reconstruction of the entire posterior mitral valve was performed in an acute 80-kg porcine model (n = 7). The posterior mitral valve leaflet and associated chordae tendineae were reconstructed with 2-ply vacuum pressed porcine small intestinal submucosa extracellular matrix. Pressure measurements and echocardiography were performed before and after intervention.

RESULTS

The reconstructed mitral valve was fully competent without any signs of regurgitation. The peak left atrial pressure for baseline and reconstruction was 9.9 ± 1.1 mmHg vs 9.9 ± 1.0 mmHg, $p = 0.676$, and the mean pressure difference across the mitral for baseline and reconstruction was 4.5 ± 2.3 mmHg vs 4.1 ± 2.3 mmHg, $p = 0.063$.

CONCLUSION

Reconstruction of the entire posterior mitral valve using 2-ply vacuum pressed porcine small intestinal submucosa extracellular matrix was possible in an acute 80-kg porcine model. The reconstructed mitral valve was fully competent; no signs of mitral valve regurgitation, stenosis, or systolic anterior motion were found.



PODIUM PRESENTATIONS

- O1 *Early detection of perioperative myocardial injury after cardiac surgery*
Zineb Chaabi et al.
- O2 *Improving Forensic Autopsies by Investigating Cause of Death using Ex-vivo Cardiac Imaging*
Sidsel Loft Nagel et al.
- O3 *In an in vitro model of aortic valve calcification, valve endothelial cells stimulate calcification by Notch-dependent mechanisms*
Daria Semenova et al.
- O4 *Consequence of open versus closed tracheostomy immediately after decannulation*
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- O5 *Pharmacological inhibition of aortic valve calcification in vitro*
Arsenii Zahirnyk et al.
- O6 *Adaptability of left atrial appendage occluders to fixed landing zone geometries with varying degree of ovality*
Tran Bao Ha et al.
- O7 *Perioperative Platelet Aggregation in Oesophageal Cancer Patients*
Tua Gyldenholm et al.



O1

Early detection of perioperative myocardial injury after cardiac surgery

Zineb Chaabi¹, Ola Hammarsten¹, Björn Redfors¹, Anders Jeppsson¹

1. Department of Cardiothoracic Surgery, Sahlgrenska University Hospital, Sweden

BACKGROUND

Perioperative myocardial injury (PMI) is associated with worsened clinical outcome in cardiac surgery patients. Early detection of PMI increases the possibilities to initiate countermeasures. PMI is normally assessed the day after surgery by measuring myocardial injury markers, such as troponins. In a recent study by Devereaux PJ et al. (N Engl J Med 2022) a high sensitive troponin I (TnI) > 5670 ng/L on postoperative day one, was associated with poor outcome. We investigated if measurement of high sensitive troponin I three hours after completed surgery identifies PMI in accordance to this cut off value.

MATERIAL AND METHODS

A total of 117 patients without recent preoperative myocardial infarction that underwent CABG and/or valve surgery at Sahlgrenska University Hospital, were included in a prospective observational study. High sensitive troponin I was measured three hours after completed surgery and on the first postoperative morning in all patients. PMI was defined as TnI > 5670 ng/L. Positive and negative predictive values, sensitivity and specificity, and C-statistics were calculated. Correlation was calculated with Spearman's test.

RESULTS

PMI defined as TnI > 5670 ng/ml on day one after surgery occurred in 15/117 patients (12.8%). Median and interquartile range troponin concentration was 1900 (1000-3450) ng/L three hours after surgery and 2300 (1300-3950) ng/L the day after surgery ($p=0.46$). The correlation coefficient between three hours and day 1 measurements was 0.78 ($p<0.001$). The positive and negative predictive values for measurements three hours after surgery were 73% and 96% respectively, and the sensitivity and specificity were 73% and 96% respectively. The area under the ROC-curve was 0.92 (95% CI 0.86-0.99).

CONCLUSION

High-sensitive troponin I measurements three hours after cardiac surgery identifies patients with clinically significant perioperative myocardial injury with acceptable sensitivity and high specificity.



