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Volume Control

# Hemodynamic Monitoring During Hemodialysis Using Bioimpedance: A Comparison of Changes in Resistance Between Different Body Segments

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## ABSTRACT

**Introduction:** Prevention of hemodynamic complications during hemodialysis remains challenging. Although whole body bioimpedance is well established in fluid status assessment, its use for dynamic or continuous recordings is limited. A segmental approach may serve this purpose better. This study investigates which body segment is best targeted to measure bioimpedance for hemodynamic monitoring.

**Methods:** In this observational study, serial bioimpedance measurements were conducted on the whole body, lower leg, upper arm, and thorax of 15 patients during two hemodialysis sessions. The resistance component of bioimpedance was used to investigate the relationship with changes in volume and systolic blood pressure (SBP).

**Findings:** Predialysis to postdialysis changes in relative resistance between the two sessions revealed the lowest intraclass correlation coefficient for upper arm (0.023) and the highest for thoracic resistance (0.728). Correlation between ultrafiltration volume and relative resistance was comparable between upper arm and thoracic segment (0.538 [0.447–0.618] and 0.537 [0.446–0.617], both $p < 0.001$, respectively) and the highest for whole-body and lower leg (0.697 [0.63–0.754] and 0.670 [0.598–0.731], both $p < 0.001$, respectively). In contrast, the correlation between changes in SBP and relative resistance was the highest in the thoracic segment (−0.33 [−0.432 to −0.219], $p < 0.001$) and the lowest for whole body measurements (−0.154 [−0.269 to −0.036], $p = 0.01$). In addition, multiple regression analysis indicated thoracic resistance as the best predictor for changes in SBP ($\beta = -0.261$ [−0.353 to −0.126], $p < 0.001$).

**Discussion:** These findings suggest that the thorax is the most suitable region for segmental bioimpedance measurements to assess hemodynamic parameters. Thoracic bioimpedance may innovate the hemodynamic monitoring of hemodialysis patients.

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**Abbreviations:** C.I., confident interval; R, resistance; SBP, systolic blood pressure; S.E., standard error time; UFR, ultrafiltration rate; UFV, ultrafiltration volume.

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## 1 | Introduction

Hemodynamic complications are common in hemodialysis patients and associate with increased risks of morbidity and mortality [1–4]. The intermittent nature of a thrice-weekly hemodialysis regimen results in significant volume fluctuations, which impose a substantial burden on the cardiovascular health and mortality in this patient population. Currently, fluid changes and their impact on blood pressure during hemodialysis can be monitored through approximations of blood volume, although the accuracy of this method remains under debate [5–9]. An interesting alternative that may serve real time hemodynamic monitoring is the bioimpedance technique. Although the whole body approach is the most widely known form of bioimpedance analysis, it is not well suited for dynamic monitoring because of the nonwearable nature of the device and its sensitivity to limb movements [10]. In addition, whole body measurements assume homogeneity in the geometric shape and size of the various body segments [11]. These limitations can be circumvented by employing a segmental approach to bioimpedance measurements. Research into calf bioimpedance during hemodialysis introduced the concept of "flatting of the resistance curve" (i.e., $R_0/R_t$, where $R_0$ represents the resistance component of the bioimpedance signal before the start of hemodialysis and $R_t$ represents resistance at timepoint $t$ during hemodialysis) [12–15]. This feature is thought to indicate the achievement of dry weight and has been proposed as a method to guide ultrafiltration volume (UFV). Its implementation has been shown to decrease postdialysis weight [13] and may also reduce left ventricle hypertrophy and predialysis systolic blood pressure (SBP) [15]. Segmental bioimpedance of the thoracic region, which addresses the central volume compartment of the body, may add relevant hemodynamic information. Given that the resistance component of bioimpedance is inversely related to segment cross sectional area [16], the thoracic segment contributes approximately 10% to whole body resistance, whereas the limbs account for 90% [17]. Consequently, hemodynamic changes that affect resistance, may be more prominently reflected in the thoracic segment.

Prior to the development of wearable bioimpedance devices, it is essential to determine which specific body segment most accurately tracks hemodynamic changes. To the best of our knowledge, no existing studies have compared the relationship between different segmental bioimpedance measurements and other hemodynamic parameters. Therefore, this study aims to identify which body segment is best targeted to monitor changes in volume and blood pressure in patients on hemodialysis.

## 2 | Materials and Methods

### 2.1 | Study Design

This work results from a prospective cohort study conducted in the dialysis unit of Ziekenhuis Oost-Limburg (Genk, Belgium). Anuric hemodialysis patients over 18 years of age able to provide informed consent and prone to intradialytic hypotension were eligible to participate. Hemodynamic instability was evaluated by screening the previous hemodialysis sessions of prevalent patients on the incidence of a nadir SBP of 90 mmHg or a drop in SBP of more than 20 mmHg compared to the predialysis SBP. Exclusion criteria were limb amputation or the need for acute hemodialysis. Written informed consent was obtained from each patient prior to study enrollment. Patients were followed up for two consecutive short interval dialysis sessions during a thrice-weekly dialysis schedule. The study complied with the Declaration of Helsinki, and the study protocol was approved by the local committee on human research (eudract/B-number B371201628917) of Ziekenhuis Oost-Limburg (Genk, Belgium) and Hasselt University (Hasselt, Belgium).

