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III Baltic Heart Failure Meeting

5–6 October 2012, Tallinn, Estonia

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III Baltic Heart Failure Meeting

October 5–6, 2012

Conference Venue

The conference will be held in Swissôtel Tallinn Conference Centre (6th floor).

Address

Tornimäe Street 3
Tallinn 10145
Estonia

Official language

The official language of the conference is English. There is no simultaneous translation provided.

Registration

The registration desk is open on the spot (6th floor):
Friday, October 5, 14:00–20:00
Saturday, October 6, 08:00–18:00

Certificate

The conference provides an EBAC certificate. You can collect your certificate on Saturday, October 6, 12:30, at the registration desk. The EBAC evaluation form which you will find in your conference folder should be completed and returned first.

Exhibition

The exhibition is open on Saturday, October 6, 10:00–17:00.

Lunch and coffee breaks

Buffet lunch and all coffee breaks are served in the conference foyer.

Welcome reception

October 5, 17:30–19:00 in the conference foyer.

Conference dinner and concert

October 6, 19:00–22:00 in the House of the Blackheads (Pikk Street 26, Tallinn)

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Conference Programme

October 5, 2012
14:00–16:00 Registration
13:00–17:00 Nurses' session (in Estonian).
16:00–17:30 Satellite Symposium **„Mechanical circulatory support devices in acute and advanced heart failure"**, sponsored by Thoratec Europe Ltd. Chairmen: Prof. R. Teesalu (Estonia) & Prof. R. Benetis (Lithuania)
16:00–16:05 Introduction
16:05–16:25 Optimal medical therapy for the advanced HF patient. Assoc. Prof. A. Kavoliuniene (Lithuania)
16:25–16:45 Patient selection and outcomes – simple selection criteria. Prof. J. Lahpor (Netherlands)
16:45–17:05 The role of the multidisciplinary team in building a successful heart failure/VAD. Dr. F. Gustafsson (Denmark)
17:05–17:20 **Case history 1**, A. Kavoliuniene **Case history 2**, J. Lahpor **Case history 3**, F. Gustafsson
17:20–17:30 Questions and conclusions
17:30–19:00 Get-together Cocktail

October 6, 2012
09:00–09:10 Opening Ceremony. Prof. P. Vardas, President of the European Society of Cardiology
Session: ACUTE AND ADVANCED HEART FAILURE
Chairmen: Prof. M. S. Nieminen (Finland), Assoc. Prof. A. Kavoliuniene (Lithuania)
09:10–09:30 Targeting heart rate in heart failure therapy. Assoc. Prof. A. Rudys (Lithuania)
09:30–09:50 Extracorporeal membrane oxygenation as salvage therapy for the treatment of refractory heart failure. Dr. M. Balciunas, Dr. G. Tomkute (Lithuania)
09:50–10:10 Volume control in advanced heart failure. Dr. A. Maca (Latvia)
10:10–10:40 Coffee break
INVITED SPEAKERS
10:40–11:20 Chronic heart failure and comorbidities: challenges and solutions. Prof. A. J. Stewart Coats (United Kingdom)
11:20–11:50 Emerging therapies for acute heart failure. Prof. M. S. Nieminen (Finland)
11:50–12:20 Lessons from the UK – outcomes for acute heart failure. Prof. T. McDonagh (United Kingdom)
12:30–13:30 Lunch

Session: CARDIAC RESYNCRONIZATION THERAPY: CRITERIA FOR PATIENTS, CAVEATS, EPIDEMIOLOGY
Chairmen: Prof. G. Marinskis (Lithuania), Prof. E. P. Vardas (Greece), Dr. H. Uuetoa (Estonia)
13:30–13:50 Cardiac resynchronization therapy: problems and complications. Prof. G. Marinskis, Dr. V. Maneikiene (Lithuania)
13:50–14:20 Echocardiography in patient selection for CRT therapy – a useful tool or waste of time and money? Dr. P. Muda (Estonia)
14:20–14:40 How to select the right patient for the right device? Assoc. Prof. O. Kalejs (Latvia)

Session: WHEN ARE THE SURGEON AND THE INTERVENTIONALIST NEEDED IN HEART FAILURE?

Chairmen: Prof. A. Erglis (Latvia), Prof. R. Benetis (Lithuania)

14:40–15:00 The role of modern interventional cardiology and regenerative medicine in treatment of heart failure. Prof. A. Erglis (Latvia)

15:00–15:20 Hybrid procedures using PliCath device for ischaemic cardiomyopathy: CONFIGURE-HF study. Dr. K. Rucinskas, Dr. I. Norkiene, Dr. V. Maneikiene, Dr. G. Zuoziene, Dr. G. Balciūnaite, Dr. V. Janusauskas, Dr. G. Davidavičius, Dr. R. Samalavičius, Dr. G. Kalinauskas (all Lithuania), Dr. Andrew S. Wechsler (USA)

15:20–15:40 New frontiers in the interventional management of heart failure. A case of catheter-based renal sympathetic denervation. Dr. H. Uuetoa (Estonia)

15:40–16:10 The role of the interventionalist and the cardiac surgeon in the treatment of heart failure. Prof. R. Benetis (Lithuania)

16:10–16:40 Coffee break

Session: MONITORING IN HEART FAILURE: TELEMONITORING, BNP-GUIDED THERAPY, HEART FAILURE CLINICS

Chairmen: Dr. T. Uuetoa (Estonia), Dr. P. Põder (Estonia)

16:40–17:00 Complex management of heart failure patients. Dr. T. Uuetoa (Estonia)

17:00–17:20 The multi-marker approach to heart failure with preserved ejection fraction. Dr. G. Kamzola (Latvia)

17:20–17:40 BNP-guided therapy for heart failure. Dr. J. Celutkiene (Lithuania)

17:40–18:00 Cardiac resynchronization therapy from remote monitoring and remote follow-ups to remote patient care. Dr. S. Pakarinen (Finland)

18:00–18:10 Closing remarks

19:00–22:00 Concert and Dinner in Tallinn Old Town, in the House of the Blackheads

Session: ACUTE AND ADVANCED HEART FAILURE

Targeting heart rate in heart failure therapy

Alfredas Rudys[1] – [1]Department of Cardiovascular Medicine, Clinic of Cardiac and Vascular Diseases, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania

Elevated heart rate (HR) has been known for a long time to be associated with heart failure (HF). The relationship between HR and systolic HF has been revealed in several animal and clinical studies. HR over 70 bpm was associated with a 53% increase in hospital admissions and 34% increased risk of cardiovascular mortality in patients with reduced systolic function (BEAUTIFUL study). The effect of medications slowing HR such as beta-blockers and ivabradine on outcomes in patients with HF has been evaluated in clinical trials.

AIM. The aim of our report is to review data on optimal strategy of HR slowing therapy in patients with HF, bearing in mind therapy of beta-blockers and ivabradine.

METHODS. We summarised data of the largest studies evaluating HR in patients with systolic and diastolic dysfunction: 5 randomised clinical trials trials (CIBIS II, MERIT-HF, COMET, BEAUTIFUL, SHIFT) and 2 meta-analyses.

RESULTS. The data of these clinical trials clearly show that elevated HR is a marker of increased mortality and that it directly worsens cardiovascular outcomes, which can be improved by HR reducing medications.

