[Abstracts]

Belgian Society of Cardiology 35th Annual Congress

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President: Prof. Agnès Pasquet

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

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

- Arrhythmias
- Basic science
- Heart failure
- Invasive
- Non-invasive

ARRHYTHMIAS

Evolution over time of antithrombotic therapies in Belgium in patients with newly diagnosed atrial fibrillation: data from the GARFIELD-AF registry. (Δ)

— Frank Cools (AZ KLINA), Bart Wollaert (ZNA), Geert Vervoort (AZ Sint Maarten), Joeri Voet (AZ Sint Nikolaas), Alex Heyse (AZ Glorieux), Stefan Verstraete (AZ Zeno), Tim Boussy (AZ Groeninge), Axel De Wolf (HH Tienen), Olivier Xhaet (UCL Mont Godinne), Geert Hollanders (De Pinte), Kurt Hermans (AZ St. Lucas), Jan Vercammen (Yperman ziekenhuis), Michel Beutels (Merksem), Dr. Wim Anné (AZ Delta), Dirk Faes (Mariaziekenhuis Noord-Limburg), Georges Mairesse (Cliniques du Sud Luxembourg), Luc Capiau (Wetteren), Pascal Godart (CHU Ambroise Paré), Peter Vandergoten (Europa Ziekenhuizen), Yohan Balthazar (Natoye), AJ Kakkar (TRI London UK)

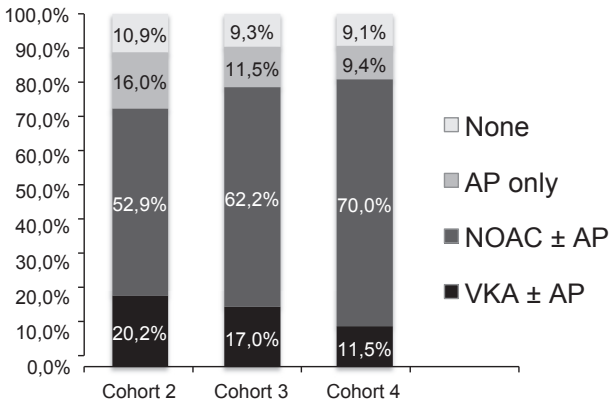
Background Changes in the use of antithrombotic therapies are described using data of Belgian patients (pts.) recruited in the Global Anticoagulant Registry in the Field (GARFIELD-AF) study, across 3 consecutive cohorts from 2012-2015.

Methods GARFIELD-AF is an ongoing, international, prospective, observational study of consecutively recruited adults (≥ 18 years) with newly diagnosed (≤ 6 weeks) non-valvular atrial fibrillation (AF) and ≥ 1 investigator-determined stroke risk factor. Patients are followed prospectively for a minimum of 2 years. Garfield is recruiting 5 cohorts of approximately 10000 patients. Belgium entered the study in cohort 2. Recruitment in cohorts 2 (June 2012-June 2013), 3 (July 2013-July 2014) and 4 (August 2014-July 2015) has now been completed: 403, 515 and 427 pts. were included respectively. Antithrombotic therapies that were initiated were analyzed per cohort.

Results At this time, baseline results are available for all 403 and 515 cohort 2 and 3 pts., as well as 384 of the 427

cohort 4 pts. (n = 1302 for all cohorts). For all cohorts, mean CHA_2DS_2-VASc score is 3,1 ± 1,6. Anticoagulants (AC) at diagnosis were started in 73,1%, 79,3% and 81,5% respectively in all pts. For the CHA_2DS_2-VASc ≥ 2 pts. this was 77,4%, 82,9% and 86,7%.

Across the 3 cohorts, the use of Vitamin K antagonists (VKA) decreased (20,2%, 17,0%, 11,5%) and use of the Non-Vitamin-K-Anticoagulants (NOACs) increased (52,9%, 62,2%, 70,0%) (Figure). Within the NOACs, Factor Xa antagonists (fXa – 61,8%, 77,4%, 81,3%) were used more frequently than direct thrombin inhibitors (DTI – 38,2%, 22,6%, 18,7%). Antiplatelet use decreased from 31,7% to 26,8% and 17,5% across the 3 cohorts.



Conclusions From 2012 to 2015, anticoagulation use in patients with newly diagnosed AF in Belgium and at least one stroke risk factor, is increasing with nowadays 86,7% of patients with a CHA_2DS_2-VASc score of ≥ 2 receiving adequate treatment. This increase is largely driven by increased use of NOACs at the cost of VKA. Within the NOACs, factor Xa antagonists are used preferentially compared to direct thrombin inhibitors. Antiplatelet use continues to decrease. More results will be available at the BSC meeting.

Long-term outcome of atrial fibrillation ablation in 1000 patients. (#) — Yves De Greef, Ian Buysschaert, Bruno Schwagten, Dirk Stockman *(ZNA Middelheim Hospital and ASZ Hospital Aalst).*

Background Pulmonary vein isolation (PVI) is an accepted treatment to relieve symptoms in patients with atrial fibrillation (AF). We studied outcome after PVI in a large cohort of patients from 2004 guided by various ablation techniques and follow-up ≥ 1 year.

Methods 1000 patients with symptomatic recurrent AF (age 60 ± 10, 72% males, CHA_2DS_2-VASc score 1 ± 1) and minimal heart disease underwent PVI (point-by-point RF ablation with Carto (manual, n = 265; stereotaxis, n = 164) or Ensite (manual, n = 138; stereotaxis, n = 9), PVAC, n = 262, HDMA-Mesh ablator, n = 59, Cryoballoon, n = 93 and nMarq, n = 10). Repeat ablation procedures consisted of point-by-point re-isolation of reconnected PVs and, if necessary, additional atrial ablation. Success was defined as freedom of documented AF after ablation with or without anti-arrhythmic drug treatment (ADT) with a blanking period of 1month.

Results After a mean follow-up duration of 46 ± 47 months, 517 patients (47 still on ADT) remained free of documented AF after a single procedure. Although most recurrences (n = 339, 70%) occurred in the first year after ablation, a substantial N of patients (n = 144, 30%) displayed a late (≥ 1year) recurrence. AF recurrence between years 1-2, 2-3, 3-4, 4-5 and > 5 years occurred respectively in 79 (55%), 33 (23%), 15 (11%), 11 (7%) and 6 (4%) patients.

After repeat ablation procedures, another 282 patients (46 still on ADT) could be rendered free of atrial fibrillation. As a final result, 80% of the patients were free of atrial fibrillation after a mean number of 1,5 ablation procedures per patient.

Conclusion Almost half of the patients undergoing AF ablation will display a documented AF recurrence during long-term follow-up. AF recurrence can still occur even after a time horizon of > 5 years. This has major implications towards "whether or not" and "when" oral anticoagulation can safely be discontinued after a presumed successful ablation in patients with a CHA_2DS_2-VASc score ≥ 1. To obtain a beneficial clinical outcome multiple procedures are often needed with 11% of patients still on chronic anti-arrhythmic drug therapy.

Safety profile of atrial fibrillation ablation versus chronic amiodarone therapy: a comparison. — Yves De Greef, Ian Buysschaert, Bruno Schwagten and Dirk Stockman *(ZNA Middelheim Hospital, ASZ Hospital Aalst).*

Aim We aimed to compare safety profile of ablation of atrial fibrillation (AF) using various techniques in a large cohort of patients from 2004 until 2014 versus a group of patients taking amiodarone before ablation.

Methods 1000 patients with symptomatic recurrent AF (age 60 ± 10, 72% males, CHA_2DS_2-VASc score 1 ± 1) and minimal heart disease underwent AF ablation (point-by-point RF ablation with Carto (manual, n = 265; stereotaxis, n = 164) or Ensite (manual, n = 138; stereotaxis, n = 9), PVAC, n = 262, HDMA-Mesh ablator, n = 59, Cryo-balloon, n = 93 and nMarq, n = 10). All procedures were performed under general anaesthesia. Before ablation, a cohort of 320 patients were on chronic amiodarone therapy. A complication of ablation was defined as any procedure-related adverse event occurring up to 1month after ablation, a side-effect of amiodarone as any reason necessitating discontinuation.

Results A total of 99 (9,9%) adverse events occurred in 1000 AF ablation procedures.

There were no peri-procedural deaths. Adverse events could be classified into 2 groups:

(1) "ablation technique independent" mainly consisting of vascular injury (40%), pneumonia (4%), bladder injury (7%), thrombo-embolic events (2%) (1 TIA, 1 coronary embolization of left atrial thrombus after transseptal puncture), transient gastro-paresis (2%) and
(2) "ablation technique dependent" such as pericardial injury (33%) (3 tamponades, 31 pericarditis requiring NSAIDs and 'fluid' retention syndrome (6%) both mainly related to point-by-point ablations using RF, transient phrenic nerve palsy (6%) mainly related to cryo-balloon ablation, and pulmonary vein stenosis (3%) mainly related to PVAC ablation.

Interruption of amiodarone therapy was necessary in 120 (38%) of 320 patients on amiodarone therapy before ablation. Reasons to interrupt were thyroid dysfunction (55%), dermal toxicity (22%), prolonged QT interval (6%), ocular toxicity (9%), pulmonary toxicity (4%) and intolerance (15%).

Conclusions Although relatively frequent, the great majority of complications of AF ablation can be treated conservatively and only seldom lead to permanent sequellae. Adverse events of AF ablation consist mainly of vascular and pericardial injury and are dependent on the ablation technique used. Although displaying a different safety profile, amiodarone therapy has an absolute higher number of adverse events.

First Belgian experience with miniaturized leadless cardiac pacemakers (Micra Transcatheter device). — Christophe Garweg, J. Ector, P. Haemers, G. Voros, R. Willems (Cardiology, University Hospitals of Leuven)

Aims Cardiac pacing is the only effective treatment for symptomatic bradycardia that improves survival in high-risk populations and reduces recurrence of syncope. Complications associated with conventional transvenous pacing systems are most often related to the pacing lead and pocket. We report the results of the first implantations of leadless cardiac pacemaker in our center.

Methods and results From july to mid-september 2015, we implanted 3 patients having a Class I indication for VVI pacing with a Micra transcatheter pacing system (Medtronic, Minneapolis, USA), from the right femoral vein and fixated in the right ventricle using four protractible tines (figure 1). The 3 patients were male, mean age 85 ± 4 years old. Primary indication for pacing was chronic atrial fibrillation with symptomatic pauses > 3 secondes and syncope. Implant success rate was 100% without need for repositioning of the device after first deployment. All procedures were performed under general anesthesia. Implant time was respectively 52, 45 and 40 minutes for the first, second and third procedure with a mean fluoroscopy time of 15 ± 4 min. The 3 devices were implanted at the RV apex. Access site closure was performed using a suture method (figure of eight stitch). No adverse events related to the procedure for the 3 patients were observed. The mean pacing capture threshold was 0.8 ± 0.2 V at 0.24 ms at implantation and was 0.56 ± 0.07 V at 0.24 ms after 1 month follow-up. Mean pacing impedance was respectively 540 ± 40 ohm and 530 ± 20 ohm at implantation and after 1 month. R-wave sensing amplitude was respectively 10.1 ± 6.2 mV and 12.3 ± 8.3 mV at implantation and after 1 month.

Conclusion The first 3 implantations of a miniaturized leadless cardiac pacemaker (Micra Transcatheter device) were successful without complications. Implantation of this new device was safe and efficient with stable pacing parameters at 1 month. Total procedure time shortened from the first to the last procedure without any complications. We will continue using this innovative technique and will present an update of our experience at the conference. We expect to have implanted > 10 devices by January 2016.

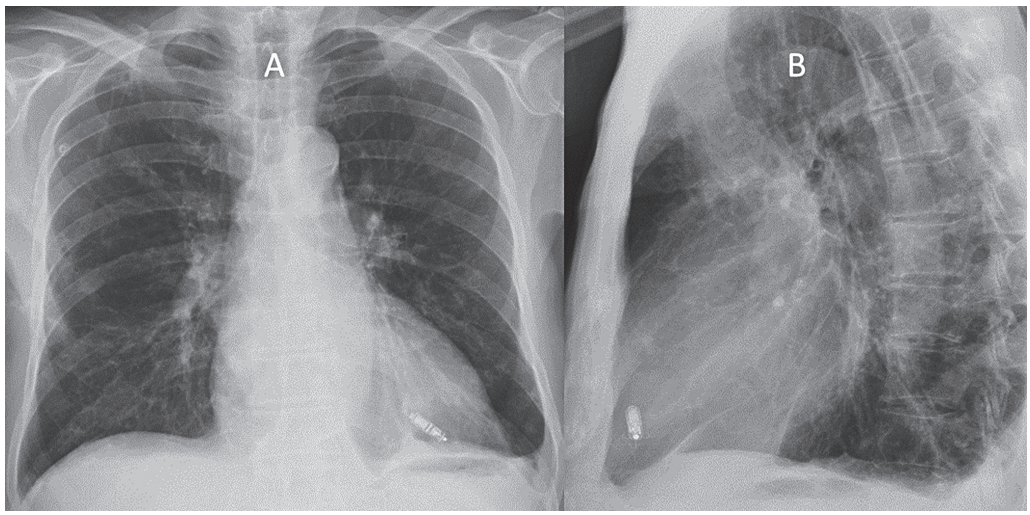


Fig. 1 Fig. 1 chest radiography (A. Face, B. Profile) after successful implantation of a leadless cardiac pacemaker (Micra Transcatheter device, Medtronic, Minneapolis, USA).

Prediction of 30-Day outcome for out of hospital cardiac arrest survivers (OHCAS). — J. Higny[1], J. Jamart[2], L. De Cannière[3], C. Boulouffe[3], X. Muschart[3], V. Gérard[3], D. Vanpee[3], A. Dive[4], P. Evrard[4], F. Feye[1], F. Foret[4], C. Hanet[1], L. Gabriel[1], V. Dangoisse[1], A. Guédès[1], E. Schroeder[1] *([1]Cardiology Unit, [2]Biostatistics Unit, [3]Emergency Unit, [4]Intensive Care Unit – CHU Dinant Godinne, B-5530 Yvoir, Belgium).*

According to current guidelines, OHCAS should undergo at admission early cerebral imaging by CT and coronary angiography in order to perform PCI culprit lesion. Early coronary reperfusion has been reported to be associated with better outcome.

Aim We sought to perform a quality control assessment on the management of OHCAS at our center and to determine predictors of 30-days outcome (survival).

Methods A consecutive series of 123 patients admitted alive to our emergency department (2012-2014) after OHCAS. STEMI was present in 24%, NSTEMI in 14%, coronary angiography was performed in 52% during the hospital stay.

Results The 30-day mortality rate was 60.2%. In comparison to survivors, deceased patients were older (69.9 vs 60.7 y. *), had longer duration of no flow (11.4 vs 3.4 min*), longer duration of low flow (34.4 vs 12.5 min*), higher lactate levels on admission (0.5 vs 4.2 mmol/L*), higher creatinine levels (1.6 vs 1.2 mg%*), higher glucose levels (244 vs 195 mg%*), lower pH (7.10 vs 7.29). 30-day mortality was increased in the group of patients without cardioconvertible rhythm (80 vs 44.1%*), witout bystanders (82.9 vs 23.9%*) without ventricular tachycardia (VT) (74.7 vs 0%*), no evidence of ACS (73.7 vs 38.3%*), no evidence of STEMI (65.6 vs 43.3%*), no evidence of NSTEMI (65.1 vs 29.4%*), with convulsions (91 vs 44%*), with renal failure (78.3 vs 37%*) during hospital stay.

By a logistic regression analysis and ascending selection, we found three variables predicting 30-day mortality: the absence of VT, the duration of no flow (OR: 1.46 – CI: 1.20-1.77) and the duration of low flow (OR: 1.13 – CI: 1.03-1.24). By using an algorythm including those 3 prehospital variables, we were able to predict correctly the 30-day outcome in 92.6%.

Conclusions In our series, 30-day outcome was mainly depending on 3 prehospital variables: the absence of ventricular tachycardia, no flow duration and low flow duration. The no flow duration seems the only modifiable (prehospital) variable – by proper training of the potential bystanders and by shortening the delay of SMUR/MUG interventions. It seems that most of the presently used diagnostic and therapeutic procedures after OHCAS have less potential to improve outcome, as the severity (duration) of the circulatory arrest seems to represent the major determinant for outcome.

* $P < 0.01$

AF free survival with the second generation cryoballoon: ready for persistent patients? — Luc Jordaens, M. Castadot, B. Dewit, A. Lozano, P. Goethals *(Hospital St Jan Brussel, Centre Medical des Iles d'Or, Brussels, Erasmus MC Rotterdam)*

Introduction The exact place for cryotherapy in the ablation of persistent and paroxysmal atrial fibrillation remains debated. With the first generation of cryoballoon catheters we addressed primarily paroxysmal AF patients, and only occasionally persistent patients. However, our results in the persistent patients were comparable to the paroxysmal patients. As the new generation cryoballoon was more powerful, it was considered to apply cryotherapy both to paroxysmal and persistent AF patients.

Methods and Results Results and complications from the first consecutive 36 patients in Brussels Heart Center (2nd generation balloon) were compared to the 48 patients treated in Erasmus MC in the year 2009 (1st generation cryoballoon) (table 1).

There were no differences between the 2 groups, except for the AF type. The event free survival for both groups is shown in the figure, showing a significantly improved result with the 2nd generation ($P < 0.01$) (figure 1).

Importantly, in the 2nd generation balloon there were no statistical differences between the subtypes of AF in respect to outcome (both recurrences were from the Persistent/Persistent + flutter group).

Procedural parameters and complications are shown in table 2.

Conclusions In spite of a more difficult patient group in the recent series, as indicated by the high number of persistent patients and patients with flutter, the 2nd generation cryoballoon was more effective than the first generation, without the need for touch up procedures, and with a substantial lower number of reinterventions. Radiation time remained equal, and the number of serious complications tended to decrease. PNP had a tendency to increase, but was transient in all. Persistent patients had anuneventful follow-up, which was similar to paroxysmal AF. Cryoablation for persistent AF merits a randomised trial.

Table 1

	2009 – Erasmus MC	2013-2014 – BHC*
Number	48	36
Male/Female	35/13	24/12
Age (Mean ± SD/Median) -yrs	58 ± 10/59	62 ± 12/66
Type	Paroxysmal: 45 (94%) (Median burden** 8%) (IQ Range 0-29%) (Mean burden 21%) Permanent: 3 (6%)	Paroxysmal: 18 (50%) Parox. + Flutter: 4 (11%) Persist. Light: 3 Persistent: 10 (39%) Pers. + Flutter: 1

*BHC: Brussels Heart Centre; ** Burden: % of daily event tracings.

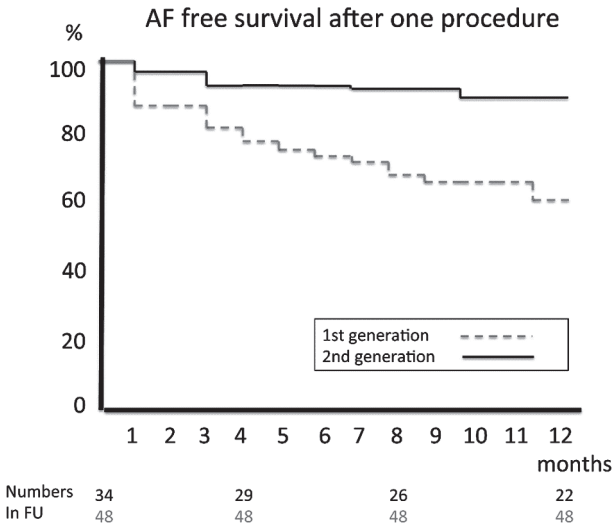


Fig. 1

Table 2

	2009 – Erasmus MC	2013-2014 – BHC
Radiation time (min)	35 ± 17	33 ± 13
	median 33	median 29
General anesthesia	18 (38%)	36 (100%)
Touch up procedure/flutter	13/0	0/2
PE/Tamponade	6/0	0/1
Phrenic Nerve Paresis* (PNP)	3	6
Groin bleeding	3	1
Other bleeding	1 hemoptoe	1 retrop. Hem.
Redo < 1 year	7	1

* all transient.

Terminal QRS axis has the potential to differentiate arrhythmogenic right ventricular cardiomyopathy from right ventricular outflow tract ectopy. — Pieter Koopman[1,3], Emilie Empsen[2], Evelyne Roets[2], Thomas Neyens[2], Anton Gorgels[3], Paul Volders[3] *([1]Heart Centre Hasselt, Jessa Hospital, Hasselt, Belgium, [2]Hasselt University, Hasselt, Belgium, [3]Maastricht University Medical Centre, Maastricht, The Netherlands).*

Aims Arrhythmogenic right ventricular cardiomyopathy (ARVC) is associated with delayed electrical activation of the right ventricle (RV). The aim of this study was to assess direction of the terminal axis (TA) of the QRS complex on 12-lead electrocardiogram (ECG) as a new method to add to the pathophysiological understanding of this condition.

Methods We retrospectively determined TA in 170 patients with a clinical diagnosis of ARVC and 26 with right ventricular outflow tract (RVOT) ectopy without structural abnormalities, as compared to 50 normal ECGs. TA was defined as the frontal plane axis of the terminal QRS activation at 20 ms before the end of the QRS and was visualized on a circular diagram.

Results TA of ARVC patients has a distinct right-sided direction (p-value: < 0.0001), whereas TA of control patients and TA of patients with RVOT ectopy is equally distributed on a circular diagram. A right-sided orientated TA yields a sensitivity of 79% for the diagnosis of ARVC. Comparison of the mean direction of TA between patients with or without a known pathogenic mutation indicates no significant difference between the two groups (p-value: 0.462).

Conclusions TA of ARVC patients is significantly directed right-sided towards the RV inflow and outflow tract, compatible to involvement of RV conduction delay in ARVC pathophysiology. In patients with benign RVOT ectopy, TA does not show this predilection. Determination of TA could be a useful additional criterium for the diagnosis of ARVC and the differentiation with benign RVOT ectopy.

First Belgian experience with the Endoscopic laser balloon Ablation System for pulmonary vein isolation. (Δ) — Pieter Koopman[1], Jeff ten Haken[2], Philippe Vanduynhoven[1], Dagmara Dilling[1], Joris Schurmans[1], Hein Heidbuchel[1], Johan Vijgen[1] *([1]Heart Center Hasselt, Jessa Hospital, Hasselt, Belgium, [2]Cardiofocus Inc, Marlborough, USA)*

Aims Pulmonary vein isolation (PVI) is a common treatment option for patients with atrial fibrillation (AF). Conventional point-by-point radiofrequency ablation is time-consuming and requires periprocedural imaging using 3D mapping systems to reliably identify the pulmonary vein (PV) – left atrial (LA) junction. Current balloon technologies are confined to a single balloon size and a preset ablation design, do not offer variable energy modes, and require periprocedural contrast injections to identify the PV – LA junction. The novel endoscopic laser balloon ablation system (EAS) consists of a compliant, sizeable balloon and allows for direct endoscopic PV visualisation and guidance of energy delivery during PVI procedures, using a new energy source for ablation. The present study aims to report feasibility, safety and acute efficacy of the novel EAS for PVI in the first 34 patients treated in Belgium.

Methods 34 patients (71% male, mean age 60 years) with AF (79% paroxysmal, 21% persistent) successfully underwent pulmonary vein isolation with the EAS in a 6.5 months period from December 2014 to July 2015. Two operators performed all procedures. A total of 132 PVs (4 patients with left common PV, 1 patient with an additional right middle PV) were treated. One right inferior PV was not treated due to occurrence of phrenic nerve palsy when isolating the right superior PV. Median follow-up was 2.5 months (0-6 months).

Results Successful PVI could be achieved in 130/132 PVs (98.5%). 121/132 veins (91.5%) were isolated on the first attempt encircling the PV by visual guidance only. Average procedure time was 149 minutes. Average fluoroscopy time was 21 minutes. Fluoroscopy time significantly declined over time. One procedure was complicated with phrenic nerve palsy (3%) and one procedure with pericardial effusion (3%). No other major adverse events occurred. Two patients had a transient recurrence of AF the day after the procedure (6%). During further follow-up, 33/34 patients (97%) remained free of AF based on symptoms and 24-hour holter ECG recordings. Palpitations but no documentation of AF occurred in the patient that was incompletely treated.

Conclusions Circumferential PVI using endoscopically guided laser balloon ablation is a valuable alternative to conventional ablation techniques and is associated with a low risk of complications. Even first time users may achieve acute PVI in a high number of patients with favorable clinical outcomes. Fluoroscopy time and procedural safety improve with growing experience.

Atrial fibrillation and long term risk for progression of mitral/tricuspid valve regurgitation. (#) — Carl Van Paesschen, Barbara Cornez, Hielko Miljoen, Paul Van Herck, Bharati Shivalkar, Chris Vrints, Marc J Claeys *(University hospital Antwerp, Belgium).*

Background While severe mitral/tricuspid regurgitation (MR/TR) is a wellestablished risk factor of atrial fibrillation (AF), it is unknown whether atrial fibrillation induces mitral/tricuspid valve regurgitation.

Objective To identify long term effects of AF on the progression of MR/TR.

Methods Mitral/tricuspid valve regurgitation was assessed over a period of 5 years in 41 patients with permanent AF, in 40 patients with non-permanent AF and in 86 control patients with persistent sinus rhythm. Consecutive AF and control patients were selected retrospectively from the outpatient cardiology clinic database and the medical check-up database. The exclusion criteria were: left ventricular ejection fraction < 55%, LV end diastolic diameter > 55 mm, significant structural or functional valve disease, follow-up period < 5 years, age < 45y. Severity of valve regurgitation was graded from 0 to 4. Significant MR/TR was defined as MR/TR grade > 2.

Results At baseline, AF patients had more severe MR/TR than control patients (see table). After 5 years, progression of ≥ 1 grade MR and TR was more prevalent in the AF patients than in the control group. Over a period of 5 years significant MR/TR developed in 10% and 25% of the patients with permanent AF, respectively, and in none of the control patients. Logistic regression analysis identified the presence of permanent AF as an independent predictor for progression of TR (OR 10.3 95% CI 1.2-85) and as a non-independent predictor for the progression of MR (OR 2.3, 95%CI 0.3-21) after adjusting for age, cardiac risk factors and baseline MR/TR severity.

Conclusion The presence of AF is associated with significant progression of MR/TR over a period of 5 years. This association is the strongest for permanent AF and for TR. These data suggest possibly a beneficial effect of sustained rhythm control on MR/TR progression in AF patients.

	Sinus n = 86	Non-permanent AF n = 40	Permanent AF n = 41	*P*-value
Age,y	50 ± 2	66 ± 8	68 ± 11	< 0.001
Baseline MR grade	0.6 ± 0.5	1.1 ± 0.5	1.3 ± 0.5	< 0.001
Baseline TR grade	0.7 ± 0.5	1.2 ± 0.6	1.2 ± 0.6	< 0.001
MR progression by ≥ 1	5.8%	19.5%	22.5%	0.01
TR progression by ≥ 1	2.3%	29.3%	32.5%	< 0.0001
MR> 2 at 5 y	0%	4.9%	10%	0.01
TR> 2 at 5 y	0%	7.3%	25%	< 0.0001

BASIC SCIENCE

Targeting of Vascular Cell Adhesion Molecule-1 by ^{18}F-labeled nanobodies for PET/CT imaging of inflamed atherosclerotic plaques. (*) — Gezim Bala[1,2], Anneleen Blykers[2], Catarina Xavier[2], Benedicte Descamps[3], Alexis Broisat[4], Catherine Ghezzi[4], Daniel Fagret[4], Guy Van Camp[2], Vicky Caveliers[2,5], Christian Vanhove[3], Nick Devoogdt[2], Tony Lahoutte[2,5], Steven Droogmans[1,2], Bernard Cosyns[1,2], Sophie Hernot[2] *([1]Centrum voor Hart-en Vaatziekten (CHVZ), UZ Brussel – Brussels, Belgium, [2]In Vivo Cellular and Molecular Imaging (ICMI) – Vrije Universiteit Brussel – Brussels, Belgium, [3]iMinds-IBiTech-MEDISIP, Department of Electronics and Information Systems, Universiteit Gent – Ghent, Belgium, [4]Radiopharmaceutiques Biocliniques, INSERM, 1039 – Université de*

Grenoble, La Tronche, France, [5]Nuclear Medicine Department, UZ Brussel – Brussels, Belgium

Background Positron emission tomography–computed tomography (PET-CT) is a highly sensitive clinical molecular imaging modality to study atherosclerotic plaque biology. Therefore, we sought to develop a new PET tracer, targeting vascular cell adhesion molecule (VCAM)-1 and validate it in a murine atherosclerotic model as a potential agent to detect atherosclerotic plaque inflammation.
Methods The anti-VCAM1 nanobody (cAbVCAM1-5) was radiolabeled using the prosthetic group N-succinimidyl-4-^{18}F-fluorobenzoate (^{18}F-SFB) and purified by size exclusion chromatography. *In vitro* cell binding studies using TNF-α stimulated bEND5 cells were carried out to assess the functionality of the tracer. *In vivo* PET/CT imaging of hypercholesterolemic ApoE$^{-/-}$ mice fed a Western diet or control mice was performed at 2h30 post-injection of [^{18}F]FB-cAbVCAM1-5 or ^{18}F-control nanobody. To demonstrate the specificity, additional ApoE$^{-/-}$ mice were injected with 70-fold excess of unlabeled anti-VCAM-1 Nb. *Ex-vivo* evaluation of plaque uptake in different aorta segments based on atherosclerosis extent was assessed by gamma well counting.
Results After ^{18}F-labeling (radiochemical purity >99%), *in vitro* cell binding studies showed specific binding of the tracer to VCAM1 expressing cells. Atherosclerotic lesions in the aortic arch of ApoE$^{-/-}$ mice injected with ^{18}F-anti-VCAM-1 Nb were successfully identified using μPET/CT imaging, while background signal was observed in the aortic arch of the control groups. These results were confirmed by *ex vivo* analyses where uptake of [^{18}F]FB-cAbVCAM1-5 in atherosclerotic lesions was significantly higher compared to control groups. Moreover, uptake increased with the increasing extent of atherosclerosis (%ID/g; score 0: 0.68 ± 0.1, score 1: 1.18 ± 0.36, score 2: 1.49 ± 0.37, score 3: 1.48 ± 0.38). High lesion-to-heart, lesion-to-blood and lesion-to-control vessel ratios were obtained (12.4 ± 0.4, 3.3 ± 0.4 and 3.1 ± 0.6, respectively).
Conclusion The [^{18}F]FB-anti-VCAM1 nanobody, cross-reactive for both mouse and human VCAM1, allows non-invasive PET/CT imaging of VCAM1 expression in atherosclerotic plaques in a murine model and may represent an attractive tool for imaging vulnerable atherosclerotic plaques in patients.