### 2.2 | Clinical Data Collection

The medical history of 15 hemodialysis patients was obtained from electronic records. Hemodialysis prescription data were checked on dialysis frequency, duration, and target weight. UFV was prescribed based on the interdialytic weight gain, the priming volume of the dialysis machine, and the estimated volume intake during the treatment, consistent with standard clinical practice. Ultrafiltration rate (UFR) was calculated as the UFV normalized to target weight and duration of the dialysis treatment, expressed as mL/kg/h. In order to investigate the relationship between UFR and changes in resistance, the hemodialysis sessions were divided into two groups based on UFR higher or lower than 8 mL/kg/h (i.e., the median of all UFR). Blood pressure was monitored predialysis and at 30-min intervals during the dialysis treatment ($T_0$, $T_{30}$, $T_{60}$, $T_{90}$, $T_{120}$, $T_{150}$, $T_{180}$, $T_{210}$, and $T_{240}$). Blood pressure measurements were taken by an automatic cuff-based blood pressure monitor. The blood pressure values are the result of the average of three consecutive measurements. Two blood pressure groups were formed based on the presence of a decrease in SBP of $\geq 20$ mmHg from predialysis to postdialysis, as this is one of the criteria for the definition of intradialytic hypotension [18]. Prior to the start of the second hemodialysis session, patients were asked if they had experienced muscle cramps during or after the first hemodialysis session.

### 2.3 | Bioimpedance Measurements

Bioimpedance measurements were conducted contralateral to the vascular access side. Standard gel electrodes were attached to the skin before the start of hemodialysis and remained in place throughout the session. To facilitate the future replacement of the current electrode configuration with patches, the targeted segments were measured compactly, rather than measuring the entire trunk (i.e., thorax + abdomen) or the entire limb (i.e., upper and lower portion). Measurements were conducted with the following electrode configuration: (1) wrist to ankle, representing whole body measurements; (2) ankle to subtuberositas tibiae, representing the lower leg; (3) ventral side of the upper arm, from the distal to the proximal biceps muscle; and (4) the thoracic segment, according to a previously determined configuration [19]. For each segmental measurement, four electrodes were used in a tetrapolar position: two for the injected electrical current and two for the measured voltage. Bioimpedance measurements were recorded predialysis (after 15 min of rest in the dialysis chair) and subsequently at 30 min during hemodialysis (in the figures represented as $T_0$, $T_{30}$, $T_{60}$, $T_{90}$, $T_{120}$, $T_{150}$, $T_{180}$, $T_{210}$, and $T_{240}$), while the patient was in fowler position. Bioimpedance measurements were performed by the Maltron BioScan 920-II device (Maltron International Ltd, United Kingdom), a multifrequency bioelectrical impedance analyzer that has been validated for fluid assessment in hemodialysis patients [20]. This device has a four-point electrode system that measures impedance at four different frequencies (5, 50, 100, and 200 kHz) for each targeted body segment [21]. The results presented in this work are obtained by analyzing the resistance component of bioimpedance at 5 kHz, represented as "*R*." This single frequency at low kHz was chosen to serve the aim of investigating the relationship with volume changes in the extracellular compartment.

### 2.4 | Bioimpedance Signal Processing

Resistance data from each segment were subjected to outlier detection, where outliers were defined as values falling outside the normal measurement range (mean of the median per session ± 3 × standard deviation). To enable comparison across different segments, the between-subject and between-segment variability were reduced by calculating the relative resistance values (expressed as percentages relative to the measurement at $T_0$).

### 2.5 | Statistical Analysis

Statistical analysis was conducted using software R version 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria). A significance level of 0.05 was considered for all tests. Descriptive statistics were performed to characterize the recruited study population and to visualize the differences in resistance across segments. Clinical characteristics are reported as mean ± standard deviation, while dichotomous data are expressed as the absolute number and frequency (%).

According to the Shapiro–Wilk test, data were not normally distributed. Therefore, the Brown–Forsythe test was used to assess the assumption of equal variances, which was not met. Consequently, changes in resistance $[(R_{T240}–R_{T0})/R_{T0}]$ during hemodialysis were analyzed using the nonparametric Wilcoxon Signed-Rank test for paired data. In addition, the correlations between relative resistance data ($R_{Tx}/R_{T0}$, expressed as percentages with x representing a specific time point during hemodialysis) and UFV (in mL at $T_x$), UFR (in mL/kg/h) and delta SBP ($\text{SBP}_{Tx}–\text{SBP}_{T0}$, in mmHg) respectively, were evaluated using the Spearman method.

Linear mixed modeling was used to compute the intraclass correlation coefficient for the changes in resistance $[(R_{T240}–R_{T0})/R_{T0}]$ between hemodialysis Session 1 and Session 2. In addition, linear mixed modeling was applied to investigate differences in relative resistance signals between groups (i.e., UFV and UFR, hypotension, muscle cramps) at specific time points.

To explore the predictive potential of the relative resistance of each segment in SBP changes, a multiple regression model was developed using a backward stepwise method with a 0.05 significance level. In addition, clinical covariates were taken into account in the final multiple regression model in a forward stepwise method with a significance level of 0.05. Given the repeated measurements (with each patient contributing 18 measurements), the assumption of independence of errors was violated (Durbin–Watson statistic 0.605) as expected. However, the variance inflation factor scores for the independent variables were all well below 10, and the tolerance statistics were all well above 0.2. In addition, the average variance inflation factor score was 1.2. Based on these calculations, we could safely conclude that there was no multicollinearity concern within our data. Furthermore, residual plots showed random dispersion, affirming model assumptions such as homoscedasticity. Results from the multiple regression models are reported as $B$ (= regression coefficient), S.E. (= standard error of $B$), $\beta$ (= standardized regression coefficient), C.I. (= 97.5% confident interval), $R^2$ (coefficient of determination).

## 3 | Results

### 3.1 | Patient Characteristics

A total of 15 patients (seven males, 46.7%) were enrolled in this study (mean age 75.1 ± 9.8 years). Table 1 displays the clinical characteristics of the study population. Each patient participated in two consecutive hemodialysis sessions, resulting in 30 sessions. A decline in SBP of ≥ 20 mmHg occurred during 13 (43.3%) sessions. Eight patients (53.3%) reported muscle cramps during or after the first session.

