determines the activation patterns during the arrhythmia. The purpose of this study is to analyze the activation frequencies during VF in isolated perfused healthy human hearts without the interference of extrinsic factors that could modulate the VF activation patterns.

Methods: Three explanted hearts not suitable for cardiac transplantation obtained from donors without structural cardiac disorders were used to obtain multiple transmural recordings with transmural needles (n=24), each equipped with four unipolar electrodes (interelectrode distance = 4 mm). Informed consent was obtained from the relatives of the deceased patients, and the study was approved by the Ethical Review Board. Hearts were perfused according to the Langendorff technique with whole blood, and the electrodes were inserted in the left, and right ventricular myocardium. Spectral techniques were applied to analyze the VF recordings obtained during the electrically induced arrhythmia. The dominant frequency of the spectrum was obtained in each channel.

Results: The highest mean dominant frequencies were obtained in the subendocardium of the posterior part of both the left ventricle (8.9±1.8 Hz vs 6.4±1.5 Hz in anterior wall, p<0.0001), and the right ventricle (7.1±1.1 Hz vs 6.3±1.0 Hz in anterior wall, p<0.05). The location of the maximum values varied in each of the three cases, corresponding to the posterior wall of the left ventricle in one case (11.3 Hz), the posterior wall of the right ventricle in another (7.8 Hz), and the posterior zone of the junction between septum and right ventricle in the third (8.6 Hz). In the left ventricle no clear endo- to epicardial gradients were observed, though the right ventricle tended towards slightly higher values in the subendocardial recordings.

Conclusion: The distribution of activation frequencies during VF shows heterogeneous patterns, with no clear endo- to epicardial gradients. The maximum dominant frequencies are obtained in the posterior zones of both ventricles.

1917 | BEDSIDE
Multi-directional ventricular conduction on magnetocardiography predicts poor prognosis after CRT implantation
T. Nakashima1, H. Takaki1, S. Usami1, Y. Yamada1, H. Ookuma1, T. Aiba1, S. Yasuda1, S. Kamakura1, W. Shimizu1, M. Sugimachi2, S. Kusamichi2
1Depts of Cardiology, National Cerebral and Cardiovascular Center Research Institute, Suita, Japan; 2Department of Cardiovascular dynamics, National Cerebral and Cardiovascular Center Research Institute, Suita, Japan

Backgrounds: Cardiovascular resonance therapy (CRT) is an established option for advanced heart failure (HF) with electro-mechanical dyssynchrony. However, it provides no benefit in an approximately one third of the patients, which is unpredictable by any clinical tool. We hypothesized that (1) magnetocardiography (MCG) capable of delineating ventricular conduction sequences with high spatio-temporal resolution identify heterogeneous (multi-directional) left ventricular (LV) intraventricular conduction (presumably indicative of local block) and (2) it would hamper the CRT effect, thereby predicting poor prognosis after CRT implantation.

Methods: We analyzed 64-ch MCGs (1kHz) in 52 patients with advanced HF (LVEF 25±9%) and QRS prolongation (147±31ms) on ECG before CRT implantation. According to the QRS current arrow mapping, they were divided into Group-A with uni-directional heterogeneous ventricular conduction patterns (n=33) and Group-B with multi-directional heterogeneous ventricular conduction patterns (n=19). CRT responder was defined when LVEF > 15% or LVEF increased > 15%.

Results: Baseline LVEF, BNP, and NYHA class were comparable between the groups. After 6 months, responders were more frequently found in Group-A (27/33) than Group-B (4/19, p<0.01). More importantly, during the mean follow-up of 12 months, Kaplan-Meier analysis revealed a marked difference in mortality (death and LVAD implant, 0/33 in Group-A, 8/19 in Group-B, p<0.001).

Conclusion: Our MCG analysis indicated that prolonged but homogeneous LV conduction may represent a characteristic of the candidate who benefits from CRT, while the presence of multi-directional heterogeneous conduction may negate the efficacy of CRT, thereby predicting poor prognosis after CRT implantation.