O2

Improving Forensic Autopsies by Investigating Cause of Death using Ex-vivo Cardiac Imaging

Sidsel Loft Nagel¹, Peter Agger¹, Lene Warner Thorup Boel², Michael Pedersen¹

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BACKGROUND

In approximately 10% of forensic autopsies the cause of death remains undetermined. Unexplained deaths are in many cases presumed to have a cardiac cause. We introduce magnetic resonance imaging (MRI) of ex-vivo hearts and coronary arteries in the forensic autopsy in order to visualize the myocardium and vascular system. This provides information for targeting biopsies of the heart to improve the chance of determining a cardiac cause of death.

METHODS AND MATERIALS

The anatomical in-vivo appearance of post-mortem hearts will be preserved by filling the cavities with a water-based polymer. The coronary arteries are visualized using a mixture of gelatin and a MRI contrast agent, Dotarem. The hearts are scanned in a Philips Achieva 1.5T clinical MRI system, and coronary angiography will be performed. Subsequently, a diffusion weighted spin-echo sequence is performed allowing for diffusion tensor calculation and quantification of myocardial architecture.

RESULTS

Pending results. The study is expected to be initiated in February 2023. Thus, no results nor conclusion can be made at this point.

PERSPECTIVES

Our study proposes a promising and simple procedure for a targeted heart examination in the forensic autopsy. This will pinpoint areas of interest in the heart, which subsequently can be subjected to conventional histological examination, and thereby increasing the chance of finding a cause of death. Furthermore, MRI will provide information on cardiac anatomy and function, leading to a better understanding of cardiac causes of death including sudden cardiac death.



O3

In an in vitro model of aortic valve calcification, valve endothelial cells stimulate calcification by Notch-dependent mechanisms

Daria Semenova¹, Arsenii Zabinnyk², Maria Bogdanova^{1,2}, Vladimir Uspensky³, Anna Kostareva³, Arkady Rutkovsky^{1,2}, Anna Malashicheva⁵, Kåre-Olav Stensløkken¹, Jarle Vaage^{1,2,4}

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OBJECTIVE

The pathophysiology of calcific aortic valve disease (CAVD) is a complex and not fully elucidated biological process. The valve interstitial cells (VIC) appear to have a major role in this process. It has been suggested that valve endothelial cells (VEC) also contribute to the calcification process. The signaling of the Notch gene has a key role in cross talk between different cell types. The aim of this study was 1. To study the role of VEC in calcification of cultured VIC; 2. To investigate the possible role of Notch in this model.

METHODS

VEC and VIC were isolated from patients with CAVD or from donors with healthy valves. VEC and VIC were co-cultivated to investigate the cross-talk mediated mechanisms. Notch was activated by lentiviral transduction. Inhibition of Notch signaling was provided by shRNA-mediated knockdown. Calcification of VIC was induced by culturing in osteogenic medium and measured spectrophotometrically by Alizarin red. Further evaluation by expression of pro-osteogenic genes.

RESULTS

VEC from CAVD patients dose-dependently (10^4 , 50^4 , 100^4 cells per well) enhanced calcification of VIC in co-culture compared to VIC monoculture (from 8.5 to 12.5 calcification intensity units) as shown by Alizarin Red staining after 21 days with osteogenic stimulation. Expression of proosteogenic markers (RUNX2, POSTN, and ALPL) and Notch target genes correlated with the number of VEC in co-culture. Notch activation in VIC increased more intensive calcification (from 8.7 to 10.5 calcification intensity units). Inhibition of Notch in VIC under osteogenic induction inhibited calcification.

CONCLUSIONS

In the present model, VEC were able to stimulate calcification of VIC by Notch-dependent mechanisms. Thus, modulation of Notch signaling might inhibit heart valve calcification.



