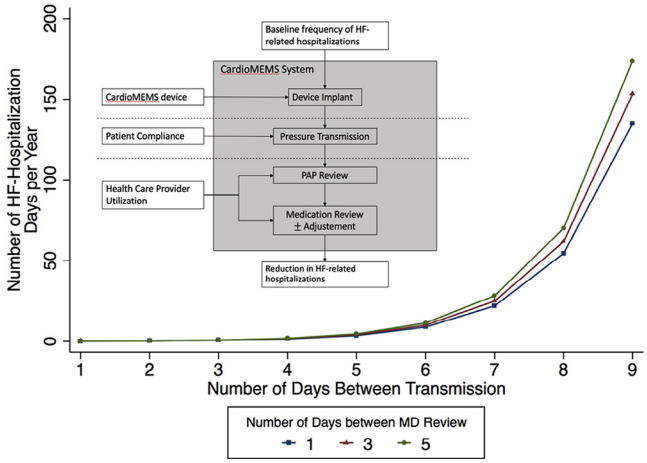

063

Fibulin-3 as a Potential Therapeutic Target for Cardiac Fibrosis

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Background: Cardiac fibrosis is the final common pathway of every cardiac disease. The consequence is a stiff, dysfunctional heart, and the long-term outcome is inevitable progression to heart failure or death. Despite its prevalence in cardiac disease, we do not have effective treatments. We have recently demonstrated that a novel extracellular matrix protein, fibulin-3 (Fib3) is significantly upregulated in the aging, fibrotic mouse heart and following experimental myocardial infarction (MI). We therefore hypothesise that Fib3 causes cardiac fibrosis in aging and diseased hearts. **Aim:** To define the role of Fib3 in cardiac fibrosis to uncover a novel therapeutic target that may be used to prevent and treat the fibrosis associated with heart failure. **Methods:** We have recently developed a Fib3 knockout mouse (Fib3-/-) to define the role of Fib3 in normal and fibrotic hearts. Experimental MI was performed on WT and Fib3-/- mice (n = 4 and 9, respectively; aged 3–4 months). Histological analysis was performed on the left ventricles of mice that survived to 28 days. Phenotypic changes in aging Fib3-/- mice vs aging WT were also investigated (aged 8–10 months). Histological analysis was performed on aortic (n = 2 and 4, respectively) and skin samples (n = 3 and 6, respectively) from these mice. **Results:** Fib3-/- mice had a higher incidence of cardiac rupture in the first week post-MI (cardiac rupture: n = 5 of 9, Fib3-/- vs n = 0 of 4, WT). Preliminary histological analysis suggested a trend towards increased infarct area (26.9 ± 12.5 vs 9.7 ± 2.8%) and circumferential extent of infarct (58.6 ± 13.9 vs 24.0 ± 6.8%) in Fib3-/- vs WT, respectively. All ageing Fib3-/- mice (n = 6) developed hernias, including inguinal hernias, pelvic prolapse and sternal hernias with xiphoid protrusion at 6–8 months (7.3 ± 0.8 months). Preliminary histological analysis suggested dilated and thickened aortic walls; and decreased subcutaneous fat. **Conclusions:** These results suggest that Fib3 is an essential component of connective tissue and plays a key role in myocardial scar formation following MI. It may therefore represent a novel therapeutic target.

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Simulation in Heart Failure: Improving the Use of Guideline-Directed Care

