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ABSTRACTS

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President: Prof. Marc Claeys

Abstracts are identified as follows: Best Abstracts by (#), Best Posters by (Δ) and abstracts of papers short-listed for the Young Investigator Award by (*). All other accepted abstracts have been invited for poster display.

Abstracts are printed in alphabetical order of the first author's name within the following categories:

- Arrhythmias/Device
- Basic science
- Heart failure
- Imaging
- Invasive/Interventional cardiology
- Other

ARRHYTHMIAS/DEVICE

(Δ) First results from ETNA AF-Europe: initial experience with edoxaban in 1321 patients in Belgium

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Background: Oral anticoagulation using non-vitamin K antagonists (NOACs), such as edoxaban, offers an alternative to vitamin K antagonists for stroke prevention in patients with non-valvular atrial fibrillation (NVAF). Edoxaban approval for stroke prevention in non-valvular AF was based on the findings of ENGAGE AF-TIMI 48 trial, and was issued in Europe in 2015. The further assessment of the drug related risks and benefits in European patients with NVAF was implemented by the Edoxaban Treatment in Routine Clinical Practice for Patients With Non Valvular Atrial Fibrillation (ETNA-AF Europe), designed in close collaboration with the European Medicines Agency. Enrolment criteria were treatment with edoxaban for stroke prevention in atrial fibrillation and no simultaneous participation in an interventional study. The first baseline data of ETNA-AF EU for the Belgian subpopulation, compared to the rest of the European subgroups are reported here.
Methods results: Different medical disciplines (cardiologists, general practitioners, internists, and neurologists) enrolled a total of 1321 patients in Belgium between December 2016 and January 2018. 1302 (9.6% of the European study population) patients were included in the baseline analysis set. Patients in the Belgian subpopulation were on average of similar age compared to the rest of the European subpopulations (72.9y vs. 73.7y) and male gender amounted to 57.9% vs. 56.6%. The mean CHA_2DS_2VASc score trended to be lower (3.1 vs. 3.3); more patients with paroxysmal AF were included (63.8% vs. 52.4%), but less with permanent AF (9.0% vs. 20.7%) (Table 1). Comorbidities that occurred more frequent

in the Belgian subpopulation were smoking, gastrointestinal disease, dyslipidaemia, vascular disease, stroke and TIA. Conversely, chronic kidney disease and hypertension were less frequent (17.1% vs. 27.8% and 64.4% vs. 78.1%) (Table 1).

In the Belgian subpopulation, compared to the rest of the European subgroups, edoxaban 60 mg OD was prescribed in 1073 patients (82.4% vs. 76.1%), and edoxaban 30 mg OD in 229 patients (17.6% vs. 23.9%). 55 (24.1% vs. 25.5%) patients receiving edoxaban 30 mg OD were considered frail and 44 (4.1% vs. 6.3%) of those receiving edoxaban 60 mg OD. 120 (9.2% vs. 18.4%) patients were switched from a vitamin K antagonist and 80 (6.2% vs. 12.5%) switched from another NOAC. 291 (22.4% vs. 14.8%) patients were on concomitant antiplatelet therapy (Table 1).

The relative amount of patients with a history of major- and clinical non-major bleeding events were higher compared to the rest of the European subpopulations in both dose regimen (2.2% vs. 1.7% for 30 mg and 0.8% vs. 0.4% for 60 mg). However patients with a history of intracranial haemorrhage were less for the 30 mg arm (0% vs. 0.7%) and same (0.4%) for the 60 mg arm (Table 2).

Conclusions: The Belgian ETNA-AF subpopulation, compared to those enrolled in the rest of the European, countries, present noteworthy differences regarding the baseline characteristics, comorbidities, history of bleeding and dosing regimen.

Table 1. Overview of the baseline characteristic of patients included in the ETNA-AF trial.

Characteristic	BE	EU w/o BEL
Patients (N)	**1302**	**12172**
HT (%)	64.4	78.1
Current smoking (%)	7.6	6.2
No alcoholic (%)	24.8	46.7
Patients ≥ 75y (%)	45.8	51.4
GI disease (%)	11.7	7.8
Dys-/hyperlipidemia (%)	55.4	41.1
Vascular disease (%)	20.0	17.5
Congestive heart failure (%)	6.5	5.7
Diabetes mellitus (%)	19.0	22.1
Ischemic stroke (%)	6.8	5.7
TIA (%)	5.7	3.1
Renal disease (%)	17.1	27.8
CHADS score (mean) (%)	1.6	1.7
Paroxysmal AF (%)	63.8	52.4
Permanent AF (%)	9.0	20.7
Previous treatment (stopped ≤ date of BL)		
VKA (%)	9.2	18.4
NOACs (other) (%)	6.2	12.5
Heparine/fondaparinux (%)	15.2	10.3
Antiarrythmic/rate control drugs (%)	12.1	4.4
antiplatelet (%)	22.4	14.8
Population at randomisation :		
30mg (%)	17.6	23.9
60mg (%)	82.4	76.1

	same
	less
	higher

Table 2. History of bleeding in patients included in the ETNA-AF trial.

Characteristics	BE		EU w/o BEL	
	30 mg*	60mg**	30mg	60mg
Patients (N)	229	1073	2912	9260
Bleeding history				
ICH (%)	0.0	0.4	0.7	0.4
Major & CRNM bleeding (%)	2.2	0.8	1.7	0.4
Major bleeding (%)	1.7	1.0	1.6	0.7
CRNM bleeding (%)	2.6	1.0	1.8	0.8
Minor bleeding (%)	2.2	0.9	1.8	0.9

Unifocal right-sided ablation for neurally mediated syncope and functional sinus node dysfunction

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Imelda Ziekenhuis

Background: Bi-atrial, extensive and complex ablation strategies have been published for the treatment of neurally mediated syncope, sinus node dysfunction. We have developed a less extensive and more specific approach, compared to previously published cardio-neuroablation strategies, called cardio-neuromodulation (CardNM). It is based on tailored vagolysis of the sinoatrial node through partial ablation of the anterior right ganglionated plexus.

Methods: We report on 22 consecutive patients enrolled between December 2016 and January 2018. They were assigned to group A if they had a positive head-up tilt test, and to group B if they presented with a pause $^{3}3$ s. The area to target during CardNM was designed offline on a computed tomograpy scan. Slow heart rates and pauses were compared during 24-h rhythm registration at baseline and 6-month follow-up. Syncope burden was assessed before the procedure and at 6-month follow-up.

Results: Twenty two patients underwent CardNM through a right-sided approach (12 in group A, 10 in group B). After a mean ± SD ablation time of 7 ± 4 min and mean ablated surface area of 11 ± 6 mm2, the P-P interval shortened by 209 ± 156 ms ($p < .001$). The number of beats <50/min during 24-h rhythm registration was reduced by a median of 100% at 6-month follow-up ($p < .001$). Syncope burden was reduced by 94% at 6-month follow-up ($p < .001$).

Conclusions: These data indicate that CardNM, through a right-sided procedure, is safe, fast, and highly reproducible in preventing inappropriate functional sinus bradycardia and syncope recurrence.

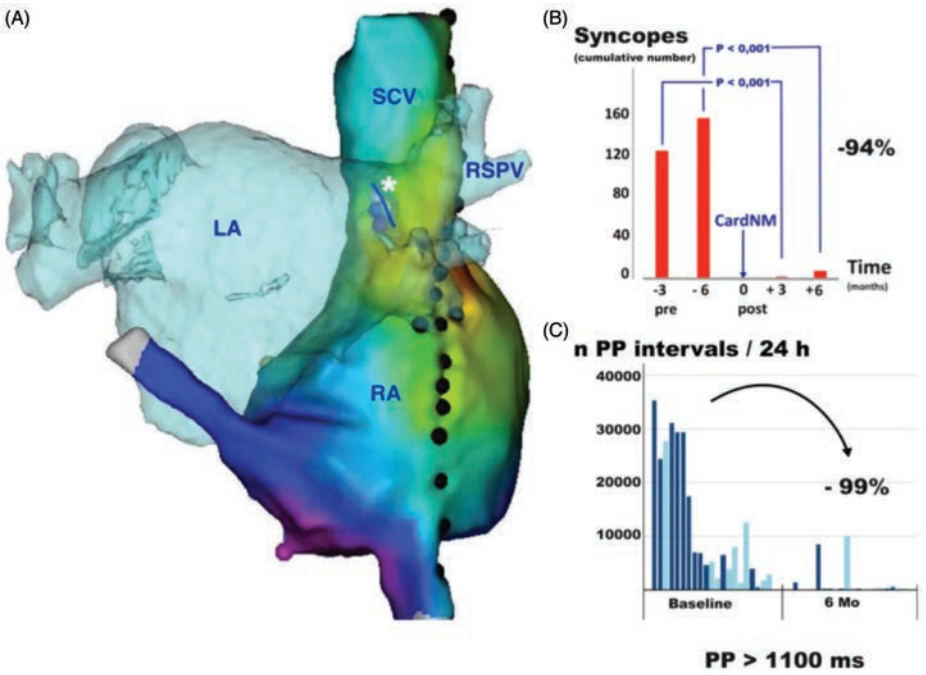
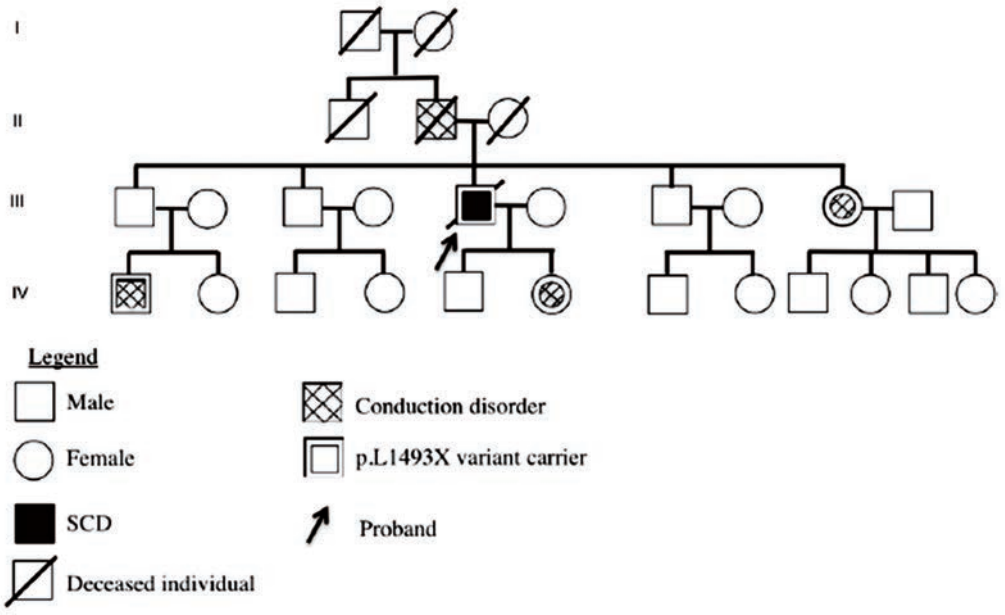


Figure 1. (A) Computed tomography scan of the left atrium and activation map of the right atrium in a posteroanterior projection. The region of the anterior right ganglionated ablated is indicated by a blue line (asterisk). Each individual ablation is indicated using a colored tag and the phrenic nerve is tagged with black dots. (B) Cumulative number of syncope episodes before and after cardio-neuromodulation at 3- and 6-month follow-up. (C) Twenty-four-hour rhythm registration data. The histograms show the number of P-P intervals >1100 ms for each patient at baseline and at 6-month follow-up.

Phenotypic variance of a SCN5A nonsense mutation in a familial transmission

Inès Dufour
Clinique Saint-Pierre

Background: Sodium voltage-gated channel alpha subunit 5 (*SCN5A)* gene is the most frequent site for mutations responsible for Brugada syndrome, an inherited cardiac disorder transmitted with an autosomal dominant pattern. Brugada syndrome can cause malignant ventricular arrhythmia and is responsible for up to 4% of sudden cardiac deaths (SCD).
Methods: Case series.
Results: We report the case of a 67-years-old male presenting with SCD associated with a nonsense mutation (p.L1493X) in the *SCN5A* gene. The familial genetic testing further identified three direct relatives with the mutation. The daughter of the patient presents an Ajmalin-induced Brugada syndrome type I pattern and an atrioventricular conduction disturbance (HV interval >70 ms). A brother and a sister have both been implanted with a permanent pacemaker for sinus node disease several years ago and are carrying the same mutation. This is the first report of a familial transmission of the p.L1493X mutation (see Figure below).
Conclusions: This case series highlights in a family the various phenotypes of a same nonsense mutation in the *SCN5A* gene, ranging from SCD to cardiac conduction disorder. It underlines the importance of genetical, pharmacological and electrophysiological investigations to confirm the diagnosis and stratify the risk for each patient.



Highly accurate detection of Dobutamine-induced hemodynamic changes by means of Kino-cardiography: a double-blind randomized cross-over placebo-controlled study

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Background: Kino-cardiography (KCG) is a non-invasive and non-intrusive technique based on body vibrations measurements produced by myocardial contraction and blood movements through the aorta. Using accelerometers and gyroscopes placed on the thorax (Seismocardiography) and in the lumbar region (Ballistocardiography), we tested the hypothesis that KCG assesses reliably Dobutamine-induced hemodynamic changes.

Methods: The ß-adrenergic agonist Dobutamine and placebo were perfused in 34 healthy volunteers (25 +/−2 years, body mass index 22+/−2 kg/m^2, 18 females). A baseline recording was followed by increasing doses of Dobutamine versus saline solutions (5, 10, 20 μg/kg.min). Stroke volume (SV) and cardiac output (CO) were determined by echocardiography at each level and followed by a 90 s KCG recording. For each subject, the total kinetic energy (KE) was sorted in ascending order. To determine KCG detection accuracy of inotropic effects of Dobutamine versus placebo, the 3 highest KE were attributed to the Dobutamine sessions by blinded investigators.

Results: Baseline CO of 4.07+/−0.8 l/min increased to 4.66+/−0.8, 6.40+/−1 and 8.77+/−1.9 l/min at 5, 10, 20 μg/kg.min of Dobutamine, respectively ($p < 0.0001$ vs. placebo). KCG detected the inotropic effects of Dobutamine with an accuracy of 96.09%, a sensitivity of 94.95% and a specificity of 96.82%. The detection of each individual level of Dobutamine was done with an accuracy of 71.92%, a sensitivity of 59.80% and a specificity of 78.42%. Records performed at 10 and 20 μg/kg.min of Dobutamine were not well differentiated. Between these two levels of Dobutamine a stagnation of SV measured by echocardiography was also observed (Figure 1). Increases in CO measured by echocardiography and KCG changes were strongly correlated ($r = +0.8$; $p < 0.0001$).

Conclusions: KCG detects hemodynamic changes induced by Dobutamine with great accuracy. Further studies will determine if this technique can monitor cardiac function changes in heart disease patients. Additional clinical validations are also planned with patients suffering from hypertension or heart failure.

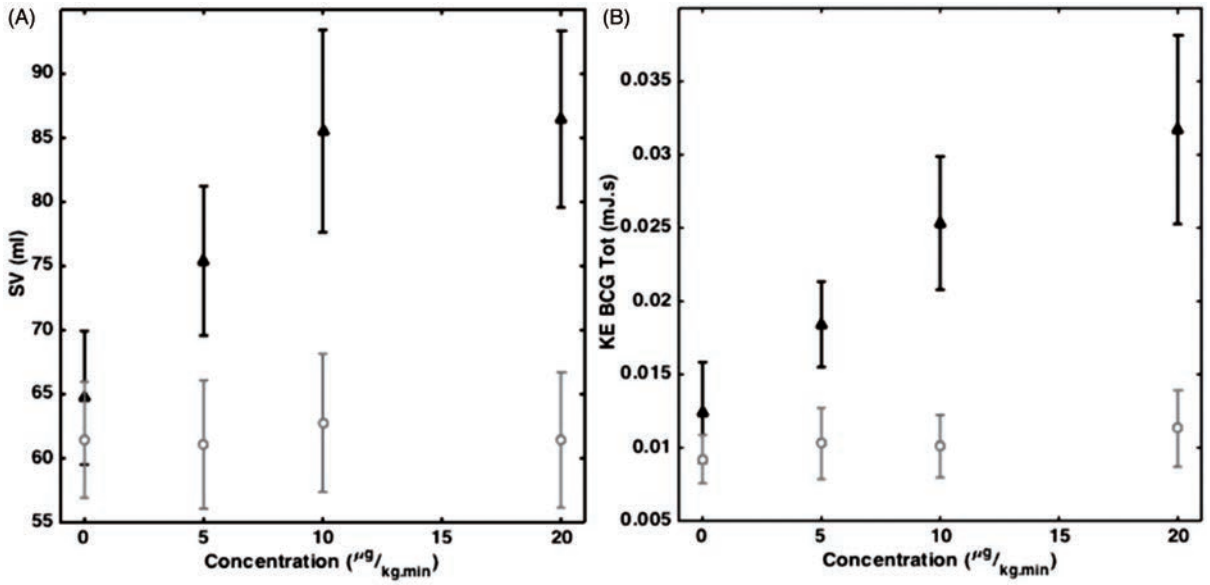

Figure 1. (A) SV and (B) KE_{Tot}^{BCG} (Mean ±95% CI) with increasing doses of dobutamine and placebo (▲ Dobutamine; ○ Placebo).

Differential presentation of AV nodal reentrant tachycardia in Athletes and Non-Athletes

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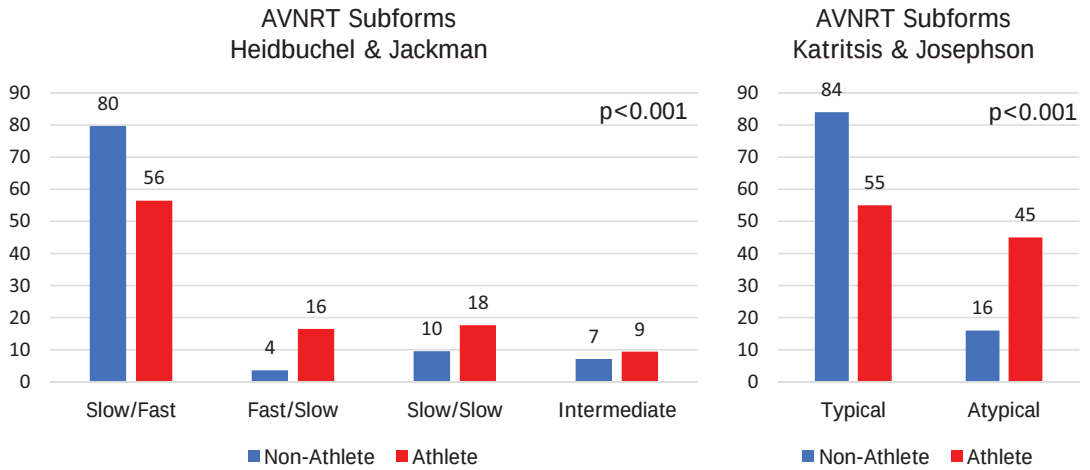
Background: Prolonged participation in exercise results in structural and electrical cardiac remodeling. The development of an athlete's heart is recognized as a risk factor for atrial arrhythmias. This study evaluates the impact of athlete heart remodeling on the presentation of AV nodal reentrant tachycardia (AVNRT).

Methods: A retrospective analysis of an ablation database selecting all patients with an electrophysiologically confirmed diagnosis of AVNRT. Athletes (defined as individuals participating in moderate to intensive sports for ≥3 hours per week and having done so for ≥5 years) were compared to healthy non-athletes. AVNRT subforms were classified according to two Methods: the ones described by Katritsis & Josephson in 2013 and by Heidbuchel & Jackman in 2014.

Results: A total of 504 AVNRT patients were fully characterized, 85 (17%) of whom were athletes. Athletes presented significantly more frequently with atypical forms of AVNRT (44–45% versus 16–20%, $p < .001$, independent of the classification method used). There was no difference in procedural success among the two groups, but the procedures in athletes were more complex, as reflected by an almost twofold increase in the use of a long sheath to reach the slow pathway ablation area.

Conclusions: Athletes present more frequently with atypical subforms of AVNRT. This is possibly related to cardiac remodelling with dilatation of the cardiac cavities leading to changed conduction properties in the septal area. Despite this difference in presentation, ablation outcome is equally effective and safe in athletes as in non-athletes.



(Δ) PACE study: pacemakers, atrial sensing changes during effort – a study on the behaviour of cardiac stimulators during standard stress tests

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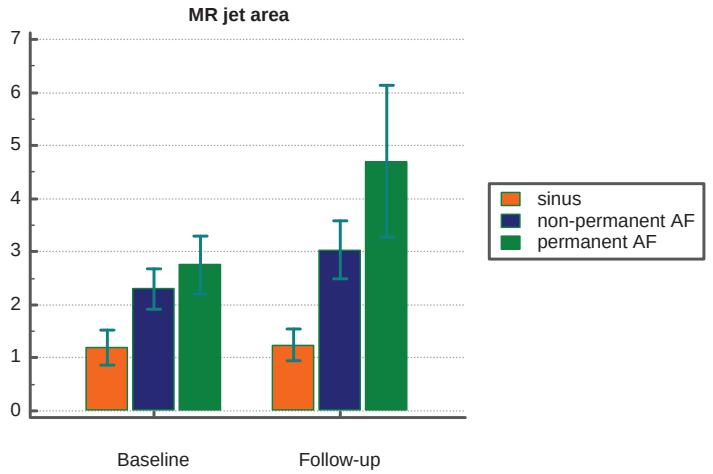
Background: Throughout the past decades, cardiac stimulators have benefited from tremendous technical improvement, peculiarly synchronous stimulation modes and bipolar leads. However, some patients relate inappropriate cardiac stimulation felt at a surprisingly low rate during effort. This leads us to suspect during these activities, atrial sensing alterations while devices are controlled as functional at rest.
Purpose: We aim to objectify a variability of atrial sensing during effort. We also attempted to screen any other potential phenomena which might account for these complaints.
Methods: In an observational monocentric prospective study, we recruited from March 2017 to May 2018 40 ambulatory patients aged between 18 and 71. All of them performed a standard stress test on a bicycle together with a control of their pacemaker. We excluded among others, defibrillators (ICDs) and resynchronisation devices (CRTs).
Results: Atrial sensing changed in 38 patients (95%). It fell by at least 10% in 30 subjects (75%), by more than 33% in 19 cases (47.5%) and by more than 50% in 9 of them (22.5%). This fall becomes greater with the age of the patients, the maximal stress load and the age of the devices (stimulators and leads alike). Most subjects (57.5%) also reached a maximal heart rate superior to the programmed upper rate. In addition, we observed what we described as unexpected events. The majority of these were normal sinus activities interpreted as premature or arrythmias (11 patients, 27.5%). Less frequent (4 patients, 10%), were ventricular activities mentioned as premature while preceded by an atrial complex and of unchanged morphology on the standard 12-lead electrocardiogram.
Conclusions: Atrial sensing tends to decrease during effort in devices which are controlled functional at rest. Most patients also reach a heart frequency superior to the programmed upper rate. Stress tests may help adjust targets in terms of atrial sensing and upper rate programming. Similar works with ICDs and CRTs may avoid potential inappropriate therapies for the former group and optimize the biventricular therapy for the latter. Further studies on the working routines and algorithms of cardiac stimulators may also explain some unexpected pacemaker behaviours.

Long term effect of permanent/non-permanent atrial fibrillation on evolution of mitral/tricuspid valve regurgitation

Lobke Pype, Laura Embrechts, Barbara Cornez, Carl Van Paesschen, Hielko Miljoen, Andrea Sarkozy, Johan Saenen, Paul Van Herck, Hein Heidbuchel and Marc Claeys
UZA

Background: While severe mitral/tricuspid regurgitation (MR/TR) is a well established risk factor for atrial fibrillation (AF), it is unknown whether atrial fibrillation induces mitral/tricuspid valve regurgitation (MR/TR). The present study aims to identify long term effects of permanent/non permanent AF on atrial remodelling and progression of MR/TR.
Methods: The severity of MR/TR was assessed at baseline and after a period of 65 ± 10 months in 37 patients with permanent AF, in 80 patients with non-permanent AF (of which 43 were treated with ablation) and in 53 control patients with persistent sinus rhythm. Cardiac dimensions and the severity of MR/TR, expressed by the jet area, were analysed off-line by one expert blinded to the clinical data. Severe MR/TR was defined as jet area >10 cm2. Consecutive AF patients were selected retrospectively from the outpatient cardiology clinic database ($n = 959$ pts) and the control group were at random selected from the medical check-up database. The exclusion criteria were: left ventricular ejection fraction <40%, LV end diastolic diameter >60 mm, significant structural or functional valve disease, follow-up period <4 years, age <45y.
Results: At baseline, AF patients had larger MR jet area than control patients (see Figure). At follow up, progression of MR, expressed as delta MR jet area, was $0.05 \pm 1.3\,cm^2$ in the control group, $0.73 \pm 2.1 cm^2$ in the non-permanent AF group and $1.95 \pm 3.6\,cm^2$ in the permanent AF group ($p = .001$). Severe MR at follow up was observed in 0%, 2.5%, 8% respectively. There was a significant positive correlation between progression of MR and increase of left atrium volume index ($r = 0.31$, $p < .001$). After adjusting for cardiac risk factors, baseline atrial dimensions and baseline MR severity, longstanding AF remained independently associated with progression of MR. Although anti-arrhythmic therapy with ablation was associated with less increase of left atrial volume as compared to non-ablated patients (delta LA vol index: -5 ± 29 ml vs $+12 \pm 28$ ml, $p = .01$), the MR evolution was comparable (delta MR jet area: 0.85 ± 2.05 vs 0.61 ± 2.12, $p = .6$). Similar findings were found for the effect of AF on TR progression.
Conclusions: The presence of longstanding AF is associated with a significant progression of MR/TR mainly due to atrial remodeling. Our data showed a beneficial effect of sustained rhythm control, either medically or by ablation, on MR/TR progression.



Early discharge possible for majority of vernakalant-treated patients from the emergency room after successful cardioversion of acute atrial fibrillation

Hugues Verloove and Hans Vandekerckhove
Algemeen Ziekenhuis Sint-Lucas

Background: Conversion of atrial fibrillation (AF) to sinus rhythm improves AF symptoms, cardiac function and output, and exercise capacity. Conversion is achievable via electrical or pharmacological methods. Vernakalant is a novel intravenously administered anti-arrhythmic drug reimbursed in Belgium for rapid AF to sinus rhythm conversion in the emergency room (ER) since June 2015. Upon the Institut national d'assurance maladie-invalidité (INAMI)/Rijksinstituut voor ziekte- en invaliditeitsverzekering (RIZIV)'s request, real-life information on Belgium-based patients with acute AF treated with vernakalant in the ER to avoid electric cardioversion and hospitalisation was collected in a survey, to support the drug's definitive reimbursement.
Methods: This post-marketing, multicentre survey was designed as an Excel questionnaire to collect information on vernakalant use to treat acute AF in the ER in Belgium. Between 25 May and 20 June 2018, the survey was completed by one investigator (with the potential help of a nurse) at each centre to collect the following information: (1) the number of patients treated with the drug for acute AF between 1 January 2017 and 15 April 2018; (2) the number of acute AF patients who avoided hospitalisation post-vernakalant in the ER; and (3) the number of acute AF patients who avoided electric cardioversion post-vernakalant in the ER.
Results: A total of 97 patients were treated with vernakalant for acute AF in the ER between 1 January 2017 and 15 April 2018 across 6 participating centres. The need for electric cardioversion and hospitalisation post-vernakalant treatment was avoided in 81.4% of all treated patients. Data per centre are shown in Table 1.
Hospitalisation post-vernakalant treatment did not appear to be centre-dependent as shown in Table 1, and the need for hospitalisation and electric cardioversion tended to be linked in all centres.
Conclusions: ER-based vernakalant treatment substantially reduced electric cardioversion and hospitalisation rates in acute AF patients in all evaluated centres in Belgium, supporting INAMI/RIZIV's decision of definitive reimbursement of the drug made on 7 August 2018.

Table 1. Multicentre survey results on patients treated with vernakalant in the ER for an episode of acute AF between 1 January 2017 and 15 April 2018 in Belgium.

Participating centres	1	2	3	4	5	6	All
Number of patients treated in ER	11	3	10	11	28	34	97
Number (%) no electric cardioversion post-treatment	9 (81.8)	3 (100)	10 (100)	7 (63.6)	19 (67.9)	31 (91.2)	79 (81.4)
Number (%) not hospitalised post-treatment	9 (81.8)	3 (100)	10 (100)	8 (72.7)	22 (78.6)	27 (79.4)	79 (81.4)

Increasing incidence of cardiac device related endocarditis over the past ten years: a single center analysis

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Background: Cardiac device related infective endocarditis (CDIE) is an increasing problem in the current cardiology practice, related to high mortality and morbidity. Recent trends have shown an increase in cardiac device placement, which remains a risk factor for developing CDIE. We performed a retrospective analysis of all patients admitted to our hospital. The aim of our study was to identify a possible correlation between the amount of device placements and the incidence of CDIE.

Methods: All patients, aged 18 years or above, diagnosed and treated for IE in our hospital in the 11 years between January 1st 2007 and December 31st 2017 were retrospectively identified. The amount of cardiac device placements was meticulously kept up to date by the administrative department. Due to the retrospective nature of our study no approval of the local ethics committee was required.

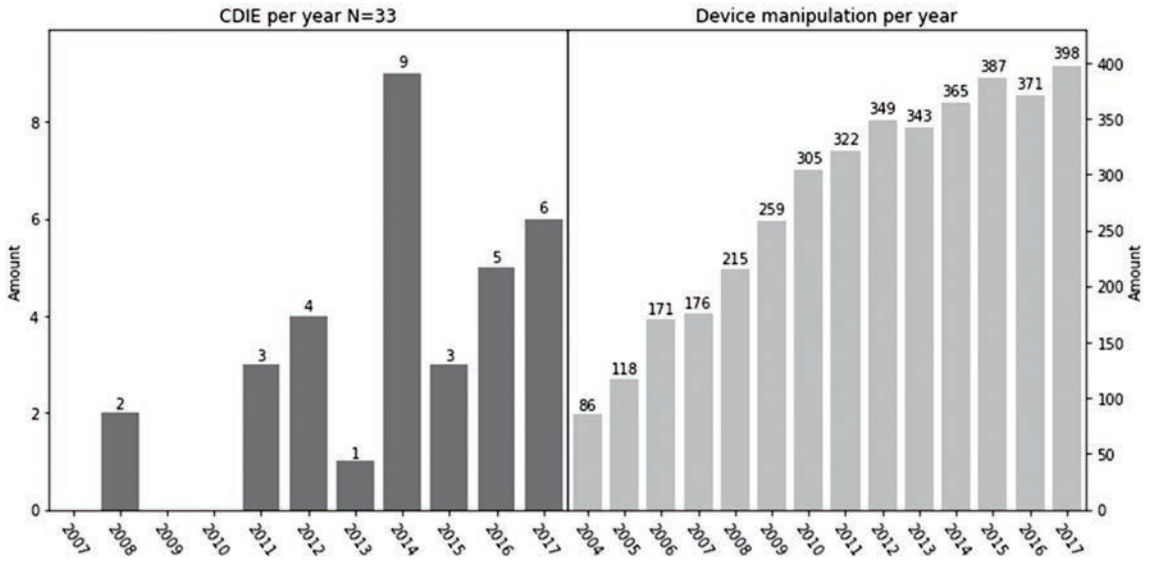
Results: A total of 33 patients with proven CDIE were identified There were no CDIE documented in 2007 2009 and 2010. 2008 showed 2 CDIE (16.7%) whereas the last 4 years of the study showed a mean incidence of 5.75 IE per year. Our population was predominantly male (84.8%) and nearly a third of the population died during hospital stay. The mean age of the population was 73.9 years old. Three quarters of the population underwent surgery and 24 patients out of these underwent device removal, the remaining 2 patients underwent valve replacement or catheter removal.

Half of the patients had early-onset or procedure-related IE (<12 months post procedure). The remaining cases were defined as late onset IE. Overall, 80% of CDIE developed within 3 years after the procedure.

The most prevalent causative organisms in our CDIE population were Staphylococci (68%) followed by Streptococci (20%). Eight out of 33 cases appeared to be culture negative (24.2%).

We sought to correlate these findings to the amount of cardiac device procedures (de novo implantations and replacements) as of 2004 (to compensate for the possible 3-year delay). The number of CD procedures increased by nearly 400% over the course of these 14 years.

Conclusions: The incidence of CDIE has increased in our population over the past 11 years. This increase runs parallel with the expansion of the number of devices implanted. About half of CDIE occur within 1 year of the procedure defined as early onset CDIE, but the presence of a cardiac device remains a risk factor for IE even thereafter. Causative organisms in our study for CDIE specifically appear to coincide with the results from other studies done in more general populations, with Staphylococci remaining the most prevalent organisms. As patients with cardiac devices implanted appear to be at increased risk for IE, one might add these to the group of patients requiring IE-prophylaxis, especially because of the high mortality rate of IE, which appears to be even higher for CDIE.



BASIC SCIENCE

Potential involvement of the IL-33/ST2 axis in the pathogenesis of Tatosubo Syndrome

Ahmad Awada and Philippe Unger
CHU Saint-Pierre Brussels

Much progress has been made to decipher the pathophysiological mechanisms underlying Takotsubo syndrome (TTS), but the exact trigger of the disease still remains to be determined. Phenotype, endomyocardial biopsy finding, and inflammatory pattern of TTS patients are similar to what is observed in inflammatory disease such as Lupus or Sjögren's Syndrome. The hypothesis of alarmin involvement such as IL-33 has never been assessed.
In this study, we aim to study the potential involvement of the IL-33/ST2 axis in TTS.
Methods: Serum levels of IL-33 and sST2 were determined by ELISA in 16 patients with TTS, 24 consecutive patients with non-TTS acute coronary syndrome (STEMI and NSTEMI) and in 15 age- and sex-matched control patients.
Results: Serum levels of sST2 were significantly higher in TTS patients as compared to controls [mean 52690 pg/ml (SEM 8716) versus 27278 (2258) pg/ml, respectively] ($p = .04$) and as compared to non-TTS acute coronary syndrome [20139 (1995) pg/ml] ($p = .0002$)]. Serum levels of IL-33 were significantly higher in TTS patients as compared to controls [38,36 pg/ml (14,52) versus 0 pg/ml, respectively] ($p = .0024$)] but, unexpectedly, lower than non-TTS ACS patients [mean 134,9 pg/ml (34,67)] ($p = .0152$). Left ventricular function was similar in TTS and ACS patients (40 and 43%, respectively, $p =$ NS). There was no correlation between sST2 and NT-proBNP levels, neither between IL-33 and Troponin T levels. Following a ROC analysis, a level of sST2 superior to 38289 pg/ml predicted the diagnosis of TTS with a sensitivity and a specificity of 93% and 56%, respectively (CI 75.7;99.1).
Conclusions: sST2 and IL-33 are both upregulated in Takotsubo Syndrome. As compared to ACS, TTS is characterized by higher sST2 and lower IL-33. sST2 might be useful to allow the diagnosis of TTS. Further studies need to be done to characterize the exact implication of IL-33/ST2 axis in the pathogenesis of Takotsubo Syndrome and to validate sST2 to diagnose TTS.

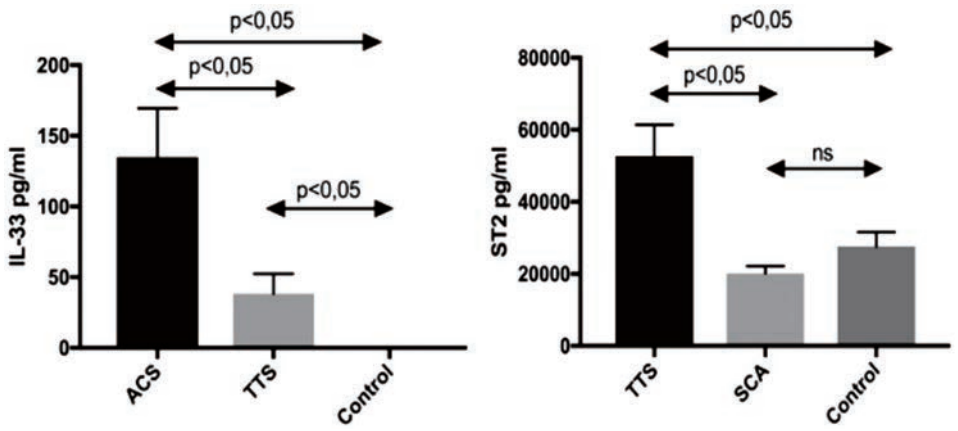


Figure 1. On the left: comparison of serum levels of IL-33 in TTS, non-TTS ACS and controls. On the right: comparison of serum levels of sST2 in TTS, non-TTS ACS and controls.

