formed the published AHEAD-U score in AHF with net reclassification improvement by 7% for total mortality and 25% for cardiovascular mortality (Table).
Conclusion: UR-HEARt score may improve the risk stratification in Asian patients with AHF. Whether or not UR-HEARt score could be generalized to other populations warrant further studies.

P6544
All you need is LE: utility of an abbreviated LACE score in predicting 30-day outcomes among patients hospitalized for Heart Failure (HF)

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Background: Length of stay, Acuity, Comorbidities, and Emergency department (ED) visits (LACE) can predict 30-day clinical outcomes when measured at the point of care (POC) in patients hospitalized for HF. However Comorbidities (C) are difficult to score and most patients likely present with high Acuity (A).
Purpose: To determine whether an abbreviated LACE score, based only on Length of stay and number of ED visits in the prior 6 months (LE), can reliably predict 30-day readmission and 30-day composite readmission/death when used at the POC in patients hospitalized for HF.
Methods: This is a sub-study of the Patient-Centered Care Transitions in HF (PACT-HF) pragmatic stepped wedge cluster randomized trial, which implemented transitional care services for HF across 10 hospitals in Canada. We included patients hospitalized for HF and discharged alive. We measured LACE and LE at the POC, and obtained 30-day clinical outcomes via linkages to administrative databases. We used log-binomial regression models with either LACE or LE as the predictor and either 30-day all-cause readmission or 30-day composite all-cause readmission/death as the outcome. We assessed risk with risk ratios (RR) and 95% confidence intervals (CI); model discrimination with C-statistic; and model calibration with a Hosmer-Lemeshow test. We adjusted all models for PACT-HF services received, and internally validated the models using bootstrapping.
Results: Of the 1,985 patients included in the analysis, 49.4% were female. Mean age was 78.1+12.1 years and mean LVEF was 45.6+14.9%. Most patients (99.0%) presented with high Acuity (A). Mean LACE and LE scores were 12.4+ 2.7 and 6.8+ 2.0, respectively. Within 30 days of discharge, 20.9% of patients were readmitted and 23.1% were either readmitted or died. LACE had modest discrimination in predicting 30-day readmission (RR 1.12 [95% CI 1.09–1.16] per unit increase; C-statistic 0.617 [95% CI 0.586–0.648]) as well as 30-day readmission/death (RR 1.14 [95% CI 1.10–1.17]/unit increase; C-statistic 0.621 [95% CI 0.592–0.651]). Compared to LACE, increments in LE predicted: (i) a higher risk of 30-day readmission (RR 1.18 [95% CI 1.13–1.23]/unit) with slightly improved risk discrimination (C-statistic 0.624 [95% CI 0.593–0.655]); and (ii) a higher risk of 30-day composite readmission/death (RR 1.25 [95% CI 1.16–1.35]/unit) with slightly improved risk discrimination (C-statistic 0.629 [95% CI 0.600–0.659]). The LE score demonstrated good model fit for the outcome of 30-day readmission (p=0.07) and 30-day readmission/death (p=0.33).
Conclusion: Among patients hospitalized for HF, the simple LE score predicted a higher risk of 30-day readmission and 30-day composite readmission/death than the more complex LACE score, with slightly improved ability to distinguish between patients who did and did not experience the outcomes. The LE score can be used instead of LACE at the POC to predict 30-day outcomes in patients hospitalized for HF.
Funding Acknowledgements: Canadian Institutes of Health Research, Ontario's Ministry of Health and Long Term Care Health System Research Fund, HHS Career Award

P6545
Does rhythm matter in acute heart failure? An insight into clinical outcomes from the British Society for Heart Failure national audit