The effect of beta-blockers on HR and eventually on outcomes was retrospectively analyzed in CIBIS II, MERIT-HF and COMET clinical trials. Investigators in these trials enrolled almost 10 000 patients with NYHA class II-IV HF. The HR reduction after two to four months of treatment in the three trials was nearly similar -10 to -20 bpm, and was associated with survival benefit. A meta-analysis (McAlister et al., 2009) of randomised placebo-controlled HF trials with over 19 000 patients revealed that the overall risk ratio for death was associated with the magnitude of HR reduction achieved within each trial. Likewise meta-analysis by Flannery et al. (2008) also showed that it is the magnitude of HR reduction that statistically is significantly associated with the survival benefit of beta-blockers. However, these studies could not distinguish the effects of HR reduction from those of other potentially important actions of beta-blockers. Maurer et al. (2009) indicate that HR reduction is responsible for about 60% of the improvement in left ventricular function, whereas 30% is due to increased contractility and a small amount is due to a reduction in systemic vascular resistance. Thackray et al. (2006) showed that reversal of beta-blockers induced bradycardia with pacing had deleterious effects on ventricular function: higher rate pacing led to higher mean left ventricular end-diastolic and systolic volumes and lower ejection fraction. More recently, the selective I(f) current inhibitor ivabradine, which specifically inhibits in the sinoatrial node to lower HR without affecting other aspects of cardiac function did reduce the combined primary endpoint of cardiovascular death and hospital admission for worsening HF in the recent SHIFT trial. In this trial it was definitely shown that in HF, HR should be reduced to 60 bpm and, if tolerated below this rate. There was relationship between HR, achieved by ivabradine after 28 days of treatment, and clinical outcomes. SHIFT trial also confirmed the continuous association between baseline HR and clinical outcomes in patients with HF: in the placebo group, patients with the highest basal HR $\geq$ 87 bpm had a more than two fold higher risk for the primary composite end point of cardiovascular death and hospitalisation for HF than patients with the lower basal HR ($P < 0.0001$). In addition, the treatment effect was neutralised after adjustment for change of HR, leading the authors to conclude that HR is not only a risk marker, but also a risk factor for patients with HF. The authors concluded that the HR lowering effect of beta-blockers plus ivabradine is more important in improving outcomes than the actual dose of beta-blocker. This information may be useful, since a substantial proportion of patients with HF do not tolerate the doses of beta-blockers used in the large clinical trials.

CONCLUSIONS. Both baseline HR and HR change significantly predicted mortality: lower HR and marked reduction of HR improve survival. If any dose of beta-blockers can result in an HR below 70 bpm, therapy with beta-blockers alone is appropriate. Adding ivabradine to beta-blockers in order to achieve HR reduction below 70 bpm is a better strategy than using only small doses of beta-blockers avoiding to increase the dose because of the fear of adverse events.

Session: ACUTE AND ADVANCED HEART FAILURE

Extracorporeal circulation as salvage therapy for the treatment of refractory heart failure

Mindaugas Balciunas[1], Gabija Tomkute[1] – [1]Centre of Anaesthesiology, Intensive Care and Pain Management, Clinic of Heart Disease, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania

BACKGROUND. Extracorporeal cardiopulmonary support (CPS) is a potentially life-saving technique used for patients with cardiopulmonary failure. We review our experience using CPS for patients with decompensated heart failure in Vilnius University Hospital Santariskiu Klinikos.

METHODS. We retrospectively analysed the data of 32 patients for whom extracorporeal circulation was initiated because of severely decompensated heart failure or postcardiotomy heart failure not responding to the otherwise optimal medical therapy at Heart Surgery Centre in Vilnius University Hospital Santariskiu Klinikos for 2010.

RESULTS. Of those who received extracorporeal CPS 29 patients underwent cardiac surgery. The extracorporeal CPS was initiated using central cannulation site (ascending aorta and right atrium) in 25 patients and for remainder (7 patients) groin vessels were used for peripheral cannulation. Two patients were connected to extracorporeal CPS before cardiac surgery because of severe left ventricle failure following acute MI. Further detailed analysis was performed on 29 operated patients of whom 17 were males (59%). The mean age was 59.9 ± 13.9 years. Fourteen patients (48%) were weaned from extracorporeal CPS and eight patients (27.6%) survived until discharge from ICU. Other perioperative data are given in the table.

Data	Value
Comorbidities	
Hypertension, n	17
Atrial fibrillation, n	19
Previous cardiac surgery, n	8
Stroke, n	4
Peripheral arteriopathy, n	0
PAH, (> 60 mmHg), n	7
COPD, n	3
Diabetus mellitus, n	3
Echocardiography	
Left ventricle EF, %	43.3 ± 13.3
Left ventricle DD, cm	5.2 ± 1.6
Risk Score	
EuroSCORE II, %	12.9 ± 15.3
Intraoperative data	
Duration of surgery, min	432 ± 183
CPB time, min	251 ± 116
AxC time, min	122 ± 59
Postoperative data	
Duration of CPS, days	9.5 ± 8.2
Duration of IABP, days	11.8 ± 7.5
Length of stay in ICU, days	18.1 ± 14.9
Vasoactive drug infusion	
Epinephrine, h	199 ± 152
Norepinephrine, h	282 ± 154
Milrinone, h	143 ± 118
Complications	
Surgical bleeding, n	14
Kidney failure, n	21
Septic complications, n	19
Stroke, n	4
Limb ischaemia, n	2

Data are given as mean and standard deviation unless otherwise stated.
AxC – aortic cross-clamp time, CPB – cardiopulmonary bypass, CPS – cardiopulmonary support, COPD – chronic obstructive pulmonary disease, DD – diastolic diameter, EF – ejection fraction, PAH – pulmonary artery hypertension.

CONCLUSION. Despite the high risk of complications associated with extracorporeal CPS, it is an additional possibility for patients with haemodynamic instability not responding to conventional therapies.

Session: ACUTE AND ADVANCED HEART FAILURE

Volume control in advanced heart failure

Aija Maca[1] – [1]Latvian Centre of Cardiology, P. Stradins Clinicial University Hospital, Riga Stradins University, Riga, Latvia

Heart failure (HF) is a major public health problem worldwide with high morbidity and mortality. The prognosis of patients with acute decompensated HF (ADHF) remains poor, with an in-hospital mortality rate of ~4%, 30-day rehospitalization rates of 23%, and a 6-month mortality rate approaching 20% in advanced HF. Admissions to hospital for ADHF continue to increase and represent a significant burden on both patients' and healthcare resources. The majority of these admissions are for the control of volume overload. Hypervolemia is associated with HF progression and increased mortality. The therapy of patients with ADHF should be aimed at eliminating fluid overload.

Intravenous loop diuretics remain the first-line therapy for ADHF and are currently prescribed for ~90% of hospitalised ADHF patients. Intravenous loop diuretics induce a rapid diuresis that reduces lung congestion and dyspnea. The main problems of usage of the loop diuretics are their side effects and development of resistance to the diuretics. These drugs may be associated with increased morbidity and mortality due to electrolyte abnormalities, enhanced neurohormonal activation, and unfavourable cardiac and renal effects. Despite decades of clinical experience with these agents, prospective data to guide the use of loop diuretics are spare. According to the last HF guidelines the optimal dose of the diuretics and route of administration are uncertain. The recently published DOSE trial is the largest prospective, double blind, randomized ADHF to evaluate initial diuretic strategies. The aim of the study was to compare the safety and efficacy of twice daily IV bolus vs. continuous IV loop diuretics infusion and of low (one time oral dose) vs. high (2.5 times oral dose) IV loop diuretic intensity in patients with ADHF. There was not difference between either of the treatment comparisons on the global assessment of symptoms and change in serum creatinine (primary endpoints). Compared with low dose strategy, the high dose strategy was associated with greater improvement in a number of secondary endpoints, but at the expense of more transient worsening of renal function.

