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ORIGINAL RESEARCH ARTICLE

Feasibility of remote speech analysis in evaluation of dynamic fluid overload in heart failure patients undergoing haemodialysis treatment

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Abstract

Aims This study aimed to assess the ability of a voice analysis application to discriminate between wet and dry states in chronic heart failure (CHF) patients undergoing regular scheduled haemodialysis treatment due to volume overload as a result of their chronic renal failure.

Methods and results In this single-centre, observational study, five patients with CHF, peripheral oedema of ≥2, and pulmonary congestion-related dyspnoea, undergoing haemodialysis three times per week, recorded five sentences into a standard smartphone/tablet before and after haemodialysis. Recordings were provided that same noon/early evening and the next morning and evening. Patient weight was measured at the hospital before and after each haemodialysis session. Recordings were analysed by a smartphone application (app) algorithm, to compare speech measures (SMs) of utterances collected over time. On average, patients provided recordings throughout 25.8 ± 3.9 dialysis treatment cycles, resulting in a total of 472 recordings. Weight changes of 1.95 ± 0.64 kg were documented during cycles. Median baseline SM prior to dialysis was 0.87 ± 0.17, and rose to 1.07 ± 0.15 following the end of the dialysis session, at noon ($P = 0.0355$), and remained at a similar level until the following morning ($P = 0.007$). By the evening of the day following dialysis, SMs returned to baseline levels (0.88 ± 0.19). Changes in patient weight immediately after dialysis positively correlated with SM changes, with the strongest correlation measured the evening of the dialysis day [slope: −0.40 ± 0.15 (95% confidence interval: −0.71 to −0.10), $P = 0.0096$].

Conclusions The fluid-controlled haemodialysis model demonstrated the ability of the app algorithm to identify cyclic changes in SMs, which reflected bodily fluid levels. The voice analysis platform bears considerable potential as a harbinger of impending fluid overload in a range of clinical scenarios, which will enhance monitoring and triage efforts, ultimately optimizing remote CHF management.

Keywords Dialysis; Acute heart failure (AHF); Remote voice analysis; Speech measure (SM)

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Introduction

Heart failure (HF) can emerge either rapidly or gradually, with minimal or subtle symptomatic eruption in either case before critical decompensation. Even frequent and routine assessments often fail to predict or alert on imminent fluid overload. New technologies developed to tighten surveillance of pulmonary fluid status include the implantable, wireless pulmonary artery pressure and heart rate monitoring CardioMEMS™ System, indicated for patients with New York

Heart Association (NYHA) Class III HF with a recent history of hospitalization,[1] and intrathoracic impedance-based assessment devices.[2,3] These technologies though are invasive and generally reserved for those with severe Class III HF and who have recently been hospitalized. Non-invasive telemedicine platforms, which involve synchronous and asynchronous transfer of measured or self-reported parameters (e.g. electrocardiogram, blood pressure, body weight, and heart rate), have had conflicting impacts on HF patient care, monitoring, and management, with some reports of no change in all-cause mortality[4] or all-cause readmission rates.[5,6] Recent advances in voice and sound analysis algorithms have raised awareness for the potential clinical benefits of non-invasively distinguishing speech features in disease settings. Such classifiers have been shown to successfully identify patients suffering from depression, pneumonia–asthma, coronary artery disease, and autism spectrum disorder.[7–11] In line with these applications, altered phonation patterns were detected in the context of pulmonary congestion, likely arising from the reduced viscosity of hyperhydrated vocal fold tissue and its consequentially atypical vibration mechanics. Murton *et al.*[12] report on measurable acoustic speech markers indicative of HF status in patients with acute heart failure (AHF).

The current study exploited the well-controlled volume status in patients with HF undergoing chronic haemodialysis treatments to further assess the capacity of the app-based algorithm to discriminate significant volume shifts. Fluid removal leads to lower circulating volume and cardiac filling pressure after each haemodialysis session, which is followed by gradual increases in fluid volume until maximizing just before the next haemodialysis session. Therefore, such patients present a 'clinical model' for the assessment of the sensitivity of vocal analysis in detecting changes in fluid status. Accordingly, fluid status-identifying speech measures (SMs) were analysed from voice recordings collected over the course of fluid management with haemodialysis of five patients with chronic HF and haemodialysis-dependent chronic renal failure.