Secondary prevention in CHD patients in Belgium: long-term Time trends based on the EUROASPIRE surveys. (#) — Delphine De Smedt, Johan De Sutter, Michel De Pauw, Hans Van de Kerckhove, Guy De Backer, Dirk De Bacquer

Background The joint European society guidelines on cardiovascular prevention have the aim to reduce cardiovascular morbidity and mortality. A particular focus is placed on the secondary prevention of coronary heart disease (CHD) patients. The aim of this study was to assess how the preventive measures have been followed in clinical practice over the latest decade.
Methods Analyses are based on data from the repeated cross-sectional EUROASPIRE (EA) surveys performed in selected geographical areas. Three Belgian hospitals located in Ghent (University Hospital, AZ Maria Middelares, AZ Sint-Lucas), took part in EA II (260 patients; in 1999-2000), EA III (287 patients; in 2006-2007) and EA IV (249 patients; in 2012-2013) allowing for a comparison over time. Patients included were patients between 18 and 70 years old, being hospitalized for myocardial infarction, coronary artery bypass graft surgery, elective or emergency percutaneous coronary intervention or acute myocardial ischemia. Patients were interviewed and examined 6 months to 3 years following hospital discharge.
Results Smoking prevalence decreased over time: 22.7% in EA II; 16.4% in EA III; 10.0% in EA IV. The proportion of obese patients (BMI≥ 30) remained more or less the same: 27.3%; 24.8% and 29.3% in the 3 surveys respectively. Likewise the proportion of central obesity remained similar: 47.3% in EA II; 46.1% in EA III; 45.9% in EA IV. The number of patients with known diabetes increased: 14.2% in EA II; 17.3% in EA III; 22.6% in EA III. The therapeutic control of blood pressure (< 140/90 mmHg (< 140/80 mmHg in patients with diabetes)), in patients on blood pressure lowering drugs, improved: 53.7% in EA II; 54.2% in EA III; 59.9% in EA IV. Likewise, the therapeutic control of LDL cholesterol (< 2.5 mmol/L), in patients on lipid lowering medication, improved substantially: 11.5%; 50.3% and 62.7% in the 3 surveys respectively. A similar trend was seen when setting the target < 1.8 mmol (1.0%, 14.8%, 16.1% respectively). The use of statins increased from 43.1% to 88.1% and 92.8% and the use of blood pressure lowering drugs remained stable (88.1% to 91.6% to 91.2% in the 3 surveys respectively).
Conclusion The management of CHD patients across Belgium showed some contrasting findings. A substantial decrease in smoking prevalence, raised blood pressure and raised LDL cholesterol was seen. Likewise, medical treatment of patients greatly improved, although target levels for LDL cholesterol are reached in only a minority of patients. However, as also seen in the general population, the prevalence of known diabetes increased and obesity as well as central obesity remain important issues which should be further targeted in the management of CHD patients.

Asynchronous electrical activation to induce dilated cardiomyopathy with left bundle branch block-like remodelling: A new ovine animal model. — Jürgen Duchenne[1], Piet Claus[1], Anna Turco[2], Kathleen Vunckx[2], Efstathios

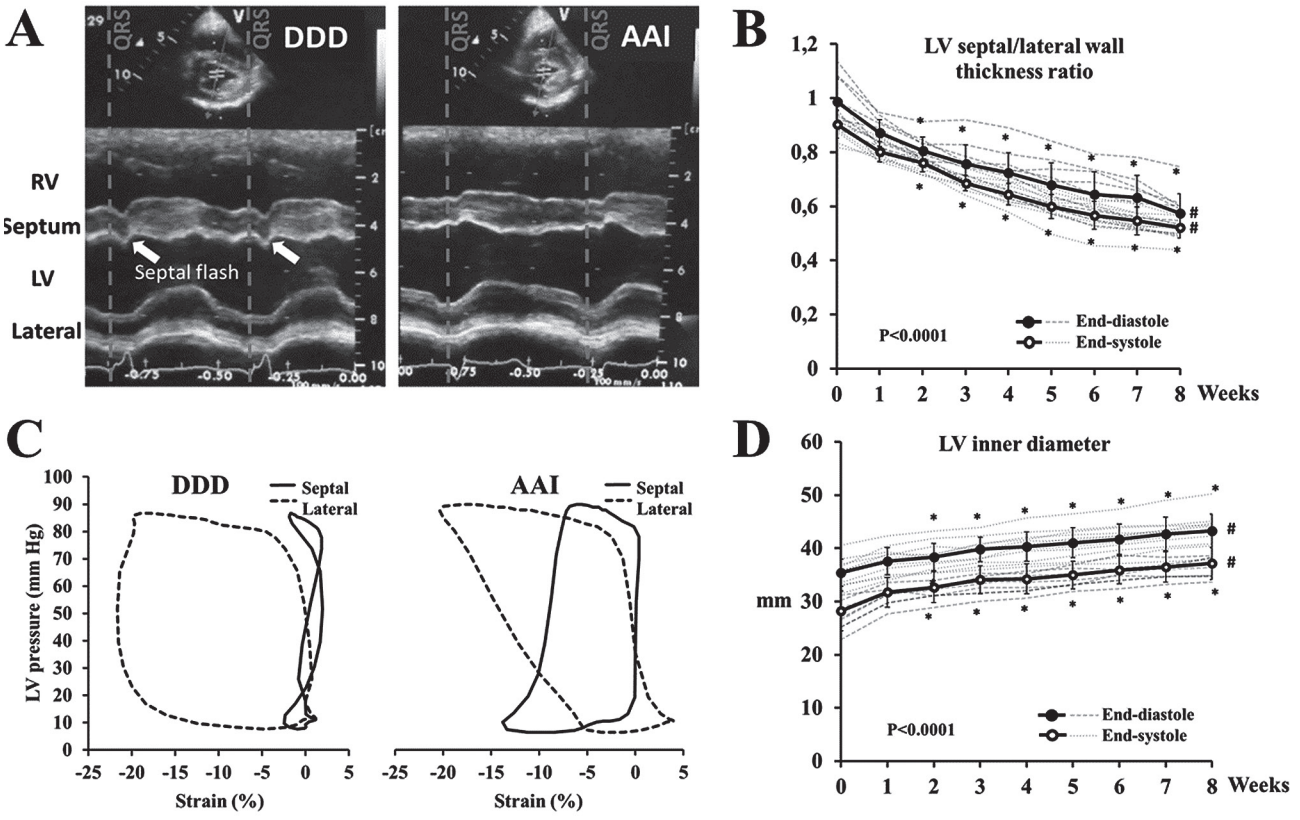
Pagourelias[1], Peter Haemers[1], Joeri Van Puyvelde[3], Olivier Gheysens[2], Filip Rega[3], Jens-Uwe Voigt[1] *([1]Department of Cardiovascular Diseases, UZ Leuven and Department of Cardiovascular Sciences, KU Leuven, Belgium, [2]Department of Nuclear Medicine, UZ Leuven and Department of Imaging and Pathology, KU Leuven, Belgium, [3]Department of Cardiothoracic Surgery, UZ Leuven and Department of Cardiovascular Sciences, KU Leuven, Belgium).*

Background The impact of regional loading and function inhomogeneities on left ventricular (LV) remodelling is not yet fully understood. We propose an animal model of rapid pacing-induced dilated cardiomyopathy (DCM) which resembles a left bundle branch block (LBBB)-like morphology and motion patterns of the LV and which allows to influence regional loading conditions and with this functional differences directly and acutely by re-programming the pacemaker.

Methods Ten sheep were subjected to 8 weeks of rapid pacing (180 bpm) on the right atrium (RA) and right ventricle (RV) mid free wall. LV regional wall thickness and diameter changes were evaluated by weekly 2D echocardiograms at end-diastole (ED) and end-systole (ES). LV volumes were also assessed by magnetic resonance imaging (MRI) at baseline and after 8 weeks. At week 8, the animals underwent invasive hemodynamic pressure-volume and simultaneous echocardiographic circumferential strain (CS) analysis. Mid-ventricular segmental pressure-CS-loops, as measure of regional myocardial work (RMW), were recorded with normal LV conduction (AAI pacing in the RA) versus LBBB-like conduction (DDD pacing in RA and RV).

Results DDD pacing acutely induced electrical and mechanical dyssynchrony of the LV, presented by an almost doubling of the QRS width ($P < 0.0001$), and the occurrence of an early septal bouncing pattern (septal flash) in both 2D echocardiography and CS (Figure A and C). Within 8 weeks of rapid DDD pacing, cardiac changes showed typical features of a DCM with LBBB: the LV septal/lateral wall thickness ratio significantly decreased by −41% at ED ($P < 0.0001$) and −42% at ES ($P < 0.0001$) (Figure B), while LV diameter significantly increased by + 21% at ED ($P < 0.0001$) and + 30% at ES ($P < 0.0001$) (Figure D), respectively. LV ED and ES volumes significantly increased by + 48% ($P < 0.0001$) and + 61% ($P < 0.0001$), respectively. After that time, acute switching from DDD to AAI resulted in a significant increase in LV stroke work of + 37% ($P = 0.034$) and a significant increase in dP/dt max by + 30% ($P = 0.025$). Furthermore, RMW more than doubled in the septal wall ($P < 0.0001$), and decreased by −30% in the lateral wall ($P = 0.005$) (Figure C).

Conclusions To our knowledge, this is the first animal model of rapid DDD pacing on the RA and RV which provides all hallmarks of DCM with LBBB which are typ-



ically found in patients. We can induce significant immediate changes in regional motion patterns and myocardial work load by switching pacing modes. This model will be instrumental to obtain new insight into the pathophysiology of LV remodelling in different cardiomyopathies.

FDG-PET as novel, non-invasive measure of regional myocardial workload in LBBB-like dyssynchrony. — Jürgen Duchenne[1], Anna Turco[2] Piet Claus[1], Kathleen Vunckx[2], Efstathios Pagourelias[1], Filip Rega[3], Olivier Gheysens[2], Jens-Uwe Voigt[1] *([1]Department of Cardiovascular Diseases, UZ Leuven and Department of Cardiovascular Sciences, KU Leuven, Belgium, [2]Department of Nuclear Medicine, UZ Leuven and Department of Imaging and Pathology, KU Leuven, Belgium, [3]Department of Cardiothoracic Surgery, UZ Leuven and Department of Cardiovascular Sciences, KU Leuven, Belgium).*

Background We hypothesize that regional myocardial energy consumption reflects regional myocardial work (RMW). This study was set up to investigate if regional myocardial glucose metabolism, as assessed by ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) can describe RMW defined by the regional left ventricular (LV) pressure-strain loop area. For this, we used a newly developed chronic rapid pacing animal model of dilated cardiomyopathy (DCM) and left bundle branch block (LBBB)-like mechanical dyssynchrony.

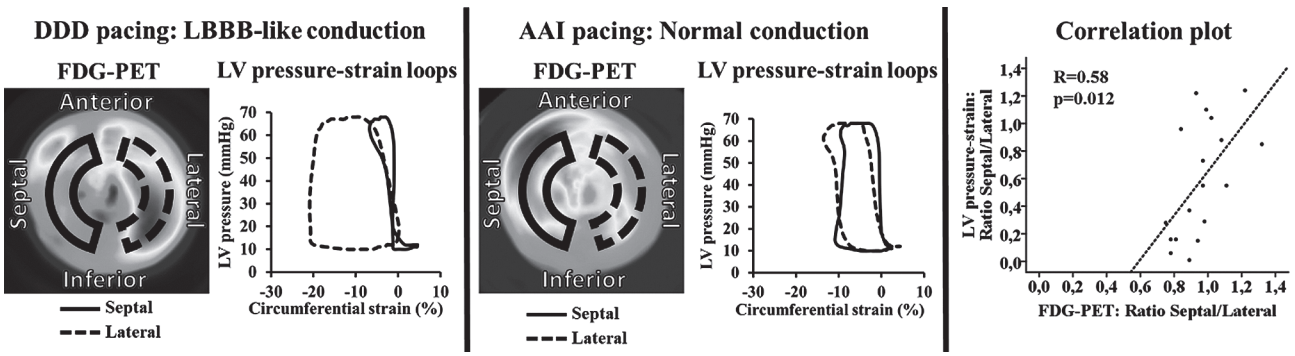
Methods Ten sheep were subjected to rapid (180 bpm) sequential pacing on the right atrium (RA) and the mid free wall of the right ventricle (RV). After 8 weeks, all animals had developed LV dilatation and asymmetric remodelling, with LBBB-like ventricular activation and, consequently, an LBBB type of LV motion and function. FDG-PET scans were performed twice, under pure RA (AAI) pacing and under sequential RA/RV (DDD) pacing, the latter inducing controllable regional function inhomogeneities. Further, all animals underwent invasive pressure-volume measurements and simultaneous echocardiographic circumferential strain acquisitions of the mid-LV segments. These data were used to calculate LV segmental pressure-strain loops, representing RMW, which were then compared to PET results.

Results While AAI stimulation caused a normal ventricular action, DDD pacing resulted in reproducible patterns of inhomogeneous RMW distribution (Figure). In DDD, we observed a significant septal to lateral wall difference in both FDG-uptake (11.7 ± 4.1 vs 13.3 ± 3.8 standardised uptake value; $P = 0.001$) and LV pressure-strain loop area (190 ± 139 vs 943 ± 374 mmHg*%; $P = 0.001$). No relevant regional difference in FDG-uptake ($P = 0.364$) or LV pressure-strain loop area ($P = 0.494$) was observed under AAI-pacing. Regional FDG-uptake and pressure-strain loop area correlated significantly (r = 0.58, $P = 0.012$) (Figure).

Conclusions Our study indicates that regional myocardial work, assessed as the regional pressure-strain loop area, is related to local FDG-uptake. AV-sequential pacing (DDD) results in a low septal and in high lateral uptake while under AAI pacing, its distribution is almost homogeneous. The influence of motion and partial volume on the reconstructed FDG-uptake in the asymmetrically remodelled hearts is currently being investigated.

Temporal shift in circulating monocyte subsets after st-segment elevation myocardial infarction and relation with myocardial injury. — Sam C Latet[1,2], Paul L Van Herck[2], Amaryllis H Van Craenenbroeck[2,3], Katrijn Van Ackeren[1], Nathalie Cools[4], Emeline M Van Craenenbroeck[1,2], Vicky Y Hoymans[1,2], Christiaan J Vrints[1,2] *([1]University of Antwerp, Cardiovascular Diseases, Department of Translational Pathophysiological Research, Wilrijk, Belgium, [2]Antwerp University Hospital, Laboratory of Cellular and Molecular Cardiology, Department of Cardiology, Edegem, Belgium, [3]University of Antwerp, Laboratory of Experimental Medicine and Pediatrics, Wilrijk, Belgium, [4]University of Antwerp, Laboratory of Experimental Hematology, Wilrijk, Belgium).*

Background The unfavourable role for excessive circulating phagocytic Mon1 in cardiac repair after ST-segment elevation myocardial infarction (STEMI) was recently suggested. Information on intermediate Mon2 and patrolling



Mon3 in humans is scarce. We investigated the temporal change in different monocyte subsets and their correlation with myocardial injury as assessed by peak troponin levels.

Methods Blood was obtained from 23 STEMI patients in the acute inflammatory (day 0), transition (day 2) and proliferative (day 5) phases and analysed with flow cytometry. Monocytes (CD45+CD86^{+}) were divided into Mon1 (CD14^{++}CD16^{-}CCR2^{+}), Mon2 (CD14^{++}CD16+CCR2^{+}) and Mon3 (CD14+CD16^{++}CCR2^{-}). As controls, 10 age- and gender-matched stable patients with coronary artery disease were included.

Results Monocyte subsets are differentially mobilized after STEMI (figure 1). Peak troponin correlates negatively with Mon1 and positively with Mon2 at day 2 (figure 2).

Conclusion STEMI induces a dynamic response of monocytes subsets that is influenced by the extent of myocardial injury. Larger infarcts appear to be characterized by a prolonged recruitment of Mon1 into the infarcted myocardium and a greater mobilisation level of Mon2. This implies an imbalance in the transition of the reparative response from the inflammatory to the proliferative phase.

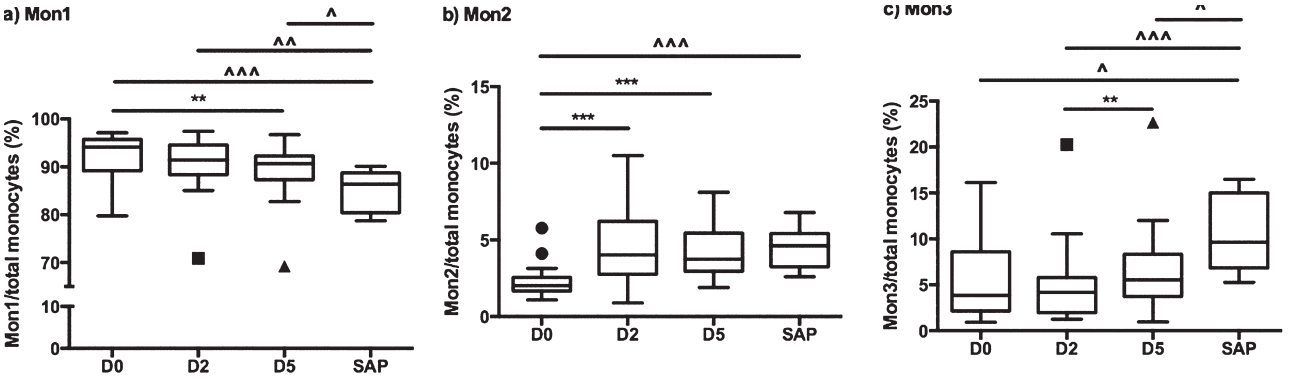


Fig. 1 Relative monocyte subsets.

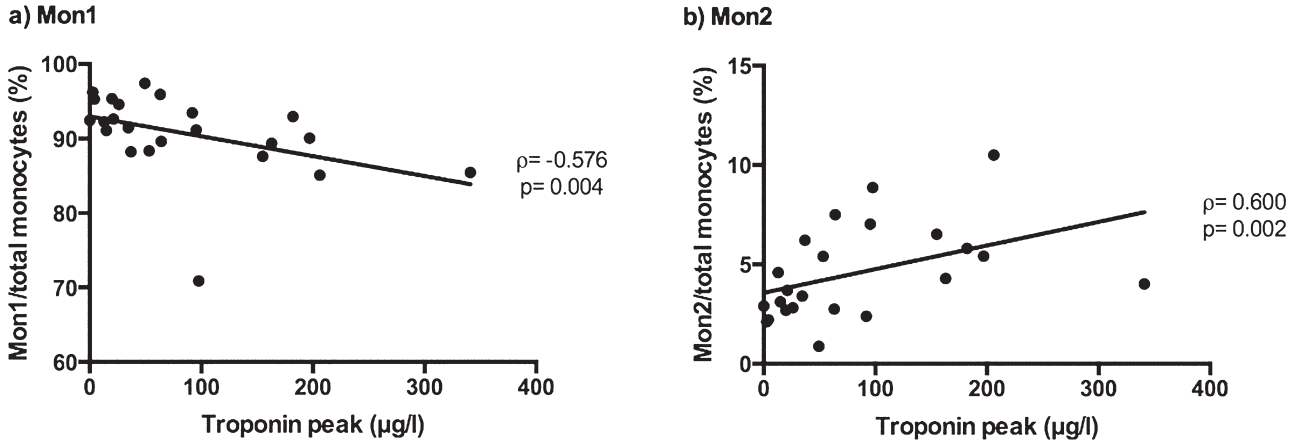


Fig. 2 Correlations between troponin and monocyte subsets at day 2.

Dynamic exercise induces acute and subacute retinal microvascular changes in rehabilitating cardiac patients.

— Tijs Louwies[1,2], Alice Schimmel[1], Fien Van Den Eynde[1], Patrick De Boever[1,2], Paul Dendale[1,3] *([1]Hasselt University, Hasselt, Belgium, [2]Flemish Institute for Technological Research (VITO), Mol, Belgium, [3]Jessa Ziekenhuis, Hasselt, Belgium)*

Background Many cardiac patients have underlying pathologies such as hypertension and atherosclerosis that attenuate endothelial function. Endothelial dysfunction may lead to disturbed flow-mediated vasodilation responses. Exercise-based cardiac rehabilitation is an effective measure to improve endothelial function and overall cardiac fitness. At the beginning of the rehabilitation program, cardiac fitness is measured with a maximal endurance cycling test. Increased cardiac output will increase blood flow in the periphery and induce flow-mediated vasodilation in the microcirculation.

This effect has not yet been investigated in the retinal microvasculature of rehabilitating cardiac patients. The retinal vessels are fully autoregulated and thus rely on endothelial function for vasodilation. As these vessels share physiological features with the coronary microvessels, they may provide insight in the functionality of coronary vessels of rehabilitating patients.

Methods 45 cardiac rehabilitating patients (average age = 61 years; 82% male), who underwent a PTCA, PCI or ACAB intervention, were recruited at Jessa Hospital. These patients participated in an exercise-based rehabilitation program. At the start of this program, a maximal endurance tests on a cycle ergometer is performed at Jessa Hospital. Fundus images were collected before and after this endurance tests. Additional images were collected 5, 10, 15 and 30 minutes after the endurance tests. Image analysis was used to calculate the width of retinal blood vessels, represented as the Central Retinal Arteriolar/Venular Equivalent (CRAE/CRVE). Mixed models were used for statistical analysis.

Results The first maximal endurance test, at the beginning of the program, has been completed. Average CRAE was increased with 2.97 μm (95% CI: 1.99 μm to 3.95 μm; $P<0.001$) after the exercise and remained increased for at least 30 minutes, when CRAE was still increased with 3.46 μm (95% CI: 2.43 μm to 4.50 μm; $P<0.001$). Average CRVE was decreased with 3.77 μm (95% CI: –3.68 μm to –0.08 μm μm; $P=0.0505$) after exercise. This decrease was attenuated after 5 minutes, when a trend to widening of CRVE became apparent.

Conclusion Assessment of exercise-induced retinal microvascular changes in cardiac rehabilitation patients is possible. These results suggest that retinal arteriolar microvessels respond to increased flow by vasodilation. This may point at a preserved endothelial function. Whether retinal microvascular changes (endothelial function) are improved (larger response) due the training program is currently being investigated.

A new paradigm to prevent cardiac hypertrophy development. — Florence Mailleux[1], R. Gélinas[1], B. Demeulder[1], A. Ginion[1], L. Hue[1], J. Hammond[2], J.-L. Balligand[2], J.-L. Vanoverschelde[1], C. Beauloye[1], S. Horman[1], L. Bertrand[1] *([1]Pole of Cardiovascular Research and [2]Pole of Pharmacotherapy, Institute of Experimental and Clinical Research, Université catholique de Louvain, Brussels, 1200, Belgium).*

Background Many studies have demonstrated that activation of the AMP-activated protein kinase (AMPK) prevents cardiac hypertrophy development. However, this paradigm has been established using indirect or unspecific AMPK activators. We recently confirmed this anti-hypertrophic action by using a more direct AMPK activator, the A769662 compound. Interestingly, our study also demonstrated that the molecular mechanisms, previously proposed to explain the anti-hypertrophic action of AMPK were not involved in this action. In the goal to elucidate the mechanism by which AMPK really blocks cardiac hypertrophy, we evaluated the possible relationship between AMPK and O-GlcNAcylation (O-GlcNAc), a post-translational protein modification recently discovered to be increased during hypertrophy.

Methods In vitro hypertrophy is induced in neonatal rat cardiomyocytes (NRVMs) using phenylephrine (PE) and AMPK is activated using 12.5 μM of A769662. Cardiomyocyte hypertrophy is evaluated by immunostaining and cell surface area measurement. In vivo cardiac hypertrophy is induced by angiotensin II (AngII) in osmotic mini-pumps and evaluated by echocardiography and cell surface area measurement. AMPK is activated by metformin in drinking water. Protein expression and phosphorylation as well as O-GlcNAc level are evaluated by western blot. We evaluate the impact of AMPK activation or deletion on the expression and/or phosphorylation state of the three enzymes regulating O-GlcNAc level, namely glutamine fructose-6-phosphate aminotransferase (GFAT), O-GlcNAc transferase (OGT) and O-GlcNAcase (OGA). Both GFAT and OGT stimulate O-GlcNAcylation whereas OGA removes O-GlcNAc moiety.

Results We show that PE-dependent NRVM hypertrophy is accompanied by an increase in O-GlcNAc level. Both hypertrophy and O-GlcNAc are prevented by A769662-mediated AMPK activation, such inhibition disappearing when AMPK is knocked down by siRNA. Inhibition of O-GlcNAc process (using two GFAT inhibitors, Azaserine or DON) inhibits PE-induced cardiomyocyte hypertrophy, mimicking AMPK activation. O-GlcNAc stimulators (PUGNAc or glucosamine) increase O-GlcNAc level and reverse the anti-hypertrophic effects of A769662, Azaserine and DON. In vivo experiments confirm our paradigm. Indeed, metformin-mediated AMPK activation is able to reduce cardiac hypertrophy in WT mice and this correlates with inhibition of the AngII-mediated increase in O-GlcNAc level. By contrast, metformin is not able to prevent AngII-induced hypertrophy and did not modify O-GlcNAc in AMPK-deficient mice. At the molecular level, we show that AngII-mediated O-GlcNAc increase in WT mice is correlated to an increase in OGT expression which is prevented by metformin. AMPK is also responsible for the increase in OGA expression and for the inhibitory phosphorylation of GFAT.

Conclusion Collectively, our results demonstrate that AMPK controls cardiac hypertrophy and O-GlcNAc through the multifaceted regulation of OGA, OGT and GFAT.

Effect of afterload increase on left ventricle mechanical dispersion and electromechanical window. — Oana Mirea, Carolina Vallecilla, Peter Haemers, Frank Rademakers, Jan D'hooge, Piet Claus *(KU Leuven, Department of Cardiovascular Sciences, Leuven, Belgium).*

Background Left ventricular mechanical dispersion (MD) and electromechanical window (EMW) have been recently proposed as predictors for arrhythmic events in patients with cardiac pathology.

Objectives Given the close relationship between diurnal variation in arrhythmic events and blood pressure rise, we sought to investigate the relation between acute increases in blood pressure and these parameters in a controlled animal model.

Methods Left-ventricular (LV) afterload was increase by the inflation of a balloon in the descending aorta in eight anaesthetised pigs (weight 30–35 kg). Two-dimensional (2D) echocardiographic LV apical (2-3-4 Chamber) views and pulsed wave (PW) Doppler recording of the LV outflow were obtained trans-diaphragmatically using a Vivid 9 system (GE Healthcare). Global mechanical dispersion (GMD) was defined as the standard deviation of time to peak longitudinal shortening in 18 LV segments obtained by Speckle tracking analysis (Echopac v13; GE, Norway). EMW is the interval between the end of the T wave (ECG) and aortic valve closure (PW Doppler, LV outflow).

Results Balloon inflations raised BP by an average of 53.9 ± 24% ($P < 0.01$) and heart rate decreased significantly ($P < 0.01$), while QT remained unchanged. LV end-systolic and end-diastolic volumes enlarged significantly during inflation ($P < 0.001$) and LV ejection fraction decreased ($P < 0.001$). GMD increased during inflation (35.5 ± 9.9 ms vs. 51.5 ± 11.6 ms, $P < 0.001$). Similarly, EMW prolonged during afterload increase (30.6 ± 26.6 ms vs. 64.9 ± 14.1 ms, $P < 0.001$), because of a delayed aortic valve closure. Both parameters showed a strong positive correlation with BP (GMD: $r^2 = 0.69$, $P < 0.05$ and EMW: $r^2 = 0.78$, $P < 0.05$)

Conclusions An acute increase of blood pressure is associated with enhanced mechanical disarray and electromechanical dissociation. These data would suggest that measuring these risk predictors during transient blood pressure increase (e.g. by a handgrip test), could unmask possible afterload-induced arrhythmic risk.

Validation of the slope of the prestretch-strain relationship as an non-invasive index of left ventricle contractility.

— Oana Mirea, C. Vallecilla, P. Claus, F. Rademakers, J D'hooge *(Department of Cardiovascular Sciences, University Hospital Gasthuisberg, KU Leuven).*

Purpose The slope of the relationship between left ventricular (LV) segmental stretch during atrial contraction (PreS) and total systolic shortening (S) has recently been proposed as a non-invasive index of LV contractility in a clinical setting. An experimental validation of this novel parameter is missing. The aim of this study was therefore to: i) correlate the PreS-S slope to invasive gold standard measurements and ii) to investigate the influence of afterload on this new parameter in a controlled experimental setting.

Methods Afterload was modulated in 13 anesthetized pigs, by a balloon inflation in the descending aorta. In an additional 6 animals contractility was increased by dobutamine infusion. During baseline and all interventions, LV pressure-volume (PV) measurements were acquired. Simultaneously, trans-diaphragmatic two-dimensional echo were acquired (2-3-4 LV chamber). The PreS-S slope was constructed from 18 segmental strain curves obtained by Speckle tracking echocardiography (Echopac v13, GE) and compared to the end-systolic PV relation (ESPVR) and the pre-load recruitable stroke work (PRSW).

Results Systolic blood pressure increased (103.8 ± 18.3 vs. 135.6 ± 30.1;p< 0.01), LV stroke volume ($P < 0.01$) and ejection fraction ($P < 0.01$) decreased during balloon inflation. Conversely, the PreSS slope was not influenced by loading ($P = 0.28$). When comparing absolute values of the PreSS slope with ESPVR and PRSW we found no correlation while when comparing the rate of change in contractility, PreSS slope correlated with PRSW ($P < 0.05$) and ESPVR ($P < 0.05$) (Figure 1).

Conclusions PreSS slope is sensitive to changes in inotropy and is comparable with the gold standard measures of LV contractility and appears to be influenced by loading in a lesser degree than the established measurements of LV function.