### 3.2 | Descriptive Bioimpedance Results

During the 30 hemodialysis sessions, bioimpedance measurements were conducted in each body segment at 9 time points from the start of the session (i.e., $T_0$, $T_{30}$, $T_{60}$, $T_{90}$, $T_{120}$, $T_{150}$, $T_{180}$, $T_{210}$, and $T_{240}$). This resulted in 270 bioimpedance measurements per body segment. Based on outlier detection methods, four (1.5%) whole body measurements were considered implausible and excluded from analysis. In the lower leg, upper arm, and thoracic segment, 2 (0.7%), 15 (5.6%), and 14 (5.2%) measurements were assigned as outliers, respectively.

Mean predialysis resistance (at $T_0$) was 614.2 ± 83.4 Ω for the whole body measurements, 169.5 ± 28.6 Ω for the lower leg segment, 106.6 ± 38.2 Ω for the upper arm, and 35.9 ± 13.7 Ω for the thoracic segment (Figure 1A).

### 3.3 | Evolution of the Resistance Signal Over Time

On average, statistically significant increases were observed across all body segments from predialysis to postdialysis ($R_{T240}–R_{T0}$) in each segment (Figure 1B, Table 2).

The intraclass correlation coefficient of the patient-specific predialysis to postdialysis changes in relative resistance between Session 1 and Session 2 is represented in Table 2. Only the thoracic measurements had a high intraclass correlation coefficient (0.728), indicating a low within-patient variability in resistance changes between hemodialysis sessions.

**TABLE 1** | Clinical and dialysis characteristics, in mean ± standard deviation or number (percentage).

| Clinical variable | Study population ($n = 15$) |
|---|---|
| Male (%) | 7 (46.7) |
| Age in years | 75.1 ± 9.8 |
| Body mass index in kg/m$^2$ | 26.1 ± 6.7 |
| Cardiac disease[a] (%) | 6 (40) |
| Diabetes mellitus (%) | 8 (53.3) |
| Shunt/Hickmann Catheter (%) | 6 (40) / 9 (60) |
| Dialysis vintage in years | 6 ± 2.9 |
| Mean UFV in liter | 2.2 ± 0.8 |
| Mean UFR in mL/kg/h | 7.5 ± 2.7 |
| Mean predialysis SBP/DBP in mmHg | 136.8 ± 17.2 / 68.4 ± 9 |
| Mean enddialysis SBP/DBP in mmHg | 126.8 ± 19.2 / 66.1 ± 9.5 |
| Mean pulse rate, predialysis and enddialysis (/min) | 70 ± 12 / 68 ± 11 |
| Mean weight, predialysis and postdialysis (kg) | 73.2 ± 18.9/70.8 ± 18.7 |
| Muscle cramps during Session 1 (%) | 8 (53.3) |
| Hemoglobin (g/dl) | 11.5 ± 1.1 |
| Albumin (g/l) | 40.1 ± 3.7 |
| Sodium (mmol/l) | 138.3 ± 3.3 |
| Potassium (mmol/l) | 4.9 ± 0.6 |
| Calcium (mmol/l) | 2.3 ± 0.1 |
| Phosphate (mmol/l) | 1.4 ± 0.4 |
| Bicarbonate (mmol/l) | 22.6 ± 2.3 |
| Renin-angiotensin-aldosteron-system blocker | 2 (13.3) |
| Calcium antagonist | 5 (30) |
| Beta-blocker | 9 (60) |

| Dialysis variable | Hemodialysis sessions ($n = 30$) |
|---|---|
| Number of hypotensive dialysis sessions[b] (%) | 13 (43.3) |
| Number of sessions with nadir < 100 mmHg (%) | 8 (26.6) |
| Hemodialysis/hemodiafiltration | 15/0 |
| Mean dialysis temperature | 36.2 ± 0.3 |
| Mean dialysate sodium | 138 ± 0 |
| Mean dialysate potassium | 2.2 ± 0.6 |
| Mean dialysate calcium | 1.5 ± 0.1 |
| Mean dialysate bicarbonate | 32.3 ± 1.3 |
| Mean Kt/V | 1.2 ± 0.3 |

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure; UFR, ultrafiltration rate; UFV, ultrafiltration volume.

[a] Cardiac disease identified as systolic or diastolic heart failure.

[b] Hypotension defined as a pre- to postdialysis decrease in systolic blood pressure of ≥ 20 mmHg, number of sessions = 30.

### 3.4 | Effect of Ultrafiltration Volume and Rate on Resistance Signal

Correlations between UFV (UFV at $T_x$–$T_0$, in mL) and relative resistance ($R_{Tx}/R_{T0}$, in %) were as follows: for whole body 0.697; for lower leg 0.669; for upper arm 0.538; and for the thoracic segment 0.537 (all $p < 0.001$, Table 3).

Relative resistance of the whole body, lower leg, and thoracic segment correlated with UFR [$r_s = 0.295$, 0.322, 0.284, respectively, all $p < 0.001$ (Table 3)]. No significant correlation was observed between upper arm resistance and UFR (Table 3).

UFV larger than 2000 mL (or 3000 mL, data not shown) did not result in a different evolution of the relative resistance over time, in any segment. On the contrary, hemodialysis sessions with a UFR > 8 mL/kg/h resulted in statistically significantly higher resistance at T120–240 in both the whole body and lower leg segment (Figure 2A,B, respectively, Table S1). Changes in upper arm or thoracic resistance did not differ between sessions with a UFR higher or lower than 8 mL/kg/h (Figure 2C,D respectively).