1918 | BENCH
Assessment of leadless pacemaker performance
M. Bonner1, M. Eggel1, J. Depal01, T. Sheldon1, E. Williams1, Medtronic, Inc
Minneapolis, United States of America; 2Marquette University, Milwaukee, United States of America

Background: Since their invention, cardiac pacemakers have provided significant lifesaving therapy for millions of people. However, a device small enough to be placed within the heart would eliminate the pocket and the lead and thereby many of the modern pacemaker complications. We have created a 7-year VVIIR pacemaker with a volume less than 1 cc that can be placed directly within the heart. In this study, we assessed the performance of the device design by comparing the pacing thresholds, R-wave amplitudes, and impedances of leadless pacemaker prototypes using three separate methods of measurement.

Methods: One prototype was placed in the RV apex in each of 16 sheep via the jugular vein for a period of 6 weeks. The prototypes were constructed of a titanium main body, a distal titanium nitride coated pacing electrode with steroid, and a proximal titanium nitride ring. To allow direct measurement of the electrode potentials and currents, the electrodes were externalized through small wires that exited the prototype at the proximal end, passed through the jugular vein, and crossed the skin between the shoulder blades. The pacing thresholds, impedance and R-wave amplitudes were measured with both a breadboard of the pacemaker circuitry and a Medtronic 2290 pacing system analyzer at implant, and each week for 6 weeks.

Results: The pacing thresholds at 0.2 ms and the R-wave amplitudes measured in the analyzer and the breadboard can be seen in Figure 1. The measurements were similar between the two methods for both the threshold and R-wave measurements. In addition, both the thresholds and the R-wave amplitudes were stable over the 6-week study.

PRACTICAL ASPECTS OF BIOMARKERS IN HEART FAILURE

1935 | BEDSIDE
Prognostic value of NT-pro-C-type natriuretic peptide (NT-proCNP) in heart failure patients with preserved and reduced ejection fraction
D.J. Lok1, Y.T. Klip2, D.J. Van Veldhuisen2, P.W. Brugts3
1LUMC, Leiden, Netherlands; 2University Medical Center Groningen, Groningen, Netherlands; 3University Hospital N Lambrecht, Nijmegen, Netherlands

Background: BNP and NT-pro-BNP are established markers in chronic heart failure (HF). C-type Natriuretic Peptide (CNP) belongs to the same peptide family. However, C-PNP data are not available of CNP asмаркermarker of HF.

Objective: To assess the prognostic power of the N-terminal pro-CNP (NT-proCNP) in HF.

Methods: In 571 patients, NT-proCNP was measured at discharge. Primary end-point was a composite endpoint of all-cause mortality and HF hospitalization after 18 months. Secondary endpoint was all-cause mortality after 3 years.

Results: Mean age was 71±11 years, 62% was male and left ventricular ejection fraction (LVEF) was 32±14%. In a multivariate linear regression model, NT-proCNP showed a positive correlation with NT-proBNP and a negative correlation with renal function and female sex. 240 Patients reached the composite endpoint and 254 died. Interaction analysis revealed a strong interaction between NT-proCNP and LVEF for both endpoints (p-value for interaction: 0.003 respectively 0.008). Therefore further analysis was stratified into patients with a reduced (HFrEF) or preserved (HFpEF) LVEF. In multivariate analyses, each doubling of NT-proCNP and NT-proBNP was associated with a 2.4-fold and 2.3 fold increase in death, respectively.
NT-proBNP was strongly predictive for both the primary (HR 1.72; 95% CI 1.28-2.32; P<0.001) and secondary endpoint (HR 1.72 (1.27-2.34; P<0.001) in patients with HFpEF, but not in patient with HFrEF.