O4

Consequence of open versus closed tracheostomy immediately after decannulation

Rasmus E. Kraghede^{1,2,3}, Karen J. Christiansen¹, Louise Devantier⁴, Alexander Emil Kaspersen², Johanne Juul Petersen⁵, Thomas Pasgaard¹, J. Michael Hasenkam^{2,3}, Michael Pedersen^{3,5}

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BACKGROUND

Tracheostomy is performed in approximately one million patients each year worldwide, predominantly for the purpose of mechanical ventilation. Decannulation following mechanical ventilation leaves the tracheostomy wound unsealed and a bandage is placed to cover the wound. However, these bandages often leak air, resulting in a compromised lung function and speech along with an increased risk of lung consolidation. This can ultimately result in decannulation failure, which is reported as high as up to 25%. Using external bandaging for tracheostomy wounds, bronchial secretion can easily pass to the wound, thereby increasing the risk of stomal infection. Recently, a new concept which enables intratracheal sealing of the tracheostomy was introduced. The concept provides an airtight sealing that potentially solves the issues of air leakage and bronchial secretion entering the wound. We aimed to investigate the feasibility of intratracheal tracheostomy sealing in relation to lung function and speech, comparing it to an open tracheostomy wound.

MATERIAL AND METHODS

Currently, ten adult patients who underwent tracheostomy at the Intensive Care Unit at Aarhus University Hospital were included. Patients with a tracheostomy tube in place for a minimum of 7 days were eligible. Decannulation was performed according to standard procedural guidelines. Immediately after decannulation, speech assessment using an equal appearing interval scale as well as spirometry was performed. Baseline measures during open stoma was obtained, using neither bandage nor seal to cover the tracheostomy wound. A handheld temporary intratracheal tracheostomy sealing device was inserted and postinterventional measures were obtained. Baseline FEV1, FVC and speech assessment were compared to postprocedural values.

RESULTS

The mean age \pm standard deviation of the ten patients was 59 ± 12 years. Mean FEV1 with 95% confidence interval (CI) at baseline was 553 (355-862) ml which increased to 785 (537-1149) ml after insertion of the device ($p=0.001$). Mean FVC with 95% CI at baseline was 660 (456-955) ml and increased to 1166 (898-1514) ml postprocedural ($p<0.001$).

CONCLUSION

In this small-scale feasibility study, FEV1, FVC, and speech improved significantly for decannulated patients after insertion of a intratracheal tracheostomy sealing disc.



O5

Pharmacological inhibition of aortic valve calcification in vitro

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BACKGROUND

Calcific aortic valve disease has no pharmacological alternative to heart surgery or catheter-based intervention with implantation of an aortic valve prosthesis. Valve calcification is an active biological process in the valve interstitial cells (VICs). Due to lack of good animal models, experimentally induced calcification of cultured human VICs is regarded as the best experimental model to study the cellular and molecular mechanisms of valve calcification. The purpose of this study was to identify drugs that may inhibit calcification in the aortic valve in vitro.

MATERIAL AND METHODS

VICs were isolated from human aortic valves harvested during surgery. Cells were cultivated at 37 °C/5% CO₂ with growth media changed twice a week until they reached confluence. Addition of osteogenic medium induced calcification, which after Alizarin Red staining was quantified spectrophotometrically. The effect on calcification of a series of small-molecular substances, which are globally used in patients for other indications, was studied.

RESULTS

Several drugs inhibited the calcification in VICs cultures. The lead compound inhibited by 91% (30 µM, p=0.002). Additional compounds from the same class of drugs inhibited calcification by 80% (30 µM, p=0.002). Inhibition of calcification was dose dependent.

CONCLUSION

A class of drugs significantly inhibited calcification in an in vitro model of aortic valve calcification. These substances are well tolerated for longtime use. Pharmacological therapy at an early stage of heart valve calcification might delay or stop heart valve calcification. It may represent a paradigm shift in therapy.



O6

Adaptability of left atrial appendage occluders to fixed landing zone geometries with varying degree of ovality

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BACKGROUND

Atrial fibrillation (AF) is the most common type of non-valvular cardiac arrhythmia. Patients with AF have a five-fold increased risk of ischemic stroke, with the predominant stroke mechanism being thrombus formation in the left atrial appendage (LAA) with subsequent embolization to the cerebral circulation. Catheter-based LAA occlusion (LAO) is a treatment option to prevent this. However, peri-device leak of the devices (PDL) may potentially leave the patient with a residual risk of thromboembolism from the LAA. Usually, the LAA orifice has an oval shape, which might cause an anatomical mismatch with the circular shape of the occluding devices, and the biomechanical interplay between device conformity and landing zone (LZ) morphology has been only sparsely described. Therefore, this study aims to investigate LAO device properties in shape fitting and their ability to ensure complete occlusion when employed in rigid LZ geometries.