Effects of air-related environmental stressors on Takotsubo cardiomyopathy

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[a]CHU St.-Pierre Brussels; [b]ULB; [c]Brussels Institute for Management of the Environment; [d]AZ VUB

Background: Air temperature and pollution are the main environmental factors influencing cardiovascular mortality and risk of myocardial infarction. Takotsubo cardiomyopathy (TCM) is a transient and reversible myocardial dysfunction whose cause and pathogenesis remain incompletely understood, but which, unlike acute coronary syndrome, does not involve obstructive coronary atherosclerosis or plaque rupture. The potential role of the environment on the risk to develop TCM remains poorly defined.
Methods: We aimed to study the effects of air temperature, particulate matter (PM) and gaseous pollutants (NO_2 and ozone) on hospitalization rate for TCM.
All hospitalizations in Belgian Hospitals for TCM (ICD 9:429.83) from 2009 to 2014 were recorded. National air pollution parameters were extracted from the Belgian Environment Agency database. A time-stratified and temperature-matched (except for air temperature effect) case-crossover analysis of the risk of TCM was performed. The main analysis focused on 0-day lag time (lag 0) between exposure and TCM; a lag structure analysis up to lag 4 was also performed.
Results: 1840 patients were included in the study (88% women). More TCM occurred during the warm compared to the cold period (Figure 1; chi^2 p value $<.05$). At lag 0, each decrease of 1 °C in ambient air temperature increased the odds ratio (OR) of TCM of 1.020 (IC $_{95\%}$: 1.003–1.035). This effect was more pronounced during the cold period and at lag 4 (RR 1.060; IC $_{95\%}$: 1.031–1.091). Conversely, during the warm period and between lag 1 and 4, an increase of 1 °C in ambient air temperature increased the RR of TCM (OR 1.053 at lag 3; IC $_{95\%}$: 1.021–1.086). No significant association was found between TCM and PM10, PM2.5, NO_2 at any lag. During the warm period, each increase in 10 μg/m^3 in ozone from lag 1 to 3 increased the risk of TCM (OR 1.089 at lag 3, IC $_{95\%}$: 1.017−1.168).
Conclusions: Air temperature strongly influences the onset of TCM. Both cold spells and heat waves seem to be associated with the development of TCM. Ozone exposure also increases the risk of TCM during the warm period, whereas particulate and NO2 pollution do not seem to play a significant role. These patterns seem to differ from those previously reported with STEMI.

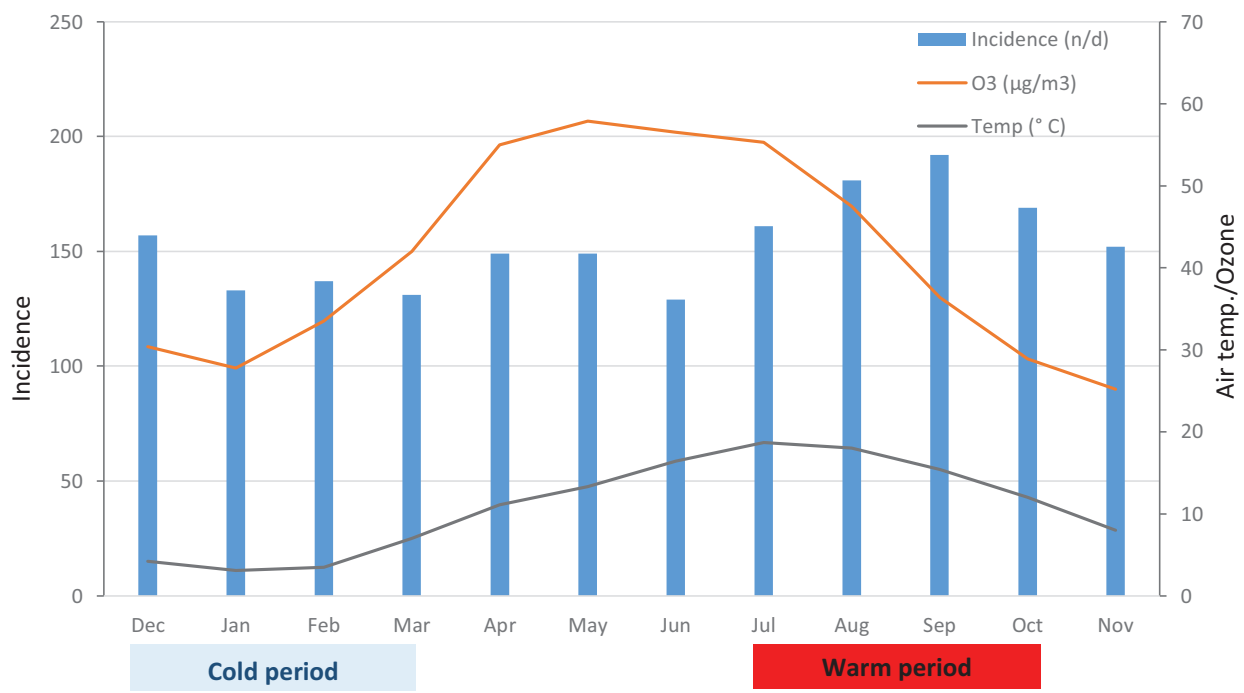

Figure 1. Monthly variation of air pollutants and TCM in Belgium.

Contribution of sodium myo-inositol transporter 1 (SMIT1) and myo-inositol transport in the regulation of cardiac fibrosis and the physiopathology of heart failure: MIHEART research project

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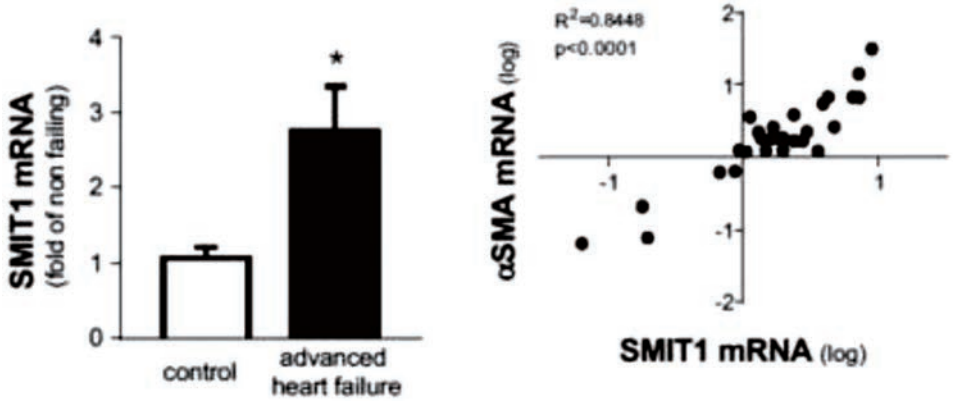
[a]UCL; [b]Cliniques Universitaires Saint Luc; [c]Université de Montréal

Background: *Myo*-inositol is a precursor of plasma membrane phospholipids and of key signaling elements. Our group demonstrated that SMIT1 is highly expressed in both rodent and human hearts. The absence of SMIT1 does not change heart function and structure under baseline condition. However, the role of SMIT1 or *myo*-inositol transport in diseased heart remains unexplored. Our current hypothesis is that *myo*-inositol transport and SMIT1 control cardiac fibrosis and therefore may contribute to the physiopathology of heart failure.

Methods: Myocardial biopsies from 23 patients at end stage heart failure were obtained during Left Ventricle Assist Device (LVAD) implantation. Control biopsies corresponded to 11 patients with mitral regurgitation or stenosis without evidence of LV remodeling and were taken during valvular surgery. Mice model of heart failure were generated by a permanent ligation of left anterior descending artery (LAD). Cardiac fibroblasts properties were studied using human cardiac fibroblasts in culture and murine cardiac fibroblasts isolated form SMIT1 wild type and knock-out mice. *Myo*-inositol transport was measured using radioactive *myo*-[2-3H]-inositol.

Results: Compared to control hearts, human failing hearts exhibited higher SMIT1 expression (see Figure below). Increase in SMIT1 was more pronounced in ischemic versus non-ischemic cardiomyopathy. Interestingly, SMIT1 expression correlated with pro-fibroblastic markers in biopsies (αSmooth Muscle Actin and Collagen Ia), suggesting that SMIT1 was tightly associated with fibrosis (see Figure below). In mice model of myocardial infraction, SMIT1 expression was 2.5-fold higher in the scar compared to remote myocardium. As in human heart, SMIT1 expression correlated with profibroblastic markers. *In vitro* study revealed that both human and murine isolated cardiac fibroblasts express SMIT1. *Myo*-inositol transport into cardiac fibroblasts depended entirely on SMIT1. Indeed, deletion of SMIT1 infibroblasts abolished *myo*-inositol transport. More importantly, we observed that changes in extracellular *myo*-inositol or SMIT1 deletion affected cardiac fibroblasts function. Increased extracellular *myo*-inositol concentration promoted human fibroblasts *myo*-differentiation, migration and proliferation whereas the absence of SMIT1 delayed murine fibroblasts proliferation.

Conclusions: SMIT1 expression is increase in ischemic failing heart, reflecting increased cardiac fibrosis. SMIT1 controls myo-inositol uptake in cardiac fibroblasts, influencing their properties. Therapeutic interventions targeting *myo*-inositol transport and SMIT1 could limit myocardial fibrosis and adverse remodelling.



Diabetic cardiomyopathy, the role of protein acetylation in early stage development

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UCL

Background: The increase prevalence of obesity in our society have been associate with a rise of associate diseases such as diabetes. The heart of diabetic patients is characterised by the loss of its metabolic flexibility via the instalment of an insulin resistance leading to the development of cardiomyopathy. Recently, our laboratory has demonstrated that leucine, an early marker of diabetes, induce a disruption of GLUT4 translocation in response to insulin, a characteristic trait of heart metabolic inflexibility. This disruption is cause by a global rise in protein acetylation due to an accumulation of acetyl-CoA downstream leucine catabolism. Beside leucine, fatty acids (FAs), also known to be elevated in diabetes, induces a similar accumulation of acetyl-CoA. The aim of my work is to study if FAs also disrupt GLUT4 translocation in response to insulin via a rise of protein acetylation in cardiomyocytes.
Methods: Isolated adult rat cardiomyocytes are treated with oleate or palmitate to evaluate their effect on glucose uptake, insulin signalling, protein acetylation and GLUT4 translocation. Involvement of protein acetylation is tested by using inhibitors of lysine acetyl-transferases (KATs).
Results: Our results show that in isolated cardiomyocytes, 20 hours of incubation with oleate and palmitate (100 and 300 μM) promote protein acetylation and inhibition of the insulin-stimulated glucose uptake. Oleate and palmitate effect can be prevented by KATs inhibitor treatment. Similarly to leucine and ketone bodies, FAs prevent GLUT4 translocation in adult cardiomyocytes.
Conclusions: Our results highly suggest that early increase of circulating FAs in prediabetic patients could lead to the instalment of cardiac insulin resistance via a rise in protein acetylation, the first step leading to diabetic cardiomyopathy.

Moderate intense exercise as a new therapeutic strategy to tackle congestion in heart failure

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Background: Congestion is an important factor contributing to worsening renal function in patients with heart failure and the cardiorenal syndrome. As a result of limited knowledge regarding the impact of congestion on organ function, the management is challenging and specific treatment options are warranted. In this respect, exercise training could be a promising non-pharmacological therapeutic strategy in congestion-related diseases. In this study, the effects of moderate intense exercise on heart and kidney function and morphology were studied in a IVCc rat model of abdominal venous congestion.
Methods: Eight male Sprague-Dawley sedentary IVCc rats (IVCc-SED) rats were compared to eight IVCc rats subjected to moderate intense exercise (IVCc-MOD). Abdominal venous congestion was induced by a permanent surgical constriction (20 Gauge) of the thoracic IVC (IVCc). Moderate intense exercise was defined as treadmill running (11 m/min, 15° inclination, 60 min/day, 5 days/week).
Results: After twelve weeks of exercise training, abdominal venous pressure was significantly lower in the IVCc-MOD group versus IVCc-SED ($p < .05$). Plasma triglycerides, epididymal fat and perirenal fat pad were significantly lower in the IVCc-MOD group versus IVCc-sed ($p < .01$), for a comparable body weight. Cardiac echocardiographic and hemodynamic parameters were not affected, except for a significantly increased left ventricular end systolic diameter ($p < .05$). Plasma cystatin C levels were significantly reduced and plasma creatinine levels were significantly increased in IVCc-MOD rats versus IVCc-SED ($p < .01$), for a comparable creatinine clearance. Indices of heart and kidney histology and morphology did not differ between groups.
Conclusions: The implementation of moderate intense exercise in a rat model of isolated abdominal venous congestion reduces abdominal venous pressure and is beneficial to kidney function. Importantly, cardiac function was not compromised by reducing the preload in this IVCc rat model or by exercise training. This study provides relevant insight concerning the beneficial impact of exercise training on abdominal venous congestion.

Depletion of cardiac glycogen content leads to improved cardiac remodeling in a mouse MI model

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Background: Glycogen (GLN) plays an vital role in the energetic stress adaptation. Nevertheless, it is a double-edged sword for the myocardium, being both protective (supplying ATP when energy is depleted) and noxious (causing injury due to H+/lactate release). High GLN content is generally considered deleterious in no-flow or prolonged ischemia, however the exact role of GLN during permanent myocardial infarction (MI) and in the long-term left ventricular (LV) remodeling post-MI, remains poorly understood. The aim of this study was to investigate whether a robust depletion of myocardial GLN can attenuate adverse LV remodeling post-MI.
Methods: We used a transgenic mouse ($GS^{R582A/R582A}$ knock-in [KI]), in which the allosteric pathway of GLN synthesis (via glucose-6-phosphate) is inhibited in muscle, leading to dramatically suppressed myocardial GLN levels. WT and KI male mouse hearts underwent *ex vivo* ischemia/reperfusion (I/R) injury (30 min ischemia followed by 35 min reperfusion) and were sacrificed following acquisition of pressure data. For the *in vivo* study, WT and KI male mice (10–12 weeks old) were subjected to MI by left anterior descending (LAD) coronary artery permanent ligation. Sham animals underwent operation without ligation. Heart function was measured by 2D-echocardiography at baseline and 56 days post-MI (Vevo 2100, Visualsonics). Mice were sacrificed 56 days post-MI and hearts were collected to measure myocardial GLN content and perform immunohistochemistry (sirius red staining for fibrosis determination) and mRNA studies.
Results: As expected, basal GLN content was dramatically depressed in KI hearts. Although KI MI hearts demonstrated worse + dp/dt max measurements 5min after initiation of *ex vivo* reperfusion (WT MI: 69.3 ± 6.4 *vs* KI MI: 44.2 ± 3.7%, $p < .01$), contractility was comparable at the end of the 35min reperfusion period (WT MI: 80.7 ± 4.0 *vs* KI MI: 82.5 ± 9.0%). Myocardial GLN was drastically reduced in WT MI mice compared to WT shams (WT sham:0.080 ± 0.015 *vs* WT MI: 0.020 ± 0.008 μmoles/ml*mg; $p < .001$) 56 days post-MI. A similar effect was not observed in KI mice (KI sham:0.008 ± 0.002 *vs* KI MI: 0.011 ± 0.002 μmoles/ml*mg). Interestingly, we demonstrated a robustly reduced LV dilatation in the KI mice 56 days post-MI, as evidenced by lower end-diastolic volume (WT MI: 167.69 ± 13.42 *vs* KI MI: 138.00 ± 4.62 μl; $p < .05$) and end-systolic volume (WT MI: 147.62 ± 14.58 *vs* KI MI: 123.15 ± 4.05 μl; $p < .05$). Moreover, KI mice exhibited attenuated global LV fibrosis (WT MI: 61.69 ± 11.10 *vs* KI MI: 37.42 ± 6.90%; $p < .05$), a significant decrease in border zone fibrosis (WT MI: 58.59 ± 12.11 *vs* KI MI: 30.33 ± 4.94%; $p < .05$) and a trend for less fibrosis in the infarct zone (WT MI: 76.80 ± 0.41 *vs* KI MI: 53.48 ± 10.90%). Surprisingly, we reported a dramatic decrease in myocardial rupture incidence in KI MI mice (WT MI: 40.00 *vs* KI MI: 6.25%), indicating involvement of matrix metalloproteases (MMPs) and tissue inhibitor of metalloproteinases (TIMPs). Lastly, a Kaplan-Meier calculation demonstrated improved survival of KI mice compared to their WT counterparts, 56 days post-MI (WT MI: 42.86% *vs* KI MI: 60%).
Conclusions: GLN depletion in KI hearts attenuates adverse LV remodeling and improves survival compared to WT 56 days after MI. Actually, there is a strong correlation between the reduction of cardiac remodeling and a drastic effect on fibrosis deposition, especially in the border zone. These data require further investigation, in order to decipher the association between low GLN content, cardioprotection and ECM deposition.

A new possible way to reverse cardiac hypertrophy development: the inhibition of O-GlcNAcylation

Justine Dontaine, Luc Bertrand, Florence Mailleux, Roselle Gélinas, Audrey Ginion, Laurent Bultot, Christophe Beauloye and Sandrine Horman

UCL

Background: It is well-known that hypertrophy is initially an adaptive response that allows the heart to maintain cardiac output. However, under chronic stimulus, hypertrophy can become maladaptive and leads to heart failure. During the last ten years, our lab has been interested in a protein able to inhibit cardiac hypertrophy development, namely **AMPK**. This protein prevents cardiac hypertrophy by regulating a specific pathway called **O-GlcNAcylation**. In order to better fit with physio-pathological conditions and reach therapeutic aim, the purpose of this study is to check if AMPK activation can also reverse a cardiac hypertrophic phenotype when already developed.
Methods: Neonatal rat cardiomyocytes (NRVMs) are treated with the prohypertrophic agent phenylephrine (PE) for 24h, a time necessary to develop significant cardiomyocyte hypertrophy. NRVMs are then treated with or without different AMPK activators (A769662, 991, AICAr and Phenformin) for an additional 24h period. To see the implication of O-GlcNAcylation in this process, we also used pharmacological O-GlcNAc inducer (PUGNAc) or inhibitor (DON). NRVM hypertrophy is evaluated by measurement of cell surface area and O-GlcNAc levels by western-blotting.

Results: As previously shown, PE-dependent cardiomyocyte hypertrophy is accompanied by an increase in protein O-GlcNAc levels. Interestingly, AMPK activation by A769662 is able to reverse this PE-mediated O-GlcNAc increase, reaching levels similar to those found in control cells. This is nicely accompanied by a reduction in cell size. The same applied using the other AMPK activators, 991, phenformin and AICAr, demonstrating the universality of our phenomenon. Moreover, siRNA-mediated knockdown of AMPK prevents the action of A769662 on cell size and O-GlcNAc levels. We next evaluated the key role of O-GlcNAc by co-treating NRVMs with the O-GlcNAc inducer PUGNAc and showed that this compound counteracts the anti-hypertrophic action of the AMPK activators. Inversely, inhibition of O-GlcNAcylation by DON mimics A769662, reducing cell size.
Conclusions: Our results reveal that AMPK activation can reverse cardiomyocyte hypertrophy development by reducing O-GlcNAcylation levels. The next step will be the demonstration of such paradigm *in vivo*.

(#) Cardiac fibroblast specific invalidation of AMPK alpha1 exacerbates left ventricular remodeling in mice via a Connexin43 mechanism

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[a]UCL; [b]Indiana University School of Medicine; [c]KUL

Background: Following myocardial infarction (MI), the necrotic area is replaced by a fibrotic scar and this is associated with deleterious left ventricular (LV) remodeling. Cardiac fibroblasts (CFs) are crucial components of the fibrotic response following MI. We have previously shown that AMPKα1 is a key regulator of CFs properties following MI. The aim of the study was to investigate whether CF-AMPKα1 is a central player in the functional and structural adaptation of the heart in response to cardiac injury.
Methods: We generated a transgenic mouse strain in which AMPKα1 is specifically deleted in CFs (CF-KO). CF-KO as well as CF-WT mice were subjected to MI (left anterior descending coronary artery permanent ligation) and cardiac function was assessed by echocardiography at baseline 7, 14, 30, 60 and 90 days post-MI. Mice were sacrificed 14 or 90 days post-surgery and hearts were collected to investigate fibrosis and to characterize LV remodeling by immunohistochemistry, histology, polarized light/electron microscopy and mRNAs/microRNAs/proteins expression studies. Blood was collected from mice and human specimens, in order to measure microRNAs levels in the plasma.
Results: At basal state, no phenotypical differences were shown between CF-KO and CF-WT hearts. While infarct size did not differ between the two genotypes, echocardiographic analysis showed that CF-KO mice exhibit exacerbated LV remodeling, as manifested by augmented diastolic (KO: 177.8 ± 12.8μl vs WT:137 ± 10.8 μl; $p < .05$) and systolic (KO: 156.2 ± 13.6 vs WT:109.8 ± 8.9μl; $p < .01$) volumes, 90 days post-MI. Histological analysis showed a robustly augmented fibrotic deposition in the infarct area of CF-KO mice compared to CF-WT, 14 days post-MI (KO: 69.5 ± 3.7% vs WT: 59.1 ± 2.1%; $p < .05$). Polarized light as well as electron microscopy investigations confirmed a more organized and denser collagen matrix in CF-KO, in striking contrast to CF-WT hearts. Immunostaining and qPCR analysis demonstrated that myodifferentiation of CFs was 2-fold increased in CF-KO infarcted hearts, while proliferation of CFs was significantly enhanced in the infarct. In cultured human CFs, we demonstrated that AMPKα1 regulates Cx43 expression by a post-transcriptional mechanism involving miR-125b. Additionally, miR-125b was found to be higher expressed in the plasma of CF-KO mice, compared to CF-WT (KO: 2.2 ± 0,4 fold vs 1.1 ± 0.2 fold; $p < .05$). Finally, we reported that miR-125b is robustly elevated in the plasma of patients developing adverse LV dilatation, compared to non-dilated patients.
Conclusions: Collectively, our data demonstrate the cardinal role of CF-AMPKα1 in cardiac remodeling, as its specific invalidation enhances CFs activity and fibrosis, leading to aggravated LV dilatation following MI. Furthermore, the deleterious effects of the CF-specific AMPKα1 deletion are mediated by Cx43 via post-transcriptional regulation by miR-125b.

Contribution of SGLT1 on glucose uptake and metabolism

Laura Ferté[a], Laurent Bultot[a], Sylvain Battault[a], Anne Van Steenbergen[a], Audrey Ginion[a], Sandrine Horman[a], Hermann Koepsell[b], Luc Bertrand[a] and Christophe Beauloye[a]
[a]UCL; [b]University of Würzburg

Background: SGLT1 combined with SGLT2 inhibitors are under wide investigations because of their ability to increase glycosuria and decrease glycemia in models of diabetes. However, little is known about the impact of these dual inhibitors on the heart since SGLT1 and SGLT2 role in this organ has not been defined yet. It is known that only SGLT1, not SGLT2, is highly expressed in the heart. Evidence based on phlorizin (SGLT inhibitor) use suggest a role of this transporter in glucose transport. However, phlorizin shares similar structure with and can be hydrolyzed into phloretin, a GLUT-specific inhibitor. Therefore, questions remain towards phlorizin potential effects on facilitated glucose transporters and the exact importance of SGLT1 in glucose uptake.

Considering those facts, the purpose of our study is to determine the contribution of SGLT1 transporter on glucose uptake and metabolism in hearts and the impact of phlorizin on this uptake.
Methods: We studied glucose uptake on cardiomyocytes from SGLT1 WT and KO mice using 2-[^{3}H]-glucose as well as glycogen content from SGLT1 WT and KO heart homogenates. Moreover, we analyzed GLUT1 and GLUT4 expression in SGLT1 WT and KO mice. Ultimately, different phlorizin concentrations were tested to determine its impact on glucose uptake.
Results: Glucose uptake was similar in SGLT1 WT and KO mice in basal, hyperglycemic and insulin-stimulated conditions. In line with this observation, glycogen content and GLUT1 and GLUT4 expression were similar or slightly decreased in SGLT1 KO compared to SGLT1 WT animals. Interestingly, high concentrations of phlorizin (10^{-3}M) completely inhibited insulin stimulated glucose uptake and this effect was equivalent for both WT and KO SGLT1 mice. Additionally, in WT and KO mice, insulin signaling appeared to be not modified by phlorizin.
Conclusions: Those results suggest that SGLT1 does not contribute to glucose uptake or metabolism. At high concentrations, phlorizin inhibits insulin stimulated glucose uptake independently of SGLT1. Phlorizin could act through an aspecific inhibition of GLUT transporters.

The ACC inhibitor TOFA decreases platelet mitochondrial function and thrombin-induced activation

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Background: Acetyl-CoA carboxylase (ACC) is phosphorylated/inhibited by AMPK upon platelet stimulation but its role in platelets has never been investigated. ACC is a key regulator of lipid synthesis and oxidation. Given the primary roles of lipids in platelet energy storage and signaling, we hypothesized that sustained ACC inhibition might have consequences on platelet bioenergetics and functions.
Methods: Platelets were treated with 30 μM TOFA, an ACC inhibitor, for 2 hours before thrombin stimulation. Mitochondrial oxygen consumption rate (OCR) was measured using the Seahorse Flux Analyzer. Platelet functions were assessed by aggregometry and flow cytometric studies.
Results: Indices of mitochondrial function assessed by OCR (pmoles/min/μg prot) before and after sequential injection of mitochondrial respiratory chain inhibitors (oligomycin, FCCP, rotenone/antimycin A) were decreased in TOFA-treated platelets relative to control (basal: control 9.01 ± 0.53, TOFA 6.81 ± 0.30; ATP-linked: control 7.79 ± 0.65, TOFA 2.70 ± 0.30; reserve capacity: control 8.19 ± 1.37, TOFA 1.77 ± 0.89; $p < .05$). In addition, TOFA also suppresses mitochondrial function in response to thrombin, notably through a decrease in reserve capacity and ATP-linked respiration. These bioenergetics changes were accompanied by a significant defect in dense granules secretion and aggregation in response to low thrombin concentrations, whereas alpha-granules secretion was not affected, suggesting that the default in aggregation likely resulted from a lower autocrine effect of ADP. Underlying mechanisms involve reduced PKC activity, and in particular two PKC substrates activity, cytohesin-2 and PKD, known to control dense granule secretion and aggregation.
Conclusions: It is concluded that the inhibitory effect of TOFA on platelet secretion and on aggregation may be mediated by the reduction of mitochondrial energy production and PKC pathway activation.

Protein acetylation, a new process involved in the inhibition of glucose metabolism in diabetic heart

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Background: At rest, the heart uses mainly fatty acids to produce its energy. Glucose becomes the main substrate of the heart in response to insulin, during an ischemic event or an increased workload as observed in hypertrophy. The diabetic heart features metabolic adaptation defaults and is no longer able to switch from one type of substrate to another resulting on a cardiac metabolism depending almost exclusively on fatty acids. This metabolic inflexibility is currently recognized to be a major factor of cardiac dysfunction linked to diabetes. Previous observations made in mouse model of obesity induced by high fat diet lead to an increase in global cardiac protein acetylation. Results from our group highlighted a correlation between an increase in cardiac global protein acetylation and a decrease in glucose uptake. We hypothesized that modulation of acetylation impact the ability of the heart to uptake glucose with a special focus on the acetylation of tubulin; a protein involved in the translocation of the glucose transporter, GLUT4, to the plasma membrane.
Methods: Glucose transport was measured following the detritiation rate of 2-^{3}H-glucose in the basal state and in response to insulin (3 nM, 30 min). Acetylation levels as well as signalling pathways were evaluated by western blotting. The impact of different pharmacological modulators of acetylation on basal and insulin-stimulated glucose uptake were experienced on primary cultured rat cardiomyocytes. Glucose uptake was evaluated in primary cultured mouse cardiomyocytes isolated from genetically modified mice lacking genes playing key roles in protein acetylation.
Results: Pharmacologically inhibiting global acetylation increases basal and insulin-stimulated glucose uptake. Modulating specifically tubulin acetylation with three different tools (1) pharmacological agent inhibiting the deacetylase of tubulin (2) overexpression of a dominant negative form of a non-acetylable tubulin (3) uses of cardiomyocytes from genetic models lacking the tubulin acetyltransferase, leads to a modulation in cardiac glucose transport. Interestingly, by targeting tubulin acetylation we were partially able to restore the inhibition of glucose transport induced by fatty acids.
Conclusions: A clear correlation between acetylation modulation and glucose uptake is established with tubulin as a potential mediator.

Pericardial diseases and cancer: a multi-center retrospective study

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Background: Recent studies have shown that the relation between pericardial diseases and cancer may be underestimated and that patients with cancer who developed pericardial diseases had a poor prognosis.
Methods: In this paper we conducted a multi-center retrospective study. We included all patients aged 14 to 99 years old who had been hospitalized in one of the 4 hospitals of the Centres-Hospitaliers-Jolimont between 2009 and 2013, and who had been diagnosed with pericarditis or pericardial effusion (based on the ICD9 and ICD10). We excluded all patients with a history of heart attack, cardiac catheterization, intra-thoracic surgery or thoracic trauma up to 30 days before the occurrence of the pericardial event. We divided these patients in two groups, those with cancer and those without cancer. We compare these two groups observing different factors such as comorbidities, ICU/coronary unit stay, and death. We also compare them to the group of all patients admitted for other cardiovascular disease between 2009 and 2013 (CVD) except from those with exclusion criteria, and to the group of all the patients hospitalized at the same period (PAT).

Results: A total of 502 patients were diagnosed with pericardial disease. The prevalence of this condition amongst hospitalized patients was 0.42%. Men were more represented (men/women ratio =1.41) and most of the patients were senior (senior/adult ratio =1.8). We excluded 176 patients. Amongst these 326 patients, 84 (25.7%) had cancer. This prevalence was 3.6 ($p < .001$) and 2.8 ($p < .001$) times higher than the prevalence of cancer amongst CVD and PAT. There was no significant difference between men and women distribution. The cancers distributions were mostly pulmonary (41%), hematological (21%), gastro-intestinal (16%), mammary (10%) and unspecified (12%). The prevalence of COPD was higher in the group of pericardial diseases with cancer (ratio of 1.8, $p = .03$). The incidence of ICU/coronary unit stay was greater in the group of patients with pericardial diseases and cancer (ratio of 1.3, $p = .002$). This incidence was 1.3 ($p < .001$) and 3.3 ($p < .001$) times greater than the incidence of ICU/coronary unit stay amongst CVD and PAT. Patients with pericardial diseases and cancer were more often readmitted to the hospital (ratio of 1.4, $p = .001$). The mortality during hospital stay was significantly higher in the group of patients with pericardial diseases and cancer (ratio of 4.8, $p < .001$). It was 7.6($p < .001$) and 5.1($p < .001$) times higher than the mortality of CVD and PAT. The mortality during the year following the pericardial event was also greater in the group of patients with pericardial diseases and cancer (ratio of 4.2, $p < .001$). Most of the death after the pericardial event amongst patients with pericardial diseases and cancer occurred during the 6 first months (88%), and survival rate at 1 year was 49%.
Conclusions: The prevalence of cancer amongst patients with pericardial diseases was significantly higher than the prevalence of cancer amongst patients with other cardiovascular diseases as well as amongst the totality of patients hospitalized during the same period. These patients had also higher prevalence of COPD, which may be linked to the high prevalence of lung cancer. They had higher rate of ICU/coronary unit stay, higher mortality during the hospital stay, and higher mortality during the year after the event, particularly during the 6 first months post-event.

This study shows that the prevalence of cancer amongst patients suffering from pericardial diseases is statistically significant, and that these patients have a very poor prognosis with high mortality and frequent readmissions to the hospital after the pericardial event.

Fe-based bioresorbable alloy inhibits platelet activation

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UCL

Background: Bioresorbable polymer stents have been used to provide a transient scaffold after coronary angioplasty. However, an increase in stent thrombosis has been observed. A current challenge is thus to develop new bioresorbable stents combining optimised mechanical and biodegradation properties together with limited thrombogenicity. In this context Fe-based alloys are amongst the good candidates for stent manufacture. In this work blood compatibility of a new Fe-based alloy was studied *in vitro* via assessment of haemolysis and platelet activation.
Methods: Human whole blood was incubated for 60 minutes with either the Fe-based alloy, pure iron, cobalt-chromium (Co-Cr) alloy (composing the bare metal stent used as a reference) or magnesium (Mg) alloy (composing a bioresorbable stent newly on the market). After centrifugation optical density (OD) of the supernatant was measured at 540 nm and haemolysis was calculated as followed:

$$Haemolysis = (OD^{test} - OD^{negativecontrol})/(OD^{positivecontrol} - OD^{negativecontrol}) \times 100\%$$

A value lower than 5% represents a judging criterion for excellent blood compatibility.

For platelet activation assays, human washed platelets were incubated for 60 minutes with each alloy before measuring their reactivity to a platelet agonist by flow cytometry, using CD62P and PAC-1 antibodies. In addition, phosphorylation of PKC substrates was evaluated by western blot. Moreover phosphatidylserines were quantified by flow cytometry to evaluate the procoagulant activity of platelets.
Results: None of the alloys induce significant red cells haemolysis. In addition, Co-Cr alloy did not affect CD62P exposure and PAC-1 presence at platelet surface upon thrombin (0.03 to 0.3 U/ml) stimulation. In contrast, Fe-based alloy and pure iron decreased significantly their response to the agonist. Mg based alloy also decreased their response but to a lesser extend (Figure 1). A drastic inhibition of the phosphorylation state of PKC substrates was also observed with the Fe-based alloy after activation with thrombin (0.03 to 0.3 U/ml). Since similar inhibitory effects were obtained when using a conditioned-reaction medium previously incubated with this Fe-based alloy, we postulate that its biocorrosion might release components counteracting platelet activation. Finally the Fe-based alloy also decreased significantly the percentage of phosphatidylserine positive platelets after activation with thrombin (0.3 to 3 U/ml).
Conclusions: The Fe-based resorbable scaffold doesn't induce haemolysis and displays anti-thrombogenic properties. Because stent implantation is currently still associated with thrombosis our stent is a promising platform for next-generation stent technologies.

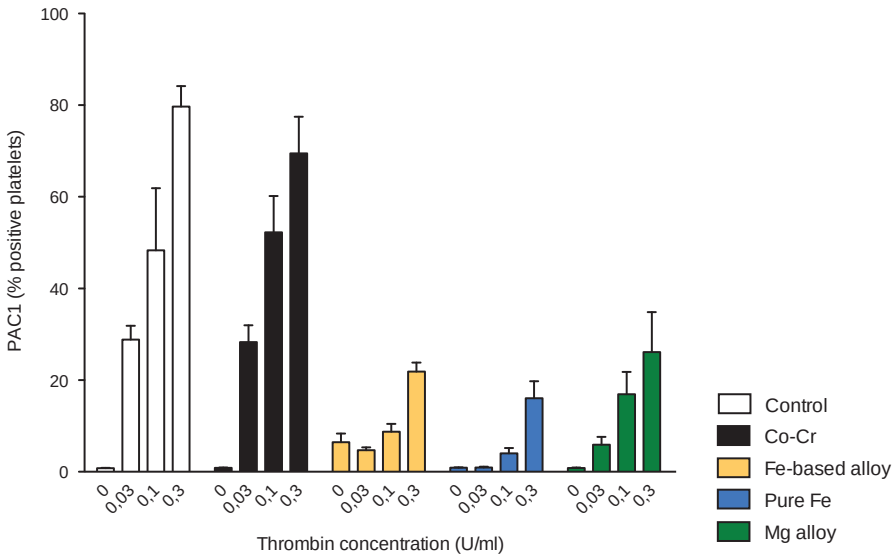

Figure 1. Human platelet activation quantified by PAC-1 following thrombin stimulation. Fe-based alloy inhibits platelet activation.