Another method to reduce fluid overload in patients with ADHF is ultrafiltration (UF). The process of ultrafiltration consists in the production of plasma water from whole blood across a semipermeable membrane in response to a transmembrane pressure gradient. In patients with fluid overload due to decompensated HF, ultrafiltration has been shown to improve signs and symptoms of congestion, increase diuresis, lower diuretic requirements and correct hyponatremia. The UNLOAD is the largest trial to clarify effects of UF in patients with ADHF. The aim of the UNLOAD (Ultrafiltration vs. Intravenous Diuretics for patients Hospitalized for Acute Decompensated Heart Failure) trial was to compare the safety and efficacy of veno-venous ultrafiltration and standard IV diuretic therapy for hospitalised patients with HF with ≥ 2 signs of hypervolemia. The results of the trial demonstrated than in ADHF, ultrafiltration safely produces greater weight and fluid loss than IV diuretics, reduces 90-day HF rehospitalisations, and is an effective alternative therapy. UF compared with diuretic's treatment is an invasive and more expensive method. According to the European guidelines, venovenous isolated UF is sometimes used to remove fluid in patients with HF, although this is usually reserved for patients who are unresponsive or resistant to diuretic therapy. Peripheral venovenous ultrafiltration has emerged as a potentially promising alternative to diuretic therapy in ADHF.

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INVITED SPEAKERS

Chronic heart failure and comorbidities: challenges and solutions

A.J. Stewart Coats[1] – [1]Norwich Research Park, United Kingdom

The favourable effects of beta-blockers on heart failure (HF) morbidity and mortality have been consistently shown by several large randomised controlled trials and meta-analyses of randomised trials overtime. Nevertheless, typically mean age of patients included in previous trials was lower than the average age of HF patients in the community, and patients with an ejection fraction (EF) < 40% were excluded.

The SENIORS (Study of the Effects of Nebivolol Intervention on Outcomes and Hospitalisation in Seniors with Heart Failure) trial showed that Nebivolol, administered on top of standard therapy to elderly (≥ 70 years) HF patients significantly reduced the composite risk of all-cause mortality and cardiovascular hospital admission, regardless of baseline EF. Nebivolol is a beta-1-selective blocker with vasodilating properties which depend on nitric oxide (NO) release. Thanks to its vasodilating properties, Nebivolol may prove effective against ischaemic injury to the myocardium. Only four beta blockers have been proven to reduce morbid/mortal events in chronic heart failure. Of these Nebivolol has the most attractive profile, having the most cardio-selectivity improving its tolerability in peripheral vascular and lung disease and has the unique vasodilatory effect via endogenous NO production enhancing endothelial function. These features make it particularly attractive in patients with co-morbidities. Ischaemic heart disease is one of the most common co-morbidities in CHF and the effect of CHF-indicated beta blockers in ischaemic heart disease is not well studied. For this reason we analysed data from 1,452 (717 placebo-treated patients and 735 assigned to Nebivolol) HF patients in whom coronary artery disease (CAD) was the underlying aetiology in a subanalysis of the SENIORS trial. The specific aim of the study was to investigate whether chronic beta-blockade by Nebivolol can reduce ischaemic events in patients with HF.

The primary endpoint was the composite of cardiac ischaemic events at 2 year follow-up: hospitalisation/death for acute myocardial infarction (MI), unstable angina or sudden death. The secondary endpoints were a composite of hospitalisation/deaths for acute MI or unstable angina and sudden death. The percentage of patients reaching the primary endpoint of composite ischaemic events was 15.9% in the placebo group and 10.7% in the Nebivolol group, with a statistically significant 32% risk reduction for ischaemic events in favour of Nebivolol. Nebivolol treatment was also associated with a significant 38% reduction in sudden death. These effects were independent of age, gender and EF.

In the setting of HF, beta-blockers are known to exert beneficial effects on progression of HF and cardiac remodeling and therefore are recommended for the treatment of HF. Nebivolol possesses additional properties that go beyond the blockade of beta-adrenergic receptors. In fact, the marked Nebivolol-induced reduction in cardiac ischaemic events in elderly patients with HF of ischaemic origin observed in this subanalysis of the SENIORS trial is, at least in part, attributable to the ability of Nebivolol to induce coronary vasodilation.

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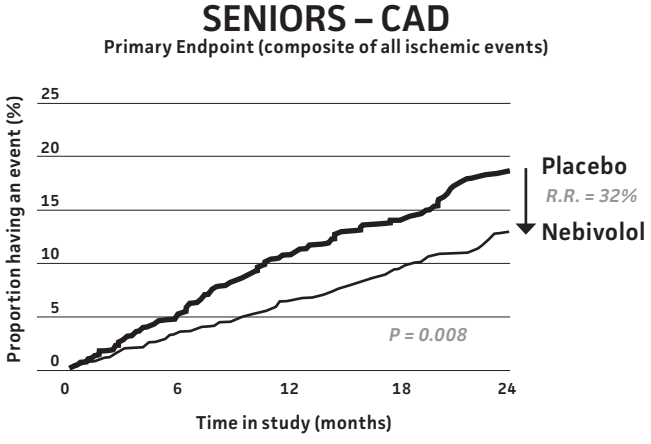

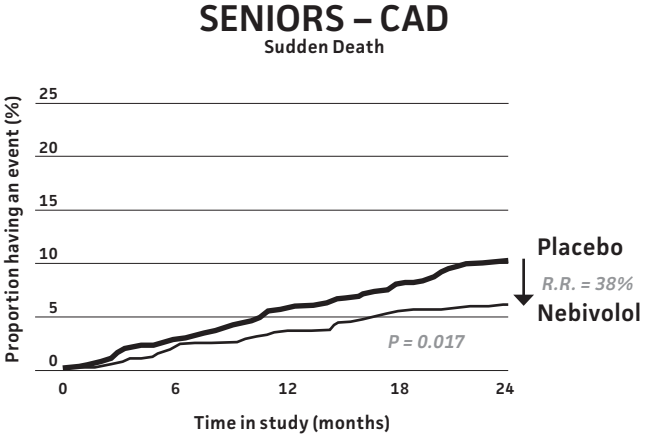

INVITED SPEAKERS

Emerging therapies for acute heart failure

Markku S. Nieminen[1] – [1]Helsinki University Central Hospital, Helsinki, Finland

The targets in acute heart failure (AHF) are related to release symptoms: dyspnea, tiredness, fluid retention, to improve haemodynamics: release vasoconstriction, decrease filling pressure, increase stroke volume and cardiac index and to improve prognosis.

Our current therapies are limited and the prognosis is poor. The current vasodilators are mainly nitrates and the main inotropes used are dobutamine, dopamine, and norepinephrine. After cardiac surgery, milrinone is frequently used in some centres.

These agents are in a way safe as they are short acting and the effects are moderate. The main problems are tachyphylaxis and, on the other hand, increase in heart rate. These therapies have been practised for decades. New therapies are welcome.