### 3.5 | Effect of Systolic Blood Pressure Decline and Muscle Cramps on Resistance Signal

Correlations between delta SBP ($SBP_{Tx}$–$SBP_{T0}$, in mmHg) and relative resistance ($R_{Tx}/R_{T0}$, in %) were as follows: whole body −0.154 ($p = 0.01$); lower leg −0.304 ($p < 0.001$); upper arm −0.223 ($p < 0.001$); and thoracic segment −0.330 ($p < 0.001$).

Figure 3 displays the relation between delta SBP and the resistance signal of each segment. Except for a single measurement at $T_{150}$ in the lower leg segment [$\beta_0 = 109.3$ (2.5), $\beta_1 = 9.5$ (3.8), $p = 0.03$, Figure 3B], only resistance signals from the thoracic segment differed between hemodialysis sessions with and without SBP decline ≥ 20 mmHg. More specifically, thoracic resistance was statistically significantly higher in the sessions with a decline in SBP from $T_{150}$ to $T_{240}$ (Figure 3D, Table S2).

Regarding muscle cramps during or after the first hemodialysis session, no significant effect on resistance signal was observed in any segment, except for the upper arm measurements at $T_{210}$ ($\beta_0 = 98.1$ [7.2], $\beta_1 = 25.6$ [9.2], $p = 0.02$).

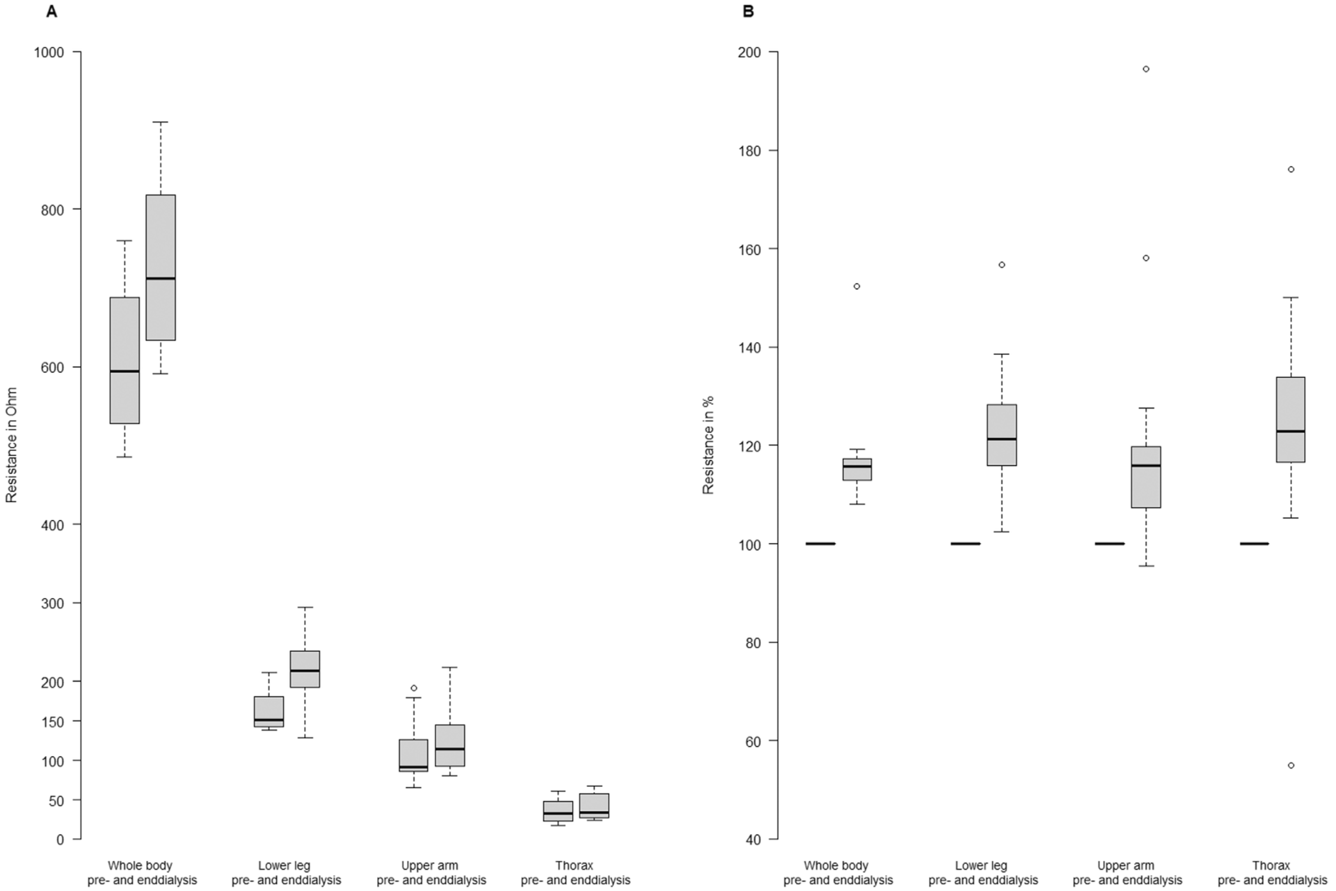

**FIGURE 1** | Boxplots of predialysis and postdialysis (corresponding to $T_0$ and $T_9$) absolute resistances (A) and relative resistance (B), for each segment ($n=30$ hemodialysis sessions). Empty circles display outliers from the boxplot.

