Underweight rather than overweight is associated with higher prevalence of hypertension: BP vs BMI in haemodialysis population

Abdulla K. Salahudeen, Erwin H. Fleischmann, John D. Bower and John E. Hall

Department of Medicine and Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, USA

Abstract

**Background.** Recent surveys have reported a higher prevalence of hypertension and obesity in the haemodialysis population, suggesting a possible link between these two parameters. Alternatively, malnutrition through proinflammatory and antiendothelial mechanisms may contribute to hypertension in malnourished, underweight patients on haemodialysis, whereas the converse may be true in overweight patients.

**Methods.** The relationship between blood pressure (BP) and body mass index (BMI) was examined in 1010 patients on chronic haemodialysis using univariate and multivariate analyses.

**Results.** Based on a systolic BP of >150 mmHg, 38% were hypertensive in the post-dialysis period. A similar figure for a diastolic BP of >90 mmHg was 21%. Unlike in the general population, there was no positive correlation between BP and BMI in simple regression analysis ($r = 0.13$, $P = 0.0005$). The percentage of patients with systolic hypertension was higher among the underweight (BMI < 20) than the normal weight (BMI 20–27.5) or overweight patients (BMI > 27.5) and were 35, 29 and 20%, respectively. Furthermore, a negative correlation, albeit weak, existed between systolic BP and markers of nutrition such as serum prealbumin ($r = -0.10$, $P = 0.03$) and serum creatinine ($r = -0.12$, $P = 0.008$), suggesting a plausible link between impaired nutrition and elevated BP. In multiple regression analysis, the lack of a positive correlation between BP and BMI persisted ($r = -0.16$, $P = 0.0007$) in spite of adjusting for case-mix characteristics and parameters related to BP and nutrition.

**Conclusions.** We demonstrate for the first time that, unlike the general population, no positive correlation exists between BP and increasing BMI in haemodialysis patients. Further analysis is necessary to verify our observation and to test the possibility of whether nutritional improvement would aid in the better control of hypertension in dialysis patients.

**Keywords:** body mass index; blood pressure; dialysis; end-stage renal disease; haemodialysis; hypertension; nutrition; obesity; survival

Background

Despite considerable advances, the mortality on haemodialysis continues to remain high [1]. Both body mass index (BMI) and blood pressure (BP) have been shown to influence mortality in the haemodialysis population [2–10]. In the general population, BP correlates positively with body weight such that overweight is associated with a higher level of BP [11,12]. Recent surveys have reported a higher prevalence of hypertension and obesity in the haemodialysis population, suggesting a possible link between these two measures [4,13,14]. Alternatively, malnutrition through proinflammatory and antiendothelial mechanisms might contribute to hypertension in malnourished, underweight patients on haemodialysis, whereas the converse might be true in overweight patients. To our knowledge, no studies have previously examined whether there is a link between BMI and BP in the dialysis population. Therefore, in this study, the relationship between BP and BMI in 1010 patients on chronic haemodialysis was determined along with their influence on patients’ 1 year survival.

Subjects and methods

The mean BP readings of 1010 patients on outpatient haemodialysis (Renal Care Group of Jackson, Jackson,
MI, USA) were calculated from 11 to 13 readings for the month of January 1997. The data set was the same as used in an earlier study [15]. This data set contained 1151 patients after excluding 21 patients who had amputation (amputation could misrepresent the BMI). One hundred and forty one patients out of 1151, who did not have data on BP, BP medication, or both, were excluded, leaving a total of 1010 for this analysis.

