Renal Replacement Therapy

RESEARCH

Open Access

Associations between body composition and intradialytic hypotension (IDH), and between IDH and prognosis, in hemodialysis patients

Sonoo Mizuiri[1*], Yoshiko Nishizawa[1], Toshiki Doi[1,4], Aiko Okubo[1,4], Kenichi Morii[1,4], Kazuomi Yamashita[1], Yukari Suga[2], Koji Usui[3], Kenichiro Shigemoto[1] and Takao Masaki[4]

Abstract

Background Previous studies describing relationships among body compositions, intradialytic hypotension (IDH), and mortality yielded inconsistent results. We studied associations between body composition and IDH, and between IDH and prognosis, in patients on hemodialysis (HD).

Methods Participants were patients on maintenance HD and predilution online hemodiafiltration (HDF) ($n=303$). IDH was defined as nadir systolic blood pressure (SBP) < 90 mmHg for ≥ 2 of 10 dialysis sessions during the exposure period (days 1–22). Clinical data at day 1 and post-dialysis body compositions using bioelectrical impedance analysis conducted once during the exposure period were collected. Differences between the IDH and non-IDH groups were analyzed. Kaplan–Meier survival curves of the IDH and non-IDH groups, logistic regression analyses of IDH, and Cox proportional hazard analyses of all-cause and cardiovascular (CV) mortality in all participants were also performed.

Results In all participants, the median (median [interquartile range]) age was 67 [56–74] years, median dialysis duration was 76 [37–145] months, and diabetes prevalence was 42.6% (129/303). Compared with the non-IDH group ($n=274$), the IDH group ($n=29$) had a lower mean pre-dialysis SBP during the exposure period, longer dialysis duration, lower serum albumin levels, and higher median fat tissue index (10.7 [8.6–14.9] versus 9.5 [6.8–11.9] kg/m^2, $P<0.05$). The IDH group had lower 3-year survival for all-cause and CV mortality ($P<0.05$). When adjusted for mean pre-dialysis SBP, mean ultrafiltration volume during the exposure period, HDF, dialysis duration, and serum albumin, fat tissue index, and lean tissue index were associated with IDH ($P<0.05$), but body mass index and overhydration/extracellular water were not. After additional adjustments for age, sex, and diabetes mellitus, only fat tissue index was a significant predictor for IDH [odds ratio: 1.12 (95% confidence interval 1.02–1.25), $P<0.05$]. IDH was also a significant predictor of 3-year all-cause and CV mortality ($P<0.05$).

Conclusions Increased fat tissue index was a significant risk factor for IDH in HD and HDF patients. Furthermore, IDH was a significant predictor of 3-year all-cause and CV mortality in HD and HDF patients.

Keywords All-cause mortality, Body composition, Cardiovascular mortality, Fat tissue index, Hemodialysis, Intradialytic hypotension

*Correspondence:
Sonoo Mizuiri
sm210@med.toho-u.ac.jp
Full list of author information is available at the end of the article

Background

There is no consensus definition of intradialytic hypotension (IDH). The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative guidelines define IDH as a decrease in systolic blood pressure (SBP) of ≥ 20 mmHg or a mean arterial pressure of ≥ 10 mmHg, as well as associated symptoms [1]. Data on IDH are often unavailable from large databases because of a lack of symptoms and intervention. Flithe et al. analyzed data from 1409 patients in the Hemodialysis (HEMO) study and 10,392 patients in the Large Dialysis Organization (LDO) study to investigate the definitions and mortality of IDH [2]. According to their report, an absolute nadir SBP of < 90 mmHg was most potently associated with overall mortality, and cases of IDH using definitions that contained symptoms, interventions, or decreases in blood pressure during the dialysis session were not associated with mortality [2]. The exposure assessment period for IDH varies widely among studies, ranging from 1 to > 100 hemodialysis (HD) treatments, and selecting among longer time-fixed exposure periods may lead to issues related to generalizability [3]. A report by Cho et al. defined IDH as > 2 hypotension episodes during 10 HD treatments [4].

It had been reported that patients undergoing HD who experienced IDH showed higher risks of all-cause mortality and cardiovascular (CV) mortality [5, 6]. Contrastingly, Tisler et al. reported no association between mortality and frequent IDH [7].

Several studies have described the relationship between body composition and IDH [8–14]. However, the timing of bioimpedance spectroscopy of body composition in these reports was variable, with measurements at pre-dialysis [9–11], post-dialysis [12], pre- and post-dialysis [14], and pre-dialysis, every hour (or 30 min) and post-dialysis [8, 13], and the results were inconsistent. Reportedly, bioimpedance measurements at pre-dialysis overestimate muscle mass and underestimate fat, suggesting that bioimpedance measurements of body composition should be taken when patients are closer to their target weight than when overhydrated [15, 16]. We also considered that bioimpedance measurements of body composition should be taken when patients are close to "dry weight" to exclude excessive interstitial body water and assess body composition more reliably and reproducibly.

In this study, we investigated the associations between post-dialysis body composition and IDH, and between IDH and prognosis, in prevalent HD patients.