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Introduction: Many physicians are not applying guideline recommendations to optimize treatment of patients with heart failure (HF). Due to a multitude of factors, including physician-associated barriers, HF is associated with a significant health burden, resulting in more than 1 million hospitalizations per year. **Hypothesis:** An online, simulation-based continuing medical education (CME) intervention could improve performance of cardiologists and primary care physicians (PCPs) in the management of patients with HF. **Methods:** The CME intervention consisted of two cases presented in a virtual patient simulation (VPS) platform that allowed learners to make clinical decisions on lab tests, diagnoses and treatments matching the scope and depth of actual practice. Clinical decisions made by the learners were analyzed using a sophisticated decision engine, and tailored clinical guidance (CG) was provided based on current evidence and expert recommendations. Learner decisions were collected post-CG and compared with each user's baseline (pre-CG) data using a 2-tailed paired T-test to determine statistical significance. The activity launched on May 25, 2016 and data were collected through August 15, 2016. **Results:** Significant absolute improvements were observed after clinical guidance:Case 1 (n = 431 cardiologists; n = 240 PCPs): • -39% improvement among cardiologists (3% pre-CG vs 42% post-CG; $P < .001$) and 15% improvement among PCPs (6% vs 52%; $P < .001$) in ability to accurately diagnose and stage HF • - 41% improvement among cardiologists (6% vs 47%; $P < .0001$) and -35% improvement among PCPs (13% vs 48%; $P < .001$) in appropriate orders to start a bioavailable loop diuretic • -15% improvement among cardiologists (53% vs 68%; $P < .001$) and -18% improvement among PCPs (48% vs 66%; $P < .001$) in orders for patient education and counseling Case 2 (n = 215 cardiologists; n = 167 PCPs): • -37% improvement among cardiologists (16% vs 53%; $P < .001$) and -45% improvement among PCPs (8% vs 53%; $P < .001$) in appropriate orders for ivabradine • -20% improvement among cardiologists (49% vs 69%; $P < .001$) and -17% improvement among PCPs (51% vs 71%; $P < .001$) in orders for weight management • -20% improvement among cardiologists (53% vs 73%; $P < .001$) and -20% improvement among PCPs (53% vs 73%; $P < .001$) in orders for coordination of care. **Conclusion:** This study demonstrates that CME utilizing VPS methodology that immerses and engages clinicians for an authentic, practical and consequence-free learning experience can improve evidence-based clinical decisions of specialists related to the management of HF. **Clinical Implications:** Using VPS-based CME to improve performance of cardiologists and PCPs has the potential to translate into improvements in clinical care and patient outcomes.

065

MAGGIC Score and Seattle Heart Failure Model are Less Reliable in Heart Failure with Preserved Ejection Fraction and Nonischemic Cardiomyopathy

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Introduction: We studied the performance of MAGGIC score and Seattle Heart failure Model (SHFM) in predicting 1-year mortality (1YM) among patients enrolled in a CHF clinic. **Methods:** Patients enrolled in the CHF clinic at least 1 year prior to the study were included for analysis (n = 134). Predicted 1YM calculated using MAGGIC and SHFM was compared to observed 1YM (death within 1 year of clinic enrolment). **Results:** 100 patients had EF < 50% (HFr+mrEF) and 34 had EF ≥ 50% (HFpEF). 74 patients had ischemic cardiomyopathy (ICM) and 60 had nonischemic cardiomyopathy (NICM). 35 patients died within 1 year of enrolment. The overall observed 1YM (26%) was slightly higher than 1YM predicted by MAGGIC (23%) and SHFM (23%). In HFpEF the observed 1YM was significantly higher (38%) than predicted by MAGGIC (20%) and SHFM (24%). Binomial logistic regression (Wald χ^2) showed significant correlation between predicted and observed 1YM in the entire cohort, HFr+mrEF and ICM but not in HFpEF or NICM (fig. 1). Predicted 1YM was higher among dead patients in the entire cohort (MAGGIC: 29% vs. 21%, $P = .005$; SHFM: 28% vs. 21%, $P = .045$) as well as patients with HFr+mrEF and ICM (figs. 2 & 3). On the contrary in HFpEF and NICM predicted 1YM was similar among patients dead or alive at 1 year (figs. 2 & 3). **Discussion:** Both MAGGIC and SHFM significantly underestimated 1-year mortality in HFpEF by 47% and 36% respectively. In HFpEF and NICM, the predicted 1YM for an individual patient did not correlate well with the observed 1YM. Also the

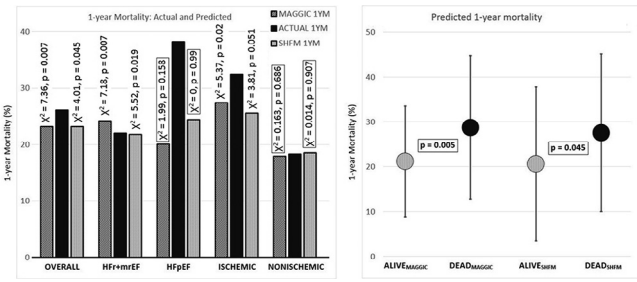

Fig. 1.