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Background: Atrial fibrillation (AF) is the most common sustained arrhythmia in patients with acute Heart Failure (AHF). The presence of AF is associated with adverse prognosis in patients with chronic Heart Failure (CHF) but little is known about its impact in acute Heart Failure.
Methods: Data was collected between April 2007 to March 2013 across 185 (>95%) hospitals in England & Wales for patients with a primary death from, or a discharge diagnosis of AHF. We investigated the association between the presence of AF and all-cause mortality during the index hospital admission and at 30 days and 1 year post-discharge using shared frailty Cox proportional hazard models.
Results: Of 96,593 patients admitted with AHF, 44,642 (46%) were in sinus rhythm (SR) and 51,951 (54%) in AF. Patients with AF were older (mean age 79.8 (79.7–80) versus 74.7 (74.5–74.7) years; $p<0.001$), but had a lower prevalence of diabetes, acute myocardial infarction and left ventricular systolic dysfunction (LVSD) than those in SR. In a multivariable analysis, AF was independently associated with mortality at all time points, in hospital (HR 1.15, 95% CI 1.09–1.21, $p<0.0001$), 30 days (HR 1.13, 95% CI 1.08–1.19, $p<0.0001$), and 1 year (HR 1.09, 95% CI 1.05–1.12, $p<0.0001$). In subgroup analyses, AF was independently associated with worse 30 days outcome irrespective of sex, ventricular phenotype and in all age groups except in those who aged between 55–74 years (Hazard ratio 1.04 (CI 0.85–1.29, p=0.69).
Conclusion: AF is independently associated with adverse prognosis in AHF during admission and up-to one-year post discharge. As the clinical burden of concomitant AF and AHF increases, further refinement in the detection, treatment and prevention of AF-related complications are necessary to effectively improve patient outcome.

NOVEL ASPECTS IN ATHEROSCLEROSIS

P6546
Thrombospondin-1 is involved in human saphenous vein graft remodelling in response to coronary hemodynamic conditions

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Background: Despite the preferred application of arterial conduits, the greater saphenous vein (SV) remains indispensable for coronary artery bypass grafting (CABG), especially in multi-vessel coronary artery disease. Early remodeling induced by altered wall mechanics has been recognized to play a key role in SV graft disease. The mechanism remains, however, unknown.
Purpose: The purpose of this work was to unveil the existence of a mechanical effect in SV graft failure, due to changes in the hemodynamic conditions occurring in SV grafts after transplantation into coronary position.
Methods: SV segments from patients receiving coronary artery bypass grafts were stimulated in a coronary "pulse-duplicator" bioreactor with either CABG or venous hemodynamic conditions. After 7 (n=6) or 14 (n=5) days, stimulated SVs were fixed, sectioned and stained by immunofluorescence. SMCs isolated from SVs of 7 patients undergoing saphenectomy were subjected to uniaxial cyclic strain (10% elongation, 1 Hz) for 24 or 72 hours using the Flexcell platform. SMC responses were analyzed with western blot, ELISA, qPCR, and mass spectrometry-based secretome analysis.
Results: CABG stimulation induced media thinning (from 345±29 to 247±40 μm at t14) due to apoptosis of medial cells (5-fold increase) in the first week. In addition, compared to venous conditions, CABG-stimulated SVs exhibited a marked decrease of cells positive for contractile SMC markers SM alpha actin (32±10 vs 79±5% in ctrl, P=0.007) and calponin (41±9 vs 71±5% in ctrl, P=0.03) at t14. Interestingly, we observed a remarkable elevation in the number of cells expressing mesenchymal (CD44) and early SMC (SM22α) markers after 14 days in the media; these cells were likely recruited from the SV adventitia. CD44+ cells also co-expressed PCNA, revealing proliferation. To allow mechanistic studies, SMCs were isolated from the SV and mechanically stretched in vitro. Results of western analysis confirmed loss of contractile marker SM alpha actin and increased expression of synthetic marker vimentin at 72 hours. Since SMC straining may induce release of factors directing CD44+SM22α+ cells, we analyzed factors released by strained SMCs by mass spectrometry. Results identified consistent Thrombospondin-1 (TSP-1) release by SMCs after both 24 and 72 hours ($P<0.05$). Mass spectrometry data were validated using Western analysis, ELISA and qPCR. TSP-1 release in the media of SVs was also confirmed ex vivo in CABG-stimulated samples. Finally, preliminary in vitro results suggest that TSP-1 functions as a chemoattractant for adventitial SV progenitor cells.
Conclusions: The present data suggest the existence of a "mechano-paracrine" effect due to CABG-specific wall strain in SV grafts. This process has consequences for recruitment of adventitial progenitor cells, and a fibrotic-like process possibly involved in pathologic programming of SV graft failure.

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Funding Acknowledgements: The present work was supported by a Health Research Grant (Ricerca Finalizzata: RF-2011-02346867).