HEART FAILURE

Angioplasty with stenting in acute coronary syndromes with very low contrast volume (<30 ml) using Cordis diagnostic catheters and improved cardiovascular and renal outcomes

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Background: To safely perform angioplasties in acute coronary syndromes with low contrast volume using 6F Cordis diagnostic catheters. Contrast induced nephropathy is a common clinical problem and it can be prevented by using low contrast volume.
Methods: In 597 patients (718 lesions/789 stents) with acute coronary syndromes angioplasty were performed with cordis 6F diagnostic catheters. Primary angioplasty was performed in 154 cases. In 74% of cases Iodixanol was used. All contrast injections were given by hand. Regular follow-up of the patients was performed at 30 days. The procedures were performed through femoral route only. Tirofiban was used in 99% cases with adjusted dosages based on the creatinine values. Pre-dilatation of the lesions with balloons was performed in 189 cases. 30 patients had creatinine more than 2mg/dl before the procedures. 23 patients had cardiogenic shock at presentation. 78% of the cases had diabetes. IVUS was used in only 2 patients. A variety of coronary drug eluting stents from various companies were used in the procedures. Buddy wires were used in 16 cases. Left main stenting was performed in 17 cases. Diabetes was managed with intermittent doses of insulin at admission and insulin mix (regular with NPH insulin) at discharge along with oral diabetic medications.
Results: The mean contrast volume used per patient was 28 ml (±7 ml) including the angiogram before the stenting. In patients with renal failure the mean contrast volume was 22 ml (±3 ml). Mild reversible contrast induced nephropathy (CIN) was observed in four patients. One another patient with creatinine 5.6 mg/dl at presentation developed acute renal failure. He was put on regular hemodialysis and later he was started on medical management after 1 m. Five mortality was observed in this series, and of these five patients four had cardiogenic shock and one patient expired after discharge due to possible acute stent thrombosis. Mild cardiac failures were seen in 16 cases, who were treated with frusemide injections and infusions. Two patients required ventilator for congestive heart failure therapy. Coronary perforation and wire breakages were not seen and proximal mild stent edge-dissections was seen in 2 cases, which were treated with additional stents. Dressler's syndrome was seen in two cases and they were managed with pericardiocentesis and low dose steroids. Antibiotics requirement was seen in 10% of the cases. Groin hematomas requiring one unit of blood transfusion was seen in 3 cases.
Conclusions: Angioplasty and stenting could be performed safely in patients with acute coronary syndromes using Cordis diagnostic catheters using low volume of contrast. Low contrast volume usage would result in lower incidence of contrast induced nephropathy and cardiac failures.

2D-RV speckle tracking predicts mortality with higher additional value than cMR-derived-RVEF in HF-rEF

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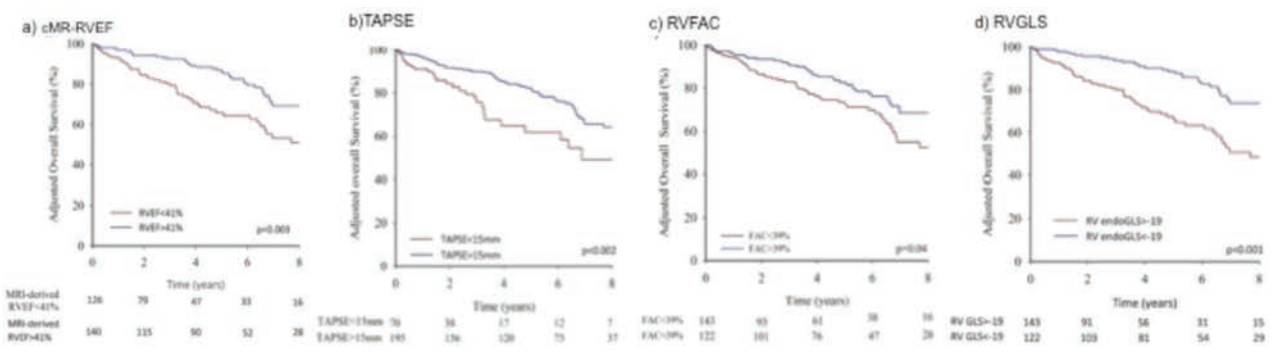
Cliniques Universitaires Saint Luc

Background: Right ventricular systolic function has been recognized as an important predictor of outcome in heart failure. Echocardiography is the first line imaging technique but there is actually no single RV echocardiographic parameter reliable enough to be universally accepted due to the complex geometrical anatomy of the RV. Recently, RV 2D speckle tracking has been proposed as a new echocardiographic method for RV evaluation.

Methods: 266 patients with HF-rEF (mean LVEF 23 ± 7%, age 60 ± 14 years; 29% female) underwent RV function assessment using cMR and 2D echocardiography and were followed for a primary endpoint of overall death and secondary endpoint of cardiovascular (CV) death. Competitive risk survival analyses were performed to predict univariate and multivariate parameters for the secondary endpoint.

Results: Average RVEF was 42% ± 15% and average RVGLS was −18.0 ±4.9%. RVGLS ($r = -0.62$), RV tricuspid annular systolic excursion (TAPSE) ($r = 0.62$) and RV fractional area change (FAC) ($r = -0.65$) correlated moderately but significantly (all $p < .001$) to cMR- RVEF. After a median follow-up of 4.7 years, 102 patients died, 84 of CV cause. RVEF, TAPSE, FAC and RV-GLS were significant univariate predictors of overall and cardiac death. In multivariate cox regression, age, ischemic etiology, diabetes, NYHA class III-IV, and beta blocker treatment were independent clinical predictors of overall mortality. cMR-RVEF ($\chi 2$ to enter = 3.9, $p < .05$), FAC ($\chi 2$ to enter 6.2, $p = .02$), and TAPSE ($\chi 2$ to enter = 4.9, $p = .04$) provided additional prognostic value over these baseline parameters, but the additional predictive value of RV-GLS ($\chi 2$ to enter = 10.8, $p < .001$) was significantly ($p < .05$) higher than the other tests. Also, RV-GLS <19% predicted overall mortality with higher additional hazard ratio (2.5 (95% CI [1.6;3.9], $p < .001$) than TAPSE <15 mm (2.15 [1.34–3.43], FAC <39% (1.6 [1.02–2.49] or RVEF <41% (1.93 [1.25–2.99]).

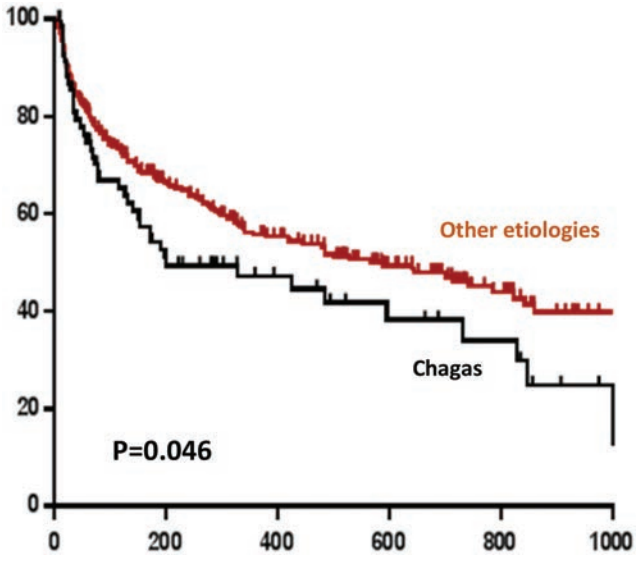
Conclusions: RV dysfunction assessed either by cMR or echocardiography predicts CV mortality with significant additional value over baseline clinical and echocardiographic parameters. Importantly, the predictive value of 2D-RV-GLS was superior to cMR and the other conventional echocardiographic parameters.



Influence of chagas cardiomyopathy in the prognosis of patients with descompensated heart failure

Victor Issa, Silvia Ayub, Paulo Chizzola, Silvia Lage and Edimar Bocchi
São Paulo University Hospital, Brazil

Background: Patients with Chagas cardiomyopathy and chronic heart failure (HF) are considered to have a worse prognosis as compared to other etiologies. However, the course of Chagas patients during episodes of decompensated HF has not been sufficiently studied. Therefore, we sought to investigate the course of Chagas patients during episodes of decompensated HF and during early follow-up after hospital discharge.
Methods: We analyzed a prospective cohort of 800 patients admitted with decompensated HF from August 2013 through December 2017; mean age was 56.7 ± 14.8 years and patients were predominantly male (473, 64.2%). Main etiologies were dilated cardiomyopathy in 274 (37.2%) patients, ischemic cardiomyopathy in 195 (26.5%) and Chagas cardiomyopathy in 162 (22%); mean left ventricle (LV) ejection fraction was 29.9 ± 11%. During the course of their hospitalization 216 (29.3%) patients died and 87 (11.8%) were transplanted; during follow-up (mean 476 days) 41(9.5%) patients died, 21(4.9) patients were transplanted and 190 (44%) were readmitted.
Results: Compared to patients with other etiologies, Chagas patients were more frequently admitted for cardiogenic shock (17.9% vs 11.1%) and arrhythmias (18.5% vs 8.9%, $p < .001$); at hospital admission they were more frequently in hemodynamic profile C (41.4% vs 29.9%, $p = .028$) and had lower heart rate (74.3 ± 20.7bpm vs 86.5 ± 25.5bpm, $p < .001$), lower arterial pressure (mean sBP 92.7 ± 62.8 vs 103.2 mmHg, mean dBP 62.8 ± 14.8 vs. 67.2 ± 16.2 mmHg, $p < .001$) and higher BNP levels (2050 ± 1572pg/mL vs 1330 ± 1274pg/mL, $p = .034$); echocardiography indicated that Chagas patients had lower LV ejection fraction (26.6 ± 8.5% vs 30.8 ± 11.5%, $p < .001$), larger LV diastolic diameter (68.9 ± 8.6mm vs 65.2 ± 11.2mm, $p < .001$), and a higher proportion of patients with moderate/severe right ventricular dysfunction (50% vs 34.4%, $p = 0.001$). Invasive hemodynamic data showed that Chagas patients had lower pulmonary artery systolic pressures (49 ± 15.5mmHg vs 54.1 ± 15.6 mmHg, $p = .05$) and lower cardiac output (3.6 ± 1L/min vs 4.2 ± 1.5L/min, $p = .016$). At discharge, Chagas patients had lower sodium level (134.6 ± 11.8 vs 136.9 ± 6, $p = .02$) and higher BNP (1790 ± 1137 vs 1101±±1147, $p = .03$). Further, Chagas patients were more likely to receive a transplant during hospitalization (20.5 vs 9.4, $p < .001$) and had a similar in-hospital mortality (30.4% vs 29.1%). After discharge, they were more likely to be readmitted, die or be transplanted at 180 days (Figure).
Conclusions: Patients with Chagas cardiomyopathy have a more severe clinical presentation during episodes of decompensated heart failure and greater degree of cardiac remodeling. Prognosis during hospitalization as well as at 180 days after discharge is poorer among Chagas patients. Our findings support specific interventions targeted to this high risk population during episodes of decompensated heart failure and early after hospital discharge.



Course of patients with cardiogenic shock supported with intra-aortic balloon couterpulsation

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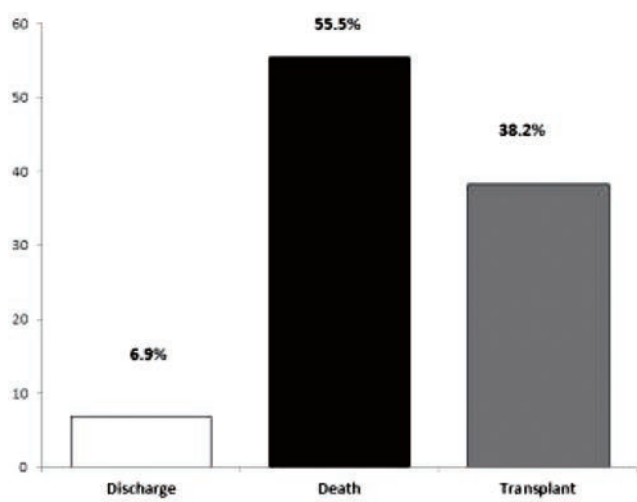
Background: The value of intra-aortic balloon couterpulsation (IABC) in cardiogenic shock after myocardial infarction has been challenged in recent clinical trials. However, the value of IABC has not been sufficiently explored in patients with chronic heart failure during episodes of acute heart failure and cardiogenic shock (HF).
Methods: We analyzed a cohort of 737 patients admitted with decompensated HF from Aug/2013-Sep/2017; 131 (17.7%) patients received a IABC; these patients were predominantly male (82, 62.6%) with mean age of 48.2 ± 12.3 years and ejection fraction of 25.9 ± 9.9%; HF etiologies were Chagas cardiomyopathy in 51 (38.9%) patients, dilated cardiomyopathy in 42 (32.1%) and ischemic in 19 (14.5%).
Results: Among the 131 patients supported with IABC, 84 (64.1%) were listed for heart transplant and 50 (59.5%) were eventually transplanted. In-hospital death occurred in 75 (55%) patients and 9 (6.9%) were discharged without heart transplant (Figure). We compared the clinical, echocardiographic and hemodynamic data of non-survivors versus transplant patients (Table) and found that transplanted patients had higher LV ejection fraction (27.9 ± 12.5 vs 24.3 ± 6.9%, *p* .035) and a tendency towards lower BNP level (1588 ± 1362 vs 2060 ± 1447, $p = .067$). Interestingly, variables potentially associated with a poor response to IABC implantation, such as presence of right ventricular dysfunction in echocardiogram or Chagas etiology, did not differ between groups (Table).
Conclusions: The use of IABC in patients with cardiogenic shock may be an adequate first step of mechanical support in centers where VADs are not broadly available. However, a significant proportion of patients may require more advanced therapies

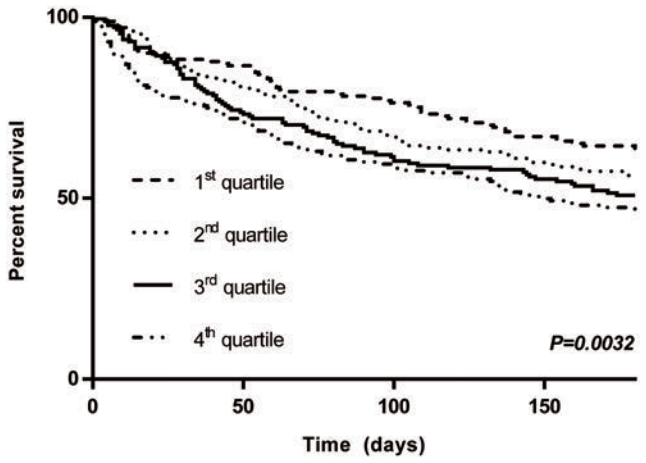
	Heart Transplant/Discharge N(%)/mean ± SD	Death N(%)/mean ± SD	*p* value
Age	47.1 + 11.1	49.6 13.5	.25
Chagas Etiology	25 (42.4)	26 (51)	.84
Admission systolic pressure	88.8 18.2	90 15.7	.7
BNP	1588 1362	2060 1447	.067
Urea	94.8 72.5	100.3 61.8	.64
LV Ejection Fraction	27.9 12.5	24.3 6.9	.035
Moderate/Severe RV dysfunction	30 (42.9)	40 (57.1)	.5
Wedge pressure	23.1 8	24.3 8	.52
Right atrium pressure	147.6	16.8 6.6	.12
Cardiac output	41.3	3.9 1.4	.84



Influence of increasing age in hospital readmission and mortality rate at 180 days in patients hospitalized for decompensated heart failure

Victor Issa[a], Rafael Lloret[b], Barbara Tamburim[b], Felix Ramires[b], Carolina Amorim[b] and Semeia Corral[b]
[a]São Paulo University Hospital; [b]Hospital do Coração (HCor) de São Paulo, Brazil

Background: The impact age has not been sufficiently studied in heart failure patients during episodes of acute decompensation. We evaluated the influence of increasing age, clinical variables and laboratory tests on the prognosis of patients admitted for heart failure.
Methods: We analyzed 721 patients admitted for decompensated heart failure and ejection fraction <40% from January 2011 through September 2017. We explored the influence of age in the rate of death or hospital readmission at 180 days.
Results: The mean age of the patients was 70.6 ± 13.2 years. Males were predominant (72%), the mean ejection fraction was 32.2 ± 7.7%. Over the period, 385 (53.4%) patients were re-admitted or died. The rate of events according to the quartiles of age was: 37.2% in the 1st quartile, 40.2% in the 2nd quartile, 46.7% in the 3rd quartile, 52.5% in the 4th quartile (Figure). When analyzed in a Cox Regression Model that included gender, heart rate, blood pressure and laboratory tests (pro-BNP, sodium, potassium, urea, creatinine, hemoglobin, increasing age (OR = 1.025, $p = .01$), as well as, ejection fraction (OR = 0.0969, $p = .04$), sodium at admission (OR = 0.944, $p = .09$) and hemoglobin at admission (OR = 0.913, $p = .036$) were independently associated with greater risk of events.
Conclusions: Age, ejection fraction, sodium and hemoglobin at hospital admission were the clinical and laboratorial variables associated with higher risk of mortality and readmission in 180 days fallow-up after hospital discharge of patients hospitalized for decompensated heart failure.



Influence of renal dysfunction on the increase in rehospitalization rates and mortality at 180 days in patients hospitalized for decompensated heart failure

Victor Issa[a], Rafael Lloret[b], Barbara Tamburim[b], Carolina Amorim[b], Semeia Corral[b] and Felix Ramires[b]
[a]São Paulo University Hospital; [b]Hospital do Coração (HCor) de São Paulo, Brazil

Background: Renal dysfunction may occur in up to one-third of patients hospitalized for decompensated heart failure, a finding that has been associated with worse prognosis. However, some recent studies have challenged this association. We sought to explore the influence of renal dysfunction in a comtemporary cohort of patients with decompensated heart failure
Methods: Renal dysfunction may occur in up to one-third of patients hospitalized for decompensated heart failure, a finding that has been associated with worse prognosis. However, some recent studies have challenged this association.
Results: The mean age of the patients was 70.6 ± 13.2 years. Males predominated (72%), the mean ejection fraction was 32.2 ± 7.74%. Throughout this period, 385 (53.4%) patients were re-admitted or died. Mean values of creatinine and urea at admission were respectively 1.65 and 73, and mean values at discharge were 1.75 and 76.4. The values of creatinine at admission (OR:0,875 $p = .429$), creatinine at discharge (OR: 1.165 $p = .282$), urea at admission (OR: 1.002 $p = .374$), urea at discharge (OR:1 $p = .977$ creatinine variation (OR: 1.072 $p = .294$) were not significantlly associated with worse prognosis (Figure). Conversely, increasing age (OR = 1.025, $p = .01$), ejection fraction (OR = 0.0969, $p = .04$), sodium at admission (OR = 0.944, $p = .09$) and hemoglobin at admission (OR = 0.913, $p = .036$) were independently associated with greater risk of events.
Conclusions: In our study renal function was not associated with readmission rates in mortality at 180 days. This finding further challenge the traditional association between admission renal function and prognosis during episodes of heart failure decompensation and offer alternative information for prognostic interpretation in this scenario.

Pulmonary hypertension does not influence outcome following implantation of a left-ventricular assist device

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Erasme Hospital

Background: Pulmonary hypertension (PH) is a common complication of heart failure (HF), especially in advanced disease when patients are candidates for left ventricular assistance device (LVAD) implantation. Significant PH leading to right ventricular failure (RVF) is associated with a worse outcome following surgery. In addition, persistent PH has been reported even in patients with successful LVAD implantation. The aims of our study were (1) to characterize the hemodynamic changes following LVAD implantation; (2) to identify predictors of outcome.
Methods: We performed a retrospective, single centre analysis of patients having a LVAD implanted between 2011 and 2017 who had a baseline and post implant right heart catheterism (RHC). The variables of interest were gathered during pre-transplant (T_0) and pre (T_1) and post (T_2) implant examinations. We drew statistical comparisons of biological, ultrasound and hemodynamic variables before and after LVAD implantation. Furthermore, the incidence and nature of complications in 30 days following LVAD implantation were collected. A Kaplan–Meier analysis was used to calculate short and long-term survival post-implantation. Using a linear regression model, the variables of interest were correlated with patients' levels of post-implant pulmonary vascular resistance (ΔPVR).
Results: Fifty-seven out of the eighty-four LVAD patients met our selection criteria, 26 of these had received a hemodynamic exam after the LVAD, on average 15 ± 10 months following implantation. Detailed hemodynamic data are shown in Table 1. PH was present in 91% of patients before LVAD (mean pulmonary artery pressure (mPAP) 37 ± 11 mmHg, PVR 3.81 ± 2.16 WU) compared to 36% after. A significant reduction in both mPAP (23 ± 8 mmHg, $p < .001$) and PVR (2.29 ± 0.93 WU, $p = .002$) was observed after LVAD. Moreover, LVAD implantation improved pulmonary arterial compliance (3.50 ± 1.42 ml/mmHg, $p = .001$) compared with before implantation (1.94 ± 0.81 ml/mmHg). LVAD implantation was complicated by severe RVF in 13 patients (22.8%) in the early 30-day post LVAD period. Four patients required temporary right ventricular assist device support. The survival, at 30 days and at 1 year, following LVAD implantation was 93% and 84% respectively. The linear regression showed that age is inversely correlated to "ΔPVR". A weaker correlation was also found between the latter and the diastolic pulmonary pressure gradient (DPG).
Conclusions: In our cohort, LVAD implantation resulted in a significant improvement of PH, mainly driven by a normalisation of left-sided filling pressures and improvement in cardiac output. This suggest that PH in end-stage HF with reduced ejection fraction is a purely passive mechanism, associated with a natural aging process, that does not influence outcome. Therefore, we believe that RVF following LVAD implantation may be explained by another mechanism independent of the pulmonary circulation.

Hemodynamic Variables	T_0 n = 36	T_1 n = 57	p value[a]	T_2 n = 26	p value[b]
HR (bpm)	80 ± 17	83 ± 17	0.893	78 ± 16	0.612
sBP (mmHg)	102 ± 16	100 ± 13	0.178		
dBP (mmHg)	67 ± 12	65 ± 11	0.283		
MAP (mmHg)	79 ± 12	77 ± 11	0.209	81 ± 21	0.346
sPAP (mmHg)	56 ± 17	54 ± 17	0.405	35 ± 12	< 0.001
dPAP (mmHg)	30 ± 9	29 ± 9	0.934	16 ± 6	< 0.001
mPAP (mmHg)	38 ± 11	37 ± 11	0.714	23 ± 8	< 0.001
PAWP (mmHg)	24 ± 8	25 ± 7	0.306	12 ± 5	< 0.001
RAP (mmHg)	12 ± 7	11 ± 6	0.668	8 ± 6	0.446
TPG (mmHg)	14 ± 8	13 ± 7	0.218	10 ± 3	0.010
DPG (mmHg)	6 ± 6	4 ± 5	0.017	4 ± 2	0.425
$S\bar{v}O_2$ (%)	54 ± 11	57 ± 11	0.374	64 ± 7	0.266
CO (L/min)	3.38 ± 1.21	3.57 ± 1.24	0.141	4.32 ± 0.89	0.089
CI (L/min/m²)	1.77 ± 0.54	1.85 ± 0.55	0.150	2.19 ± 0.48	0.064
PVR (Wood Unit)	4.76 ± 2.83	3.81 ± 2.16	0.012	2.29 ± 0.93	0.002
C_{PA} (ml/mmHg)	1.92 ± 1.21	1.94 ± 0.81	0.607	3.50 ± 1.42	0.001

Values are expressed as mean ± standard deviation. T_0: pre-transplant examination; T_1: pre-implant examination; T_2: post-implant examination. p value[a]: comparison T_0 and T_1; p value[b]: comparison T_1 and T_2. p value ≤ 0.05 was considered statistically significant.

HR: heart rate; **sBP**: systolic blood pressure; **dBP**: diastolic blood pressure; **MAP**: mean arterial pressure; **sPAP**: systolic pulmonary artery pressure; **dPAP**: diastolic pulmonary artery pressure; **mPAP**: mean pulmonary artery pressure; **PAWP**: pulmonary artery wedge pressure; **RAP**: right atrial pressure; **TPG**: transpulmonary pressure gradient; **DPG**: diastolic pulmonary pressure gradient; **$S\bar{v}O_2$**: mixed venous oxygen saturation; **CO**: cardiac output; **CI**: cardiac index; **PVR**: pulmonary vascular resistance; **C_{PA}**: pulmonary arterial compliance

(Δ) Sacubitril/valsartan reduces ventricular arrhythmias and appropriate ICD-interventions in heart failure with reduced ejection fraction

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Ziekenhuis Oost Limburg

Background: Sacubitril/valsartan reduced the occurrence of sudden cardiac death in the PARADIGM-HF trial. However, limited information is available about the mechanism.
Methods: Heart failure (HF)-patients receiving sacubitril/valsartan for a class-I indication equipped with an implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT) with remote tele-monitoring were retrospectively analyzed. Device registered arrhythmic-events were determined (ventricular tachycardia/fibrillation[VT/VF], appropriate therapy, non-sustained VT [NsVT;>4 beats and <30 seconds], hourly premature-ventricular-contraction [PVC]-burden), following sacubitril/valsartan initiation (incident-analysis) and over an equal time-period before initiation (antecedent-analysis). Reverse remodeling to sacubitril/valsartan was defined as an improvement of left ventricular ejection fraction (LVEF) of ≥5% between baseline and follow-up.
Results: A-total of 151 HF-patients with reduced LVEF (29 ± 9%) were included. Patients were switched from ACE-I or ARB to equal doses of sacubitril/valsartan (expressed as %-target-dose; before =58 ± 30% vs. after =56 ± 27%). The mean follow-up of both the incident and antecedent-analysis was 364-days. Following the initiation, VT/VF-burden dropped (individual-patients with VT/VF pre_n = 19 vs. post_n = 10, total-episodes of VT/VF pre_n = 51 vs. post_n = 14, both $p < .001$), resulting in reduced occurrence of appropriate therapy (pre_n = 16 vs. post_n = 6; $p < .001$). NSVT-burden per patient also dropped (See Table). There was no impact on atrial-fibrillation burden (see Table). PVC-burden dropped significantly, which was associated with an improvement in BiV-pacing in patients with <90% BiV-pacing at baseline. A higher degree of reverse remodeling was associated with a lower burden of NsVT and PVCs (both $p < .05$). Following initiation of sacubitril/valsartan 44% of patients exhibited beneficial reverse remodeling with an increase of LVEF >5%.
Conclusions: Initiation of sacubitril/valsartan for a class-I indication, is associated with a lower degree of VT/VF, resulting in less ICD-interventions. This beneficial effect on ventricular arrhythmias might be related to cardiac reverse remodeling.

Table 1. Arrhythmias and pacing parameters before and after sacubitril/valsartan over similar time period.

Parameter	Before initiation (N=151)	After initiation (N=151)	P-value
Ventricular arrhythmias			
Number of patients ≥1 VT/VF episode	19	10	<0.001
Total amount of VT/VF-episodes	51	14	<0.001
Number of patients with ≥1 appropriate therapy	16	6	0.007
Total amount of appropriate therapy-episodes	20	6	0.007
Number of patients with ≥1 inappropriate therapy	3	2	0.319
Total amount of inappropriate therapy-episodes	3	2	0.319
NsVT (mean episodes/patient)	7.7±11.8	3.7±5.4	<0.001
Mean NsVT-duration (seconds)	6.3±5.2	5.3±3.8	0.041
Mean PVCs per hour	14 (4-22)	2 (0-4)	<0.001
Atrial arrhythmias			
Median percent of time per day in AF	9 (5-14)	9(5-14)	0.332
Patients with ≥1 paroxysmal AT/AF-episode > 30s	48	33	0.159
Pacing parameters			
% of Atrial pacing	7 (1-14)	7 (1-14)	0.578
% of Biventricular pacing	96±4	99±1	<0.001
BiV-pacing < 90%	5 (4.7%)	1 (0.9%)	0.045

The optimal plasma volume status in heart failure in relation to clinical outcome

Pieter Martens, Petra Nijst, Matthias Dupont and Wilfried Mullens
Ziekenhuis Oost Limburg

Background: Progressive plasma volume (PV) expansion is a hallmark of chronic heart failure (CHF), ultimately contributing to decompensated heart failure. Monitoring PV might offer prognostic information and might be a target for tailored therapy.
Methods: The correlation between technetium-(^{99}Tc)-labeled red blood cell measured PV and calculated PV was first determined in a **validation cohort**. Afterwards the relationship between PV-status (PVS; a marker how much the actual PV deviated from the ideal PV) and outcome was analyzed using cox-proportional modeling in a prospective **outcome cohort** of CHF-patients
Results: Thirty-one CHF-patients were prospectively included in the validation cohort. Calculated PV (=aPV) correlated well with technetium-(^{99}Tc)-measured PV (r = 0.714; $p = .001$). A total of 1173-patients (HFrEF $n = 872$, HFmrEF $n = 229$, HFpEF $n = 72$) were prospectively included in the outcome cohort. The mean PVS in the outcome cohort was $-6.7 \pm 10\%$, indicating slight PV-contraction (see formula and distribution Figure panel A). A higher PVS was independently associated with an increased risk for heart failure hospitalization and all-cause mortality (HR =1.016; CI = 1.006−1.027 per 1% increase in PVS; $p = .002$). ROC-curve analysis indicated that an PVS of −6.5% optimally predicted absence of adverse outcome. Hazard ratio analysis indicated that CHF-patients were less equipped in tolerating PV-expansion in comparison to PV-contraction (see Figure panel B). The use of ACE-I/ARBs and MRAs in higher dosages were independently associated with a higher odds for having an optimal PVS in HFrEF and HFmrEF but not in HFpEF (see Table 1).
Conclusions: Calculated PV correlates well with measured PV in CHF-patients. An increase in PV is independently associated with a higher risk for adverse outcome and a slight contraction of the predicted PV seems to be related to less adverse events. Higher dosages of Renin-Angiotensin-Aldosterone blockers are associated with a higher odds for having an optimal PV-status.

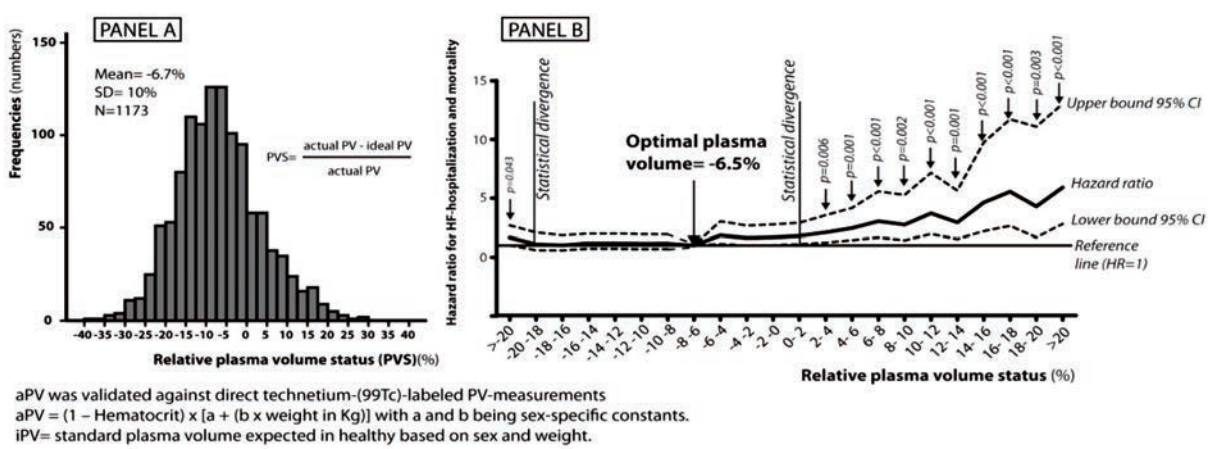

Figure 1. Distribution and formula of PVS (panel A) and relation between PVS and outcome (panel B).

Table 1. Relation between the odds for having an optimal PVS and dosages of CHF-therapies.

Parameter	HFrEF (N=872)		HFmrEF (N=229)		HFpEF (N=72)	
	OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value
RAS-I-dose *(10% increase)*	1.1 (1.0–1.1)	**0.008**	1.1 (1.00–1.2)	**0.047**	0.9 (0.8–1.1)	0.476
BB-dose *(10% increase)*	1.0 (0.9–1.1)	0.139	1.0 (0.9–1.1)	0.473	1.0 (0.9–1.2)	0.780
MRA-dose *(12.5mg increase)*	1.2 (1.0–1.3)	**0.009**	1.2 (1.0–1.4)	**0.037**	1.1 (0.8–1.5)	0.529
Loop diuretic *(per 40mg furosemide equivalent)*	0.9 (0.9–1.0)	0.160	0.9 (0.8–1.2)	0.721	0.5 (0.2–1.1)	0.101

Indications and diagnostic yield of endomyocardial biopsies for unexplained cardiomyopathy

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Ziekenhuis Oost Limburg

Background: Endomyocardial biopsies (EMBs) remain the golden standard to diagnose underlying pathophysiologic process in heart failure (HF), when potential therapeutic decisions cannot be made by non-invasive techniques. However, changes in the field of noninvasive diagnostic testing might have an impact on the need for performing an EMB in certain scenarios.
Methods: We performed a retrospective analysis of consecutive EMBs performed in a single, non-academic, center. EMBs were performed between February 2009 and March 2018. Baseline characteristics including non-invasive imaging and hemodynamic profile were assessed. Indications of EMBs were analysed in accordance with the 2007-AHA/ACC/ESC-scientific statement on EMBs (14 scenarios when to or not perform an EMB).
Results: A total of 57 patients (74% male) were included. The overall diagnostic yield was 58%, with a trend towards a higher diagnostic yield in left ventricular (64%) vs right ventricular EMBs (45%; $p = .346$). The majority of patients (88%) underwent EMBs for a class IIa-recommendation, 9% for a class-I recommendation and the remaining patients for a class IIb-indication (see Table). Of the EMBs for a class IIa indication, 82% ($n = 47$) was for an unexplained restrictive cardiomyopathy, in which 53% ($n = 25$) revealed a diagnosis (of whom $n = 23$ patients had amyloidosis). Subtyping of the EMBs with a pathologic diagnosis of amyloidosis revealed that 52% ($n = 12$) had transthyretin amyloidosis (ATTR) and 43% ($n = 10$) had light-chain amyloidosis. Overall one major (1.7%; tamponade requiring surgery) and one minor (1.7%; pericardial effusion requiring pericardiocentesis) complication occurred following the EMB-procedure.
Conclusions: When following the AHA/ACC/ESC-scientific statement on EMBs, the performance of EMBs had a high diagnostic yield, with acceptable complication rates. However, in patients presenting with an unexplained restricted cardiomyopathy, technetium-labeled bone scanning could offer a non-invasive approach to establishing the diagnosis of ATTR, mitigating the need for EMBs in a subset of patients.

Table. Overview of biopsies performed with diagnostic yield per AHA/ACC/ESC clinical scenario.