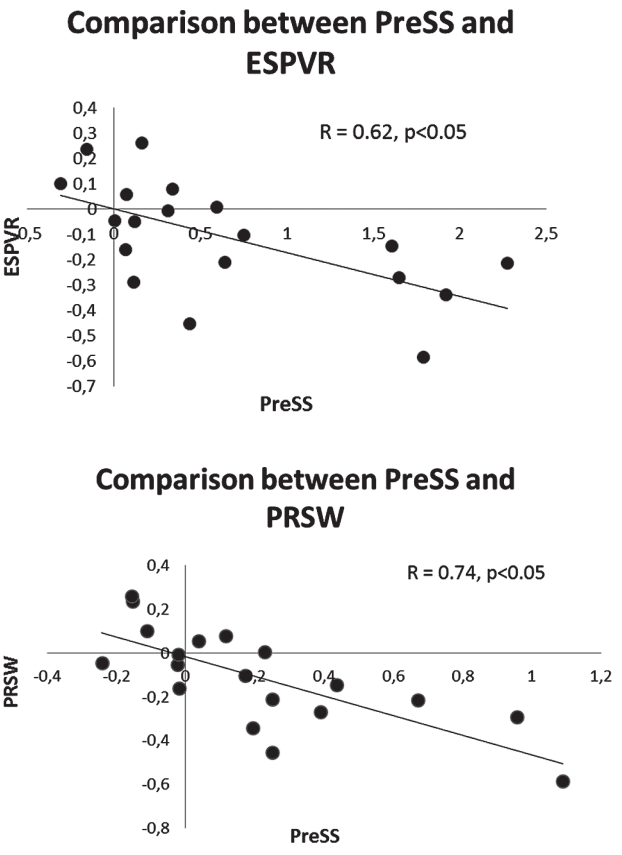


Fig. 1

Evaluation of management of dyslipideamia in Moroccan women. — Najat Mouine[1], Z. Lakhal[1], I. Asfalou[1], M. Raissouni[1], M. Sabry[1], A. Chaib[1], A. Benyass[1], E. Zbir[1] *([1]Mohammed V University Souissi, mohamed v military hospital, cardiology department, Rabat, Morocco).*

Background National guidelines for lipid management have been updated in 2011 by European society of cardiology. The objective of this study was to assess clinical practices based on these recommendations in Moroccan women compared to men.

Materials and methods A representative sample of patients was admitted to cardiology consultation for management of their dyslipidemia, they have been questioning, clinical examination and dosage of LDL cholesterol, HDL cholesterol, total cholesterol and triglycerides.

Results We included 103 patients [42 women, 61men], who had a lipid-lowering treatment that was consistent with the guidelines. Depending on the number of cardiovascular risk factor, there is no significant difference between men and women in LDL-cholesterol target, 67% of women had a lower threshold of LDL-cholesterol target versus 33% had not a lower threshold of LDL cholesterol target and 65,4% of men had a lower threshold of LDL-cholesterol target versus 34,6% had not a lower threshold of LDL cholesterol target Conclusion: Lipid management was consistent European society guidelines in majority of our patients, men and women; it stresses the importance of respect of guidelines to have more well-treated patients.

Bone marrow-derived progenitor cell dysfunction in ischemic heart disease and its relation to inflammation. — Evelien Nollet[1], Hoymans VY[1], Rodrigus I[2], De Bock D[2], Van Hoof VO[3], Dom M[4], Vanassche B[5], Vercruysse H[5], Van Ackeren K[1], Vrints CJ[1,6], Van Craenenbroeck EM[1,6] *([1]Cardiovascular Diseases, Department of Translational Pathophysiological Research, University of Antwerp, [2]Department of Cardiac Surgery, Antwerp University Hospital, [3]Department of Clinical Chemistry, Antwerp University Hospital, [4]Department of Oral and Maxillofacial Surgery, General Hospital Sint-Maarten, [5]Department of Oral and Maxillofacial Surgery, General Hospital AZ Monica, [6]Department of Cardiology, Antwerp University Hospital, Antwerp, Belgium).*

Purpose Stem cell dysfunction could contribute to the disappointing outcome of autologous bone marrow stem cell administration in ischemic heart disease. In this regard, bone marrow stem/progenitor cell numbers and function were studied in coronary artery disease (CAD) patients and increased inflammation was further explored as possible underlying mechanism.

Methods Bone marrow (BM) and peripheral blood (PB) was obtained from 23 CAD patients (SYNTAX score range 6-32, age 61 ± 11 yrs) and 11 healthy age-matched subjects (HS), during respectively cardiac and maxillofacial surgery. BM mononuclear cells (MNC) were evaluated in vitro for migration towards SDF1α/VEGF and differentiation capacity to granulocyte macrophage colony forming units (GM-CFU). We quantified the number of hematopoietic (HPC; $CD45^{dim}CD34+SSC^{low}$) and endothelial (EPC; $CD45^{dim}CD34+KDR^{+}$) progenitor cells in BM and PB by flow cytometry. Plasma IFNy, TNFα, IL-6, VEGF and bFGF levels were measured in PB and BM using Meso Scale Discovery. The expression level in BM-MNC of the cytokine receptors TNFR1 and 2, IFNyR1, IL-6R, CXCR4 and VEGFR2 was determined by RT-PCR.

Results (Table 1). The GM-CFU differentiation capacity of BM-MNC was decreased in patients with CAD compared to HS. Whereas migration capacity of BM-MNC did not differ between groups, it decreased with increasing CAD complexity, as assessed by SYNYAX score ($r=-0.657$, $P=0.002$). Furthermore, a depletion of HPC, but not EPC in BM was observed in the setting of CAD, accompanied with a recruitment of EPC into the circulation. In CAD patients, IFNy and TNFα levels were elevated in BM but did not correlate with any numerical or functional assessment. Moreover, no differences in cytokine receptor expression on BM-MNC were found between CAD and HS.

Conclusion Whereas spontaneous recruitment of EPC was increased in CAD, the functional deficit of BM-MNC and the depletion of HPC could contribute to the reduced efficacy of autologous bone marrow stem cell therapy. However, the observed increase in inflammatory status in BM from CAD patients was not related to the observed BM dysfunction, suggesting that other mechanisms are at play.

Table 1 Numerical and functional assessments of progenitor cells and cytokine levels in BM and PB. Data prestned as median (IQR

	CAD (n=23)	HS (n=11)	*p-value*
BONE MARROW			
Migration (%) BM-MNC	30 (25-27)	32 (23-39)	*0.730*
GM-CFU (N)	42 (22-58)	73 (55-82)	*0.003*
BM HPC (/10^6 $CD45^+$ BM-MNC)	11500 (8461-16871)	16703 (12076-20914)	*0.038*
BM EPC (/10^6 $CD45^+$ BM-MNC)	293 (96-518)	242 (80-508)	*0.845*
IFNy	4.39 (3.36-4.81)	1.07 (0.20-3.20)	*0.005*
TNFα	1.77 (1.45-2.75)	1.29 (1.05-1.63)	*0.027*
IL-6	0.55 (0.17-1.06)	0.18 (0.05-0.48)	*0.122*
VEGF	68.66 (59.30-146.24)	229.06 (70.85-282.83)	*0.236*
bFGF	103.54 (57.66-258.08)	136.76 (81.78-334.45)	*0.633*
PERIPHERAL BLOOD			
PB HPC (/10^6 $CD45^+$ PB-MNC)	881 (508-1355)	672 (589-798)	*0.121*
PB EPC (/10^6 $CD45^+$ PB-MNC)	78 (51-168)	29 (17-39)	*0.001*
IFNy	4.90 (3.85-5.82)	4.34 (2.44-4.66)	*0.161*
TNF	2.19 (1.58-2.65)	1.74 (1.32-2.00)	*0.133*
IL-6	0.51 (0.13-1.31)	0.37 (0.11-0.51)	*0.475*
VEGF	16.52 (13.33-58.30)	83.34 (23.59-101.65)	*0.070*
bFGF	2.42 (1.77-4.05)	2.51 (0.77-19.16)	*0.962*

The extent of BM-derived progenitor cell dysfunction in ischemic heart disease and chronic heart failure in relation to inflammation. — Evelien Nollet[1], Hoymans VY[1], Rodrigus I[2], De Bock D[2], Van Hoof VO[3], Dom M[4], Vanassche B[5], Vercruysse H[5], Van Ackeren K[1], Kristien Wouters[6], Vrints CJ[1,7], Van Craenenbroeck EM[1,7] *([1]Cardiovascular Diseases, Department of Translational Pathophysiological Research, University of Antwerp, [2]Department of Cardiac Surgery, Antwerp University Hospital, [3]Department of Clinical Chemistry, Antwerp University Hospital, [4]Department of Oral and Maxillofacial Surgery, General Hospital Sint-Maarten, [5]Department of Oral and Maxillofacial Surgery, General Hospital AZ Monica, [6]Department of Scientific Coordination and Biostatistics, Antwerp University Hospital, [7]Department of Cardiology, Antwerp University Hospital, Antwerp, Belgium).*

Purpose The efficacy of autologous bone marrow stem cell therapy in ischemic heart disease could be hampered by intrinsic bone marrow dysfunction. We assessed the function and numbers of bone marrow-derived progenitor cells in a broad range of cardiovascular disease to determine whether myocardial ischemia or rather a reduced cardiac output is the primum movens for BM progenitor cell dysfunction. Moreover, inflammatory markers were studied in relation to BM dysfunction.

Methods Bone marrow (BM) and peripheral blood (PB) samples were obtained from 17 patients with coronary artery disease (CAD, SYNTAX range 6-35, LVEF 62 ± 2%), 8 patients with heart failure (HF) due to ischemic cardiomyopathy (ICM, SYNTAX range 9-32, LVEF 26 ± 4%), 7 patients with non-ischemic HF (non-ICM, LVEF 44 ± 3%) and 11 healthy subjects (HS). BM mononuclear (MNC) were evaluated for granulocyte/macrophage (GM-CFU) and erythroid (BFU-E) differentiation capacity and in vitro migratory response towards SDF-1α/VEGF. We quantified the number of hematopoietic (HPC; $CD45^{dim}CD34+SSC^{low}$) and endothelial (EPC; $CD45^{dim}CD34+KDR^{+}$) progenitor cells in BM and PB by flow cytometry. Plasma levels of IFNγ, TNFα, IL-6, VEGF and bFGF in BM and PB were measured using Meso Scale Discovery. The expression of the cytokine receptors TNFR1 and 2, IFNGR1, IL-6R, CXCR4 and VEGFR2 was determined by RT-PCR analysis.

Results Both GM-CFU ($P=0.002$) and BFU-E ($P=0.012$) differentiation capacity of BM-MNC was impaired in patients with IHD (CAD and ICM group), but not in non-ICM. Whereas migratory capacity did not differ between groups, it was inversely related to the complexity of CAD, as assessed by the syntax score (r=-0.682, $P<0.001$). In BM, no alterations in HPC or EPC numbers were observed, while circulating EPC numbers ($P<0.001$) were strongly increased in patients with IHD, suggesting an active EPC recruitment. In HF, only a significant HPC recruitment was observed ($P=0.011$). Yet, the circulating EPC numbers correlated negatively with LVEF (r=-0.628, $P=0.026$). Cytokine profiling revealed IL-6 increase in BM ($P=0.021$) and PB (0.012) in patients with HF and elevated VEGF levels in BM in IHD ($P=0.047$) and HF ($P=0.021$) patients. However, no relevant correlations with numerical and functional assessments of BM-derived progenitor cells were and no differences in cytokine receptor expression on BM-MNC were found.

Conclusion BM-derived progenitor cells are functional impaired in patients with severe IHD, which could contribute to a reduced efficacy of autologous stem cell therapy. This functional impairment is not observed in non-ICM. These findings suggest ischemia as important determinant on the progenitor cell function rather that reduced cardiac output. Cytokine analysis revealed that inflammation is not related to the observed BM dysfunction in IHD, suggesting that other mechanisms are at play. In contrast, elevated EPC recruitment observed in IHD will benefit neovascularization.

Influence of Pregnancy on Cardiovascular Disease in Marfan syndrome. — Renard Marjolijn[1], Manalo Elise[2], Tufa Sara[3], Muiño Mosquera Laura[1], Keene Douglas[3], De Backer Julie[1], Sakai Lynn[2] *([1]Center for Medical Genetics Ghent, Ghent University Hospital, Ghent, Belgium. [2]Department of Biochemistry and Molecular Biology, Shriners Hospital for Children, Portland, Oregon, USA. [3]Micro-Imaging Center, Shriners Hospital for Children, Portland, Oregon, USA).*

No abstract available.

Genetic retesting with targeted capture sequencing of prior genotype negative – phenotype positive patients with inherited primary arrhythmia syndrome or cardiomyopathy. — Tomas Robyns[1], Cuno Kuiperi[2], Jeroen Breckpot[2], Koenraadt Devriendt[2], Johan Van Cleemput[1], Rik Willems[1], Dieter Nuyens[3], Gert Matthijs[2], Anniek Corveleyn[2] *([1]University Hospitals (UZ) Leuven, Department of Cardiovascular Diseases, Leuven, Belgium, [2]University Hospitals (UZ) Leuven, Center for Human Genetics, Leuven, Belgium, [3]Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium).*

Background In inherited primary arrhythmia syndromes (PAS) and cardiomyopathies (CMP) the yield of genetic testing varies between 20% and 75% in different diseases. These numbers are mainly derived from studies evaluating only the most frequently affected genes. Next generation sequencing (NGS) allowed us to design and validate a panel of 75 PAS and CMP susceptibility genes for targeted capture and massive parallel sequencing.

Purpose We evaluated the additional yield of NGS based panel testing in PAS and CMP patients and

determined if genetic retesting was worthwhile in previously genotype negative – phenotype positive probands.

Methods We examined the database of our hereditary heart disease clinic and selected patients with a clear phenotype who remained genotype-negative after genetic analysis of the main genes implicated in their specific phenotype. Targeted sequencing of the coding regions of 75 genes implicated in PAS and CMP was performed. Variant interpretation and classification was done according to a stringent scoring system implementing different in-silico analyses, population frequencies and paralogous and orthologous conservation. Sanger sequencing was performed to confirm the presence of class 3 (variant of unknown significance), class 4 (probably pathogenic) and class 5 (pathogenic) variants. Co-segregation was done when DNA and clinical data of family members was available.

Results 96 patients were included: 25 with LQTS, 8 with BrS, 5 with CPVT, 7 with idiopathic VF, 42 with HCM, 8 with DCM and 1 with ARVC. A total of 42 variants of class 3, 4 or 5 were identified. Co-segregation was performed on 21 variants. Three class 3/4 variants were downgraded to a benign variant due to lack of co-segregation. In contrast, 12 were upgraded to class 4 or 5 after critical evaluation of published functional studies or co-segregation analysis. In total, 22 variants of class 3 and 17 mutations (class 4/5 variants) in 16 patients were identified, resulting in a genetic yield of 17% (14% in CMP and 20% in PAS). The initial detection failures had several causes: detection of a mutation in a new gene in 8 cases, not reported variant by an external lab in 3, allelic dropout with DHPLC in 2, functional reclassification in 1, heterozygous calling with sequencing failed in 1 and a wrong initial diagnosis in 1.

Conclusion Genetic retesting in clinically overt PAS and CMP cases, who were genotype-negative with older scanning techniques, resulted in an additional genetic diagnosis in up to 17% of the cases. This clearly supports genetic retesting with NGS based panels.

Expression of genes involved in myocardial remodelling in children with congenital cardiac defect depends on type of hemodynamic overload. — H. Rouatbi[1], A. Gerard[1], R. Heying[2], M-C Seghaye[1] *([1]Dept. of Pediatrics, [2]University Hospital Liège, Dept. of Pediatric Cardiology, KU Leuven).*

Background Hemodynamic overload related to congenital cardiac defects initiates myocardial remodelling that involves inflammation, growth and apoptosis and ultimately deteriorates ventricular function.

Our study was designed to clarify whether the type of hemodynamic overload would influence myocardial expression of genes participating to remodeling in children with congenital cardiac ,defect.

Methods 16 children with ventricular septal defect (VSD) ($n=7$), atrial septal defects (ASD) ($n=5$) and Tetralogy of Fallot (TOF) (n = 4) scheduled for primary surgical repair were investigated.

RT-PCR was performed in the right atrial myocardium taken before connexion to the extracorporeal circulation to study the expression of genes involved in myocardial inflammation, growth, fibrosis and apoptosis, respectively (IL1β, TNFα, IL6, IL10, HSP90, Collagen III, cardiotrophin 1, IGF1, TGFβ, VEGF, Bcl-xl, BAK).

Results Levels of mRNA encoding for IL1β and IL6 were significantly higher in patients with VSD compared to the other groups ($P<0{,}005$, respectively) whereas levels of mRNA encoding for HSP-90-, Bcl-xl- and VEGF-mRNA were higher in patients with ASD as compared with the other groups ($P<0{,}05$), respectively.

Expression of the other genes was not different between groups.

Conclusions Our results show differential expression of genes involved in myocardial remodelling in children with congenital heart disease with inflammatory signals in patients with left ventricular volume overload and heart failure (VSD), and protective, anti-apoptotic signals and vascular growth signals in those with volume overload of the right atrium and right ventricle (ASD).

Skeletal muscle myoblasts from chronic heart failure patients exhibit a pro-inflammatory phenotype, reduced proliferation capacity and a disturbed adiponectin pathway. — Tahnee Sente[1], A.M. Van Berendoncks[2], R.J. Rodenburg[3], A. Wouters[4], V.Y. Hoymans[5], C.J. Vrints[1,2] *([1]Cardiovascular Diseases, Department of Translational Pathophysiological Research, University of Antwerp, Belgium. [2]Department of Cardiology, Antwerp University Hospital, Edegem, Belgium. [3]Nijmegen Center for Mitochondrial Disorders, Department of Paediatrics, Radboud University Medical Centre, Netherlands. [4]Center for Oncological Research (CORE) Antwerp, University of Antwerp, Wilrijk, Belgium).*

Background Skeletal muscle alterations including wasting and impaired energy metabolism are common findings in chronic heart failure (CHF). Of particular interest is the insulin-sensitizing adipocytokine adiponectin. Increased levels of adiponectin have been documented in CHF patients and linked to poor prognosis. Recently, we demonstrated a functional adiponectin resistance at the level of the skeletal muscle in CHF. There is a further need to determine the mechanisms by which adiponectin affects outcome in CHF. We characterized for the first time primary muscle cultures from CHF patients and investigated whether adiponectin resistance is preserved *in vitro*.

Methods Myoblast and myotubes cultures were initiated from muscle biopsies (*m. vastus lateralis*) of 10 CHF patients (LVEF< 45%; NYHA Class II-III) and 10 age-and

gender matched healthy donors. Cultures were processed for morphological and differentiation analyses by immunohistochemistry and flow cytometry. Dynamic high-resolution assessments of myoblast proliferation were performed using the xCELLigence technology. mRNA expression levels of adiponectin-related genes and TNF-alpha receptors (TNFR1 and TNFR2) were quantified by RT-PCR. Senescence was assessed by SA-β-gal activity and expression of acetyl-p53. Circulating adiponectin concentrations were measured using ELISA whereas supernatant levels of cytokines were analyzed by multiplex ELISA.

Results CHF muscle cells did not differ from controls in terms of morphology or differentiation capacity ($P=0.065$). No differences were observed in myogenic markers (Pax3, Pax7, Myogenin, MyoD1 and MRF4; $P>0.05$) between groups. CHF myoblasts demonstrate a reduced proliferation rate compared to myoblasts from healthy donors ($P=0.001$). Proliferation rate was strong positively associated with leg lean mass ($r=0.832$, $P=0.001$) and exercise capacity (VO_2 peak, $r=0.665$, $P=0.003$; max. workload, $r=0.746$, $P<0.001$) and moderate positively with work efficiency ($r=0.535$, $P=0.022$). Expression of acetyl-p53 was similar in muscle biopsies ($P=0.307$) and cultures ($P=0.590$) of CHF patients and controls. In addition, CHF myoblasts demonstrated an equal number of SA-β-gal positive cells as controls ($P=1.000$). A decreased expression of the survival receptor TNFR2 ($P=0.017$) was apparent and accompanied by a reduced IL-6 secretion in CHF myoblasts ($P=0.016$). No differences in TNF-α, IL-10, IL-1β and IFN-γ production were observed between both groups. Furthermore, both serum ($P=0.038$) and mRNA expression (38.51 ± 1.14 versus 40.12 ± 1.24) of adiponectin were increased in CHF cultures, whereas AdipoR1 was downregulated ($P=0.051$) accompanied by reduced expression of downstream-located genes involved in lipid metabolism (AMPK, $P=0.022$; pAMPK/AMPK, $P=0.046$; HK2, $P=0.059$). Immunohistochemistry confirmed the presence of adiponectin protein expression in CHF cultures ($P=0.058$).

Conclusion CHF muscle cultures exhibit a pro-inflammatory phenotype as indicated by a diminished IL-6 secretion and a reduced expression of TNFR2, both related to the slower proliferation kinetics of CHF myoblasts. The features of adiponectin resistance were preserved *in vitro*. Therefore, primary muscle cultures from CHF patients are an attractive tool for further *in vitro* exploration of adiponectin resistance and underlying mechanisms of muscle wasting in CHF.

AdipoR1 deficiency and increased inflammation are associated with adiponectin resistance, mitochondrial dysfunction and impaired myogenesis in the skeletal muscle of patients with chronic heart failure. — Tahnee Sente[1,2], AM. Van Berendoncks[1,2], E. Franssen[3], VY. Hoymans[1,2], CJ. Vrints[1,2] *([1]Laboratory for Cellular and Molecular Cardiology, Antwerp University Hospital, Edegem, Belgium, [2]Cardiovascular Diseases, Department of Translational Pathophysiological Research, University of Antwerp, Wilrijk, Belgium, [3]StatUa Center for Statistics, University of Antwerp, Antwerp, Belgium).*

Background Skeletal muscle metabolic alterations including adiponectin resistance and mitochondrial dysfunction are common features in chronic heart failure (CHF). We previously demonstrated that CHF patients are characterized by a functional adiponectin resistance at the level of the skeletal muscle. The purpose of the present study was to examine the role of adiponectin receptor 1 (AdipoR1) and TNF-α on adiponectin signalling and mitochondrial function in skeletal muscle.

Methods Myoblasts and myotubes cultures were initiated from muscle biopsies *(m. vastus lateralis)* of 10 CHF patients (LVEF; $31.30\pm2.89\%$) and 10 age-and gender matched healthy controls. Cultures from healthy donors were transfected with siAdipoR1 and/or treated with TNF-α (10 ng/ml; 72h).

Results Primary CHF myotubes preserve the features of adiponectin resistance *in vitro* as evidenced by a tendency toward increased adiponectin expression ($P=0.058$) and a downregulation of AdipoR1 ($P=0.051$) and its underlying signalling pathway ($P<0.05$). Upon siRNA-mediated silencing of AdipoR1, phosphorylated AMPK and AMPK activation were reduced (pAMPK, pAMP/AMPK, $P<0.01$). In addition myoblast proliferation, evaluated with the xCELLigence RTCA, demonstrated a delayed growth rate ($P<0.0001$). Moreover, the expression of AdipoR1 was negatively correlated with the time needed to reach the maximal cell index ($r=-0.7319$, $P=0.003$). Incubation with TNF-α decreased the mRNA expression levels of genes involved in lipid (PPARα, ACADM), glucose (AMPK, HK2) and mitochondrial (FOXO3) metabolism ($P<0.0001$), and led to impaired myogenesis (MyoD1, Myogenin; $P=0.047$ and $P=0.031$; respectively). In addition, an increased cellular senescence, as evidenced by SA-β-gal activity and p53 acetylation ($P<0.05$) was apparent and accompanied by increased secretions of IL-1β, IL-6, IL-10 and IFN-γ (Meso Scale Discovery; $P<0.05$). TNF-α treatment partially restored the siAdipoR1-induced delay in myoblast proliferation ($P<0.001$).

Conclusion Primary CHF muscle cells exhibited characteristics typical to *in vivo* skeletal muscles of CHF patients including a conserved adiponectin resistance. Silencing of AdipoR1 attenuated the proliferation of muscle cells and the activation of AMPK. In contrast, inflammation induced impairment of adiponectin signalling, myogenesis and mitochondrial biogenesis, suggesting that an increased inflammatory constitution contributes to adiponectin resistance and skeletal muscle dysfunction in CHF patients.

Osteoglycin prevents cardiac dilatation and dysfunction after myocardial infarction through infarct collagen strengthening. (*) — Lucas Van Aelst[1,2], Sandra Voss[3], Paolo Carai[1,4], Sandra Sanders-van Wijk[4], Eric Verbeken[5], Stuart A Cook[6,7,8], Hans-Peter Brunner-La Rocca[4,9], Helge Möllmann[3], Anna-Pia Papageorgiou[1,4], Stephane Heymans[1,4,10] *([1]Center for Molecular and Vascular Biology, Box 911, Department of Cardiovascular Sciences, Catholic University of Leuven, Herestraat 49, 3000 Leuven, Belgium, [2]Department of Cardiology, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium, [3]Department of Cardiology, Kerckhoff Heart Center, D-61231 Bad Nauheim, Germany, [4]Department of Cardiology, Cardiovascular Research Institute Maastricht (CARIM), University Hospital Maastricht, 6229 HX Maastricht, the Netherlands, [5]Department of Pathology, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium, [6]National Heart and Lung Institute, Sydney Street, Imperial College London, London, UK SW3 6NP, UK, [7]National Heart Centre Singapore, 5 Hospital Drive, Singapore, 169609 Singapore, [8]Duke-NUS, 8 College Road, 169857 Singapore, [9]Department of Cardiology, University Hospital Basel, Switzerland, [10]ICIN–Netherlands Heart Institute, Utrecht, The Netherlands).*

Background To maintain cardiac mechanical and structural integrity after an ischemic insult, profound alterations occur within the extracellular matrix. Osteoglycin (OGN) is a small leucine-rich proteoglycan previously described as a marker of cardiac hypertrophy, yet its role in scar formation and cardiac remodeling following myocardial infarction (MI) is unknown.
Methods Permanent ligation of the descending coronary artery was performed in OGN null mice and wild type (WT) littermates. Sections of infarcted and remote myocardial tissue were examined by light and electron microscopy. Cultured fibroblasts were stimulated with TGFß following OGN knockdown or supplementation. Circulating levels of OGN were compared in patients with heart failure (HF) of ischemic and non-ischemic etiology.
Results OGN expression is associated with collagen deposition and scar formation in mouse and human MI. Absence of OGN in mice resulted in significantly increased rupture-related mortality with tissue disruption, intramyocardial bleeding and increased cardiac dysfunction, despite equal infarct sizes. Surviving OGN null mice had greater infarct expansion in comparison to WT mice due to impaired collagen fibrillogenesis and maturation in the infarcts as revealed by electron microscopy and collagen polarization. Absence of OGN did not affect cardiomyocyte hypertrophy in the remodeling remote myocardium. In cultured fibroblasts, OGN knockdown or supplementation did not alter TGF-ß signaling. Adenoviral overexpression of OGN in WT mice significantly improved collagen quality, thereby blunting cardiac dilatation and dysfunction following MI. In OGN null mice, adenoviral overexpression of OGN was unable to prevent rupture-related mortality due to insufficiently restoring OGN protein levels in the heart. Finally, circulating OGN levels in HF patients were significantly increased in the patients with a previous history of myocardial infarction compared to those with non-ischemic HF and correlated with survival, left ventricular volumes and other markers of fibrosis.
Conclusion Increased OGN expression in the infarct scar promotes proper collagen maturation and protects against cardiac disruption and adverse remodeling following MI. In human HF, OGN is a promising biomarker for ischemic HF.

Identification of a glucose sensor in the heart. — Anne Van Steenbergen[1], Balteau M[1], Koepsell H[2], Vanoverschelde JL[1], Hue L[1], Horman S[1], Bertrand L[1], Beauloye C[1] *([1]Université catholique de Louvain (UCL), Institut de Recherche Expérimentale et Clinique (IREC), Pôle de Recherche Cardiovasculaire, Brussels, Belgium, [2]Institute of Anatomy and Cell Biology, University of Würzburg, Würzburg, Germany).*

Background In the heart, hyperglycemia stimulates reactive oxygen species (ROS) production through NOX2 activation, the major isoform of NADPH oxidase. We previously demonstrated that NOX2 activation is independent of glucose metabolism but requires a sodium-glucose transporter (SGLT). Seven SGLT's isoforms (SGLT1 to 6 and SMIT1) have been described although their expression and function in heart remain elusive. Our working hypothesis is that one of SGLTs confers to the cardiomyocyte the ability to detect increased glucose concentration and therefore, acts as a glucose sensor. It could contribute to the pathophysiology of diabetic cardiomyopathy.
Purpose The aim of this work is to investigate the expression of SGLTs in heart and identify the isoform responsible for hyperglycemia-induced NOX2 activation.
Methods We systematically investigated the expression of SGLT isoforms in mouse, rat and human heart. The contribution of each SGLT in NOX2 activation was evaluated, based on their substrate affinity (galactose transported by SGLT1, 1DOG by SGLT3 and myoinositol by SMIT1). Genetic demonstration was performed in SGLT1-/- cardiomyocytes and after adenoviral SMIT1 overexpression in rat cardiomyocytes. NOX2 activation was assessed by p47phox translocation to the plasma membrane and ROS production.
Results SGLT1 and SMIT1 were expressed in mice and rat heart as well as in isolated cardiomyocytes. SGLT3b corresponding to the human SGLT3 was marginal. SGLT2, SGLT5 and SMIT2 were not detected. SGLT4 was only expressed in rat heart. The human heart only expressed SGLT1 and SMIT1. More interestingly, SMIT1 expression

increased in failing human heart. Under 5mM glucose background, incubation of adult rat cardiomyocytes with 16mM galactose or 1DOG did not activate NOX2. By contrast, addition of myoinositol completely reproduced toxic effects of hyperglycemia (21mM glucose), favoring NOX2 activation and ROS production. Myoinositol-induced NOX2 activation resulted from increased PKCβ2 activation, similar to that observed with hyperglycemia. Taken together, sole the glucose analog transported through SMIT1 was able to reproduce glucotoxicity. These results were confirmed using genetic models. The absence of SGLT1 did not prevent hyperglycemia to activate NOX2. Adenoviral SMIT1 overexpression in rat cardiomyocytes sensitized cardiomyocytes towards glucose and exacerbates glucotoxicity. Under this condition, NOX2 activation and subsequent ROS production were more than doubled at 10mM glucose, being nearly maximal (which was normally observed at 21 mMglucose). These results have been reinforced using an in vivo model of glucotoxicity and diabetic cardiomyopathy (after streptozotocin injection).

