



# Pre-dialytic Systolic Blood Pressure is an Independent Predictor of Intradialytic Hypertension

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## Abstract

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**BACKGROUND:** Since endothelial dysfunction and activation of renin-angiotensin aldosterone system are the primary mechanism of intradialytic hypertension (IDHT), the assessment of pre-dialytic blood pressure might provide an important information for the prediction of IDHT.

**AIM:** The objectives of the study were to assess the association between pre-dialytic blood pressure and the risk of IDHT.

**METHODS:** We conducted a cross-sectional study in Universitas Muhammadiyah Malang Hospital. The inclusion criteria were all hemodialysis patients aged more than 18 years, and the exclusion criteria were patients with hemodialysis duration of <3 months, patients with poor compliance to consume antihypertensive drugs, and hemodynamically unstable. The predictor variable was pre-dialytic systolic blood pressure and the outcome was the incidence of IDHT. The association between pre-dialytic blood pressure and the risk of IDHT was assessed using multiple logistic regression.

**RESULTS:** A total of 36 patients with IDHT and 60 patients without IDHT were enrolled in our study. Our study identified that pre-dialytic systolic blood pressure was associated with the risk of IDHT, with mean difference was 10.90 mmHg between patients with IDHT and without IDHT. Our study confirmed that the levels of pre-dialytic systolic blood pressure 135 mmHg were the optimal cutoff, and we found that patients with pre-dialytic systolic blood pressure  $\geq$  135 mmHg had 4.60-fold to develop IDHT compared to patients with pre-dialytic systolic blood pressure < 135 mmHg.

**CONCLUSION:** Our study reveals that pre-dialytic systolic blood pressure is an important predictor of IDHT.

## Introduction

Intradialytic hypertension (IDHT), defined as an elevated levels of blood pressure during or immediately after hemodialysis, is a serious issue and has a fatal impact in hemodialysis patients [1]. The incidence of this circumstance was predicted between 15% and 18% among hemodialysis patients [2], [3]. IDHT had been reported to affect adverse outcomes such as ischemic coronary disease, heart failure, and mortality [1], [4]. The report revealed that the mortality caused by IDHT was approximately 20% [5] and the survival rate between patients without IDHT and IDHT was 96.8% versus 77.3% [6]. To date, no specific recommendation for the management of IDHT, and the current recommendation only suggested for the correction of dry weight, administration of carvedilol, and a reduction in sodium concentration in the dialysate. The current recommendation only suggested for the correction of dry weight, administration of carvedilol, and a reduction in sodium concentration in the dialysate [4]. However, the

management of IDHT is complex and it might depend on the underlying illness. Therefore, the identification of potential predictors of IDHT was crucial to prevent IDHT and to determine the appropriate management.

The pathogenesis of IDHT is complex, and the precise etiology and risk factors of IDHT are undefined properly. While the theory reveals that several conditions such as volume overload, smaller dry weight, malnutrition, and low-level potassium dialysate are considered the potential risk factors of IDHT, the evidence remained conflicting [4]. On the other hand, the identification of potential causes of IDHT is an important approach to anticipate the existing of IDHT among hemodialysis patients. As widely known that vascular resistance, sympathetic overactivity, and the activation of renin-angiotensin aldosterone system are the potential underlying condition proposed to contribute in the development of IDHT [1], the assessment of pre-dialytic blood pressure might provide the valuable predictor for estimating IDHT. Therefore, the aims of our study were to assess the association between

pre-dialytic blood pressure and the risk of IDHT among hemodialysis patients.

## Methods

### Design and participants

We performed a cross-sectional study in Universitas Muhammadiyah Malang Hospital, Malang, Indonesia, to assess the association between pre-dialytic systolic blood pressure and the risk of IDHT. Corresponding to the estimated prevalence of hemodialysis patients was 10.6–13.4% with 5% margin error and 95% confidence interval, we required a minimal of 92 patients to enroll in our study. All hemodialysis patients with age more than 18 years old were included in our study. We excluded patients with hemodialysis duration of <3 months, patients with poor compliance to consume antihypertensive drugs, and hemodynamically unstable. The checklists of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and the principles outlined in the Declaration of Helsinki were adapted to set the appropriate protocols in our study. The STROBE checklist in our present study is outlined in the supplementary files [7]. Our present study had been registered and approved by the local ethical committee of Universitas Muhammadiyah Malang Hospital (No: E5a/264/KEPK-UMM/XII/2021). Before recruit in the study, the participants were explained on the aims, benefits, and risks of the study. Participants were also explained that they could quite from our study at any time. Participants were voluntary, and no incentive was given.