Patients and methods

Study population

In this retrospective, observational study, data from 303 consecutive Japanese patients who underwent maintenance HD or predilution online hemodiafiltration (HDF) in September 2018 at our hospital were examined.

Data collection, and exposure and outcome assessment periods

Figure 1 shows the analytical timeline for IDH in this study. Patients' medical records were followed up with until death, transfer to another facility, or 3 years (1095 days) post-baseline, whichever came first. Day 1 was classified as baseline; days 1–22 (10 dialysis sessions) were classified as the exposure assessment period, including the session on day 1; and day 23 to the end of the study (3 years post-baseline) was classified as the outcome assessment period. Pre-dialysis SBP, pre-dialysis diastolic blood pressure (DBP), nadir SBP, and ultrafiltration from day 1 to the end of the exposure assessment period (10 dialysis sessions) were assessed in all patients. IDH was defined as a nadir SBP of < 90 mmHg or the

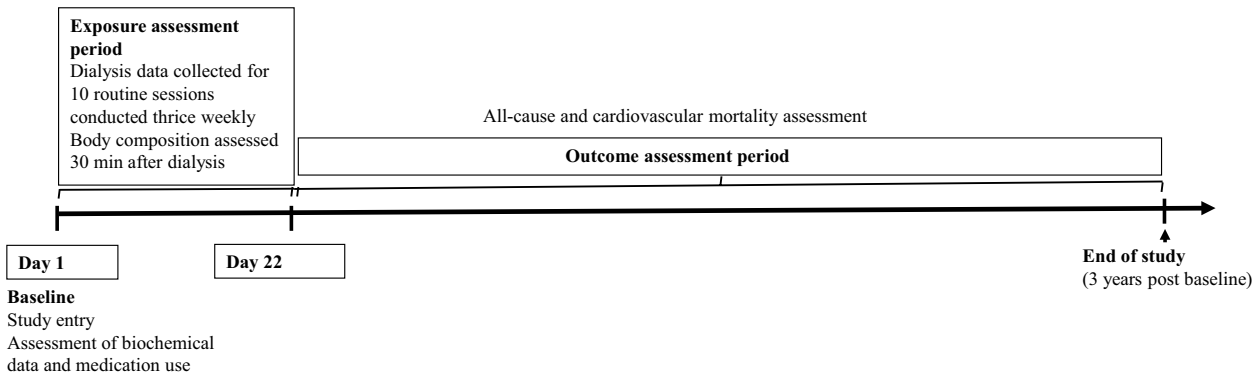

Fig. 1 Timeline for analysis of intradialytic hypotension in this study of 303 patients undergoing hemodialysis (HD). Baseline was day 1; the exposure assessment period was from days 1 to 22 (10 HD sessions), including the session on day 1; and the outcome assessment period was from day 23 to the end of study (3 years post-baseline)

requirement for vasopressor (etilefrine hydrochloride ≥ 20 mg/session) and/or saline (≥ 100 mL/session) infusion during at least 2 of 10 dialysis sessions [4] during the exposure assessment period (days 1–22) of this study. As the outcome assessment, all-cause and CV mortality during the outcome assessment period were confirmed by documentation. Exclusion criteria were as follows: age < 20 years, dialysis duration < 3 months, a history of advanced cancer, infection in the month leading up to the study, and organ transplantation. All patients had vascular access providing a blood flow rate of ≥ 200 mL/min and underwent HD or HDF for 4 h using high-flux membranes three times per week. Substitution volume for HDF was 40 L/session in all patients on HDF. A standard bicarbonate dialysis fluid (140 mEq/L sodium, 2.0 mEq/L potassium, 3.0 mEq/L calcium, 1.0 mEq/L magnesium, and 100 mg/dL glucose), which was delivered using a central dialysis fluid delivery system, was used for HD and HDF. Patient baseline characteristics, including age, sex, primary kidney disease, presence of diabetes mellitus, dialysis duration, and antihypertensive medications, were obtained from the institutional database. Hemoglobin, serum albumin, and C-reactive protein (CRP) levels were obtained on day 1, just before the first dialysis session of the week. Kt/V_{urea} at baseline was also obtained. Intradialytic weight loss was considered to represent the ultrafiltration volume. Body composition data were collected using a bioimpedance spectroscopy device (BCM®; Fresenius Medical Care, Buzen City, Japan) once, 30 min after a dialysis session conducted during the exposure period (days 1–22), and post-dialysis body mass index (BMI) was calculated on the same day. For bioelectrical impedance analysis (BIA), patients were placed in the supine position, two conventional electrodes were placed on the hand, and two were placed on the foot contralateral to the vascular access. Fat tissue index, lean tissue index, total body water, intracellular water, extracellular water (ECW), and overhydration (OH) were measured [17, 18]. The difference between normal ECW and measured ECW is OH (i.e., excess fluid) [18]. Coronary artery calcification was assessed using the Agatston coronary artery calcium score (CACS) [19], once during the exposure assessment period (days 1–22) based on electrocardiography (ECG)-gated chest multidetector computed tomography (CT). ECG-gated chest multidetector CT was performed using the IVY Model 3000T (IVY Biomedical, Branford, CT, USA) and the Aquilion 64 TSX-101A (Toshiba Medical Systems, Tokyo, Japan). Clinical biochemical analyses were performed at our hospital laboratory.