Inotropic mechanism	Drugs
Na-K ATPase inhibition	Digoxin
Beta-adrenergic stimulation	Dobutamine, Dobamine
PDE-inhibition	Enoximone, Milrinone
Calcium sensitization	Levosimendan (inodilator)
Na-K ATPase inhibition+ Serca-activation	Istaroxime
Acto-myosin cross-bridge activation	Omecantivmecartil
SERCA-activation	Gene transfer
SERCA-activation+Vasodilatation	Nitrosyl donor, CXL-1020
Ryanodine receptor stabilization	Stabilizer, S44121
Energetic modulation	Etomoxir pyruvate

Some disappointment has been expressed regarding the safety of these agents and thus the only drug at the moment in consensus use is levosimendan. It is an inodilator, with clear and long acting vasodilatation, with some inotrophic effect and a mild inotropic effect exerted through calcium sensitization based on troponin C.

Also a number of vasodilators are in phase II studies, but their efficacy and safety data are still lacking.

On the other hand, these agents are quite similar in action to nesiritide, a natriuretic peptide analogue, which has been associated with adverse effects like hypotension.

Vasodilators:
Levosimendan (inodilator, - dilator)
Guanylate cyclase activator
Nesiritide
Relaxin
Urodilatan
Adrenomedullin
Neuropeptide calcitonin gene-related peptide (CGRP) – controversial data, receptor upregulated
Glucagon-Like Peptide, exenatide, liraglutide, albiglutide

The problem with all emerging therapies, is that they are more potent than dobutamine and nitrate, but their half life is 1 to several hours, and when given as a bolus with continuous infusion, their efficacy is definitely achieved but hypotension is frequently unexpectedly encountered.

Thus haemodynamic monitoring is needed, and when used, filling pressure has to be monitored together with other targets of haemodynamic safety.

INVITED SPEAKERS

Lessons from the UK – outcomes for acute heart failure

Theresa McDonagh[1] – [1]King's College Hospital, London, United Kingdom

Despite major advances in the treatment of chronic heart failure over the last twenty years, morbidity and mortality for acute heart failure remains high. Data which has accumulated over the last few years from the UK National Heart Failure Audit shows in patient mortality rates of 11%, and 33 % of patients die in the first year after admission to hospital. In addition at least 25% of patients are readmitted to hospital with heart failure during the following year. These frequent and prolonged hospitalizations (the median length of stay is 11 days) care the main reason for the huge fiscal cost of heart failure to the NHS (up to 2% of the total NHS budget). National efforts are now focusing on improving these outcomes.

The National Heart Failure Audit demonstrates that specialist care improves mortality for heart failure patients. Those admitted to a cardiology wards have mortality rates which are 50% lower than those admitted to general medical wards. Even when adjusting for age, severity of disease and comorbidity in multivariate statistical models having access to cardiology care is an independent predictor of better survival in hospital and in the first year post discharge. Cardiology care seems to be the gate keeper to appropriate diagnosis, investigation, treatment and specialist cardiology and heart failure multidisciplinary follow up. All of these are known to improve morbidity and mortality for heart failure patients.

The challenge is for us to adapt our models of acute heart failure care to allow patients being admitted to hospital with heart failure more access to specialist cardiology care.

Session: CARDIAC RESYNCRONIZATION THERAPY: CRITERIA FOR PATIENTS, CAVEATS, EPIDEMIOLOGY

Cardiac resynchronization therapy: problems and complications

Germanas Marinskis[1], Vyte Maneikiene[1] – [1]Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania

AIM. To evaluate procedural data and long-term results in patients with implanted cardiac resynchronization therapy (CRT) devices.

METHODS. Periprocedural details and follow-up data were evaluated in 266 patients with CRT-P and CRT-D devices implanted in our institution. In 210 patients, primary implantation was done, in 19 – upgrading from the DDD system, in 37 – upgrading from the VVI system. Duration of follow-up varied from 3 to 110 months.

RESULTS. The following problems were encountered in our patients during implantation and after it: subclavian venous occlusion after previous system implantation (in 6 upgrade patients (pts)); absence of the lateral coronary sinus (CS) venous branch suitable for lead implantation (36 pts); dissection of the coronary sinus and/or its branches during the procedure (7 pts); phrenic nerve pacing (initially observed in 66 pts); left ventricular (LV) lead dislodgement (8 pts); proarrhythmia probably due to the LV pacing (1 pt); infectious complications not manageable by conservative measures and thus requiring system removal (3 pts). These problems were managed as follows: in all 6 patients with vein thrombosis, contralateral vein was used and the LV lead was successfully placed and connected to the generator after tunnelling the subcutaneous tissues across the sternum. In patients with absent lateral CS branch, in 18 cases LV pacing was possible by guiding the electrode via retrograde or anterior intraventricular vein collaterals, in 6 pts epicardial LV lead had been placed surgically. Phrenic nerve pacing was managed by replacing the pacing lead (46 pts) and/or reprogramming the device to lower voltage and longer stimulus duration, and changing pacing vector (12 pts). Despite successful LV capture, in significant number of patients (53 pts) no anticipated response to the CRT was observed.

CONCLUSIONS. Despite possible problems and complications, effective left ventricular pacing is possible in about of 90 per cent of patients with attempted biventricular system placement. The results, however, are additionally worsened by "no response" problem.

Session: CARDIAC RESYNCRONIZATION THERAPY: CRITERIA FOR PATIENTS, CAVEATS, EPIDEMIOLOGY

Echocardiography in patient selection for CRT therapy – a useful tool or waste of time and money?

Piibe Muda[1] – [1]Tartu University Hospital, University of Tartu, Tartu, Estonia

The magnitude of benefit from cardiac resynchronization therapy (CRT) varies significantly among its recipients; approximately 30% of CRT patients do not report clinical improvement.

According to the current heart failure guidelines of the European Society of Cardiology, only echocardiographic parameter included in the patient selection for the CRT is ejection fraction.

Over the last 10 years, many echocardiographic parameters have been proposed to predict response to CRT. Numerous methods have been described to estimate cardiac interventricular and left ventricular (LV) dyssynchrony by means of echocardiographic indices measured both with conventional echocardiography, tissue Doppler imaging and, more recently, using the speckle tracking technique. Although results from single-center studies have proved promising, the multicenter study – Predictors of Response to CRT (PROSPECT) raised substantial concerns about the intraoperator/interoperator repeatability and reproducibility of these methods. Moreover, the complexity of these techniques and associated costs prevent them from becoming widely accepted and used.

Currently there are some promising studies showing that echocardiography can identify responders. Presence of LV contractile reserve during low-dose dobutamine stress echo and interventricular dyssynchrony are independent predictors of CRT response (99% specificity and 83% sensitivity in detecting responders).

Two-dimensional (2D) speckle tracking has been used as a direct measure of strain. A cutoff value of 130 ms between the time to peak radial strain between the anteroseptum and the posterior wall of the in the short axis of midventricle appears to be a promising predictor of response to CRT.

Echocardiographic evaluation of transmural scar burden predicts CRT response. Myocardial wall at the region of transmural scar is usually thin (an end-diastolic wall thickness ≤ 5 mm) associated with increased acoustic reflectance. Also speckle-tracking 2D radial strain amplitude < 10% helps to identify myocardial scar. Pacing transmural scar tissue reduces left ventricle reverse remodelling after CRT and carries a greater risk of mortality and morbidity than pacing non-scarred myocardium.

Three-dimensional (3D) echocardiography enables to assess the regional volume changes of each segment of LV. The systolic dyssynchrony index (SDI) is defined as the standard deviation of the average time needed to reach the minimum systolic volume for 16 segments of LV expressed as a percentage of the cardiac cycle obtained with 3D echocardiography. A cut-off value for SDI of 5.6% has been shown in small studies to predict acute echocardiographic CRT response to CRT with a sensitivity of 88% and specificity of 86%. Speckle tracking strain analysis has been developed in 3D to overcome limitations of the 2D measurements. More studies are needed to evaluate the utility of this modality.

