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Chapter: HF Voice Biomarker



### Chapter 1: Systematic Review on Clinical Research

- In patients with acute decompensated heart failure, discharge recordings were successfully tagged as distinctly different from baseline (wet) in 94% of cases, with distinct differences shown for all 5 SMs in 87.5% of cases.<sup>[1]</sup>
- Univariate binary logistic regression analysis identified 5 voice features that were associated with CAD (P<.05 for all). Multivariate binary logistic regression with adjustment for ASCVD risk score identified 2 voice features that were independently associated with CAD (odds ratio [OR], 0.37; 95% CI, 0.18-0.79; and 4.01; 95% CI, 1.25-12.84; P=.009 and P=.02, respectively).<sup>[2]</sup>
- Each SD increase in the biomarker was associated with a significant 32% increased risk of death during follow-up (95% CI, 1.24-1.41, P<0.001) and that compared with the lowest quartile, patients in the highest quartile were 96% more likely to die (95% CI, 1.59-2.42, P<0.001).<sup>[3]</sup>
- Changes in patient weight immediately after dialysis positively correlated with Speech Measures (SM) changes, with the strongest correlation measured the evening of the dialysis day [slope:  $-0.40 \pm 0.15$  (95% confidence interval: -0.71 to -0.10), P = 0.0096]. [4]
- An increase in the mean voice biomarker by 1 unit was associated with a high Pulmonary Artery Pressure (PAP), odds ratio 2.31, 95% CI 1.05-5.07, p = 0.038.<sup>[5]</sup>

<sup>[1]</sup> Amir, Offer, et al. "Remote Speech Analysis in the Evaluation of Hospitalized Patients With Acute Decompensated Heart Failure." Heart Failure (2021).

<sup>[2]</sup> Maor, Elad et al. "Voice Signal Characteristics Are Independently Associated With Coronary Artery Disease." Mayo Clinic proceedings vol. 93,7 (2018): 840-847.

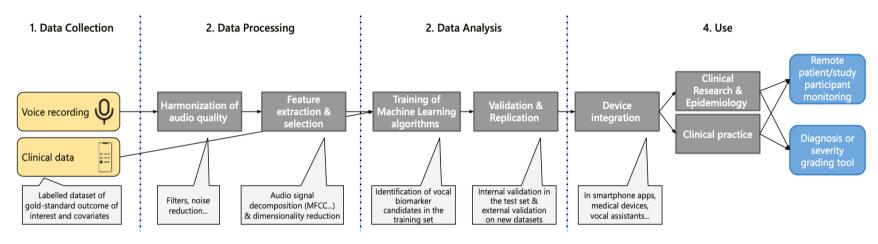
<sup>[3]</sup> Maor, Elad, et al. "Vocal biomarker is associated with hospitalization and mortality among heart failure patients." Journal of the American Heart Association 9.7 (2020): e013359.

<sup>[4]</sup> Amir, Offer, et al. "Feasibility of remote speech analysis in evaluation of dynamic fluid overload in heart failure patients undergoing haemodialysis treatment." ESC Heart Failure (2021).

<sup>[5]</sup> Sara, Jaskanwal Deep Singh, et al. "Non-invasive vocal biomarker is associated with pulmonary hypertension." PloS one 15.4 (2020). e023 441. BIOFOURMIS. ALL RIGHTS RESERVED



## Chapter 2: Systematic Review on Technique Research



Pipeline for vocal biomarker identification, from research to practice<sup>[1]</sup>

- Types of voice recordings (to derive vocal biomarkers for various health conditions, not limited to HF)<sup>[1]</sup>:
  - 1. Verbal (read-aloud or spontaneous conversation)
    - isolated words, short sentence repetition, reading passage, running speech
  - 2. Vowel/syllable
    - sustained vowel phonation
    - diadochokinetic task
  - 3. Nonverbal vocalizations
    - Coughing<sup>[2]</sup>/breathing

<sup>[1]</sup> Fagherazzi, Guy, et al. "Voice for Health: The Use of Vocal Biomarkers from Research to Clinical Practice." Digital biomarkers 5.1 (2021): 78-88.

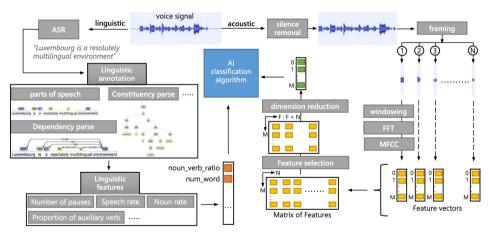
<sup>[2]</sup> Windmon, Anthony, et al. "Tussiswatch: A smart-phone system to identify cough episodes as early symptoms of chronic obstructive pulmonary disease and congestive heart

<sup>4</sup> failure." IEEE journal of biomedical and health informatics 23.4 (2018): 1566-1573.

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## Systematic Review on Technique Research (CONT)

- Audio feature extraction (to derive vocal biomarkers for various health conditions, not limited to HF)<sup>[1]</sup>:
  - Acoustic features such as temporal, frequency, cepstral, wavelet, and time-frequency domains can capture motor speech impairments
    - Prosodic (pitch, formants, energy, jitter, shimmer) or spectral characteristics (spectral flux, slope, centroid, entropy, roll-off, flatness), voice quality (zero-crossing rate, harmonic-to-noise ration, noise-to-harmonic ratio) or phonation (fundamental frequency, pitch period entropy).
    - Nonlinear dynamic features (correlation dimension, fractal dimension, recurrence period density entropy, Lempel-Ziv complexity).
    - Segmental features, such as MFCC (usually the first 8-13 MFCC coefficients), perceptual linear prediction coefficients, and linear frequency cepstral coefficients.
  - Linguistic features such as the parts of speech, vocabulary diversity, lexical and grammatical complexity, syntactic structures, semantic skills, and sentiment can capture cognitive impairments



Representation of a typical voice signal pre-processing and feature extraction using MFCCs<sup>[1]</sup>

[1] Fagherazzi, Guy, et al. "Voice for Health: The Use of Vocal Biomarkers from Research to Clinical Practice." Digital biomarkers 5.1 (2021): 78-88.



### Appendix: Well-known authors

- Daryush D. Mehta, PhD. Clinical voice and speech science and technology. https://scholar.harvard.edu/dmehta/publications
- Olivia Murton, PhD. Her dissertation is in voice biomarkers to monitor health conditions including voice disorders and heart failure. <a href="https://www.mghihp.edu/olivia-murton-phd">https://www.mghihp.edu/olivia-murton-phd</a>
- Ongoing research project (2020-2024): Speech-based biomarking of heart failure. https://research.aalto.fi/en/projects/speech-based-biomarking-of-heart-failure/publications/
- Evaluation of speech biomarkers: review and recommendations. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7670321/