Methods

Patients and study design

This single-centre, observational, single-arm study was approved by the ethics committee of Hadassah Medical Center, Jerusalem, Israel.

Adult (>18 years) patients with acute and chronic Class C, NYHA Classes II–IV, congestive HF, undergoing haemodialysis 2–3 times weekly, with a fluid overload of 2–4 L above their currently known dry weight, peripheral oedema of ≥2, and pulmonary congestion-related dyspnoea were eligible to participate in the study. Patients with significant chronic obstructive pulmonary disease, a congenital heart disease, evidence of an active infection or restrictive cardiomyopathy, or constrictive pericarditis were not eligible to participate in the study. Signed informed consent was obtained from each participant.

Patients undergoing routine haemodialysis treatment were asked to record five sentences, in their native language (Hebrew or Arabic) into a standard smartphone 3–4 times immediately before (wet state) dialysis. They were then asked to record the sentences an additional four times at home: 2–3 h following haemodialysis end (noon/early evening) in the late evening/before bed time, in the morning following dialysis, and before breakfast, and in evening of the day following dialysis. The duration of each recording was 2–5 s. Patient weight before and after dialysis was recorded to determine the volume of fluid removed during each cycle. Each patient was monitored over multi-dialysis cycles.

Speech analysis application

The HearO™ voice capturing application (Cordio Medical Ltd., Or Yehuda, Israel) runs on a standard smartphone/tablet, and transmits data to an analysis software which executes on a server in the cloud. The analysis algorithm compares SMs between utterances collected at a baseline state and different points of interest. In this study, baseline is the pre-dialysis SM and different points of interest are the post-dialysis SMs (Supporting Information).

Speech analysis

The generation of speech sounds can be modelled as the passage of an excitation signal, originating from the lungs, through a linear filter. The filter represents the shape of the vocal tract, which includes the air pathways from the glottis upwards to the lips and nostrils.

Speech measure represents the dissimilarity (larger values mean greater dissimilarity) between patient utterances of a reference set R, when the patient was at a baseline physiological state, and a test set T, obtained later when the patient's state may have changed. The method is based on a *similarity measure* $D(t,r)$ between a test and reference utterances, which is a weighted sum of short-term spectral (transformed filter) distortions between non-linear aligned frames in the test and the reference utterances. The SM can formally be defined as

$$\mathrm{SM}(T, R) = \mathrm{median}_{r \in R} D(t, r).$$

That is, for each test utterances, the similarity measures are computed relative to every one of the reference utterances and the median distortion is presented as the

representative distortion. The SM between the repeated utterances within each class measures *intra-class* variability, whereas the SM between the test and the reference classes measures *inter-class* variability. Thus, if SM(*T*,*R*) is significantly larger than SM(*R*,*R*), this indicates a difference between the underlying physiological conditions.

Table 2 Descriptive statistics of median speech measures

Recording time point	SM (median)					
	N	Mean	SD	Min	Median	Max
Dialysis day morning	5	0.87	0.17	0.64	0.91	1.04
Dialysis day noon	5	1.07	0.15	0.87	1.10	1.23
Dialysis day evening	5	1.04	0.20	0.76	1.14	1.23
Non-dialysis Day 1 morning	5	1.14	0.23	0.80	1.09	1.38
Non-dialysis Day 1 evening	5	0.88	0.19	0.64	1.00	1.03

SD, standard deviation; SM, speech measure.

Results

Voice recordings were collected from five patients, each of whom underwent haemodialysis treatments two to three times each week. On average, patients participated throughout 25.8 ± 3.9 dialysis treatment cycles, during which they lost a mean 1.93 ± 0.19 kg. No acute respiratory events or inflammations were reported throughout the study period. Patients provided a mean 94.4 recordings; in total, 472 recordings were analysed. Four patients were male, and one was female; mean patient age was 78.8 ± 7.8 years. In three cases, chronic HF was classified as NYHA 2 and in two cases as NYHA 3. Baseline N-terminal prohormone brain natriuretic peptide levels averaged 7016.6 ± 3404.0 pg/mL. Co-morbidities included coronary artery disease (*n* = 3), diabetes (*n* = 3), and hypertension (*n* = 4) (*Table 1*).