Concomitant right ventricular (RV) failure is a common comorbid condition, which may indicate the advanced nature of heart failure. RV function is usually evaluated by echocardiography. Poor RV function is associated with poor CRT response.

A combination of methods that include finding the site of the latest activation, presence of interventricular dyssynchrony, myocardial scar localization, the presence of viable myocardium and identifying concomitant heart pathology may help to predict the response to CRT therapy.

Session: CARDIAC RESYNCRONIZATION THERAPY: CRITERIA FOR PATIENTS, CAVEATS, EPIDEMIOLOGY

How to select the right patient for the right device?

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While no new ICD RCT has been completed since the publication of the 2008 guidelines, there have been several important RCTs using CRT that have changed the recommendations. Other technologies including a wearable defibrillator vest and implantable monitors (either 'stand-alone' or incorporated into other devices) are of research interest, but do not yet have enough evidence behind them to support guideline recommendations.

Approximately half of the deaths in patients with HF, especially in those with milder symptoms, occur suddenly and unexpectedly, and many, if not most, of these are related to ventricular arrhythmias (whereas others may be related to bradycardia and asystole). Prevention of sudden death is therefore an important goal in HF. While the above mentioned key disease-modifying neurohumoral antagonists reduce the risk of sudden death, they do not abort it. Specific antiarrhythmic drugs do not decrease this risk (and may even increase it). For this reason, ICDs have an important role to play in reducing the risk of death from ventricular arrhythmias.

Two large RCTs have shown that CRT is of benefit in patients with mild (NYHA class II) symptoms as well as in those who are more severely symptomatic. There is little doubt that patients expected to survive with good functional status for 1 year should receive CRT if they are in sinus rhythm, their LVEF is low (= 30%), QRS duration is markedly prolonged (=150 ms), and an ECG shows a left bundle branch morphology, irrespective of symptom severity. There is less consensus about patients with right bundle branch block or interventricular conduction delay (based on subgroup analyses) and those in AF (because most trials excluded these patients and because a high ventricular rate will prevent resychronisation). Another area of debate is what to do with an HF-REF patient without an indication for CRT who needs a conventional pacemaker. The possibility that patients with a QRS duration of 120 ms may have 'mechanical dyssynchrony' (detectable by imaging) and might benefit from CRT is another area of research interest but remains to be proven.

The two commonly encountered clinical situations where there is little sound evidence for (or against) CRT is AF and when a patient with a reduced EF has an indication for conventional pacing and no other indication for CR. One small, single-blind study [Multisite Stimulation in Cardiomyopathies (MUSTIC)] included 59 HF-REF patients with persistent/permanent AF, slow ventricular rate necessitating permanent ventricular pacing, and a paced QRS duration = 200 ms. The study had a crossover design (3- month conventional pacing vs. 3-month CRT). The drop-out rate was high (42%) and there was no difference in the primary endpoint of 6-min walk distance. All key large RCTs of CRT have excluded patients with AF, with the exception of RAFT. RAFT included 229 patients with permanent AF or flutter either with a controlled ventricular rate (60 bpm at rest and 90 bpm during a 6-min walk test) or with planned AV junction ablation. Further analysis did not show a significant relationship between baseline rhythm and treatment effect, but this subgroup represented only a small proportion of the overall population. Other data suggesting that patients with AF (without AV nodal ablation) may benefit from CRT are limited as being observational in nature. All major RCTs of CRT, with the exception of RAFT, excluded patients with a conventional indication for pacing. RAFT included 135 patients with a paced QRS duration = 200 ms, a subgroup too small for meaningful analysis. Conventional right ventricular pacing, however, alters the normal sequence of cardiac activation in a similar way to LBBB, and experimental and observational data suggest that this may lead to deterioration in LV systolic function. It is on this basis that CRT is recommended as an alternative to conventional right ventricular pacing in patients with HF-REF who have a standard indication for pacing or who require a generator change or revision of a conventional pacemaker.

The top questions remain the same: Where are super-responders for CRT implantation? Despite this success of CRT and the recent expansion of its role in the treatment of patients with CHF, there remain many inherent limitations to the technology and its delivery. A significant minority of patients (~30%) continue to remain non-responsive to this pacing strategy.

How can we identify responders among the whole heart failure patient population? What is the first choice of diagnostic tools – ECG or ECHO? As many as 30% of heart failure patients presenting with a wide QRS complex do not show LV mechanical dyssynchrony. It has been suggested that CRT could induce LV mechanical dyssynchrony in this subgroup of patients, leading to impaired LV performance and, subsequently, to poor clinical outcome. However, to date, no study has evaluated the potential induction of LV mechanical dyssynchrony after CRT implantation in this subgroup

of patients and, more important, the long-term clinical consequences of this acutely induced LV dyssynchrony remain unknown.

CRT or CRT-D or ICD? Which one for which patient?

Can we apply CRT in patients only with wide QRS, or also in the case of some clinical findings in patients with narrow QRS? Why? QRS complex width is presently used to select patients for CRT as a measure of LV dyssynchrony. However, electrical dyssynchrony is not equivalent to LV mechanical dyssynchrony and a poor correlation between QRS duration and LV dyssynchrony has been reported. Furthermore, heart failure patients with narrow QRS complex may show echocardiographic mechanical LV dyssynchrony amenable to be corrected with CRT.

What can we do with patients with right branch block? Also, a number of studies, including the Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) study and Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE), presented RBBB patients in the same subset as nonspecific interventricular conduction defect and thus they could not be included.

There are pathophysiological reasons to expect a response to CRT in at least some patients with RBBB and cardiomyopathy. An electroanatomic mapping study found conduction delay in both bundles; indeed, delay in left ventricular endocardial activation was seen in most patients with RBBB and left-axis deviation. Echocardiographic studies have shown evidence of significant left ventricular intraventricular mechanical dyssynchrony in many patients with RBBB. However, current data do not support the use of mechanical dyssynchrony assessment to select patients for CRT. There is more to be learned about the relationship between conduction delay (electrical dyssynchrony), mechanical dyssynchrony, and response to CRT.

What must we consider first: QRS dimension or QRS morphology? Non-left bundle branch block (LBBB), as the baseline electrocardiogram morphology before CRT implantation, is much more prevalent in real-world practice than in randomized clinical trials; echocardiographic and clinical response to CRT is determined by baseline QRS morphology in the first place and to a lesser degree by QRSd, and those with LBBB had better response rates than those with non-LBBB; and event-free survival (from death, heart transplantation or left ventricular assisting device) is better in CRT-treated patients with baseline LBBB and QRS ≥ 150ms. However, this difference is not significant after adjusting for baseline characteristics. The key findings can be summarized as follows: 1) non-LBBB, as the baseline ECG morphology before CRT implantation, is much more prevalent in real-world practice than in randomized clinical trials; 2) echocardiographic and clinical response to CRT is determined by baseline QRS morphology in the first place and to a lesser degree by QRSd; 3) event-free survival (from death, heart transplantation, or LVAD) is better in CRT-treated patients with baseline LBBB and QRS ≥ 150 ms. However, this difference is not significant after adjusting for other baseline characteristics.

