

**Original Article**

## Providing Intradialytic Parenteral Nutrition Therapy Does Not Improve Anthropometric Status in Hemodialysis Patients with Malnutrition

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ARTICLE INFO	ABSTRACT
<p><i>Article history:</i> Received: March 22, 2024 Accepted: April 19, 2024 Published Online: April 24, 2024</p> <p><i>Corresponding Author:</i> Satriyo Dwi Suryantoro, Kidney-Hypertension Division, Faculty of Medicine, Airlangga University, satriyo.dwi.suryantoro@fk.unair.ac.id</p>	<p><b>Background:</b> Malnutrition is prevalent among hemodialysis patients and significantly impacts prognosis. It can result from reduced food intake and protein loss during hemodialysis. Nutritional status is determined through anthropometric examinations, which include upper arm circumference (UAC), body mass index (BMI), hand grip strength, bicep, and tricep fold thickness. Laboratory examinations such as total cholesterol and Malnutrition Inflammation Score (MIS) or Subjective Global Assessment (SGA) are also utilized. Intradialytic Parenteral Nutrition (IDPN) is expected to maintain or improve the nutritional status of hemodialysis patients.</p> <p><b>Objective:</b> To assess the impact of parenteral nutrition therapy on the anthropometric status of malnourished hemodialysis patients</p> <p><b>Methods:</b> This cross-sectional study, a sub-analysis of a larger nutritional therapy study, involved 24 hemodialysis patients experiencing malnutrition based on SGA B and C criteria, with 1-10 years of hemodialysis. IDPN therapy was provided, and anthropometric measurements, as well as total cholesterol levels, were taken at baseline and three months after the initiation of nutritional therapy. Data processing utilized comparative statistical analysis.</p> <p><b>Results:</b> The mean age was 45.33 years, with 14 males and 10 females. After 3 months, there were no significant differences in UAC (mean difference = 0.13; <math>p = 0.69</math>), BMI (mean difference = 0.13; <math>p = 0.50</math>), hand grip strength (mean difference = -0.96; <math>p = 0.282</math>), biceps skinfold thickness (mean difference = 0.13; <math>p = 0.69</math>), triceps skinfold thickness (mean difference = 0.59; <math>p = 0.134</math>), or total cholesterol (mean difference = -1.5; <math>p = 0.71</math>).</p> <p><b>Conclusion:</b> Three months of IDPN therapy did not improve the anthropometric status of malnourished hemodialysis patients.</p> <p><b>Keywords:</b> hemodialysis, intradialytic parenteral nutrition, anthropometry, chronic kidney disease.</p>

### Introduction

Patients undergoing hemodialysis (HD) frequently experience protein-energy malnutrition. The causes of protein-energy malnutrition are varied, although there is agreement on the need to assess nutritional status in HD patients using non-standard methods. Additionally, in patients with chronic kidney

disease (CKD), low-grade chronic inflammation occurs, exacerbating the condition and further increasing the degree of malnutrition.<sup>1, 2</sup>

Anthropometric status is a key parameter for measuring improvements in malnutrition. Common anthropometric measurements used to evaluate improvements in

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malnutrition conditions include body mass index (BMI), body weight, hand grip strength, upper arm circumference, calf circumference, bicep and triceps skinfold thickness, among others. Numerous studies demonstrate that nutritional therapy can enhance the anthropometric status of HD patients.<sup>1, 3-5</sup>

Nutritional therapy for HD patients may involve counseling, oral supplementation, or intradialytic parenteral therapy (IDPN). Counseling therapy educates patients on managing their diet independently. Oral supplementation may include providing additional nutrients in the form of solid or liquid supplements. IDPN is administered intravenously to patients unable to tolerate enteral or oral nutrition due to gastrointestinal tract malfunction, vomiting, chronic nausea, anorexia, or those who have not responded to counseling and oral therapy.<sup>2, 6</sup>

Previous research suggested that IDPN did not improve the patients' clinical condition. However, contrasting findings from other studies indicated improvements in patients' quality of life and pre-albumin levels after four weeks. Few studies have linked IDPN with improvements in anthropometric status.<sup>4,7-10</sup> This study aimed to examine the effects of intradialysis parenteral nutrition therapy on several anthropometric parameters.

## Methods

### Design and participants

This cross-sectional study was a sub-analysis of a larger study conducted in 2020, investigating the provision of nutritional therapy to HD patients. It involved 24 HD patients experiencing malnutrition according to Global Assessment (SGA) B and C criteria, with a HD duration ranging from 1 to 10 years. IDPN

therapy was administered to these patients, and their anthropometric status was assessed using measurements of upper arm circumference (UAC), BMI, hand grip strength, biceps and triceps skinfold thickness. Total cholesterol levels were measured through laboratory tests. Anthropometric measurements were taken at baseline and three months after nutritional therapy initiation. All patients provided informed consent before receiving nutritional therapy. This study adhered to the guidelines of Dr. Soetomo (Approval No: 0090/KEPK/XI/2020).