### Study covariates

The predictor covariate in our present study was pre-dialytic systolic blood pressure. The outcome measure of our study was IDHT, defined as rise in mean arterial pressure >15 mmHg within or immediately post-dialysis [8]. Pre-dialytic systolic blood pressure and interdialytic blood pressure were considered as the mean of blood pressure in the past 30 days of the baseline period. The measurement of blood pressure was conducted using standard protocols by an automated device integrated in the hemodialysis machine on the non-access arm with the patients seated in the dialysis chair. We also collected the baseline characteristics among groups, retrieved from medical records, including age, gender, body weight, body height, body mass index, mid-upper arm circumference, job type, educational levels, smoking status, comorbidity, and laboratory findings.

### Statistical analysis

Data were presented in mean  $\pm$  SD or n (%). The

numerical covariates in our study were tested for normality using Kolmogorov–Smirnov test. Data were considered normal if the p value more than 0.05 was considered. All baseline characteristics between groups were analyzed for homogeneity using Chi-squared for categorical covariates and unpaired t-test for numerical covariates. Data were considered having homogeneity if the p value more than 0.05 was considered. The association between pre-dialytic hypertension and IDHT among hemodialysis patients was assessed using multiple logistic regression.  $p < 0.05$  was considered statistically significant. The effect estimate was determined by calculating mean difference (MD) for numerical data and odds ratio with 95% confidence interval (OR 95% CI) for categorical data. The cutoff point of pre-dialytic blood pressure was determined by calculating J index. The highest J index was considered the best cutoff point. The software of Statistical Package for the Social Sciences (SPSS) version 17 (IBM SPSS, Chicago, IL) was used to analyze the data.

## Results

### Patient selection

During the study period, a total of 121 hemodialysis patients were enrolled in our study. Of those, a total of 25 patients were excluded due to the hemodialysis duration which was <3 months, poor compliance to consume antihypertensive drugs, and hemodynamically unstable. Finally, a total of 96 hemodialysis patients were included in our study. The flowchart of patient selection in our study is presented in Figure 1, and the baseline characteristics of patients among groups are outlined in Table 1. Our data suggested that our study participants between groups were age and sex matched. The raw data of patients in our study are outlined in the Supplementary files [7].