Our facility requires the following conditions for determination of dry weight: (1) normal blood pressure (pre-dialysis SBP < 140 mmHg); (2) absence of edema; (3) normal size cardiothoracic ratio (< 50%) on chest X-ray; (4) OH between −1.1 and +1.1 L using BIA [17]; and (5) no symptoms, including dry mouth, light-headedness, cramping, nausea, cold extremities, or tachycardia.

This study was approved by the Ethical Committee of Ichiyokai Harada Hospital (Approval No. 202303), which conformed to the provisions of the 2013 version of the Declaration of Helsinki. Due to the anonymity of the patients included and the nonintrusive nature of the research, the requirement for written consent was waived.

Statistical analyses

Statistical analyses were performed using Easy R (EZR) [20], which is a modified version of R designed to add statistical functions frequently used in biostatistics.

Data for categorical variables are shown as frequencies (percentages), and data for continuous variables are shown as means ± standard deviations (SDs), or medians and interquartile ranges (IQRs), as appropriate. The significance of intergroup differences was analyzed using Student's *t*-test for normally distributed variables, the Mann–Whitney *U* test for non-normally distributed variables, or the chi-squared test for categorical data, as appropriate. Kaplan–Meier survival curves of the IDH and non-IDH groups, logistic regression analyses of IDH, and Cox proportional hazard analyses of 3-year all-cause and cardiovascular (CV) mortality in all participants were also performed. In all statistical tests, a P value < 0.05 was considered to indicate statistical significance.

Results

In the 303 patients undergoing HD or HDF, primary renal diseases were diabetic nephropathy [$n = 118$ (38.9%)], chronic glomerulonephritis [$n = 97$ (32.1%)], nephrosclerosis [$n = 50$ (16.5%)], autosomal-dominant polycystic kidney disease [$n = 14$ (4.6%)], other diseases [$n = 14$ (4.6%)], and unknown conditions [$n = 10$ (3.3%); Table 1].

Pre-dialysis SBP, pre-dialysis DBP, and ultrafiltration were based on mean values of 10 HD sessions conducted during the exposure assessment period in each participant. The medians [IQRs] for age, dialysis duration, and prevalence of diabetes mellitus in the overall cohort ($n = 303$) were 67 [56–74] years, 76 [37–145] months, and 129/303 (42.6%), respectively. The patients were classified into two groups: IDH ($n = 29$, 9.6%) and non-IDH ($n = 274$, 90.4%). Compared with the non-IDH group, the IDH group had a significantly longer dialysis duration and significantly lower values of the following: mean pre-dialysis SBP and DBP at 10 HD sessions conducted during the exposure assessment period, serum albumin concentration, geriatric nutritional risk index (GNRI), and usage frequency of antihypertensive drugs except

Table 1 Baseline characteristics of the study population according to IDH

	Total ($n=303$)	IDH group ($n=29$)	Non-IDH group ($n=274$)	*P*-value
Age (years)	67 (56–74)	68 (62–74)	67 (55–74)	0.17
Sex	204/303 (67.3)	15/29 (51.7)	189/274 (62.4)	0.07
Diabetes mellitus, *n* (%)	129/303 (42.6)	14/29 (48.3)	115/274 (42.0)	0.52
HDF (%)	227/303 (74.9)	18/29 (62.1)	209/274 (76.3)	0.11
Dialysis duration (months)	76 (37–145)	122 (65–193)	70 (36–143)	< 0.05
†Pre-dialysis SBP (mmHg)	149 ± 19	131 ± 26	151 ± 17	< 0.0001
†Pre-dialysis DBP (mmHg)	80 ± 11	70 ± 12	81 ± 10	< 0.0001
†Ultrafiltration volume (L/session)	2.2 ± 0.7	2.3 ± 0.8	2.1 ± 0.7	0.39
CACS	976 (327–2540)	1385 (637–2514)	952 (271–2540)	0.30
Kt/V_{urea}	1.51 (1.32–1.71)	1.61 (1.36–1.72)	1.50 (1.31–1.70)	0.15
Hemoglobin (g/dL)	11.5 (10.7–12.1)	11.9 (10.9–12.6)	11.5 (10.7–12.1)	0.10
Serum albumin (g/dL)	3.6 (3.4–3.8)	3.4 (3.3–3.8)	3.7 (3.4–3.8)	< 0.01
GNRI	94 (90–97)	91 (87–97)	94 (91–97)	< 0.05
Body mass index (kg/m^2)	22.8 (20.3–25.8)	23.8 (20.3–26.8)	22.7 (20.2–25.5)	0.28
C–reactive protein (mg/dL)	0.12 (0.04–0.35)	0.16 (0.05–1.10)	0.12 (0.04–0.35)	0.08
Antihypertensive drugs, *n* (%)	237/303 (78.2)	16/29 (55.2)	221/274 (80.7)	< 0.01
Calcium channel blockers, *n* (%)	171/303 (56.4)	8/29 (27.6)	163/274 (59.5)	< 0.001
α–blockers, *n* (%)	55/303 (18.2)	0/29 (0)	55/274 (19.7)	< 0.01
β–blockers, *n* (%)	29/303 (9.6)	4/29 (13.8)	25/274 (9.1)	0.51
RAS inhibitors, *n* (%)	160/303 (52.8)	8/29 (27.6)	152/274 (55.5)	< 0.01