Conclusion Heart expresses SGLT1 and SMIT1. SMIT1 but not SGLT1 senses any increase in glycaemia, inducing NOX2 activation. This work strongly supports that SMIT1 acts as a glucose sensor in the heart and contributes to diabetic cardiomyopathy.

Platelet Endothelial Aggregation Receptor 1: a novel modifier of neo-angiogenesis. (*) — Christophe Vandenbriele *(Center for Molecular and Vascular Biology, KU Leuven).*

No abstract available.

HEART FAILURE

Serial sST2 measurement to evaluate volume status in acute decompensated heart failure. — Frederic De Roeck, MD*, P. Mortelmans, MD*, D. Hansen, PhD, M. Houbrechts, RN, P. Dendale, MD PhD *(Department of Cardiology, Jessa Hospital, Hasselt, Belgium).*
**equally contributing*

Background ST2 is a receptor for interleukin (IL) 33 and exists in 2 forms: a transmembrane receptor (ST2L) and a soluble receptor (sST2). The ST2 gene is induced by mechanical stress in both cardiac fibroblasts and cardiomyocytes. The IL-33/ST2L signaling axis has cardioprotective effects by counteracting maladaptive hypertrophy and fibrosis.
sST2 acts as a decoy receptor for IL33, preventing the beneficial effects of the IL33/ST2L pathway. sST2 has been shown to be a promising biomarker in heart failure, as high circulating concentrations are associated with worse outcome. More recently its value in diagnosing heart failure and its complementarity with brain natriuretic peptide (BNP) has been suggested.
The clinical usefulness of serial sST2 measurements during hospitalization for acute decompensated heart failure has not been studied. We aimed to assess the correlation between volume status – as illustrated by diuretic-induced weight loss – and serial sST2 measurements.

Methods In this single center prospective clinical trial 25 patients admitted to our hospital with acute decompensated heart failure were included. sST2 and body weight were measured repeatedly, including at admission and discharge. Patients with terminal renal failure, acute coronary syndrome or isolated right heart failure were excluded.

Results 15 women (60%) and 10 men (40%) were included. The mean age was 75.4 [31-89] years. 11 patients (44%) had heart failure with preserved ejection fraction (HFpEF), the remaining 14 patients had a reduced ejection fraction (HFrEF). The mean hospitalization length was 6.4 days. Mean weight loss was 3.7 [-0.3-13.3] kg or 4.7%, while mean sST2 decrease was 65.8 [2.4– 218.3] ng/ml or 46.4%. No correlation could be found between the evolution of body weight and sST2 decrease during hospitalization neither in absolute nor relative terms. This finding was consistent over time for both repeated measurements (Spearman $\rho = 0.163/P = 0.126$ *absolute*) and admission/discharge values (Spearman $\rho = 0.300/P = 0.145$ *absolute* and Spearman $\rho = -0.001/P = 0.997$ *relative%*).

Conclusion Our study suggests that serial measurement of sST2 is not useful to assess volume status evolution nor to guide optimal diuretic therapy in HFrEF or HFpEF patients admitted with acute decompensated heart failure.

Prognosis of heart failure: the added value of 1, 25-dihydroxyvitamin D to PTH(1-84) ratios. (Δ) — Damien Gruson, Sylvie A. Ahn and Michel F. Rousseau *(Cliniques Universitaires St-Luc and Université Catholique de Louvain, Brussels, Belgium).*

Background A growing body of evidence supports the role of vitamin D and parathyroid hormone (PTH) in cardiac remodeling and worsening of heart failure (HF). However, the prognosis value of the 1,25-dihydroxyvitamin D ($1,25(OH)_2D$), the most potent biologically active metabolite of vitamin D, remains unclear. Our objective was therefore to determine $1,25(OH)_2D$ levels in HF patients as well as the predictive value of the ratio of $1,25(OH)_2D$ to PTH(1-84) for cardiovascular death.

Methods Our study included 170 chronic HF patients (females n = 36; males n = 134; NYHA II-IV; mean age: 67 years; etiology: ischemic n = 119, dilated cardiomyopathy

n = 51; mean LVEF: 23%). The primary outcome was cardiovascular death. Circulating levels of $1,25(OH)_2D$, PTH(1-84), 25(OH) vitamin D (25(OH)D), B-type natriuretic peptide (BNP), N-terminal proBNP (NT-proBNP), Galectin-3 (Gal-3), and Fibroblast Growth Factor 23 (FGF23) were determined.

Results Serum levels of $1,25(OH)_2D$ decreased markedly with increase in HF severity. Medians were 33.3 pg/mL for NYHA-II patients, 23.4 pg/mL for NYHA-III, and 14.0 pg/mL for NYHA-IV patients ($P < 0.001$). Most patients had levels of 25(OH)D below 30 ng/mL, and stratification by NYHA functional class did not show significant differences ($P = 0.249$). The $1,25(OH)_2D$ to PTH(1-84) ratio, and the $(1,25(OH)_2D)^2$ to PTH(1-84) ratio were found to be the most significantly related to HF severity. After a mean follow-up of 4 years, 106 out of 170 patients reached the primary endpoint. Cox proportional hazard modeling revealed $1,25(OH)_2D$ and the $1,25(OH)_2D$ to PTH(1-84) ratios to be strongly predictive of outcomes. in ROC analysis the area under the curve (AUC), criteria defined as CV death at the end of the follow-up, for $1,25(OH)_2D$ and the ratios of $1,25(OH)_2D$/PTH(1-84) and $(1,25(OH)_2D)^2$/PTH(1-84) were 0.722 (95% CI: 0.648-0.788), 0.741 (95% CI: 0.668-0.805), and 0.749 (95% CI: 0.677-0.812) respectively, which was similar to BNP (AUC 0.744 [(95% CI: 0.671-0.808]), but clearly higher than 25(OH)D (AUC 0.529 [(95% CI: 0.451-0.606]). Clinically accepted biomarkers had AUCs as follows: NT-proBNP (AUC 0.730 [(95% CI: 0.657-0.796]), Gal-3 (AUC 0.660 [(95% CI: 0.583-0.731]), FGF-23 (AUC 0.702 [(95% CI: 0.624-0.773]), CgA (AUC 0.663 [(95% CI: 0.587-0.733]), and PTH(1-84) (AUC 0.641 [(95% CI: 0.564-0.713]).

Conclusions Levels of $1,25(OH)_2D$ are decreased in HF patients and related to disease's severity. Furthermore, the $1,25(OH)_2D$ to PTH(1-84) ratios strongly and independently predict cardiovascular mortality in chronic HF.

Prognostic significance of improvement in right ventricular systolic function during cardiac resynchronization therapy. (Δ) — Frederik Helsen[1,2], Alexander Van De Bruaene[2], Charlien Gabriels[1,2], Els Troost[2], Gábor Vörös[2], Rik Willems[1,2], Jens-Uwe Voigt[1,2], Werner Budts[1,2] *([1]KU Leuven – University of Leuven, Department of Cardiovascular Sciences, Division of Cardiology, B-3000 Leuven, Belgium, [2]University Hospitals Leuven, Department of Cardiology, B-3000 Leuven, Belgium).*

Background Right ventricular (RV) systolic function can improve during cardiac resynchronization therapy (CRT). However, it is unclear if this is related with improved long-term clinical outcome.

Methods Patients with de novo implantation of a CRT device between January 2009 and December 2011 and subsequent echocardiographic follow-up in our institution were eligible for inclusion in this retrospective analysis. RV systolic dysfunction was defined as a RV fractional area change (FAC) < 35%, left ventricular (LV) reverse remodeling as a reduction of LV end-systolic volume ≥ 10%, clinical response as a reduction in New York Heart Association (NYHA) class ≥ 1, and RV response as an improvement of RV FAC in patients with RV systolic dysfunction at baseline (RVdys group). First, we evaluated NYHA class and echocardiographic response to CRT at one year. Second, we assessed covariates associated with RV response at one year. Third, we looked at the composite endpoint of all-cause mortality or heart transplantation at latest follow-up, stratified for RV FAC < 35%.

Results Medical records of 69 patients (25% female, mean age 62.8 ± 9.2 years, mean LV ejection fraction 27 ± 8%, and mean RV FAC 34 ± 11%) were reviewed. Baseline RV systolic dysfunction was present in 37 patients (54%). Forty-five patients (65%) experienced LV remodelling and 42 patients (61%) were considered clinical responders. CRT elicited only a significant improvement in RV FAC in the RVdys group (Z = –3.16, $P = 0.002$). Twenty-four patients (65%) in the RVdys group were RV responders and had a mean increase in RV FAC of 13 ± 6%. At one year, LV remodelling was significantly associated with an increase in the likelihood of RV response (OR 4.80, 95% CI 1.13-20.46, $P = 0.034$), and more severe mitral regurgitation with a decrease in the likelihood of RV response (OR 0.32, 95% CI 0.12-0.89, $P = 0.029$). For all patients, there were 23 events over a median follow-up period of 4.2 (IQR 3.5-4.9) years. Baseline RV FAC was not associated with the composite endpoint of all-cause mortality or heart transplantation. However, RV FAC at one year (HR 0.90, 95% CI 0.86-0.94, $P = < 0.001$) and the change in RV FAC (HR 0.93, 95% CI 0.90-0.96, $P < 0.001$) were, independently of NYHA class and LV remodelling, associated with the occurrence of the combined endpoint. In the RVdys group, RV response was associated with a lower risk of the combined endpoint (HR 0.15, 95% CI 0.05-0.51, $P = 0.002$).

Conclusion RV systolic function can improve during CRT. This seems mainly due to an improvement in left-sided hemodynamics and LV remodelling. Improvement in RV systolic function is identified as a factor independently associated with improved long-term clinical outcome.

Plasma volume in stable chronic HFrEF patients is contracted and independent of neurohumoral activation and heart failure therapy. — Petra Nijst[1,2], Frederik H. Verbrugge[1,2], Pieter Martens[1], Matthias Dupont[1], Olivier Drieskens[1], Liesbeth Mesotten [1], Joris Penders[1,3], W.H. Wilson Tang[4], Wilfried Mullens[1,3] *([1]Department of Cardiology, Ziekenhuis Oost-Limburg, Genk, Belgium, [2]Doctoral school for Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium, [3]Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Diepenbeek,*

Belgium, [4]Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, OH, United States of America).

Background Both intravascular volume overload as well as under-filling are associated with hospitalizations and mortality in heart failure (HF) patients. (1,2) Currently, little is known of plasma volume (PV) in chronic stable HF patients with reduced ejection fraction (HFrEF) treated with neurohumoral blockers.

Methods PV with ^{99}Tc-labeled red blood cells (3) as well as body-surface area predicted ideal PV (4) were determined in 24 stable HFrEF patients under optimal medical HF therapy and without any clinical sign of volume overload. Potential relation between parameters associated with HF severity and PV regulation were assessed.

Results 67% of patients had a contracted PV (measured PV< ideal PV) with 42% even demonstrating hypovolemia (measured PV < 90% of ideal PV), and only 8% had hypervolemia (measured PV > 110% of ideal PV). BSA was the only parameter significantly related to PV ($R^2 = 0{,}519$; $P < 0{,}001$) in a multiple regression analysis including all variables which correlated significantly with plasma volume ($P < 0{,}2$) in bivariate analysis, (table 1).

Conclusion An accurate assessment of PV cannot be made by clinical exam. Secondly, in contrast with general belief, PV was significantly lower than predicted values in two thirds of patients while hypervolemia was exceptional. Surprisingly, none of the factors involved in the classic pathophysiologic concept of PV regulation as neurohumoral activity, diuretic use, HF maintenance therapy, renal function or LVEF were related to PV status.

Table 1 Baselinge characteristics

Age (years)	68±11
Body surface area (m^2)	1,9±0,2
Heart rate (bpm)	65,8±11,9
Systolic blood pressure (mmHg)	124±17
Diastolic blood pressure (mmHg)	54±12
Laboratory values	
Hemoglobine (g/dl)	12±1,2
Serum creatinine (mg/dl)	1,5±0,7
Serum aldosterone (ng/l)	275±169
Plasma renin activity (ng/ml/h)	22±27
pro-BNP (pg/ml)	1554,0±1738,4
Plasma volume	
Measured (L)	3±0,6
Ideal (L)	3,2±0,4
Mean difference (%)	-6±13
hypovolemia	*42%*
hypervolemia	*8%*
Medication use	
Renin-angiotensin system blocker	83%
Beta blocker	96%
Aldosterone antagonist	83%
Loop diuretic	62%
Thiazides	21%

Ejection Fraction/Global Strain ratio for differential diagnosis in left ventricular hypertrophy. — Efstathios Pagourelias, J. Duchenne, O. Mirea, J. Van Cleemput, M. Delforge, J. Bogaert, T. Kuznetsova, J.U. Voigt *(Department of Cardiovascular Diseases, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium, Department of Radiology, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium, Department of Hematology, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium.)*

Background We hypothesize, that the relation between ejection fraction (EF) and global longitudinal

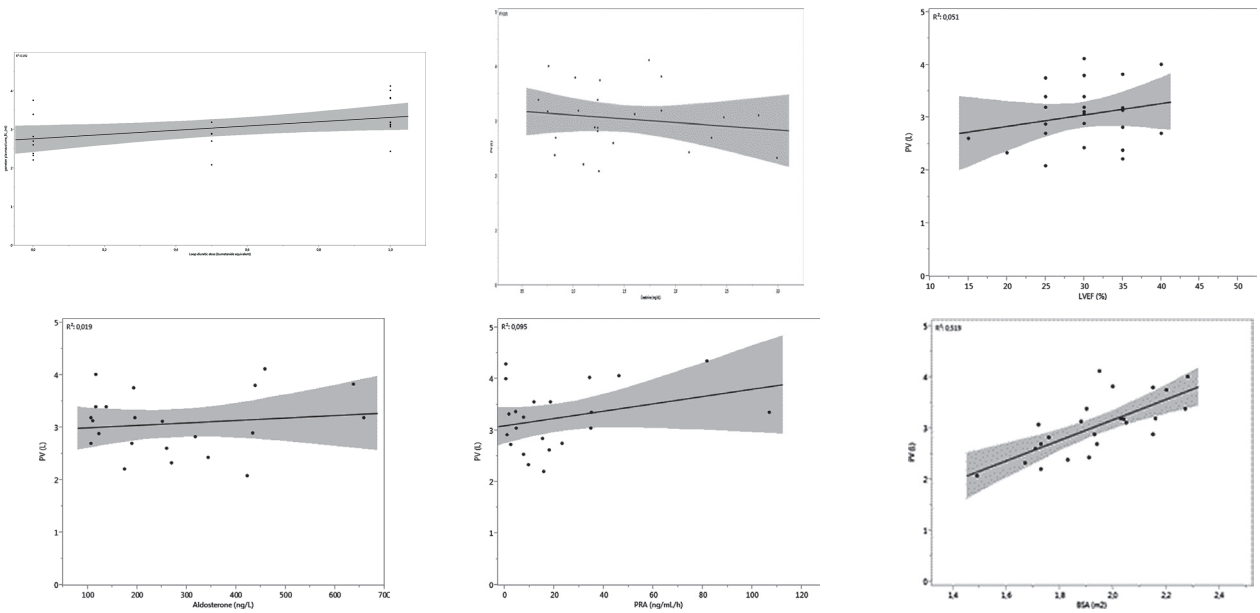


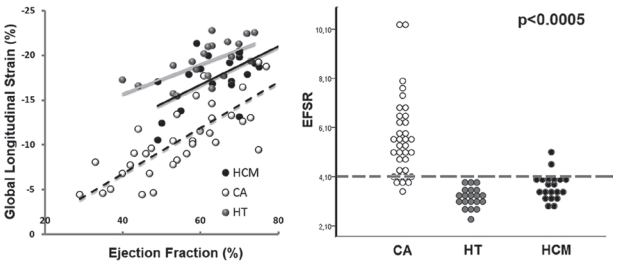
Fig. 1 Correlation between PV and loop diuretic dose, creatinine, left ventricular ejection fraction (LVEF), plasma renin activity (PRA), aldosterone (all $P > 0{,}05$) and body surface area (BSA) ($P < 001$).

strain (GLS) may be influenced by left ventricular (LV) function, LV morphology and underlying pathology. This study aimed at investigating the relationship between EF and various global strain components in hypertrophic hearts and at determining if the EF/global strain ratio can differentiate cardiac amyloidosis (CA) from other hypertrophic substrates such as in hypertrophic cardiomyopathy (HCM) or hypertension (HT).

Methods We included 75 subjects of which 35 were patients with biopsy-proven CA (65.9 ± 11.1 years, 65.7% male, 60% AL type), 20 HCM patients matched for maximum LV wall thickness (51 ± 17 years, 85% male) and 20 age and body habitus matched HT patients (62.3 ± 8.1, 80% male) with LV hypertrophy. Apart from EF and speckle tracking derived global longitudinal strain (GLS), regional and global circumferential (CGS) and radial (GRS) strain indices along with LV twist were analyzed.

Results After including GLS, GCS, GRS, LV twist, left ventricular mass index (LVMI) and patient group in a multiple linear regression model, only patient group and GLS were found to be significant regressors of EF with a linear equation: EF = 20.7-2.3*GLS + 10.3*GROUP (0 for HCM + HT and 1 for CA), (model $R^2 = 0.76$, $P < 0.0005$ both for GLS and patient Group). A graphical representation of this equation (figure) revealed a novel index, EF strain ratio (EFSR = EF/|GLS|) which was significantly higher among CA patients compared to other groups (5.7 ± 1.7 in CA vs 3.7 ± 0.6 in HCM vs 3.2 ± 0.4 in HT, $P < 0.0005$) (figure). ROC analysis showed that EFSR was better (compared to other validated parameters) to differentiate CA from other hypertrophy substrates [AUC = 0.951, 95%CI(0.91-1.0), $P < 0.00005$)], even among patients with mild (< 16 mm) hypertrophy [AUC = 0.95, 95%CI(0.89-1.0), $P < 0.001$)]

Conclusions Our study demonstrated that in patients with thickened hearts, the relation between EF and GLS is dependent on the underlying pathology. A novel index EFSR has shown an excellent differentiating capacity for CA among patients with thickened hearts.



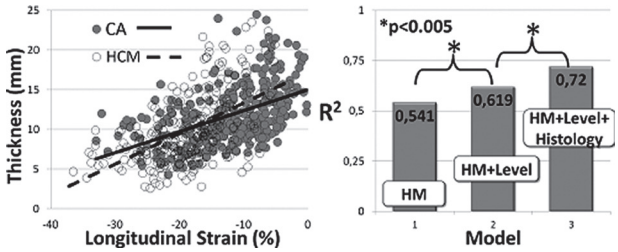
Impact of wall thickness, hypertrophy pattern and histology on strain measurements. — Efstathios Pagourelias, J. Duchenne, O. Mirea, M. Delforge, J. Van Cleemput, J. Bogaert, JU. Voigt *(Department of Cardiovascular Diseases, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium, Department of Hematology, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium, Department of Radiology, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium).*

Background To investigate the relationship between segmental hypertrophy magnitude (HM) and local peak longitudinal strain (LS) under different pathologic substrates. Additionally, to determine the impact of additional factors [left ventricular (LV) level of hypertrophy and histology] on LS measurements.

Methods We included 25 patients with biopsy-proven cardiac amyloidosis (CA) (65.9 ± 11.1 years, 68% male, 60% AL type) and 20 patients with hypertrophic cardiomyopathy (HCM) matched for maximum LV wall thickness (51 ± 17 years, 70% male). The LV was divided into three levels (base, mid, apex) with 6 segments each (18 segment model). Segmental LS was assessed with speckle tracking echocardiography. HM was measured in short-axis magnetic resonance cine loops. Segments with > 13 mm wall thickness were considered hypertrophic.

Results In total, 810 segments were evaluated of which 147 (32.7%) in CA and 84 (23.3%) in HCM were hypertrophic (maximum thickness 16.1 ± 2.8 mm in CA vs 16.6 ± 2.8 in HCM, $P = 0.554$). For the same HM, segmental LS was more impaired in CA (–8.1 ± 5.2% vs –13.4 ± 4.5% in HCM, $P = 0.0008$) (Figure). Correlation between HM and LS was slightly larger among HCM hypertrophic segments (r = 0.357, $P = 0.006$ vs r = 0.274, $P = 0.005$ in CA). Regression analysis revealed that the combination of HM, level and histologic substrate accounted for 0.72 of segmental LS variability ($P < 0.0005$) with thickness explaining about half of it ($R^2 = 0.541$, $P < 0.0005$) (Figure).

Conclusions Our study indicates that thickness explains more than half of segmental LS variability and it is an important factor to be taken into consideration when regional myocardial function is to be evaluated by longitudinal strain measurements.



Evolution of functional mitral regurgitation in heart failure patients with reduced ejection fraction and its prognostic implications. (#) — Lauranne Van Assche,

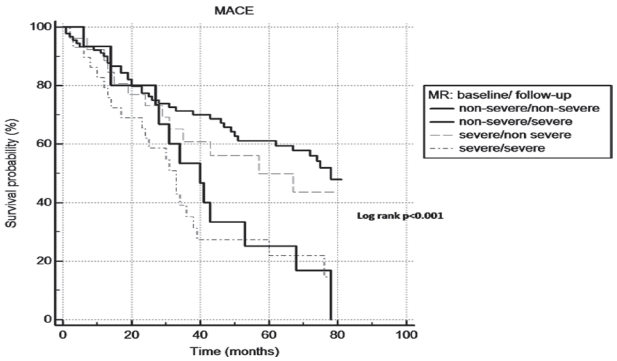
R Nasser, A Vorlat, T Vermeulen, E Van Craenenbroeck, V Conraads, C Vrints, MJ Claeys *(University Hospital Antwerp, Belgium).*

Background Functional mitral regurgitation(FMR) in heart failure patients (pts) with reduced ejection fraction (HFrEF) is associated with a worse prognosis. It is uncertain to what extent HF medication may alter severity of FMR and its prognosis.

Methods The extent of FMR was assessed at baseline and during an average follow-up of 43 ± 25 months in 164 consecutive HFrEF pts from the HF outpatient clinic. Severe FMR was defined as MR grade 3-4 based on a validated integrative method. All patients received maximal tolerable HF medication. Major adverse cardiac event (MACE) was defined as a composite of death, need for heart transplantation or hospitalisation for heart failure and/or malignant arrhythmia's.

Results A total of 57 (35%) pts showed severe MR and had a baseline risk profile comparable to HF pts without severe MR except for slightly worse EF (27% vs 30%,p = 0.05). During follow-up 46% of the severe FMR pts showed improvement to non-severe FMR (MR grade< 3) whereas 14% of non-severe FMR pts developed severe FMR despite optimal HF treatment. Deteriorated FMR was associated with a poor outcome comparable with the outcome of pts with sustained severe FMR (MACE 86% vs 77%, adjusted HR 1.2 (95%CI 0.6-2.7)) whereas outcome of improved FMR was as good as with sustained non-severe FMR. (50% vs 45%, adjusted HR 1.4 (95%CI 0.7-2.7)).

Conclusion Severe FMR is present in more than one third of patients with HFrEF and can be successfully treated with medication in almost 50%. However, severe FMR despite optimal HF treatment is associated with a dramatic prognosis and may need a more invasive approach.



Soluble ST2 as a useful marker in the diagnosis of acute heart failure. — Van hunsel Tine*[1], Van der Goten Kato*[1], Neyens Thomas[4], Hens Niel[4], Mewis Alex[3], Frederix Ines[1,2], Dendale Paul[1,2] *([1]Faculty of Medicine and Life Sciences, Hasselt University, [2]Heart Centre Hasselt Jessa Hospital, [3]Clinical Laboratory Jessa Hospital, [4]Censtat, Hasselt University).*

Background Soluble suppression of tumorigenicity 2 (sST2) is an emerging biomarker of cardiac remodeling and fibrosis. Previous studies indicate the diagnostic and prognostic utility of this protein in patients with heart failure (HF). This study examined the existence of an sST2 threshold value, above which the diagnosis of heart failure is beyond doubt. We investigated the additional diagnostic and prognostic value of ST2 to B-natriuretic peptide (BNP) measurements in emergency department (ED) patients with suspected acute heart failure.

Methods 48 ED patients (56% male, 44% female; aged 69 ± 14 years) with acute dyspnea were included in the study between May and June 2014. Serum samples (sST2 and BNP measurements) and clinical variables (systolic and diastolic blood pressure, edema, ejection fraction etc.) were analyzed. ELISA was used for ST2 and BNP measurements. The primary endpoint was a final clinical diagnosis of heart failure. To identify heart failure patients the physicians relied on classic diagnostic parameters for HF (cardiomegaly, jugular distention, peripheral edema, body mass index (BMI), ejection fraction etc.). A second primary endpoint was the 6-and 9-month readmission or mortality rate. Statistical analysis comprises univariate and multivariate logistic regression, receiver operator curve (ROC) analysis, Wilcoxon rank sum test, Kaplan Meier analysis etc.

Results In the 48 dyspneic subjects, of whom 48% (n = 23) were diagnosed with heart failure, the median sST2 was 52.6 ng/ml (IQR = 85,3). sST2 levels were significantly associated with the diagnosis of heart failure ($P = 0.0083$). This high diagnostic utility was confirmed through ROC analysis with an area under the curve (AUC) of 0.9112 (AUC BNP = 0.8522).

The optimum cut-point for the sST2 levels determined by ROC was 42.61 ng/ml. Among patients with an sST2 value > 42.61 ng/ml and a baseline BNP level > 285.24 ng/L, 100% (n = 15/15) suffered from heart failure, contrary to the 10% (n = 1/10) of the patients with marker values below these reference level.

Baseline ST2 levels were correlated with baseline BNP levels (r = 0.47; $P = 0.0007$).

After 6 months, 38% (n = 18) of the patients had experienced an adverse event. Median concentrations of ST2 at presentation to the emergency department were higher among the group with an adverse event within 6 months. However the Wilcoxon rank sum test demonstrated that this difference was not significant between the two groups. By both the Kaplan Meier analysis and the Cox regression analysis, we concluded that sST2 levels were not associated with readmission or mortality in our study.

Conclusions Based on our results, serum ST2 measurement has additional diagnostic value to BNP for the

diagnosis of heart failure in ED patients presenting with acute dyspnea as cardinal symptom. The combination of these two biomarkers has the highest sensitivity but it is also the most expensive option. Therefore, this combined approach is recommended for the clinical mode of operation.
Our study results did not confirm the prognostic value of ST2.

Response and Tolerance to Oral Vasodilator Uptitration after Intravenous Vasodilator Therapy in Advanced Decompensated Heart Failure. (Δ) — Frederik H. Verbrugge, M. Dupont, M. Finucan, A. Gabi, N. Hawwa, W. Mullens, D.O. Taylor, J.B. Young, R.C. Starling, W.H.W. Tang *(Ziekenhuis Oost-Limburg/Cleveland Clinic).*

Background Oral hydralazine/isosorbide dinitrate (HYD/ISDN) is often used to maintain a favourable hemodynamic response achieved with intravenous vasodilator therapy in advanced decompensated heart failure (ADHF). However, there is a paucity of information on hemodynamic response and tolerance to HYD/ISDN uptitration in ADHF.
Methods Medical records of 147 consecutive ADHF patients who underwent placement of a pulmonary artery catheter and received intravenous vasodilator therapy were reviewed. Beneficial hemodynamic response was defined as pulmonary arterial wedge pressure (PAWP), central venous pressure ≤8 mmHg, and cardiac index ≥2.20 L/min/m², without emergent hypotension.
Results Intravenous sodium nitroprusside and sodium nitro-glycerine was the intravenous vasodilator agent used in 143 and 32 patients, respectively. Sixty-one percent of patients were subsequently converted to oral HYD/ISDN combination therapy through a standardized conversion protocol (Table). Those patients had a significantly higher PAWP upon admission, compared to patients not converted (28 ± 7 versus 25 ± 8 mmHg, respectively; *P*-value = 0.024). Beneficial hemodynamic response was achieved in a similar proportion of patients receiving oral HYD/ISDN or not (32% versus 29%; *P*-value = 0.762). Those patients had a significantly better right ventricular stroke work index at baseline compared to patients who did not reach hemodynamic targets (11.0 ± 3.7 versus 8.4 ± 3.6 g/m²/beat; *P*-value = 0.028). The incidence of inotrope and vasopressor use, left ventricular assist device placement, and orthotopic heart transplantation was significantly higher in the group that was not converted from the intravenous vasodilator agent to oral HYD/ISDN combination therapy. HYD/ISDN dosing was progressively and consistently decreased up to the moment of hospital discharge and during outpatient follow-up, primarily due to incident hypotension.
Conclusion The use of a standardized hemodynamically-guided uptitration protocol for conversion from intravenous to oral vasodilators is safe, but may warrant subsequent dose reductions upon stabilization.

Subclinical Volume Overload in Stable Outpatients with Chronic Heart Failure. — Frederik H. Verbrugge, L. Boonen, P. Nijst, P. Noyens, P. De Vusser, D. Verhaert, J. Van Lierde/M. Vrolix/M. Dupont/W. Mullens, *(Ziekenhuis Oost-Limburg/Hasselt University).*

Background Bioelectrical impedance analysis (BIA) allows estimation of total body water and might detect subclinical volume overload in chronic heart failure (CHF).
Methods Venous blood sampling and BIA were performed in consecutive CHF patients (n = 58) free from clinical signs of volume overload and treated with oral loop diuretics. Subclinical volume overload was defined as excess extracellular water on BIA.
Results Patients with (n = 34) versus without (n = 24) subclinical volume overload were significantly older (72 ± 10 versus 65 ± 9 years; *P*-value = 0.016), had higher systolic blood pressure (126 ± 20 versus 114 ± 17; *P*-value = 0.012), and took angiotensin-converting enzyme

	Starting dose	Uptitration schedule
Isosorbide dinitrate	10 mg	After 2 h, ↑ to 20 mg if previous dose tolerated After 10 h, ↑ to 40 mg if previous dose tolerated After 18 h, ↑ to 60 mg if previous dose tolerated Continue 60 mg TID if previous dose tolerated If previous dose is not tolerated, administer highest dose tolerated TID
Hydralazine	25 mg (10 mg if low MAP or unstable patient)	After 2 h, ↑ to 50 mg if previous dose tolerated After 8 h, ↑ to 75 mg if previous dose tolerated After 14 h, ↑ to 100 mg if previous dose tolerated Continue 100 mg QID if previous dose tolerated If previous dose is not tolerated, administer highest dose tolerated QID

MAP, mean arterial blood pressure; QID, 4 times daily; TID, 3 times daily.

inhibitors more often (65% versus 33%; *P*-value = 0.032). Dyspnea symptoms were similar among both groups (Figure). Subclinical volume overload was associated with low serum albumin (*P*-value = 0.014) and protein levels (*P*-value = 0.041). In contrast, serum sodium levels (141 ± 3 versus 139 ± 2 mEq/L; *P*-value = 0.033) but not chloride levels (99 ± 14 versus 101 ± 3 mEq/L; *P*-value = 0.980) were significantly higher in patients with versus without subclinical volume overload, respectively. The former versus latter group also demonstrated lower plasma aldosterone levels [276 (195-475) versus 400 (306-717) ng/L, respectively; *P*-value = 0.032].