**TABLE 2** | Mean changes in relative resistance from the start of dialysis for each segment. *p* value represents the significance of the mean changes from predialysis to postdialysis according to the Wilcoxon signed-rank test. Intraclass correlation coefficient (ICC) represents the between-subject variability of the changes in resistance of one session, relative to the within-subject variability of the resistance changes between Session 1 and 2, in each segment.

| | Mean Δ resistance in % ± S.D., Session 1 | *p* | Mean Δ resistance in % ± S.D., Session 2 | *p* | ICC |
|---|---|---|---|---|---|
| WB | 115.7 ± 9.2 | < 0.001 | 116.9 ± 10.8 | < 0.001 | 0.126 |
| LL | 120.7 ± 12.9 | < 0.001 | 126.2 ± 13.3 | < 0.001 | 0.389 |
| UA | 132.1 ± 26.9 | < 0.001 | 121.3 ± 25 | < 0.001 | 0.023 |
| TH | 120.8 ± 30.8 | 0.04 | 123.6 ± 26.2 | 0.009 | 0.728 |

Abbreviations: LL, lower leg segment; TH, thoracic segment; UA, upper arm segment; WB, whole body.

### 3.6 | Segmental Bioimpedance as Predictor of Systolic Blood Pressure Changes

To evaluate the predictive potential of segmental bioimpedance measurements for intradialytic hypotension, a multiple regression analysis was performed using a backward stepwise model (Table 4A,B). Thoracic resistance was identified as an independent predictor of SBP changes ($\beta=-0.261$ [$-0.353$ to $-0.126$], $p<0.001$, Table 4B), whereas the relative resistances from the other segments were not (Table 4A).

An additional regression model, adjusted for possible covariates of blood pressure changes (i.e., age, gender, vintage, UFV, UFR, diabetes mellitus, and heart failure) was developed (Table 5). Univariate analysis identified thoracic resistance as the variable with the highest adjusted $R^2$ (0.064). The final multiple regression model, which included the relative thoracic resistance changes (%), gender, dialysis vintage, and UFR was statistically significant [$F_{(4,232)}=9.476$, $p<0.001$] (Table 5), accounting for 12.6% of the variance in SBP changes. The relative change in thoracic resistance at 5 kHz from predialysis to postdialysis was a significant predictor of SBP changes, $t_{(232)}=-0.133$, $p=0.04$, indicating a negative relationship.

The cross-validity of this model was confirmed using Stein's formula, resulting in a calculated $R^2=0.107$, and closely approximating the observed adjusted $R^2$ (0.126), demonstrating good cross-validity.

**TABLE 3** | Spearman correlation analyses between hemodynamic parameters and segmental resistance. Spearman's Rho correlation coefficient is represented as $r_s$ (± C.I.).

| Relative change in resistance (%) | Ultrafiltration volume | | Ultrafiltration rate | | Δ systolic blood pressure | |
|---|---|---|---|---|---|---|
| | $r_s$ (C.I.) | $p$ | $r_s$ (C.I.) | $p$ | $r_s$ (C.I.) | $p$ |
| WB ($n=266$) | 0.697 (0.63–0.754) | <0.001 | 0.295 (0.182 to 0.4) | <0.001 | −0.154 (−0.269 to −0.036) | 0.01 |
| LL ($n=267$) | 0.67 (0.598–0.731) | <0.001 | 0.322 (0.211 to 0.425) | <0.001 | −0.304 (−0.409 to −0.192) | <0.001 |
| UA ($n=254$) | 0.538 (0.447–0.618) | <0.001 | 0.016 (−0.103 to 0.135) | 0.8 | −0.223 (−0.333 to −0.107) | <0.001 |
| TH ($n=253$) | 0.537 (0.446–0.617) | <0.001 | 0.284 (0.171 to 0.391) | <0.001 | −0.33 (−0.432 to −0.219) | <0.001 |

Abbreviations: LL, lower leg segment; TH, thoracic segment; UA, upper arm segment; WB, whole body.