Scenario	Description of AHA/ACC/ESC clinical scenario	class	Number biopsies (NB) ; diagnostic yield (DY) ; diagnosis (D/)
1	New-onset HF of <2 wks associated with a normal-sized or dilated LV and hemodynamic compromise	I	**NB**=2 ; **DY**= 50% ; **D**/ viral myocarditis
2	New-onset HF of 2 wks to 3 months associated with a dilated LV and new ventricular arrythmias, second- or third-degree heart block, or failure to respond to usual care within 1 to 2 weeks	I	**NB**=3 ; **DY**= 66% ; D/ 1x Sarcoidosis and 1x Rheumatic carditis
3	HF of >3 months' associated with a dilated LV and new ventricular arrythmias, second- or third-degree heart block, or failure to respond to usual care within 1 to 2 weeks	IIa	**NB**=0
4	HF associated with a DCM of any duration associated with suspected allergic reaction and/or eosinophilia	IIa	**NB**=0
5	HF with suspected anthracycline cardiomyopathy (ACM)	IIa	**NB**=2 ; **DY**= 100% ; **D**/ 2x ACM
6	HF with unexplained restrictive cardiomyopathy	IIa	**NB**=47 ; **DY**= 53% ; **D**/ 23x amyloidosis, 2x suspicion lysosomal storage disease
7	Suspected cardiac tumors	IIa	**NB**=1 ; **DY**= 100% ; **D**/ 1x angiosarcoma
8	Unexplained cardiomyopathy in children	IIa	**NB**=0
9	New-onset HF of 2 weeks' to 3 months' associated with a LV, without new ventricular arrythmias or second- or third-degree heart block, that responds to usual care within 1 to 2 weeks	IIb	**NB**=0
10	HF of >3 months' associated with a dilated LV, without new ventricular arrythmias or second- or third-degree heart block, that responds to usual care within 1 to 2 weeks	IIb	**NB**=0
11	HF associated with unexplained HCM	IIb	**NB**=2 ; **DY**= 100% ; **D**/ 2x HOCM
12	Suspected ARVD/C	IIb	**NB**=0
13	Unexplained ventricular arrythmias	IIb	**NB**=0
14	Unexplained atrial fibrillation	III	**NB**=0

sST2 and mortality in acute heart failure

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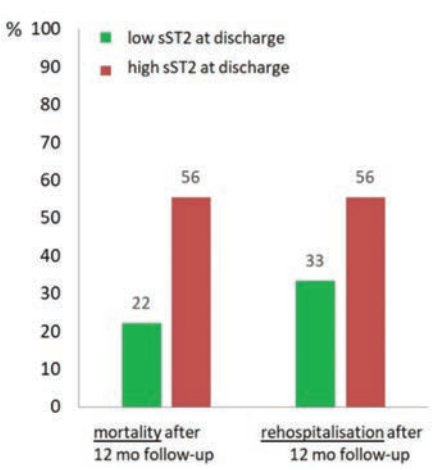
Background: ST2 is a protein belonging to the interleukin-1 receptor family. Circulating soluble ST2 (sST2) concentrations increase as a result of cardiomyocyte stress and cardiac fibrosis. This relatively new and promising biomarker has recently demonstrated to be a strong predictor of mortality in acute heart failure.
Purpose: We determined the circulating levels of sST2 in patients with acute heart failure. We aimed to assess the relation between a single measurement as well as serial measurements with mortality.
Methods: Twenty patients admitted because of acute heart failure were included (males $n = 11$; females $n = 9$; mean age: 82 years; etiology: ischemic $n = 11$, non-ischemic $n = 9$; mean ejection fraction: 34%). Levels of sST2 were measured at admission, after 48 hours and at discharge. The primary outcome was all-cause mortality within 1 year after admission. The normal value of the sST2 assay was <35 ng/mL.
Results: 11 patients died within 1 year after admission. The overall sST2 concentration decreased between admission and discharge as a result of diuretic therapy (median concentration at admission: 170 ng/mL, at discharge: 50 ng/mL). Survivors after 1 year of follow-up had a tendency toward a lower sST2 concentration at discharge: 42 ng/mL versus 65 ng/mL [$p = .17$]. When serial measurements of sST2 were taken into account, patients with greater sST2 reductions between admission and discharge had a better survival. The mortality within 1 year was significant lower in patients with a reduction of sST2 greater than the median reduction (mortality of 11%) compared to a reduction of sST2 smaller than the median reduction (mortality of 67%) [$p = .047$].
Conclusions: sST2 is a promising prognostic biomarker for assessment of adverse events in patients with acute heart failure. A single measurement as well as serial measurements could be useful for the prediction of mortality in the patient with acute heart failure.



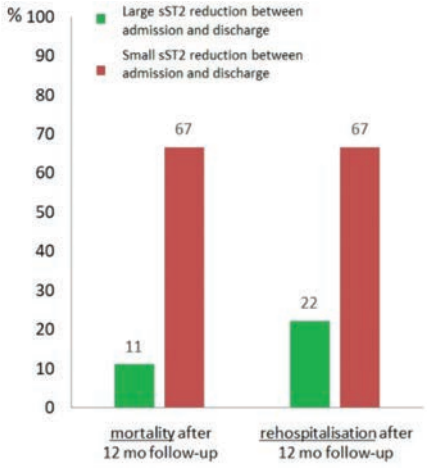


Figure 1 (left). Relation between sST2 at discharge and mortality (left) or rehospitalisation (right) within 1 year. The division of 'low sST2' versus 'high sST2' was based on the median sST2 value.

Figure 2 (right). Relation between sST2 reduction during hospitalisation (between admission and discharge) and mortality (left) or rehospitalisation (right) within 1 year. The division of 'large sST2 reduction' versus 'small sST2 reduction' was based on the median sST2 reduction.

(*) Phenotyping heart failure with preserved ejection fraction: focus on fibrosis markers (Extracellular volume by cMR and biomarkers) and their prognostic impact

Clotilde Roy, Anne-Catherine Pouleur, Alisson Slimani, Christophe de Meester, Mihaela Amzulescu, Audrey Ginion, Benjamin Ferracin, Agnès Pasquet, David Vancraeynest, Christophe Beauloye, Jean-Louis Vanoverschelde, Sandrine Horman, Damien Gruson and Bernhard Gerber

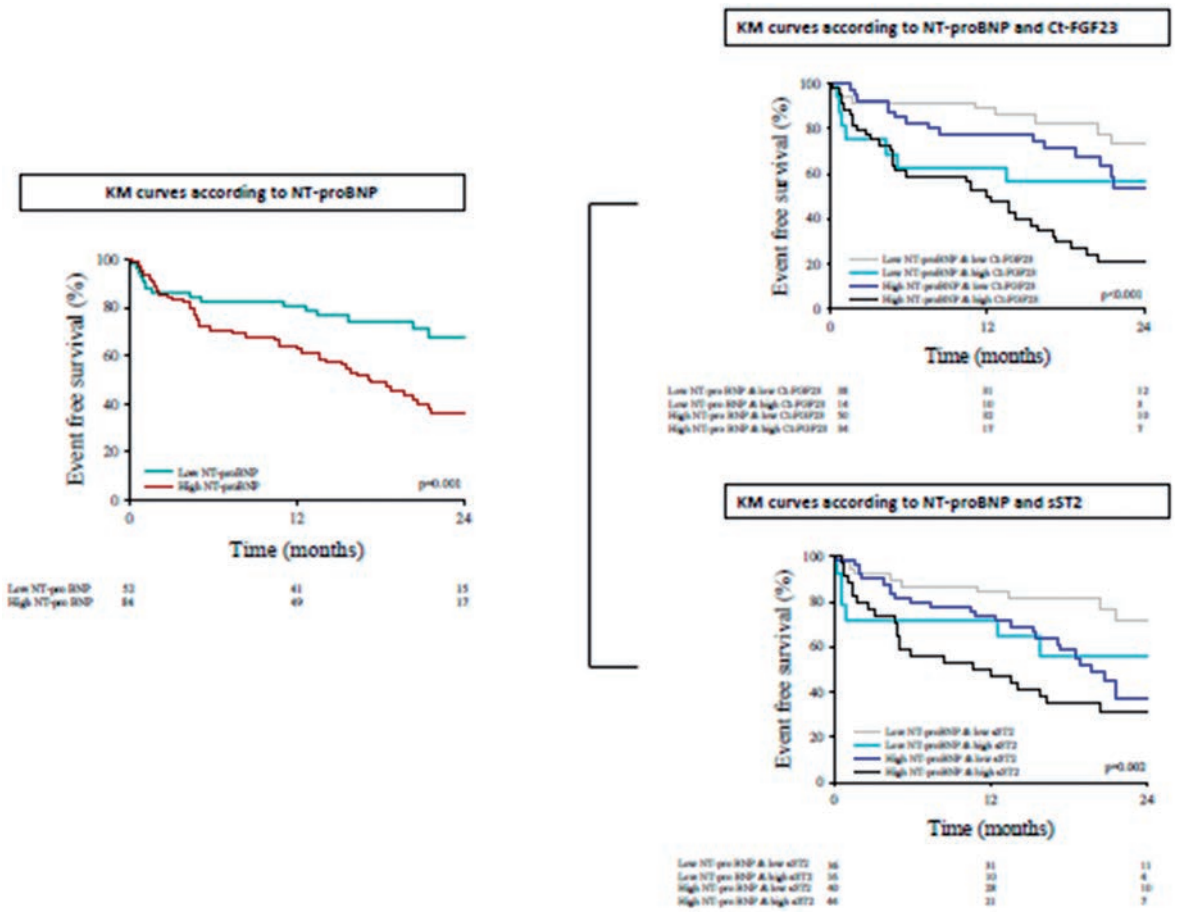
Cliniques Universitaires St.-Luc

Aims: Increased myocardial fibrosis may play a key role in heart failure with preserved ejection fraction (HFpEF) pathophysiology. Extracellular volume (ECV) calculated by cMR has already been associated with prognosis in HFpEF. Fibroblast growth factor 23 (FGF23) and sST2 have been associated with cardiovascular risk in heart failure (HF) but data in HFpEF remain scarce. The aim of this study was to determine circulating levels, clinical and imaging correlates and prognosis value of FGF23 and sST2 in HFpEF.

Methods: We prospectively included 84 controls (57 ± 19 y, 44% female) and 143 consecutive HFpEF patients (78 ± 8 y, 61% female). Patients underwent a complete 2D echo and cardiac magnetic resonance (cMR) to assess ECV, an indirect index of myocardial diffuse fibrosis. FGF23 and sST2 were also measured at time of enrolment.

Results: Mean ECV value was significantly higher in HFpEF patients than in controls separated in controls ($n = 53$) and age-sex-matched controls ($n = 31$) (32.7 ± 4.9% versus 25.9 ± 3.2% and 27.8 ± 2.4% respectively, $p < .001$). Median Ct-FGF23 and sST2 were significantly higher in HFpEF patients compared to controls and age and sex matched controls (247 RU/ml vs 57 and 61 RU/ml and 42 ng/ml vs 27 and 24 ng/ml, $p < .001$ respectively). Over a mean follow-up of 22 ± 7 months, 72 HFpEF patients reached the combined outcome of all cause death or first HF hospitalization. In univariate cox regression analysis, ECV (HR 1.26 [1,00;1,58]; $p = .048$), Ct-FGF23 (HR 1.46 [1,19;1,80]; $p < .001$) and sST2 (HR 1.42 [1,12;1,81]; $p = .004$) were significantly associated with combined outcome. In multivariable Cox regression analysis, a reference model showed that NT-proBNP (HR 1.57[0.93; 2.65], $p = .091$), diabetes (HR = 1.58[0.99;2.52], $p = .056$), GFR (HR 0.99[0.98;1.00], $p = .072$) and E wave velocity (HR 1.01[1.00;1.02], $p = .032$) were independent predictors of combined outcome. After adjusting for this preliminary model, the individual inclusion of sST2 (c2 to improve: 4.62; $p = .032$) and Ct-FGF23 (c2 to improve: 5.79; $p = .016$) improved the prediction, but when included together, only FGF23 was significantly associated with combined outcome. Kaplan Meier curves showed the prognostic according to the different biomarkers (Figure).

Conclusions: In HFpEF, above and beyond NT-proBNP, Ct-FGF23 is the strongest predictor of worst outcome compared to sST2, even after adjusting for confounding factors.



Idarucizumab for the reversal of dabigatran in patients undergoing heart transplantation

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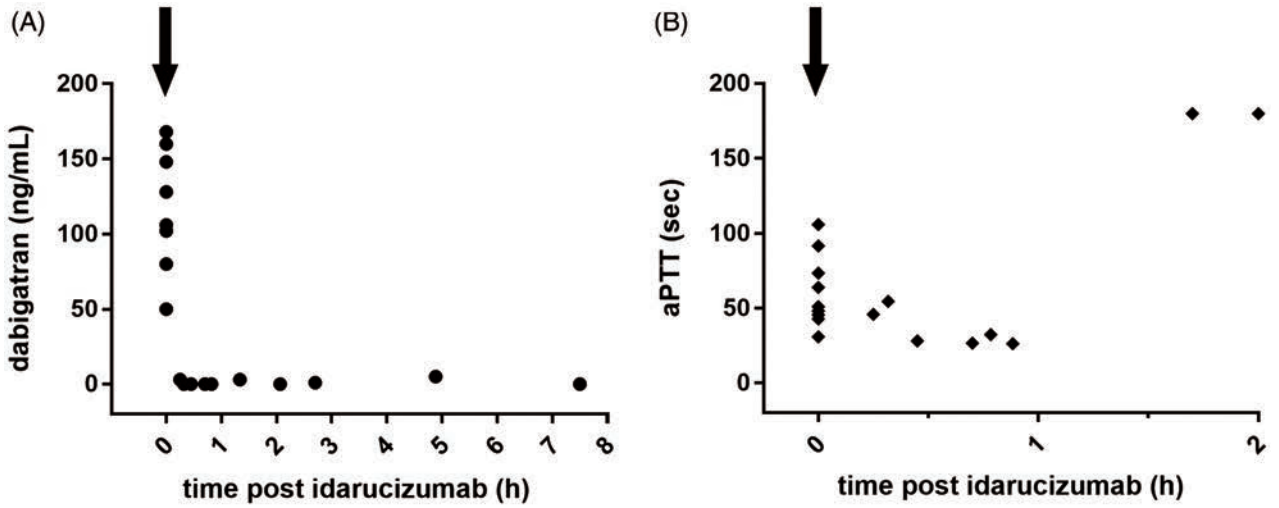
UZ Leuven

Background: Atrial fibrillation is common among patients with advanced heart failure who are listed for transplantation. Idarucizumab is a monoclonal antibody fragment that was developed to neutralize the activity of the direct thrombin inhibitor dabigatran. We describe the experience of dabigatran reversal with idarucizumab in 10 patients undergoing heart transplant surgery at the University Hospitals Leuven.
Methods: At the time of listing for heart transplantation, patients requiring anticoagulation because of non-valvular atrial fibrillation, CHA2DS2VASc score $\geq$2 and without ventricular assist device or end-stage renal failure, were started on or switched to dabigatran. Upon availability of a donor organ, dabigatran was neutralized with 5 g of intravenous idarucizumab, immediately prior to induction of anaesthesia.
Results: Ten patients have received a heart transplant using this protocol since its implementation at our centre on October 1st, 2015. Mean age was 57.9 years, 9 of the 10 patients were male, median CHA_2DS_2VASc score was 3 and mean eGFR at time of transplantation 53 mL/min. Mean time since last intake was 6.2 h. Evolution of dabigatran concentration (measured by a calibrated diluted thrombin time assay) and activated partial thromboplastin time (aPTT) in function of time after idarucizumab administration are represented in Figure 1. Mean dabigatran level before administration of idarucizumab was 117.8 ng/mL. All dabigatran concentrations post idarucizumab were unmeasurably low. Mean aPTT (reference range 25.1–36.5 s) was 55.8 s prior to idarucizumab and 35.4 s immediately post idarucizumab. During surgery, patients received on average 1.0 unit of packed cell transfusion, 4.1 units fresh frozen plasma, 0.9 pools platelets and 587 mL blood that was recovered via cell salvage. Two patients (20.0%) needed re-intervention because of bleeding. No adverse reactions or unexpected events that could potentially be related to idarucizumab administration were noted. There were no thrombotic complications.
Conclusions: This is the largest report describing the use of idarucizumab to normalize coagulation in patients on dabigatran awaiting heart transplantation. Administration of 5 g of idarucizumab led to a sustained and complete biochemical reversal, without thrombotic complications, and without interfering with heparinization for cardiopulmonary bypass. However, there still were some bleeding events. The availability of an immediately-acting complete reversal agent makes dabigatran an attractive choice for non-VAD patients with non-valvular atrial fibrillation who are listed for heart transplantation.



Functional mitral regurgitation in pts with HFrEF, HFmrEF and HFpEF: the good, the bad and the ugly?

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OLV Aalst

Background: The 2016 heart failure(HF) guidelines introduced a new classification of heart failure based on ejection fraction – HFrEF, HFmrEF and HFpEF. The aim of this study was to evaluate and compare the prevalence and evolution of functional(F) mitral(M) regurgitation(R) in HFrEF, HFmrEF and HFpEF pts admitted with an episode of acute decompensated heart failure.
Methods: We retrospectively analyzed data of 1453 de novo heart failure(HF) patients consecutively admitted with an acute episode of heart failure in a tertiary HF center (mean length of stay: 18 ± 16 days) . Ejection fraction was measured during index hospitalization and functional mitral regurgitation(FMR) was assessed at time of discharge. Severe FMR $\geq$2 was present in 40% of pts. Mean age of the patients was 74 ± 12 years, 52% of them were men. After a mean FU of 1045 ± 702 day, 63% of pts were still alive. According to ESC criteria we identified 45.3% patients with HFrEF, 18.8% patients with HFmrEF and 35.9% patients with HFpEF.
Results: Pts with HFpEF were younger ($p < .001$), had lower NTproBNP ($p < .001$), less cardiac readmissions ($p < .001$) and better RV function as evidenced by TAPSE($p = .003$). HFrEF pts had significantly higher incidence of severe FMR $\geq$2 at time of discharge (50.8% vs 33.1% vs 38.8%; $p > .001$) and had higher LVEDD (60 ± 9 mm vs 54 ± 8 mm vs 48 ± 7 mm; $p < .05$) compared to HFpEF, HFmrEF pts. Interestingly in HFrEF as well as in HFpEF pts optimisation of the HF therapy resulted in a significant improvement in FMR. No difference in survival was noted between HFpEF, HFmrEF and HFrEF pts. However, only in the HFrEF group a significant difference in survival was noted beween those pts with and without severe FMR ($p < .001$).
Conclusion: Interestingly in HFrEF and HFmrEF but not in HFpEF pts optimisation of HF therapy resulted in a significant improvement in MR. Although FMR is prevalent in pts with HFpEF and HFmrEF it only bears prognostic information in HFrEF pts. Therefore we speculate that HFrEF pts with persistent severe FMR after recompensation should be followed intensively in a dedicated heart failure clinic.

Is there a role for cardiac inflammation in the development of diabetic cardiomyopathy?

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Hasselt University

Background: In 2014, 422 million people were diagnosed with diabetes, corresponding to a prevalence of 8.5% among the adult population worldwide. The prevalence of diabetes is increasing with an alarming rate and is estimated to exceed 10% by 2030. Diabetic cardiomyopathy (DCM) is a major chronic complication of type 2 diabetes mellitus (T2DM), defined as diabetes-associated structural and functional changes in the myocardium, not directly attributable to other confounding factors such as coronary artery disease or hypertension. It is currently speculated that oxidative stress, fibrosis, apoptosis, impaired autophagy and altered Ca handling are important factors in the aetiology of DCM. Recent published data demonstrate that Western diet (high sugar combined with high fat diet) given to healthy rats mimics the human phenotype of DCM. Whether inflammation contributes to the development of DCM is unclear. In that context, we performed a longitudinal study, examining progression of DCM phenotype with cardiac inflammation.
Methods: Forty-two healthy male Sprague-Dawley rats were randomly assigned a 'Western diet' ($n = 20$) or a normal chow-fed diet ($n = 22$) for 18 or 30 weeks. Cardiac function was evaluated non-invasively via echocardiography and invasively via hemodynamic measurements. An oral glucose tolerance test (OGTT) was performed to measure glucose and insulin levels. Cardiac fibrosis and TNF-α levels were investigated in harvest tissue samples. Lipid profile was evaluated from blood samples.
Results: Western diet given to healthy rats induces hyperglycaemia, hyperinsulinemia, in association with an altered lipid profile already after 18 weeks diet. After 18 weeks, left-ventricle (LV) hypertrophy and increased interstitial fibrosis were observed in diabetic rats and were further worsened after 30 weeks diet. Conventional echocardiographic analysis did not reveal significant changes between groups regarding ejection fraction, fractional shortening, heart rate, cardiac output, end-diastolic and end-systolic volumes after 18 weeks Western diet. However, after 30 weeks, systolic function was observed, characterized by an increased end-systolic volume and a decreased ejection fraction and fractional shortening. In addition, end-diastolic pressure was significantly increased after already 18 weeks diet. Finally, cardiac TNF- α levels were unchanged after 18 weeks Western diet. However, after 30 weeks, tissue TNF-α levels were significantly increased in rats fed with Western diet and negatively correlated with ejection fraction ($R^2 = 0.024$ $p < .05$).
Conclusions: After 18 weeks, Western diet induces DCM, characterized by wall hypertrophy and increased cardiac fibrosis. After 30 weeks diet, DCM displays additional systolic dysfunction and is associated with increased cardiac tissue inflammation. Our data suggest that inflammation could be a key factor involved in the switch from diastolic to systolic failure in DCM. Underlying mechanisms remain to be determined in order to evaluate the importance of reducing cardiac inflammation in diabetic patients.

Diastolic left ventricular function in relation to circulating metabolic biomarkers in a population study

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Background: We studied the association of circulating metabolic biomarkers with asymptomatic diastolic left ventricular (LV) dysfunction (LVDD), a risk-carrying condition that affects 25% of the population.
Methods: In 570 randomly recruited people, we assessed in 2005–2010 and in 2009–2013 the multivariable adjusted correlations of e' (early LV relaxation) and E/e' (LV filling pressure) measured by Doppler echocardiography with 43 serum metabolites, quantified by magnetic resonance spectroscopy.
Results: In 2009–2013, e' cross-sectionally increased (Bonferroni corrected $p \leq .016$) with the branched-chain amino acid (BCAA) valine (per 1 SD increment, +0.274 cm/s [95% confidence interval, +0.057, +0.491]) and glucose + the amino acid (AA) taurine (+0.258 cm/s [+0.067, +0.481]), while E/e' decreased ($p \leq .017$) with valine (0.264 [0.496, 0.031]). The risk of developing LVDD over follow-up (9.4%) was inversely associated ($p \leq .0059$) with baseline glucose + AA taurine (odds ratio, 0.64 [0.44, 0.94). In partial least squares analyses of all the baseline and follow-up data, markers consistently associated with better diastolic LV function included the AAs 2 aminobutyrate and 4 hydroxybutyrate and the BCAAs leucine and valine, and those consistently associated with worse diastolic LV function glucose + AA glutamine and fatty acid pentanoate. BCAA metabolism ($\log10p = 12.6$) and aminoacyl tRNA biosynthesis (9.9) were among the top metabolic pathways associated with LVDD.
Conclusions: The associations of LVDD with circulating AAs and BCAAs were consistent over a 5 year interval and suggested a key role of BCAA metabolism and aminoacyl-tRNA biosynthesis in maintaining diastolic LV function.

IMAGING

Validation study of upper limit of normal values for proximal aortic diameters in patients with thoracic aortic disease

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Background: Thoracic aortic dilatation (TAD) requires accurate and timely detection in order to prevent progression to aortic dissection. The detection of TAD necessitates the availability of cut-off values for normal aortic diameters. Initially published nomograms used to predict normal proximal thoracic aortic diameters obtained by echocardiography were mostly based on small reference populations with varying age groups and/or applicable for the sinuses of Valsalva (SoV) only. To overcome this problem we previously developed gender and BSA specific formulas for upper limit of normal (ULN) calculation for both SoV and ascending aorta (AA) based on established guidelines and applicable in a wide age range. We now aimed to validate different available ULN formulas in a cohort of TAD patients.
Methods: We selected six articles establishing ULN formulas using the ASE- and EACVI guidelines for measuring proximal aortic diameters and subsequently applied them on a cohort of 593 TAD patients (3-90y) including bicuspid aortic valve (BAV, N = 280, female 31.8%), Marfan syndrome (MFS, N = 193, female 47%) and Turner syndrome (TS, N = 120). ULN values are compared separately for subjects <18 y (N = 109) and >18 y (N = 484) as most formulas include different age ranges. Differences between the various ULN values were obtained by subtracting the ULN calculated with our formulas from those of literature.
Results: MFS subjects have significantly larger SoV diameters (median SoV diameter 39 mm (IQR 34; 44 mm)) compared to AA diameters and to the other TAD groups ($p < .001$). BAV subjects have significantly larger AA diameters (median AA diameter 34 mm (IQR 29.4; 40 mm)) in comparison to the other TAD groups ($p < .001$). In subjects <18 y our ULN values provide equivalent information about dilatation of the SoV compared to two other available formulas in 82 and 86% of cases, resp. (median difference −1.29mm (IQR −1.8; −0.87 mm) and 1.9 mm (IQR 1.19; 2.3 mm), resp.). Only one other study provide ULN formulas for the AA in children and yields a strong agreement in classification of dilated and non-dilated AA with our formulas of about 98% (median difference 0.05mm (IQR −0.44; 0.43 mm)). The importance of gender becomes apparent above the age of 15y resulting in large scattering in ULN values not accounting for gender above 15 y. In adults >18 years differences in ULN values of the SoV were smallest when comparing to ULN formulas that account for gender and use age as a continuous variable (median difference 0.67mm (IQR −0.14; 1.41 mm), with 94% agreement in classification in dilated and non-dilated SoV). For the AA, only one other study was available for comparison, but showed incongruent results with our values due to categorization in small age groups.
Conclusions: ULN values obtained with our previously published formulas correlate well and lie within the range of those calculated with the other available formulas. ULN formulas implementing gender, age as a continuous variable and BSA provide equivalent information on aortic dilatation in about 86 to 94%. Gender should be taken into account due to its impact on aortic dimensions from adolescence on.

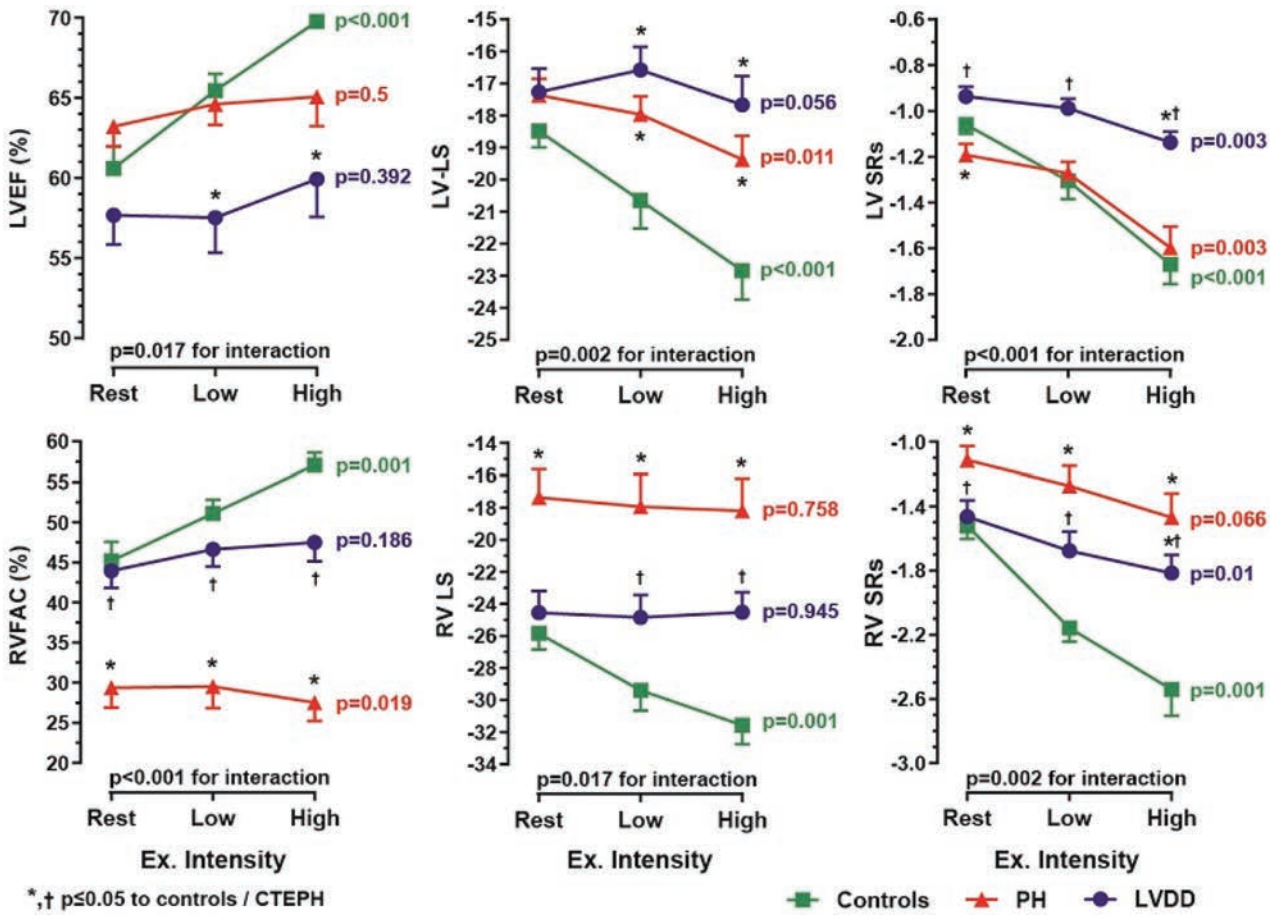
(#) Impaired biventricular contractile reserve in patients with diastolic dysfunction

Mathias Claeys[a], Rik Willems[a], Thibault Petit[b], Andre La Gerche[c], Piet Claus[a], Jens-Uwe Voigt[a], Marion Delcroix[a], Stefan Janssens[a] and Guido Claessen[a]
[a]UZ Leuven; [b]Virga Jesse ZH Hasselt; [c]Baker Heart & Diabetes Instiute

Background: Exercise capacity is a strong prognostic factor in heart failure and patients are mainly symptomatic during exercise, yet cardiac imaging is generally performed at rest. To gain insight into the mechanisms of exercise intolerance, we compared cardiac function during exercise in left ventricular diastolic dysfunction (LVDD) with precapillary pulmonary hypertension (PH) patients and healthy controls.
Methods: Bicycle stress echocardiography was performed in 48 subjects (10 controls, 21 PH patients and 17 LVDD patients). LVDD was defined as either a diagnosis of HFpEF ($n = 11$) or concentric remodelling with signs of diastolic dysfunction ($n = 6$). LV ejection fraction (LVEF), RV fractional area change (RVFAC), LV & RV peak systolic longitudinal strain (LV-LS, RV-LS) and strain rate (LV-SRs, RV-SRs) were analysed from apical grey-scale images obtained at rest, low (25% of peak VO_2) and high (66% of peak VO_2) intensity exercise. Cardiac output (Q) and mean pulmonary artery pressure (P) were estimated by Doppler techniques.

Results: LVDD patients (age 71 y ± 9, 41% male) were older then both controls (age 46y ± 10, 80% male) and PH patients (age 57y ± 16, 62% male)($p < .001$ for age, $p = .157$ for gender). At rest, left and right ventricular function did not differ between controls and LVDD patients while RV function was impaired in PH patients ($p < .05$ to controls). During exercise, ventricular performance differed across the groups (all $p < .05$ for interaction). Notably in controls, LV & RV function increased (all $p \leq .001$) while in PH patients RV function either did not increase (RV-LS & RV-SRs) or even declined (RVFAC). Interestingly, in addition to a lower left ventricular reserve (no increase in LVEF, LV-LS and only a modest increase in LV-SRs) also RV functional parameters did not increase with exercise in LVDD patients. Both PH (7.2 ± 3.9) and LVDD (3.5 ± 1.7) patients had an abnormal (i.e. >3 mmHg/L/min) P/Q slope as opposed to controls (1.7 ± 0.8) ($p < .001$ between groups).

Conclusions: Patients with LVDD have a reduced biventricular reserve while RV functional impairment predominates in precapillary PH. Exercise imaging provides insight into disease mechanisms and uncovers ventricular dysfunction not evident at rest.



Epicardial adipose tissue and myocardial fibrosis in aortic stenosis: relationship with symptoms and outcomes

Laurent Davin, Raluca Dulgheru, Alain Nchimi, Stella Marchetta, Christophe Martinez, Olivier Gach, Mathieu Lempereur, Patrick Marechal, Cecile Oury and Patrizio Lancellotti
CHU Liège

Background: The onset of symptoms is a critical point in the natural history of aortic stenosis (AS) and the cardinal indication for valve replacement (AVR). Actually, the clinical outcome significance of myocardial replacement fibrosis in asymptomatic patients remains controversial. Other local and systemic factors might contribute to the severity of left ventricular (LV) remodelling, symptoms and patients outcome. Epicardial Adipose Tissue (EAT) is a source of several pro-inflammatory and pro-atherogenic cytokines, which can biologically influence the myocardium and epicardial coronary arteries through paracrine or vasocrine actions. Coronary artery disease and AS share similar disease pathways.
Methods: This study assessed the respective contribution of EAT and myocardial fibrosis to the symptomatic status and outcome of patients with AS. Between March 2008 and October 2016, a total of 118 patients with moderate to severe AS (81 asymptomatic and 37 with symptoms) by echocardiography and who underwent Cardiac Magnetic Resonance (CMR) to assess LV replacement fibrosis via Late-Gadolinium Enhancement (LGE) and EAT volume, were included in this study.
Results: In multivariable analysis, after adjustment for age, gender, cretatinine, atrial fibrillation, coronary artery disease, LV ejection fraction, and blood pressure; aortic mean pressure gradient ($p = .014$), Brain Natriuretic Peptide (BNP) levels ($p = .001$), Body mass index (0.032) and LV fibrosis ($p = .043$) emerged as independent cofactors associated with symptoms. During a mean followed-up of 36 ± 22 months, 51 (63%) asymptomatic patients experienced events. In multivariable Cox-regression analysis, aortic valve area ($p = .007$), relative LV wall thickness ($p = .008$), creatinine ($p = .011$) and EAT volume index ($p = .006$) were independently associated with cardiovascular events. When used as a categorical variable, EAT volume >60 ml/m2 accurately predicted the occurrence of events in the multivariable analysis. Myocardial fibrosis was not predictive of the outcome in these asymptomatic patients.
Conclusions: In patients with AS, symptoms are associated with the degree of obstruction and the severity underlying myocardial adverse remodelling. However, focal fibrosis and BNP level do not predict outcome of asymptomatic AS patients. On the other hand, evaluating EAT volume may allow better identification of patients with asymptomatic AS at higher risk of developing cardiovascular events during follow-up. Indeed, excess EAT could contribute to the inflammatory burden of AS by producing pro-atherogenic cytokines, which in turn promote the calcification process of aortic valves leaflets, and the progression of valvular obstruction.

Global myocardial work during exercise echocardiography and outcome in patients with asymptomatic severe aortic stenosis

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Background: The management strategy in asymptomatic patients with severe aortic stenosis (AS) and preserved left ventricular ejection fraction (LVEF) is controversial. Aortic valve replacement (AVR) is associated with significant morbidity and mortality, while there is a risk for heart failure (HF) and sudden cardiac death (SCD) with conservative management. Exercise testing is recommended in asymptomatic AS, but the prognostic value of dynamic changes in mean pressure gradient (MPG) and LV contractility is still debated. Moreover, the evaluation of both Global Longitudinal Strain (GLS) and Global Myocardial Work (GMW) indexes has demonstrated to be more sensitive than LVEF to detect subclinical myocardial dysfunction.
Purpose: The aim of the present study was to evaluate the additional value of GLS and GMW indices during exercise echocardiography for predicting the need for AVR in asymptomatic patients with severe AS and preserved LVEF ($>50\%$).
Methods: We enrolled 77 truly asymptomatic patients (mean age 69 ± 12) with severe AS and preserved LVEF, who underwent exercise echocardiography at our institution with adequate images for the evaluation of GLS and GMW indices both at rest and during exercise. Occurrence of AS-related events (onset of symptoms, HF or symptoms driven AVR) were collected after 1-year follow-up.
Results: AS-related events occurred in 24 patients (32%). No differences in baseline demographic and echocardiographic characteristics were found between the 2 groups. Double product (DP) was also similar. Patients with AS-related event were less likely to show contractile reserve (defined as an increment $>5\%$ in LVEF) ($p = .013$, log-rank survival analysis $=0.015$). GLS at baseline and during exercise were similar between groups. Patients with AS-related events had lower values of exercise GMW index (GMWI) (2214 ± 661 vs 2615 ± 772 mmHg%, $p = .045$) and a bigger decrease of GMWI with exercise (Δ%GMWI of $16 \pm 28\%$ vs $2 \pm 35\%$, $p = 0.015$). On multivariable analysis, after adjustment for presence of contractile reserve, only Δ%GMWI was a predictor of AS-related events at 1-year follow-up (HR 1.027, CI95% 1.004–1.1051, $p = .02$). Moreover, by ROC curve analysis, a cut-off value of 7% of Δ% GMWI was associated with AS-related events (sensitivity of 63% and specificity of 60%).
Conclusions: GMW analysis during exercise could provide additional information for risk stratification in asymptomatic patients with severe AS and preserved LVEF, above and beyond assessment of contractile reserve and GLS analysis at rest and during exercise. This finding is probably related to the higher sensitivity of the parameter, associated with a relative load independency.

Acute effects of a short endurance exercise on the right ventricle: a myocardial speckle tracking study

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[a]Cliniques Universitaires St.-Luc; [b]CHU Dinant- Godinne

Background: Few studies have documented right ventricular dysfunction after (ultra)-endurance sport, especially in middle or long distances. We aimed to evaluate the impact on the right ventricle (RV) of short distances races.
Methods: 37 adults participated in two different trail races: a short race (S) (15 km), $n = 25$ and a long race (L) (45 km), $n = 12$. Echocardiography was performed at baseline and immediately after the race. The evaluation of RV function was defined by the RV basal diameter and other classical parameters. Myocardial speckle tracking provided RV longitudinal strain.
Results: A significant modification of the RV strain (−25% to –22.7%, $p < .05$) was observed in the two groups of runners. The RV strain was also significantly alterated (−24.9% to –22.6%, $p < .05$) in group S. No correlation was found between the variation of the strain and the variation of the basal diameter of the RV nor the variation of the classical parameters of the right ventricular function.
Conclusions: Alteration of myocardial deformation in right ventricle was observed immediately after an endurance exercise,even in a short distance race. The long-term effect of these alterations remains unknown.