P6547
Relation of relative telomere length and cardiovascular disease in the population

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Introduction: Telomeres are tandem repeats of DNA sequences located at the chromosomal ends that function to stabilise the genetic structure. The relevance of telomeres has been shown for different human disorders including cardiovascular disease. Yet, the majority of these studies was performed in disease specific cohorts with small samples sizes.
Purpose: The aim of this study was to evaluate the association of relative telomere length (RTL) with cardiovascular risk factors and cardiovascular disease in a large population based cohort.
Methods: RTL was measured according to a previously validated real-time quantitative polymerase chain reaction technique in subjects of the Gutenberg Health Study (n=5000). An association study of RTL with cardiovascular risk factors smoking status, LDL, HDL, triglycerides, BMI, systolic and diastolic blood pressure as well as an association study of RTL with cardiovascular diseases heart failure with reduced ejection fraction (HF-REF), heart failure with preserved ejection fraction (HF-PEF), myocardial infarction (MI), family history of MI, coronary artery disease (CAD) and atrial fibrillation (AF) was performed.
Results: A significant association was found between RTL and smoking status (effect -0.016, p=0.048), however, no association was found with lipid levels, blood pressure and BMI. For cardiovascular disease, a moderate association was found with heart failure with preserved ejection fraction (effect: -0.030, p=0.062). Interestingly, RTL also associated significantly with the surrogate biomarkers of heart failure NT-proBNP (effect: -0.007, p=0.009) as well as Troponin I (effect: -1.495, p=0.040). In contrast, no association of RTL was found with HF-REF, MI, family history of MI, CAD, AF.
Conclusion: In a large population based study, RTL showed only moderate association to smoking and markers of heart failure, however for the majority of cardiovascular diseases no significant association was detected.

P6548
Werner syndrome gene mutation is responsible for cardiac aging with transition from diastolic to systolic LV dysfunction

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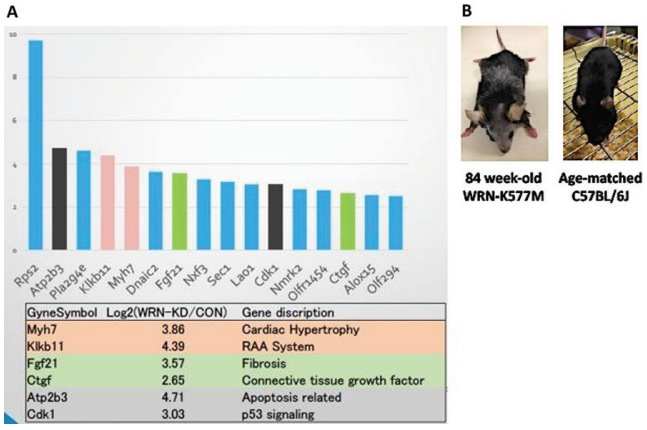
Background/Introduction: Werner syndrome is a premature aging disorder caused by dysfunction of the DNA-helicase-regulatory protein (WRN). However, there is little information whether progeria may link to cardiac aging. Amino acid (AA) substitution of WRN at position 577 (WRN-K577M) has been reported to abolish the ATPase and helicase activities and its mutant mice exhibits accelerated skin aging.
Purpose: We aimed to elucidate whether WRN-K577M is responsible for cardiac aging in mice.
Methods: C57/BL6-based mutant mice harboring WRN-K577M were evaluated at 18 week-old and 84 week-old.
Results: At 18-week-old (18w-WRN-K577M), appearance of WRN-K577M was normal. However, cardiac aging markers (p53 and γH2AX) and apoptosis detected by TUNEL were augmented in 18w-WRN-K577M (p53 in WRN-KD versus CON; 1.20 fold increase, γH2AX in WRN-KD versus CON; 1.78 fold increase, $P<0.05$). Body weight of 18w-WRN-K577M was similar to the age-matched control mice, however, 18w-WRN-K577M exhibited cardiomegaly (in mg; 130±7 for 18w-WRN-K577M and 113±5 for wild). 18w-WRN-K577M exhibited diastolic left-ventricular (LV) dysfunction, whereas their systolic LV function was preserved, with concomitant cardiac fibrosis and hypertrophy. Consistently, hypertrophy-associated signaling was elevated (mTOR in WRN-KD versus CON; 1.4 fold, AKT; 1.4 fold, ERK; 1.4 fold). DNA microarray analysis of 18w-WRN-K577M heart revealed that the 253 genes was upregulated compared to wild-type. Among them, 16 genes were increased >4 fold higher than wild (Figure A). KEGG ontology revealed that characteristics of these genes were as follows: hypertrophy (Myh7, Klkb11), fibrosis (Fgf21, Ctgf), and inflammatory molecules (Ap1s3, Pla2g2e, Has1, MMP9). Notably, 18w-WRN-K577M exhibited normoglycemia. In contrast, at 84-week-old, WRN-K577M exhibited significant hair loss, retarded locomotive behavior (Figure B), systolic LV dysfunction (LVFS; 26.2±2%) and decline in LV wall thickness with consistent decrease in cardiomyocyte size and increase in cardiac fibrosis and apoptosis.
Conclusion(s): We report the impact of WRN-K577M on chronical cardiac aging. The WRN-K577M at earlier age is responsible for diastolic LV dysfunction related to cardiac hypertrophy and fibrosis via enhanced gene alteration related to cardiac remodeling and inflammation independently of glucose metabolism. The WRN-K577M mutation is responsible for not only phenotype of systemic progeria but also for transition from the diastolic to systolic LV dysfunction observed in progeria.