Mean ± SD of median wet-state SM was 0.87 ± 0.17, which rose to 1.07 ± 0.15 by the end of the dialysis session (noon) and remained at a similar level until the following morning. By the evening of the day after dialysis, mean SM dropped to 0.88 ± 0.19 (*Table 2*). Similarly, from the MMRM analysis model, the estimate ± standard error (SE) of wet-state SM was 0.982 ± 0.086, which rose to 1.176 ± 0.086 by the end of the dialysis session (noon) and remained at a similar level until the following morning. By the evening of the day after dialysis, mean SM dropped to 0.98 ± 0.086 (*Table 3* and *Figure 1*). There was a statistically significant difference between median SMs measured

Table 3 Adjusted means of median speech measures from MMRM[a] analysis

Recording time point	Estimate	SE	*P*-value	Lower 95% CI limit	Upper 95% CI limit
Dialysis day morning	0.98	0.09	0.0027	0.68	1.28
Dialysis day noon	1.18	0.09	0.0017	0.88	1.47
Dialysis day evening	1.15	0.09	0.0018	0.85	1.44
Non-dialysis Day 1 morning	1.24	0.09	0.0014	0.95	1.54
Non-dialysis Day 1 evening	0.99	0.09	0.0026	0.69	1.29

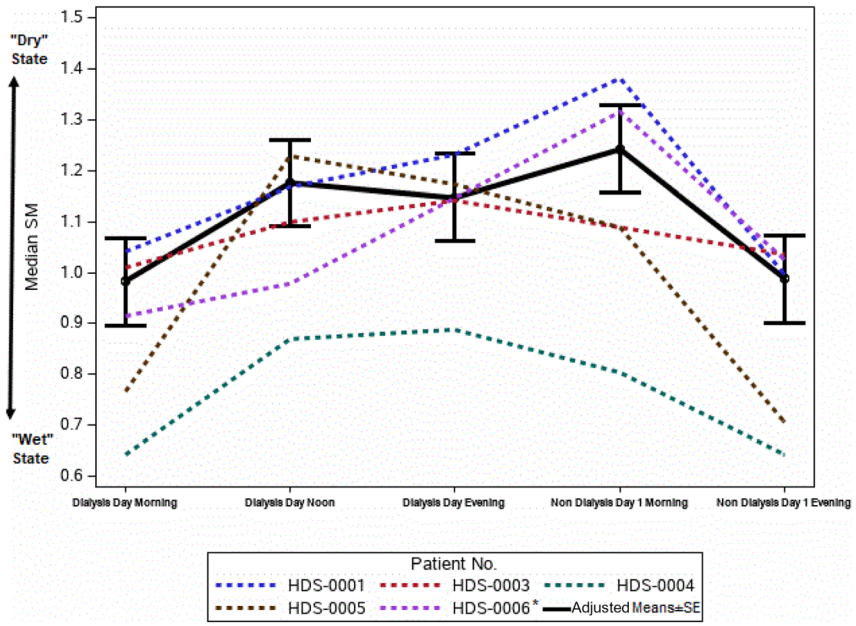
CI, confidence interval; MMRM, mixed model repeated measures; NT-proBNP, N-terminal prohormone brain natriuretic peptide; SE, standard error.
[a]Explanatory variables: day and time, age, NT-proBNP, and gender.