Opinion varies as to what level of BP constitutes hypertension in the dialysis population, what level constitutes control of hypertension and whether levels should be based on pre-dialysis, post-dialysis or a mean of the both [16]. Here we have used a BP of >150/90 mmHg, a slightly conservative estimate compared with the recommendation for the general population, and one that was used in an earlier BP analysis in the dialysis population [17]. The BMI was calculated as pre- and post-dialysis weight in kg/height in m$^2$. The data were obtained for all the patients over the entire observation period and the data in their entirety was used for the analysis. The data on patient survival for the ensuing 12 months was used in this analysis, as we have performed before [4,15]. The BMI was divided into three groups based on the National Health and Nutritional Examination Service criteria of BMI for overweight [18]. A BMI $>27.5$ was classified as overweight, 20–27.5 as normal weight and $<20$ as under-weight, as previously described [4].

**Statistical analysis**

The Statistical Package for Social Sciences computer program, Version 10.1.3 and StatView, Version 5 were used for data analysis. The relationship between BMI and BP was assessed using simple regression analysis, and the influence of other variables on this relationship was assessed using a multivariate approach. The relative risk for dying (RR) was determined by the Cox proportional hazard model for BP with and without the adjustment for BMI categories. Data are presented as mean ± SD or mean with a 95% confidence interval (CI); a $P$-value $<0.05$ is considered statistically significant.

**Results**

**Patients’ characteristics**

Forty five percent were male, and the mean age was 56 ± 16 years. Eighty nine percent of the 1010 patients were African Americans, and the rest were Caucasians. The reported causes of renal failure were hypertension (39%), diabetes (31%), glomerulonephritis (11%), polycystic kidney disease (10%) and others including uncertain causes (9%). The patients had been on haemodialysis for an average of $4.3 ± 3.6$ years.

**BP measurements**

Prevalence of hypertension and the influence of dialysis on BP are given in Figure 1. Assuming a BP of $>150/90$ mmHg as hypertension, 61% and 38% had a systolic BP $>150$ mmHg, in the pre- and post-dialysis

![Graphs showing frequency distribution of BP obtained before and after dialysis.](image-url)
periods, respectively. If one were to apply a liberal systolic hypertension cut-off of >130 mmHg, the same numbers would be 84% and 62%, pre- and post-dialysis, respectively. Similar figures for a diastolic BP of >90 mmHg, were 42% and 21%. Based on these figures, dialysis appears to acutely reduce the prevalence of hypertension by \( \sim 20\% \).

**BP medications**

Based on a computerized home medication record, 54% were on one or more antihypertensive medications, and among them 31, 17 and 6% were on one, two and three antihypertensive medications, respectively. They were, in the order of frequency, calcium channel blockers, hydralazine, beta-blockers, ACE inhibitors, minoxidil, clonidine and other antihypertensives.

**BMI**

The mean post-dialysis BMI of the study population was 26.8 ± 6.7. Out of 1010 patients, underweight, that is a BMI <20, was noted in 11.9% (BMI 17.9 ± 1.1), normal weight, a BMI 20–27.5, was noted in 47.9% (23.7 ± 2.2) and overweight, a BMI >27.5, was found in 40.2% (33.6 ± 5.8). A quarter (24.4%) of the population was obese based on a BMI of \( \geq 30 \). Since interdialysis weight gain may relate to BMI, weight gains were determined for BMI categories. These were 5.4 ± 4.2 kg for overweight, 4.8 ± 3.9 kg for normal weight and 3.8 ± 3.2 kg for underweight \( (P < 0.05) \) between overweight and underweight groups, but the gain as a percentage of dry weight was not different \( (6.2, 6.5 \text{ and } 6.0\% \text{ in the overweight, normal weight and underweight groups, respectively}) \). As we have previously reported in this patient population, the age among the different groups was also not different \( (54.9 \pm 14, 55.4 \pm 18.2 \text{ and } 56.6 \pm 16.6\text{ years in the overweight, normal weight and underweight groups, respectively}) \).

With regard to BP medications, the respective percentages of patients on various agents among the underweight, overweight and normal weight patients were: calcium channel blockers, 24, 23 and 31%; beta blockers, 17, 8 and 9%; ACEI, 14, 21 and 14%; hydralazine, 10, 9 and 16%; minoxidil, 21, 9 and 3%; and clonidine, 12, 7 and 7%.