Conclusions Subclinical volume overload assessed by BIA in stable CHF is associated with low serum protein levels, increased serum sodium but not serum chloride, as well as decreased neurohumoral activation.

Hyponatremia Patterns during Hospitalization for Acute Heart Failure. — Frederik H. Verbrugge, J.L. Grodin, W. Mullens, D.O. Taylor, R.C. Starling, W.H.W. Tang *(Ziekenhuis Oost-Limburg/Cleveland Clinic).*

Background Hyponatremia is associated with worse outcome in acute heart failure (AHF), but its pathophysiology is complex and heterogeneous. The temporal pattern of hyponatremia development during hospitalization for AHF may carry prognostic relevance.

Methods A post-hoc analysis of the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) and Diuretic Optimization Strategies Evaluation in Acute Heart Failure (DOSE AHF) study was performed (n = 716). Patients were stratified according to their pattern of hyponatremia development: (1) no hyponatremia; (2) *persistent hyponatremia* present from admission till discharge; (3) *decompensation hyponatremia* disappearing with decongestive treatment; and (4) *treatment-induced hyponatremia*, emerging with decongestion.

Results Persistent and decompensation hyponatremia patients had more pronounced neurohumoral activation at baseline, illustrated by significantly elevated blood urea nitrogen/creatinine ratios (*P*-value< 0.001), plasma renin activity (*P*-value< 0.001), and plasma aldosterone levels (*P*-value< 0.001). Persistent hyponatremia patients also had significantly lower arterial blood pressure compared to patients without hyponatremia (*P*-value< 0.001). In contrast, patients with treatment-induced versus no hyponatremia had very similar baseline characteristics, comparable natriuretic peptide levels, and both groups had little neurohumoral activation at baseline. Loop diuretic efficacy, defined as net fluid balance [mL] per 40 mg furosemide-equivalent dose administered, was lower in patients with persistent or treatment-induced hyponatremia versus decompensation hyponatremia or no hyponatremia, respectively. The former versus latter groups also had more pronounced neurohumoral activation with decongestive treatment. The risk for all-cause mortality [HR(95%CI) = 2.50 1.50-4.19); *P*-value 0.001] and death or heart failure readmission [HR(95%CI) = 2.18 (1.60-2.97); *P*-value< 0.001] was significantly elevated in patients with persistent versus no hyponatremia, with the risk of decompensation and treatment-induced hyponatremia situated in-between.

Conclusions The temporal pattern of hyponatremia development in patients with AHF provides prognostic information and mechanistic insight. Tretment-induced hyponatremia is harmful.

INVASIVE

Meta-analysis of randomized trials comparing drug-eluting stents with coronary artery bypass grafting. — Alban Dibra, Sokol Xhepa, Laureta Dibra *(University Hospital Center "Nene Tereza", Tirana).*

Background There is limited information from clinical trials about the long term differences between percutaneous coronary intervention (PCI) with drug-eluting stents (DES) and coronary artery bypass grafting (CABG) in patients with complex coronary artery disease (CAD). Additionally, most of these trials have not been powered to evaluate outcomes such as death. To address these issues we performed a meta-analysis of randomized trials on this topic.

Methods We searched for randomized trials comparing DES with CABG in patients with multivessel CAD and/or left main disease reporting clinical outcome for a minimum of 12 moths. Data sources included PubMed and conference proceedings. Outcomes of interest included death, repeat revascularization and stroke.

Results A total of 7 trials with 6089 patients were included in this analysis. Reported follow-up was 1 year in one of the studies, 2 years in another study and about 5 years in the remaining studies. Mean age of study patients was 64 years and more than 60% of the patients had diabetes. Males constituted more than 70% of the population. Syntax score varied from 22.1 to 28.7. About 29% of the patients had 2-vessel coronary artery disease. From the total study population, 10% died, 13% required a repeat revascularization procedure and 3% suffered stroke. The risk of death was higher among patients treated with DES as compared to patients treated with CABG (odds ratio 1.3, 95% CI 1.1 to 1.5; *P* = 0.004); similarly the risk of repeat revascularization procedures was markedly higher among patients treated with DES as compared to patients treated with CABG (odds ratio 2.3, 95% CI 1.9 to 206; *P* < 0.001). On the other hand, patients treated with DES had a lower

risk of suffering stroke compared to patients treated with CABG (odds ratio 0.6, 95% CI 0.4 to 0.8; $P=0.007$).

Conclusion While both PCI and DES can be used to treat patients with multivessel CAD and or left main disease, CABG is markedly superior among patients with a high angiographic risk profile and diabetes mellitus.

5-Year Clinical Follow-up of the PYTON (Prospective Evaluation of the TRYTON Side-Branch Stent with an additional XIENCE-V Everolimus-Eluting Stent in Coronary Bifurcation Lesions) Study. — Johan Bennett, Nick Hiltrop, Tom Adriaenssens, Peter Sinnaeve, Walter Desmet, Christophe Dubois *(Department of Cardiovascular Medicine, University Hospitals Leuven, Leuven, Belgium).*

Background Dedicated bifurcation stents have been proposed as a potential alternative for treatment of true coronary bifurcation lesions. This study sought to evaluate the healing responses with optical coherence tomography (OCT), and angiographic and clinical outcome after bifurcation stenting with the TRYTON Side-Branch stent™.

Methods Twenty consecutive patients with coronary bifurcation lesions and significant involvement of the side-branch (SB) were treated with the TRYTON Stent in the SBand an additional XIENCE-V™ everolimus-eluting stent in the main vessel (MV). At 9 months, the ratio of uncovered to total stent struts (RUTSS) with OCT, angiographic late luminal loss (LLL), and in-stent and in-segment restenosis, were assessed. Clinical follow-up was performed at 1, 3 and 5 years. The clinical endpoints included the rate of major adverse cardiac events (MACE) and their components, target lesion revascularization (TLR), non-target lesion revascularisations (non-TLR) and stent thrombosis; MACE were defined as any of the following: all-cause death, myocardial infarction (MI) and ischemia-driven target lesion revascularization (TLR).

Results Clinical follow-up was obtained in all patients (n = 20). At 5 years, 7 patients had undergone TVR (35%), of which 5 were TLR (25%). Four target lesion restenoses occurred in the first year post stenting with 1 occurring after almost 4 years. Three were silent (detected at planned angiographic and OCT follow-up at 9 months). All but 2 restenoses occurred at the ostium of the SB or the proximal MV stent edge. Three patients suffered an MI (15%), two of which were peri-procedural and without clinical consequences. The third MI was in a patient who developed new Q-waves on the electrocardiogram as well as severe anterior hypokinesia, secondary to a silent sub-occlusive restenosis in the MV. Following revascularization, the patient's ventricular wall motion abnormalities normalised and there was complete resolution of the Q-waves. Two patients underwent non-TLR. There was 2 non-cardiac deaths (10%) which occurred 28 and 59 months after stent implantation. There were no stent thromboses. The composite MACE rate was 40%. Kaplan Meier event-free survival curves are presented in figure 1.

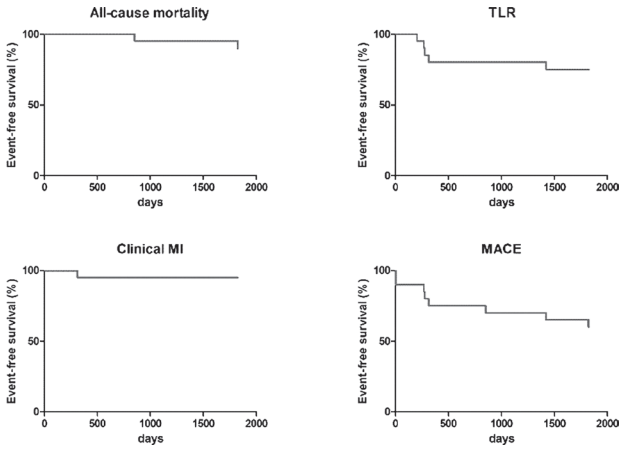


Fig. 1 Kaplan Meier survival Curves.

Conclusions Percutaneous coronary bifurcation revascularisation with TRYTON stents does not meet expectations of contemporary bifurcation lesion treatment with high rates of TLR and MACE.

An in-vivo multi-modality imaging study of the Absorb everolimus-eluting bioresorbable scaffold in complex coronary bifurcations. — Johan Bennett, Maarten Vanhaverbeke, Nina Vanden Driessche, Tom Adriaenssens, Peter Sinnaeve, Walter Desmet, Christophe Dubois *(Department of Cardiovascular Medicine, University Hospitals Leuven and Department of Cardiovascular Sciences, KU Leuven, Leuven, Belgium).*

Background This in-vivo study sought to provide insights regarding the feasibility of performing complex bifurcation techniques with the Absorb everolimus-eluting bioresorbable vascular scaffold (BVS).

Methods 20 New Zeeland white rabbits were anaesthetized and a 6 Fr arterial sheath was placed in the carotid artery extending to the distal aorta. Bifurcation stenting procedures of the aorta-iliac bifurcation were performed with 3.0x28 mm BVS using the following stenting techniques: main-vessel (MV) stenting with ballooning of side branch (SB) through the BVS struts (Provisional stenting, n = 5), T-and protrusion (TAP, n = 5), modified T (mini-crush of BVS in SB first, n = 5) and culotte (n = 5) stenting. POT with 3.5 mm non-compliant (NC) balloons at 16 atm and mini-kissing balloon post-dilatation with 3.0 NC balloons at 5 atm were performed in all procedures. Angiography, optical coherence tomography (OCT) and post-procedural micro-computed tomography (micro-CT) were performed.

Results In all procedures angiographic results were excellent with no evidence of dissection or SB compromise. Re-crossing through struts with guidewires was always successful and subsequent crossing with balloons and a second BVS (only in TAP + culotte procedures) was smooth. Provisional stenting optimally opened the SB ostium without deforming the MV BVS. On OCT there was no malapposition in the MV and micro-CT revealed good SB aperture and a single connector fracture was present in the MV in 1 of the 5 cases. Modified T stenting and TAP stenting resulted in complete coverage of the SB ostium and carina. Both techniques resulted in minimal double-strut layers at the carina and at the proximal SB ostium on OCT with no significant malapposition. On Micro-CT, no strut fractures were present following modified T stenting (figure 1), whilst in 3 out of 5 TAP procedures single strut fractures were noted, these did not cause luminal compromise. Culotte stenting resulted in complete coverage of the bifurcation with an extensive proximal segment of double-layered scaffold struts. In 3 of the 5 culotte procedures, OCT revealed significant circumferential malapposition at the bifurcation. On micro-CT there was distortion of MV and SB scaffolds at the level of the bifurcation with single strut fractures present in all 5 cases affecting the MV BVS. These fractures did not cause luminal compromise.

Conclusion In this non-diseased aorto-iliac bifurcation model, it was feasible to perform complex bifurcation stenting using Absorb BVS with excellent angiographic results. When a 2-stent technique is planned, modified T-stenting was the most promising with no evidence of significant malapposition or scaffold disruption on OCT and micro-CT, respectively. Finally, culotte stenting frequently caused circumferential malapposition, scaffold distortion and strut fractures, the clinical impact of which is unknown.

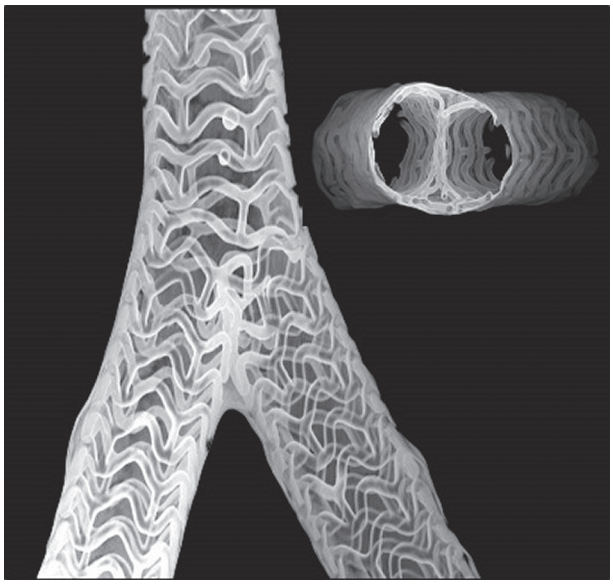


Fig. 1 Example of 3D Micro-CT reconstruction of modified T stenting.

Percutaneous mitral valve repair in patients at high surgical risk: 1-year results from the prospective Belgian MitraClip Registry (MITRABEL).

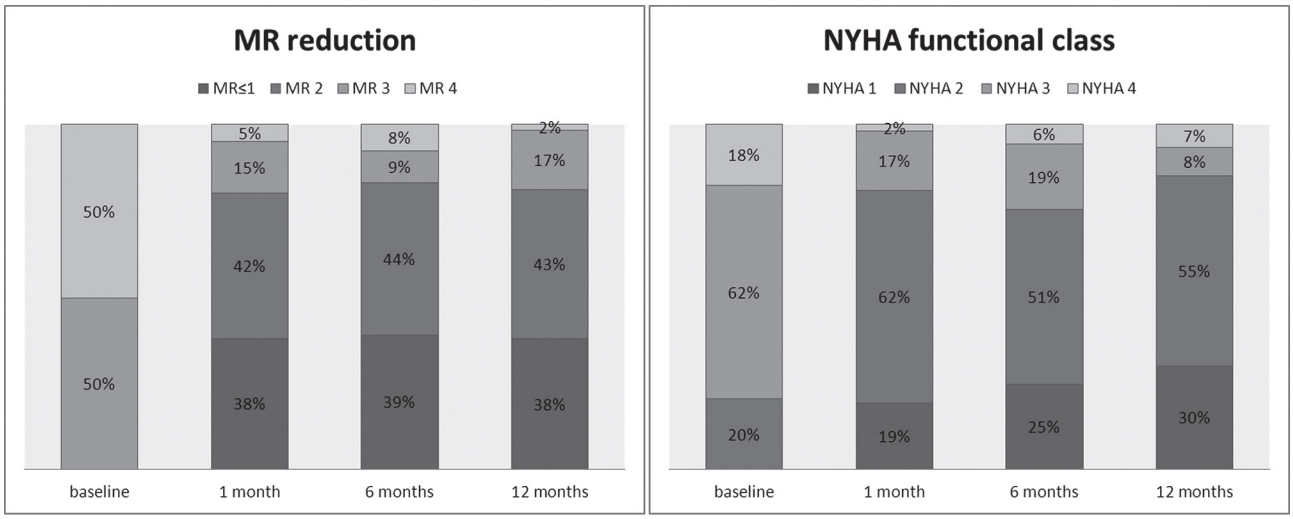
(Δ) — Philippe B. Bertrand, Philippe Debonnaire, Patrick Coussement, Jozef Bartunek, Marc Vanderheyden, Georges Saad, Suzanne Pourbaix, Bert Ferdinande, Anne-Catherine Pouleur, Dina De Bock, Bernard Paelinck, Marc J. Claeys *(Universitair Ziekenhuis Antwerpen, AZ Sint Jan Brugge, AZ OLV Aalst, CHR de la Citadelle Liège, Ziekenhuis Oost-Limburg Genk, UCL St-Luc Brussel).*

Background Percutaneous edge-to-edge mitral valve repair (MitraClip®) offers treatment for severe mitral regurgitation (MR) in patients at high or prohibitive surgical risk. We report the 1-year results of the Belgian MitraClip Registry.

Methods Patients who underwent MitraClip® implantation in a Belgian hospital between October 2010 and May 2015 were prospectively included in the registry. Procedural safety, treatment efficacy, and major adverse cardiac events (MACE), defined as the combined endpoint of death, surgical mitral valve intervention, and hospitalization for heart failure (HF), were evaluated at 1 month, 6 months and 1 year follow-up.

Results A total of 113 consecutive patients with symptomatic severe (3 or 4+) MR underwent MitraClip® therapy at 6 Belgian sites (73 ± 10 years old; 63% male; left ventricular ejection fraction (LVEF) 37 ± 13%; New York Heart Association (NYHA) functional class III or IV in 80%, logistic EuroSCORE 18% (IQR 9-30%), 84% functional MR).

The clip implant rate was 95%. Acute procedural success (clip implant and reduction of MR to ≤ 2+) was obtained in 96 (85%) patients, with more than one clip placed in 40 (35%). A total of 3 patients (2.7%) died within 30 days after the MitraClip® procedure. Hospital length of stay was 5 (IQR 3-8) days. Significant improvement in the severity of MR was maintained at 12 months ($P < 0.001$ compared with baseline), with 81% of surviving patients free from MR> 2 (Figure). Moreover, 85% of patients were in NYHA functional class I or II at 12 months ($P < 0.001$ versus baseline). Hospitalization for HF was significantly reduced to 19% of patients in the first year post-clip versus 62% of patients in the 2 years before the procedure ($P < 0.001$). The Kaplan-Meier survival at 1 year was 76%; freedom from MACE at 1 year was 63%. Nine patients (8%) required mitral valve surgery within 12 months after the procedure. Predictors of MACE in multivariate Cox regression analysis were chronic obstructive pulmonary disease (HR 2.5, 95% CI: 1.2-5.0), HF hospitalization in



* 35 pts surviving no 1 year FU yet

the 2 years before the procedure (HR 3.7, 95% CI: 1.3-10.9) and post-clip MR (HR 1.8, 95% CI 1.1-2.9).

Conclusion High-risk patients with predominantly functional MR are typically targeted with MitraClip® therapy in Belgium. In these patients, MR ≤ 2 + and NYHA class ≤ II are obtained in > 80% with low procedural mortality and maintained up to 1 year follow-up. Chronic obstructive pulmonary disease, preoperative HF hospitalization and incomplete MR reduction during the procedure are independent predictors of worse outcome after the therapy.

Duration of hospitalization for minimally invasive CABG versus CABG through sternotomy; a stepwise linear regression analysis. — Senne Broekx[1*], Jef Driesen[1*], Marc Hendrikx[1,2], Urbain Mees[2], Boris Robic[2], Alaaddin Yilmaz[2], Niel Hens[3], Thomas Neyens[3], Paul Dendale[1,3] *([1]Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium, [2]Department of Cardiothoracic Surgery, Jessa Hospital, Hasselt, Belgium, [3]Research Institute Center for Statistics (CENSTAT), Hasselt University, Hasselt, Belgium, [4]Department of Cardiology, Jessa Hospital, Hasselt, Belgium, *These authors contributed equally to this work).*

Background Until now, Coronary Artery Bypass Grafting (CABG) through sternotomy has been the standard of care for patients suffering from Coronary Artery Disease (CAD). Today mini-thoracotomy, a minimally invasive alternative to this procedure, is gaining ground. Its success is primarily due to the perceived reduction in recovery time after surgery.

Methods We set out to determine the impact of the surgical approach on duration of hospitalization as a primary objective. EuroSCORE II values were calculated for each subject included in our study. A total of 593 patients, treated between 2013 and 2015, were divided into two main groups according to incision type. One group accommodates patients treated with mini-thoracotomy (n = 190), the other group patients with conventional sternotomy approach (n = 403). A stepwise linear regression analysis was performed. Duration of hospitalization was used as the dependent variable in the regression model. Incision type and EuroSCORE II were used as input variables. By including EuroSCORE II values in our model, we were able to study the effect of incision type on hospitalization, while taken into account the difference in predicted operative mortality between different study subjects. In addition, an identical investigation was performed with two different types of mini-thoracotomy: Endoscopic Atraumatic Coronary Artery Bypass Grafting (endo-ACAB; n = 126) and Endoscopic Coronary Artery Bypass Grafting (endo-CABG; n = 64).

Results Stepwise linear regression revealed both EuroSCORE II ($P = 0.0176$) and incision type ($P < 0.0001$) to be significant predictors of duration of hospitalization. Parameter estimates for incision type showed a decrease in duration of hospitalization when treating patients through mini-thoracotomy (mean length of stay = 8.34 days), compared to conventional sternotomy (mean length of stay = 11.56 days). The same conclusions can be drawn after identical statistical analysis for both endo-ACAB (mean length of stay = 8.67 days) and endo-CABG (mean length of stay = 7.69).

Conclusion Based on our study, the minimally invasive approach seems to have a significant effect on reducing the duration of hospitalization in patients suffering from CAD. Similarly significant effects were also noticeable when comparing endo-ACAB and endo-CABG.

Evaluation of geriatric parameters before and after transcatheter aortic valve implantation in patients with severe, symptomatic aortic valve stenosis patients. — Valérie M. Collas[1,2], Yie Man Chong[3], Bernard P. Paelinck[4], Inez E. Rodrigus[4], Tine E. Philipsen[4], Christiaan J. Vrints[1,2], Maurits Vandewoude[3], Johan M. Bosmans[1,2] *([1]University of Antwerp – Cardiovascular Diseases, [2]Antwerp University Hospital – Department of Cardiology, [3]ZNA Sint-Elisabeth – Department of Geriatrics, [4]Antwerp University Hospital – Department of Cardiac Surgery).*

Background Transcatheter aortic valve implantation (TAVI) is suggested in patients with severe, symptomatic aortic valve stenosis not eligible for surgical aortic valve replacement, in order to improve their prognosis and quality of life. The aim of this study was to evaluate the evolution of quality of life and geriatric parameters before and after (6 weeks and 6 months) TAVI.

Methods Patients with severe, symptomatic aortic valve stenosis underwent multidimensional geriatric assessment before and after TAVI (follow up1: after 6 weeks and follow up 2: after 6 months). This assessment included the following domains: 1) quality of life (general health, SF12, Katz independent); 2) nutritional state (decreased appetite, loss of weight: more than 3 kg, nutritional problems); 3) cognition (Mini-Mental State Exam) and depression (Geriatric Depression Scale); 4) function (exhaustion, 6 minute walking test).

Results 69 patients were evaluated before TAVI and 59 patients 6 weeks after TAVI (6 deceased). 41 patients were evaluated 6 months after TAVI (1 deceased additionally). Mean age was 81 ± 6 years and 43.5% were male. Median logistic EuroSCORE was 15.2 (9.8-19.9)%. On a scale from 0 (worst) to 10 (excellent), general health increased from 6.6 ± 2.1 to 7.5 ± 1.4 (n = 58, $P = 0.005$). This remained stable 6 months after TAVI (7.4 ± 1.8, n = 39, $P = 0.574$). The other parameters and their evolution can be found in table 1. The proportion of patients with "decreased appetite" decreased significantly from 36.8% (6 weeks) to 13.2% (6 months post TAVI, n = 38, $P = 0.022$). All other parameters remained stable up to 6 months after TAVI.

Conclusion Although the proportion of patients independent for Katz decreased, quality of life, cognition and function improved within 6 weeks and remained stable 6 months after TAVI.

Functional performance and quality of life in high-risk comorbid patients undergoing transcatheter aortic valve implantation for symptomatic aortic valve stenosis. — Nick Hiltrop, Ann Belmans, Marina Claes, Miek Hornikx, Bart Peeters, Johan Flamaing, Tom Adriaenssens, Filip Rega, Herbert De Praetere, Marie-Christine Herregods, Walter Desmet, Paul Herijgers and Christophe Dubois *(Department of Cardiovascular Medicine and Cardiac Surgery/University Hospitals Leuven).*

Background Despite beneficial haemodynamic effects of transcatheter aortic valve implantation (TAVI) in patients with aortic valve stenosis (AS), the impact of this procedure on functional performance and quality of life in a high-risk patient population with multiple comorbidities remains unclear.

Methods We prospectively evaluated New York Heart Association (NYHA) functional class, six minute walking distance (6MWD) and quality of life (QoL) at baseline, 30 days and 6, 12 and 24 months after TAVI. 6MWD was analysed in absolute distance (meters) and as percentage of predicted

Table 1	Baseline	Follow up 1	N	P	Follow up 1	Follow up 2		P
Quality of life								
Better health compared to last year/ before TAVI – n (%)	3 (5.1)	45 (76.3)	59	<0.001	29 (76.3)	30 (78.9)	38	1.000
SF12 – Physical Score (%)	44 ± 11	48 ± 8	53	0.011	49 ± 7	49 ± 8	33	0.952
SF12 – Mental Score (%)	52 ± 9	52 ± 8	53	0.897	52 ± 10	53 ± 8	33	0.732
Katz independent – n (%)	41 (69.5)	30 (50.8)	59	0.003	22 (57.9)	20 (52.6)	38	0.688
Nutrition								
Decreased appetite – n (%)	20 (34.5)	20 (34.5)	58	1.000	14 (36.8)	5 (13.2)	38	0.022
Loss of weight – n (%)	26 (45.6)	26 (45.6)	57	1.000	19 (48.7)	22 (56.4)	39	0.581
Nutritional problems – n (%)	2 (3.6)	3 (5.4)	56	1.000	3 (7.9)	1 (2.6)	38	0.500
Cognition and depression								
Mini-Mental State Exam	27 (25-29)	28 (26-30)	43	0.013	26 (26-30)	28 (26-30)	8	0.343
Mini-Mental State Exam ≥27 – n (%)	29 (67.4)	27 (62.8)	43	0.754	3 (37.5)	5 (62.5)	8	0.500
Geriatric Depression Scale	3 ± 2	3 ± 3	59	0.874	3 ± 3	2 ± 2	41	0.192
Geriatric Depression Scale ≥5 – n (%)	12 (20.3)	13 (22.0)	59	1.000	7 (17.9)	6 (15.4)	39	1.000
Function								
6 minute walking test (m)	300 (250-350)	325 (255-378)	23	0.053				
Exhaustion – n (%)	23 (41.8)	12 (21.8)	55	0.019	6 (17.1)	6 (17.1)	35	1.000

distance. Quality of life was evaluated using the validated Dutch version of the EuroQol-5D (EQ-5D) assessment.

Results Between January 2009 and December 2014 a total of 145 patients underwent TAVI with the SAPIEN or SAPIEN XT valve (Edwards LifeSciences) (age 82.8 ± 5.9y, 49% female, 68.3% previous coronary artery disease, 27.5% previous heart surgery, 40% previous stroke, 33.8% chronic obstructive pulmonary disease). Median STS-score was 7.2 (5.3; 9.71), median log-EuroSCORE was 25.0 (17.0; 34.54) and median EuroSCORE II was 7.3 (4.88; 14.89). Distribution of transfemoral and transapical procedures was 61 vs. 39% (89 vs. 56 procedures), respectively. All-cause mortality at 30 days, 6, 12 and 24 months was 6.9%, 11.9%, 21.6% and 41.6% respectively, of which 50% had a non-cardiovascular cause.

All patients were eligible for analysis. NYHA functional class improved significantly at 30 days and 6, 12 and 24 months follow up ($P < 0.001$ for all) (Figure 1). Absolute 6MWD improved significantly at 30d (+19.3m ± 8.2; $P = 0.0166$) and at 6m (+23.3m ± 8.1; $P = 0.0048$). When expressed as percentage of predicted distance, improvement was also significant at 30d (+3.3% ± 1.6; $P = 0.0166$) and 6m (+4.3% ± 1.7; $P = 0.0048$). A favorable trend was maintained at 12m (+17.1m ± 8.8 or + 2.1% ± 1.9; $P = 0.094$ for both), while at 24m 6MWD was similar to baseline values. A significant improvement in QoL (EQ5D) was observed from baseline (0.602 [0.366; 0.805] to 30d (0.737 [0.396; 0.861]; $P = 0.016$) and 6m (0.691 [0.364; 0.843]; $P = 0.0048$). This improvement in QoL was no longer significant at 12 and 24m.

Conclusion In high-risk comorbid patients with symptomatic AS, TAVI results in a significant improvement of functional capacity at 30 days and 6 months follow-up, when evaluated by objective measures as a 6MWD and up to 24 months when using the NYHA functional class. In our population, TAVI resulted in a significant but temporary improvement in quality of life up to 6 months follow-up, most likely related to multiple comorbidities driving the outcome of the EQ-5D assessment.