Table 1 Patient demographics and baseline characteristics

Subject	Gender	Age (years)	Race	LVEF (%)	CAD	History of MI	History of CABG/PCI	Diabetes	HT	NT-proBNP (pg/mL)	Blood pressure (mmHg)	NYHA	Concomitant medications
HDS-0001	F	83	Caucasian	>70	No	No	No	No	Yes	5710	166/93	3	Anti-platelet
HDS-0003	M	69	Caucasian	24	Yes	Yes	Yes	Yes	No	3872	136/55	2	Anti-platelet Hyperlipidaemic Vasodilator Loop diuretics
HDS-0004	M	83	Caucasian	41–50	Yes	Yes	No	No	Yes	5446	145/43	2	Anti-platelet Loop diuretics Hyperlipidaemic Ca^{+} channel blocker
HDS-0005	M	72	Caucasian	45–50	No	No	No	Yes	Yes	7367	130/52	2	Anticoagulant Beta-blocker Cardiac glycoside
HDS-0006	M	87	Caucasian	50–55	Yes	Yes	Yes	Yes	Yes	12 688	151/62	3	Ca^{+} channel blocker ACE inhibitor Beta-blocker Anti-platelet Hyperlipidaemic

CABG, coronary artery bypass grafting; CAD, coronary artery disease; HT, hypertension; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NT-proBNP, N-terminal prohormone brain natriuretic peptide; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

Figure 1 Speech measures (SMs) of acute heart failure patients during haemodialysis cycles. Five chronic heart failure patients undergoing haemodialysis two to three times weekly recorded five sentences using the HearO™ app, before and immediately after dialysis, as well as later that same evening, and the next morning and evening. Median SMs per patient are shown, as well as the adjusted mean ± standard error (SE) SMs, estimated from a mixed model repeated measures analysis, which included median SM as the response variable and time, gender, age, and N-terminal prohormone brain natriuretic peptide at baseline as explanatory variables and compound symmetry as variance covariance matrix structure. *Excluding subject HDS-0006 dialysis day evening data that included only three cycles.



immediately before vs. immediately after dialysis [−0.19, SE = 0.08, *P*-value = 0.04, 95% confidence interval (CI): −0.37 to −0.01]. There was also a significant difference between SMs measured immediately before dialysis and those measured the following morning (−0.26, SE = 0.08, *P*-value = 0.0070, 95% CI: −0.44 to −0.08) (*Table 4*). Changes in patient weight immediately after dialysis positively correlated with SM changes, with the strongest correlation measured the evening of dialysis [slope ± SE: −0.40 ± 0.15 (95% CI: −0.71 to −0.10), *P* = 0.0096], which paralleled the window in which SM changes were highest and patients were likely driest.

Discussion

The present study utilized a highly accessible clinical model to assess the ability of a sound-based algorithm to distinguish between wet and dry states in patients with AHF undergoing haemodialysis. The voice analysis platform identified significant changes in SMs, which paralleled the cyclic haemodialysis treatment-removal fluid patterns. Specifically, pre-dialysis SMs were distinct from those of recordings collected immediately after or the morning following treatment. These differences waned with gradual systemic fluid accumulation as patients progressed towards their next treatment

Table 4 Difference of adjusted means of median speech measures from MMRM[a] analysis model

Comparison	Estimate	SE	*P*-value	Lower 95% CI limit	Upper 95% CI limit
Dialysis day morning–dialysis day noon	−0.19	0.08	0.04	−0.37	−0.01
Dialysis day morning–dialysis day evening	−0.17	0.08	0.069	−0.34	0.01
Dialysis day morning–non-dialysis Day 1 morning	−0.26	0.08	0.0070	−0.44	−0.08
Dialysis day morning–non-dialysis Day 1 evening	−0.01	0.08	0.94	−0.19	0.17
Dialysis day noon–dialysis day evening	0.03	0.08	0.74	−0.15	0.21
Dialysis day noon–non-dialysis Day 1 morning	−0.07	0.08	0.44	−0.25	0.11
Dialysis day noon–non-dialysis Day 1 evening	0.19	0.08	0.041	0.01	0.37
Dialysis day evening–non-dialysis Day 1 morning	−0.10	0.08	0.27	−0.27	0.08
Dialysis day evening–non-dialysis Day 1 evening	0.16	0.08	0.078	−0.02	0.34
Non-dialysis Day 1 morning–non-dialysis Day 1 evening	0.25	0.08	0.0082	0.08	0.43