MATERIAL AND METHODS

Different models representative of a wide range of LAA LZ sizes were developed and 3D printed based on three device sizes for both the Watchman FLX and Amplatzer Amulet. The LZ models represented a circular, slightly oval, and highly oval diameter, based on an eccentricity index of 0, 0.2 and 0.5. Once the devices were inserted into the LZ geometry, the degree of leakage was measured through back lighting followed by image analysis, providing a quantitative measure. The degree of symmetry of the expansion was qualitatively assessed. To estimate how fixated the devices were in the model, the peak stress was measured using a force meter during pull out of the devices.

RESULTS

The results of the image analysis showed a significant tendency of higher leak percentage in geometries with a high degree of ovality. When testing the device types (Watchman FLX vs Amplatzer Amulet) against each other, within ovality and size, the Watchman FLX had the highest leak and lowest peak stress, with significant p-values for the image analysis and stress measurements. Furthermore, the Watchman FLX displayed a more irregular expansion of its outline compared to the Amulet.

CONCLUSION

With the results of the Amplatzer Amulet having less PDL and higher peak stress than the Watchman FLX, the former might have greater adaptation abilities when implanted in a rigid prescribed structure.



O7

Perioperative Platelet Aggregation in Oesophageal Cancer Patients

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BACKGROUND

Thrombosis is the most common cause of death in cancer patients after the cancer itself. Cancer activates the coagulation, leading to an increased thromboembolic tendency. The risk of thrombosis is further exacerbated when patients undergo surgery.

MATERIALS AND METHODS

We are performing a trial examining the coagulation activity in oesophageal cancer patients before, during and after they undergo intended curative surgery. Here, we present interim data on the platelet aggregation of the 38 patients that had undergone surgery at the time of writing. Blood samples were taken just before surgery, when surgery ended, and on the first postoperative day. Platelet aggregation was analysed by impedance aggregometry using three agonists: ADP, ASPI, and TRAP. Results are reported as area under the curve (AUC).

RESULTS

Median AUC for ADP was 830 (interquartile range: 619-1064), 986 (795-1174) for ASPI and 1281 (985-1431) for TRAP in the preoperative sample, which are all within reference range. Median aggregation stayed within the reference ranges for all three agonists during surgery, though there was a statistically significant increase from the preoperative sample to the sample taken just after surgery for ADP ($p=0.001$) and TRAP ($p=0.002$). There was no significant difference between the preoperative sample and the day 1 postoperative sample.

CONCLUSION

Most patients have a normal platelet aggregation before surgery. During surgery, the aggregation increases and then returns to baseline within 24 hours.

PERSPECTIVES

A topic for future study, when the full cohort is included, will be to isolate those patients with an aggregation above reference range and examine whether they display an increased risk of thrombosis.



POSTER PRESENTATIONS

- P1 *Effects of oxygen therapy on pulmonary perfusion and ventilation in a porcine model of acute pulmonary embolism*
Mette Wørmer Poulsen et al.
- P2 *Early detection of chronic heart failure by visualizing the pH of the heart with MR-hyperpolarization*
Henrik Mulbjerg et al.
- P3 *A Novel Method for on-line Intraoperative Visualization of Blood vessels and Tissue Perfusion*
Frederik Thørholm Andersen et al.
- P4 *Current practices and long-term outcome of myocardial revascularization*
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- P5 *The effects of Bone Morphogenetic Protein 10 in pressure overload induced right ventricular failure - A preclinical study*
Caroline Damsgaard Jensen et al.



P1

Effects of oxygen therapy on pulmonary perfusion and ventilation in a porcine model of acute pulmonary embolism

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BACKGROUND

Every year 300.000 people die of acute pulmonary embolism (PE) in Europe alone. Oxygen is a key element of acute PE treatment, although knowledge about the exact mechanism is sparse, and the amount of oxygen given is not agreed upon. Dual Energy CT (DECT) is a useful tool for assessing lung perfusion and ventilation changes before and after acute PE. It offers absolute, quantitative values for perfusion while also providing images for the evaluation ventilation, and traditional CT pulmonary angiogram. The aim of this study is to evaluate pulmonary perfusion and ventilation changes at different fractions of inhaled O₂ (FiO₂) in acute PE by utilizing novel software for the DECT technology.