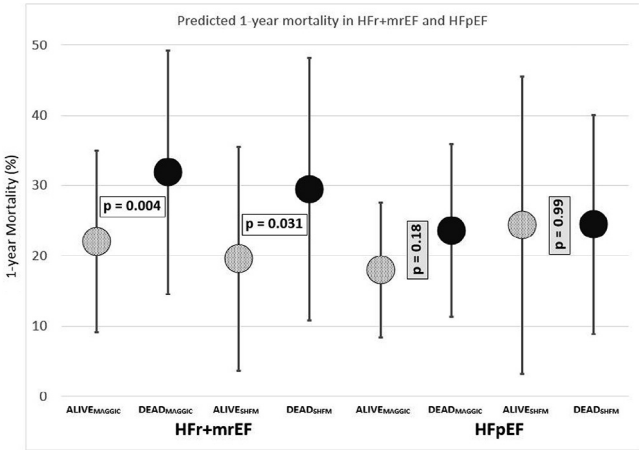

Fig. 2.

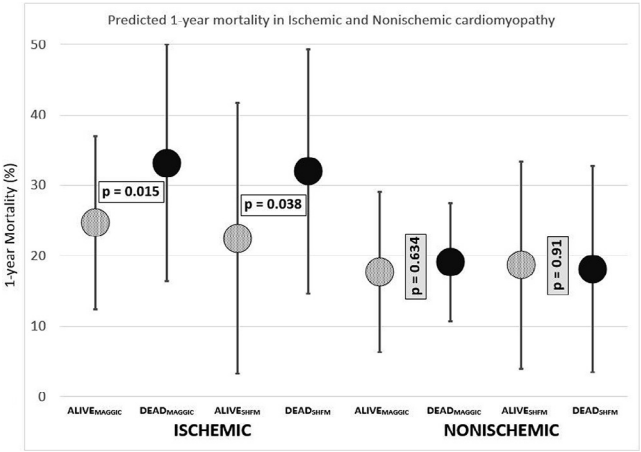

Fig. 3.

predicted 1YM among dead patients was similar to patients alive at 1 year in HFpEF and NICM. This affects the reliability of MAGGIC or SHFM in predicting 1 year mortality in patients with HFpEF or NICM. **Conclusion** MAGGIC and SHFM are less reliable for predicting 1 year mortality in HFpEF and NICM compared to HFr+mrEF and ICM.

066

Real-Time Assessment of Patient Reported Outcomes in Heart Failure Clinic

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Introduction: Patient-reported outcomes (PROs) are commonly used in clinical trials to assess patient health-related quality of life (hrQoL), but PRO implementation in daily practice is rare. We sought to develop a novel approach to integrate PROs within routine clinical practice at a heart failure (HF) clinic. **Methods and Results** Technical implementation of PRO capture was facilitated by the University of Utah mEVAL Personal Health Assessment team. We deployed a computer program on portable computers (iPad) to collect PRO instruments of interest—Kansas City Cardiomyopathy Questionnaire & physical function, depression, fatigue, and satisfaction with social roles domains of Patient-Reported Outcomes Measurement Information System—PROMIS. We initiated an automated algorithm through which patients are identified at registration for clinic, provided with iPAD and asked to complete the PROs (Fig. 1A). Through secure data transfer, PROs are scored and made immediately available in the electronic health

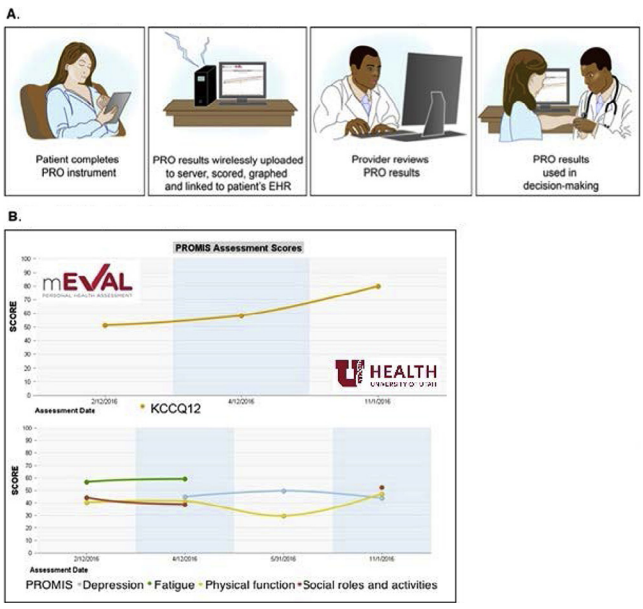

Fig. 1. A. Flow of PRO capture, scoring, upload to EHR and use in clinical care. B. Graphical display of PRO results in eletronic health record.