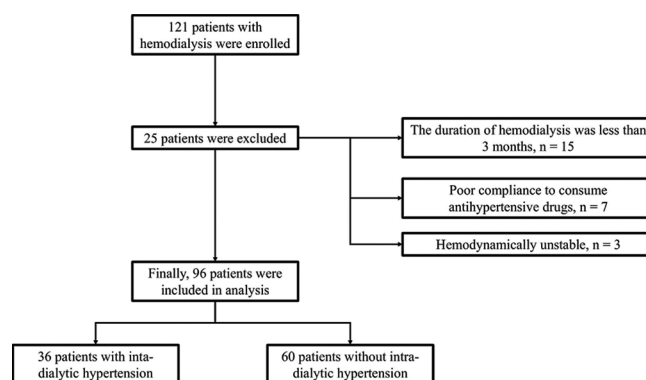


Figure 1: A flowchart of patient selection in our study

### Pre-dialytic systolic blood pressure and the risk of IDHT

Our study revealed that patients with

**Table 1: Baseline characteristics of patients included in our study**

Characteristics	IDHT (n = 36)	Control (n = 60)	p
Age (years)	55.3 ± 12.1	53.2 ± 12.1	0.4100
Male (n [%])	17 [47.2]	33 [55.0]	0.4610
BW (kg)	58.1 ± 10.1	61.2 ± 13.1	0.2230
BH (cm)	160.0 ± 7.4	161.0 ± 7.0	0.5070
MUAC (cm)	26.2 ± 3.7	27.0 ± 4.9	0.3980
BMI (kg/m <sup>2</sup> )	22.6 ± 3.0	23.4 ± 3.7	0.2720
Job			
Housewife (n [%])	19 [52.8]	26 [43.3]	0.3700
Civil servant (n [%])	4 [11.1]	3 [5.0]	0.2770
Entrepreneur (n [%])	13 [36.1]	30 [50.0]	0.1870
Educational levels			
Primary (n [%])	4 [11.1]	1 [1.7]	0.0790
Junior high school (n [%])	11 [30.6]	24 [40.0]	0.3530
Senior high school (n [%])	14 [38.9]	26 [43.3]	0.6690
Diploma (n [%])	2 [5.6]	1 [1.7]	0.3170
University (n [%])	5 [13.9]	8 [13.3]	0.9390
Smoking (n [%])	5 [13.9]	10 [16.7]	0.7170
Comorbidity			
Diabetes mellitus (n [%])	12 [33.3]	24 [40.0]	0.5140
Hypertension (n [%])	20 [55.5]	35 [58.3]	0.7900
Renal stone (n [%])	1 [2.8]	1 [1.7]	0.7150
CGN (n [%])	0 [0.0]	2 [3.3]	0.4670
Uric acid (n [%])	3 [8.3]	1 [1.7]	0.1530
Laboratory findings			
Hemoglobin (gr/dl)	9.4 ± 2.4	9.4 ± 1.6	1.0000
Urea (mg/dl)	120.8 ± 27.1	117.1 ± 33.3	0.5730
Creatinine (mg/dl)	17.2 ± 15.5	15.3 ± 16.9	0.5820
HD duration (months)	28.9 ± 20.4	24.6 ± 10.1	0.1680
UF	2.1 ± 0.8	2.1 ± 1.0	1.0000
Qb	238.0 ± 25.9	239.0 ± 27.2	0.8590

Note, data were presented in mean ± SD or n (%); IDHT: Intradialytic hypertension, BW: Body weight, BH: Body height, MUAC: Mid-upper arm circumference, BMI: Body mass index, CGN: Chronic glomerulonephritis, BP: Blood pressure, HD: Hemodialysis.

higher pre-dialytic systolic blood pressure were associated with increased risk of IDHT (MD: 10.90; 95% CI: 6.07–15.73). Furthermore, our analysis in ROC identified that 135 mmHg was the optimal cutoff point of pre-dialytic systolic blood pressure, and we found that patients with pre-dialytic blood pressure ≥135 mmHg were associated with 4.60-fold to have IDHT than those with pre-dialytic blood pressure <135 mmHg (OR: 4.60; 95% CI: 1.88, 11.23) (Table 2 and Figure 2).

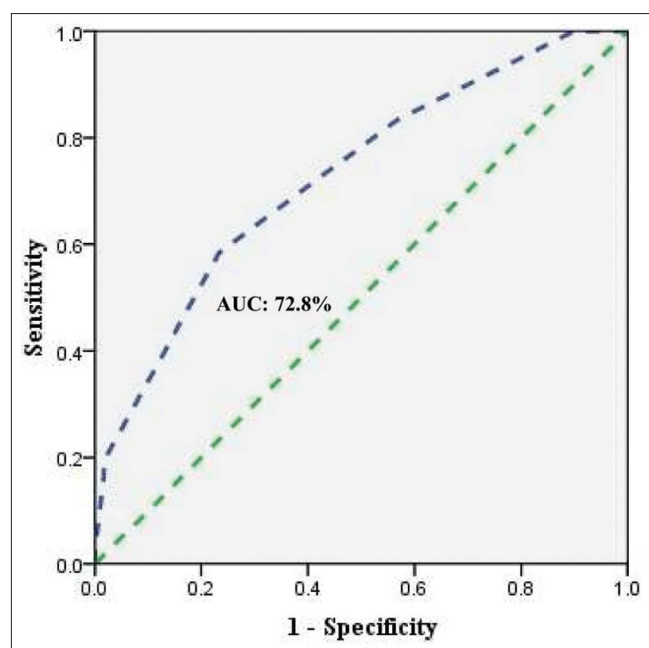


Figure 2: ROC of the association between pre-dialytic systolic blood pressure and the risk of intradialytic hypertension (AUC, 72.8%; J, 0.35; sensitivity, 58.3%; specificity, 76.7%; and cutoff, 135 mmHg)

**Table 2: The summary of the association between pre-dialytic systolic blood pressure and the risk of intradialytic hypertension**

Parameters	IDHT (n = 36)	Control (n = 60)	MD/OR	95%CI	p
Pre-dialytic systolic blood pressure	138.1 ± 13.3	127.2 ± 10.6	10.90*	6.07–15.73	<0.0001
Pre-dialytic systolic blood pressure (≥135 vs. <135 mmHg)	21 (58.3)	14 (23.3)	4.60**	1.88–11.23	0.0010

Note, data were presented in mean ± SD or n (%); MD: Mean difference, OR: Odds ratio, CI: Confidence interval, \*indicated MD, \*\*indicated OR, IDHT: Intradialytic hypertension.