IDH intradialytic hypotension, *HDF* predilution online hemodiafiltration, *CACS* Agatston coronary artery calcium score, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *GNRI* geriatric nutritional risk index, *RAS* renin–angiotensin system

† Mean of 10 dialysis sessions conducted during the exposure assessment period [days 1–22 (10 dialysis sessions)]

β–blockers (total antihypertensive drugs, calcium channel blockers, α–blockers, and renin–angiotensin system inhibitors; $P<0.05$). Other parameters were not significantly different between the two groups. The prevalence of male individuals was 51.7% in the IDH group and 62.4% in the non-IDH group ($P=0.07$). The prevalence of diabetes mellitus was 48.3% in the IDH group and 42.0% in the non-IDH group ($P=0.52$). The prevalence of HDF was 18/29 (62.1%) in the IDH group and 209/274 (76.3%) in the non-IDH group ($P=0.11$). The mean ultrafiltration volume at 10 HD sessions conducted during the exposure assessment period was 2.3 ± 0.8 L/session in the IDH group and 2.1 ± 0.7 L/session in the non-IDH group ($P=0.39$). The median [IQR] CACS (measured over days 1–22) was higher in the IDH group (1385 [637–2514]) than in the non-IDH group (952 [271–2540]), but the difference was not significant ($P=0.30$).

Table 2 shows body composition parameters of patients in the IDH and non-IDH groups. The IDH group showed a significantly higher median [IQR] fat tissue index compared with the non-IDH group (10.7 [8.6–14.9] versus 9.5 [6.8–11.9] kg/m^2, $P<0.05$). Lean tissue index, OH, and OH/ECW were not significantly different between the two groups.

Among the 303 patients, 50 all-cause deaths, 23 CV deaths, and 24 hospital transfers occurred over 3 years.

Table 2 Body composition parameters in IDH and non-IDH groups

Variables	Total ($n=303$)	IDH group ($n=29$)	Non-IDH group ($n=274$)	*P*-value
Lean tissue index (kg/m^2)	12.2 (10.6–14.2)	11.1 (9.9–14.0)	12.3 (10.6–14.3)	0.06
Fat tissue index (kg/m^2)	9.7 (7.1–12.2)	10.7 (8.6–14.9)	9.5 (6.8–11.9)	< 0.05
OH (L)	1.20 (0.30–2.30)	1.20 (0.15–2.25)	1.20 (0.40–2.30)	0.71
OH/extracellular water (%)	8.5 ± 9.4	7.7 ± 12.2	8.6 ± 9.1	1.00

IDH intradialytic hypotension, *OH* overhydration (the difference between normal extracellular water and measured extracellular water) [18]

Figure 2 shows the Kaplan–Meier survival curves for 3-year all-cause mortality and 3-year CV mortality. Among the 303 patients, those with IDH ($n=29$) had lower 3-year cumulative rates of survival free from all-cause death (64.5% versus 84.4%, log-rank test, $P<0.01$) and CV death (80.3% versus 93.2%, log-rank test, $P<0.05$) compared with those without IDH ($n=274$).

The results of logistic regression analyses, which aimed to identify body compositions and BMI associated with IDH in all patients, are shown in Table 3. Fat tissue index and lean tissue were significantly associated with IDH, but BMI, OH and OH/ECW were not associated in the unadjusted models. When adjusted for the mean pre-dialysis SBP of 10 dialysis sessions conducted during the exposure assessment period, the mean ultrafiltration volume of 10 dialysis sessions conducted during the exposure assessment period, HDF, dialysis duration, and serum albumin (Model 1), we found that fat tissue index {odds ratio (OR): 1.15 [95% confidence interval (CI)1.04–1.26]} and lean tissue index [OR: 0.78 (CI 0.63–0.96)] were significant predictors for IDH ($P<0.05$). However, after additional adjustments for age, sex, and presence of diabetes mellitus in Model 1 (Model 2), only fat tissue index

