Predicting Adverse Events and Dry Weight with Non-Invasive Monitoring

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BACKGROUND

New devices – like the toSense CoVa™ Monitoring System (the 'Necklace') - make non-invasive measurements prior to and during dialysis possible. The purpose of this study was to investigate if adverse events can be identified prior to occurrence through non-invasive monitoring. Additional objectives were to estimate true 'dry weight' and to determine if evaluation of physiological waveforms could identify hyperkalemia. The Necklace (**Figure 1**) is a non-invasive device that measures vital signs, thoracic impedance (TI) [1], stroke volume (SV) , and cardiac output (CO) [2]. A next-generation system will also cufflessly measure blood pressure (BP) and SpO2 [3]. All measured data are wirelessly sent via a Gateway and then forwarded to a Web-based System.

Figure 1: CoVa™ Monitoring System

METHODS

35 patients receiving dialysis at UF Health Shands Dialysis Center (Outpatient) and 37 patients receiving dialysis at UF Health Shands Hospital (Inpatient) were monitored using the Necklace during one or more dialysis sessions. Demographic information and a summary of the data captured are presented in **Table 1**. Before dialysis, research personnel applied the Necklace to patients. During dialysis, it made frequent measurements of SV, CO, TI, heart rate (HR), respiration rate (RR), and ECG waveforms. Additional data captured and analyzed included patients' weight before and after each dialysis session, blood pressure (BP), fluid removed, ultrafiltration rate (UF), adverse events during the dialysis session, and lab values (if available) prior to the dialysis session.

Establishing Dry Weight

In this study the difference between pre and post-weight and TI changes during dialysis sessions versus net fluid removed during a dialysis session were evaluated. Early analysis indicates that net fluid removed correlates better with with changes in weight, as compared to TI. However, weight is not always available. While this parameter is currently the best estimator for UF goals, too much fluid, or not enough fluid, may be removed when weight is the only metric. Evaluation of the trends in TI and SV, and BP, during a dialysis session may provide insights into a patient's true dry weight, and therefore guide UF rate as well as UF goals. For patients with normal ejection fraction, it is expected that TI would rise and SV would go down with UF. If TI is unchanged, that may indicate that the UF rate could be increased and along with possibly the UF goal. Our hypothesis, as well as rate and goal recommendations for UF, are shown in **Table 2**. Further data analysis and additional trials are needed to confirm these hypotheses and UF recommendations.

Table 2: Hemodynamic Changes During Dialysis and UF Recommendations

Parameters Compared Post - Pre	Number of Sessions	Percent	Hypothesis	UF Rate Recommendations	UF Goal Recommendations
TI Up SV Down	36	11%	Optimal UF goal and rate in a patient with a normal ejection fraction	Optimal	At or near optimal dry weight
TI Up SV Up	56	18%	Optimal UF goal and rate in a patient with a reduced ejection fraction	Optimal	If patient does not have CHF, UF goal may be sub-optimal
TI Up SV Unchanged	106	34%	Good UF rate	Optimal	Could attempt to pull off more fluid over a longer period of time to see if SV decreases
TI Unchanged SV Down	17	5%	Less than optimal UF rate	Could increase UF rate	Could increase UF goal, cautiously
TI Unchanged SV Up	9	3%	Less than optimal UF rate	Could increase UF rate	Could increase UF goal, cautiously
TI Unchanged SV Unchanged	90	29%	Less than optimal UF rate	Could increase UF rate	Could increase UF goal, aggressively

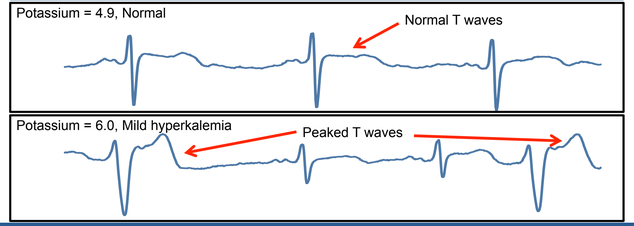
Table 1: Demographic Information / Data Captured

Total Patients	**72**
Inpatient [n (%)]	**37 (51)**
Female [n (%)]	**33 (46)**
Outpatient body mass index (kg/m^2) [average]	**27.0**
Total sessions	**330**
Inpatient sessions [n (%)]	**79 (24)**
Outpatient sessions [n (%)]	**251 (76)**
Sessions per patient [n]	
1 to 3 sessions [n (%)]	**32 (44)**
4 to 6 sessions [n (%)]	**14 (20)**
7 to 10 sessions [n (%)]	**26 (36)**
Adverse events [n]	**60**
Cramping [n (%)]	**31 (52)**
Nausea/vomiting [n (%)]	**3 (5)**
Hypotension [n (%)]	**17 (28)**
Altered mental status [n (%)]	**2 (3)**
Not feeling well [n (%)]	**5 (8)**
Lightheadedness [n (%)]	**2 (3)**
Identified hyperkalemia sessions [n]	**28**
Mild (Potassium >5.1 & <6.0) [n (%)]	**19 (75)**
Moderate (Potassium >6.1 & <7.0) [n (%)]	**7 (21)**
Severe (Potassium >7.1) [n (%)]	**1 (4)**

Hyperkalemia Analysis

During the trial, potassium values were received daily for inpatients and monthly for outpatients. The number/type of hyperkalemia events is shown in **Table 1**. Analyzing hyperkalemia events indicated that 86% of the events could be predicted with an algorithm that analyzes ECG waveforms. Patient inclusion in the analysis required one or more sessions while they had normal potassium levels as well as one or more session where they were hyperkalemic. **Figure 2** shows ECG waveforms in a patient with a normal potassium level (p=4.9, top) and elevated potassium level (p=6.0, bottom) two days later.

Figure 2: ECG Waveforms



Predicting Adverse Events

Focusing on the hypotension and cramping adverse events, analysis indicates that BP and SV/CO were good predictors of a potential adverse event as shown in **Table 3**. In 27% of the events, CO was the first indicator of an event, while in 25% of the events, BP was the first indicator. 50% of the events were preceded by an increase in HR **(Figure 3)**. This suggests that a constellation of parameters may give the best indicator of an impending adverse event. Note: adverse events that occurred after the session ended were not included in the analysis.

Figure 3: Adverse Events during Dialysis

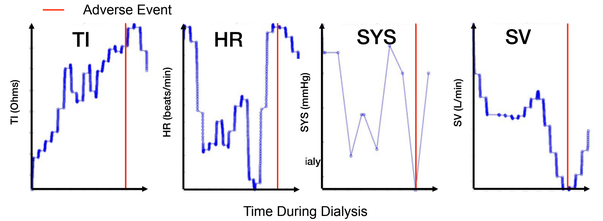


Table 3: Predicting Adverse Events

Predictor of Adverse Events	Overall	Earliest
Blood Pressure	**100%**	**25%**
Stroke Volume/Cardiac Output	**92%**	**27%**
Heart Rate	**50%**	**0%**

CONCLUSIONS

This study indicates that measurements made by the Necklace, coupled with data-driven algorithms, may be able to guide UF rates and help determine the optimum UF goal. The Necklace's non-invasive measurements of SV/CO/HR may be able to predict adverse events during dialysis. Future measurements of BP and SpO2 could enhance the algorithm, providing even earlier notification of hypotensive and cramping events during dialysis, while improving the dialysis experience. The Necklace may also have the ability to provide insight into hyperkalemia in patients without needing to perform invasive lab analysis.

REFERENCES

[1] 510(k) approval – K142087
[2] 510(k) approval pending - K160899
[3] pending FDA 510(k) submission 1Q2017