From the early days of CRT, it was noted that a substantial subset of patients fail to benefit from this treatment. Although this is in no way different from treatment with medications, CRT has received considerable attention because of the cost and invasive nature of this therapy. Attempts to predict and subsequently minimize nonresponders have focused on better patient selection by analysing data from subgroups of the original randomized trials. Patients with non-LBBB morphologies, often underrepresented in clinical trials, or shorter QRSd on their baseline ECG were repeatedly reported to gain less or even no benefit. Stratifying patients, however, according to both the morphology and the duration of the QRS complex has been less frequently done.

Session: WHEN ARE THE SURGEON AND THE INTERVENTIONALIST NEEDED IN HEART FAILURE?

The role of modern interventional cardiology and regenerative medicine in treatment of heart failure

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The main objective of invasive strategy in heart failure patients is to reduce heart failure symptoms, to improve the quality of life and survival, and to support long-term medical treatment. According to guidelines, coronary and percutaneous revascularization is indicated for relief of angina pectoris in patients with reduced ejection fraction heart failure or heart failure with preserved ejection fraction. CABG is recommended for patients with chronic HF and systolic LV dysfunction and alternative strategy can be percutaneous coronary angioplasty. Besides coronary revascularization, nowadays interventional cardiologists also perform other percutaneous procedures to improve the quality of life and survival of heart failure patients.

TAVI is one of invasive treatment strategy for symptomatic HF patients with severe aortic valve stenosis and LV systolic dysfunction who are otherwise fit for surgery. Since 2010 in Latvia there have already been performed more that 100 TAVI procedures with good results.

There is a wealth of preclinical and clinical data showing the safety, feasibility, and efficacy of cell therapy in patients with cardiovascular disease. However, stem cell delivery remains a major challenge in the development of cardiac stem cell therapy strategies. Since 2008 there are three ongoing clinical trials in Latvia: transplantation of autologous bone marrow mononuclear cells for patients with acute myocardial infarction, chronic heart failure and diabetes mellitus using intracoronary delivery or injections in branches of splenic artery during balloon angioplasty. Since 2011 another delivery technique has been applied in Latvia: transendocardial intramyocardial stem cell application using NOGA XP (three-dimensional electromagnetic cardiac mapping system).

Another new invasive technique which is used patients with ischaemic heart failure with reduced ejection fraction and LV aneurism is percutaneous implantation of Parachute implant ventricular partitioning device. Preliminary clinical data shows that Parachute device implantation improves left ventricle haemodynamic and functional capacity in the 12 months following the procedure. There are three ongoing clinical trials (two in Europe and one in United States) for Parachute device.

Heart failure is a serious complication with symptoms reducing the quality of life. Interventional cardiology and regenerative medicine could be good strategy for reducing these symptoms and even for improving survival.

Session: WHEN ARE THE SURGEON AND THE INTERVENTIONALIST NEEDED IN HEART FAILURE?

Hybrid procedures using PliCath device for ischaemic cardiomyopathy: CONFIGURE-HF study

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OBJECTIVE. The CONFIGURE HF study is a multi-centre, prospective, single-armed, study designed to evaluate the safety and feasibility of the BioVentrix PliCath HF Epicardial Catheter-based Ventricular Reduction (ECVR) System for left ventricular volume reduction in heart failure. We are presenting the data of a single center experience.

METHODS. Study inclusion criteria were: age 18–76 years, left ventricular ejection fraction 15–35 %, acontractile (akinetic and/or dyskinetic) scar located in the antero-septal-apical region involving at least the anterior 1/3 of the septum (60 cc/m² ≥ LVESV/I ≤ 120 cc/m²), viability of myocardium in regions remote from area of intended scar exclusion.

The implantable elements of the PliCath HF System were delivered through a catheter directly across the epicardial surface of the LV via sternotomy. The LV volume and radius were reduced through excluding a portion of the circumference of LV wall where it had been replaced by the antero-septal scar.

All study patients were undergoing scheduled follow-up evaluations at hospital discharge, 30, 90 and 180 days after initiation of their treatment. During follow-up visits imaging procedures (TTE, MRI), heart failure biomarkers and evaluation of physical capacity tests were done.

RESULTS. From November 2011 to July 2012, fourteen patients (12 male and 2 female) underwent PliCath procedure. The mean age of the patients was 58 years (38 to 74). Six patients (42%)) were operated off pump. Concomitant revascularization was performed for 6 (42%) patients, 3 (21%) of them were revascularised by performing of pump CABG and 3 (21%) patients underwent PTCA. Prophylactic IABP support was instituted to 7 patients. 10 patients completed 1 year follow-up.

Medium increase of LVEF postoperatively was 27%, the improvement was sustained for 12 months for majority of patients. Average Minnesota heart failure score had decreased from 48 to 41 points (15%). Six minute walking distance had increased to 431m (27%).

Two patients required postoperative ECMO support for heart failure. One patient had pulmonary artery valve replacement more than one year after surgery (suspected pulmonary artery damage during the procedure). There were no deaths in study patient group.

CONCLUSIONS. Use of this device replicates the geometric reconfiguration of the ventricle achieved through surgical Left Ventricular Reconstruction, but this takes place on a beating, unsupported heart, thereby creating the option of avoiding the use of cardiopulmonary bypass pump. This procedure is safe and effective in selected patients with end stage ischaemic cardiomyopathy.

Session: WHEN ARE THE SURGEON AND THE INTERVENTIONALIST NEEDED IN HEART FAILURE?

New frontiers in the interventional management of heart failure. A case of catheter-based renal sympathetic denervation

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Various hypertensive conditions are characterized by sympathetic hyperactivity, including (some forms of) essential hypertension, metabolic syndrome/obesity, sleep apnea and chronic kidney disease. Even in the absence of hypertension, heart failure is often associated with sympathetic hyperactivity. Sympathetic hyperactivity is an important component of heart failure and primary hypertension. Decreased parasympathetic and increased sympathetic tone increase peripheral vascular resistance, reduce renal blood flow, and increase sodium retention, while impairing glucose handling and contributing to adverse cardiac and vascular remodelling. Increased sympathetic activity is present in patients with heart failure and it is correlated with functional class. The renal afferent sympathetic activity might contribute to this phenomenon, so effective modulation by renal denervation might help to treat patients with heart failure. Increased renal sympathetic activity might also play a role in the development of resistance to atrial natriuretic peptide. Research over the past two decades has convincingly shown that the kidneys are important in the pathogenesis of sympathetic hyperactivity.

Renal artery denervation procedure is a newly rediscovered tool in fight against drug resistant hypertension, helping to reduce sympathetic overactivity in these patients. After successful denervation procedure, the norepinephrine spill-over is significantly reduced and that effect maintained in clinical studies for several years. Furthermore, whole-body sympathetic activation is reduced by the ablation of afferent renal nerves, which stimulate sympathetic outflow in the hypothalamus. Thus, in contrast to beta-blockers, renal denervation diminishes both beta- and alpha-receptor–mediated hyperactivity. It seems attractive to hypothesize that apart from a direct effect of the intervention on blood pressure by renal denervation, there may be a second level of efficacy, i.e. the slow reversal of structural vascular abnormalities. In earlier study, renal denervation significantly improved cardiac functional parameters. Renal sympathetic nerve ablation reduced left ventricular volumes, increased the ejection fraction, and improved diastolic dysfunction, such as myocardial relaxation and end-diastolic pressures as indicated by left ventricular mitral valve E/E' and LA size, which have been linked to improved prognosis in pharmaceutical interventional trials. Reduction of left ventricular filling pressure and regression of left ventricular wall thickness will have improved diastolic dysfunction after renal denervation. A potential impact of renal denervation on myocardial fibrosis remains speculative. Although pressure overload per se affects myocardial collagen content, reduction of sympathetic and renin-angiotensin-aldosterone system activity, known to occur after renal denervation, might also facilitate regression of myocardial fibrosis. Consistent with the prior studies, there is a strong logic behind the idea that renal denervation procedure may be beneficial in heart failure patients, both with and without hypertension.