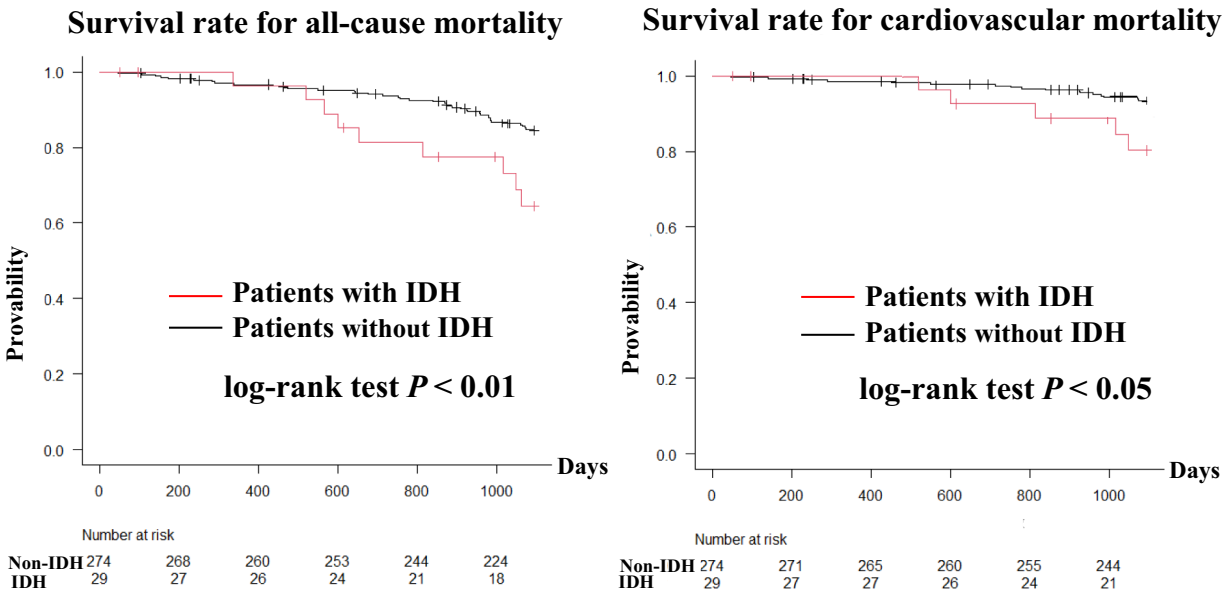

Fig. 2 Kaplan–Meier survival curves for 3-year all-cause and cardiovascular mortality in patients undergoing hemodialysis or predilution online hemodiafiltration, with and without intradialytic hypotension (IDH)

Table 3 Logistic regression analyses for IDH ($n=303$)

Variables	Unadjusted			Adjusted					
				Model 1			Model 2		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Body mass index (kg/m^2)	1.04	0.96–1.14	0.33	1.10	0.99–1.23	0.09	1.11	0.98–1.25	0.10
Fat tissue index (kg/m^2)	1.08	1.00–1.17	< 0.05	1.15	1.04–1.26	< 0.01	1.12	1.02–1.25	< 0.05
Lean tissue index (kg/m^2)	0.85	0.71–1.00	< 0.05	0.78	0.63–0.96	< 0.05	0.88	0.69–1.11	0.27
OH (L)	0.91	0.71–1.18	0.48	1.02	0.78–1.34	0.88	1.06	0.77–1.45	0.73
OH/extracellular water	0.99	0.95–1.03	0.54	1.01	0.97–1.05	0.73	1.01	0.96–1.06	0.74

Model 1 is adjusted for pre-dialysis SBP, ultrafiltration volume, HDF, dialysis duration, and serum albumin. Model 2 is adjusted for pre-dialysis SBP, ultrafiltration volume, HDF, dialysis duration, serum albumin, age, sex, and presence of diabetes mellitus. Pre-dialysis SBP is the mean pre-dialysis systolic blood pressure value of 10 dialysis sessions conducted during the exposure assessment period [days 1 to 22 (10 dialysis sessions)]. Ultrafiltration volume is the mean ultrafiltration volume during the exposure assessment period [days 1 to 22 (10 dialysis sessions)]. OH (overhydration) is the difference between normal extracellular water and measured extracellular water [18]. *IDH* intradialytic hypotension, *OR* odds ratio, *CI* confidence interval *SBP* systolic blood pressure, *HDF* predilution online hemodiafiltration

remained as a significant predictor for IDH [OR (CI): 1.12 (1.02–1.25), $P < 0.05$].

Table 4 shows the associations between IDH and 3-year all-cause or CV mortalities using Cox proportional hazard analyses ($n = 303$). The analyses for all-cause mortality and CV mortality were carried out separately. As shown in the upper panel, IDH was significantly associated with 3-year all-cause mortality in the univariable analysis. In the multivariable analysis, after adjusting for age, sex, and HDF (Model 1), IDH was a significant predictor of 3-year all-cause mortality ($P < 0.05$). After additional adjustment for CRP, GNRI, and presence of diabetes mellitus in Model 1 (Model 2), IDH was confirmed as a significant predictor of 3-year all-cause mortality [hazard ratio (HR): 2.19 (95% CI 1.02–4.74)], $P < 0.05$]. As shown in the lower panel, IDH was also significantly associated with 3-year CV mortality in the univariable analysis. In the multivariable analysis, after adjusting for age, sex, and HDF (Model 1), IDH was a significant predictor of 3-year CV mortality ($P < 0.05$). After additional adjustment for CRP, GNRI, and presence of diabetes mellitus in Model 1 (Model 2), IDH was confirmed as a highly significant predictor of 3-year CV mortality [HR: 3.09 (95% CI1.09–8.78), $P < 0.05$].