**Relationship between BP and BMI: simple regression analyses**

Unlike in the general population, the BP did not correlate positively with BMI in our patients. Instead, a weak negative correlation was noted, most significantly between post-dialysis BMI and post-dialysis systolic BP \( (r = -0.13, P = 0.0005) \), and less so for post-dialysis diastolic BP \( (r = -0.11, P = 0.04) \) (Figure 2). A similar finding was also observed between pre-dialysis BMI and pre-dialysis systolic \( (r = -0.11, P = 0.05) \) and diastolic BP \( (r = -0.12, P = 0.01) \). Since post-dialysis BMI reflects the ‘true’ BMI and post-dialysis systolic BP had the best association with post-dialysis BMI, further analyses to understand the relationship between BP and BMI in these patients were carried out using these two parameters. The percentage of patients with systolic hypertension in the post-dialysis period was higher for the underweight group (35%) vs the rest (29% and 20%). Examination of the effect of the antihypertensive prescription on the relationship between post-dialysis systolic BP and BMI continued to show a significant negative relationship even in patients who were prescribed antihypertensives \( (r = -0.11, P = 0.03) \), compared with patients not prescribed, \( r = -0.13, P = 0.01) \).

**Relationship between post-dialysis systolic BP and other relevant variables: simple and multiple regression analyses**

Table 1 displays the simple regression data on post-dialysis systolic pressure vs variables related to BP and nutrition such as age, duration on dialysis, delivered
dialysis dose, BMI and serum calcium-phosphate product, creatinine, prealbumin and albumin. Significant negative relationships were noted for Kt/V \((r = 0.10, P = 0.004)\), BMI \((r = -0.13, P = 0.0005)\), serum creatinine \((r = -0.12, P = 0.008)\) and prealbumin \((r = -0.11, P = 0.04)\).

The relationship between post-dialysis systolic BP and BMI was reanalyzed in the multivariate regression model by including four variables that were significant in the simple regression model along with age, race, gender and presence or absence of diabetes. The results provided in Table 2 shows the persistence of the lack of any positive correlation between post-dialysis systolic BP and BMI, in spite of adjusting for a number of relevant variables (partial correlation coefficient \(-0.12, P = 0.002)\).

**Table 1. Simple regression analysis: relationship between post-dialysis systolic BP and related variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Post-dialysis systolic BP</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>-0.05</td>
<td>0.140</td>
<td></td>
</tr>
<tr>
<td>Duration of dialysis (months)</td>
<td>0.04</td>
<td>0.160</td>
<td></td>
</tr>
<tr>
<td>Hct</td>
<td>-0.05</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Kt/V</td>
<td>0.10</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Calcium-phosphate product</td>
<td>0.02</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>0.014</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>-0.12</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>Serum prealbumin (mg/dl)</td>
<td>-0.10</td>
<td>0.032</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>-0.13</td>
<td>0.0005</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Multiple regression analysis: relationship of post-dialysis systolic BP with BMI in the presence of age, race, gender and diabetes, and variables significant in Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Post-dialysis systolic BP</th>
<th>(r^a)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>-0.11</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.01</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>-0.15</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Kt/V</td>
<td>0.06</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>-0.06</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Serum prealbumin (mg/dl)</td>
<td>-0.01</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>-0.11</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Partial correlation.