Stroke volume response and pulmonary venous atrial function of patients with a systemic right ventricle

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UZ Leuven

Background: In adults with complete transposition of the great arteries after atrial switch (TGA-Mustard/Senning), impaired atrial function could be an important factor limiting exercise capacity. Therefore, we aimed to assess both the stroke volume response during a physiological exercise test and the pulmonary venous atrial function in these patients versus patients with congenitally corrected TGA (ccTGA).
Methods: Thirty-three adults with a systemic right ventricle (sRV) (70% TGA-Mustard/Senning, 37 ± 9 years of age, 24% female, 94% NYHA class I-II) underwent cardiovascular magnetic resonance (CMR) imaging, both during exercise and at rest. At rest, a stack of retrospective-gated cine images horizontal long-axis plane was acquired for volumetric assessment of the pulmonary venous atrium (PVA), and 12 radial long-axis cine images (each with a rotation of 15°) encompassing the whole PVA for strain analysis. Afterwards, patients performed free breathing bicycle exercise at four exercise stages within the CMR bore using a cycle ergometer with adjustable electronic resistance and a real time CMR acquisition protocol.
Results: During exercise, TGA-Mustard/Senning experienced a significant 8% fall in stroke volume, whereas ccTGA could increase their stroke volume by 15%. Strain analysis was possible in 30 patients. PVA strain during the reservoir phase and the contraction phase, and volumetric PVA emptying fraction were lower in TGA-Mustard/Senning patients compared to ccTGA patients (7.8 ± 2.6 vs. 13.3 ± 2.7%, −2.8 ± 1.9 vs. –6.4 ± 2.2%, and 22 ± 7 vs. 37 ± 9%, all $p < .001$). TGA-Mustard patients ($n = 7$) had lower atrial strain during the reservoir phase (6.1 ± 2.3 vs. 8.6 ± 2.4%, $p = .037$) and during the contractile phase (−1.3 ± 0.8 vs. −3.5 ± 1.9%, $p = .001$) compared to TGA-Senning patients ($n = 16$); there was a significant age difference between both groups (43 ± 8 vs. 31 ± 4 years of age, $p < .001$). In the group of TGA-Mustard/Senning patients, PVA strain during the reservoir phase was correlated with the global longitudinal strain of the sRV ($r = -0.418$, $p = .047$) and maximal PVA volume ($r = 0.418$, $p = .047$).
Conclusions: During exercise, TGA-Mustard/Senning patients have an abnormal fall in stroke volume which is different from the increase in stroke volume observed in ccTGA patients. This could be due to rigid baffles and a stiff PVA in the former. Preliminary results of the strain analysis suggest that (1) there are lower atrial strain values in atrial switch patients compared to ccTGA patients; (2) TGA-Mustard patients have lower strain values compared to TGA-Senning patients; and (3) PVA strain during reservoir phase seems correlated with sRV systolic function and PVA volume in TGA-Mustard/Senning patients. Larger series, validation of strain measurements with invasive pressure measurements, and strain measurements during exercise are needed.

Does Mitral Annular Calcification predict mortality in renal transplant recipient: a 14 year follow up study

Caroline Henrard[a], Agnes Pasquet[a], Annie Robert[b], Maelle Lucion[b], Robin Thirionet[b], Emmanuel Coche[b] and Michel Jadoul[b]

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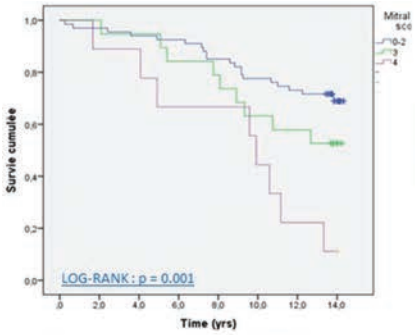
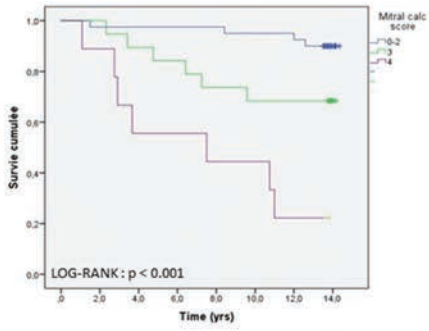
Background: Several studies have demonstrated that Mitral annular calcifications (MAC) are significantly related to cardiovascular event and mortality in different patient's population. Patients with kidney failure have more frequent and more severe MAC. The aim of this study is to assess the prognosis role of MAC in renal transplant recipient (RTR).
Methods: between feb 2004 and jan 2005, all the RTR followed in the nephrology department were asked to take part this study and underwent a complete 2D echocardiography and a vascular scanner. All the echos were reanalysed for MAC. MAC extent and distribution were graded semiquantitatively (0 = no calcification, 4 severe calcification) using 2D echocardiography. Demographic and clinical characteristics (biological data, data related to renal failure and transplant) were extracted from the medical file. Follow up data was obtained from nephrology database, contact with referring nephrologist or GP.
Results: From the 300 RTR, echodata could be analysed for 279 RTR, mean age 52 ± 13years (168 (80% males), dialysis time before renal transplant (RT): 2.3 ± 2.3 y, time after RT 7.6 ± 8.3y). Mean creat: 1.6 ± 0.8 mg/dl. During a mean follow up of 11 ± 3 years, 114(48%) patients died. Because survival was related to time after RT, we divided our population in 3 groups: <5years, 5−10 years and >10 years after RT. In cox multivariate analysis adjusted for time after RT, survival was significantly related to: age ($p = .027$), ejection fraction ($p < .005$), posterior wall thickness ($p = .005$), MAC score ($p = .021$), aorta scanner calcification score ($p < .001$). Figure show the Kaplan meyer survival curve according to time after RT.

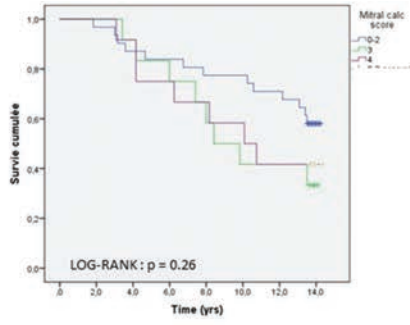
According to the 5 covariates isolated by the cox analysis, we could propose a risk score for prediction of survival in RTR: **Risk Score RTR =0,64 ($\log_{10}$[Ao +1]) – 0,04 EF +0,05 PWD +0,3 Mitral calc score +0,04 âge (EF: ejection fraction, PWD: posterior wall thickness))**
Conclusions: In RTR, MAC are an important risk factor for mortality specially in the first years after RT. This emphasizes the importance of the control of cardiovascular risk factor in this population.



Survival according to MAC
RTR > 5 years



Survival according to MAC
> 5 RTR < 10 years



Survival according to MAC
> 10 years RTR

(Δ) Prediction of outcome in primary and secondary mitral regurgitation using the average pixel intensity method on echocardiography

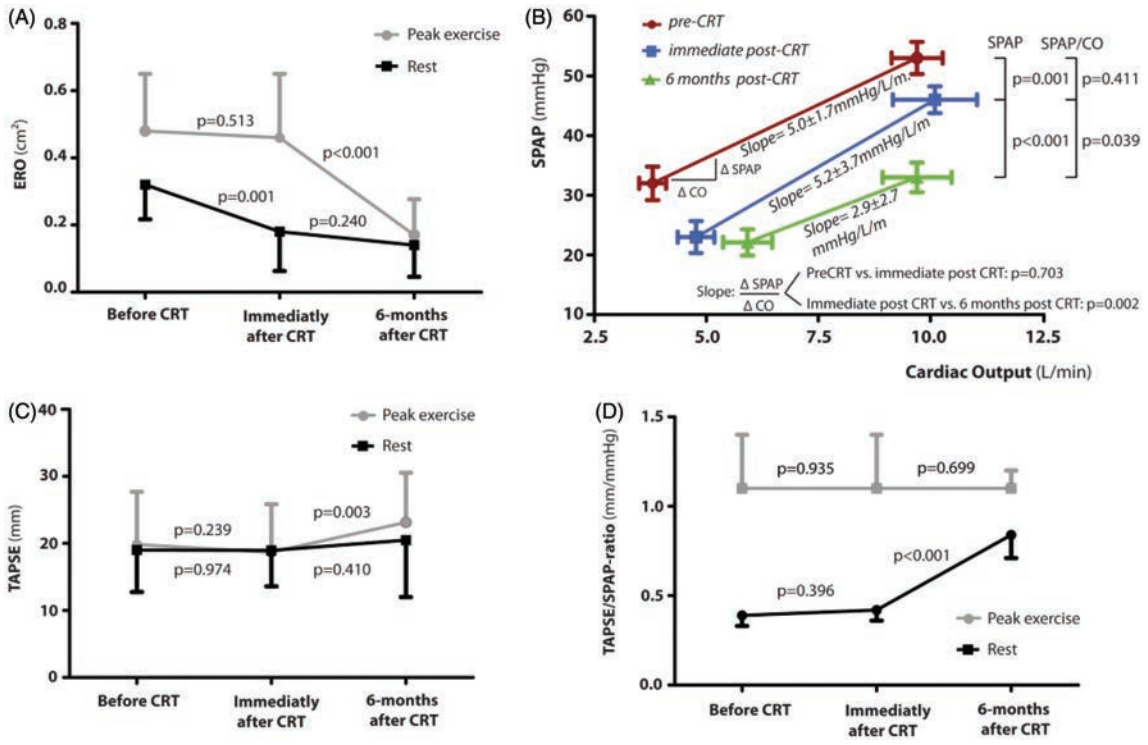
Victor Kamoen, Milad El Haddad, Marc De buyzere, Tine De Backer and Frank Timmermans
UZ Gent

Background: Mitral regurgitation (MR) can be either primary due to prolapse of the mitral valve (MVP-MR) or can result from ventricular dysfunction (secondary or functional MR (FMR)). The echocardiographic grading of MR is challenging and the recommended grading parameters have several important limitations. We developed and validated a novel echocardiographic parameter to grade MR, the average pixel intensity (API) method, based on pixel intensity analysis of the Continuous Wave Doppler signal.
Purpose: In this study, we assessed the long-term predictive value of the API method on clinical endpoints.
Methods: Transthoracic echocardiography was performed in consecutive MVP-MR ($n = 135$) and FMR patients ($n = 148$, ejection fraction <50%). MR was assessed using the API method, color Doppler, vena contracta width (VCW), effective regurgitant orifice area (PISA-EROA) and regurgitant volume (PISA-RV). The primary clinical outcome was major adverse cardiac event (MACE) in MVP-MR and cardiovascular mortality in FMR.
Results: The API method was feasible in 90% of all MR patients, which was significantly higher than the guideline-recommended parameters such as VCW, PISA-EROA and PISA-RV.
In MVP-MR, during a mean follow-up period of 17 months, 41 patients (34%) had a clinical event during the follow-up period (all-cause mortality (4%), mitral valve surgery (27%), percutaneous mitral intervention (2%) or heart failure hospitalization (2%)). On Mantel-Cox test, the degree of MR severity by the API method was highly significant for the prediction of events ($p < .001$) with a higher sensitivity and specificity compared to PISA-EROA and VCW.
In FMR, 36 patients (25%) died of heart failure during a mean follow-up period of 27 months. On multivariate Cox regression analysis, the API method was predictive for cardiovascular mortality and this was independent of ejection fraction.
Conclusions: The API method is a feasible and reproducible MR grading tool that is predictive for clinical outcome in primary and secondary MR. Therefore, the API method may be considered for the echocardiographic grading of MR severity in clinical practice.

(*) An exercise hemodynamic evaluation of the acute and chronic effects of CRT on right ventricular-arterial coupling and pulmonary vascular reserve

Pieter Martens[a], Frederik Verbrugge[a], Philippe Bertrand[a], David Verhaert[a], Pieter Vandervoort[a], Matthias Dupont[a], WH Wilson Tang[b], Stefan Janssens[c] and Wilfried Mullens[a]
[a]Ziekenhuis Oost Limburg; [b]Cleveland Clinic; [c]UZ Leuven

Background: The acute and chronic effects of cardiac resynchronization therapy (CRT) on pulmonary pressures, right ventricular (RV) function and right ventricular-arterial coupling during exercise are insufficiently understood. Yet, these factors are strongly associated with functional status and outcome.
Methods: Heart failure patients with reduced ejection fraction (HFrEF) indicated for CRT were prospectively included to undergo exercise echocardiography simultaneously with cardiopulmonary exercise testing (CPET) before (pre_CRT), 1-day after (post_CRT) and 6-months (post6_CRT) after CRT-implant. Right ventricular-arterial coupling was assessed by the TAPSE/SPAP-ratio. Pulmonary vascular reserve was assessed as the slope of ΔSPAP/ΔCardiac Output (CO) -ratio.
Results: A total of thirty-one HFrEF-patients (age = 66 ± 13 years), were prospectively included. CRT resulted in an immediate reduction in inter- and intraventricular dyssynchrony, resulting in a reduction in rest SPAP (pre_CRT = 32 ± 16mmHg vs. post_CRT = 23 ± 16 mmHg; p = 0.006) and rest effective regurgitant orifice (ERO; pre_CRT = 0.32 ± 0.1 vs. post_CRT = 0.18 ± 0.2; $p = .001$) without changes in the degree of exercise induced mitral regurgitation (MR – panel A) or exercise SPAP indexed for cardiac-output (panel B). Six-months following CRT, in parallel with left ventricular reverse remodeling and a reduction in exercise MR and exercise E/e'-ratio, the exercise SPAP/CO significantly improved (post_CRT = 5.6 ± 3.1 mmHg/L.m^{-1} vs. post6_CRT = 4.3 ± 2.9 mmHg/L.m^{-1}; $p = .039$), which was also illustrated by a reduced slope of ΔSPAP/ΔCO (post_CRT = 5.2 ± 3.7 mmHg/L.m^{-1} vs. post6_CRT = 2.9 ± 2.7mmHg/L.m^{-1}; $p = .002$; panel B). CRT did not result in an acute or chronic effect on TAPSE or TAPSE/SPAP-ratio at rest. However, exercise revealed the presence of right ventricular-arterial uncoupling before CRT-implant which was not affected by an acute CRT effect ($p = .396$) but only improved by a chronic CRT effect ($p < .001$; TAPSE/SPAP-ratio: pre_CRT = 0.39 ± 0.6 mm/mmHg; post_CRT = 0.42 ± 0.5 mm/mmHg; post6_CRT = 0.84 ± 0.12 mm/mmHg; Panel C/D). Of all exercise echocardiography variables, the TAPSE/SPAP-ratio demonstrated the strongest correlation with VO2 peak (r = 0.475), VE/VCO2 (r = −0.585) and workload (r = 0.476) during CPET ($p < .05$ all). Multivariate predictors determining improvement in exercise ventricular-arterial coupling following CRT included metrics of residual exercise MR and systolic and diastolic LV-function.
Conclusions: A chronic CRT-effect (reverse remodeling), but not an acute CRT-effect (resolution of dyssynchrony) beneficially influences pulmonary pressures, pulmonary vascular reserve and right ventricular arterial coupling during exercise, with the latter strongly relating to functional status. These findings are mechanistically linked to left ventricular reverse remodeling with improved interventricular-dependence and a reduction in exercise MR.



(#) The detrimental effect of right atrial pacing on left atrial function and clinical outcome in cardiac resynchronization therapy

Pieter Martens, Sébastien Deferm, Pieter Vandervoort and Wilfried Mullens
Ziekenhuis Oost Limburg

Background: Data on the effects of right atrial (RA)-pacing on left atrial (LA) synchronicity, function and structure after cardiac resynchronization therapy (CRT) and its relation to clinical outcome are scarce.
Methods: Two CRT-cohorts were collected. First, a prospective *imaging cohort* of heart failure (HF)-patients in sinus rhythm and a guideline indication for CRT, to assess the impact of RA-pacing on LA-function, morphology and synchronicity. 2D atrial speckle tracking was performed by an independent and blinded investigator at baseline (pre-implant) and at 6-months following CRT-implant. Second, a retrospective *outcome cohort* of all consecutive HF-patients undergoing CRT-implantation between 2008 and 2016 was collected to assess the relation of RA-pacing with outcome, defined as reverse remodeling 6-months following CRT-implant, occurrence of new onset atrial fibrillation (AF) and HF-hospitalization and all-cause mortality. High versus low atrial pacing burden was defined as atrial pacing above or below 50% in both cohorts.
Results: Thirty-six patients were prospectively included in the *imaging cohort* (age = 68 ± 11 years). Six-months after CRT, patients with high RA-pacing burden showed less improvement in LA-maximum volume, minimum volume and total emptying-fraction ($p < .05$ for all). Peak atrial longitudinal strain, reservoir and booster strain-rate but not conduit strain-rate improved after CRT in patients with low pacing burden and worsened in patients with high pacing burden (see Figure – panel A). Only a high pacing burden induced significant intra-atrial dyssynchrony (maximum-opposing-wall-delay; 44 ± 13 msec vs 97 ± 17 msec, $p = .022$; – panel B). A total of 569-patients were included in the *outcome-cohort*. A high burden of RA-pacing independently predicted a diminished LV end-systolic volume reduction 6-months after implant ($\beta = -0.164$, 95%CI = [−16.006;-4.917], $p = .001$), higher burden of new-onset AF (41% vs. 22% at 37 ± 18 months follow-up; $p < .001$; after extensive multivariate correction), and a higher HF-hospitalization and mortality rate ($p = .002$).
Conclusions: RA-pacing in CRT patients negatively influences LA-morphology, function and synchronicity, which is associated with worse clinical outcome including diminished LV- reverse remodeling, increased risk for new onset AF, HF-hospitalization and mortality. Strategies reducing RA-pacing burden might be warranted, in order to optimally sustain LA synchronicity and function following CRT-implant.

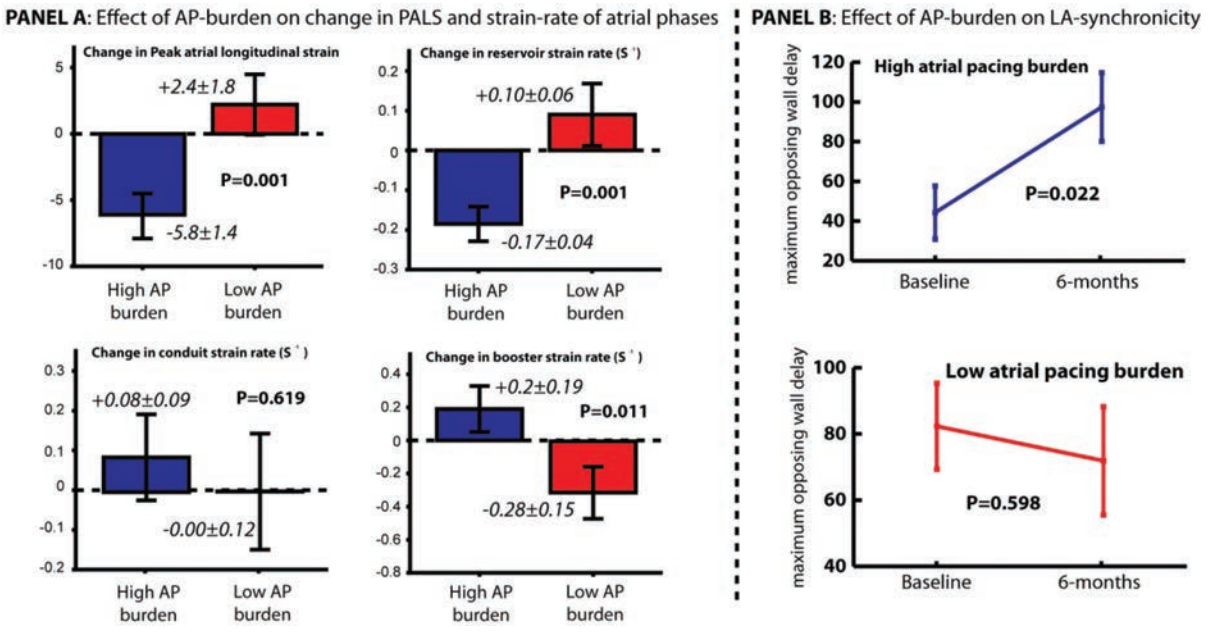


Figure. Effect of RA-pacing on LA function (panel A) and synchronicity (panel B).

Isolated left ventricular non compaction: revelation modes, predictors of mortality, and mri utility: experience of the first moroccan department of cardiac MRI through 26 cases

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Mohammed V Military Hospital, Morocco

Background: Isolated left ventricular non compaction (ILVNC) is a rare congenital cardiomyopathy resulting from the failure of myocardial development during embryogenesis. Its main characteristic is the existence of many prominent ventricular trabeculae and deep intertrabecular recesses, mostly localized in the apex of the left ventricle.

Methods: -A retrospective, descriptive and analytical study was conducted on a series of 26 patients diagnosed with ILVNC by echocardiographic and MRI criteria, coming from various areas of Morocco, over a period of nine years -between January 1st, 2009 and September 1st, 2018.

- The 26 patients were selected according to the criteria of Oechslin: (1) Absence of coexisting cardiac abnormalities (others that 2-4 below). (2) Thickened myocardium with a two-layered structure consisting of a thin compacted epicardial layer/band (C) and a much thicker, non-compacted endocardial layer (N) or trabecular meshwork with deep endomyocardial spaces; N/C ratio >2.0. (3) Predominant location of the pathology: mid-lateral, mid-inferior, and apex. (4) Colour Doppler evidence of deep intertrabecular recesses filled with blood from the left ventricular cavity.
- The data were introduced on the software IBM SPSS statistics20.

Results: −15% of the patients were asymptomatic with: a nonspecific pathological EKG, a systematic assessment of an extracardiac pathology or a family investigation.

- Our echocardiographic results join the ones of literature as the preferential localization of ILVNC is mid-latero-apical in 86% and mid-inferior in 62% of the cases.
- Coronarography was conducted in order to research an anomaly of birth of the coronary arteries or an ischaemic heart disease. Coronaries were healthy in 70% of the cases.
- 14 patients (54%) of our series were followed for a dilated cardiomyopathy of unspecified origin during a period of one -3 years. MRI had enabled the diagnosis of ILVNC.
- Mortality in our series is about 14%.
- The identified factors of mortality are: DTDVG >65 mm ($p = .003$), iterative pushes of IVG ($p = .002$), one FEVG <30% ($p = .01$), chronic F ($p = .04$), a BBG ($p = .01$), a report NC/C >2,2 ($p = .01$) and a number of not compacted segments >6 ($p = .02$) with an IC with 95%.

Conclusions: The echocardiography remains the tool of reference and the MRI should probably be used more systematically because of its best resolution. This diagnosis implies a family assessment and sometimes genetics which remain non accessible in a Third World country like Morocco, Our series remains conclusive even if the number is restricted.

Two D echocardiographic evaluation of left ventricular diastolic function after beating heart closed mitral valvotomy (CMV) in rheumatic mitral stenosis

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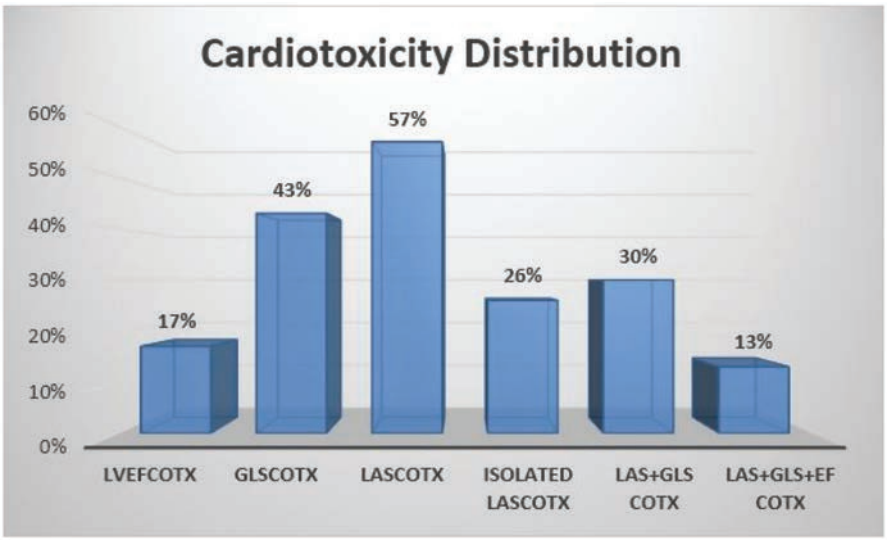
Background: Diastolic dysfunction is seen in patients of rheumatic severe mitral stenosis. This study investigates the effects of left ventricular diastolic function on outcome in patients with rheumatic mitral stenosis undergoing closed mitral valvotomy.
Methods: This is a single centre two year comparative study consisting of 60 patients. We evaluated preoperative and post operative transthoracic Two D echocardiographic parameters of diastolic function and compared both data to evaluate improvement of diastolic function.
Statistical analysis: The statistical analyses were performed on SPSS (Statistical Package for Social Sciences). A two-sided (fi =2) p value less than 0.05 ($p < .05$) was considered statistically significant.
Results: Maximum patients were in New York heart association (NYHA) grade 3. Wilkins score ranged from 6 to 10. Mitral valve area (MVA) increased from 0.77 ± 0.13 to 2.32 ± 0.26, Ejection fraction (EF) increased from 61.38 ± 4.61 to 64.79 ± 3.22, Deceleration time, (DT ms) decreased from 231.55 ± 49.31 to 168.28 ± 14.30, E/A ratio reverted to 1.70 ± 0.54 from 0.89 ± 0.39. Total ejection isovolume (TEI) index improved from 0.50 ± 0.03 to 0.39 ± 0.06, Mitral inflow propagation velocity, (MIPV cm/sec) increased from 47.28 ± 3.71 to 57.86 ± 3.19. Peri-operative and follow up was uneventful
Conclusions: Surgical closed mitral valvotomy produce excellent and comparable early hemodynamic improvement, significant improvement in clinical stage of disease and improvement in diastolic function. It remains a simple, safe, and effective means of treating mitral stenosis in regions where socioeconomic changes have not yet reduced the incidence of rheumatic heart disease and where resources for its treatment are limited there is still a place for this procedure.

Left atrial cardiotoxicity in breast cancer patients undergoing chemotherapy

Evangelos Stefanidis, Asim Katbeh, Anna Pipertzi, Etel Silva, Anastasios Milkas, Zsuzsanna Balogh, Kathy De Knijf, Martin Penicka and Guy Van Camp
OLV Aalst

Background: In breast cancer patients, chemotherapy (CHEM) is known to be associated with left ventricular (LV) dysfunction due to cardiotoxicity. However, data on the effects on left atrial (LA) function in patients receiving CHEM are scarce. Therefore, we aimed to compare effects of CHEM on LA contractile strain (LAS) with effects on LV global longitudinal strain (LV GLS) and ejection fraction (LVEF) in breast cancer patients undergoing CHEM including Anthracyclines, Alkylating agents, Taxanes and Trastuzumab.
Methods: We have prospectively enrolled 23 consecutive breast cancer patients (age 53 ± 10 years, 100% females) with normal LVEF (>50%) undergoing CHEM. All patients were treated with Epirubicin and Cyclophosphamide followed by either Docetaxel (30%) or Paclitaxel (70%). Trastuzumab was administered in 18 (78%) individuals. No patient had history of cardiovascular or internal disease. Comprehensive transthoracic echocardiography was performed at baseline and then at 3-month intervals. Cardiotoxicity was defined in three different ways according to each parameter as a >5% symptomatic or >10% asymptomatic decrease in LVEF to <50% (LVEFctox), by a reduction of LV GLS magnitude >12% (GLSctox) or LAS magnitude by >15% (LASctox), from baseline.
Results: LVEFctox was observed in 4 (17%), GLSctox in 10 (43%) and LASctox in 13 (57%) patients ($p = .021$) (Figure). A total of 4 (100%) and 3 (75%) patients with LVEFctox had also GLSctox and LASctox, respectively. In patients with GLSctox, a concomitant LASctox was noted in 7 (70%) patients. Isolated LASctox occurred in 6 (26%) patients. Significantly more patients who received Docetaxel developed GLSctox than those having received Paclitaxel (86% vs 6%, $p = .019$). In contrast, similar proportion of patients with LASctox (57% versus 56%, ns) was observed in both treatment arms. On the other hand, the isolated LASctox was overwhelmingly observed (100%) in patients having received Paclitaxel.
Conclusions: Left atrial cardiotoxicity, both isolated and concomitant with LV cardiotoxicity, occurs in a large proportion of breast cancer patients undergoing CHEM. The potential impact of the left atrial cardiotoxicity on clinical outcome needs to be investigated in a long-term prospective study.



Clinical characteristics and outcomes of aortic valve endocarditis: a single center experience

Laurence van der Haert, Agnes Pasquet, Berhnard Gerber, David Vancraeynest, Jean-Louis Vanoverschelde and Jean Cyr Yombi

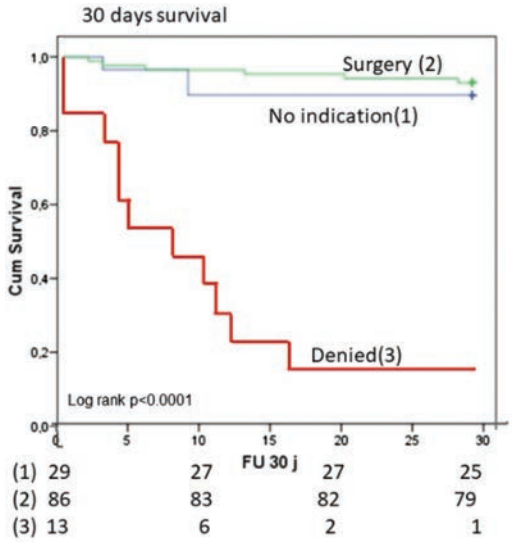
Cliniques Universitaires Saint-Luc

Background: Despite improvement in diagnosis and management, infectious endocarditis (IE) remains associated with high mortality and serious complications. Therefore we decided to review our experience in patients with isolated acute IE on native aortic valve (IENAV). The aim of this study was to assess mortality and determine risk factors associated to poor prognosis.

Methods: IENAV patients were recruited from 3 databases (cardiothoracic surgery, echolab, minimum clinical summary). Patients with IE on other valves than aortic valve, on prosthesis or device were excluded. Demographic and clinical characteristics (echocardiographic, biological data, and data related to IE) were extracted from the medical file. Follow up data was obtained from surgery database, contact with referring cardiologist or GP. For each patient, diagnosis of IE was verified according to Duke's modified criteria and the Euroscore and Charslton score were calculated. Mortality at 30 days, 1 year and at the end of follow up was calculated.

Results: In total, 128 patients with IENAV were included. The mean age was 59 ± 15 years (range 24-85) and 103 (80%) male. During a mean follow up of 51 ± 55 months (range 0–187), 61 (48%) patients died. Survivors were younger (55 ± 13 vs 63 ± 11 y $p < .01$), had a lower Euroscore 4.5 ± 6.2 vs 8.5 ± 10 $p < .01$, and less frequently shock. According to Dukes modified criteria, EI was definite in 102 (86%) patients and possible in 26 (20%) patients. No germ was demonstrated in 13 (10%) patients, staphylococci was present in 45 (35%). Mean duration of antibiotics treatment was (38 ± 17 days), 90 (70%) were treated with 2 antibiotics and 31 (24%) with only 1 antibiotics. 86 (67%) patients were treated by surgery (34 (40%) bioprosthesis, 27 (31%) homograft) and 42 (33%) in whom 13 (31%) were denied for surgery and 29 (69%) did not have surgical indication, were treated medically. 18 (14%) patients died at 30 days,3 in the group without surgical indication (3 shock, 1 infection), 4 in the surgical group (2 infectious shock, 1 neurologic complication, 1 acute coronary syndrome) and 11 in the group denied for surgery (2 infection, 3 neurological complication, 3 heart failure, 1 haemorrhagic shock, 2 cardiogenic shock) ($p < .0001$) (figure). At 1 year, 36 (28%) died, 10 (34%) in group without indication of surgery, 13 (40%) in the surgical group (p = ns for survival), all the patients denied for surgery died. In patients treated by surgery, staphylococci was associated with a worse prognosis ($p < .05$). Cox univariate analysis determinant 1 year survival, were: Charlston score ($p < .005$), Euroscore ($p < .001$), haemoglobin at admission ($p < .05$), kidney failure ($p < .01$), germ ($p < .05$), shock ($p < .01$), surgery ($p < .001$). Emboli, age, diabetes were not related. In multivariate analysis, only kidney failure ($p = .002$), Euroscore ($p = .002$), staphylococci ($p = .03$) and surgery ($p < .001$) precited 1 year survival.

Conclusions: Nowadays, IENAV remains a disease with a high mortality rate at 30 days and one year. Kidney failure and staphylococcus remain high risk factors. Surgery had a favourable impact on survival. All Patients with indication of surgery who were denied for surgery died. It is therefore important to manage IE with multidisciplinary team dedicated for IE.

