Table 1

Analyzed models	c-stat (95% CI)
Established rik factors	0.54 (95% CI 0.48–0.61)
+ NT-proBNP	0.60 (95% CI 0.54–0.66)
+ panel of 7 miRNAs	0.66 (95% CI 0.60–0.72)
+ NT-proBNP and panel of 7 miRNAs	0.68 (95% CI 0.63–0.74)
panel of 7 miRNAs only	0.67 (95% CI 0.60–0.74)

Conclusion: Our findings suggest that a baseline model for risk prediction, using only established risk factors, performs poorly in the prediction of CV death and hospitalization rate. Adding NT-pro-BNP to this model increases the capacity of the model to predict risk, but the strongest contributor to the prediction model appeared to be the panel of 7 miRNAs.

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4380
Vocal biomarker predicts long term survival among heart failure patients

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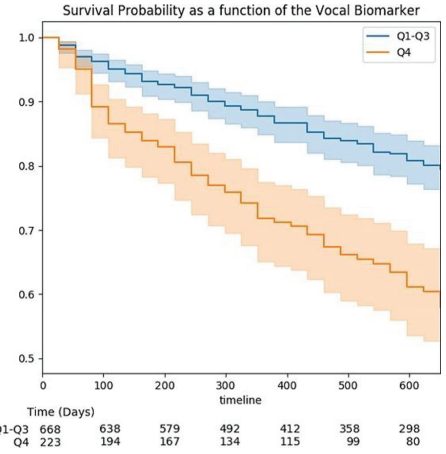
Home telemedicine holds the potential to reduce costs and improve outcome among patients with congestive heart failure (CHF). We recently reported a possible relationship between vocal biomarkers and coronary artery disease. The purpose of the current study was to test the hypothesis that vocal biomarkers are associated with long term survival among CHF patients.

Methods: Study cohort included 2,282 patients who were registered to a large HMO's call center of patients suffering from chronic conditions including CHF. 940 acoustic features were extracted from 20 secs of speech for each of the patients. A biomarker was then developed based on a train cohort (N=1,391) using machine learning techniques optimized according to an age cutoff of 75. The biomarker was then tested on a final mutually exclusive CHF study cohort (N=891). The biomarker was evaluated as a continuous variable, as well as dichotomized to two groups: high (upper quartile) and low.

Results: Mean age of the CHF study population was 74±12, 67% were men. During an average follow-up of 32±15 months, 246 (28%) patients died. Kaplan Meier survival analysis showed significantly higher cumulative probability of death among subjects in the higher vocal biomarker group (41%±19% vs. 30%±20%, $p<0.001$; FIGURE). Consistently, cox regression analysis of the vocal biomarker as a continuous variable in the model, and with adjustment to known predictors of poor survival, demonstrated that each standard deviation increase in the vocal biomarker was associated with a significant 15% increased risk of death during follow-up (95% CI 1.02 - 1.3, p=0.02).



Kaplan Meier Survival Analysis Curve

Conclusions: This is the first study to document a relationship between a vocal biomarker and long-term survival among CHF patients. The results have important clinical implications for telemedicine and CHF patient care.

Funding Acknowledgements: Beyond Verbal Communications

4381
Prognostic implications of pathogenic truncating variants in the TTN gene

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Prognostic implications of pathogenic truncating variants in the TTN gene

Background: TTN truncating mutations are the most common genetic cause of dilated cardiomyopathy. However, few data about prognosis is available in genetic carriers.

Purpose: To evaluate the prognostic implications of truncating pathogenic variants in the TTN gene.

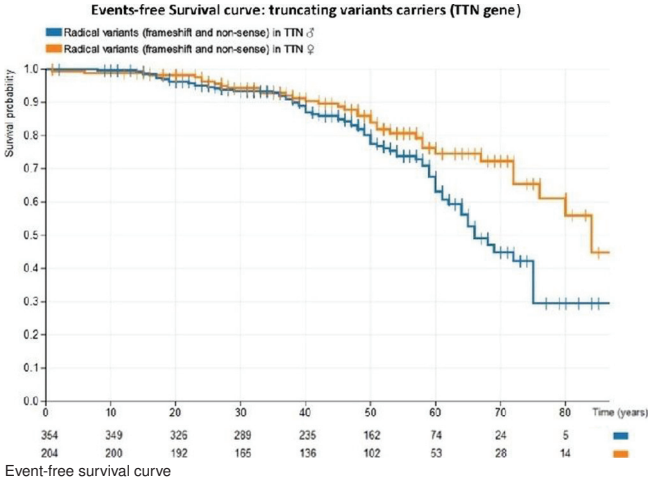
Methods: Through a systematic literature research, we collected in a dedicated database clinical and genetic data about all the carriers and affected relatives of families with nonsense and frameshift pathogenic or likely pathogenic variants in TTN gene, according to the ACMG criteria.

We evaluated available follow up data and constructed Kaplan-Meier survival curves free from cardiovascular death (sudden death, heart transplant, heart failure death, appropriate implantable cardiac defibrillator discharge and stroke related death). Long-rank test was used to compare event-free survival time between males and females.

Results: 573 individuals were included in the final analysis (354 males; 204 females, 15 unknown sex), carrying 347 different variants (186 frameshift; 161 nonsense). 266 were index cases and 307 first-degree relatives. 357 had titin truncating variants phenotypes: 309 dilated cardiomyopathy; 28 muscular diseases; 20 isolated left ventricular non-compaction. Of the remaining, 58 were healthy carriers, 97 had not phenotypic data, and 61 had unrelated phenotypes to the one expected.

112 patients suffered events: 63 sudden deaths (46 males; 17 females), 22 transplants (19 males; 3 females), 23 heart failure deaths (11 males; 12 females) and 4 stroke-related deaths (2 men; 2 women). No cardiac defibrillator discharges were reported.

Incidence of cardiovascular death was higher in males than females ($p<0.01$). Annual incidence of cardiovascular death between ages 30 to 70 was 1.3%/year in males (almost 60% of these were sudden death) and 0.6%/year in females.



Event-free survival curve

Conclusions: TTN truncating variants are associated with a relevant risk of cardiovascular death, which is higher in males, especially after age 30. More than 50% of the events were sudden deaths, suggesting that ICDs could have been under-indicated in this population.

CMR INNOVATION FOR CLINICAL USE

4382
Fully automated assessment of filling and ejection rates of the ventricle. Reference values for healthy volunteers from the UK-biobank cohort

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Introduction: Atrial and ventricular ejection and filling rates and atrial contribution to filling are sensitive markers of myocardial function, especially in early disease. Cardiac Magnetic Resonance is a gold standard for cardiac volumetrics and allow accurate quantification of volume changes over time. But obtaining these values has so far been labour intensive, limiting their use. Recent development of automated segmentation algorithms greatly improve the ability to use such measures for early detection of cardiac disease.

Purpose: Using a previously validated human-level ventricular segmentation algorithm [1], we set out to investigate ventricular ejection and filling characteristics