Table 1. Scores of completed patient-reported outcome assessments

Instrument Name	Sample Size	Median Score	25th Percentile	75th Percentile
KCCQ-12	804	57	39	74
PROMIS-Depression	714	50	45	57
PROMIS-Fatigue	788	55	48	61
PROMIS-Physical Function	719	41	35	47
PROMIS-Satisfaction Roles Activities	791	45	39	51

record (EHR) (Fig. 1B). We also conducted provider training in PRO score interpretation. In 2016, serial PRO assessments were done in 685 patients (age 60.1 ± 16.3 yrs, 66% male, average completion time 6.7 min), which represented a 58% completion rate among eligible patients. PRO results indicated marked reduction in hrQoL in a large number of the patients—Table 1. The original design was to collect PROs at 3 month intervals; early experience indicated that it was more useful to collect these at each visit and share the results with patients. This is expected to improve completion rates. **Conclusion** PRO capture during routine clinical care with real-time EHR uploads is feasible in a large HF outpatient population. Ongoing efforts will better determine how best to share this information with patients and will provide data regarding the utility of routine PRO use in clinical care. While PROs are being proposed as required metrics of quality of health care delivery, our approach intends to make these measures actionable in real-time clinical care.

067

Stroke and Myocardial Infarction Risk among Newly Diagnosed Heart Failure Patients with Reduced, Borderline, and Preserved Left Ventricle Ejection Fraction

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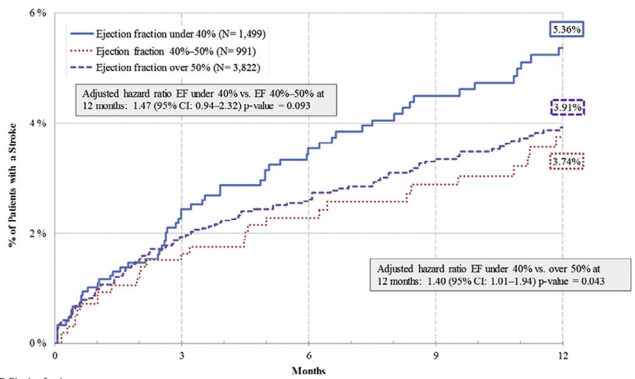
Introduction: There is limited data on contemporary cardiovascular (CV) event rates among heart failure (HF) patients with preserved or reduced ejection fraction (EF) in community practice. Our goal was to determine the association between EF and CV events in the HF population. **Hypothesis:** Among HF patients, those with reduced EF [<40%] will have higher CV event rates than those with borderline [40%-50%], or preserved [≥50%] EF (2013 ACC/AHA/HFSA guidelines). **Methods:** Using Integrated Claims/EHR data from Optum, we analyzed a cohort of adult patients newly diagnosed with a HF hospitalization or an emergency room visit between 07/2009 and 09/2016. Patients with a measurement of EF within a window of ±90 days around the index date were stratified by EF. Subsequent adverse CV events after index HF discharge were identified by a primary diagnosis documented during a hospitalization. Kaplan-Meier rates for stroke and acute myocardial infarction (MI) were evaluated over a 1-year period and differences were assessed using Cox proportional hazard models adjusting for baseline characteristics. **Results:** A total of 7,005 HF patients were included in the study of which 1,622, 1,095, and 4,288 formed the reduced, borderline and preserved EF cohorts, respectively. Patients in the preserved EF (pEF) cohort were older (74 vs. 72–73 years) and were mostly female (55% vs. 36–38%) compared with both reduced and borderline EF (rEF and bEF) cohorts. Compared with those with bEF and pEF, those with rEF had higher observed rates and adjusted risk for stroke at 1 year (5.4% vs 3.7% [bEF] and 3.9% [pEF], adjusted HR [95% CI]: 1.47 [0.94 - 2.32]; $P = .093$, and 1.40 [1.01 - 1.94]; $P = .043$, Fig. 1) despite a significantly lower prevalence of atrial fibrillation in the rEF patients. Similarly, patients with rEF had higher risk of MI at 1 year compared with bEF and pEF patients (7.5% vs 5.9% and 3.2%;



EF: Ejection fraction
* Identified as a primary diagnosis of stroke during a hospitalization.
Hazard ratio were calculated using a Cox proportional hazard model adjusting for age, gender, region, race, ethnicity, insurance type, year of index date, baseline hospitalizations, atrial fibrillation, comorbidities with a prevalence >5% (i.e. hypertension, hyperlipidemia, diabetes, depression, obesity, COPD, myocardial infarction, previous VTE), and baseline anticoagulants.

Fig. 1. Kaplan-Meier rates of Ischemic stroke* - excluding patients with stroke at baseline.