Discussion

Infusion of vasopressor and saline is usually provided before a nadir SBP of < 100 mmHg in patients who experience recurrent IDH episodes at our hospital. Considering previous reports [2–4], and the treatment for recurrent hypotension during HD or HDF in our hospital, IDH was defined as a nadir SBP of < 90 mmHg or the requirement for vasopressor and/or saline infusion during at least two of 10 dialysis sessions during the exposure assessment period, and our outcome assessment period was 3-years post-baseline. A recent meta-analysis reported that the prevalence of IDH is < 12% for both the European Best Practice Guideline definition and the Nadir < 90 definition [21], which is much lower than that stated in most reviews. Prevalence of IDH was 9.6% in this study, consistent with the meta-analysis above.

Our study showed that higher fat tissue index and lower lean tissue index in post-dialysis BIA were each associated with IDH, although higher fat tissue index was the most significant predictor for IDH. Furthermore, patients with IDH showed a significantly lower 3-year survival rate for all-cause and CV mortality than patients without IDH in this study, in consistent with the previous reports [5, 6].

Marcelli et al. reported that both lean tissue index and fat tissue index within the 10th–90th percentiles of an age- and sex-matched healthy population were associated with best survival [22]. Consistent with our results, several studies have revealed that low lean tissue index and high fat tissue index are risk factors for IDH [10–12]. Zhou et al. reported that soft lean mass ratio and skeletal muscle ratio were significantly decreased, while fat mass ratio, percentage body fat ratio, and visceral fat area were significantly increased in the IDH group compared with those in the intradialytic normotension group among 127 HD patients [10]. Tian et al. also reported that high fat tissue index and low lean tissue index measured by a body composition monitor rather than BMI were independently associated with greater odds of having IDH, indicating that lean tissue is beneficial, while fat mass is detrimental, in terms of IDH occurrence [11]. Son et al. reported that low skeletal muscle mass to body weight and low handgrip strength indicated higher odds of IDH and suggested that a higher fat tissue index with a low lean tissue index should be interpreted as poor-quality muscle [12]. It is possible that other factors were induced by the increase in fat tissue index in the IDH group in this study, which in turn may have induced IDH. It has been reported that increased arterial stiffness is associated with IDH, and the pre-dialysis subendocardial viability ratio, an index used to evaluate myocardial perfusion, could complement screening for IDH [23, 24]. Although we did not collect data on arterial stiffness for this study, obesity and visceral fat tissue are reportedly positively

Table 4 Associations of intradialytic hypotension (IDH) and 3-year all-cause or cardiovascular (CV) mortality in the Cox proportional hazard analyses ($n = 303$)

Variable	Unadjusted			Adjusted					
				Model 1			Model 2		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value	HR	95% CI	*P*-value
IDH (for all-cause mortality)	2.52	1.22–15.19	< 0.05	2.12	1.01–4.42	< 0.05	2.19	1.02–4.74	< 0.05
IDH (for CV mortality)	3.19	1.18–8.61	< 0.05	3.00	1.10–8.21	< 0.05	3.09	1.09–8.78	< 0.05

The analyses for all-cause mortality and CV mortality were carried out separately. Model 1 was adjusted by age, sex, and HDF. Model 2 was adjusted by age, sex, HDF, C-reactive protein, geriatric nutritional risk index and presence of diabetes mellitus. *HR* hazard ratio, *CI* confidence interval, *HDF* predilution online hemodiafiltration

correlated with parameters of arterial stiffness (pulse wave velocities) in renal transplant recipients [25].

However, different results for associations among the fat tissue index, IDH, and survival in HD patients have also been reported [9, 26]. Katalinic et al., defining IDH as a decrease in SBP of ≥ 20 mmHg over a 12-month observation period, regardless of the frequency, reported that an increase in the fat tissue index led to fewer IDH episodes in 50 HD patients [9]. However, we consider the number of patients in their study ($n = 50$) to be too small to evaluate the significance of the fat tissue index for IDH. We also find it unusual that only 4 of their 50 patients reportedly experienced a decrease in SBP ≥ 20 mmHg more than once in all the HD sessions conducted over 12 months. Yajima et al. reported that higher fat tissue indexes were independently associated with reduced risks of all-cause mortality in 162 HD patients [26]. The timing of bioimpedance spectroscopy was after dialysis, and the participants were Japanese in their study, the same as in our study and had a similar age, but the aims of their study and ours were slightly different; namely, they described all-cause mortality, but not IDH and CV mortality, in HD patients. In our study, a higher fat tissue index was a significant risk factor for IDH, and IDH was a significant risk factor for 3-year all-cause and CV mortality in HD and HDF patients. However, the risk factors for all-cause and CV mortality in dialysis patients include not only IDH, but also age, sex, diabetes mellitus, and albumin and serum CRP levels [27, 28]. Kwan et al. reported that fat mass might have dual competing effects on survival in dialysis patients—a protective effect mediated through nutrition and a deleterious effect mediated through adipokines—and proposed that the level of kidney function modifies the relative importance of these effects [29]. They reported that an increase in fat mass in HD patients is associated with inflammation, insulin resistance, atherosclerosis, and coronary calcification, and there is no reverse epidemiology of the associations among traditional and nontraditional risk factors and disease with adiposity in these patients [29]. We could not rule out the possibility that IDH was mediated by increased fat tissue index with a deleterious effect in dialysis patients of our study.