Session: MONITORING IN HEART FAILURE: TELEMONITORING, BNP-GUIDED THERAPY, HEART FAILURE CLINICS

Complex management of heart failure patients

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Heart failure (HF) is a growing epidemic, especially in the Western world. Approximately 50% of HF patients are rehospitalized within 6 months of discharge and with the aging of the population this trend will continue to rise. Understanding the epidemiology and pathophysiology of the syndrome, identifying the predictors and the strength of their association with outcomes, and cost-effectively using the available diagnostic modalities are essential in order to implement novel therapeutic approaches to curb this epidemic.

HF disease management (HFDM) programs are common in North America, Europe, and Australia. Programs have been widely introduced following recommendations from international clinical guidelines. The use of comprehensive HFDM programs have involved specialty care and a multidisciplinary team; the goals of the HFDM programs have included optimization of drug therapy, intensive patient education, vigilant follow-up with early recognition of problems, and identification and management of patients' comorbidities. HF patients who were cared for in these programs were shown to have significantly fewer rehospitalizations, lower healthcare costs, improved functional and symptom status, and better quality of life as compared either with their preintervention status or with HF patients treated with conventional care.

Meta-analysis of HFDM programs through 1999 has concluded that multidisciplinary teams providing direct specialized follow-up care statistically significantly reduced hospitalization and healthcare costs, whereas studies that used telephone contact to coordinate primary care services seemed to have no effect. Randomised clinical trials have established that certain HFDM programs improve prescribing practices and reduce the risk of hospitalization, costs, and mortality; successful programs have included patient education, multidisciplinary teams, and specialized follow-up procedures. In contrast, telephone-based systems designed to enhance follow-up with primary care providers have yielded mixed results and the effectiveness of these programs has not been fully established. Healthcare providers, insurers, and policymakers should now recognize that when it comes to HFDM programs, no class effect exists. HFDM programs should strive to adhere to the principles set forth by the European Society of Cardiology and include the elements found to be efficacious in clinical trials – multidisciplinary teams, improved use of evidence-based guideline-recommended therapy, emphasis on patient education and self-management, and enhanced access to specialized clinics or home visits. Although some HFDM programs have been proven to be effective, others have not, and significant additional attention is needed in testing and demonstrating best practices and sharing information about successful program components across a variety of care settings.

Currently available trial results may seem rather ambiguous and confusing. Nevertheless, it appears that the randomised controlled trials tend to be in favour of telemonitoring. Importantly, an improved quality of life – a soft end-point gaining more and more clinical significance – has been reported in all studies, whereas telemonitoring was highly acceptable by chronic HF patients. Key components that patients with HF encounter through their contact with healthcare services should be sampled in order to design larger scale studies that could test their value. Another urgent need is the identification of patients that would actually be benefited by such interventions. Since the resources are getting scarce and in a time when cutbacks and cost reductions are getting bigger, sustainability of telemonitoring approaches seems difficult. Consequently, a key factor that will influence the future implementation of telemonitoring strategies is the availability of human and economic resources.

Session: MONITORING IN HEART FAILURE: TELEMONITORING, BNP-GUIDED THERAPY, HEART FAILURE CLINICS

The multi-marker approach to heart failure with preserved ejection fraction

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Heart failure with preserved ejection fraction (HFPEF) accounts for approximately one half of all heart failure patients and carries a significant morbidity and mortality burden. Diagnosis of HFPEF is frequently challenging and relies upon careful clinical evaluation, the finding of non-dilated left ventricle with preserved ejection fraction and the evidence of diastolic dysfunction.

While early research focused on the importance of diastolic dysfunction in the pathophysiology of HFPEF, recent studies have revealed that multiple non-diastolic abnormalities in cardiovascular function also contribute to it. Mathematically, ejection fraction is the stroke volume, but it does not take into account systolic function in the longitudinal axis. A number of studies have shown that left ventricular (LV) longitudinal function is reduced not only in diastole but also in systole even though LV ejection fraction is within normal limits. A preserved ejection fraction often merely indicates that the radial or circumferential fibres of the ventricle have compensated for dysfunction of the longitudinal fibres, but it does not necessarily imply that the systolic function is normal. Speckle tracking (2D strain) and colour tissue Doppler imaging (TDI) can be useful techniques to evaluate significantly impaired systolic and diastolic longitudinal function in these circumstances. This confirms that HFPEF is not an isolated disorder of diastole.

Routine echocardiographic parameters of diastolic dysfunction include mitral inflow Doppler measurements, tissue Doppler imaging-derived early diastolic myocardial velocities, measured at the mitral annulus, pulmonary venous flow velocity patterns, left atrial volume index (LAVI) etc. The ratio of mitral early diastolic inflow velocity (E) to mitral early annular lengthening velocity (E') exceeding 15 provides evidence for raised left ventricular filling pressure – the major functional abnormality in HFPEF as a consequence of diastolic dysfunction. Shuai X et al. (2011) in their studies have found out that lateral E/E', LAVI and Ar-A have the greatest value in diagnostics of HFPEF, while the role of left ventricular mass index is controversial. Current guidelines for the diagnosis of HFPEF are based on measurements at rest, however, ventricular dysfunction in HFPEF is more apparent on exercise. It shows additive value of stress echocardiography for individual patients. There is no single echocardiographic parameter that can be used to diastolic dysfunction in isolation, therefore accurate diagnosis of HFPEF requires a comprehensive assessment of all relevant two-dimensional ad Doppler measurements.

Abnormal diastolic filling pressure results in the release of plasma natriuretic peptides in proportion of heart failure severity. Unfortunately, many previous studies have found that natriuretic peptides levels in HFPEF patients are less elevated than in patients with heart failure with reduced ejection fraction and the levels are especially low in HFPEF patients presenting in an outpatient clinic with complaints of limited exercise tolerance. DIAST-CHF study shows sensitivity of 65% for diagnosis of HFPEF when using the recommended N-terminal proBNP cut-off value 220 pg/ml. Relationships between plasma natriuretic peptides and echocardiographic findings have not been yet established.

In contrast to natriuretic peptides, recent studies of new fibro-inflammatory biomarkers raise higher expectations due their advantage of reflecting the chronic myocardial remodelling process of HFPEF. For example, matrix metalloproteinase 2 (MMP2) may be more useful than BNP in the identification of HFPEF. Growth differentiation factor 15 (GDF-15) also has good correlation with echocardiographic markers of diastolic function and elevated filling pressures. But the sensitivity and specificity of these new markers for detecting of HFPEF should be clarified in future research.

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Session: MONITORING IN HEART FAILURE: TELEMONITORING, BNP-GUIDED THERAPY, HEART FAILURE CLINICS

BNP-guided HF therapy for heart failure

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In managing the ongoing treatment of HF patients, clinicians have limited tools to aid in decisions to adjust patient treatment regimens. The majority of heart failure (HF) patients do not achieve the dose levels of their medications recommended by clinical practice guidelines.