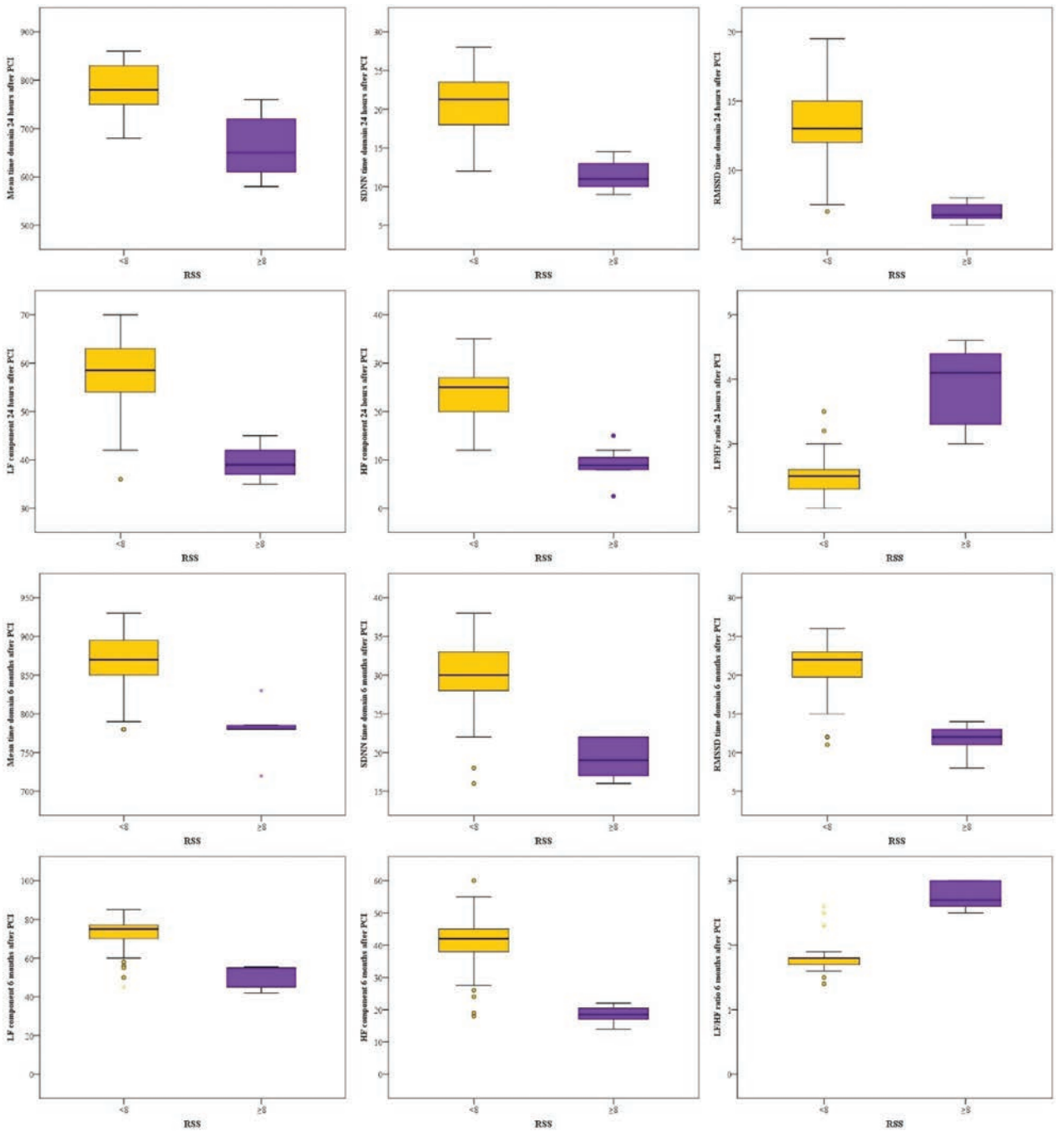


Invasive/Interventional cardiology

The impact of completeness of revascularization by percutaneous coronary intervention in patients with coronary artery disease on the autonomic modulation of the heart

Mahmoud Abdelnabi, Moataz Zaki, Mohamed Sadaka and Moustafa Nawar
Alexandria University, Egypt

Background: Type of revascularization has been the main concern for better clinical outcome in CAD patients.To evaluate the impact of completeness of revascularization assessed by Residual SYNTAX Score (RSS) in coronary artery disease (CAD) patients undergoing elective PCI on the cardiac autonomic modulation assessed by heart rate variability (HRV).
Methods: A prospective study included 100 patients undergoing elective PCI when indicated either by patient's symptoms or if there is an evidence of ischemia either by a stress test or post-acute coronary syndromes (ACS) excluding patients with contraindication to contrast, dual antiplatelet therapy, patients with atrial fibrillation or multiple premature beats, patients receiving anti-arrhythmic drugs except class II, IV and patients who underwent previous Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG). SYNTAX score (SX) and RSS were calculated before and after PCI to determine the completeness of revascularization using SYNTAX score calculator software. Complete revascularization (CR) was defined as RSS <8 while incomplete revascularization (IR) was defined as RSS ≥ 8. A short-term HRV measurement was performed before PCI, 24 hours and 6 months after PCI at the same time of the day using CheckMyheart^{TM} handheld HRV device from DailyCare BioMedical Inc, Taiwan. HRV data were interpreted by CheckMyheart^{TM} 5-min HRV analysis software using the standard methods for HRV measurement as discussed in the Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology.
Results: Baseline patient characteristics included 85 males and 15 females, with a mean age of 56.89 ± 10.7 years. As regards risk factors, 41 patients were diabetics, 47 hypertensives, 54 smokers, 11 had a family history of CAD, 8 dyslipidemic and 4 had miscellaneous diseases. 6 patients had typical ischemic symptoms, 8 had a positive stress test, while 86 had a history of ACS. mean heart rate was 77.95 ± 11.79 beats/minute, mean ejection fraction was $54.03 \pm 11.08\%$. mean SX score was 13.11 ± 8.52. 42 had multi-vessel CAD while 58 had a single vessel CAD. TVR was a single vessel in 69 patients, 31 was multi-vessel. Mean RSS was $2.0 \pm 5.77.90$ patients had CR, while 10 had IR. There was a statistically significant difference between time and frequency domain HRV parameters 24 hours and 6 months after PCI in patients who had CR with those who had IR. Time domain parameters included mean time, SDNN, RMSSD which was lower in patients with RSS ≥ 8 and statistically higher in patients with RSS <8 (p-value $<.001$). Frequency domain parameters included LF, HF which was lower in patients with RSS ≥ 8 and statistically higher in patients with RSS <8 (p-value $<.001$) and LF/HF ratio was higher in patients with RSS ≥ 8 and statistically lower in patients with RSS <8 (p-value $<.001$).
Conclusions: CR was associated with an improved autonomic modulation assessed by HRV after PCI. Based on the results of the current study, CR whenever feasible is recommended in CAD patients for an improved autonomic modulation and overall survival.



Comparison between HRV parameters with CR and IR 24 hours and 6 months after PCI

The impact of different characteristics of coronary artery disease patients on the cardiac autonomic modulation

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Background: Several patient characteristics are involved in affecting cardiac autonomic function. Autonomic dysfunction is associated with increased cardiovascular morbidity and mortality. So we aimed to study the impact of different clinical and angiographic characteristics of coronary artery disease (CAD) patients on the cardiac autonomic modulation assessed by heart rate variability (HRV) measurement.
Methods: A prospective study which included 100 patients undergoing elective coronary angiography when indicated either by patient's symptoms or if there is an evidence of ischemia either by a stress test or post-acute coronary syndromes (ACS) excluding patients with contraindication to contrast or dual antiplatelet therapy, patients with atrial fibrillation or multiple premature beats, patients receiving anti-arrhythmic drugs except class II, IV and patients who underwent previous PCI or CABG. Throughout clinical history and examination, electrocardiographic, echocardiographic and angiographic assessment with SYNTAX score (SX) calculation using SYNTAX score calculator software was done. short-term HRV measurement was performed using CheckMyheart^{TM} handheld HRV device from DailyCare BioMedical Inc, Taiwan. HRV data were interpreted by CheckMyheart^{TM} 5-min HRV analysis software using the standard methods for HRV measurement as discussed in the Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology.
Results: Baseline patient characteristics included 85 males and 15 females with mean age of 56.89 ± 10.75 years. 41 diabetics,47 hypertensives,54 smokers,11 patients had a family history of CAD,8 had dyslipidemia and 4 had other miscellaneous diseases. 6 had CSA-CCS II, III, 8 had a positive stress test, while 86 had a history of ACS, mean SX score was 13.11 ± 8.52 with 87 patients had a low SX, 9 had intermediate SX and 4 had a high SX. 42 patients had multi-vessel CAD while 58 had a single vessel CAD. Multivariate linear analysis logistic regression of the different patient characteristics that affect HRV revealed that the type of CAD whether single or multi-vessel and SYNTAX score are the strongest independent factors that affect HRV in CAD patients.
Conclusions: Complexity of CAD quantified by SYNTAX score is by far the strongest independent factor in patients with CAD affecting the cardiac autonomic modulation assessed by HRV measurement

Long-term outcome of medical treatment in patients with angiographic intermediate coronary stenosis and a negative fractional flow reserve-measurement: a cohort study

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[a]Antwerp University; [b]Heilig Hart Ziekenhuis; [c]AZ Klina

Background: Fractional flow reserve (FFR) is a valuable tool to guide therapeutic decisions on angiographically intermediate coronary stenosis. Current evidence supports deferral of revascularization for lesions with FFR values >0.80. Little data are available, however, on the long-term outcome of medical therapy in patients with FFR-negative intermediate lesions.
Purpose: To investigate the long-term clinical outcome of patients with an FFR-value of >0.80 who were treated with medical therapy, and to investigate the effects of risk factors for occurrence of major adverse cardiac events (MACE) in this cohort.
Methods: The files of patients who underwent FFR measurement for angiographically intermediate coronary lesions in our university hospital between January 2009 and December 2014 were retrospectively evaluated. All patients in whom revascularization was deferred, based on FFR >0.80, were included. Baseline patient characteristics were collected, including cardiovascular risk factors, and characteristics of the coronary lesions at the time of FFR measurement. At the last known follow-up medication use was registered. The occurrence of MACE, defined as cardiac death, acute myocardial infarction or target vessel revascularization, during the longest available clinical follow-up was recorded. To quantify the effect of the variables on the outcome, a cox-proportional hazards survival analysis was performed. Additionally, a propensity weighted analysis was performed to study the potential effect of statin use on the outcome.
Results: A total of 708 patients (489 (69%) men and 219 (31%) women) with 957 coronary lesions were included in the study. The median age of the included patients was 67 years (IQR = 59–74). Most of the lesions were in the LAD, respectively followed by the RCX, RCA, LMCA and venous bypass grafts. The median FFR value was 0.89 (IQR 0.86-0.93). During a median follow up of 34 months (IQR = 20–48) 101 patients (14%) experienced a MACE. Target lesion revascularisation in 79 patients (11%) was the most frequent encountered MACE. The effect on MACE of the following variables was studied in a multivariable analysis: arterial hypertension, dyslipidaemia, diabetes mellitus, smoking status, BMI, cardiovascular history (ACS, PCI and/or CABG), chronic kidney disease, FFR value and medication use at follow up. Cox-regression demonstrated that the absolute FFR-value (HR: 0.93 95% CI 0.90–0.97; $p < .01$), any cardiovascular history (HR: 1.58 95% CI

1.10–2.29; $p = .02$), and chronic kidney disease (HR: 2.33 95% CI 1.50–3.61; $p < .01$) were significantly associated with the occurrence of MACE. Similar results were found using only target vessel revascularisation as endpoint. Propensity weighted analysis to correct for confounders could not demonstrate a significant relation between the use of statin (at the latest follow up) and MACE (HR 0.99, 95% CI 0.55–1.79), even after correction for cholesterol levels at last follow up.
Conclusions: After a median follow-up of 3 years, 86% of the included patients treated medically for FFR-negative intermediate coronary stenosis had a favourable outcome. No significant association between medication usage and MACE could be found in our heterogeneous study population. The inverse relation of the absolute FFR value and the risk for MACE, mainly driven by late revascularisation, was confirmed. Patients with any cardiovascular history and/or with chronic kidney disease had the highest risk for MACE.

(#) Time quality indicators for ST elevation myocardial infarction and relation to in hospital mortality: results from the Belgian STEMI database

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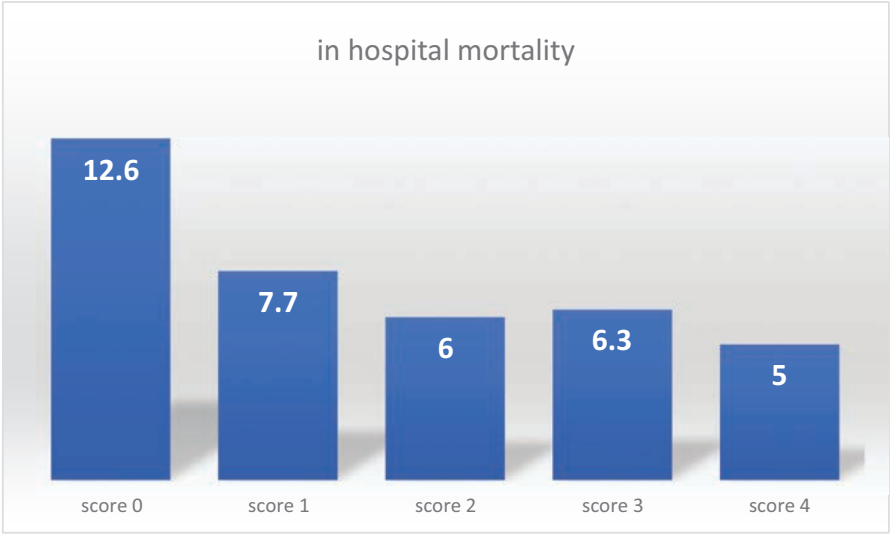
Background: Applications of established quality indicators for ST elevation myocardial infarction (STEMI) are only valid if there is a gap between evidence and practice and whether this gap results in worse outcome. Previous evaluation of the Belgian STEMI database revealed good adherence to most of the STEMI recommendations except for time delays between diagnosis and treatment. The present study aims to investigate the relationship between variation in time delay and in hospital mortality in Belgium STEMI patients treated with primary percutaneous coronary intervention (pPCI).
Methods: A total of 5776 STEMI patients, admitted in 55 Belgian hospitals during the period 2015–2017 were enrolled in the STEMI database and had complete time data available. Diagnosis-to-balloon time (DiaTB) and door-to-balloon (DoTB), defined as time between arrival in the PCI center and first balloon inflation, were correlated to in hospital mortality with correction for differences in baseline risk profile (TIMI risk score). A time quality score (0–4) was assigned to each patient according to summation of following rules: DiaTB >120 min = 0; DiaTB 90–120 min = 1, DiaTB <90 min = 2 and DoTB >90 min = 0; DoTB 60–90 min = 1; DoTB <60 min = 2.
Results: The average time quality score was 2.9 ± 1.3 with good adherence to recommended time lines (score 4) in 47% of the patients and lack of adherence (score 0) in 7.6% of the patients. In hospital mortality was 6.2%. There was a significant independent correlation between the time quality score and the in-hospital mortality (adjusted OR 0.81 (95% CI 0.7–0.89) with observed mortality rates of 12.6% in pts with score 0 and of 5.0% in patients with score 4 (see Figure). Additional analysis revealed that DoTB was a better outcome predictor than DiaTB. The time quality score increased from 2.8 in 2015 to 3.1 in 2017 ($p = .001$) but without significant effect on mortality.
Conclusions: Good adherence to recommended time lines was present in only half of the Belgian STEMI patients and was associated with the lowest in hospital mortality rate. A more systematic implementation of this time quality indicator will help to improve current inequities in quality of care in Belgium.



In vivo and *in silico* study of the flow-obstruction secondary to two devices measuring fractional flow reserve

Stéphane Carlier[a], Astrid Delpature[b], Alessandro Scalia[b], Julien Saussez[b] and Gregory Coussement[b]
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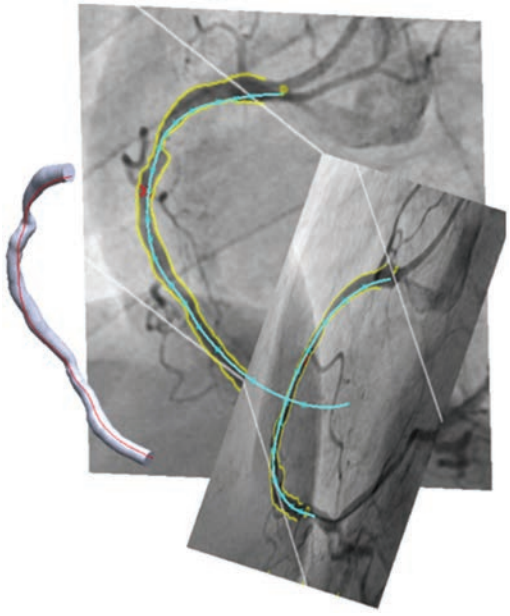
Background: Fractional flow reserve (FFR) can be measured with a wire or a monorail microcatheter with built-in pressure-sensor. We sought to quantify the flow-obstruction and secondary increased pressure gradient (ΔP) of each device *in silico* and *in vivo*. We reviewed also our clinical experience with both systems.
Methods: Idealized 15-mm long coronary stenosis of 40, 50 and 60% in diameter in vessels of 2.5, 2.75 and 3.0 mm were constructed with meshes of 1.10^6 nodes. ΔP for flow rates (Q) up to 100 ml/min with or without the presence of a FFR device across the stenosis were assessed by computational fluid dynamic solving the Navier-Stokes equations. In vivo, 2 orthogonal angiographic views were recorded to reconstruct in 3-D coronary arteries of patients with mild-to-moderate stenosis. An approximate mesh of the artery and the catheter inside was reconstructed from the path of its projection and ΔP for different flow rates were also derived from simulation and compared to FFR recordings under iv adenosine.
Results: Without a stenosis, ΔP at $Q = 100$ ml/min was $\sim$8 mmHg in a simulated artery of 3 mm, with or without a 0.014″ FFR-wire or a 0.022″ FFR microcatheter, when both systems were close to the wall. Gradients were twice larger with a device in the centre of the lumen. *In silico* other geometries showed an increased influence of any device on ΔP for smaller vessel and increased diameter stenosis. Similar flow-obstruction issues were calculated on *in vivo* 3-D reconstructed coronary arteries. The relative error on the pression gradient defined as $(\Delta P_{\text{with FFR device}} - \Delta P_{\text{w/o device}})/\Delta P_{\text{w/o device}}$ and the relative diameter of the FFR device defined as $\text{Dia}_{\text{FFRcatheter}}/\text{Dia}_{\text{Stenosis}}$ were exponentially highly correlated ($R^2 = 0.9$). For example, in a 50% diameter stenosis in a vessel of 2.5 mm, a 0.014″ wire increases ΔP by 4 mmHg, but a 0.022″ microcatheter by 9 mmHg, potentially crossing the grey-zone for a FFR$\sim = 0.8$, and artificially increasing its physiological significance.

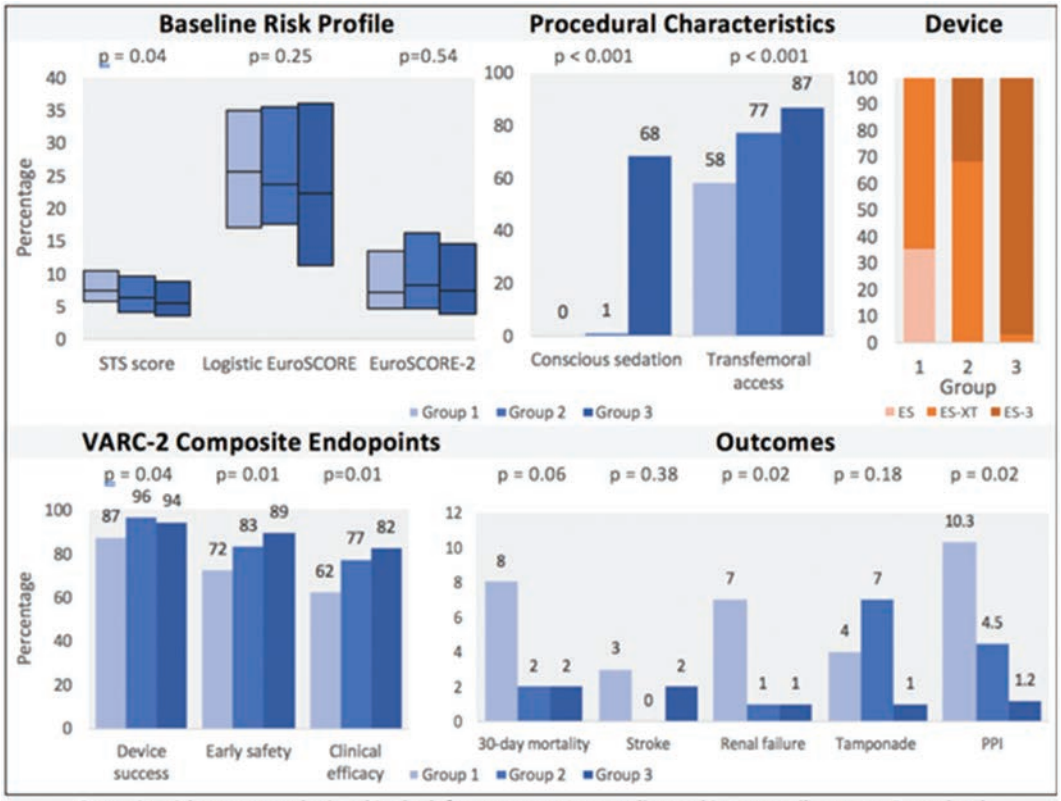
Conceptually, a pressure-wire might not cross difficult lesions while a workhorse wire would, on which a FFR-microcatheter could be advanced. However, in our clinical data base reviewed over 2 years, among 1009 coronary angiography and 315 PCI, we used 41 FFR-microcatheters and failed to cross 3 times lesions, while we could cross all attempted stenosis with 73 FFR wires.
Conclusions: Clinically significantly higher pressure gradients are measured in small simulated diseased coronary arteries with a microcatheter than with a FFR wire. In daily practice, these microcatheters showed a higher failure rate to cross tortuous lesions. This highlights the influence of a device used to measured FFR, mainly in small coronary arteries, that might lead to falsely pathological FFR results.



(#) Temporal trends in 10 years of transcatheter aortic valve implantation: 30-day outcomes in a single Belgian center

Henri Gruwez, Christophe Dubois, Peter Verbrugghe, Tom Adriaenssens, Steven Jacobs, Steffen Rex, Johan Bennett, Bart Meuris, Walter Desmet, Filip Rega, Marie-Christine Herregods and Paul Herijgers
UZ Leuven

Background: Transcatheter aortic valve implantation (TAVI) has become a widely-recognized treatment for patients with severe aortic valve stenosis (AS) who are at high or prohibitive surgical risk. The aim of this study was to assess performance trends and 30-day clinical outcomes of all TAVI procedures in our center over a 10-year period.
Methods: All TAVI performed for native AS at a single tertiary center between March 2008 and February 2017 were included in the registry. The patient population ($n = 300$) was divided in three consecutive cohorts of 100 patients for analysis of temporal trends. Clinical outcomes are reported according to the Valve Academic Research Consortium II.
Results: Main results are presented in Figure 1. Overall perioperative risk according to the STS score was significantly higher in the early cohort (median [interquartile range] 7.4 [5.7–10.5]; 6.2 [4.1–9.7]; 5.6 [3.5–8.7]%; $p = .04$), while logistic EuroSCORE (25.7 [17.0–35.0]; 23.6 [17.6–35.4]; 22.4 [11.4–36.2]%; $p = 0.25$) or EuroSCORE-2 (7.2 [4.8–13.6]; 8.2 [4.7–16.2]; 7.5 [3.8-14.7]%; $p = .54$) did not differ significantly. In cohort one, two and three, the rates of all-cause mortality and new permanent pacemaker implantation were 8%, 2%, 2% ($p = .06$) and 10.3%, 4.5% and 1.2% ($p = .02$), respectively. Device success, early safety and clinical efficacy improved significantly over time, from 87%, 72% and 62% in the first cohort to 94%, 89% and 82% in the latest cohort, respectively (p values were 0.04, 0.01 and 0.01, respectively).
Conclusions: 10 years of progressive changes in operator experience, implantation technique and device innovation led to significant improvements in the clinical results of TAVI in a single Belgian center, while the perioperative surgical risk remained invariably high. Overall major adverse cardiovascular event rate was low, despite the high-risk profile of patients. New permanent pacemaker implantation decreased to extremely low rates, and conscious sedation was implemented successfully.



Operative risk scores are depicted in the left upper corner as median and interquartile ranges. Procedural characteristics, device, VARC-2 composite endpoints and outcomes are depicted as frequencies. STS: Society of Thoracic Surgeons; ES: Edwards Sapien; ES-XT: Edward Sapien XT; ES-3: Edward Sapien 3; VARC-2: Valve Academic Research Consortium 2; PPI: Permanent pacemaker implantation; Renal failure is defined as acute kidney injury stage 2 or 3, following the Acute Kidney Injury Network (AKIN) classification

Figure 1.

Temporal changes in the practice of interventional cardiology related to belgian legislation adaptation: a real-life retrospective analysis in a single high- volume centre

Olivier Gach
CHU Sart Tilman Liége

Background: In 2014, a modification of the Belgian legislation enabled under strict conditions new B1-B2 cardiology centres to perform interventional cardiology therapy leading to the creation of new B2 centres.
Purpose: The objective of this study was to evaluate the clinical and medical impacts on our B3 high-volume centre.
Methods: 2 periods of activity in our institution have been analysed: Pre new B2 period (P1) from 01/01/2014 to 30/06/2014 and post new B2 period (P2) from 01/01/2017 to 30/06/2017. During these periods, all patients admitted in our centre for interventional cardiology procedure (diagnostic and therapeutic) were enrolled in the present study. Clinical, procedural, biological characteristics of the population and in hospital outcomes were compared.
Results: In the P1 period, 1726 patients were admitted whereas only 1394 patients were observed in the P2 period (−19.2%). Compared to the P1 period, in the P2 period we observed a significant reduction in elective PCI, in secondary transfer and in prescription of anti-platelet therapy ($p < .001$, $p < .001$ and $p = .05$, respectively), while there was a significant increase in structural interventions, urgent procedures and length of hospital stay ($p < .001$, $p < .001$ and $p = .05$, respectively). After logistic multivariate regression analysis performed to evaluate independent predictive factors of hospitalisation length stay, 8 parameters were found to be statistically significant (age, myocardial infarction, structural intervention, elective PCI, procedural complication, stents implantation and secondary transfer, $p < .001$ for all).
Conclusions: In the last years, after Belgian legislation adaptation, in a high-volume PCI centre, there was a significant decrease in the number of procedures performed during a 6-month period but an increase in length of hospital stay secondary to the modification of the treated patient's profile in term of co-morbidities, risk and prognosis. Economic impact of these modifications should be analysed by the authorities to allow funding adaptation. Yet, no data from new B2 centres have been published.

(Δ) Initial clinical experience and 6-month follow-up by coronary computed tomography angiography of a new bioresorbable magnesium-based stent

Chadi Ghafari, Nicolas Brassart, Philippe Brunner, Philippe Delmotte, Kathleen Thayse and Stephane Carlier
CHU A. Paré Mons

Background: Drug-eluting stents (DES) are the gold standard in percutaneous coronary interventions (PCI), but leave a permanent metallic "caging" of the treated vessels. Absorbable scaffolds were initially designed to overcome this limitation but the first generation stents made of poly-L-lactic acid demonstrated higher thrombosis rates. A new bioresorbable magnesium-based (Mg) stent coated by a biodegradable polymer eluting sirolimus has been developed, with promising results in the BIOSOLVE II and III studies.
Aim: We sought to characterize PCI results by coronary computed tomography angiography (CTA) at 6-month follow-up of patients treated with at least one Mg-based stent in our institution.
Methods: In this prospective observational study, since January 15, 2017, younger patients with de novo lesions were preferably treated by this new generation Mg-bioresorbable stent after pre-dilatation. Post-dilatation was systematically performed using a non-compliant balloon. Procedural and clinical data at hospital discharge and 6-month follow-up were collected along with the assessment of vessel size and in-stent minimal lumen area, well measured without any scaffold struts blooming artefact on CTA.
Results: To date, 22 Mg stents (mean diameter: 3.2 ± 0.3 mm, length 20.5 ± 4.3 mm) were successfully implanted in 20 patients. Acute coronary syndrome was the presenting diagnosis in 91% ($n = 18$) with acute myocardial infarction in 64% ($n = 14$). The left anterior descending artery was treated in 64% ($n = 14$). Mean age was 53 ± 6 years with male:female ratio 5:1. Calcifications on angiography were found in 8 lesions (36%). Post-dilatation mean balloon diameter was 3.5 ± 0.3 mm inflated at a mean 18 ± 2 atm. No major adverse cardiac events were noted up to 6-mo follow up. On CTA ($n = 6$ to date, further follow-up are ongoing and will be presented), proximal and distal stent markers were well visualized while scaffold struts were not discernible. Mean proximal and distal reference lumen area were respectively 8.8 ± 2.6 mm^2 and 5.4 ± 1.2 mm^2. Mean in-stent minimal lumen area (MLA) was 5.9 ± 2.9 mm^2, with no statistical difference

with the mean of the proximal and distal references (7.1 ± 1.8 mm^2, $p = .4$, Wilcoxon rank test). Significant in-stent restenosis was noted in only one patient who remains so far asymptomatic (MLA = 1.1 mm^2; reference vessel lumen area 5.5 mm^2).
Conclusions: Coronary CTA-scans at follow-up of patients treated by a second-generation Mg-based stent is fully interpretable. Stent struts do not produce any blooming artefact, allowing precise assessment of 6-month minimal lumen area in the stent. This offers an accurate non-invasive assessment of the late PCI results. In our limited experience, optimal stent deployment and late artery patency could be achieved without major adverse cardiac events. This highlights the potentials of this new Mg-bioresorbable stent and the use of coronary CTA for the clinical follow-up of the treated patients.

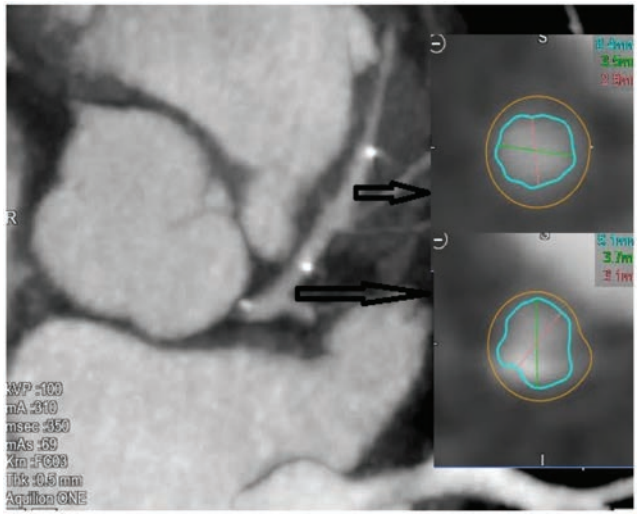


Figure 1. Cross sectional cut of proximal left anterior descending artery and in-stent minimal lumen area. The two radiopaque spots are the markers at the proximal and distal edges of the stent, without discernible struts in between.

Percutaneous balloon mitral valvuloplasty during pregnancy: our experience at IBN SINA Hospital

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Ibn Sina Hospital, Bangladesh

Background: Rheumatic mitral stenosis (MS) remains endemic in developing countries, it is also the most common form of valvular heart disease revealed or complicated during pregnancy. Percutaneous balloon mitral valvuloplasty (PBMV) is one of the treatment options available if the valve anatomy is suitable for balloon dilatation, it replaced surgical mitral commissurotomy as the preferred treatment of rheumatic MS. The objective of this study is to assess the immediate results of PBMV in symptomatic pregnant women with severe MS.
Methods: From November 2016 to February 2018, 10 pregnant women with symptomatic severe mitral stenosis underwent PBMV by Inoue balloon catheter technique in the department of Cardiology A at Ibn Sina hospital in Rabat. Statistical analysis was conducted by SPSS (Statistical Package for the Social Sciences) version 24.
Results: Mean age of patients was 31.5 ± 6.9 years, and mean gestational age was 6.9 ± 0.9 months. After the procedure, mitral valve area (MVA) increased from 0.9 ± 0.2 to 2.3 ± 0.3 cm2 ($p < .0001$). Mean mitral gradient recorded during transthoracic echocardiography decreased from 21 ± 6.6 to 6.9 ± 1.9 mmHg ($p < .0005$). Mean left atrial pressure measured during catheterization decreased from 34.8 ± 7.6 to 15.2 ± 5.9 mmHg ($p < .0001$). 2 cases of new-onset mild mitral regurgitation were observed after PBMV without statistical significance. During and immediately after the procedure, there were no maternal or fetal complications.
Conclusions: PBMV can be performed safely during pregnancy, with good immediate results.

Retrospective real-life registry of patients implanted with a bioresorbable vascular scaffold: a single center experience

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[a]CHU Mont Godinne; [b]Saint-Luc Bouge

Background: Bioresorbable vascular scaffold (BVS) consists of poly-L-lactic acid (PLLA), which is completely metabolized within 18 to 24 months. Recent data showed bad long-term outcomes in terms of late and very late scaffold thromboses compared to non-resorbable drug eluting stents.
Purpose: We reviewed the clinical outcome of a consecutive series of all-comer patients after BVS implantation in a non-academic hospital.
Methods and Results: Between November 2012 and June 2016, 84 patients (mean age 56 ± 9 years; 87% of males) were implanted with 93 BVS in our center. Follow-up was available in 83 of them for a mean duration of 27 ± 13 months. Clinical presentation was stable coronary disease in 77% of patients and acute coronary syndrome in 23% (including 17% of NSTEMI and 6% of STEMI). Almost half of the cohort had a previous history of revascularization by CABG (8%) or PCI (39%). BVS (length 21 ± 5mm, diameter 2.9 ± 3 mm) implantations mostly concerned LAD (58%) and 23% were FFR-guided. Pre-dilatation of the lesion was frequent (90%) but only 22% were pre- and post-dilated.

During the follow-up, two patients died of non-cardiac causes and four patients had target-vessel myocardial infarction [TVMI] with proven definite scaffold thrombosis treated by direct PCI. Target lesion failure [TLF] defined as a composite of cardiac death, TVMI, or ischemia-driven target vessel revascularization [ID-TLR] occurred in 13 patients (14%). Nine TLF (69%) occurred on DAPT, three (23%) on Aspirin and one on OAC monotherapy (8%). Most TLF (84%) occurred in the first 12 months after BVS implantation. Among the 9 ID-TLR, 5 were treated by PCI and 4 by CABG, including one patient who got both. By multivariate analysis, no factor significantly influenced the occurrence of TLF (especially pre- and post-dilatation) but calcified lesions approached the statistical threshold (OR 3 [0.69 – 12.7] p= 0.076).
Conclusions: In our all-comer population, a TLF rate of 14% was observed over a mean follow-up of 27 ± 13 months after BVS implantation. Most of these TLF (84%) occurred within the first year.

Long-term outcomes after foramen ovale closure

Mathieu Lempereur, Catherine Paris, Raluca Dulgheru, Stella Marchetta, Laurent Davin, Olivier Gach, Christophe Martinez, Patrick Maréchal and Patrizio Lancellotti
CHU Liège

Background: Patent foramen ovale (PFO) is a known cause of cryptogenic stroke, especially in individuals younger than 60 years old. One third of ischemic strokes are classified as cryptogenic. Recent randomized controlled trials have shown a benefit of PFO closure with a significant reduction in the rate of recurrent cerebrovascular events. We describe long-term outcomes after PFO closure for secondary prevention in cryptogenic TIA/stroke in our centre.
Methods: A total of 159 patients who underwent percutaneous PFO closure at CHU Sart-Tilman, Liège University Hospital, between January 2004 and December 2016 were included. Closure was obtained with the Cardia® or Amplatzer® devices in 118 and 35 patients, respectively. The mean duration of follow-up was 6.6 ± 3.8 years with a total of 1055 patient-years. The primary end-point assessed the efficacy of the procedure and was defined as the recurrence of transient ischemic attack (TIA) or ischemic stroke. The secondary end-points assessed the security of the procedure and were defined as the apparition of atrial fibrillation (AF) on one hand, and a composite endpoint of other adverse events on the other hand, including death, device dislocation, tamponade, cardiac ischemia, thrombosis, device malposition, complete heart block, and bleeding.
Results: Mean age was 48 ± 9 years with 60.4% of males. Indications for closure was cryptogenic cerebrovascular events in all patients (stroke: 78.6%, TIA: 21.4%). Most PFO had high-risk anatomy characteristics: atrial septal aneurysm (44.6%), spontaneous shunt (34.0%) and/or strongly positive microbubbles study (64.8%). During follow-up, the rate of non-cerebrovascular events was 15%. The recurrence rate of TIA was 1.2% per patient-year and the rate of stroke 0.09% per patient-year. The AF rate was 1.20% per patient-year. The head-to-head comparison of the two devices Cardia® and Amplatzer® showed a lower risk of TIA/stroke at 1-year with the Cardia® device but the two groups were heterogeneous at baseline. The evolution of the security of the procedure overtime showed a decrease of the peri-procedural TIA rate and of the length of the hospital stay across the years. We did not find any significant predictive factors for TIA/stroke recurrence.
Conclusions: Long-term outcomes after percutaneous closure of PFO for secondary prevention in cryptogenic TIA/stroke in our population showed similar rates of recurrent TIA/stroke and AF onset as in reference trials.

Cardiovascular risk profile among patients treated by PCI and impact of this treatment and prevention nurse advice on smoking cessation

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Background: Cardiovascular disease is the first cause of mortality in the world and smoking cessation has a major impact on cardiovascular outcomes.
The purpose of this study is to evaluate the impact of advice given by a specialized nurse in cardiovascular prevention on smoking withdrawal after percutaneous coronary angioplasty (PCI).
Methods: We compared retrospectively active smoker patients ($n = 171$) who underwent PCI from January to June 2017 and prospectively active smoker patients ($n = 34$) treated by PCI in march 2018 who received advice on smoking cessation by a dedicated education nurse. The impact of PCI and specialized advice on smoking cessation at 1 and 3 months was evaluated by a phone call.
Results: In the two group, impact of PCI was no significant on smoking withdrawal but a statistical significant difference was found in the number of patients in smoking cessation at 1 month (46 vs 54.5%, $p = .032$) and 3 months (35,5 vs 51.6%, $p = .037$) after specialized advice given by the prevention nurse. Moreover, patients who changed their smoking behaviour and didn't smoke inside anymore were much more after nurse advice (20.6% before, 46.7% at 1 month and 53.3% at 3 months, $p = .004$).
Conclusions: The intervention of a dedicated nurse in cardiovascular prevention has a significant impact at 3 months on smoking cessation and on smoking behaviour after PCI. Secondary prevention after a coronary event must be personalized for each patient and can be reinforced by the intervention of a dedicated nurse in cardiovascular prevention in the process and the motivation of smoking withdrawal.