Our findings have important clinical implications that bioimpedance analyses in HD and HDF patients are important since higher value in fat tissue index is bad, at least for IDH occurrence and IDH was a significant predictor for 3-year all-cause and CV mortality.

Limitations

First, this was a single-center study with a retrospective design. Second, the prevalence of diabetes mellitus in the IDH and non-IDH groups was not uniform, although the difference was not significant. Third, clinical and laboratory data were only assessed at baseline. Fourth, the exposure assessment period for IDH was rather short (10 dialysis sessions). Fifth, our cohort included only Japanese patients, whose average body size is much smaller than patients in Western countries.

Conclusions

Increased fat tissue index was a significant risk factor for IDH in HD and HDF patients. Furthermore, IDH was a significant predictor for 3-year all-cause and CV mortality in HD and HDF patients.

Abbreviations

IDH	Intradialytic hypotension
HD	Hemodialysis
HDF	Predilution online hemodiafiltration
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
CV	Cardiovascular
CRP	C-reactive protein
BMI	Body mass index
BIA	Bioelectrical impedance analysis
OH	Overhydration
ECW	Extracellular water
CACS	Agatston coronary artery calcium score
ECG	Electrocardiography
CT	Computed tomography
IQR	Interquartile range
GNRI	Geriatric nutritional risk index
OR	Odds ratio
CI	Confidence interval
RAS	Renin–angiotensin system

Acknowledgements

We thank M.E. Kazuyoshi Karasuda from Ichiyokai Harada Hospital for help with statistical analysis.

Author contributions

Conception or design of the work, or acquisition, analysis, or interpretation of the data: Sonoo Mizuiri, Yoshiko Nishizawa, Toshiki Doi, Aiko Okubo, Kenichi Morii, Kazuomi Yamashita, Yukari Suga, and Koji Usui. Supervision or mentorship: Kenichiro Shigemoto and Takao Masaki. Each author contributed important intellectual content during the drafting of the manuscript, and all the authors approved the final version of the manuscript.

Funding

No specific grant from any funding agency in the public, commercial, or not-for-profit sectors was received for this study. This study was supported by the private foundation of Ichiyokai Harada Hospital.

Availability of data and materials

The datasets analyzed in this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the ethical standards of the 2013 Declaration of Helsinki and its later amendments or comparable ethical standards. It was approved by the Ethical Committee of Ichiyokai Harada Hospital (approval no. 202303). Because of the anonymity of the patients studied and the nonintrusive nature of the research, the requirement for written consent for publication was waived via the opt-out method on the hospital's information.

Consent for publication
Not applicable.

Competing interests
The authors report no conflict of interest.

Author details
[1]Division of Nephrology, Ichiyokai Harada Hospital, 7-10 Kairoyama-cho, Saeki-ku, Hiroshima 731-5134, Japan. [2]Division of Dialysis Therapy Registry, Ichiyokai Harada Hospital, 7-10 Kairoyama-cho, Saeki-ku, Hiroshima 731-5134, Japan. [3]Ichiyokai Ichiyokai Clinic, 10-3 Asahien, Saeki-ku, Hiroshima 731-5133, Japan. [4]Department of Nephrology, Hiroshima University, 1-2-3 Kasumi Minami-ku, Hiroshima 734-8551, Japan.