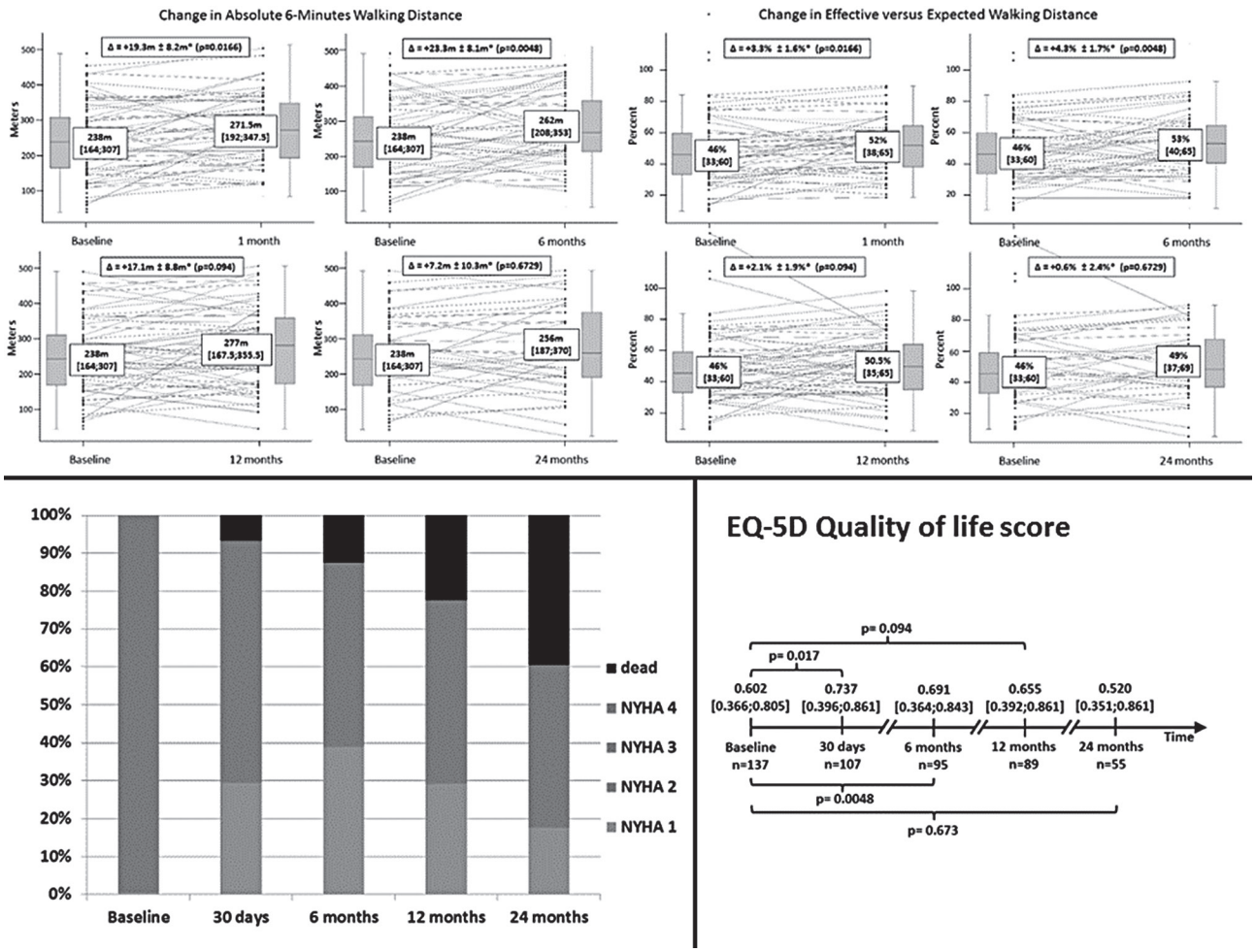


Fig. 1 Evolution of 6 minute walking distance, functional NYHA class and quality of life after TAVI.

Circumflex coronary artery injury after mitral valve surgery: A report of two cases and comprehensive review of the literature. — Nick Hiltrop, Johan Bennett, Tom Adriaenssens, Paul Herijgers, Walter Desmet *(Department of Cardiovascular Medicine and Cardiac Surgery, University Hospitals Leuven, Leuven, Belgium).*

Background The circumflex coronary artery (LCx) runs in close relation to the mitral valve annulus and is therefore susceptible to mitral valve surgery related injury. A variety of underlying possible mechanisms, predisposing factors and different therapeutic strategies have been suggested, but no large case series have been published and disagreement exists.

Methods Using a MeSH terms-based PubMed search, we were able to detect a total of 42 cases of mitral valve surgery related LCx injury, including our 2 cases. (Figure 1) We performed a comprehensive analysis regarding reported predisposing factors, diagnostic signs and outcome of available therapeutic strategies.

Results Preoperative coronary angiography was performed in 55% (n = 23). After additional diagnostic angiographies, overall prevalence of coronary abnormalities was 12% (n = 5). Coronary dominance was reported in 71% (n = 30), predominantly showing a left (74%, n = 22) or balanced (13%, n = 4) circulation. Right coronary dominance was present in 13% (n = 4). Ischemia was detected in the perioperative or early postoperative phase in 87% (n = 28). Delayed symptoms were present in 12% (n = 5), including 3 patients with a time interval of more than 30 days. Echocardiography demonstrated new or dynamic regional wall motion abnormalities in 79% (n = 23). In 21% (n = 6), echocardiography was negative despite coronary compromise. Electrocardiography showed myocardial ischemia in 97% (n = 32), and regional ST-segment elevations were present in 66% of these patients (n = 21). (Figure 1) Primary treatment was surgical in 38% (n = 13) and percutaneous in 62% (n = 21). Surgical success was 92% (n = 12), while PCI was successful in 81% (n = 17).

Conclusions We confirm the previously reported augmented risk of LCx injury during mitral valve surgery in a co-dominant or left-dominant coronary anatomy. Preoperative knowledge of coronary anomalies and a right coronary dominance however do not preclude LCx injury. An anomalous LCx arising from the right coronary cusp was overrepresented in the case series, and could therefore be identified as a separate entity, putting the patient at an augmented risk for perioperative injury. Larger registries however are needed to further investigate this relation. Monitoring of ECG and use of intraoperative TEE are paramount to ensure a timely diagnosis. Both surgical and interventional procedures report excellent results, although publication bias could influence these results since only 42 patients have been reported so far.

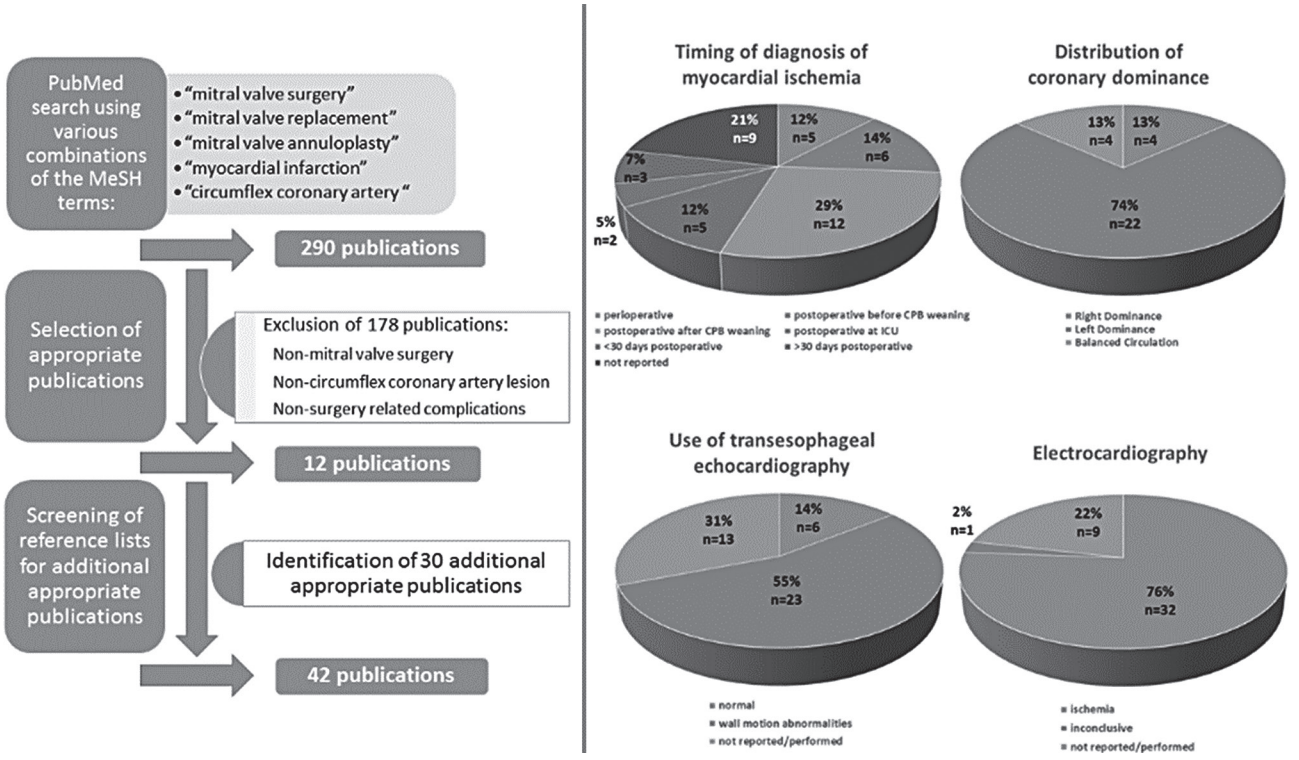


Fig. 1 Flow chart outlining the PubMed search and chart demonstrating frequency of preoperative coronary angiography, distribution of coronary dominance and timing of ischemia diagnosis.

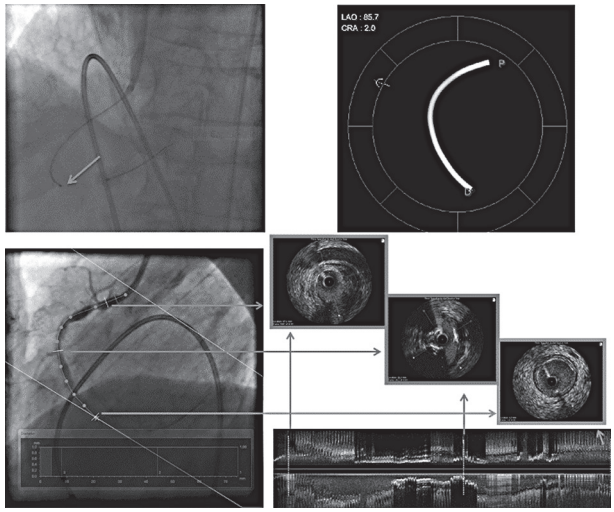
A multicenter evaluation of a new method for co-registration of IVUS and 3D angiograms. — K Houissa[1], N.L. Cruden[2], N. Uren[2], J. Escaned[3], C. Macaya[3], T. Slots[4], S. Carlier[1,5] *([1]UMons, Belgium, [2]Royal Infirmary of Edinburgh, Edinburgh, UK, [3]Hospital Clinico Universitario San Carlos, Madrid, Spain, [4]Pie Medical Imaging BV, Maastricht, The Netherlands, [5]Hôpital Ambroise Paré, Mons, Belgium).*

Background in order to optimally guide a percutaneous coronary intervention (PCI) with intravascular ultrasound (IVUS), the operator should be able to map each cross-sectional image of the pullback on the angiogram without misjudgment of location of side-branches or moderate lesions. If the angiogram remains the roadmap to perform any stent implantation, this foreshortened projected shadow of the lumen offers much less information than IVUS. Currently, available co-registration methods have several disadvantages: manual indication of common anatomical positions needed in both modalities, need for 2 angiographic projections filled with contrast, excessive X-ray exposure if real-time angiographic tracking of the position of the imaging transducer during pullback is necessary,... We present the *in-vitro* validation and the first multicenter *in-vivo* evaluation of a new co-registration of IVUS, or optical coherence tomography (OCT), using the 3D catheter path of the imaging wire.

Methods with the imaging catheter inserted in the coronary artery to be imaged, two angiograms at least 30 degrees apart are acquired, one with a contrast injection to serve as the roadmap image. Angiograms are sent via DICOM to the co-registration workstation (CAAS Workstation IV-LINQ) that streams in real-time the IVUS during the pullback. In both angiograms the 2D path of the catheter is marked, starting on the IVUS transducer in order to calculate the true 3D catheter path. Co-registration is then possible using a distance mapping algorithm knowing the true length on the angiogram and the position of the first IVUS frame.

Results *in vitro*, angiograms of a ball on which three pigtails with markers at known distance (30, 90 and 174 mm) were filmed in multiple projections. The mean ± sd difference between the reference length and the one measured of the 3D reconstructed path was –0,01 ± 0,4 mm using 37 paired projections. The intraobserver variability was 0,4%. *In vivo*, our ongoing feasibility study has already included 19 patients. Pullback issues (stalling), breathing during acquisition and displacement of the table between the 2 angiograms were the main factors identified limiting a reliable co-registration finally obtained in 18 of 19 attempts (95%). In these, side-branches on both imaging modalities were used as reference landmarks for comparison and were found < 1 mm apart, a precision that allows an acceptable co-registration accuracy for the selection of healthy proximal and distal landing zones to stent a lesion. Preliminary evaluation demonstrated also the feasibility of this approach for OCT in our lab.

Conclusions our new method for co-registration of IVUS or OCT and 3D catheter path from two angiograms appears a robust, feasible and accurate tool to guide percutaneous coronary interventions.



The IOCVA method: a solution for placement of transvenous leads across total chronic occlusions. (Δ) — Jimmy Jacobs, L. Riahi, B. Schwagten, R. Prisecaru, Y. De Greef, P. Van Den Heuvel, D. Stockman, P. Vermeersch, B. Scott *(Hartcentrum ZNA campus AZ Middelheim – Antwerp – Belgium).*

Background Placing a transvenous cardial lead is a challenge in the presence of bilateral venous obstruction of the upper extremities. Alternate access options, such as switching to the contralateral side or epicardial approach exist, but are associated with greater morbidity. Elayi et al recently described a promising new method of vascular access that allows endocardial implantation of a lead on the side of the venous occlusion.
The purpose of this study is to show the feasibilty of the inside-out central venous access (IOCVA) method to gain vascular access in patients with complex central venous occlusions.

Methods Six patients with central venous occlusions were referred for cardiac device implantation. Inside-out central venous access (IOCVA) was obtained via a percutaneous femoral approach. A catheter-dilator system was advanced via the right atrium to the most central point of venous occlusion. The occluded vein segment was punctured with a directionally guided needle (Brockenbrough), which was advanced along intravascular or extravascular tissue planes towards the subclavicular or lower neck region. A solid wire needle was oriented towards the skin surface and advanced through the soft tissue until exit from the body was obtained. The wire was then used to pull a

rigid dilator through the occluded segment and the skin. Standard transvenous leads were implanted through the newly created channel.

Results From June 2013 until June 2014, 6 patients underwent cardiac device implantation using the IOCVA method. The mean age was 71 years (3 males and 3 females). All of them had a total central venous occlusion. In 5 patients, it was an initial device implantation and the sixth patient had an upgrade to a CRT-D device. They all had successful preprectoral device implants (2 ICDs, 2 PMs, and 2 CRT-Ds). Fluoroscopy and procedural times were longer than average. One patient suffered pneumodiastinum, which was treated conservatively and healed without sequelae. Upon follow-up (mean 17 months), no device or lead dysfunctions occured. One patient died due to a non-cardiac cause, one month after implantation procedure.

Conclusion IOCVA is a feasible method to implant a transvenous lead for patients with ipsilateral central venous occlusions. Although procedural and fluoroscopy time was longer, compared to conventional implantation data, this method avoids switching to a de novo implantation on the contralateral side or obviates the need for a thoracotomy approach.

Role of clopidogrel pretreatment before PCI in stable coronary heart disease patients. — Sabrina Joachim[1], Charles Pirlet[1], Laurent Davin[1], Olivier Gach[1], Christophe Martinez[1], Victor Legrand[1] *([1]CHU de Liège, Liège, Belgium).*

Background Before diagnostic coronary angiography for stable coronary heart disease, European Society of Cardiology guidelines recommend dual anti-platelet therapy comprising of aspirin (500 mg) and clopidogrel (300 to 600 mg) 6 to 24 hours prior to procedure.

Although older studies with clopidogrel pre-treatement showed a reduced risk of ischaemic events, this strategy has never shown a decrease in all-cause mortality in the setting of a randomized controlled trial.

Moreover, pre-treatment with clopidogrel increases the risk of procedure relatedbleeding and we now know that major bleeding is independently associated with an increase in mortality and adverse cardiac events more than one year after the procedure.

Therefore, it seems important to raise the following question with regards to the risk/benefit ratio and the timing of clopidogrel in stable coronary heart disease: could clopidogrel be given after coronary angiography, after decision to proceed to PCI has been made in order to avoid unnecessary loading in patients that will require medical treatment or surgical revascularization?

Methods Our study included 202 patients that underwent PCI for stable coronary heart disease during a nine-month period in 2015 in a single tertiary hospital (CHU de Liège). Patients were assigned to receive either 600 mg of clopidogrel plus 500 mg of aspirin the day before PCI if they were admitted on odd-numbered days or 500 mg with no clopidogrel pre-loading the day before PCI if they were admitted on even-numbered days. The latter group received 600 mg of clopidogrel two hours after the procedure. Thereafter, clopidogrel (75 mg o.d.) and aspirin (80 mg o.d.) were given for one month after bare metal stent implantation and for 6 to 12 months after drug eluting stent implantation.

Analysis of the results was two-fold:

- a prospective study to determine the benefit, if any, offered by pre-treatment with clopidogrel before diagnostic coronary angiography for stable coronary heart disease;
- a retrospective, post-hoc study to determine the risk of procedure-related bleeding and procedure-related ischemic events.

Results Our study does not show a reduction in periprocedural ischaemic events in patients pre-treated with clopidogrel undergoing PCI for stable coronary heart disease. It does not reveal an increase in major or minor bleeding.

Moreover, our retrospective study did not allow us to determine the clinical or biological risk factors related with bleeding. Nevertheless, previous trials have shown that female gender, kidney disease, obesity, femoral access and pretreatment with more than 300 mg of clopidogrel were significantly associated with hemorrhagic events.

Conclusion This study does not confirm the role of clopidogrel pretreatment before PCI in stable coronary heart disease patients.

The major limitation of our trial is related to the small cohort of patients in light of the low incidence of bleeding or ischaemic events.

The role of preventive dual-antiplatelet therapy with aspirin and clopidogrel prior to diagnostic coronary angiography in patients with stable coronary heart disease should be evaluated in a prospective trial with a larger cohort given the low incidence of events.

Validation of the hybrid techniques for the percutaneous treatment of coronary Chronic Total Occlusions: the RECHARGE registry. (#) — Joren Maeremans[1], Alexandre Avran[2], Paul Knaapen[3], Simon Walsh[4], Colm Hanratty[4], Benjamin Faurie[5], Pierfrancesco Agostoni[6], James Spratt[7], Erwan Bressollette[8], Peter Kayaert[9], Dave Smith[10], Alexander Chase[10], William Smith[11], Alun Harcombe[11], Julian Strange[12], John Irving[13], Alan Bagnall[14], Mohaned Egred[14], Margaret McEntegart[15], Paul Kelly[16], Nicolas Lhoest[17], Jo Dens[1,18] *([1]Faculty of Medicine and Life Sciences – Universiteit Hasselt, Hasselt, Belgium, [2]Clinique de Marignane, Marseille, France, [3]VU university medical center, Amsterdam, the Netherlands, [4]Belfast City Hospital, Belfast, United Kingdom, [5]Groupe Hospitalier Mutualiste, Grenoble, France, [6]Universitair Medisch Centrum Utrecht,*

Utrecht, the Netherlands, [7]Royal Infirmary of Edinburgh, Edinburgh, United Kingdom, [8]Nouvelles Cliniques Nantaises, Nantes, France, [9]Universitair Ziekenhuis Brussels, Brussels, Belgium, [10]Morriston Hospital, Swansea, United Kingdom, [11]Nottingham University Hospital, Nottingham, United Kingdom, [12]University Hospital of Bristol, Bristol, United Kingdom, [13]Ninewells Hospital Dundee, Dundee, United Kingdom, [14]Freeman Hospital Newcastle, Newcastle, United Kingdom, [15]Golden Jubilee Hospital, Glasgow, United Kingdom, [16]Basildon University Hospital, Basildon, United Kingdom, [17]Clinique de l'Orangerie, Strasbourg, France, [18]Ziekenhuis Oost-Limburg, Genk, Belgium).

Background The hybrid algorithm has been developed with the primary aim of improving procedural outcomes of contemporary coronary CTO-PCI. The prospective, multicenter 'REgistry of Crossboss and Hybrid procedures in FrAnce, the NetheRlands, BelGium and UnitEd Kingdom ('RECHARGE) aims to validate the efficacy of this algorithm by collecting data on 1200 hybrid procedures.

Methods Patients treated with PCI for a coronary CTO, according to the hybrid algorithm, were prospectively and consecutively enrolled in 18 centers. The primary endpoint is procedural success. Data were collected on demographics, angiographics and procedural characteristics. CTOs were classified according to the J-CTO difficulty score. Procedural characteristics included data on the applied (hybrid) techniques and corresponding outcomes. The hybrid algorithm consists of four techniques: antegrade wire escalation (AWE), antegrade dissection & re-entry (ADR), retrograde wire escalation (RWE) and retrograde dissection & re-entry (RDR). Multiple techniques could be applied per procedure.

Results From Jan 2014 to Sep 2015, 1057 CTOs were included. Overall procedural success corresponded to 86%. The average J-CTO score equaled to 2.2 ± 1.3. Easy, intermediate, difficult and very difficult CTOs could be treated successfully in 100% (99/99), 96% (203/211), 88% (287/328) and 77% (323/419) respectively. Each of the hybrid techniques (AWE, ADR, RWE, RDR) was used 849 (80%), 252 (24%), 182 (17%) and 242 (23%) times during the 1057 procedures at any time respectively. Success was reached in 62% (530/849), 64% (162/252), 26% (47/182) and 71% (173/242). As a primary strategy, each technique was successful in 63% (508/802), 65% (52/80), 26% (20/76) and 71% (70/99), resulting in a total success of 61% (650/1057). If necessary, the application of a second, third and/or fourth bail-out strategy resulted in an additional success of 56% (261/468), with ADR and RDR most preferred and successful (63% (109/172) and 72% (103/143) respectively).

Conclusion(s) This data from a prospective multicenter registry show that the hybrid approach to CTO-PCI leads to high success rates, especially when different strategies are combined. Future analyses will provide detailed information on the specific failure modes of each technique

Quality control of interventional cardiology: objective assessment by the NCDR Cath PCI risk score system: a single center experience (1997-2014).

— Erwin Schroeder, B. Bihin, Cl. Tatar, P. Chenu, O. Gurné, A. Guédès, V. Dangoisse, L. Gabriel, J.L. Paquay, Ph. Colles, E. Morandini, JY. Triquet, C. Hanet

To fullfill the legal obligation of quality control in the setting of the B2 (PCI) program, we recorded prospectively all in-hospital complications after PCI.
Observed intrahospital mortality was compared to the predicted rate based on the well validated NCDR Cath PCI risk score of the ACC.

Methods A consecutive series during the period 01.01.1997-31.12.2014 of 10.799 hospital stays where at least one PCI was performed in our center. The only exclusion criteria was referral back to referring hospital the day of PCI (N: 2.431).
The patient/clinical characteristics were: mean age = 65 y, history of cerebrovascular disease: 11%, history of peripheral vascular disease: 13%, COPD: 10%, previous CABG: 12%, acute coronary syndromes: 57%, recent (< 24 hours) myocardial infarction: 11%, cardiogenic shock: 1.9%.
Procedural data: multivessel therapy: 13.7%, full angiographic success: 91.9%, failure: 4.1% and incomplete success: 4.1%.

Results The following post-procedural events occurred: myocardial infarction: 4.3%, stent thrombosis: 0.8%, puncture-related bleeding (TIMI major): 0.4%, non puncture-relative bleeding (TIMI major): 0.8%, dialysis: 0.67%, cerebrovascular event (Ranking _ 1): 0.24%, emergent CABG: 0.33%, death: 1.85%. The expected mortality (NCDR Cath PCI) was 2.63%. The performance of the model to predict mortality for the entire group was excellent (AUC: 0.88). The temporal evolution evidenced an

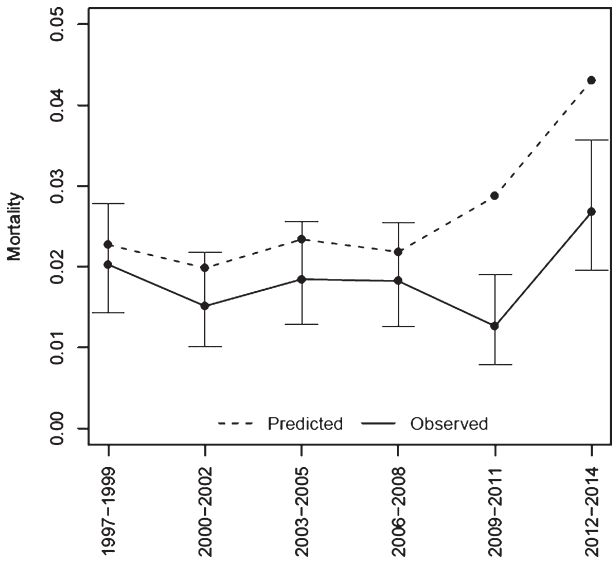


Fig. Temporal evolution of predicted vs obeserved IH mortality.

increase of the observed mortality from 2.0% to 2.5%*, and of the expected mortality from 2.1% to 4.2%*. The proportion of PCI in the setting of STEMI increased from 5% to 20%*. *(* $P < 0.01$)*

Conclusions In this single center registry, we observed a lower mortality than the predicted by the NCDR Cath PCI risk score. Increase over time of mortality after PCI may be explained by an increase of procedures at higher risk, such as STEMI. Our data should be evaluated at a national level by using the QUERMID data base linked to the National Institute of vital statistics.

Impact of digital stent enhancement technique on decision making during percutaneous coronary revascularisation. — Claudiu Ungureanu[1], A de Meester[1], Ph. Jl Vandenbossche[2] *([1]Jolimont Hospital, La Louviére, [2]CHU Saint Pierre Brussels).*

Background The digital enhancement of stent image is a technique based on a software capable of improving fluoroscopy visualisation of metallic prosthesis. This technique could improve the assessment of correct stent deployment and theoretically help the PCI operator to chose a strategy leading to an optimal result with a diminution of thrombosis or restenosis events. The purpose of the study was to assess the usefulness and impact of digital enhancement stent image in routine practice.

Methods StentBoost (StB) is a software that averages selected frames and creates an enhanced image of the stent by improving signal-to-noise ratio. A total of 139 consecutive patients were prospectively included. An analysis of StB image was performed after every stent implantation by the first PCI operator. A second analysis was performed off line by another PCI operator, not involved in the procedure and without knowing if the patient had or not an optimalisation of the result by ballon angioplasty. All the peri-procedural technical decisions were taken after visualisation of the StB interpretation and the conventional fluoroscopy image. The primary endpoint was the correlation between the result of StB and his impact in the periprocedural technical decisions of the first operator. The secondary endpoint criteria was the correlation between the result of StB and the offline interpretation made by the second cardiologist.

Results A total of 146 stents were analysed. The mean age was 64,8 ± 11, with 82,1% male patients. The first operator agreement with StB analysis was 93,41% in case of optimal stent deployment but the periprocedural decision to perform or not a final ballon angioplasty was not significantly influenced by StB system even in case of under expansion or stent deformation by StB analysis. The second cardiologist agreement with StB analysis was 82,42% in case of optimal stent deployment. The decision to perform a final ballon angioplasty based only on the fluoroscopy image was encountered in 43,64% cases, a very similar result with the first operator decision.

Conclusion The stent boost enhancement technique didn't have a significant impact regarding the decisions in coronary PCI procedures in the routine practice. Currently the utilisation of the StB is based on subjective criteria without any strong recommandations and without any clear criteria defining the deformation or under deployment of the metallic prosthesis.

Long-term outcome after percutaneous left atrial appendage occlusion with PLAATO LAA Occlusion system® and AMPLATZER™ Cardiac Plug. — Bert Vandeloo, Dirk Stockman, Benjamin Scott, Stefan Verheye, Paul Vermeersch *(Antwerp Cardiovascular Center, ZNA Middelheim, Antwerp, Belgium).*

Background Left atrial appendage (LAA) occlusion has emerged several years ago as an alternative to oral anticoagulants (OAC) for the prevention of ischemic stroke in patients with non-valvular atrial fibrillation (AF) and has been implemented into the treatment guidelines. Closure of the LAA, the site of 90% of thrombi in these patients, has shown to be effective in reducing thromboembolic events and reducing major bleeding. However some doubts were raised on the long-term outcome. This study aimed to evaluate long-term results of this technique.

Methods In this single center, retrospective study, we examined all patients who underwent LAA closure more than 5 years ago (September 2004 – August 2010).

Results Nineteen patients were included in this study. Median age at closure was 76 years (61-86 y). Eight (42%) patients underwent closure with the PLAATO LAA Occlusion system®, the other 11 (58%) with the AMPLATZER™ Cardiac Plug. Procedural success was obtained in 18 (94.7%) patients, with 1 (5.3%) procedural-related adverse event (air embolism). Due to procedural failure or incomplete follow-up data, 3 patients were excluded from further analysis. Median CHA_2DS_2-VASc score was 5 (IQR 4-7) and median HAS-BLED score was 3 (IQR 3-5). During a total follow-up period of 100 patient years, 2 strokes and 2 transient ischemic attacks were observed, resulting in a total systemic thromboembolism annual rate of 4.0%, compared to an expected annual rate of 10.4%. The major bleeding annual rate was 2.0%, compared to an expected annual rate of 6.6%. No intracranial hemorrhages occurred.

Conclusions Percutaneous closure of the LAA in patients with high thrombo-embolic and bleeding risk has a favourable outcome for the prevention of AF-related thrombo-embolism and major bleeding over an average period of follow-up of 6.3 years.

Gene expression patterns identifying the inflammatory response in patients with acute coronary syndrome: a prospective cohort study. (#) — Maarten Vanhaverbeke[1], Denise Veltman[1], Sander Trenson[1], Thibault Petit[1], Heinrich J Huber[1], Tom Adriaenssens[2], Johan Bennett[2], Christophe Dubois[2], Walter Desmet[2], Stefan Janssens[1,2], Peter Sinnaeve[1,2] *([1]K.U. Leuven, Department of Cardiovascular Sciences, Leuven, Belgium, [2]U.Z. Leuven, Department of Cardiovascular Diseases, Leuven, Belgium).*

Background The inflammatory response in acute coronary syndromes (ACS) is correlated with infarct size and residual cardiovascular risk. High-sensitivity CRP (hsCRP) identifies patients at risk after an ACS, but the underlying pathways leading to this persisting inflammatory burden are not well understood. We investigated the different gene expression patterns in ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) over time and evaluated whether it correlates to hsCRP or infarct size.

Methods A total of 80 patients with STEMI, NSTEMI or stable disease were prospectively enrolled and blood samples were collected on admission, after 3 days, 30 days and 1 year. This pilot analysis reports the results of the first 34 ACS patients on admission and at 30-day follow-up. Total RNA was extracted from whole blood at both time points and micro-array analysis was performed (Affymetrix Human Transcriptome 2.0). The results were validated with Polymerase Chain Reaction (PCR) and correlated to clinical characteristics and biomarkers.