(#) Quality of life after surgical and transcatheter aortic valve replacement in patients and their informal caregivers: real-world data contributing to establish value-based medicine in East Denmark

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Background: The concept of value-based medicine (VBM) is increasingly implemented in therapeutic decision-making processes, but only few data on patient-perceived values are available in the field of aortic stenosis (AS) treatment. This study aimed to deliver data on patient-perceived values and health-related quality of life (HRQoL) after surgical and transcatheter aortic valve replacement (SAVR/TAVR) in a real-world patient population.
Methods: Questionnaires were sent to 637 patients, 18 ± 4 months after elective SAVR or TAVR, performed between September 2015 and August 2016. The questionnaires were specifically designed to capture HRQoL and physical/mental impact of the entire AVR process on patients and their nearest relative, and were completed by 429 patients (SAVR, $n = 265$; TAVR, $n = 164$).
Results: In both groups, 10% of patients reported no change in HRQoL, whereas HrQoL improved in 76% vs. 83% ($p = .092$) and became worse in 14% vs. 7% ($p = .040$) in, respectively, the SAVR and TAVR populations. Both physical and mental impact of the intervention and its recovery period were experienced more stressful by the SAVR group as compared to the TAVR group. Also, nearest relatives of SAVR patients experienced the entire process mentally more stressful and enduring than TAVR relatives.
Conclusions: HRQoL improved in both SAVR and TAVR groups, although a majority of patient-perceived values tends to favor TAVR. Given the increasing importance of VBM, patient-perceived data will have to be considered in future therapeutic decision-making processes, both at individual and public policy-making level.

Percutaneous left atrial appendage closure following transcatheter aortic valve replacement: results from the ATTRACTIVE study

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Background: Atrial fibrillation is present in 30 to 40% of patients undergoing transcatheter aortic valve replacement (TAVR). Usually these patients are in need for anticoagulant therapy due to the elevated risk for stroke or thromboembolism (TE). Simultaneously, they often have an increased bleeding risk due to their high age and multiple comorbidities. In this study we investigate the safety and efficacy of percutaneous left atrial appendage closure (LAAC) in combination with TAVR as treatment option for patients with severe aortic stenosis (AS), atrial fibrillation (AF) and high bleeding risk.
Methods: During a 14-month period, 308 patients underwent TAVR. Of these, 118 patients (38%) were known with AF. Twenty patients with a high bleeding risk were treated with LAAC (TAVR + LAAC group) versus 98 patients were continued on medical therapy for stroke prevention (TAVR + medical group). In case of combined TAVR + LAAC, TAVR was performed first, followed by LAAC 4 to 10 days later. Clinical one-year follow-up data were available for all patients and multi-detector computed tomography was performed in 74 patients three months after the procedure.
Results: In the TAVR + LAAC group, both TAVR and LAAC procedures were performed successfully without any major procedural complication. Following LAAC, all patients, except one, received double anti-platelet therapy for a period of three months, followed by single anti-platelet therapy. At one-year follow-up, there were no reports of stroke, TE or major bleeding in the TAVR + LAAC population, whereas in the TAVR + medical group, a stroke/TE was reported in 4 patients (5%; $p = .236$) and a major bleeding was noted in 8 patients (10%; $p = .036$).
Conclusions: Treatment of patients with severe AS, AF, and a high bleeding risk with combined TAVR and LAAC is feasible and safe with no procedural complications. Medium-term safety and efficacy outcomes are promising. Large-scale studies and longer-term follow-up are warranted to confirm these findings.

Septal hematoma post CTO procedure

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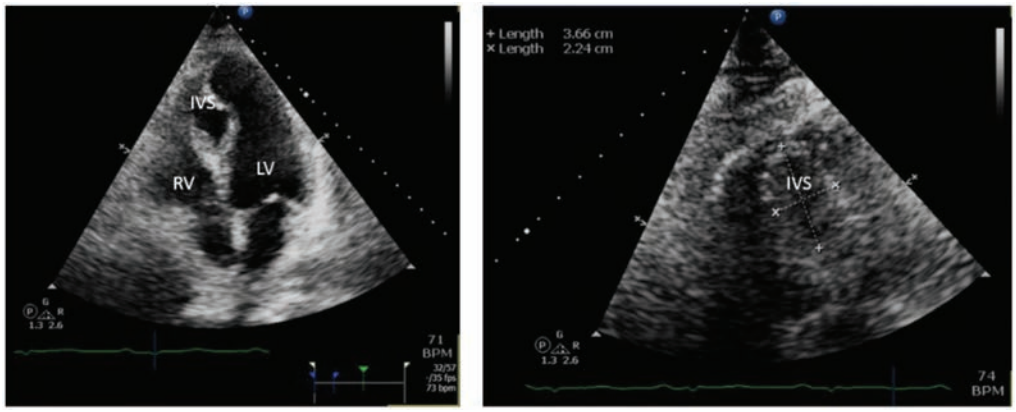
Background: An interventricular septal (IVS) hematoma is a rare finding and mainly occurs post myocardial infarction. It has previously been described as a complication of percutaneous chronic total occlusion (CTO). Severity can range from benign to life threatening. It seems that the clinical implications do not only correlate with size of the hematoma but also with location. Complications that occur can be mechanical or arrhythmic.
Methods: We present a patient with a large ventricular septal hematoma draining into the right ventricle post CTO-procedure. A 62-year-old man was transferred to our hospital for CTO procedure. Through retrograde dissection re-entry with retrograde access via a septal branch, the distal RCA occlusion was treated with implantation of four drug-eluting stents. During the procedure, a small laceration of the septal branch was noted but the patient reported no symptoms nor were there ECG changes or hemodynamic instability. Two hours later, the patient developed acute chest pain, typical for angina in combination with ECG changes and frequent monomorphic ventricular extra systole (VES). Two dimensional transthoracic echocardiography (TTE) visualised a septal hematoma with a maximal diameter of 37mm draining to the right ventricle (RV). The hematoma was located on the midportion of the septum and expanded apically without signs of outflow tract obstruction. Conservative management with beta-blockage, intravenous (IV) nitrates and pain relief was initiated.
Results: We observed multiple runs of non-sustained ventricular tachycardia (up to 24 beats). The arrhythmia diminished in frequency and duration and disappeared after 48 hours. The patient remained hemodynamically stable and symptoms resolved. The patient was discharged after 72 hours on a low dose of bisoprolol (2.5mg OD) in addition to the aspirine and clopidogrel. Four weeks later, he remained asymptomatic. TTE showed non-dilated, mildly septal hypertrophic left ventricle with normal global contractility. There was a small akinetic patch in the mid septum correlating with the position where the septal hematoma was previously.
Conclusions: As CTO PCI procedures are becoming more prevalent, clinicians should be aware of possible complications such as a septal hematoma. This complication is potentially life threatening. However, with conservative management, even when VSD is present, the hematoma can resorb within a few weeks.



OTHER

Pattern of prosthetic valve infective endocarditis – a single center experience

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Background: Infective Endocarditis (IE) is one of the disease entities that severely affect the heart and its function. The incidence of prosthetic valve infective endocarditis (PVIE) varies from 1 to 3% and it is most commonly seen in the aortic position with mechanical valve type. PVIE is classified according to its timing after surgery into two types, early (less than 6 months after surgery) and late (more than 6 months after surgery).
Methods: We studied the pattern of PVIE in the patients presented to our tertiary care center from January 2015 till December 2017 (2 years). Patients characteristics, type of PVIE, patient risk factors, history of previous IE, blood culture and sensitivity results as well as the fate of the patients were all studied.
Results: As regards patient characteristics and risk factors, a total number of 24 patients had PVIE with a mean age of 45 ± 13 years with 15 (62.5%) males. 4 (16.7%) had history of IE while 20 (83.3%) had mechanical prosthesis. 5 (20.8%) diabetics, 10 (41.7%) hypertensives, 5 (20.8%) had atrial fibrillation, 1 (4.2%) had ischemic heart disease, 13 (54.2%) had rheumatic heart disease and 6 (25%) had early IE. Blood culture and sensitivity, 1 (4.2%) patient had methicillin sensitive staphylococcus aureus, 5 (20.8%) had methicillin resistant staphylococcus aureus, 4 patients (16.7%) had streptococcus, 1 (4.2%) had enterococcus, 1 (4.2%) had other organism while 12 (50%) had negative blood culture. Patient prognosis, 12 (50%) were managed conservatively and 6 (25%) had a re-do surgery while in-hospital death occurred in 6 patients (25%).
Conclusions: PVIE reported in 1-3% of cases, more commonly in aortic valve position, in our experience we had encountered high incidence of culture negative IE that can be explained with the misuse of antibiotics also, delayed diagnosis with associated with high incidence of in-hospital death. Prompt diagnosis and proper treatment are mandatory to reduce its mobility and mortality

1- Patient Characteristics and risk factors ($n = 24$)	
Age (years)	45 ± 13
Male Sex	15 (62.5%)
History of IE	4 (16.7%)
Mechanical Valve	20 (83.3%)
Diabetes	5 (20.8%)
Hypertension	10 (41.7%)
Atrial Fibrillation	5 (20.8%)
Ischemic Heart Disease	1 (4.2%)
Rheumatic Heart Disease	13 (54.2%)
Early IE	6 (25%)
2- Blood culture and sensitivity ($n = 24$)	
Methicillin Sensitive Staphylococcus Aureus (MSSA)	1 (4.2%)
Methicillin Resistant Staphylococcus Aureus (MRSA)	5 (20.8%)
Streptococcus	4 (16.7%)
Enterococcus	1 (4.2%)
Other	1 (4.2%)
Culture Negative	12 (50%)
3- Fate of the patients ($n = 24$)	
Surgical re-do	6 (25%)
Medical management only	12 (50%)
In-hospital death	6 (25%)
Lost follow up	0 (0%)

Data are represented as mean(±SD) or number (Percentage).

Patient specific long QT syndrome type 3 cardiomyocytes can be used for clinical drug safety assessments

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Long QT syndrome is a heart rhythm disorder with a prolonged QT interval which can result in a torsade de pointes tachycardia and ventricular fibrillation leading to sudden cardiac death. To date, there are 14 subtypes known with multiple different genes and locations of the mutation causing the disease that is either inherited or caused by de-novo mutations. In addition, a prolonged QT interval can be acquired due to adverse drug effects mostly blocking the outward rectifying potassium channel (hERG).
Cardiomyocytes (CM) were generated from a Long QT syndrome type 3 (LQT.3) patient using the same SMAD-activated differentiation approach as for a healthy control cell line (CorV.4U). LQT.3 CMs were subjected to electrophysiological analysis using patch-clamp-, multi electrode array- (MEA), calcium cycling-, impedance- and contractile force-measurements. Pharmacological analysis was done with model substances to evaluate the drug effects and arrhythmogenic potential. For the comparative analysis CorV.4U were used as a healthy control cell line. Furthermore, LQT.3 CMs were electrically paced to induce arrhythmias.
The MEA experiments demonstrate a higher sensitivity in measuring prolongation of field potential duration using the LQT.3 CMs model as compared to other CM models in pharmacological studies. Field potential prolongation and QT prolongation can be directly linked and are thus associated with a higher risk in arrhythmic events. This enables this CM model to be used in pharmacological safety testings to detect cardiac adverse drug effects in early pre-clinical phases. Moreover, LQT.3 CMs can be used to study the pathophysiology of the Long QT syndrome.

E-cigarette decreases arterial oxygen tension in smokers with coronary artery disease: a randomized controlled pilot trial

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Background: Whereas high wattage electronic cigarettes (e-cigarettes) vaping (V) is increasingly popular, its health effects are largely unknown. We tested the hypothesis that pure propylene glycol/glycerol e-liquid vehicles V decreases arterial oxygen partial pressure in heavy tobacco smokers suspected of coronary artery disease.
Methods: After their coronary angiogram, twenty tobacco smokers participated in an open-label randomized parallel study where serial intra-arterial blood samples were performed before and after 1-gram propylene glycol/glycerol e-cigarette V at 60 Watts or sham-vaping (SV). Peripheral pulse oximetry, transcutaneous gas tension and microcirculatory blood flow were assessed throughout the experimental sessions.
Results: Eighty % of the patients were hypertensive and 45% had a left ventricular ejection fraction $<50\%$. Established coronary artery disease was found in 65% patients, of whom 62% underwent a coronary stent procedure during the index angiogram. Compared to SV, V decreased the following parameters 5 minutes after the exposure: (1) Δ-arterial oxygen partial pressure (SV: $+5.4 \pm 3.3$mmHg *vs.* V: -5.4 ± 1.9mmHg; $p = .012$) (difference between groups; 10.8 [95%CI, 8.4-13.2]mmHg); (2) Δ-arterial oxygen saturation (SV: $+0.9 \pm 0.6\%$ *vs.* V:$-0.8 \pm 0.3\%$; $p = .023$); 3) Δ-oxyhemoglobin fraction (SV: $+1 \pm 0.5\%$ *vs.* V: $-0.6 \pm 0.3\%$; $p = .028$); (4) Δ-peripheral oxygen saturation (SV: $+1.3 \pm 0.4\%$ *vs.* V: $-1.3 \pm 0.5\%$; $p < .0001$); and 5) Δ-transcutaneous oxygen partial pressure (SV: $+6 \pm 3.4$mmHg *vs.* V: -1.2 ± 2.1mmHg; $p = .041$). The decrease in Δ-peripheral oxygen saturation (SV: $+0.7 \pm 0.6\%$ *vs.* V: $-0.7 \pm 0.5\%$; $p = .036$) persisted up to 20 minutes after V compared to SV.
Conclusions. Acute high wattage e-cigarette V in smokers with heart disease induces arterial hypoxemia with subsequent tissue hypoxia. The latter could be related to ventilation/perfusion mismatches. (ClinicalTrials.gov identifier: NCT03404011)

Clinical characteristics and genetic predisposition to combined post-capillary and pre-capillary pulmonary hypertension in left heart diseases

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Background: Pulmonary Hypertension (PH) in left heart diseases (LHD) has been redefined as isolated post capillary PH (IpcPH) when the diastolic pressure gradient (DPG or diastolic pulmonary artery pressure – pulmonary artery wedge pressure, PAWP) is <7 mmHg and combined post-capillary and pre-capillary PH (CpcPH) when the DPG is ≥7 mmHg. The latter form is uncommon in LHD and predicting factors have not yet been fully identified. Predisposing constitutional and/or environmental factors may play a role in the development of CpcPH, as suggested by the variability in the adaptation of pulmonary circulation to the elevation of PAWP. We sought to determine whether a genetic predisposition to CpcPH could be identified.
Methods: Based on our right heart catheterization database from January 2007 to January 2015, we selected patients diagnosed with PH-LHD (MPAP ≥25 mmHg and PAWP and/or Left Ventricular Diastolic Pressure, LVDP >15 mmHg). Clinical and hemodynamic variables were used to compare IpcPH to CpcPH. In addition, patients with CpcPH underwent an analysis of genetic variations in the genes known to predispose to heritable PH, using next generation sequencing.
Results: Ninety-three patients presented with PH-LHD, of which 30% met the definition of CpcPH. Clinical presentation was similar in both groups, except for higher morphometric features in the CpcPH group. Pulmonary pressures as well as pulmonary resistance were higher in CpcPH patients while the arterial and venous oxygen saturations were lower in the same group (Table 1). A potentially pathogenic variation of the BMPR2 gene was identified in one CpcPH patient. The patient had one of the most severe forms of PH in the CpcPH group.

Table 1. Clinical and Hemodynamic characteristics.

Characteristics	**CpcPH (*n* = 30)**	**IpcPH (*n* = 63)**	*p* value
Mean age, years	63 ± 2.5	64.1 ± 1.7	.715
Feminine gender, % (*n*)	43.3 (13)	58.7 (37)	.187
BMI, kg/m^2	**30.3 ± 0.9**	**27.8 ± 0.7**	**.032**
Etiology			.593
HFrEF, % (*n*)	36.7 (11)	39.7 (25)	
HFpEF, % (*n*)	56.7 (17)	47.6 (30)	
Valvulopathy, % (*n*)	6.7 (2)	12.7 (8)	
NYAH, moy	2.8 ± 0.1	2.8 ± 0.1	.591
I, % (*n*)	0.0	0.0	
II, % (*n*)	30.0 (9)	31.7 (20)	
III, % (*n*)	70.0 (21)	65.1 (41)	
IV, % (*n*)	0.0	3.2 (2)	
Walking test, m (*n*)	354.3 ± 33.0 (19)	286.2 ± 24.0 (37)	.103
VO2 peak, ml/min*kg	13.4 ± 0.8 (21)	14.3 ± 0.8 (36)	.453
Hemodynamic values			
HR, bpm	72.4 ± 2.3	70.3 ± 1.7	.464
MPAP, mmHg	**48.7 ± 1.7**	**34.5 ± 0.9**	**<.001**
PAWP, mmHg	23.8 ± 1.1	22.9 ± 0.6	.466
RAP, mmHg	13.6 ± 1.2	12.0 ± 0.7	.217
SaO2, % (*n*)	**93.7 ± 0.8 (*n* = 27)**	**96.5 ± 0.3 (*n* = 61)**	**.002**
SvO2, % (*n*)	**59.0 ± 1.6 (*n* = 26)**	**64.6 ± 1.1 (*n* = 58)**	**.005**
CI, l/min/m2	2.1 ± 0.1	2.2 ± 0.1	.255
PVR, mmHg	**7.0 ± 0.7**	**3.0 ± 0.1**	**<.001**
TPG, mmHg	**24.8 ± 1.4**	**11.7 ± 0.5**	**<.001**
DPG, mmHg	**11.0 ± 0.8**	**1.9 ± 0.2**	**<.001**

Data are presented as mean ± SE or % and No (*n*).

(#) PATHway-I: Feasibility and preliminary efficacy of a technology-enabled home-based cardiac rehabilitation system

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Background: Cardiac rehabilitation (CR) is highly effective as secondary prevention for cardiovascular diseases (CVD). Uptake of CR remains suboptimal (30% of eligible patients) and long-term adherence to a physically active (PA) lifestyle is even lower. New innovative and cost-efficient strategies are needed that result in increased uptake and long-term adherence to a healthy and PA lifestyle. We developed the technology-enabled PATHway system (Physical Activity Towards Health) to provide a comprehensive, remotely monitored home-based CR program for CVD patients. The PATHway-I study aimed to investigate its feasibility and clinical efficacy.
Methods: In a multicenter randomized controlled pilot feasibility trial, patients with CVD were randomized on a 1:1 basis to the PATHway intervention group (PW) or usual care control group (UC). PATHway uses an internet-enabled and sensor-based home exercise platform as the core component of a personalized, comprehensive lifestyle intervention programme. Outcome measures assessed at completion of phase II CR and at 3 months and 6 months follow-up included PA (Actigraph GT9X link), physical fitness (peak oxygen uptake, handgrip strength, isometric and isokinetic upper leg strength, 30-second sit-to-stand test), modifiable cardiovascular risk factors (body mass index, fat mass, waist and hip circumference, blood pressure, blood glucose and blood lipids), endothelial function (flow mediated dilatation of the right brachial artery), intima-media thickness of the common carotid artery and quality of life (SF-36). System usability and patients' experiences were only evaluated in PW. A mixed-model ANOVA with Bonferroni adjustment was used to analyse between-group effects over time. Missing values were handled by means of an intention-to-treat analysis using the last-value-carried-forward approach. Statistical significance was set at a two-sided alpha level of 0.05. Data are reported as mean ± SD.
Results: A convenience sample of 120 CVD patients (60.3 ± 9.2 years, 22 women), completing phase II CR was randomised to PW or UC. The PATHway system was successfully deployed in the homes of the 60 participants randomised to PW. Mean system usability score was 65.7 ± 19.7 (scale 5-100), which indicates average usability by participants. An increase from baseline to 6 months follow-up for daily average minutes of moderate to vigorous intensity PA could only be established for PW (PW: 127 ± 58 min to 141 ± 69 min, UC: 146 ± 66 min to 143 ± 71 min; p-interaction = 0.039) while diastolic blood pressure increased in the UC group (PW: 79 ± 11 to 79 ± 10 mmHg, UC: 78 ± 9 to 83 ± 10 mmHg; p-interaction = 0.004). A decrease in usage of the PATHway system was observed over time with a significantly ($p = .03$) lower number of uploaded exercise sessions in the final two months.
Conclusions: This pilot study demonstrated the feasibility and acceptability of a technology-enabled, remotely monitored, home-based CR program. Although efficacy was demonstrated, several challenges were identified that could influence adoption of PATHway.

This project has received funding from the European Union's Horizon 2020 Framework Programme for Research and Innovation Action under Grant Agreement no.643491.

PATHway: Technology enabled behavioural change as a pathway towards better self-management of CVD.

(Δ) Spontaneous coronary artery dissection in women <60 years: not so rare!

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Background: Spontaneous coronary artery dissection (SCAD), defined as a spontaneous separation of the wall of the coronary artery, is an underdiagnosed cause of acute coronary syndrome (ACS), especially in women <60 years. The pathognomonic angiographic form (type 1) with visualisation of a flap or multiple radiolucent lumina is only present in a minority of the SCAD patients, making the diagnosis challenging.
Aim: The aim of this study was to evaluate the occurrence of SCAD in low-risk women (<60 y and no or little risk factors) and to evaluate the potential association with fibromuscular dysplasia (FMD) in proven SCAD patients.

Methods: We performed a single centre retrospective analysis of ACS cases in women <60 years, who were admitted in our hospital (tertiary care centre with B2 and B3 facilities) between 05-2007 and 05-2017. The coronary angiograms of women with a low cardiac risk profile (<2 of the following: smoking, diabetes, total cholesterol >220 mg/dL) and absence of clear atherosclerotic findings of the coronaries or other major arteries were reviewed by 2 independent interventional cardiologists and classified as 'definite' or 'probable' or 'no' SCAD. "Definite" or "probable" SCAD patients were further analysed.
Results: During the study period 208 women <60 years were admitted with an ACS. Of these, 146 (69.9%) had more than 1 of the pre-specified risk factors or had clear signs of atherosclerosis of the coronary arteries or other arteries. After thorough re-assessment of the remaining 62 coronary angiograms, 8 (12.9%) were classified as 'definite' SCAD, 7 of these had already been diagnosed before (6 at the index event and 1 during follow up). Sixteen patients (25.8%) were considered 'highly probable' SCAD.

The mean age of all SCAD patients ($N = 24$) was 47,8 years. More than half presented with STEMI (58.3%), 2 patients presented with out of hospital cardiac arrest (8.3%) and 2 patients were resuscitated for ventricular fibrillation in the hospital (8.3%). Extreme emotional stress preceding the event was registered in 8.3% of women and 38.9% mentioned chronic stress. The LAD artery was the most affected artery (62.5%), followed by the Cx (25%). PCI was attempted in the majority of cases ($N = 20$, 83.3%), 25% of these PCI attempts failed or were complicated. The remaining patients were managed conservatively and none of the patients underwent urgent CABG. A minority of the SCAD patients had a systemic inflammatory condition ($N = 2$) or a hereditary connective tissue disease ($N = 1$, Marfan syndrome). A screening for FMD had already been performed in 5 of the patients with definite SCAD, 4 of these (80%) had FMD lesions on a head to pelvis CT-angiography. Of the remaining patients one had suffered a carotid dissection before SCAD and a second was treated with a carotid stent after SCAD, both cases are "very suggestive for" FMD.
Conclusions: We found that 38.7% of female ACS patients <60 years with low risk profile and no signs of peripheral or coronary atherosclerosis had a 'definite' or 'highly probable' SCAD. This is in accordance with literature and stresses the need for more awareness. PCI failed or was complicated in 1 out of 4 patients, supporting a conservative approach when flow is maintained. FMD was diagnosed in 80% of the screened cases while two other patients suffered a neurological event compatible with FMD. Further screening for FMD has been proposed to these 2 patients as well as the remaining patients.

(*) Platelet acetyl-CoA carboxylase phosphorylation: a risk stratification marker evidencing platelet-lipid interplay in CAD patients

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Background: Activation of the adenosine monophosphate (AMP)-activated protein kinase (AMPK) leads to phosphorylation of acetyl-CoA carboxylase (ACC) on serine 79 (phosphoACC) and its subsequent inhibition. Given the role of AMPK-ACC signaling in platelet lipid metabolism and function, this pathway could be affected in the platelets of patients with coronary artery disease (CAD), where the atherogenic environment has an impact on platelet biology.
Aims: We hypothesized that platelet AMPK-ACC signaling is activated by atherogenic lipids and could be considered as a metabolic signature in high-risk CAD patients. We also explored the association of platelet phosphoACC with platelet lipid metabolic profile.
Methods: Blood samples from 188 consecutive patients admitted for coronary angiography were processed. Lipid extracts from the platelets of 31 patients were subjected to lipidomic analysis.
Results: PhosphoACC level in circulating platelets of CAD patients were significantly increased and highly correlated with acute coronary syndrome (OR: 6.71, 95% CI: 2.06–21.91; $p = .002$). The triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C) ratio, a well-known atherogenic marker, was strongly associated with increased phosphoACC in our CAD cohort. TG/HDL-C ratio correlated with oxidized low-density lipoprotein (oxLDL) levels in our entire population. Consistently, oxLDL activated AMPK-ACC signaling through a CD36-dependent pathway. Lipidomic analysis revealed that increased phosphoACC led to a down-regulation of intraplatelet TG, particularly of those containing C14:0 fatty acid chains.
Conclusions: Platelet phosphoACC is a potential marker for risk stratification in suspected CAD patients and reveals an interaction between platelets and lipids. Inhibitory phosphoACC impacts platelet lipid content by down-regulating TG, which in turn may affect platelet function (ACCTHEROMA, NCT03034148).

Alteration of right ventricular to pulmonary artery coupling in systemic sclerosis

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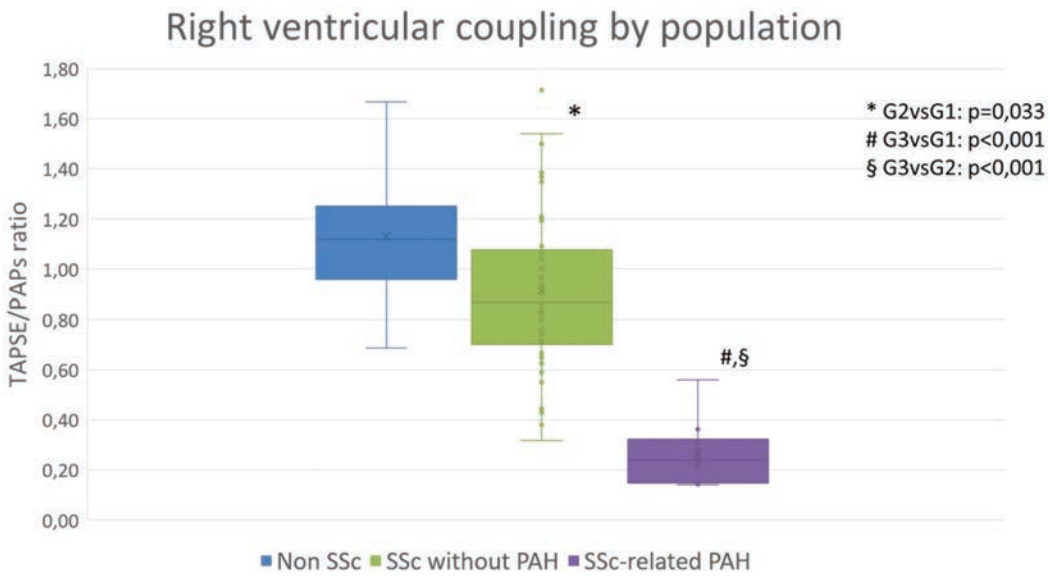
Background: Pulmonary arterial hypertension (PAH) associated with systemic sclerosis (SSc) has a worse prognosis than idiopathic PAH. This poor prognosis may be explained, at least in part, by an uncoupling of the right ventricle (RV) to the pulmonary artery (PA)[1]. It has been shown by Guazzi that the RV/PA coupling may be assessed non-invasively by echocardiograpy, using the TAPSE/PAPs ratio[2]. We therefore sought to determine whether the ratio TAPSE/PAPS was impaired in SSc and whether this may be associated with other variables assessing the RV function.
Methods: In our retrospective, single center analysis, 3 groups of subjects were compared: (1) a group of healthy subjects; (2) a group of SSc patients without cardiac or pulmonary impairment; (3) a group of SSc-related PAH patients. We collected anthropometrics, clinical, functional, biological and echocardiographic (focusing the right ventricle function) data. We also analyzed some hemodynamic data of patients who had a right-heart catheterization (RHC), according to international guidelines.
Results: The TAPSE/PAPs ratio, obtained among 10 patients with SSc-related PAH (Mean ± S.D: 0.26 ± 0.13), 66 SSc-patients without PAH (0.91 ± 0.30) and 34 healthy subjects (1.13 ± 0.24) was significantly different between the 3 groups, even after correction for age and sex (Figure). The decrease of the RV coupling was related, in the SSc group PAH-free, with a decreased s' wave and an increased blood level of NT-proBNP. In the PAH group, there is a relation between the decrease of the RV-arterial coupling and a decreased s'wave, an increased PVR and a decreased right ventricular ejection volume.
Conclusions: The right ventriculo-arterial coupling, assessed by the TAPSE/PAPs ratio, is impaired in systemic sclerosis, regardless of the presence of PAH. A decrease in TAPSE/PAPs is correlated with the level of NT-proBNP and the s' wave. This suggest a myocardial impairment in SSc which is non-related to the vascular complications.



References

[1] Tedford RJ, Mudd JO, Girgis RE et al. Right ventricular dysfunction in systemic sclerosis-associated pulmonary arterial hypertension. Circ Heart Fail. 2013;6:953–963.
[2] Guazzi M, Bandera F, Pelissero G et al. Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis. Am J Physiol Heart Circ Physiol 2013;305:H1373–H1381.

Partial anomalous pulmonary venous return in adults. Insight into pulmonary hypertension. A single center experience

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Cliniques Universitaires St.-Luc

Background: Partial anomalous pulmonary venous return (PAPVR) is a rare congenital disease where pulmonary veins drain into systemic circulation leading to a left-to-right shunt. PAPVR is not well known and often mismanaged despite its potential serious consequences, ie pulmonary hypertension (PH). To date, predictors of PH are not well established. The aims of this study were (1) to determine the prevalence of PAPVR based on a chest computed tomography (CT) database, (2) to determine the follow-up rate in patients having an incidental discovery of PAPVR, (3) to identify the impact of PAPVR on the right ventricle, (4) to identify the predictive factors of PH development, and (5) to evaluate the respect of surgery criteria in the clinical practice.
Methods: In this prospective monocentric cohort study, patients were selected from our medical center's database. Patients aged $\geq$18 years with a non-operated PAPVR and patients operated before the age of 18 years were enrolled. Patients with other potential causes of PH than PAPVR were excluded. All the non-operated patients had a transthoracic echocardiography and a NT-ProBNP measurement between April 2017 and July 2018. Data of the operated patients were analyzed retrospectively. PH was defined based on right heart catheterization (RHC). For patients without RHC, the transtricuspid regurgitation pressure gradient and echocardiographic indirect signs were used according guidelines to identify PH.
Results: In total, 29 patients were included. Mean patient age was 53 ± 18 years with a 59% female predominance. PAPVR was mostly arising from the right side (66% of cases) and was associated with congenital heart disease in 12 patients (41%). Most of them (9/12) were sinus venosus atrial septal defect (ASD). PAPVR was diagnosed by chest CT in 25 patients (86%). The reported prevalence of PAPVR was 0.2% (25/12466 chest CT reports). 48% of them were discovered fortuitously and 7 patients (58%) didn't have a cardiac follow-up. A pre-capillary PH was identified in 8 patients of the cohort (28%). Systolic pulmonary artery pressure was 59 ± 24 mmHg compared to 29 ± 4 mmHg ($p = .001$). No predictive factor of PAH was identified. Patients with PH had an increased size of their pulmonary artery (25 ± 5 *vs.* 20 ± 5 mm; $p = .015$), a decreased fractional area change (FAC) (24 ± 11 *vs.* 37 ± 11 mm, $p = .01$) and a decreased right ventricular global longitudinal strain (13.3 ± 5.9 *vs.* −21.0 ± 7.6 $p = .01$). Surgical repair was performed in 9 of the 29 patients (31%). All these patients were operated according to guidelines criteria. Among the non-operated patients (20 patients), 50% of them had at least one surgical criteria. Among them, 2 have not been informed by their referring physician about their diagnostic.
Conclusions: Prevalence of PAPVR is estimated at 0.2% of the population based on a chest computed tomography (CT) database. Among the patients incidentally diagnosed, half of them were not followed up. One third of the patients with PAPVR developed PH and no predictive factor was identified. All the patients were operated according guidelines criteria. However, one half of the non-operated patients presented at least one surgery criteria.

Fail to improve daily walking after acute cardiac event: is it so important?

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Background: Rehabilitation is a key factor of the treatment after an acute cardiac event (Ia evidence). During the program, patient increase his exercise capacity and learn to better managed the risk factors. The observed increased of exercise capacity should incite the patient to continue the training and "move more" in the daily life, the exercise feeling seeming less triyng.
Purpose: The aim of the study is to determine if the increase of exercise capacity is related to the increase of walking habits during the rehabilitation period.
Method: 17 patient engaged in a rehabilitation program after an acute cardiac event, have been recruited (STEMI, NSTEMI, CABG, RVAo, RVMi). A cardiopulmonary exercise testing (CPET) is realized after 4 sessions and 20 sessions later. To evaluate the number of step realized each days, patient are asked to wear a podometer for 7 days, during respectively each week they performed the CPET. We finally evaluate the quality of life with a SF36 questionnaire (ref ethic C: P2017/470/CCB B406201733631).
Results: No adverse event have been reported during the study. Our population present a typical exercise capacity of patient enrolled in cardiac rehabilitation (VO2p at 72+/−22% of the predicted value of Wasserman). Between the 2 CPET (20 sessions), VO2p increase by 3.2 ml/Kg.min (17%, $p < .001$) and Wmax by 32 W (26%, $p < .001$) for a comparable RER. In the same time, total step/day increase only by 8% ($p = .3$) but quality of life score (SF36) increase significatively ($p < .001$).

We didn't find any correlation between the increase of CPET parameters and increase of step/day. Different hypotheses/weakness could explain those results:

- Patient have much more "free time" to walk at the beginning of their rehabilitation program compared to 7 weeks later
- The season or the meteo during the respective weeks tested
- The device allow us only to count walking activities

Conclusions: Exercise capacity increase largely during the observation period but we didn't observe significative modification of walking habits in the same time. This underline that exercise capacity seems to increase principally by rehabilitation program than by a simple increase of walking habits.

An update meta-analysis of antiplatelet therapy in high risk patients for primary prevention

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Background: Antiplatelet therapy with aspirin is widely accepted for secondary prevention in patients with atherosclerotic cardiovascular disease. However, the indication of aspirin in asymptomatic patients for primary prevention is unclear. It is argued that aspirin reduced ischemia events at the cost of bleeding. The absolute benefits of aspirin is debated. Randomized clinical trials (RCTs) are regarded as the golden standard, thus we try to perform an update meta-analysis to elucidate the problem.
Methods: We conducted a search for RCTs in Medline, Embase, Cochrane database and major international conferences. We conducted the search from 2008 to 2018 and the language was restricted in English. Low dose aspirin was compared with placebo in these trials. The titles and abstracts were reviewed, and the data from studies which met the inclusion criteria was collected. Conflicts between reviewers were resolved by discussion in three reviewers. Internal validity of RCTs were assessed. Efficacy endpoints included myocardial infarction, ischemia stroke, cardiovascular mortality and all cause mortality. Safety endpoint were gastrointestinal bleeding, hemorrhagic stroke and major bleeding. Studies did not report the risk estimates or relevant outcomes were excluded. In cases of duplicate publications, we included the publication with the longest follow-up duration or the largest number of study participants. Risk Ratio (RR) and 95% confidence interval (CI) were used as the summary statistic. Fixed-effects model was used in our analysis when heterogeneity was low.
Results: Seven RCTs were enrolled with 68374 patients. Surprisingly, there was only a mild trend towards favoring aspirin for the rate of myocardial infarction (RR = 0.92, 95%CI: 0.83–1.03). Similarly, there was no statistically significant difference in the rate of ischemia stroke (RR = 0.91, 95%CI 0.81–1.01). In terms of cardiovascular mortality, aspirin treatment showed no benefit compared with the control group (RR = 0.99, 95%CI: 0.88–1.12). There was a no markedly difference in the rate of all cause mortality either (RR = 0.96, 95%CI: 0.89–1.03). On the other hand, there was significant harm with aspirin for primary prevention (RR = 1.69, 95%CI: 1.47–1.94). Meanwhile, aspirin therapy resulted in more risk in respect to major bleeding (RR = 1.35, 95%CI: 1.22–1.50). Finally, there was no difference for hemorrhagic stroke (RR = 1.21, 95%CI: 0.93–1.57).
Conclusions: In our meta-analysis, aspirin did not reduced ischemia events significantly in asymptomatic patients for primary prevention, while increased the risk of bleeding. There should be good evidence that benefits outweigh harms. Hence, aspirin for primary prevention should be individualized and the trade-off should be taken into full consideration.