CI, confidence interval; MMRM, mixed model repeated measures; NT-proBNP, N-terminal prohormone brain natriuretic peptide; SE, standard error.
[a]Explanatory variables: day and time, age, NT-proBNP, and gender.

session. A deviation from this cyclic pattern was consistently noted on the evening of haemodialysis, which may be related to the patients being in their minimal fluid overload on the day of the haemodialysis itself.[13]

The potential of SMs to inform on pathophysiological states is likely rooted in the hydration-sensitive viscoelastic properties and associated oscillatory behaviour of the vocal fold tissue and in respiratory muscle biomechanics. Well-known clinical examples of fluid state-related voice changes include the characteristically deep and hoarse voice of patients with Reinke's oedema, a condition in which fluid accumulates below the outer layer of the vocal cords, subsequently reducing their vibration frequency.[14] Similarly, bronchophony, whispered pectoriloquy, and egophony[15] are common presentations of alveolar or interstitial space fluid overload. Aligning with these are the reports on the negative fluid balance effect of haemodialysis on vocal acoustics parameters,[16–19] respiratory muscle strength and endurance,[20] and total lung capacity,[21,22] all with bearings on phonation aerodynamics. These effects resonate with the commonly reported transient ($\leq$24 h) post-dialysis hoarseness,[23,24] shown to correlate with decreased vocal fold thickness.[25] Indeed, in a previous study assessing voice recordings of patients with AHF at hospital admission and at discharge, HearO discriminated between recordings collected at admission and those collected at discharge, following intense diuretic treatment and reduction of extracellular fluid. In the current controlled AHF model, the algorithm immediately translated the reduced systemic fluid overload achieved with haemodialysis into discriminating SMs extractable from simple voice recordings.

In the context of the increasing attention being placed on remote access technologies of transitional care programmes, this algorithm promises to serve as a valuable monitoring and triage tools in HF management protocols. Such an addition to the expanding alternatives to traditional in-person follow-up visits is expected to advance the global efforts towards optimized HF healthcare response and patient care.

Several limitations of the current study should be noted. The study tested a small cohort of patients and was a single-centre, open-label study. In addition, patients with HF on dialysis treatment do not necessarily represent the classical worsening pattern of HF. Nevertheless, as in this unique model, each patient had multiple and separate dialysis cycles, and the data analysed here actually represent a larger cohort. Further studies will be needed to assess the performance of the voice analysis algorithm in larger cohorts of HF patients under less rigorous clinical surveillance. In conclusion, this unique clinical model of patients with HF undergoing haemodialysis assisted in the validation of this smartphone app algorithm and its ability to deploy sophisticated vocal analysis to determine the pulmonary hydration status of patients with HF.

Conflict of interest

O.A. is a paid consultant to Cordio Medical Ltd. S.D.A. reports receiving grant support from Abbott and Vifor Pharma and fees from Abbott, Bayer, Boehringer Ingelheim, Cardiac Dimension, Impulse Dynamics, Novartis, Servier, and Vifor Pharma and is a consultant to Cordio Medical Ltd. I.G. has no interest to declare. W.T.A. is a consultant to Cordio Medical Ltd. and has received consulting fees from Abbott, Boehringer Ingelheim, CVRx, Edwards Lifesciences, and Respicardia; salary support from V-Wave Medical; and research support from the US National Institutes of Health/National Heart, Lung, and Blood Institute. S.P.P. is a consultant to Cordio Medical Ltd. and has received consulting fees from Abbott, CareDx, Medtronic, NuPulse, and Procyrion. D.B. is a consultant to Cordio Medical Ltd. I.D.S. is the Chief Technology Officer of Cordio Medical Ltd. R.H. is the Clinical SrVP at Cordio Medical Ltd. E.R.E. is supported in part by a grant from the US National Institutes of Health (NIH R01 49039) and is a paid consultant to Cordio Medical Ltd. C.L. is a board member of Cordio Medical Ltd. and receiving lecture fees from Boehringer Ingelheim.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1. Supporting Information.

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