Results On admission, 125 inflammatory transcripts were differentially expressed when compared to 30 days after the event. From the top-ranking genes, 4 significantly upregulated genes on admission were validated by PCR: CLEC4E (fold change 2.2, $P<0.001$), FKBP5 (fold change 2.3, $P<0.001$), IL18RAP (fold change 1.6, $P=0.002$) and the inflammasome-related NLRC4 (fold change 1.8, $P<0.001$). At 30-days follow-up, there was no difference in hsCRP between STEMI and NSTEMI patients (1.27 mg/dl vs. 1.98 mg/dl, $P=0.50$). However, the expression of FKBP5, a marker of oxidative stress, was significantly higher in STEMI than in NSTEMI patients on admission (3.36 fold, $P<0.001$), and remained higher at 30-days follow-up (1.29 fold, $P<0.05$). We observed a significant correlation between peak hsTnT and expression of FKBP5, both on admission and at follow-up ($P=0.004$ and $P=0.011$), reflective of infarct size. However, no linear correlation could be shown between the expression of the genes and peak CRP or hsCRP on admission and at follow-up.

Conclusion Peripheral blood gene expression profiles reflect acute inflammatory responses in ACS. FKBP5 expression, a marker of oxidative stress, distinguishes STEMI from NSTEMI in the acute phase as well as at follow-up, reflective of initial infarct size but irrespective of residual 30-day hsCRP levels. Whether these expression profiles correlate with outcome needs further investigation.

NON-INVASIVE

Physiopathological determinants of secondary mitral regurgitation in patients with aortic stenosis and preserved ejection fraction. — Jean-Marc Bantu-Bimbi*, Liliane Jahjah, Dominique Schulze, Tin Tran, Jean-Luc Vandenbossche, Thierry Pepersack, Philippe Unger *(Cardiology Department, CHU Saint-Pierre and *Erasme Hospital, Université libre de Bruxelles, Brussels, Belgium).*

Background Secondary mitral regurgitation (SMR) is a common finding in patients with aortic stenosis (AS), and can be observed even if left ventricular ejection fraction (LVEF) is preserved. Its determinants are poorly defined. We aimed to assess the mechanisms responsible for SMR

Methods Patients presenting a maximal aortic velocity ≥ 2.5 m/s and a LVEF ≥ 50% were prospectively included and underwent an echocardiographic examination including a longitudinal strain analysis (Vivid 7, GE Healthcare). Primary mitral regurgitation, ≥ moderate aortic regurgitation, previous aortic or mitral valve surgery, left ventricular outflow tract obstruction, and unfeasible proximal isovelocity surface area method for MR quantification were considered as exclusion criteria.

Results Sixty patients were included; among them, 36 (60%) presented SMR, with a mean mitral effective regurgitant orifice (ERO) of 9 ± 5 mm² (range 3-23 mm²). Two patients had an ERO >20 mm². As compared to patients without MR, larger left atrial volume, larger mitral E/A and E/e' ratio, lower mitral annular S wave and larger mitral annulus diameter were observed in patients with SMR (Table 1). By contrast, LVEF, maximal aortic velocity and valve area, and global and segmental longitudinal strain were similar in the 2 groups. By univariable analysis, significant associations between ERO and mitral annular diameter, E/e' ratio and left atrial volume, and between regurgitant volume

Table 1

Parameter	SMR +	SMR -	p
Number of patients	36	24	
Left atrial volume (ml/m²)	45±15	37±18	0.03
LVEF (%)	62±8	62±7	0.87
LV end-diastolic volume (ml)	85±26	80±29	0.50
Global longitudinal strain (%)	-15.4±3.7	-15.5±7.5	0.98
Maximal aortic velocity (cm/s)	3.74±0,72	3.73±0,79	0.85
Aortic valve area (cm²)	0.93±0,37	0.96±0,27	0.42
E/A	0.93±0,44	0,80±0,50	0.03
E/e'	17.8±6,5	12.8±5,6	0.005
Mitral annular diameter (cm)	3.28±0.25	3.12±0.33	0.04

and mitral annular diameter, left ventricular mass, E/A, E/e' ratio, mitral annular septal S wave and left atrial volume were observed. By multivariable analysis, only E/e' ratio was associated with ERO ($P=0.003$), and mitral annular diameter with regurgitant volume ($P=0.046$).

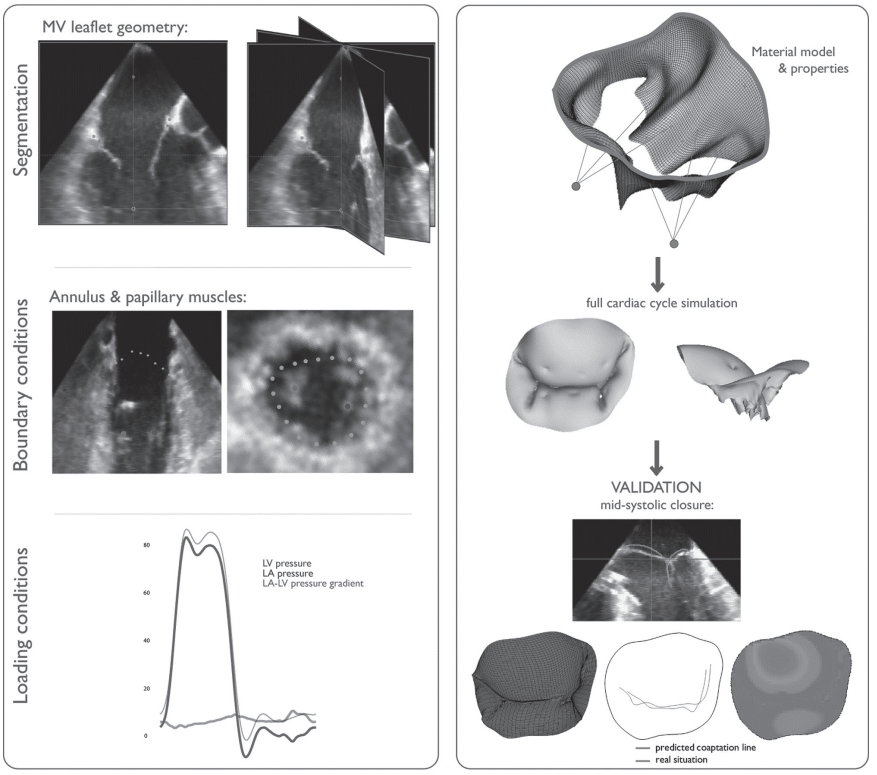
Conclusions In our series, SMR was only seldom severe. The observed associations between the magnitude of SMR and E/e' ratio and with mitral annular diameter likely reflect the haemodynamic load of SMR. However, these findings are also consistent with a scenario where left atrial dilatation resulting from increased left ventricular filling pressures dilates mitral annulus, thereby increasing SMR which further dilates left atrium. This vicious circle, where SMR begets SMR, should be further validated using longitudinal studies.

Patient-specific numerical modelling of the mitral valve apparatus using 3-dimensional echocardiography. (#)

— Philippe B. Bertrand, Tim Dezutter, Nic Debusschere, Henri De Veene, Mathias Vrolix, Piet Claus, Pascal Verdonck, Pieter M. Vandervoort, Matthieu Debeule *(Ziekenhuis Oost-Limburg, Genk; Department of Biomechanical Engineering, Ghent University, Ghent; Doctoral School for Medicine and Life Sciences, Hasselt University, Hasselt; Medical Imaging Research Center, KULeuven, Leuven)*.

Background A correct interplay of mitral valve (MV) leaflets, annulus, papillary muscles and chordae is essential for normal MV function; any imbalance might cause valvular regurgitation. A patient-specific, quantitative model of the complex 3-dimensional MV geometry and dynamics might improve pathophysiologic insight and enhance therapeutic efficacy by predicting the effect of interventions. This study aimed to develop a patient-specific numerical model of the mitral valve apparatus based on 3-dimensional transoesophageal echocardiography (3D-TEE) and to validate this model in predicting MV dynamics in different hemodynamic loading conditions.

Methods The geometry of the MV apparatus was extracted from full volume 3D-TEE by manual segmentation of one end-diastolic frame and transferred into a finite element mesh (Figure, left panel). Patient-specific boundary conditions (annular and papillary muscle position and dynamics) were manually extracted from the 3D-TEE images for the entire cardiac cycle. Leaflets were modelled as transversely isotropic hyper-elastic material with characteristics from *in vitro* mechanical testing; chordae were modelled as hyper-elastic connections between papillary muscles and leaflets. The end-diastolic finite element mesh, material properties, and boundary conditions were combined to numerically calculate MV dynamics when applying a certain hemodynamic load. For validation, datasets from 5 normal MVs were prospectively collected during elective percutaneous closure procedures of a patent foramen ovale during which left atrial and ventricular pressures were invasively measured and 3D-TEE was simultaneously acquired.



Results The model realistically predicted opening and closure of the MV leaflets in all datasets (Figure, right panel). Comparison of the predicted mid-systolic closure versus real-time 3D-TEE imaging showed good accuracy with an average prediction error (root mean square) ranging from 1.4 mm to 2.9 mm. Furthermore, the position of the coaptation line was predicted with an average error ranging from 0.6 mm to 2.0 mm. Point-to-point error between predicted and real-time leaflet position was the highest in the intertrigonal area due to bulging in the simulated leaflets (Figure, right panel).

Conclusion 3D-TEE based patient-specific numerical MV modelling allows a realistic prediction of valvular dynamics in physiological loading conditions. The strategy developed in this study with *in vivo* validation holds great promise to improve insight in MV pathophysiology and enhance therapeutic efficacy by enabling pre-intervention planning and simulation.

Technology use and interest for technology enabled cardiac rehabilitation among cardiac patients. — Roselien Buys, Deirdre Walsh, Nils Cornelis, Kieran Moran, Werner Budts, Catherine Woods, Véronique Cornelissen *(KU Leuven, Dublin City University).*

Background Cardiac rehabilitation (CR), a secondary prevention programme consisting of exercise training and lifestyle education, has been shown to slow or reverse the progression of cardiovascular disease (CVD). While supervised ambulatory CR improves outcome, uptake of community-based CR, the long-term rehabilitation phase, is low. E-cardiology and E-health evolve rapidly and have particular potential in CVD prevention and management. Furthermore, technology solutions for physical activity uptake and monitoring are becoming available and seem interesting for use in CR. In this view, evidence is needed regarding current technology usage of CVD patients, and their needs and interests for technology enabled CR.

Methods A technology usage questionnaire with 30 questions (8 about baseline characteristics, 9 about technology use and 13 about interests, needs and wants from technology-based, virtual CR) was administered. Patients were recruited from a supervised ambulatory CR program and an adult congenital heart disease consultation, and from 2 community based CR programs. Analysis of survey responses was largely descriptive. Spearman rank correlation coefficients were used to relate scores with age ($P < 0.05$).

Results Of 310 responders, 298 patients (77% male; mean age 61,7 ± 14,5 years; median 65, range 17-83) completed at least 25 questions of the survey and were included in the analysis (completion rate of 96%).

Most patients had a mobile phone (97% of which 58% had a smartphone) and used the internet (91%). The majority of patients (78%) never used a computer based physical activity game. Heart rate monitors were used by 35% of the respondents, but 68% of them reported that they found heart rate monitoring important during home exercises. The use of physical activity monitoring in daily life was reported by 12% of the respondents.

Respondents were interested in receiving CR support via internet (77%) and mobile phone (68%). Moreover, 67% of the patients reported interest in a game-based CR training program. The idea of a virtual rehabilitation class was positively received by 58% of the respondents. At least a medium interest in technology enabled CR was reported by 75% of the patients. Interest decreased with increasing age (r=-0.16; $P=0.005$).

Advice on exercise ideas, exercise prompts, information on local exercise opportunities, healthy meal ideas and practical ideas to manage stress received the highest ratings for inclusion in a technology enabled CR platform.

Conclusion This study documents the interest for technology enabled home-based CR and could guide the design of a technology-based, virtual CR intervention.

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.

Electrocardiographic characteristics of the paced QRS complex according to different positions of the left ventricular lead in CRT patients. — Jan De Pooter, MD[1], F. Van Heuverswyn, MD[1], A. Baeyens[1], M. El Haddad, PhD[1], L. Timmers, MD[1], R. Stroobandt, MD, PhD[1], L. Jordaens, MD, PhD[1] *([1]Ghent University Hospital, Heart Center, Ghent, Belgium).*

Background The position of the left ventricular (LV) lead in cardiac resynchronization therapy (CRT) influences clinical outcome of CRT patients. Published data on electrocardiographic characterisation of QRS complexes during LV and biventricular (BV) pacing at different sites remain scarce. Existing methods are often inconvenient and different strategies report conflicting results. The goal of this study was to assess whether biplane QRS axis and QRS duration of paced QRS complexes differs among varying positions of the LV lead.

Methods Retrospective analysis of 90 paced ECGs (45 LV pacing and 45 BV pacing) of 45 CRT patients was performed. All patients had an apical position of the right ventricular lead. QRS axis in the frontal and horizontal plane of the standard twelve lead ECG and global QRS duration ($QRSD_{global}$) were assessed using custom made software. LV lead positions were assessed on fluoroscopy, using a right anterior oblique (RAO) 30° and left anterior oblique (LAO) 45°, according to American Heart Association standardized 17 segments model.

Results The RAO view distinguished between an apical position (n = 21) versus non apical position (n = 24) of the LV lead. The LAO view distinguished between anterior (n = 4), anterolateral (n = 10), lateral (n = 12), inferolateral (n = 16) and inferior (n = 3) positions.

The horizontal QRS axis during LV pacing was significantly different between the apical (median + 175°) versus non apical group (+121°, $P = 0.009$, Fig. 1), whereas no significant differences were observed using the frontal axis. The frontal axis during LV pacing was significantly different among the LAO defined groups: anterior (+131°), anterolateral (+164°), lateral (−163°), inferolateral (−143°) and inferior (−66°, $P = 0{,}001$, Fig. 2). No differences between the LAO defined groups were observed using the horizontal plane. With BV pacing, neither the frontal nor the horizontal axis could differentiate between the RAO and LAO defined groups.

$QRSD_{global}$ during LV and BV pacing could not discriminate between the RAO or LAO defined groups. Although with BV pacing a trend to broader QRS durations with an apical position was noted compared to a non apical position (Table 1).

Conclusion Determination of biplane QRS axis may be a simple strategy to differentiate LV paced ECGs of different LV lead positions, provided that RAO and LAO positions are assessed separately. $QRSD_{global}$ with LV pacing or BV pacing was not dependent on the position of the LV lead.

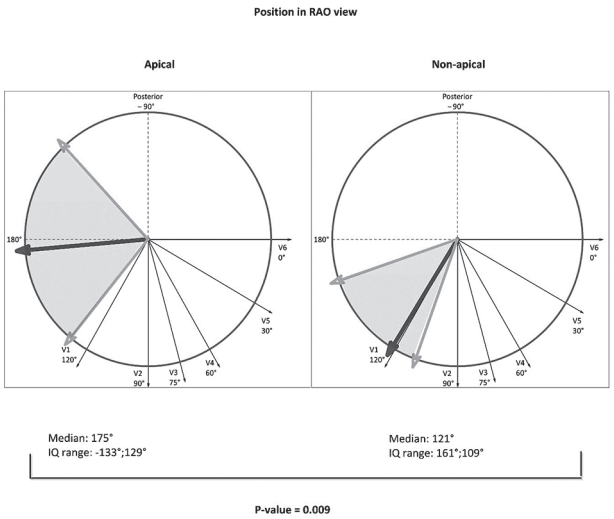


Fig. 1 Horizontal axis during LV pacing for RAO defined positions
RAO: right anterior oblique view. IQ: Interquartile range with percentile 25 and 75.

Table 1 $QRSD_{global}$ with LV pacing and BV pacing

QRSD during LV pacing				QRSD during BV pacing			
	$QRSD_{global}$				$QRSD_{global}$		
RAO view	Apical (n=21)	206 [174:275]	p value NS	RAO view	Apical (n=21)	153 [136:165]	p value NS
	Non Apical (n=24)	201 [187:269]			Non Apical (n=24)	137 [121:148]	
LAO view	ANT (n=4)	243 [187:267]	p value NS	LAO view	ANT (n=4)	129 [88:151]	p value NS
	AL (n=10)	195 [152:269]			AL (n=10)	127 [117:151]	
	LAT (n=12)	211 [191:275]			LAT (n=12)	147 [136:178]	
	IL (n=16)	201 [191:243]			IL (n=16)	143 [132:151]	
	INF (n=3)	162 [135:238]			INF (n=3)	166 [103:190]	

$QRSD_{global}$: global QRS duration RAO: right anterior oblique view. LAO: left anterior oblique view.

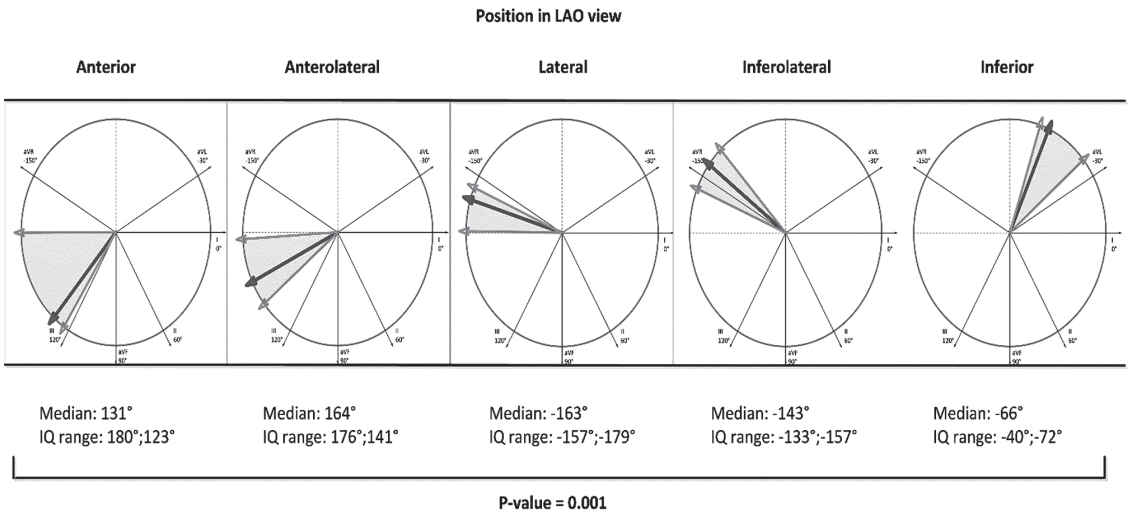


Fig. 2 Frontal axis during LV pacing for LAO defined positions.
LAO: left anterior oblique view IQ: Interquartile range with percentile 25 and 75.

Efficacy of training programs on weight loss in obese patients at high risk for cardiovascular disease. — Maxim Dendale[2], Ines Frederix[1,2], Inge Gielen1, Rita Guilliams[1], Paul Dendale[1,2] *([1]Heart Centre Hasselt, Jessa Hospital, Hasselt, Belgium, [2]Faculty of Medicine & Life Sciences Hasselt University, Hasselt, Belgium).*

Background In 2014, more than 1,9 billion adults were overweight of which more than 600 million were obese; this represents more than 13% of the world's population who are at risk of cardiovascular diseases. Patients try different approaches to lose weight but little is known about the most effective program for specific groups of patients. The objective of this study is to provide a better understanding of the influence of different programs on weight loss.

Methods This is a retrospective study in which 322 obese patients participated. Patients were included into a group or individual program according to their own choice. The patients trained 3 times one hour a week for 3 months. In the individual program, they had a meeting with a dietician every 2-4 weeks. In the group program, they participated in 16 sessions led by psychologists or dieticians for 6 months. At the start of the program the VO_2max and the BMI were measured. At the end of the program their weight was measured to calculate their percentage weight loss. Also the length of the training program (in months) and the age of the patients were used in the multiple linear regression analysis.

Results Mean percentage weight loss was 6,4 ± 5,9%, and mean duration of the program followed was 3,9 ± 2,1 month, which corresponded to 1,7 kg per month. Multiple regression analysis showed that following parameters had a significant effect on percentage weight loss: VO_2max at the start of the program (0,002 ± 0,001 ml/min), $P < .001$, CI [0.001;0,003] and length of the training program (1,188 ± 0.152), $P < .001$, CI [0.890;1,487]. In contrast, BMI at the start of the program had no significant effect on the percentage weight loss, ($P = 0.94$). Also the age of the patient had no significant effect ($P = 0.32$). When using a logistic regression on the 2 different training programs against weight loss there was no significant difference between the individual and group program ($P = 0.71$).

Conclusions This study showed that patients with a better physical condition are more likely to lose a significant amount of weight. Also as one would expect, the duration of the training and whether the patient succeeds in completing the program influences the success rate. This study shows the potential of personally adjusting obesity programs to patients with different medical backgrounds and different physical condition.

Electrically assisted cycling: a novel mode for meeting physical activity guidelines in coronary artery disease patients? — Ines Frederix[1,2], Dominique Hansen[1,2], An Soors[1], Valerie Deluyker[1], Paul Dendale[1,2] *([1]Faculty of medicine & life sciences, Hasselt university, Agoralaan gebouw D, 3590 Diepenbeek, Belgium, [2]Department of cardiology/Heart centre Hasselt, Jessa hospital, Stadsomvaart 11, 3500 Hasselt, Belgium).*

Background Exercise training is proven effective in secondary prevention programs for coronary artery disease patients. Unfortunately, long-term benefits are often poor due to lack of adherence to exercise prescription. Therefore, novel strategies such as electrical assisted bicycles (EAB) are pushed forward to increase exercise adherence rates, especially for the least-motivated and least-fit patients not being able to overcome challenges associated with classical cycling (such as strong contrary wind, hilly courses). The aim of this study was to assess the acute physiological load of EAB to test its potential as an alternative method to continue to perform exercise training.

Methods This study was a mono-center, prospective, randomized cross-over clinical trial in which 15 coronary artery disease patients (2 females, 13 males), aged 64 ± 7 years participated. They cycled a predefined route of 10 km at a self-selected comfortable speed. using 3 different supporting settings: classical bike (no support), EAB with low support (EAB_{low}) and EAB with high support (EAB_{high}). The exercise oxygen consumption (VO_2) was measured (averaged every 10 seconds) by analysis of expired gases using a mobile ergospirometer.. Cycling time was determined by chronometry, ratings of perceived exertion were assessed at 3 km and 7 km of cycling, and total cycling route caloric expenditure was calculated.

Results The level of electrical support had a significant main effect on mean VO_2 (ml/min) for the cycling sessions, $F(2, 28) = 4.632$, $P = 0.018$. Mean VO_2 for the EAB_{high} (1,729 ± 139 ml/min) was lower, compared to the EAB_{low} (1,890 ± 160 ml/min), $P = 0.038$. But, cycling sessions with both the classical bicycle, the EAB_{low} and the EAB_{high} were sufficiently high to contribute to the moderate-intensity standard (3-6 MET) of exercise training standards for secondary prevention in coronary artery disease patients. Ratings of perceived exertion were significantly lower for EAB_{high} (9 ± 0.6), when compared to EAB_{low} (11 ± 0.5), $P = 0.014$ and classical bicycle sessions (11 ± 0.6), $P = 0.007$. When cycling with $EAB_{high,}$ patients burned less kcal (249 ± 14 kcal) than when cycling with low support (301 ± 15 kcal), $P < 0.001$ or no support at all (312 ± 12 kcal), $P < 0.001$.

Conclusions These results show that EAB reduces ratings of perceived exertion, while maintaining a sufficiently high exercise intensity level according to the European Society of Cardiology's recommendations for secondary prevention programs of coronary artery disease patients. Cycling session duration with EAB needs to be

longer in order to burn the same amount of kcal, when compared to cycling sessions using a classical bicycle. EAB has the potential to take away barriers for the least-fit and discouraged patients, improving their adherence to exercise training.

Monocentric prospective study of patients dismissed from follow-up after closure of isolated congenital shunt lesions. — Charlien Gabriels[1], Alexander Van De Bruaene[1], Frederik Helsen[1], Philip Moons[2], Kristien Van Deyk[1], Els Troost[1], Werner Budts[1] *([1]Department of Congenital and Structural Cardiology, University of Leuven, University Hospitals Leuven, [2]Department of Public Health and Primary Care, University of Leuven, Leuven, Belgium).*

Background Dismissal from follow-up after closure of small isolated congenital shunt lesions in childhood or adolescence is common. The aim of the present study was to recall these patients to evaluate their health and hemodynamic status.

Methods Adult patients included in our local database with closure of isolated atrial septal defect (ASD) type secundum or ventricular septal defect (VSD) before the age of 18 years and latest clinical control ≥ 5 years ago, were invited for clinical check-up. Data on catheterization and defect closure were retrieved. Demographic and clinical data, electrocardiographic and echocardiographic measurements were prospectively acquired.

Results Twenty-one of 138 (15%) patients with ASD closure had died. Forty-six patients (63% female, mean age 30 ± 7 years) responded. Median defect size was 16 (IQR 11-20) mm. Median age at ASD repair was 6 (IQR 4-8) years. Forty (87%) ASDs were closed surgically (22 primary, 15 patch, 3 unspecified), 6 percutaneously (Amplatzer Occluder). Mean Qp/Qs ratio was 2.4 ± 0.5, pulmonary hypertension (PH) was present in 1 (2%).

All but one functioned in NYHA class I. Eight (17%) patients reported palpitations, no arrhythmia were documented. All patients were in sinus rhythm. Median SF-36 Norm-based Score for Physical Health was 56 (IQR 53-57), for Mental Health 55 (IQR 51-57). No patient had residual shunt. No patient developed PH. Right ventricular (RV) dilatation was present in 7 (15%). RV dysfunction was not uncommon (RV fractional area change < 35% in 7 (15%), TAPSE < 17 mm in 12 (26%)).

Twenty-one of 133 (16%) patients with VSD closure had died. Forty-seven patients (57% male, median age 34 (IQR 29-40) years) responded. Most (95%) VSDs were perimembranous. Median defect size was 9 (IQR 7-10) mm. Median age at VSD repair was 4 (IQR 1-5) years. All patients had surgical repair (15 primary, 29 patch, 3 unspecified). Mean Qp/Qs ratio was 2.6 ± 0.8, PH was present in 21 (45%).

Six (13%) patients functioned in NYHA class II, the others in class I. Seventeen (36%) patients reported palpitations, no arrhythmia were documented. All were in sinus rhythm. Median SF-36 Score was 56 (IQR 51-58) for Physical Health, 54 (IQR 48-57) for Mental Health. A residual shunt was present in 6 (13%). Four (9%) patients presented PH. RV dilatation was present in 6 (13%). RV dysfunction was surprisingly frequent (RV fractional area change < 35% in 7 (15%), TAPSE < 17 mm in 17 (36%)). Seven (15%) patients had a dilated ascending aorta.

Conclusions Patients with closure of isolated ASD type secundum in childhood do well and do not seem to warrant systematic follow-up. Although, as in the VSD group, some presented RV dilatation and dysfunction. In contrast, more patients after VSD closure were symptomatic and presented problems as PH and ascending aortic dilatation, requiring systematic follow-up.

How long does the gender gap in coronary artery disease in women persist? Results from the Monica-Bellux registry. (Δ) — Bernhard Gerber, Michel Jeanjean, Sophie Kaddach, Jean-Louis Vanoverschelde *(Cliniques St. Luc UCL).*

Background Women present less coronary stenosis severity on coronary angiograms. This is believed to result from protective effects of estrogen, and has been shown to persist up to 10 years after menopause. Yet the prevalence of coronary artery disease in elderly women has been less studied and it remains is unknown if the gender difference in coronary artery disease severity persists in very elderly women.

Methods The Monica-Bellux registry records the rate of coronary artery disease related events of inhabitants (inh.) of the province Luxembourg. We analyzed the number and results of diagnostic coronary angiograms, and the incidence of significant single and multivessel coronary artery disease in the first coronary angiograms performed in inhabitants of the province Luxembourg between 2005 and 2011 according to gender and age groups (45-54, 55-64, 65-74 and 75-84 years).

Results In men, the proportion of patients presenting with significant coronary artery disease on first coronary angiogram remained relatively stable over time (increasing slightly from 56% in males aged 45-54 years to 62% in males >75 years). By opposition, in women, the prevalence of significant coronary artery disease detected on first coronary angiogram increased progressively with growing age (from 30% in women aged 45-54 years to 43% in women aged >75 years). Yet in every age group it remained always significantly less than in men, and the proportion of coronary angiograms not showing significant disease remained still high (57% in women >75 years vs 38% in men of the same age). The incidence of detection of new coronary artery

disease in women increased from 63/100000 inhabitants aged 45-54 years to 1263/100000 inhabitants aged 75-84 years. Yet, in each age group it remained always fourfold less than in men (ie 294/100000 inhabitants in male aged 45-54 and 4783/100000 inhabitants in men aged 75-84 years).

Conclusion Although coronary artery disease severity rises with increasing age in post-menopausal women, even in octogenarian women, severity of coronary artery disease on first coronary angiograms remains lower than in men and the proportion of normal coronary angiograms remains high. On a population basis, the incidence of new detected coronary disease remains fourfold lower in women than in men even at high age.

Long-term outcome after infective endocarditis: a report from the Ghent endocarditis registry. — Schaubroeck Hannah[1], Willems Anne-Marie[2], Vande Kerckhove Barbara[3], De Corte Thomas[1], De Backer Tine[1,3], De Sutter Johan[2,3] *([1]Department of cardiology, Ghent University Hospital, Belgium, [2]Department of cardiology, AZ Maria Middelares Hospital, Ghent, Belgium, [3]Department of internal medicine, Ghent University, Belgium).*

Background The epidemiology of infective endocarditis (IE) is changing due to ageing of the general population and the increase of invasive procedures and intracardiac devices. In this study we evaluated clinical presentation, management and long-term outcome after IE in a regional IE registry in Belgium.

Methods We collected all patients with definite IE admitted or referred to 2 centers performing cardiac surgery in Ghent, Belgium, between 2006 and 2012. Mean follow-up for all-cause mortality was 47 ± 22 months.

Results In total 174 patients (age 62 ± 15 years) were included. 69% of all patients presented with native valve IE, 24% with prosthetic valve IE and 12% with device or catheter related IE. Staphylococci were found in 40%. 29% of all patients had an invasive procedure less than 3 months before admission. Overall in-hospital mortality was 19%, varying from 11% in surgically treated patients, to 27% in patients undergoing device/catheter extraction, and 48% in patients treated conservatively. After discharge, 1-year survival was 92% and 5-year survival 69%. Independent predictors for all-cause mortality during follow-up were age, history of stroke, diabetes and reduced renal function. Patients undergoing device/catheter extraction and patients treated conservatively had a higher in-hospital and long-term mortality as compared to patients undergoing cardiac surgery.