**Table 3. Cox model analysis of the influence of systolic BP on relative mortality risks (RR)**

<table>
<thead>
<tr>
<th>BP</th>
<th>RR</th>
<th>95% CI</th>
<th>(P)</th>
<th>(n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-dialysis systolic BP</td>
<td>0.993</td>
<td>0.984–1.002</td>
<td>0.11</td>
<td>994</td>
</tr>
<tr>
<td>Pre-dialysis systolic BP (^a)</td>
<td>0.98</td>
<td>0.97–0.99</td>
<td>0.0004</td>
<td>997</td>
</tr>
<tr>
<td>Underweight</td>
<td>0.99</td>
<td>0.99–1.01</td>
<td>0.734</td>
<td>93</td>
</tr>
<tr>
<td>Normal weight</td>
<td>0.98</td>
<td>0.97–0.98</td>
<td>0.005</td>
<td>534</td>
</tr>
<tr>
<td>Overweight</td>
<td>0.98</td>
<td>0.98–0.99</td>
<td>0.02</td>
<td>320</td>
</tr>
</tbody>
</table>

\(^a\)The RR-reducing effect of pre-dialysis systolic BP was re-examined by splitting the analysis further with BMI categories and adjusting simultaneously for age, duration on dialysis, presence of diabetes, gender, race and antihypertensive medications. Higher pre-dialysis systolic BP in underweight patients was not associated with a lower relative mortality risk.

**Effect of systolic BP and BMI on patients’ survival**

In the Cox proportional hazard analysis for the entire population, pre-dialysis but not post-dialysis systolic BP exhibited a significant negative correlation with mortality \((r = -0.03, P < 0.001)\) (Table 3). However, when the former analysis with pre-dialysis systolic BP was reanalyzed by splitting for BMI subcategories and adjusted for age, duration on dialysis, presence of diabetes, gender, race and antihypertensive medications, the significant negative correlation persisted only for normal weight and overweight patients, but not for underweight patients (Table 3).

**Discussion**

The novel finding in our study is that unlike in the general population no positive correlation exists between BP and increasing BMI in haemodialysis patients. A weak but significant negative correlation also existed between systolic BP and markers of nutrition suggesting a plausible link between impaired nutrition and elevated BP in haemodialysis patients.

The negative relationship between BP and BMI in our patients was a weak one. However, it is to be noted that to have a weak negative correlation in our patients, the correlation had to move from a positive correlation observed in the general population to a negative one in haemodialysis patients; this point is schematically depicted in Figure 3. The mechanisms for the unexpected negative correlation between BMI and BP noted in this study are not readily apparent. The negative relationship may be the result of a combination of lower BP in overweight patients and higher BP in underweight patients. A heightened renal tubular sodium reabsorption is implicated in the pathogenesis of obesity-related hypertension in the general population [19]. This cannot be a mechanism to explain for the higher BP in underweight dialysis patients in the absence of functioning kidneys. Other factors such as

![Fig. 3. Schematic representation of our findings. The negative relationship \((r = -0.13)\) between post-dialysis systolic BP and BMI in our haemodialysis patients is quite weak. However, since a good positive relationship exists between these two variables in the general population, what we find as a weak negative correlation is in fact a sizeable shift in the intercept slope (indicated by the arrow) from what is expected in the general population with larger BMI to what is seen in our haemodialysis patients with larger BMI.](image-url)
cardiac output, vascular resistance, blood volume, use of antihypertensive medications and delivered dose dialysis can determine the BP in dialysis patients.

However, a difference in BP medication intake between overweight and underweight patients cannot be the main reason for the BP difference, as an inverse relationship existed even after adjusting for these medications. Furthermore, there were more patients in the underweight group receiving potent antihypertensive medications; thus, prescribing less potent antihypertensives appears less of a reason for the higher prevalence of hypertension among underweight patients. Under-dialysis cannot be a factor for hypertension in underweight patients because these patients tend to receive higher doses of dialysis per unit body weight compared with overweight patients [15]. Pre-dialysis salt and water gain contributes to hypertension in the dialysis population, but that alone cannot be an important factor in the hypertension, since negative correlation persisted between BMI and systolic BP in spite of dialysis. It is plausible that higher relative volume shifts frequent in underweight patients can trigger an increased sympathetic outflow from the remnant kidneys [20], thus possibly contributing to higher systolic BP in underweight patients. In our patients, however, the weight change as a percent of body weight among the three BMI categories was not different. Finally, since the data is based primarily on African Americans, whether the current findings would be equally applicable to a predominantly Caucasian population is also uncertain.