AIM. To analyze key findings of NT-proBNP/BNP-Guided Heart Failure Therapy Trials and to find out if there is sufficient evidence to translate BNP-guided HF therapy to clinical practice.

METHODS. To collect data of randomized clinical trials and 2 meta-analyses and to analyse differences in outcomes between conventional and BNP-guided treatments groups.

RESULTS. A total of 10 RCTs with published results were identified evaluating NT-proBNP/BNP guided therapy for HF patients versus clinically guided therapy.

4 studies showed that NT-proBNP / BNP guided therapy resulted in better patient outcomes including:	**6 studies showed no difference in primary end-points with NT-proBNP / BNP guided therapy.**
· Reductions in cardiovascular events · Reductions in HF-related hospitalizations · Reductions in HF-related and all-cause death	However, some studies mentioned trends for improvement in secondary endpoints and other measures with natriuretic peptide -guided HF therapy
Positive Studies:	**Negative / Neutral Studies:**
· Troughton1 · STARS-BNP2 · Berger3 · PROTECT4	· BATTLESCARRED5 · TIME-CHF6 · PRIMA7 · STAR-BRITE8 · SIGNAL-HF9 · NorthStar10,11

Meta-analyses by both Felker et al. and Porapakkham et al. show decreased mortality risk ratios [RR 0.76 (95% CI 0.63–0.91; p = 0.003) by Porapakkham] for biomarker-guided therapy in data pooled across both positive and neutral / negative clinical trials of natriuretic peptide-guided HF therapy.

Two subpopulations have better responses to NT-proBNP/BNP guided therapy: HF patients with compromised LVEF and patients younger than 75 years. In a subgroup analysis based solely on TIME-CHF and BATTLESCARRED, the only studies to report the necessary data, patients younger than 75 years had an all-cause mortality RR for guided therapy of 0.52 (95% CI 0.33–0.82; p = 0.005).

In general, patients on guided management achieved target ACE-inhibitor and beta-blocker dosages about twice as often as those managed conventionally.

PROTECT was halted at an enrolment of 151 patients out of planned 300 when management guided by NT-proBNP showed a significant advantage for the primary end point at one year. The difference – in a composite that included worsening heart failure, HF hospitalisation, and CV death – was significant at p = 0.008.

Several trials did not treat trial subjects aggressively or adjust therapy in response to elevated peptide levels. These included TIME-CHF, SIGNAL HF, and PRIMA.

Those RCTs showing positive outcomes for natriuretic peptide-guided HF therapy had the following features: low target values were set for the biomarker, elevated biomarker levels triggered treatment modifications, treatment was pursued aggressively to lower biomarker concentrations until the target level was reached, younger HF patients were recruited for the study, only patients with left ventricular systolic dysfunction were included in the study.

CONCLUSIONS. Recommendations for the use of natriuretic peptides for the guidance of HF care:

- NT-proBNP / BNP should be considered as the biochemical gold standards for HF prognosis.
- Serial measurements of NT-proBNP / BNP should be taken.

Recommended target concentrations to ensure successful biomarker-guided therapy	**Meaningful changes in biomarker concentrations**
· BNP ~125 pg/ml	· BNP: ± 40%
· NT-proBNP = 1000 pg/ml	· NT-proBNP: ± 25%

- NT-proBNP / BNP concentrations above target levels should always be treated as a sign of concern, even if the patient appears to be stable.
- The focus of NT-proBNP / BNP guided therapy should be on treatments with mortality benefit for chronic HF: ACEIs, ARBs, β-blockers, aldosterone antagonists, exercise therapy, placement / optimisation of cardiac resynchronization therapy.

Session: MONITORING IN HEART FAILURE: TELEMONITORING, BNP-GUIDED THERAPY, HEART FAILURE CLINICS

Cardiac resynchronization therapy from remote monitoring and remote follow-up to remote patient care

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In the era of wireless communication technology, new options are now available for following-up patients with implanted cardiac pacing devices. Major pacing device companies offer pacing devices with wireless capabilities to communicate with home transmitter, which then pass data to the physician, thereby allowing remote patient follow-up and daily based monitoring. These remote monitoring systems are being widely used in the USA and Europe mainly with ICD and CRT-D patients.

With remote monitoring systems the physician can receive diagnostic information from the patient without the patient having to visit the hospital. It allows transmissions of intra-cardiac ECGs including arrhythmia episodes and other diagnostic data from the pacing device and this can be done even on 24/7 basis.

Results form the recent studies have shown that remote monitoring is a safe alternative to conventional in clinic follow-ups. With remote monitoring arrhythmias and device-related events will be recognized and therapeutic actions will be taken earlier than the next scheduled visit to the clinic. Thus major reductions in inappropriate and unnecessary shocks and hospitalizations have been shown with remote monitoring. Within large cardiological centres remote monitoring has already become a new standard of care for follow-up of ICD and CRT-D patients.

Referral Criteria for Heart Failure

Patients with more than one of the following risk factors and who are NYHA Class III or IV should be considered for referral for MCS and/or cardiac transplantation evaluation.[1]

Functional Assessment

- Inability to walk 300 m without shortness of breath
- Intolerant or refractory to ACE inhibitors, angiotensin receptor blockers, or beta-blockers
- One heart-failure–related hospital admission in the past 6 months[2]
- CRT nonresponder
- High diuretic dose (eg, 120 mg/d furosemide)

Lab Assessment

- Serum sodium < 136 mmol/L
- BUN > 40 mg/dL or serum creatinine > 1.8 mg/dL
- Hematocrit < 35%

Art		
Indication	**Destination Therapy**	
Etiology	**Idiopathic Cardiomyopathy**	
	Baseline	**24 Months Post-Implant**
NYHA Class	**IV**	**I**
Cardiac Output (Lpm)	**2.4**	**7.1**
Serum Creatinine (mg/dL)	**2.3**	**1.8**
BUN (mg/dL)	**43**	**21**
Total Bilirubin (mg/dL)	**0.6**	**0.5**
Minnesota Living with Heart Failure Score	**70**	**21**
Kansas City Cardiomyopathy Score	**49**	**87**

— Art, age 75
NYHA Class I

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— Professor Michael Buerke, HF Cardiololgist, Germany.

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Nebivolool

For the treatment of chronic heart failure
(patients 70 years and older)

- In a mortality–morbidity trial performed in 2128 patients ≥ 70 years with stable chronic heart failure, nebivolol, on top of standard therapy, significantly prolonged the time to occurrence of deaths or hospitalisations for cardiovascular reasons (primary end-point for efficacy) with a relative risk reduction of 14%.[1,2]
- This risk reduction developed after 6 months of treatment and was maintained for all treatment duration (median duration: 18 months).[1,2]
- A decrease in sudden death was observed in nebivolol treated patients (4.1% vs 6.6%, relative reduction of 38%).[1,2]

DOSAGE

CHRONIC HEART FAILURE (patients 70 years and older)

The treatment has to be initiated with a gradual uptitration of dosage at 1-2 weekly intervals until the optimal individual maintenance dose is reached:

Initial dose 1,25 mg x 1 → 2,5 mg x1 → 5 mg x 1 → The maximum recommended dose 10 mg x 1

Indications:
- Treatment of essential hypertension.
- Treatment of stable mild and moderate chronic heart failure in addition to standard therapies in elderly patients ≥ 70 years.

Prescription medicine.
Package: 5 mg tablets, N28 or N90

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1. Summary of product characteristics. www.ravimiamet.ee
2. Flather MD et al.; Eur Heart J 2005;26:215-225

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