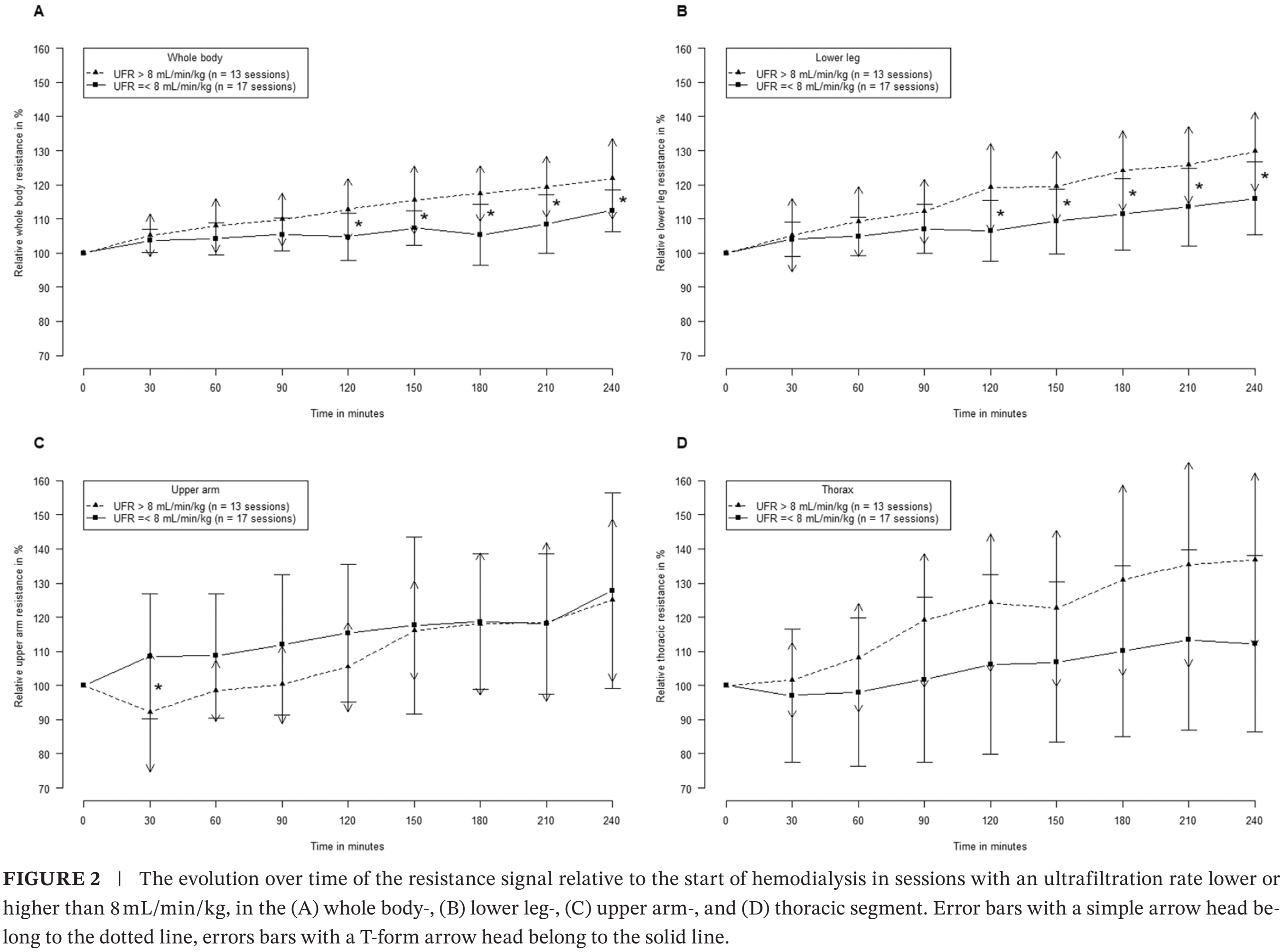

**FIGURE 2** | The evolution over time of the resistance signal relative to the start of hemodialysis in sessions with an ultrafiltration rate lower or higher than 8 mL/min/kg, in the (A) whole body-, (B) lower leg-, (C) upper arm-, and (D) thoracic segment. Error bars with a simple arrow head belong to the dotted line, errors bars with a T-form arrow head belong to the solid line.

## 4 | Discussion

This study aimed to identify the most relevant body segment for bioimpedance measurements in monitoring hemodynamics during hemodialysis. It appeared that thoracic bioimpedance measurements had the strongest predictive capability for SBP changes during hemodialysis, surpassing measurements from the whole body, lower leg, and upper arm.

Bioimpedance measurements of the upper arm and the thoracic segment generated more outliers compared to whole body or lower leg measurements. The increased outlier frequency in the upper arm and thoracic measurements may be attributed to different factors. For the upper arm, outliers likely resulted from movement-related segmental changes, while thoracic outliers may be due to suboptimal electrode attachment [22]. In that case, one would expect to detect outliers in serial occurrence.

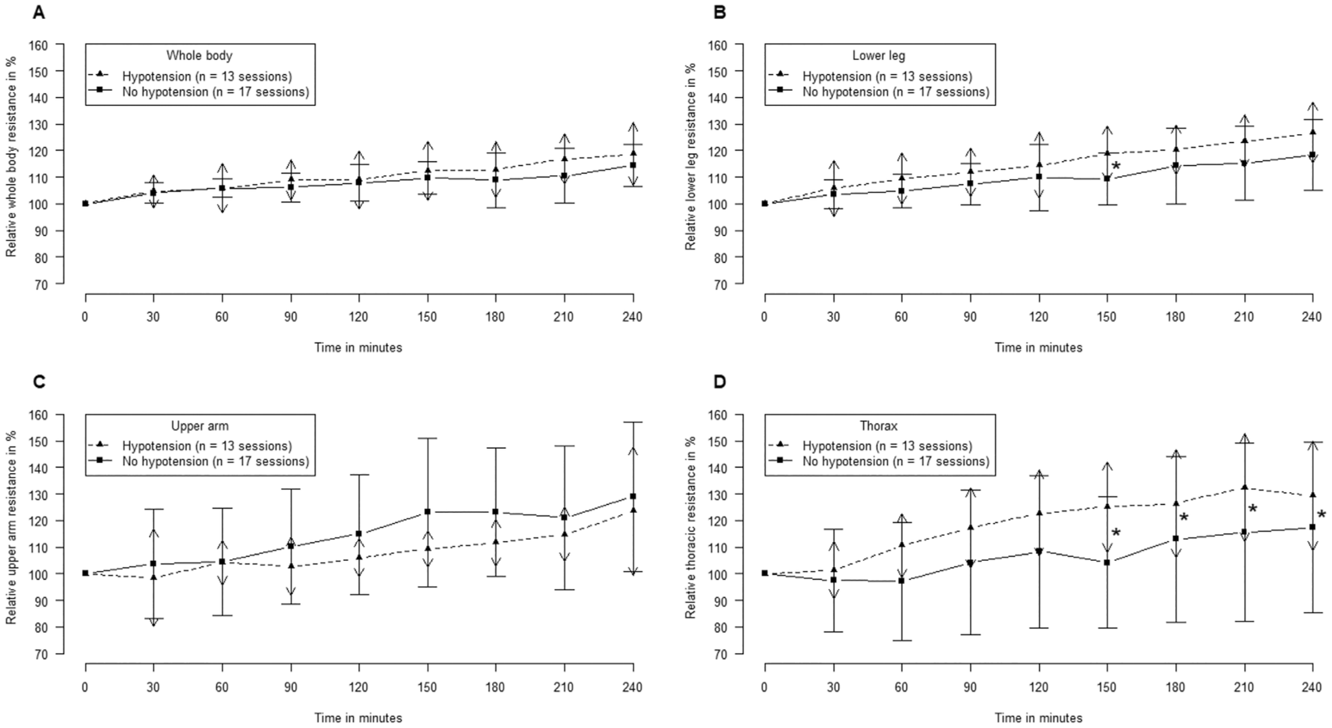

**FIGURE 3** | The evolution over time of the resistance signal relative to the start of hemodialysis during sessions with and without decline in systolic blood pressure, in the (A) whole body-, (B) lower leg-, (C) upper arm-, and (D) thoracic segment. Error bars with a simple arrow head belong to the dotted line, errors bars with a T-form arrow head belong to the solid line.