Conclusion IE is still associated with high in-hospital mortality (19%). Long-term outcome is mainly related to age and comorbidities. Patients undergoing device/catheter extraction and patients treated conservatively had a higher in-hospital and long-term mortality as compared to patients undergoing cardiac surgery.

Keywords Infective endocarditis, epidemiology, long-term outcome, comorbidities

Cardiopulmonary exercise capacity in patients early after endoscopic atraumatric CABG (endo-ACAB) surgery: implications for rehabilitation and treatment. — Dominique Hansen[1,2], Ruben Roijakkers[1], Lore Jackmaert[1], Boris Robic[3], Marc Hendrikx[3], Allaadin Yilmaz[3], Ines Frederix[1,2], Michael Rosseel[4], Paul Dendale[1,2] *([1]REVAL – Rehabilitation Research Center, BIOMED- Biomedical Research Center, Faculty of Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium, [2]Jessa Hospital, Heart Centre Hasselt, Hasselt, Belgium,[3]Jessa Hospital, Department of Cardiothoracic Surgery, Hasselt, Belgium, [4]Algemeen Stedelijk Ziekenhuis, Department of Cardiology, Aalst, Belgium).*

Background Cardiopulmonary exercise tolerance early after endoscopic atraumatric coronary artery bypass (endo-ACAB) surgery has not been studied. This may lead to suboptimal exercise prescription and/or treatment. The aim of this study was to examine exercise tolerance and cardiopulmonary function during exercise in patients early (within one month) after endo-ACAB surgery.

Methods Twenty endo-ACAB surgery patients, 20 coronary artery bypass graft (CABG) surgery patients, and 15 healthy subjects (matched for body mass index, age, gender, timing after surgery) executed a maximal cardiopulmonary exercise test, with assessment of cycling power output (W), oxygen uptake (VO2), carbon dioxide output (VCO2), respiratory gas exchange ratio (RER), end-tidal O2 (PETO2) and CO2 (PETCO2) pressure, equivalents for VO2 (VE/VO2) and VCO2 (VE/VCO2), heart rate (HR), oxygen pulse (VO2/HR), expiratory volume (VE), tidal volume (Vt), respiratory rate, at peak exercise and ventilatory threshold. In surgery patients forced expiratory volume and forced vital capacity was also measured. These parameters were compared between groups.

Results VO2, VCO2, VE, Vt, VE/VO2, VE/VCO2, PETO2, PETCO2 at peak exercise (matched RER at peak exercise between groups) and ventilatory threshold were significantly worse in surgery patients vs. healthy controls ($P < 0.05$, observed $\alpha > 0.80$). All these parameters, as well as lung function, were however comparable between CABG and endo-ACAB surgery patients ($P > 0.10$): they achieved 74 ± 17% and 72 ± 15% of their normal VO2peak, respectively.

Conclusion Exercise tolerance and cardiopulmonary function during exercise is significantly compromised early after endo-ACAB surgery and of comparable level as

opposed to CABG patients. These data signify the need for rehabilitation intervention and provide important insights in exercise prescription and treatment early after endo-ACAB surgery.

Keywords exercise tolerance, cardiac surgery, endo-ACAB, CABG

Left Atrial Function as Predictor of Recurrent Stroke or Paroxysmal Atrial Fibrillation in Patients with Cryptogenic Stroke. — Jens Jeurissen[1*], Bram Verdonck[1*], Jan Verweft[2], Thomas Neyens[3], Nina De Klippel[4], Ines Frederix[1,2], Paul Dendale[1,2] *([1]Faculty of Medicine, Hasselt University, Hasselt, Belgium, [2]Department of Cardiology, Jessa Hospital, Hasselt, Belgium, [3]Department of Statistics, Hasselt University, Hasselt, Belgium, [4]Department of Neurology, Jessa Hospital, Hasselt, Belgium, * equally contributing authors).*

Background Stroke is an important cause of disability and the third leading cause of death.

Approximately 30 to 40% of all strokes are estimated to be cryptogenic (i.e. no cause can be found). There have been few previous studies regarding risk stratification for stroke recurrence in patients with cryptogenic stroke. We want to evaluate the predictive value of left atrial function for the risk of stroke recurrence and/or atrial fibrillation by transthoracic echocardiography in patients with no proven atrial fibrillation and no indication for anticoagulants.

Methods We analyzed all patients who were admitted for cerebrovascular accident (CVA) or transient ischemic attack (TIA) between 2011 and 2014. We searched for patients who had a recurrent CVA/TIA and/or who were diagnosed with atrial fibrillation (AF) during the study duration. Patients with non-cryptogenic stroke were excluded from entry into the study.

From these patients echocardiographic, laboratory and clinical markers were measured.

The primary outcome of this study was the recurrence of a CVA/TIA. The secondary endpoint was the discovery of an episode of AF.

Univariate and multivariate analysis were performed using the Cox proportional hazards model with backward elimination model selection.

Results 1529 patients were admitted for CVA or TIA between 2011 and 2014. 544 patients (36%) with cryptogenic stroke were included in the study. 54 of the 544 (10%) patients were re-admitted to the hospital for recurrent CVA/TIA. AF was discovered in 21 of the 544 patients (4%). 6 of the 544 patients (1%) developed a recurrent CVA/TIA as well as AF. 475 of the 544 patients (87%) did not develop recurrent CVA/TIA nor AF during the study duration.

The mean time until recurrence of CVA/TIA was 263,28 days (standard deviation [SD] of 286,08). The mean time until discovery of AF was 352,81 days (SD of 321,80). The mean study follow-up duration was 576,17 days (SD of 408,19 days).

Hypertension (β=-1,93; P=0,09), peak systolic longitudinal left atrial strain (LA-Ss; β<0,001; P=0,99), interatrial conduction delay (β=-0,09; P=0,004), glomerular filtration rate (GFR; P=0,03), the interaction between hypertension and LA-Ss (β=-0,12; P=0,02), and the interaction between GFR and interatrial conduction delay (β=0,06; P=0,003) were significant predictors for recurrence of stroke in multivariate analysis at α=0,05.

Mitral valve deceleration time (MV DecT; β=0,009; P=0,002) was the only significant predictor for occurrence of AF in multivariate analysis at α=0,05.

Conclusion Echocardiographic (interatrial conduction delay) and laboratory (GFR) parameters predict an increased risk for stroke recurrence in patients with cryptogenic stroke.

MV DecT can be used to assess increased risk for atrial fibrillation in patients with prior stroke.

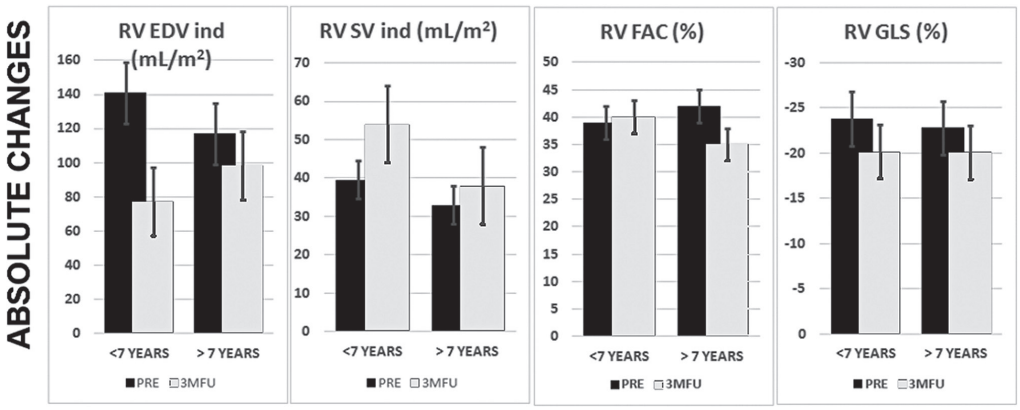
Right Ventricular Structural and Functional Remodelling after Transcatheter Pulmonary Valve Implantation: Time matters! (#) — Efstathios Pagourelias, A.M. Daraban, R. Mada, J. Duchenne, J. Bogaert, M. Gewillig, J.U. Voigt *(Department of Cardiovascular Diseases, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium, Department of Radiology, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium, Department of Pediatric Cardiology, University Hospital Gasthuisberg, Catholic University of Leuven, Leuven, Belgium).*

Background Surgical correction of Fallot's Tetralogy (ToF) leads to pulmonary valve insufficiency (PI), which is further associated with late adverse events. Percutaneous pulmonary valve implantation (PPVI) for ToF patients with severe PI has been shown to be beneficial, however, the optimal age for the procedure still remains subject of debate. Therefore, aim of this study was to determine the potential impact of PPVI time point on global and segmental right and left ventricular (RV &LV) structure and function as well as on myocardial function recovery.

Methods Twenty patients [age 13.9±9.2 years, (range 4.3-44.9), male 70%] with severe PI (≥3 grade) secondary to previous correction of ToF, underwent Melody valve (Medtronic, Minneapolis, MN, US) implantation, with a pre-stent placement in the majority of them (85%). Full echocardiographic assessment (including both traditional and speckle tracking analysis) and cardiovascular magnetic resonance (CMR) evaluation [for 14 (70%)] of the enrolled patients were performed in 2 time points: (1) afternoon before the procedure; (2) at 3 months follow-up after PPVI.

Results PPVI was accompanied by remodelling of RV characterized by significant decrease of RV transverse diameters and volumes evidenced both by echo and CMR [indexed RV end diastolic volume (RV EDV ind) from 123.1 ± 24.1 to 101.5 ± 18.3, $P = 0.005$]. Despite RV output increase [RV effective stroke volume indexed (RV SV ind) (mL/m2) from 38.4 ± 9.5 to 51.4 ± 10.7, $P = 0.005$] we observed a significant decrease of all indices considered to reflect RV systolic function [-13.3 ± 21.5% relative reduction in fractional area change (FAC), a −12.8 ± 10.9% in RV global longitudinal strain (GLS)]. Among potential predictors of greatest RV remodelling after PPVI, time after last surgical correction causing PI was the only significant regressor [$R^2 = 0.60$, beta = 0.387, 95%CI(0.07 to 0.7), $P = 0.019$]. Volume depletion and functional gaining were more prominent among patients treated with PPVI earlier than 7 years after last correction (Figure).

Conclusions Following a cohort of patients with corrected ToF who underwent PPVI due to severe secondary PI, we have shown that: i) biventricular remodelling with output increase might be evident even 3 months after the valve implantation and ii) earlier intervention (<7 years after last RVOT operation) is associated with better short-term outcomes. Our data indicate, that earlier interventions using stented valves may be beneficial, which may have direct impact on current guidelines for the clinical management of ToF patients.



The long-term effects of aerobic interval versus continuous training in patients with coronary artery disease: one-year follow-up data from the SAINTEX-CAD study. — Nele Pattyn (presenting author), L. Vanhees, V. Cornelissen, E. Coeckelberghs, C. De Maeyer, G. Frederix, K. Goetschalckx, N. Possemiers, K. Wuyts, E. Van Craenenbroeck, P. Beckers *(Departments of Cardiovascular Rehabilitation, UZ Leuven and UZ Antwerpen).*

Background Aerobic interval training (AIT) and continuous training (ACT) both improve physical fitness (peak VO_2) in coronary artery disease (CAD) patients. However, little is known on the long-term effects of AIT and ACT on peak VO_2 and exercise adherence.

Methods In this multicentre study, 200 CAD patients (90% men, mean age 58.4 ± 9.1 years) were randomized to either AIT or ACT. A total of 163 patients were assessed after 12 weeks of AIT or ACT and 12 months after their enrolment. Physical fitness (peak VO_2, maximal graded cardiopulmonary exercise test on bicycle ergometer) and physical activity measures (SenseWear Pro3™ Armband; worn for 5 days) served as primary outcomes, and peripheral endothelial function, cardiovascular risk factors and quality of life as secondary outcomes.

Results After the 12 week intervention, during which 26 patients dropped out, 11 additional patients were lost to follow-up. Drop-outs (n = 37) were significantly more women (completers 6.7% women; drop-outs 24.3% women; $P = 0.001$) and had a significantly lower peak VO_2 compared to completers (n = 163) (completers 23.2 ± 5.5 ml/kg/min; 20.7 ± 5.9 ml.kg/min; $P = 0.017$). Physical fitness (VO_2, heart rate and workload at peak, at first and second threshold) and physical activity (steps, active energy expenditure (kcal) and physical activity duration (min)) were preserved nine months after completing the interventions. A significant correlation was found between peak VO_2 and active energy expenditure at 12 weeks (spearman $\rho = 0.40$; $P < 0.001$), only a trend appeared for changes (spearman $\rho = 0.18$; $P = 0.06$). Forty percent of patients increased peak VO_2 and follow-up values were significantly above the predicted peak VO_2. Fifty-eight percent of patients increased active energy expenditure at the follow-up measurements. In the AIT and ACT group respectively, 95.9% and 91.9% of all patients met the recommended levels of 150min/week of moderate physical activity (*p*-group NS). In addition, peripheral endothelial function, cardiovascular risk factors and quality of life remained stable from 12 weeks to 12 months after the start of the intervention

(*P*-time NS). Both AIT and ACT were equally effective (*P*-interaction NS).
CONCLUSION This multicentre study shows that the short-term improvements of centre-based AIT or ACT on peak VO_2, physical activity levels, peripheral endothelial function, cardiovascular risk factors and quality of life are sustained after one year follow-up. Physical fitness levels were higher than the predicted values and the majority of all patients (>90%) met the recommended physical activity levels of 150min/week.

Is the number of attended cardiac rehabilitation sessions influential on prevention of recurrent ischemic cardiac disease? — B. Schuermans[1], W. Tack[1], T. Neyens[1], N. Hens[1], J. Berger[2], I. Frederix[1,2], P. Dendale[1,2] *([1]Hasselt University, Hasselt, Belgium, [2]Jessa Hospital, Hasselt, Belgium).*

Background In Belgium, cardiovascular disease is the most common cause of death and thus a great concern for healthcare providers. Previous studies have concluded that participating in a cardiac rehabilitation (CR) program for ischemic heart disease significantly reduced morbidity as well as mortality.
This study aims to investigate the influence of the number of attended CR training sessions on reducing morbidity and recurrence following an ischemic event. The primary goal is to study the effect of the number of phase II CR training sessions a patient completed on the time to first event. The secondary goal is to identify subpopulations of ischemic heart disease patients with comorbidities like diabetes or hypertension that might derive significantly more benefit by participating in CR than patients without comorbidities.
Methods Data was acquired from patient files from a regional hospital. The study included all ischemic heart disease patients who took part in a CR program in 2006, and were seen for yearly examinations after the completion of the program. The follow-up period was 9 years. Survival analysis was applied to the data, using Kaplan-Meier graphs and Cox proportional hazard models, in order to study the influence of session participation and other parameters such as comorbidities and environmental factors on time to event. An event was defined as rehospitalisation due to occurence of ischemic disease or cardiac death.
Results 281 patients (216 male, 65 female; aged 64±10 years) participated in a CR program in 2006, after an ischemic event. The mean (± SD) number of attended CR sessions was 22 (± 9). The number of sessions had a significant effect ($P=0.0004$) on the time to event. The average (95% confidence interval (CI)) time to first event was 2627.91 (2338.10-2917.73) days for patients participating >30 sessions and 2011.74 (1595.78-2427.71) days for patients participating in <10 sessions; the former were 50% less likely to endure a recurrent event. CR was not found to be significantly more beneficial in certain subpopulations as other parameters did not have a significant effect on time to event.
Conclusion Cardiac rehabilitation is significantly more effective when a patient participates in more training sessions. Therefore it is important that patients complete the full CR program and participate in all training sessions to best reduce the chance of recurrence. To achieve this goal patients must be motivated and facilities must be put into place to ensure participation is as easy as possible. The studied comorbidities were not of significant influence meaning CR should be recommended to all subpopulations of patients.

Reverse remodeling after early surgery for severe aortic or mitral regurgitation: Do patients come back to normal? — Stéphanie Seldrum *(CHU Mont-Godinne et UCL St-Luc Bruxelles).*

Background Surgery for correction of severe aortic regurgitation (AR) or mitral regurgitation (MR) tends to be performed earlier nowadays, with techniques often allowing valve repair. It's not known how this management influences reverse remodeling and if patients may recover fully normal left ventricular (LV) dimensions and function post-operatively.
The aim of this study was to evaluate reverse remodeling in patients undergoing surgical correction for severe mitral or aortic regurgitation quite early in disease, and compare them with normal volunteers.
Methods We included patients operated on for pure isolated chronic mitral or aortic regurgitation, with conserved LV ejection fraction (LVEF >45%). They underwent cardiac magnetic resonance (CMR) imaging pre-operatively and 6 to 12 months post-operatively for comprehensive assessment of LV volumes and function.
Healthy volunteers of similar ages were recruited in order to assess normal values in a similar population and with similar tools.
Results 89 patients were included: 29 with AR and 60 with MR, mean follow-up was 222±57 days. Unsurprisingly, at baseline AR patients were younger than MR patients (46±13 versus 56±12 years old, $P=0.0001$), and they had larger LV mass and volumes (LV mass indexed ($LVmass_{ind}$) 94±19 versus 66±15 g/m², $P<0.0001$; LV end-diastolic volume indexed (LVEDVi) 148±33 versus 125±27 ml/m², $P=0.0005$; LV end-systolic volume indexed (LVESVi) 69±19 versus 49±13 ml/m², $P<0.0001$), but lower LVEF (54±6 versus 61±6%, $P<0.0001$).

Post-operatively, significant regression of $LVmass_{ind}$, LVEDVi and LVESVi was observed in both groups ($P < 0.0001$ for all). LVEF significantly decreased in MR patients (61 ± 6 versus 53 ± 7%, $P < 0.0001$) while it remained unchanged in AR patients (54 ± 6 versus 55 ± 6%, $P = 0.20$). However, compared to age-matched healthy volunteers, $LVmass_{ind}$ and LVESVi remained increased in both groups (respectively 70 ± 11 versus 52 ± 9 g/m², $P < 0.0001$ and 43 ± 11 versus 36 ± 7 ml/m², $P = 0.02$ in AR versus volunteers; 55 ± 10 versus 45 ± 11 g/m², $P = 0.0004$ and 39 ± 12 versus 34 ± 6 ml/m² for MR versus volunteers), while LVEDVi normalized. Compared to volunteers, LVEF normalized in AR patients, unlike in MR patients with values significantly higher pre-operatively and significantly lower post-operatively (from 61 ± 6 to 53 ± 7%, versus 57 ± 4% in volunteers; $P < 0.01$ for both).

For AR as for MR patients, pre-operative LV mass and volumes, as well as regurgitation size were good predictors of reverse remodeling.

Conclusion Early intervention in severe aortic and mitral regurgitation allows significant reverse remodeling of the LV, nevertheless it does not completely reach normal values compared to age-matched healthy volunteers.

Aortic stenosis in the setting of a non referral hospital: does speckle tracking global longitudinal strain add predicitive information regarding symptoms and severity?

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Background In several heart diseases, it has been demonstrated that global longitudinal strain (GLS) allows to detect subclinical changes in left ventricular function before the left ventricular ejection fraction (LV EF) decreases. In the medical literature, it has been advocated that GLS < –15 is a useful cut off value for the predication of symptoms and worse outcome in patients with aortic stenosis (AS).

Methods In the setting of a non referral hospital, we searched for a correlation between GLS and presence of symptoms and severity of the AS in patients with AS and preserved LV EF. Speckle tracking GLS was measured on a Vivid 7 GE Ultrasound echocardiograph. To be included in the analysis, the patients had to have peak velocity of at least 2.8 m/s and LV EF had to be preserved. Exclusion criteria were concomitant aortic valve regurgitation or presence of at least moderate mitral valve disease.

According to the ESG guidelines, the AS was classified as mild, moderate or severe. Patient characteristics and presence of symptoms were obtained from the medical records.

Results 101 patients were included. The patient characteristics were as follows: mean age 75 years (range 42-100), M/F ratio: 65/36. The AS was classified as mild, moderate and severe in respectively 5, 53 and 43 cases. In 3 cases of state of symptoms was not well documented. Of the remaining 98 patients, 59 patients were asymptomatic and 39 had symptoms.

Table 1 lists the distribution of presence of symptoms among the groups with normal or abnormal strain, using the cut off value of GLS -15. There was no significant correlation found. (Chi square stastitic is 1.1957. $P = 0.274$)

Table 2 summarizes the correlations between speckle tracking GLS and echocardiographic parameters of AS and age. A significant correlation was found between GLS and AS VTI ratio and LV EF. There was a trend towards significance between GLS and mean gradient. However, using the cut off value of GLS -15, we were unable to demonstrate a correlation between GLS and the classification of severity (severe or mild/moderate) of AS. Chi square static is 0.496, $P = 0.481$.

Conclusion Our study shows a correlation between speckle tracking GLS and AS VTI ratio and LV EF in patients with AS and preserved LV EF. There was also a trend toward significance between GLS and mean gradient. However, the cut off value of GLS < -15 was not helpful in predicting symptoms and severity of AS.

Table 1

Speckle tracking GLS	Asymptomatic	Symptomatic	Total
GLS < –15	36 (63.2%)	21 (36.8%)	57
GLS > –15	23 (56.1%)	18 (43.9%)	41

Table 2

Speckle tracking GLS	AV max	Mean gradient	Peak gradient	AVA	AS VTI ratio	LV EF	Age
Pearson correlation	0.161	0.193	0.171	–0.185	–0.229	–0.228	–0.133
Significance (2 tailed)	0.107	0.054	0.087	0.068	0.022	0.023	0.186

AV max: peak velocity over the aortic valve, AVA: aortic valve area, AS VTI ratio: aortic stenosis velocity time integral ratio.

Rest and exercise hemodynamics in relation to symptomatic status after MitraClip therapy for functional mitral regurgitation. (Δ) — Van De Heyning Caroline[1], Bertrand Philippe[2], Debonnaire Philippe[3], De Maeyer Catherine[1], Vandervoort Pieter[2], Coussement Patrick[3], Paelinck Bernard[1], De Bock Dina[1], Vrints Christiaan[1], Claeys Marc[1] *([1]Universitair Ziekenhuis Antwerpen, Edegem, [2]Ziekenhuis Oost-Limburg, Genk, [3]AZ Sint-Jan, Brugge).*

Background Percutaneous mitral valve repair using MitraClip offers symptomatic benefit in patients with severe mitral regurgitation (MR) that are at high or prohibitive surgical risk. Data are lacking regarding the effect of MitraClip therapy on cardiac output (CO) and systolic pulmonary artery pressure (SPAP) during exercise and its relation to symptomatic status.

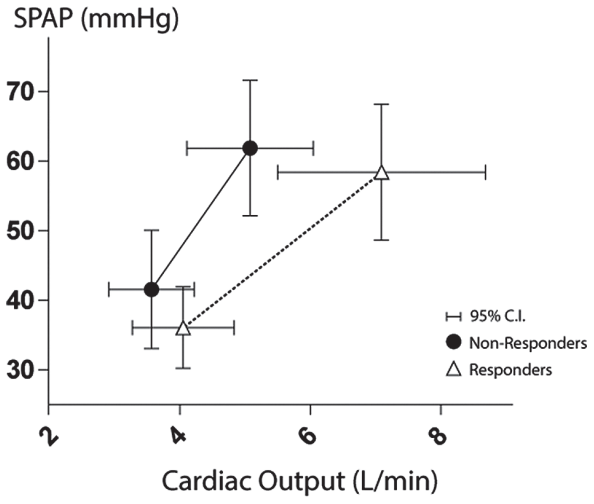
Methods Patients from 3 Belgian centers with symptomatic severe functional MR were prospectively evaluated by comprehensive transthoracic echocardiography at rest and during a symptom-limited exercise test on a semi-supine bicycle pre and 6 months post MitraClip procedure.

Results A total of 26 patients (71 ± 11 years, 62% male) was evaluated.

At rest 6 months post versus pre MitraClip, reduced MR grade (1.8 ± 0.8 vs 3.0 ± 0.6, $P = 0.003$), increased CO (3.9 ± 1.3 vs 3.3 ± 1.0 L/min, $P = 0.042$) and a trend towards lower SPAP (39 ± 10 vs 43 ± 11 mmHg, $P = 0.10$) was found. Symptomatic benefit, defined as New York Heart Association class improvement ≥ 1 grade occurred in 17/26 patients (65%, responders), while 9/26 did not improve (35%, non-responders). SPAP at rest was more reduced in responders versus non-responders (-9.5 ± 10.1 vs + 2.4 ± 10.4 mmHg, $P = 0.016$) for a similar CO at rest (4.0 ± 1.5 vs 3.6 ± 0.9 L/min, $P = 0.4$).

During exercise 6 months post versus pre MitraClip, higher workload (69 ± 26 vs 58 ± 24 Watt, $P = 0.036$), a trend towards higher peak CO (6.4 ± 2.9 vs 5.4 ± 1.7 L/min, $P = 0.065$) and a similar peak SPAP (60 ± 16 vs 63 ± 13 mmHg, $P = 0.3$) at these higher flow rates were noted. Responders versus non-responders had more favourable exercise hemodynamics shown by a similar peak SPAP (58 ± 17 vs 62 ± 13 mmHg, $P = 0.6$) at a higher peak CO (7.1 ± 3.1 vs. 5.1 ± 1.3 L/min, $P = 0.028$), implying a less steep SPAP/CO slope during exercise.

Conclusions Symptomatic benefit 6 months after MitraClip therapy for functional MR relates to improved hemodynamics both at rest and during exercise.



QTc risk classification predicting 30 day all-cause mortality highly depends on correction formulae. — Bert Vandenberk[1,2], Vandael E.[3], Garweg C.[1,2], Vandenberghe J.[4], Foulon V.[3], Ector J.[1,2], Willems R.[1,2] *([1]University of Leuven, Department of Cardiovascular Sciences, [2]University Hospitals Leuven, Cardiology, [3]University of Leuven, Department of Pharmacology, [4]University of Leuven, Department of Neurosciences).*

Background QT prolongation carries risk for cardiac arrhythmia and mortality. The impact of different QT correction on risk assessment is unknown.

Methods All ECGs in patients > 18y with sinus rhythm and normal QRS duration (≤ 120 ms) and rate < 90 bpm in the University Hospitals of Leuven during a 2 month period were included (first ECG per patient). Age, gender, heart rate and QT were collected. QT correction was performed with Bazett (QTcB), Fridericia (QTcFri), Framingham (QTcFra), Hodges (QTcH) and Rautaharju (QTcR). All-cause mortality rates after 30 days were collected.

From this cohort an age- and sex-matched population of 212 patients, ranging 18 to 70y of age, without any cardiac history or cardiac/QT prolonging medication was selected as controls and 99% upper limit of normal (ULN) reference values were determined using most recent CLSI criteria (Clinical and Laboratory Standards Institute).

Correction formula were compared using QTc/RR linear regression slopes ($QTc = B \times RR + cst$) with a B-value closest to zero indicating the least remaining influence by the RR-interval. Multivariate Cox Regression analysis including age, heart rate and prolonged QTc was performed reporting hazard ratios (HR) with the 95% confidence interval (CI) for 30 day all-cause mortality.

Results A total of 6609 ECGs were included: age 59.8 ± 16.2 y; 53.6% male and heart rate 68.8 ± 10.6 bpm. The 30 day all-cause mortality incidence was 0.9% (61 patients). The findings are shown in the table.

Rate adjustment was near optimal using QTcFri or QTcFra, QTcB performed worst. The 99% ULN showed expected gender differences and QTcB having ULN far above current clinical reference values. HR, sensitivity (Sens) and specificity (Spec) for prediction of 30 day all-cause mortality appeared superior using QTcFri or QTcFra.

	B	99% ULN male	99% ULN female	Prolonged QTc	Sens	Spec	HR (95% CI)
QTcB	−0.071	472 ms	481 ms	3.2%	19.7%	97.0%	4.5 (2.3-8.7)
QTcFri	0.004	450 ms	468 ms	5.2%	27.9%	95.0%	6.0 (3.3-10.6)
QTcFra	−0.005	450 ms	467 ms	4.6%	27.9%	95.6%	7.3 (4.1-13.0)
QTcH	0.024	447 ms	465 ms	5.7%	26.2%	94.5%	6.2 (3.4-11.2)
QTcR	−0.033	465 ms	469 ms	3.5%	23.0%	96.7%	6.3 (3.4-11.6)

Conclusions In normal heart rate ranges QTcB has the worst rate adjustment compared to QTcFri or QTcFra, which performed nearly optimal. We propose to base in-hospital QTc-monitoring on QTcFri or QTcFra.

Point-of-Care Heart-type Fatty Acid Binding Protein versus High-Sensitivity Troponin T Testing in Emergency Patients at High Risk for Acute Coronary Syndrome.

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Background High-sensitivity cardiac troponin testing is used to detect myocardial damage in patients with acute chest pain. Heart-type fatty acid binding protein (H-FABP) may be an alternative, available as point-of-care test.

Methods Patients (n = 203) referred by general practitioners for suspected acute coronary syndrome (ACS) or presenting with typical chest pain and one major cardiovascular risk factor at the emergency department were prospectively included in a single-centre cohort study. High-sensitivity cardiac troponin T (hs-TnT) and point-of-care H-FABP testing were concomitantly performed at admission and after 6h.

Results Maximal hs-TnT levels above the 99th percentile were observed in 152 patients (75%) with 127 (63%) fulfilling criteria for myocardial infarction. Upon admission, hs-TnT and H-FABP were associated with an AUC (95%CI) of 0.83 (0.77-0.89) and 0.79 (0.73-0.85), respectively, to predict myocardial infarction, which increased to 0.93 (0.90-0.97) and 0.88 (0.84-0.93), respectively, after 6h. The diagnostic accuracy for non-ST-segment elevation myocardial infarction was somewhat lower with AUCs (95%CI) of 0.80 (0.72-0.87), 0.90 (0.84-0.96), 0.73 (0.64-0.81), and 0.77 (0.67-0.86), respectively. When assessment was performed within 3h of chest pain onset, diagnostic accuracy of H-FABP versus hs-TnT was similar (Figure). Each standard deviation increase in admission H-FABP was associated with a 68% relative risk increase of all-cause mortality (*P*-value = 0.027) during 666 ± 155 days of follow-up.

Conclusions Point-of-care H-FABP testing has lower diagnostic accuracy compared to hs-TnT assessment in patients with high pre-test ACS probability, but might be of interest when assessment is possible early after chest pain onset.