Lack of vascular compliance in haemodialysis patients has been suggested as a mechanism for the high frequency of hypertension among the dialysis population. However, a simple relationship between calcium-phosphate products and BP was not seen in this study and this accords with the lack of positive correlation between BP and vascular calcification in patients with end-stage renal disease [21]. A lower BP in our obese patients could be partly due to reduced myocardial function in these patients. Although no cardiac function measures are available for our patients, obesity in dialysis patients was reported to be associated with better survival [2]. We also considered the possibility that underweight patients might be older and, therefore, old age might be a reason for higher BP in underweight groups. However, age was not different among the groups. Furthermore, in our patients, unlike in the general population, aging was not a significant determinant of BP, possibly due to the presence of other powerful determinants of BP such as renal failure and altered myocardial function and peripheral vascular resistance.

Because of the association of systolic BP with underweight and reduced levels of nutritional markers in our study, an important consideration for the mechanism of systolic hypertension in these patients would be the excessive presence of proinflammatory cytokines (IL-1, IL-6, TNF-α and others) in underweight and malnourished patients that may alter the endothelial function and, hence, the vascular tone [22,23]. This, although attractive, is an inchoate speculation and as such requires further supportive evidence.

The finding herein of an association between higher BP and lower BMI and the two earlier observations of a paradoxical association, one, higher BP with better survival and, two, lower BMI with higher mortality, may pose a seeming contradiction. That is, that we find higher BP among underweight patients yet better survival was independently reported in patients with higher BP or higher BMI. In this and earlier studies, higher pre-dialysis, and not post-dialysis, BP was attended by a better survival probability [9,10]. Higher pre-dialysis BP in patients with better survival may be an indication of patients with better myocardial function, a point previously suggested by others [9,10]. Furthermore, our finding that the survival advantage of higher systolic BP was not found for underweight patients when reanalyzed for BMI categories, suggests that under-nutrition continues to exert a greater negative influence on dialysis patients survival. Stated differently, an overweight haemodialysis patient with normal BP is likely to out-survive an underweight patient with hypertension.

There are limitations to our study. Being a database analysis, despite a larger overall sample size of 1010 patients, no uniform protocol was used for measuring BP at the dialysis units. On the other hand, the BP obtained here is what is generally obtainable in the clinical practice setting. Our patients, being a prevalent population, unforeseen bias could have segregated systolic hypertension with underweight patients. Furthermore, the data is correlative and thus, no cause and effect assumption can be made between malnutrition and hypertension. Moreover, as discussed above, the relationship between malnutrition and hypertension is weak and should be considered as suggestive rather than definitive.

In summary, our study demonstrates a novel observation that, unlike in the general population, no positive correlation exists between systolic BP and increasing BMI in haemodialysis patients. The finding of a weak but significant negative correlation between systolic BP and markers of nutrition suggests a possible link between under-nutrition and elevated BP in haemodialysis patients. Further analysis is necessary to verify our observation and to test the possibility of whether improvement in nutrition may aid the control of hypertension in dialysis.

Acknowledgements. The authors appreciate the support of the administrative, nursing and dietetic staff of the Renal Care Group, Jackson, MS, particularly, the contributions of Ms Nancy Teal. This study is made possible in part by a grant from the Kidney Care Inc. Foundation, Jackson, MS, to A.K.S.

Conflict of interest statement. None declared.

References
5. Leavey SF, McCullough K, Hecking E, Goodkin D, Port FK, Young EW. Body mass index and mortality in ‘healthier’ as compared with ‘sicker’ haemodialysis patients: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplant* 2001; 16: 2386–2394

Received for publication: 25.4.03
Accepted in revised form: 1.9.03