MATERIAL AND METHODS

Female pigs (n=10) underwent five DECT-scans at four different levels of FiO₂, with 15-minute intervals between scans, before and after acute pulmonary emboli (PE). Autologous PE were given one at a time until mean arterial pressure (MAP) was reduced by $\geq 50\%$, mean pulmonary arterial pressure (mPAP) was doubled, cardiac output was decreased by $\geq 20\%$, or if administration of vasopressors was needed. Images were then uploaded into two stand-alone, machine-learning based software for quantitative analyses of perfusion and ventilation. The results from these analyses were compared to invasive pulmonary and systemic pressures and blood gasses obtained at the same timepoints as the scans.

RESULTS

The study is a research year project running from September 1st, 2022 until august 31st, 2023. Imaging analysis has not been initiated, as the project is still in progress (January 2023). We plan to include 10 pigs during the fall 2022 and winter 2023 and preliminary results will be presented at the conference if available.

PERSPECTIVES

This study will explore the effects of oxygen on pulmonary perfusion and ventilation in acute pulmonary embolism, be it beneficial or harmful, and will help evaluate the clinical usefulness of DECT and machine-learning based software for automatic quantification of pulmonary perfusion.



P2

Early detection of chronic heart failure by visualizing the pH of the heart with MR-hyperpolarization

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BACKGROUND

Chronic heart failure is associated with significant diagnostic difficulties. The available diagnostic tools correlate poorly with clinical symptoms. It would benefit patients and clinicians alike to have a reliable assessment and quantification of disease. Such a tool is not readily available but hyperpolarized magnetic resonance imaging provides a potential solution. The technique has proven useful in several organ systems, and we seek to expand its use in a cardiovascular setting further.

METHODS

The study will be conducted in a porcine animal model of chronic heart failure. Fifteen pigs will be included. Over 16 weeks, the pigs will be scanned with conventional MRI and with hyperpolarisation at 4-week intervals. In this way structural, functional, and metabolic changes can be assessed in the myocardium. In addition, the intervention group will be randomised to receive pharmacological treatment to elucidate if the metabolic changes can be counteracted pharmacologically.

EXPECTED RESULTS

The study will show the potential of hyperpolarized magnetic resonance scans in relation to chronic heart failure in a porcine animal model. Preliminary results will be presented at the conference if available.

PERSPECTIVES

Hyperpolarized cardiac magnetic resonance imaging has previously been proven viable for heart failure detection and can detect the lurking disease before conventional diagnostic methods in a controlled preclinical setting. Significant advantages such as its non-radiating, non-toxic and minimally invasive nature make it an ideal candidate for incorporation in an actual clinical setting. Here, it could provide clinicians with otherwise unobtainable insights into disease mechanisms, which in turn would provide a basis for personalised management and treatment of heart failure.

ACKNOWLEDGEMENTS

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P3

A Novel Method for on-line Intraoperative Visualization of Blood vessels and Tissue Perfusion

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BACKGROUND

Blood vessel identification is an essential and challenging task during surgeries in order to avoid ischemia and/or excessive bleeding. Therefore, a technology which allows for visualization of vessels in the operative field is very much sought after. The start-up company Perfusion Tech (PT) has recently developed a novel technology based on indocyanine green (ICG) micro-dosing, PerfusionWorks (PW), which allows for continuous intraoperative assessments of tissue perfusion as well as artery, and vein visualization in real time. We hypothesize that the method can reliably provide blood vessel mapping and detect perfusion changes. Therefore, the aim of this study was to assess the validity of the method in an animal experimental feasibility setting.

MATERIAL AND METHODS

Eight healthy 60kg pigs were enrolled for the study. The course of a subcutaneous arterial branch and vein, located in the porcine groin, was denoted on epidermis under guidance of ultrasound, and the intra-luminal diameters were measured. This was followed and compared with PW transcutaneous blood vessel visualization of the same vessel courses and dimensions. A minimally invasive laparoscopic set-up was used to visualize the gastroepiploic artery inside its investing connective tissue using PW, and a subsequent laparotomy was performed to provide reference values based on ultrasound. The renal perfusion was quantified using PW and transit time flow measurements (TTFM) concomitantly under controlled flow adjustment using a vascular clamp. The jugular vein and common carotid artery were exposed which allowed for macroscopic comparisons when PW eventually was used to visualize the courses of the same vessels.