Study or Subgroup	Aspirin Events	Aspirin Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
PAPADAD 2008	55	638	56	638	8.5%	0.98 [0.69, 1.40]	2008
AAA 2010	62	1675	68	1675	10.3%	0.91 [0.65, 1.28]	2010
JPPP 2014	20	7220	38	7224	5.8%	0.53 [0.31, 0.90]	2014
JPAD 2017	22	992	22	1168	3.1%	1.18 [0.66, 2.11]	2017
ARRIVE 2018	88	6270	98	6276	14.9%	0.90 [0.68, 1.20]	2018
ASPREE 2018	167	9529	184	9589	27.9%	0.91 [0.74, 1.12]	2018
ASCEND 2018	191	7740	195	7740	29.6%	0.98 [0.80, 1.19]	2018
Total (95% CI)		**34064**		**34310**	**100.0%**	**0.92 [0.83, 1.03]**	
Total events	605		661				

Heterogeneity: Chi² = 5.32, df = 6 (P = 0.50); I² = 0%
Test for overall effect: Z = 1.46 (P = 0.14)

Pregnancy in women with congenital heart disease – outcome in a single tertiary care center

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Background: An increasing number of women with congenital heart disease is reaching reproductive age. Pregnancy in these patients is associated with a higher risk of maternal, obstetric, fetal and neonatal complications. Improved knowledge regarding the outcome of pregnancy within this heterogeneous patient population is needed to create standardized protocols for preconceptional advice and management during pregnancy, delivery, and postpartum phase.
Methods: The aim of this retrospective monocentric study was to map the outcome of pregnancy in women with congenital heart disease in a tertiary care center. The data were compared to the available literature and an attempt was made to explain the differences and their root causes. This was used to evaluate the management of these patients in order to explore potential future improvements.
In this study, 69 pregnancies in 55 patients were recorded between January 2009 and February 2017. Data were collected r trospectively from the electronic patient files and the ROPAC registry (Registry Of Pregnancy And Cardiac disease). Descriptive statistics were performed and data were compared to data in the general population and published data from the ROPAC registry.
Results: Nine women (16.4%) with cardiomyopathy, 21 women (38.2%) with an aortic disease and 25 (45.4%) women with other congenital heart diseases were included. The diagnosis was known before pregnancy in 94.0% of patients, and 87.5% were counseled preconceptually. The average maternal age was 28.7 yrs (±3.5), which is significantly lower compared to the general Flemish pregnant population (30.4yrs) and the ROPAC registry (30 yrs). Nulliparity was observed more frequently (70.6%) in comparison to these populations. The majority of patients was NYHA (New York Heart Association) class 1 (83.9%) and could be classified as WHO (World Health Organization pregnancy risk) class 1 (29.1%) or 2 (58.2%).
Cardiac complications occurred in 4.4% of the pregnancies. In patients with aortic pathology, the diameter of the ascending aorta was significantly larger after birth. A miscarriage, either spontaneous or therapeutic, occurred in 4.3%. The median duration of gestation was significantly lower than in the general Flemish population (38.4 w vs 40 w respectively, $p = .001$). During pregnancy, 15 patients (22.4%) were hospitalized for cardiac, obstetric or other complications (no delivery). Obstetric complications occurred in 5.9% of pregnancies. The majority of patients delivered vaginally (71.2%), a significantly higher number compared to the ROPAC registry (59%, $p = .044$). Women received epidural anesthesia in 91.6% of deliveries, which is significantly more than in the general Flemish population (69.7%, $p < .001$). Neonatal complications occurred in 28.1% of pregnancies and 20.6% neonates were born prematurely, a significantly higher percentage compared to the general population (8%, $p < .001$). Average birth weight was significantly lower than in the general Flemish population (2985 g 3288 g, $p < .001$). Intrauterine growth retardation and dysmaturity were seen in 10% and 10.9% respectively. Neonatal mortality occurred in 1.5% of cases. No maternal or fetal mortality was observed. Late complications occurred in 1.7% of pregnancies. In 15.3% NYHA classification changed after pregnancy compared to previous values.
Conclusions: A comparison to available literature shows that the outcomes of pregnancy in patients with congenital heart disease seen at our tertiary care center are similar or more favorable than those in the data reported in literature. Continuing close follow up and further registration of outcomes in these patients can result in more evidence regarding management during and after pregnancy. This way, general guidelines for follow up of pregnant patients with congenital heart disease can be created and outcomes can be optimized.

(#) Real-world usage of glucose lowering agents in heart failure patients with type 2 diabetes

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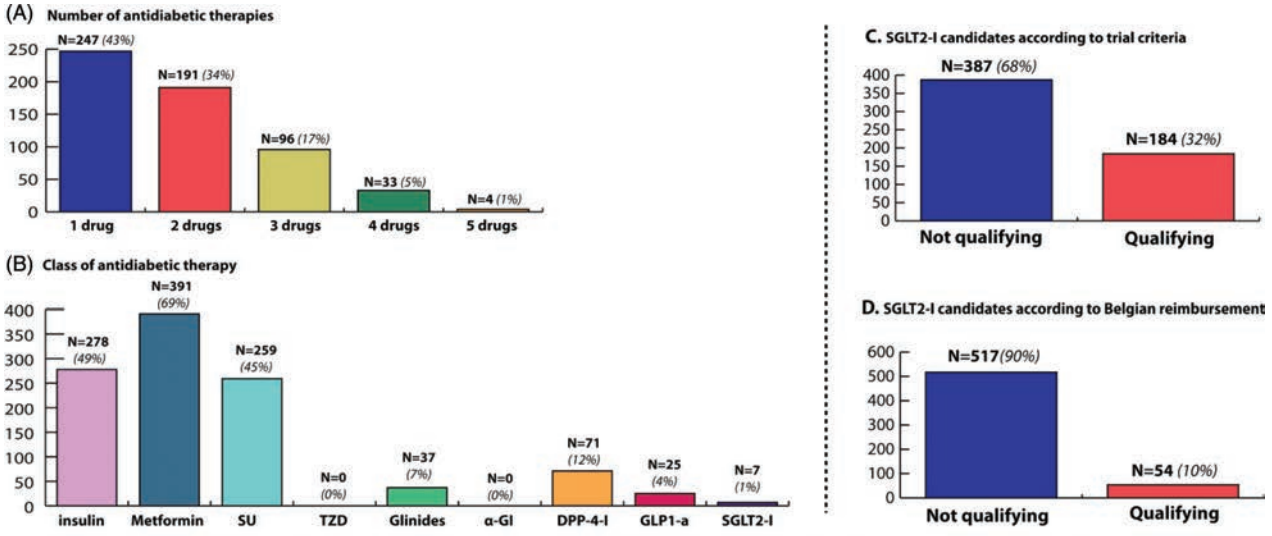
Ziekenhuis Oost Limburg

Background: The choice of glucose lowering agents in heart failure patients can have a strong impact on heart failure related adverse events, with some classes increasing and other classes reducing the risk for developing an acute heart failure episode. Little data is available about the choice of glucose lowering agents in real world patients with both heart failure and type 2 diabetes.
Methods: We performed a cross-sectional single center point analysis of all patients with both a diagnoses of heart failure and diabetes. Medical records were used to determine the choice of current glucose lowering agents. Clinical data at the time of cross-sectional analysis was used to determine potential eligibility to a sodium glucose linked transporter 2 inhibitor (SGLT2-inhibitor) based on the enrollment criteria of the EMPAREG-OUTCOME and CANVAS-trial.

Results: A total of 571 HF-patients with diabetes were assessed on June the first 2017. The majority of patients were either managed with one or two glucose lowering agents (43% respectively 34%; see figure – panel A), with metformin ($N = 391$; 61%), Insulin ($N = 278$; 49%) and sulfonylurea ($N = 259$; 45%) being the most frequently employed treatments (see figure – panel B). SGTL2-inhibitor use was low ($N = 7$; 1%). According to trial inclusion-criteria 184 patients (32%) theoretically qualified for an SGLT2-inhibitor (panel C). The main reasons for ineligibility to an SGLT2-inhibitor was a HbA1C below 7% ($N = 324$) or a glomerular filtration rate (GFR) below 30ml/min ($N = 154$). However 54% of patients with a HbA1C $< 7\%$ were treated with ≥ 2 glucose lowering agents from a class other than SGLT-2-inhibition, none of which confront protection against heart failure readmission. When assessing eligibility to an SGLT2-inhibitor according to the Belgian reimbursement criteria, the theoretical eligibility dropped from 32% to 10%, due to the more stringent criteria for GFR (>60 ml/min) in the Belgian reimbursement criteria versus the trial inclusion criteria.
Conclusion: Despite potential eligibility, SGLT2-inhibition remains an underused glucose lowering agent in this cross-sectional analysis of contemporary heart failure patients. From the Belgian perspective, stringent reimbursement criteria limiting the use of SGLT2-inhibitors in patients with a GFR below 60 ml/min, might explain the low uptake. Additional research is necessary for strategies enhancing uptake of SGLT2-inhibitors in eligible patients.

Figure 1.



Abbreviations: SU sulfonylurea, TZD thiazolidinediones, α-GI α-glucosidase inhibitors, DPP4-I dipeptidyl peptidase 4 inhibitor, GLP1-a glucose linked peptide 1 agonists.

Evaluation of cardio respiratory capacities after cardiac rehabilitation

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Léopold Bellan Hospital, France

Introduction: Cardiac rehabilitation consists of measures that allow a patient to recover their functional capacity through physical exercise and secondary prevention measures. The aim of our study is to evaluate the impact of cardiac rehabilitation on cardio respiratory capacities
Materials and methods: It's a retrospective study, including 1132 patients admitted in cardiac rehabilitation center, Léopold Bellan Hospital, Paris. All of them had clinical examination, electrocardiogram, transthoracic echocardiography, biological test and Ergospirometry.
Results: The average age of patients was 62.5 ± 11.8 years, with male predominance, they have more than three cardiovascular risk factors, dominated by Hypertension and diabetes, they have overweight with BMI to $28.14 \pm 5.4\,kg/m^2$, clinical examination is normal, transthoracic echocardiography showed preserved left ventricular ejection fraction ($54.2 \pm 12.03\%$).
After 20 sessions of cardiac rehabilitation, they have decreased in BMI ($26.4 \pm 4.8\,kg/m^2$), a significant decrease in blood pressure level and in heart rate, they had an improvement in the maximal work load (from 89.02 ± 34.5 to 109.67 ± 43.65 watt, $p = .01$) and VO2max (from 19.87 ± 5.7 to 22.2 ± 6.2 ml/kg/min, $p = .02$).
Conclusion: This study demonstrated that cardiac rehabilitation is clearly benefic for patients to improve their exercise capacities and improve their cardio respiratory level.

Patient and caregiver productivity loss and indirect costs after acute coronary syndrome and stroke in Belgium

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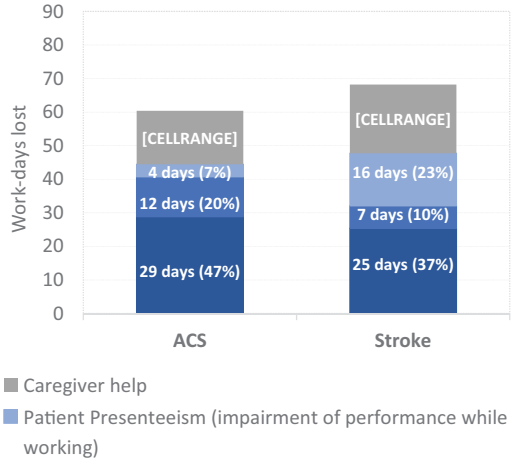
Background: Data on productivity loss and indirect costs due to cardiovascular events (CVE's) are scarce.
Purpose: To estimate patient and caregiver productivity loss/indirect costs in the first year after an acute coronary syndrome (ACS) or stroke in Belgium.
Methods: Productivity loss of Belgian ACS and stroke patients (absenteeism, and presenteeism) and caregiver help in the previous 4 weeks was collected cross-sectionally via a validated Productivity Cost Questionnaire (iPCQ). The questionnaire was administered to the patients during a routine cardiologist or neurologist visit within 3–12 months post-index hospitalization. Reported lost hours were converted into 8-hour workdays, extrapolated to 1 year, combined with the duration of the initial hospitalisation and post-hospitalization sick leave, and valued according to the Belgian's labour cost (Eurostat: €39.8/hour, 2017).
Results: Fifty-three Belgian patients were included in the study. Of those 30 had ACS (83% myocardial infarction; mean left ventricular ejection fraction 61.7%; all had re-vascularisation) and 23 had stroke (96% ischaemic; Modified Rankin scale 0–1: 83%). Mean (SD) age of the patients was 55 (9) years, 85% were men, 23% were smokers, 11% had diabetes type 2, 47% had hypertension, and 79% of the patients had a LDL >70 mg/dL despite lipid lowering treatment. ACS patients and caregivers together lost on average 60 (SD = 78) work-days during the first year after the event: patients lost 29 (27) work-days at index hospitalisation followed by initial sick-leave, 12 (37) days due to absenteeism after return to work, and 4 (8) work-days lost due to presenteeism at work; 16 (67) work-days were lost by caregivers helping the ACS patients. Average productivity loss for stroke patients and their caregivers was 68 (81) work-days: 25 (25) days were lost by patients for initial hospitalization and sick leave, after having retuned to work they lost 7 (30) days due to absenteeism and 16 (40) – due to presenteeism; caregivers of the stroke patients lost 21 (57) work-days (Figure 1). Average total indirect costs during the first year after the event were €19,234 (€24,903) and €21,732 (€25,927) for ACS and stroke respectively.
Conclusions: Our results suggest that productivity loss and indirect costs to patients and caregivers during the first year after a CVE in Belgium are substantial. Total annual productivity loss by patients amounts on average to 20% of working days; caregivers lost 7% of their working days. The main driver of productivity loss in patients is absenteeism due initial hospitalization and sick leave.

Figure 1. Productivity loss during the 1st year after ACS and stroke in Belgium



(Δ) Clinical utility of thromboelastography (TEG) in off pump coronary artery bypass grafting (CABG)

Kumar Rahul
King George's Medical University, India

Background: Thromboelastography enables a complete evaluation of the process of clot initiation and the structural characteristics of the formed clot and its stability. Many studies have previously assessed the predictive role of thromboelastography in on-pump cardiac surgery. However, there are no clear guidelines about its role or use in off-pump coronary artery bypass grafting. The aim of this study is to evaluate the use of thromboelastography and its relevance during the post operative period.
Methods: This is a two-year prospective study consisting of 550 patients undergoing off-pump coronary artery bypass grafting for coronary artery disease. Thromboelastography was performed as a bedside investigation in the Cardiothoracic & Vascular Surgery Intensive Care Unit.
Results: The association between Maximum amplitude and a total blood loss of <500 ml compared to a blood loss of >500 ml was found to be statistically significant ($p < .001$). Using Receiver Operator Characteristic Curve analysis, it was seen that with increasing maximum amplitude values, a decrease in blood loss was observed. Cut off value for maximum amplitude of <49.63 was regressed to have a predicted sensitivity of 100% and a predicted specificity of 89.3% for prediction of blood loss of >500 ml.
Conclusions: Thromboelastographic parameters show a reliable correlation for an increased blood loss in off-pump coronary artery bypass grafting surgeries and predict patients with an increased chance of blood requirement as well as for those at risk of a hypercoagulable state.

A new invasive validation method for non-invasive central blood pressure measurement using a suprasystolic sphygmomanometer

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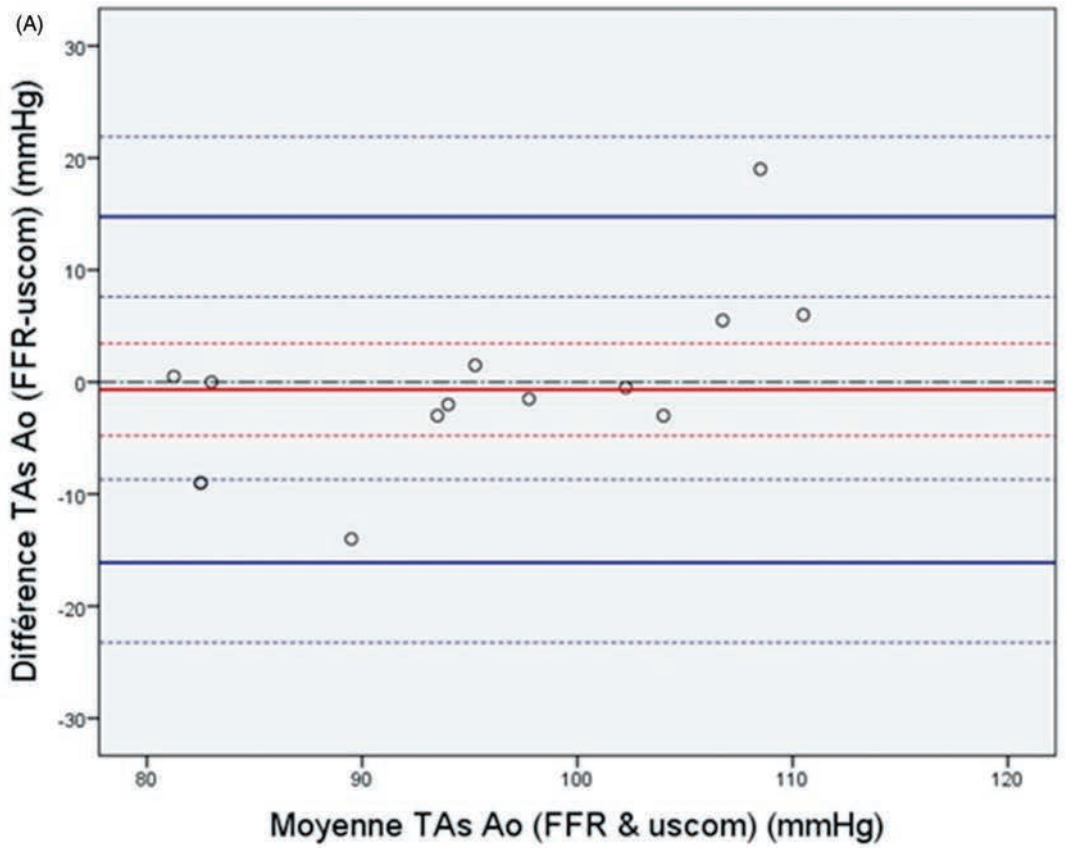
[a]CHU A Paré; [b]CHU A Paré & UMONS; [c]UMONS

Background: Central blood pressure (cBP) is a better predictor of the damage caused by hypertension in comparison with peripheral blood pressure (pBP). Although challenging to measure, numerous devices are trying to reliably estimate cBP non-invasively. Pulse wave velocity (PWV) is another important independent cardiovascular risk factor.
Aim: We sought to deploy a new validation method using a high-fidelity pressure wire as the invasive gold standard measurement for sphygmomanometer devices estimating cBP. Moreover, we invasively calculated the PWV to investigate its relationship to the non-invasively estimated cBP.
Methods: In 50 patients requiring a cardiac catheterization, we measured the blood pressure in the ascending aorta (AAo) with a fluid-filled (FF) guiding catheter (NaCl 0.9%). We compared these values with the results derived simultaneously with a novel sphygmomanometer that estimates cBP from the analysis of brachial artery suprasystolic pressure waves, based on the pressure-wave propagation of a water-hammer acoustic model. On 14 of these patients, we placed a 0.014" high-fidelity pressure wire in the AAo to measure cBP, when it was clinically indicated to evaluate one or more coronary stenosis by Fractional Flow Reserve (FFR). Ultimately, the wire was pulled back into the humeral artery (HUM). PWV was then calculated from the length of the pullback and the time delay between AAo and HUM pulses by gating to the R-wave of the ECG for both measurements, using MatLab software.
Results: Bland-Altman analysis of the sphygmomanometric cBPsys and the FFR wire (left on figure) demonstrates less scatter than with the FF catheter (right). The mean difference with the sphygmomanometrically derived cBPsys was -1.2 ± 4.7 mmHg (CI95%: -3.84; 1.82) for the FFR wire and $6{,}0 \pm 9{,}8$ mmHg (CI95%: 3.2; 8.9) for the FF catheter. Central diastolic and mean BP were both overestimated by the sphygmomanometer, with respectively -7.8 ± 6.8 mmHg (CI95%: $-11{,}4$; $-4{,}2$) and -5.5 ± 6.1 mmHg (CI95%: -8.6; -2.3) compared to the FFR wire and -10.3 ± 6.7 mmHg (CI95%: -12.2; -8.3) and -5.5 ± 6.5 (CI95%: -7.3; -3.6) for the FF catheter. The average PWV was 7.0 ± 1.4 m/s. No significant relationship of PWV and cBP was identified ($p = .189$). The PWV was 0.8 m/s lower in patients with ≤ 1 cardiovascular risk factors versus >1, but without reaching statistical significance.
Conclusions: Using an FFR wire in the AAo as a high-fidelity pressure reference, we demonstrated that cBPsys derived from the sphygmomanometer was accurate, with a non-significant bias (<5 mmHg) and high precision (standard deviation <8 mmHg) as recommended, criteria not met using the FF guiding catheter measurements. PWV measurements were also easily obtained from the FFR wire method.


(A)
Différence TAs Ao (FFR-uscom) (mmHg)
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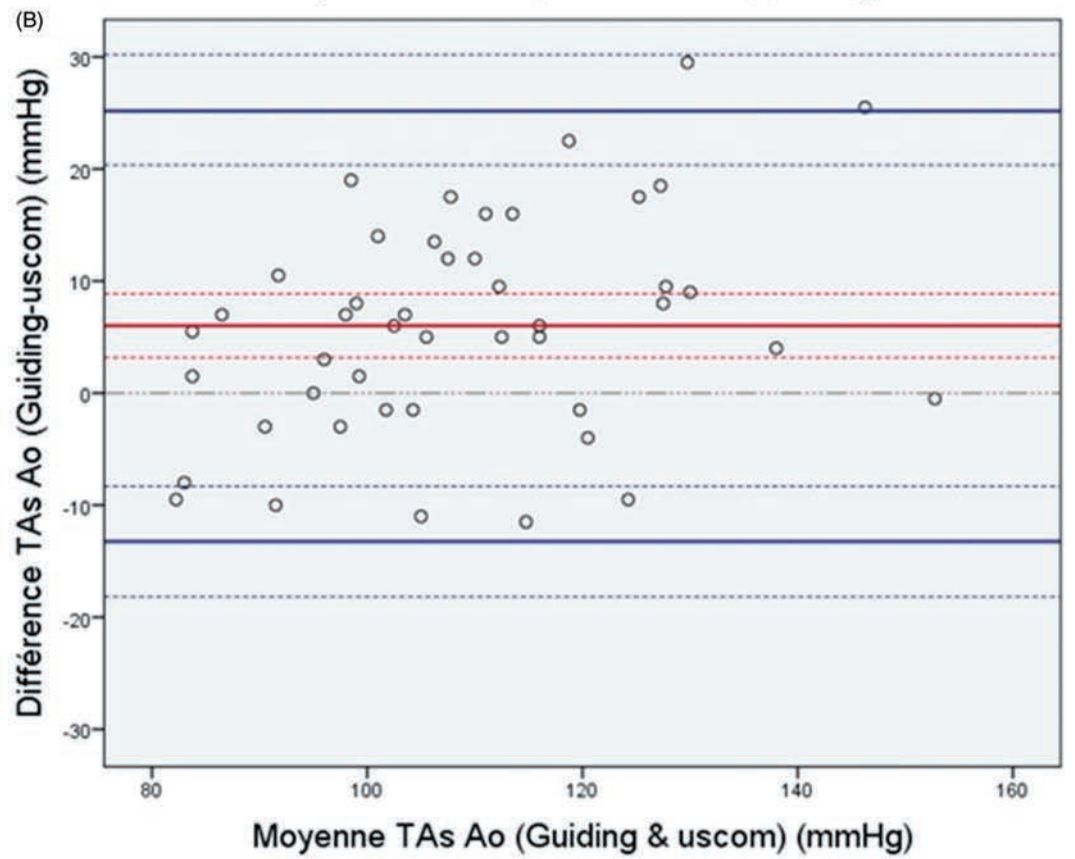
Moyenne TAs Ao (FFR & uscom) (mmHg)


(B)
Différence TAs Ao (Guiding-uscom) (mmHg)
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140
160
Moyenne TAs Ao (Guiding & uscom) (mmHg)

Longitudinal changes in diastolic function and exercise capacity under the influence of cardiometabolic disease

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[a]Cliniques universitaires Saint-Luc; [b]Brussels Brabant Heart Center; [c]KCE

Background: The relationship between cardiovascular risk factors and the development of diastolic dysfunction (DD) as well as the effect of DD on exercise capacity is still underestimated. Our aim was to evaluate the longitudinal evolution of diastolic function and exercise capacity in patients with cardiometabolic disease.
Methods: Forty-three patients (53 ± 11 years, 35% women) with a single (diabetes type II, arterial hypertension or hypercholesterolemia) or no cardiovascular risk factor in 2007 underwent a 2D echocardiography and an exercise test at visit 1 (2007) and 2 (2016) with a mean interval of 9 years.
Coronary artery disease was excluded by CT-SCAN.
Results: The comparison of cardiovascular risk profiles between visit 1 and 2 showed that the participants tended to accumulate cardiovascular risk factors over time. Sixteen participants presented DD at visit 1, and twenty-seven at visit 2. DD progressed in 44%, remained stable in 42% and regressed in 14%. Systolic function remained stable and preserved. We noticed a significant decline in exercise capacity with a reduction in the power provided during the exercise test ($p = .001$), a decrease in the maximal O2 consumption ($p = .006$), the amount of METS ($p = .039$) and in the maximum cardiac rate ($p < .001$). Multivariate logistic regression showed that a higher ejection fraction (HR = 0.78, 95% CI 0.64-0.94, $p = .009$) and a higher number of METS delivered at exercise test in 2007 (HR = 0.58, 95% CI 0.36-0.94; $p = .027$) seem to be protective factors for development of DD over time. No cases of cardiovascular death or acute heart failure were observed during the interval.
Conclusions: DD tends to progress in a community based cohort with cardiometabolic disease. A maintained EF and a high number of METS provided during exercise test seem to be protective factors in the development and progression of DD.

	Visit 1 2007	Visit 2 2016	p-value
Number of participants	43	43	-
Gender (female)	15 (35%)	15 (35%)	-
Age (years)	53 ± 11	62 ± 10	<0.001
Participants without cardiometabolic disease	10 (23%)	6 (14%)	0.71
Participants with arterial hypertension	12 (28%)	21 (49%)	0.002
Participants with hypercholesterolemia	11 (26%)	18 (42%)	0.070
Participants with diabetes type II	10 (23%)	13 (30%)	0.083
Smokers	14 (33%)	6 (14%)	0.003
Echocardiographic parameters			
Mitral E wave velocity (cm/s)	59 ±12	61 ± 14	0.49
E wave deceleration time (ms)	181 ± 29	174 ± 42	0.47
E/A ratio	0.93 ± 0.26	0.88 ± 0.28	0.47
Septal E/E' ratio	7.9 ± 1.6	10.2 ± 3.5	<0.001
Lateral E/E' ratio	5.9 ± 1.5	8.1 ± 2.8	<0.001
Ejection fraction of the left ventricle (%)	58 ± 5	59 ± 9	0.48
Shortening fraction of the left ventricle (%)	40 ± 8	40 ± 9	0.85
Exercise test parameters			
Power (watts)	156 ± 42	142 ± 52	0.001
Maximal VO_2 (ml/min/kg)	78 ± 19	82 ± 22	0.006
METS	6.5 ± 2.2	6.05 ± 1.8	0.039
Maximum cardiac rate (beats/min)	149 ± 16	139 ± 21	<0.001

(Δ) Predictors of the usage of a cardiac-based e-learning platform in ischemic heart disease patients

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Background: Despite effectiveness of cardiac rehabilitation (CR) in ischemic heart disease (IHD) patients, time and travel required to attend CR in specialized centres severely impede participation rates. E-learning may be the first step to offer CR to patients at home, but may also be a qualitative memory support in addition to on-site educational lectures. Several studies suggest that online learning and CR may improve self-care behaviour.

Purpose: This study investigates whether sociodemographic factors and medical history influence cardiac-based e-learning usage. This may be useful in daily clinical practice to identify IHD patients who are more likely to use e-learning and have the possible benefits of it.

Methods: This prospective, multicentre trial with 508 IHD patients was conducted in two Belgian hospitals. All patients received one-month access to an online cardiac-based e-learning platform containing sixty videos, in addition to conventional cardiac care. In these 1-2-minute videos, (para)medics and patients lectured about different topics concerning living with IHD. The explored sociodemographic and medical variables of the subjects comprised age, gender, educational attainment, vocational status, smoking, in-centre CR participation, type of cardiac pathology, treatment of IHD, diabetes mellitus, peripheral artery disease, arterial hypertension, hyperlipidemia, family history of IHD and ejection fraction. The primary endpoint was the proportion of patients who watched videos on the e-learning platform. The secondary endpoint comprised the time subjects spent watching the e-learning videos. By modelling multiple logistic and linear regressions, the influences of the sociodemographic and medical variables on the outcome measures were investigated. Multiple imputation was used to handle missing patient variables.

Results: Half (50.4%) of the subjects opened the videos of the e-learning platform at least once and the median time they watched the videos was 23'17". Regression analyses with all variables included show that in-centre CR participation ($p = .0130$) and educational attainment ($p = .0228$) significantly affect the probability that a patient uses the e-learning platform after receiving free access. Of the subjects who attended in-centre CR 53.8% used the platform, while this was only 35.2% for subjects who never attended in-centre CR. Depending on the educational attainment, 44.0% (primary education), 46.4% (secondary education), 64.7% (higher education) or 50.6% (university) of the subjects watched the videos. Furthermore, there seems to be a significant negative influence of age ($p = .0498$) on the logarithm of the time patients spent watching videos. All other variables had no significant effect on the outcome measures.

Conclusions: This study suggests that in-centre CR participation, educational attainment and age may influence cardiac-based e-learning usage in IHD patients. Future research should assess whether the investigated factors also influence the clinical effectiveness of e-learning.

A decade of infective endocarditis in a single large cardiac center: contemporary insights into an ancient illness

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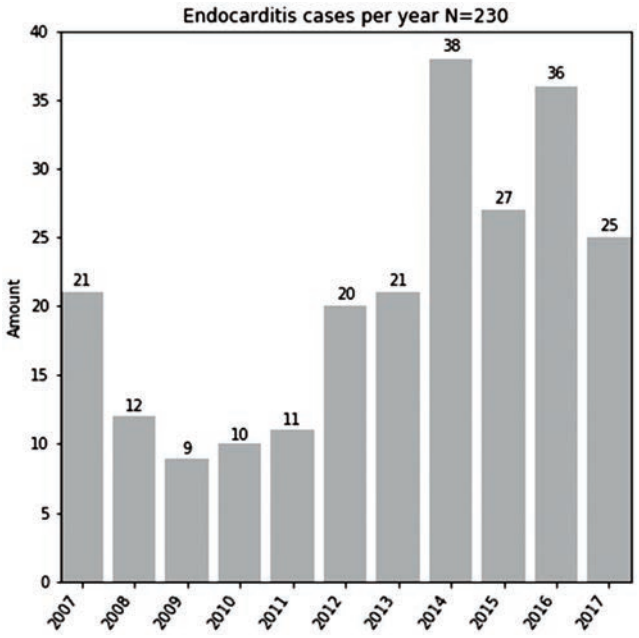
Background: Recent studies have shown an increase in incidence of Infective Endocarditis (IE), which, despite medical advancements, still carries a significant mortality rate.
Many speculations have arisen to explain this increase in incidence, mainly the aging of the population or the (guideline-based) limiting of IE prophylaxis, as well as the growing number of intra-cardiac devices and valve replacements. The aim of our study was to verify if these trends were also seen in a large tertiary center in a country with easy access to a high standard medical care.
Methods: All patients, aged 18 or above, diagnosed and treated for IE in our hospital in a period of 11 years between January 1st 2007 and December 31st 2017 were retrospectively identified. Due to the retrospective nature of the study no approval of the local ethics committee was required.
Results: A total of 230 cases were identified, out of these 33 patients (14.3%) had a Cardiac Device related IE (CDIE) and 59 patients (25.7%) had prosthetic valve endocarditis. The incidence of overall IE increased over the course of years (from 10 IE/year to 25 IE/year).
Our population was predominantly male (63.9%). The mean age was 67.7 years old. The patients treated by surgery combined with antibiotics had a significantly better prognosis (mortality 19.6%) compared to those who were treated conservatively with antibiotics only (mortality 31.3%, $p = .05$). Women had a significantly higher mortality (33.7% vs 21.8%, $p = .047$).
One sixth of the population were classified as culture-negative and in those with positive blood cultures Staphylococci were the most prevalent (49.7%) followed by Streptococci (27.7%) and Enterococci (12.8%). A single case of Coxiella burnetti IE was identified (0.5%). Mortality was the highest for Staphylococcus infections (though not significant, $p = .134$).
Older patients appeared to have a higher risk for mortality (mean age for survivors was 66 years compared to 72 years at time of death).
Interestingly, our study showed a higher (though not significant) mortality rate for native valve IE compared to prosthetic valve IE (33.3% vs 21.9%, $p = .406$). Women were less likely to undergo surgery.
Conclusions: From one of the largest reported single-center cohorts of IE patients, it is obvious that the incidence of IE has also increased in our population over the past 11 years. This trend is consistent through all subgroups. The "typical" causal microorganisms remain responsible for the vast majority of infections.
Interesting differences in outcome between the sexes and between different m anagement modalities (surgery or not) are apparent, however statistical significance remains uncertain. Mortality remains more than 20% despite modern medical management of this condition. Analysis of a larger cohort (for instance, by creating a national endocarditis-database for instance) and monitoring trends over time could certainly lead to better insights.



A decade of prosthetic heart valve endocarditis in a single large cardiac center: contemporary insights into an ancient illness

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Background: Recent medic al advancements have caused a shift from rheumatic heart valve disease towards degenerative heart valve disease in developed countries. This in combination with the ageing of the population has caused an increase in heart valve replacements and a change in type of heart valve replacement towards biologic prosthesis. Heart valve replacement remains a risk factor for infectious endocarditis (IE), which up to this day, despite medical advancements, retains a high mortality and morbidity. We performed a retrospective study in our hospital including all patients with a prosthetic valve infectious endocarditis. The aim of our study was to identify possible trends in change in incidence, causative organisms and mortality.
Methods: All patients, aged 18 or above, diagnosed and treated for IE in our hospital in the 11 years between January 1st 2007 and December 31st 2017 were retrospectively identified by data-mining the cardiac ultrasound database and cross-referencing with patient records as well as disease coding for endocarditis and lead-extraction, the subpopulation of Prosthetic valve IE cases were then identified and examined. SPSS and Matplotlib combined with Scipy were used for statistical analysis. Due to the retrospective nature of the study, no approval from the local ethics committee was required.
Results: A total of 64 patients with prosthetic valves and infective endocarditis were identified, out of these a total of 59 cases with proven prosthetic valve endocarditis were included. The remaining 5 patients were classified as a Cardiac Device related Infective Endocarditis.
Two thirds of our population were male and the median age was 75 years old (min 42–max 92). A fifth of the population died during hospital stay. Nearly forty percent underwent valve replacement surgery during hospital stay. 3 patients had a relapse, 2 within 1 year and 1 within 3 years of original diagnosis. Six patients died during the 5-year follow-up due to all-cause mortality.
The most prominent location of infection was the aortic valve (59.3%) followed by the mitral valve (49.2%). Seven cases had multiple valve involvement.
Eight cases were classified as culture negative and the most common causative organisms were Streptococci (31.4%), Enterococci (27.5%) and Staphylococci (25.5%). One single case of Coxiella burnetti IE was identified. The mean incidence of prosthetic valve endocarditis increased from 2 cases per year during the first half of the study to 8.2 cases per year during the second half of the study. More men underwent surgery (46.2%) compared to women (25%) and women had a higher mortality (30% versus 12.8%)
Conclusions: The incidence of prosthetic valve infective endocarditis has markedly increased over the past ten years and still carries a high mortality and morbidity. Contrary to other IE studies, the most prevalent causative organisms were Streptococci, as was seen many years ago, and not Staphylococci.