Hazard ratios for doubling of NT-proBNP

<table>
<thead>
<tr>
<th>NT-proBNP (doubling)</th>
<th>HFpEF</th>
<th>p-value</th>
<th>HFpEF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality 3 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvariable</td>
<td>1.41 (1.15–1.72)</td>
<td>0.001</td>
<td>1.91 (1.50–2.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 1</td>
<td>1.37 (1.11–1.69)</td>
<td>0.001</td>
<td>1.81 (1.42–2.30)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.04 (0.82–1.33)</td>
<td>0.714</td>
<td>1.74 (1.26–2.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 3</td>
<td>0.89 (0.66–1.19)</td>
<td>0.418</td>
<td>1.72 (1.28–2.30)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Model 1: adjusted for age and sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2: adjusted for model 1 and additionally adjusted for NT-proBNP levels (doubling)</td>
<td>Model 3: adjusted for model 1 and additionally adjusted for all CCM risk engine variables (age, sex, diastolic blood pressure, pulse pressure, previous heart failure hospitalization, sodium level, renal and a medical history of stroke, myocardial infarction, diabetes, atrial fibrillation or peripheral artery disease).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: NT-proBNP is a strong independent marker for outcome in patients with HFpEF.

1938 | BEDSIDE

Plasma level of NT-proBNP in elderly population in Poland - the PolSenior study

P. Nadrówski1, J. Chudek1, T. Grodzicki2, M. Mossakowska4, M. Skrzypk6, A. Wieck6, K. Kozakiewicz1. 1Upper Silesian Heart Centre, 3rd Department of Cardiology, Katowice, Poland; 2Medical University of Silesia, Department of Pathophysiology, Katowice, Poland; 3 Jagiellonian University Medical College, Department of Internal Medicine and Gerontology, Krakow, Poland; 4International Institute of Molecular and Cell Biology, Warsaw, Poland; 5Medical University of Silesia, Department of Epidemiology, Katowice, Poland; 6Medical University of Silesia, Department of Nephrology, Endocrinology and Metabolic Diseases, Katowice, Poland

Purpose: Left ventricular remodelling following ST-elevation myocardial infarction (STEMI) is associated with the occurrence of increased NT-proBNP in elderly patients with HFpEF, but not in patients with HFrEF.

Background: The brain natriuretic peptides (BNP, NT-proBNP) are useful diagnostic markers of Heart Failure (HF), as exemplified by the ESC Heart Failure guidelines. The PolSenior project was an epidemiological study carried out to examine medical, psychological and socioeconomic aspects of aging in Poland. The aim of this study is an etiological and descriptive analysis of HF based on elderly population from the PolSenior Study, stratified by NT-proBNP concentration values.

Material and methods: The research sample included 4979 respondents (2567 males and 2412 females) split into six equally sized age groups of elderly subgroups. The study consisted of three visits performed by trained nurses and included a questionnaire survey, comprehensive geriatric assessment and blood and urine sampling with more than 50 biochemical parameters measured. Serum NT proBNP was measured by Electrochemiluminescence method (ECLIA).

Results: The prevalence of Chronic Kidney Disease (CKD) (77.8%) and atrial fibrillation (39.5%), number of hospitalizations (23.7%) and a history of cardiovascular disease. The relationship between age and the 5th centile of EF derived from the PolSenior Study, stratified by NT-proBNP values. The PolSenior project was an epidemiological study carried out to examine medical, psychological and socioeconomic aspects of aging in Poland. The aim of this study is an etiological and descriptive analysis of HF based on elderly population from the PolSenior Study, stratified by NT-proBNP concentration values.

Conclusions: We conclude that CKD and atrial fibrillation but not hypertension are associated with the occurrence of increased NT-proBNP in elderly population. On contrary, overweight or obesity are associated with lower level of NT-proBNP in elderly.

1937 | BEDSIDE

Admission NT-proBNP levels better predict subsequent left ventricular remodelling than infarct size and salvage index assessed by cardiac magnetic resonance

N.A. Razni1, L.L. Ng2, G.P. Macnair3, I.B. Squire2. 1NIHR Leicester Cardiovascular Biomedical Research Unit, Leicester, United Kingdom; 2University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom

Purpose: Left ventricular remodelling following STElevation myocardial infarction (STEMI) is associated with worse outcomes. NT-proBNP is a predictor of LV systolic impairment and adverse outcomes. We assessed the relationship of NT-proBNP with infarct characteristics assessed by cardiac magnetic resonance (CMR) in patients presenting with first STEMI treated by primary percutaneous coronary intervention (PPCI).