**TABLE 4** | Results of the entire (A) and reduced (B) multiple regression analyses With the predialysis to postdialysis systolic blood pressure change as dependent variable and the change in relative resistance of each body segment as independent variables ($n = 237$).

| **A** | | | | | |
|---|---|---|---|---|---|
| | **Entire regression model containing resistance of all segments** | | | | |
| | ***B* (S.E.)** | ***t*** | ***β* (C.I.)** | ***p*** | **Adjusted $R^2$** |
| Intercept | 31.469 (16.969) | 1.854 | — | 0.07 | 0.063 |
| WB | 0.095 (0.252) | 0.378 | 0.039 (−0.401 to 0.592) | 0.7 | |
| LL | −0.197 (0.219) | −0.896 | −0.11 (−0.63 to 0.236) | 0.4 | |
| UA | −0.079 (0.068) | −1.156 | −0.075 (−0.213 to 0.055) | 0.2 | |
| TH | −0.181 (0.075) | −2.425 | −0.198 (−0.328 to −0.034) | 0.02 | |
| **B** | | | | | |
| | **Reduced regression model (backward stepwise method)** | | | | |
| Intercept | 17.623 (6.582) | 2.677 | — | 0.008 | 0.064 |
| TH | −0.239 (0.058) | −4.149 | −0.261 (−0.353 to −0.126) | <0.001 | |

Abbreviations: LL, lower leg segment; *p*, *p*-value; *t*, t-statistic; TH, thoracic segment; UA, upper arm segment; WB, whole body.

Notably, 9 out of the 14 thoracic outliers came from consecutive time points during one hemodialysis session of two patients. In contrast, this was not the case for the outliers in the upper arm segment. In addition, upper arm data demonstrated the lowest intraclass correlation compared to the other segments. This indicates high within-patient variability between the two sessions and may be explained by segmental movements or differences in electrode positioning. Some caution should be taken in the clinical interpretation of these findings, as these data were not corrected for the surface area of the measured segment [23]. However, as the presented findings result from relative values, corrections for segment length or surface area do not impose. These results suggest that bioimpedance measurements of the upper arm are more exposed to variability and therefore may be less reliable compared to measurements of other segments.

**TABLE 5** | Results of the univariate (A) and multiple (B) regression analyses with the predialysis to postdialysis systolic blood pressure change as dependent variable.

**A**

| | **Univariate regression analysis, predicting changes in SBP from the start of dialysis** | | | | |
|---|---|---|---|---|---|
| | **$\beta_0$ (S.E.)** | **$\beta_1$ (S.E.)** | ***F*** | ***p*** | **Adjusted $R^2$** |
| Gender | −12.927 (2.087) | 7.195 (2.85) | 6.371 | 0.01 | 0.022 |
| Age | −6.161 (11.309) | −0.038 (0.149) | 0.007 | 0.8 | −0.004 |
| Vintage | −1.1628 (3.224) | −1.239 (0.482) | 6.616 | 0.01 | 0.023 |
| BMI | −20.206 (5.761) | 0.421 (0.211) | 3.98 | 0.05 | 0.013 |
| Diabetic | −12.685 (2.11) | 6.639 (2.86) | 5.387 | 0.02 | 0.018 |
| Cardiac[a] | −21.75 (4.256) | 9.16 (2.901) | 9.969 | 0.002 | 0.036 |
| UFV | −5.277 (2.229) | −0.004 (0.002) | 4.909 | 0.03 | 0.016 |
| UFR | 4.687 (4.056) | −1.844 (0.510) | 13.07 | $<0.001$ | 0.049 |
| WB | 28.565 (16.803) | −0.347 (0.155) | 5.053 | 0.03 | 0.017 |
| LL | 34.567 (12.76) | −0.392 (0.114) | 11.84 | $<0.001$ | 0.044 |
| UA | 5.391 (7.686) | −0.129 (0.068) | 3.667 | 0.06 | 0.011 |
| TH | 17.623 (6.582) | −0.239 (0.058) | 17.22 | $<0.001$ | 0.064 |

**B**

| | **Multiple regression model (step forward method)** | | | | |
|---|---|---|---|---|---|
| | ***B* (S.E.)** | ***t*** | **$\beta$ (C.I.)** | ***p*** | **Adjusted $R^2$** |
| Intercept | 20.156 (6.898) | 2.922 | — | 0.004 | 0.126 |
| TH | −0.133 (0.062) | −2.079 | −0.146 (−0.259 to −0.007) | 0.04 | |
| Gender | 8.55 (2.96) | 2.889 | 0.193 (2.719 to 14.381) | 0.004 | |
| Vintage | −1.623 (0.515) | −3.151 | −0.217 (−2.637 to −0.608) | 0.002 | |
| Ultrafiltration rate | −1.231 (0.564) | −2.154 | −0.153 (−2.341 to −0.12) | 0.03 | |

Abbreviations: BMI, body mass index; *F*, F-statistic; LL, lower leg segment; *p*, *p*-value; SBP, systolic blood pressure; *t*, t-statistic; TH, thoracic segment; TH, thoracic segment; UA, upper arm segment; UFR, ultrafiltration rate; UFV, ultrafiltration volume; WB, whole body.

[a] Cardiac disease identified as systolic or diastolic heart failure.