GyneSymbol	Log2(WRN-KD/CON)	Gene discription
Myh7	3.86	Cardiac Hypertrophy
Klkb11	4.39	RAA System
Fgf21	3.57	Fibrosis
Ctgf	2.65	Connective tissue growth factor
Atp2b3	4.71	Apoptosis related
Cdk1	3.03	p53 signaling

Figure 1

P6549
Inflammasome-induced endothelial microparticles impair cellular function in arterial smooth muscle cells

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Background: The inflammasome is a multimeric protein complex that is activated by danger signals such as cholesterol crystals, oxidized LDL or ATP to stimulate inflammatory responses in atherogenesis through proinflammatory mediators like caspases and cytokines. Microparticles (MP) are extracellular vesicles that are released by activated or apoptotic cells. Although MP also serve as a physiological mechanism of communication between cells, deleterious effects of microparticles have been found in numerous diseases. The body of evidence indicates that endothelial microparticles contribute to the development and complications in atherosclerosis. With this study we sought to elucidate the effects microparticles, that are discharged by inflammasome activated endothelial cells, exert on arterial smooth muscle cells.
Methods and results: RTPCR experiments showed that activation of human coronary artery endothelial cells (HCAEC) with inflammasome activators (LPS+Nigericin) leads to NLRP3-Inflammasome-specific upregulation of NLRP3, Caspase-1 and IL1β. Analysis of the supernatant of aforementioned cells via FACS- and electron microscopy experiments revealed time dependent release of endothelial microparticles (EMP), while western blot demonstrated that EMP enclose active Caspase-1.
Fluorescence microscopic imaging illustrated incorporation of EMP by heart coronary artery smooth muscle cells (HCASMC). Examining the effect EMP exert on HCASMC, a detrimental biological effect was detectable, as Scratch Assay showed decreased migration and proliferation, and viability assay proved an extenuated number of viable cells after 8h treatment. Moreover, a significant increase in mRNA-levels of NLRP3, IL1β and VCAM was verified by RTPCR, while IL1β-ELISA showed increased secretion of selfsame cytokine. Treatment of EMP with NLRP3-Inflammasome inhibitors isoliquiritigenin (ILG) and dimethyl sulfoxide (DMSO) revealed diminishment of cytotoxic effects. Examination of cellular reactions of HCASMC upon conventional activation of the NLRP3-Inflammasome (LPS+Nigericin) revealed that HCASMC also release microparticles, as shown by flow cytometry and electron microscopy. Similar to EMPs smooth muscle cell microparticles (SMP) demonstrated cytotoxic properties when incubated with endothelial cells.
Conclusion: Our findings verify that MPs released from inflammasome-activated HCAEC are incorporated by HCASMC which in turn sustain a reduction of cell viability, migration and proliferation. EMP effectuate activation of the NLRP3-Inflammasme in their target cells. The cytotoxic effects of EMP are suppressed by inhibitors of the NLRP3-Inflammasome. Furthermore inflammasome-activated HCASMC exhibit the ability to release microparticles equally.
Our findings indicate that inflammasome activation is transferable through microparticle-associated communication which in turn facilitates cell death.
Funding Acknowledgements: Else Kröner-Fresenius-Foundation

P6550
Apoptotic and non-apoptotic circulating microparticles appear to exert opposing effects on the endothelial function and inflammatory status of patients with acute coronary syndromes

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Background: Endothelial apoptotic microparticles (MPs) have been implicated

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