Methods: Forty-seven consecutive patients (mean age 60.5±12.3 years, 42 male) with first STEMI treated by PPCI (median time to reperfusion 150 minutes, IQR 120 minutes) had NT-proBNP levels sampled during admission (median 42 hours, IQR 25 hours). Patients underwent CMR examination (median day 2, IQR 2 days) with follow up CMR at 4 months. Spearman’s rank correlation was used to assess the association between admission NT-proBNP and infarct characteristics, and subsequent left ventricular end systolic volume index (LVESVI) and ejection fraction (EF) at 4 months. Regression analysis of CMR assessed infarct characteristics was used to determine univariate and multivariate predictors of NT-proBNP.

Conclusions: NT-proBNP was compared to CMR assessed infarct characteristics - to determine remodelling assessed as LVESVI and EF at four months.

NT-proBNP, IS, MVO, IMH and AAR correlated significantly with 4 month EF while NT-proBNP, MVO and IMH correlated significantly with ESVI at 4 months. These were entered into multivariate linear regression analysis for predictors of ESVI and EF. NT-proBNP was the only significant predictor of ESVI (r=0.407, P<0.0005) and EF (r=0.465, P<0.0005) at 4 months.

Results: Infarct size (IS), microvascular obstruction (MVO), intramyocardial haemorrhage (IMH), Oedematous Area-at-risk (AAR) and myocardial salvage index (MSI) all correlated with admission NT-proBNP, and were significant univariate predictors of NT-proBNP. On multivariate regression analysis entering all infarct measures, MVO remained the only significant predictor of NT-proBNP (r=0.572, P<0.019).

Conclusions: NT-proBNP is a better predictor of LV remodelling (ESVI and EF at 4 months) than infarct size and CMR assessed infarct characteristics.

Early NT-proBNP measurement at admission might select patients at subsequent risk of LV remodelling.

1938 | BEDSIDE

What is normal left ventricular ejection fraction? a global individual person data meta-analysis of the distribution across ethnicity, gender and age

K.K. Pope on behalf of The EchoNoMAL Collaboration. The University of Auckland, Auckland, New Zealand

Purpose: Left ventricular (LV) ejection fraction (EF) is a ubiquitous measurement of systolic function used to define and assess the severity of LV dysfunction, guide management and assess prognosis. However consistent regarding the lower limit of normal EF is lacking. This study explores the distribution of EF to determine normative reference values by gender and ethnicity.

Methods: We performed an individual person data meta-analysis of population-based echocardiographic (echo)studies of volunteers. Demographics, clinical history, height, weight, BP, glucose, and echo measurements were collated. In this analysis we studied EF in adults without hypertension, diabetes, renal or cardiovascular disease. The relationship between age and the 5th centile of EF derived from 2D volume estimates (Simpson single or biplane, or area-length methods) was modelled using quantile regression. The predicted value of the 5th centile was considered the lower reference value (LRV) and is presented with a 95% confidence interval. Gender-specific models were created within each ethnic group. Data are reported for people of European (E), Asian (A) and South Asian (SA) descent, aged ≤70 years.

Results: 21317 healthy subjects from 41 studies, 50% men. EF available in: 6398 E, 926 A, 1324 SA. Among E, the LRV for EF at 50 years was 49% for men and 50% for women. Among A, EF at 50 years was 56% for men and 57% for women. Among SA men, EF at 50 years was 54% which was higher than but lower than A. Among SA women, EF was the same as A women (57%). There were small but significant increases in the LRV across age in E men and women, and a difference in LRV suggested between genders for SA (table).

LRV (95% Cl) of ejection fraction (%) by gender and age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80-89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: This large study shows that reference values for EF in healthy adults are associated with ethnicity, and among SA may be associated with gender. Ethnicity and gender are important factors to consider when assessing left ventricular systolic function.