Received: 16 December 2023 Accepted: 23 May 2024
Published online: 18 June 2024

References

1. K/DOQI Workgroup. K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. Am J Kidney Dis. 2005;45(4 Suppl 3):S1–153.
2. Flythe JE, Xue H, Lynch KE, Curhan GC, Brunelli SM. Association of mortality risk with various definitions of intradialytic hypotension. J Am Soc Nephrol. 2015;26:724–34.
3. Assimon MM, Flythe JE. Intradialytic hypotension definition of intradialytic hypotension. Semin Dial. 2017;30(6):464–72.
4. Cho A, Lee YK, Oh J, Yoon JW, Shin DH, Jeon HJ, et al. The relationship between intradialytic hypotension and vascular calcification in hemodialysis patients. PLoS One. 2017;12:e0185846.
5. Dasgupta I, Thomas GN, Clarke J, Sitch A, Martin J, Bieber B, et al. Associations between hemodialysis facility practices to manage fluid volume and intradialytic hypotension and patient outcomes. Clin J Am Soc Nephrol. 2019;14:385–93.
6. Chou JA, Kalantar-Zadeh K, Mathew AT. A brief review of intradialytic hypotension with a focus on survival. Semin Dial. 2017;30:473–80.
7. Tisler A, Akócsi K, Borbás B, Fazakas L, Ferenczi S, Görögh S, et al. The effect of frequent or occasional dialysis-associated hypotension on survival of patients on maintenance haemodialysis. Nephrol Dial Transplant. 2003;18:2601–5.
8. Koziolek MJ, Gauczinski S, Kahler E, Bramlage CP, Scheel AK, Mueller GA, et al. Bioimpedance analysis and intradialytic hypotension in intermittent hemodialysis. Clin Nephrol. 2006;66:39–50.
9. Katalinic L, Krtalic B, Jelakovic B, Basic-Jukic N. The unexpected effects of L cartinine supplementation on lipid metabolism in hemodialysis patients. Kidney Blood Press Res. 2018;43:1113–20.
10. Zhou Q, Wang J, Xie S, Yuan S, Zhong L, Chen J. The Correlation between body composition measurement by bioelectrical impedance analysis and intradialytic hypotension. Int Urol Nephrol. 2020;52:953–8.
11. Tian M, Zha Y, Qie S, Lin X, Yuan J. Association of body composition and intradialytic hypotension in hemodialysis patients. Blood Purif. 2020;49:334–40.
12. Son HE, Ryu JY, Lee K, Choi YI, Kim MS, Park I, et al. The importance of muscle mass in predicting intradialytic hypotension in patients undergoing maintenance hemodialysis. Kidney Res Clin Pract. 2022;41:611–22.
13. Haroon S, Tai BC, Yeo X, Davenport A. Changes in total and segmental extracellular and intracellular volumes with hypotension during hemodialysis measured with bioimpedance spectroscopy. Artif Organs. 2022;46:666–76.
14. Tangvoraphonkchai K, Davenport A. Changes in extracellular water with hemodialysis and fall in systolic blood pressure. Int J Artif Organs. 2022;45:140–5.
15. Panorchan K, Nongnuch A, El-Kateb S, Goodlad C, Davenport A. Changes in muscle and fat mass with haemodialysis detected by multi-frequency bioelectrical impedance analysis. Eur J Clin Nutr. 2015;69:1109–12.
16. El-Kateb S, Davenport A. Changes in intracellular water following hemodialysis treatment lead to changes in estimates of lean tissue using bioimpedance spectroscopy. Nutr Clin Pract. 2016;31:375–7.
17. Wabel P, Chamney P, Moissl U, Jirka T. Importance of whole-body bioimpedance spectroscopy for the management of fluid balance. Blood Purif. 2009;27(1):75–80.
18. O'Lone EL, Visser A, Finney H, Fan SL. Clinical significance of multi-frequency bioimpedance spectroscopy in peritoneal dialysis patients: independent predictor of patient survival. Nephrol Dial Transpl. 2014;29:1430–7.
19. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol. 1990;15:827–32.
20. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statics. Bone Marrow Transpl. 2013;48:452–8.
21. Kuipers J, Verboom LM, Ipema KJR, Paans W, Krijnen WP, Gaillard CAJM, et al. The prevalence of intradialytic hypotension in patients on conventional hemodialysis: a systematic review with meta-analysis. Am J Nephrol. 2019;49:497–506.
22. Marcelli D, Usvyat LA, Kotanko P, Bayh I, Canaud B, Etter M, et al. Body composition and survival in dialysis patients: results from an international cohort study. Clin J Am Soc Nephrol. 2015;10:1192–2200.
23. Iwashima Y, Fukushima H, Horio T, Rai T, Ishimitsu T. Blood pressure, arterial waveform, and arterial stiffness during hemodialysis and their clinical implications in intradialytic hypotension. Hypertens Res. 2023;46(3):697–707.
24. Mogi M. Prediction of intradialytic hypotension. Hypertens Res. 2023;46(3):774–5.
25. Heleniak Z, Illersperger S, Brakemeier S, Dębska-Ślizień A, Budde K, Halleck F. Obesity, fat tissue parameters, and arterial stiffness in renal transplant recipients. Transplant Proc. 2020;52(8):2341–6.
26. Yajima T, Arao M, Yajima K, Takahashi H, Yasuda K. The associations of fat tissue and muscle mass indices with all-cause mortality in patients undergoing hemodialysis. PLoS ONE. 2019;14: e0211988.
27. Ma L, Zhao S. Risk factors for mortality in patients undergoing hemodialysis: a systematic review and meta-analysis. Int J Cardiol. 2017;238:151–8.
28. Mukai H, Villafuerte H, Qureshi AR, Lindholm B, Stenvinkel P. Serum albumin, inflammation, and nutrition in end-stage renal disease: C-reactive protein is needed for optimal assessment. Semin Dial. 2018;31(5):435–9.
29. Kwan BC, Beddhu S. Cardiovascular and survival paradoxes in dialysis patients: a story untold: adiposity, adipokines and outcomes in dialysis population. Semin Dial. 2007;20(6):493–7.

Publisher's Note