By analyzing relative resistances from predialysis to postdialysis, the variability between segments can be minimized. Although the differences between the segments were small, the thoracic segment showed the smallest mean predialysis to postdialysis changes in relative resistance. This is in line with previous research, stating that the body prioritizes maintaining central volume located in the thorax during volume changes [17, 24, 25].

UFV and relative resistance correlated statistically significant in all segments. The strongest correlation was observed with whole body resistance, closely followed by lower leg resistance, whereas the correlation was lowest for thoracic and upper arm segments. However, no body segment could show a difference in resistance signal between hemodialysis sessions with a large versus a low UFV. On the other hand, UFR showed comparable correlations with whole body, lower leg, and thoracic resistance. Moreover, bioimpedance measurements of whole body and lower leg revealed significantly higher resistances during the second half of hemodialysis sessions with UFR exceeding 8 mL/kg/h, whereas no effect of UFR on the resistance of the upper arm or thorax was noticed. Given their small cross-sectional area, the limbs contribute more than 90% to the whole body resistance. In addition, it is known that the lower leg pools excess fluid due to gravity. Therefore, changes in volume causing changes in resistance will be expressed most in the lower leg. Consequently, the high correlation between UFV and both whole body and lower leg may be attributed to limbs' cross-sectional area. The concept that the extracellular space is not a homogeneous pool has been studied and confirmed for many years [26, 27]. Therefore, the lower leg has been the body segment of prolonged interest to measure segmental bioimpedance [10, 12–15, 28–31]. Nevertheless, there are a few studies comparing the lower leg and trunk segments in relation to fluid changes during hemodialysis [17, 24–26, 32]. These studies describe that although the increase in resistance from predialysis to postdialysis was consistently higher in the trunk than in the leg segment [10, 33], the relative changes in relation to whole body resistance were lower in the trunk compared to the leg [10, 17, 33]. These findings support the theory that the body prioritizes the preservation of central volume by redistributing fluid from the legs toward the trunk. Indeed, when resistance values (Ω) were converted to volume estimates, the leg has emerged as the segment with the largest changes in extracellular volume during hemodialysis, which likely explains the occurrence of muscle cramps during or after hemodialysis [24, 25]. However, in the present study, no effect of muscle cramps on relative resistance was observed in any segment, also not in the lower leg. On the contrary, the trunk has also been identified as the segment associated with the highest proportion of fluid removal [10, 17, 26]. Since the trunk encompasses both thorax and abdomen, this statement is difficult to compare with those presented here. Additionally, one study found that the arm had the largest fluid reduction compared to the calf and trunk [34]. The observations of the current study confirm that segmental bioimpedance measurements of the lower leg can be used for fluid management and may offer a valuable alternative to whole body measurements. Notably, the correlation coefficient between UFV and relative whole body resistance was lower than our previous work [35]. This difference may be attributed to the inclusion of lower UFV in the current study population, which would otherwise have strengthened the correlations observed in earlier research.

SBP and relative resistance at 5 kHz correlated negatively significant in all segments. While the upper arm lost significance in univariate analysis, thoracic resistance had the strongest correlation compared with the other segments. This is in line with previous work, comparing whole body versus thoracic resistance at low frequency [35]. The presented results from the multiple regression analysis add the importance of the thoracic segment in predicting SBP changes during hemodialysis. Although some assumptions were not fully met, and the model only explained a small proportion of the variance in blood pressure changes, the thorax was the only segment that contributed significantly to the model. In addition, the cross-validation was also robust. These results confirm earlier work [36] and further support the thorax as the preferred segment for hemodynamic monitoring during hemodialysis over whole body, lower leg or upper arm. Future studies should show whether changes in thoracic bioimpedance can predict intradialytic hypotension.

Some limitations of this study have to be mentioned. First, the sample size was relatively small, though it is consistent with the average number of participants in the referred literature. Second, the analysis was based on resistance data measured at a single frequency (5 kHz), despite the availability of other frequencies. This choice was made to maintain clarity in the presented results. By all means, these data may contain valuable information in addition to single frequency analysis. Third, not all assumptions of the multiple regression model were met. Therefore, some caution is warranted when interpreting the results. Lastly, measurements were performed during hemodialysis and cannot be extrapolated to the interdialytic interval.

### 4.1 | Clinical Implementation and Future Perspectives

The finding that thoracic bioimpedance measurements may have a predictive potential for blood pressure changes during hemodialysis reaches out for several clinical implementations. Integrating thoracic bioimpedance into hemodynamic monitoring could innovate hemodialysis treatment. For example, once a patient reaches a critical resistance threshold, physicians could adjust the UFR to prevent hypotensive episodes and endure residual renal output. The wearable format of thoracic bioimpedance enables its use as well as during center hemodialysis as during home hemodialysis treatments.

Technically, the bioimpedance device should be further developed into a user-friendly configuration (e.g., a patch or an implantable) [37]. Hereby, multifrequency measurements and continuously monitoring capacities are warranted. By analyzing multifrequency bioimpedance signals during hemodialysis, novel features such as impedance ratio could be investigated. A continuous application of impedance ratio may optimize hemodynamic monitoring, guide UFR, and reduce the incidence of intradialytic hypotension.

## 5 | Conclusion

This study elucidates the pivotal role of thoracic bioimpedance in the hemodynamic monitoring of hemodialysis patients. Compared to whole body, lower leg, or upper arm bioimpedance measurements, thoracic bioimpedance was found to be an independent predictor of SBP changes during hemodialysis. Future work should focus on the miniaturization of a bioimpedance device and further investigate its predictive potential in both clinical and remote hemodynamic monitoring.

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### Disclosure

This work did not receive any grants, fees, or funding. University Hasselt did not have any role in study design; collection, analysis, and interpretation of data; writing the report; and the decision to submit the report for publication. Study data is available upon request.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## Supporting Information

Additional supporting information can be found online in the Supporting Information section.