RESULTS

Results are pending.

PERSPECTIVES

Intraoperative visualization of vasculature and perfusion assessment, such as provided by PW, has the potential to abbreviate operation time and prevent bleeding-related complications by providing visual guidance during surgery. Furthermore, perioperative quality assessment forms the basis for rapid intraoperative diagnostics, followed by an immediate corrective intervention if needed. Consequently, PW has potential to reduce the economic burden and reduce the complication rate associated with surgery.



P4

Current practices and long-term outcome of myocardial revascularization

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BACKGROUND

Myocardial revascularization is recommended in patients suffering from coronary artery disease with moderate to severe symptoms persisting after adequate medical therapy, or for whom the outcome could be improved. Possible revascularization procedures include coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), and hybrid myocardial revascularization. CABG has been found to provide mid-term survival benefit and a lower risk of repeat revascularization compared to PCI in patients with complex coronary artery disease. Current knowledge regarding optimal treatment of less complex disease is limited. Evidence regarding the impact of varying degrees of guideline adherence on clinical outcome is scarce. We aim to investigate current myocardial revascularization practices and compare long-term outcome of different surgical revascularization strategies, PCI, and hybrid myocardial revascularization in patients with chronic coronary syndrome, treated in Denmark or Sweden between 2000 and 2020.

MATERIALS AND METHODS

In this Scandinavian, multicentre, observational cohort study, adult, elective patients who underwent either first-time isolated CABG, first-time isolated PCI, or hybrid myocardial revascularization between 2000 and 2020 in Denmark or Sweden will be identified by NCSF surgical intervention codes in the SWEDEHEART registry and the Western Denmark Heart Registry. Pre-, peri-, and postoperative variables will be obtained from the Swedish and Danish National Patient Registers according to ICD 10. The primary endpoint will be all-cause mortality.

RESULTS

So far, no results have been obtained. The current myocardial revascularization guidelines warrant a need of large studies examining the long-term clinical aspect of isolated surgical revascularization, PCI, or combined as hybrid myocardial revascularization.

CONCLUSION

No conclusions can be drawn, but long-term results from large registry-based studies are an important supplement to randomized controlled trials, since results from randomized controlled trials do not always mimic real life. An increased knowledge regarding the best choice of revascularization strategy is needed.



P5

The effects of Bone Morphogenetic Protein 10 in pressure overload induced right ventricular failure - A preclinical study

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BACKGROUND

Right ventricular (RV) failure is the predominant cause of death in patients with pulmonary arterial hypertension (PAH) and there is an unmet need for new treatment strategies to support the failing RV in these patients remains. Current treatment strategies only focus on dilating the pulmonary vessels even though RV function can further decline even after control of pulmonary pressure. We aim to investigate if administration of exogenous (Bone morphogenetic protein 10) BMP10 or palovarotene can prevent RV failure in an animal model of isolated RV failure.

MATERIALS AND METHODS

Rats (n=38) will undergo pulmonary trunk banding (PTB) and will be randomized into three groups one week after the procedure. Two groups will receive treatment for four weeks: one with BMP10 (n=12) and one with palovarotene (a drug increasing endogenous BMP10, n=12). The third group (n=14) without treatment will serve as a control group. Five weeks after PTB, RV function will be evaluated by echocardiography, magnetic resonance imaging and invasive pressure-volume measurements and compared between groups. Histological and molecular analyses will be performed on cardiac tissue samples and will also be compared between groups.

RESULTS

The study is ongoing and data collection is expected to be concluded in February 2023. Preliminary results will be presented at the 31st Annual Meeting in SSRCTS.

CONCLUSION

We aim to investigate whether administration of exogenous BMP10 or palovarotene, which increases endogenous production of BMP10, can attenuate the development of RV failure.

PERSPECTIVES

If administration of exogenous BMP10 or palovarotene can prevent RV failure in an animal model of isolated RV failure, BMP10 may be a potential new target for medical therapy of RV failure that can be tested in a clinical setting of patients with PH.

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