## Discussion

Our study found that patients with elevated pre-dialytic systolic blood pressure had higher risk to develop IDHT. Moreover, we confirmed that the pre-dialytic systolic blood pressure >135 mmHg had 4.60 odds to develop IDHT compared to those with the pre-dialytic systolic blood pressure <135 mmHg. Our current study was consistent with the report of the previous studies. The studies conducted in Greece [9], the US [10], [11], Italy [12], [13], and Iran [14] also found that pre-dialytic systolic blood pressure and its variability were the important predictor in patients with IDHT. However, in those previous studies, the incidence of IDHT was also affected by other predictors such as age and dialysis setting. In our study, we confirmed that the other potential predictors such as age and dialysis setting were homogeneous between case and control, and therefore, our study might serve the better evidence.

The theory underlying between pre-dialytic systolic blood pressure and IDHT remains inconclusive. Normally, in hemodialysis patients, the reduction of intravascular volume may occur due to ultrafiltration process, and the concentration gradient between blood and dialysate may cause the solute diffusion and may lead to the reduction of extracellular osmolarity. Those circumstances may be responsible to affect the decreased in blood pressure in hemodialysis patients [15]. However, in patients with the existing of elevated levels of blood pressure before hemodialysis, the response may differ to those normal hemodialysis patients. In patients with increased pre-dialytic systolic blood pressure, the activation of various paracrine and neurohormonal system may occur in response to minimizing the hemodynamic instability. This response may affect the failure of blood pressure reduction and furthermore may contribute to the elevated blood pressure [16]. On the other hand, in patients with elevated pre-dialytic blood pressure, the various degrees of vascular resistance may be existed and may contribute to the development of IDHT [17]. In addition, some previous studies had shown that the elevated levels of biomarkers having the pivotal role in the development of vascular resistance such as asymmetric dimethylarginine [18], endothelin-1 [10], and nitride oxide [19] were proven to affect IDHT. Those potential biomarkers may have the important role

affecting the damage of vascular system and contribute to the development of IDHT [10].

In our study, we had found that pre-dialytic systolic blood was the independent risk factor of the development of IDHT among hemodialysis patients. Our current study might suggest that hemodialysis patients with elevated levels of systolic blood pressure should be a concern to anticipate the occurrence of IDHT. On the other hand, we also suggested that the appropriate management in blood pressure control in hemodialysis patients should be a priority to prevent elevated pre-dialytic systolic blood pressure and IDHT. However, further investigations might also be required to elucidate the precise potential predictors of IDHT, and the scoring system might also be needed to compile for early detection of IDHT.

Our present study had some limitations. First, the possibility of confounding factors, for example, the levels of potential biomarkers of endothelin-1, nitride oxide, and asymmetric dimethylarginine which may affect the endothelial function [15], was not included in the study. Second, the relatively limited sample size in our study might provide the false-positive results. Therefore, further investigations with including larger sample size were needed. Third, our current study was retrospective data analysis. Therefore, the risk of analysis bias might be existed. Further investigations with better study design might be required.

## Conclusion

Our study reveals that hemodialysis patients with the levels of blood pressure >135 mmHg in pre-dialysis are associated with increased risk of IDHT. Our current study might provide the new insight regarding the role of pre-dialytic systolic blood pressure in the development of IDHT.

## Declarations

### **Ethics approval and consent to participate**

Participants had provided written informed consent before involve in the study. Our study had been approved by local ethical committee (No: E5a/264/KEPK-UMM/XII/2021).

### **Availability of data and materials**

The supplementary data were presented in Figshare (<https://doi.org/10.6084/m9.figshare.17152814.v1>)

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## Authors' contributions

Idea/concept: AR and DS. Design: AR and DS. Control/supervision: JKF and AG. Data collection/processing: AR and DS. Extraction/Analysis/interpretation: JKF. Literature review: AR, DS, JKF, and AG. Writing the article: JKF. Critical review: AG. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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