### Statistical analysis

Statistical analysis for this study utilized SPSS version 24.0 software (Chicago, IL, USA) for data analysis. Descriptive statistics include categorical variables reported as percentages (n, %) and continuous variables presented as mean and standard deviation (mean, SD). Comparative statistical analysis was conducted using paired t-tests for normally distributed data. Alternatively, the Wilcoxon test was employed for non-normally distributed data.

## Results

Patient characteristics revealed an average age of 45.33 years, with 14 males and 10 females included in the study. Among them, 10 patients reported eating three times a day, while 12 patients had a frequency of two meals per day, and only 2 patients reported eating once a day. The average dietary calorie intake was 16,490.60 kcal. The average systolic blood pressure was 144 mmHg, with a diastolic blood pressure of 82.08 mmHg, and an average duration of HD of 49.88 months. The initial mean values for anthropometric status were as follows: upper arm circumference = 25.25 cm; BMI = 23.23; hand grip strength = 22.67 kg; triceps skinfold thickness = 8.10 mm; biceps skinfold thickness = 4.52 mm (Table 1).

**Table 1.** Characteristics of patients receiving parenteral intradialytic nutritional therapy

	Total	Minimal	Maximum	Mean	Std. Deviation
Age	24	28	58	45.33	8.92
Sex					
Male	14				
Female	10				

Eat frequency					
1x	2				
2x	12				
3x	10				
Calori of diet	24	771,10	2390,60	1649,60	430,22
Duration HD month)	24	7	120	49,88	30,67
Heart Rate	24	78,00	96,00	87,33	4,57
Systolic blood pressure (mmHg)	24	110,00	170,00	144,16	15,29
Diastolic blood pressure (mmHg)	24	70,00	90,00	82,08	8,33
UAC(cm)	24	15,50	34,00	25,25	3,96
SfT tricep (mm)	24	2,20	16,50	8,10	4,21
SfT bicep (mm)	24	1,30	10,90	4,52	3,04
Handgrip strength (kg)	24	9,70	37,20	22,67	7,62
BMI early	24	13,27	33,20	23,23	4,39
Cholesterol (mg/dl)	24	76,00	230,00	161,42	33,66

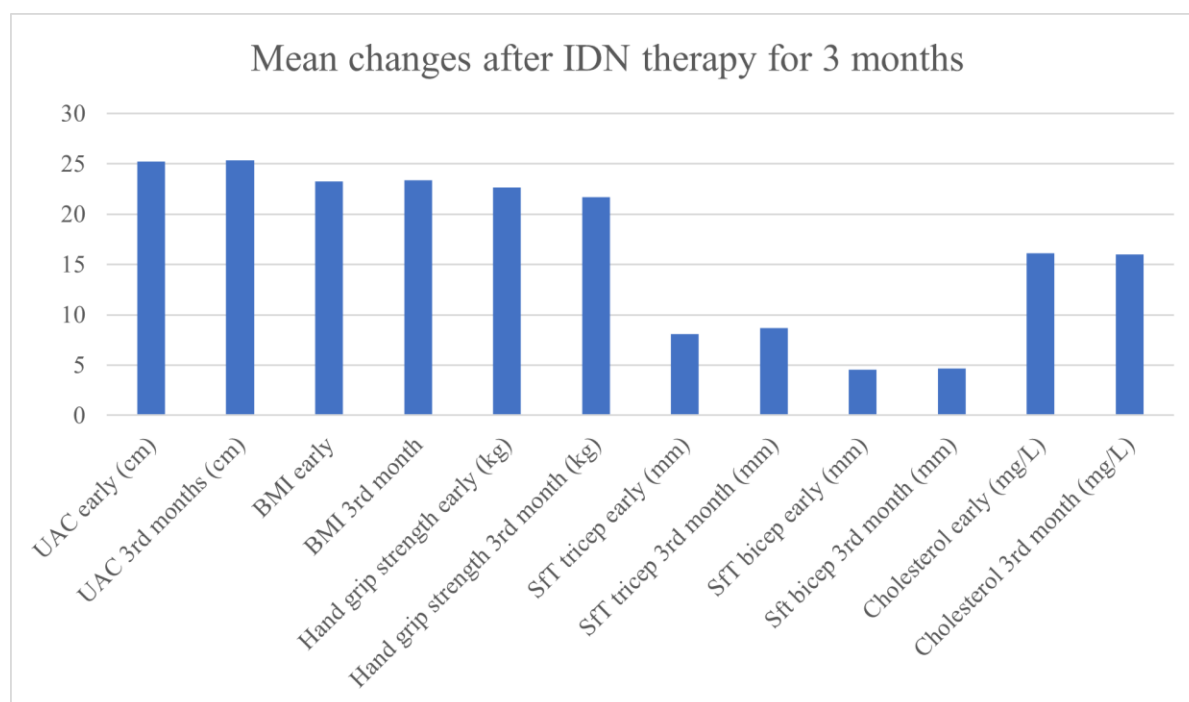
All parameters, including UAC, BMI, hand grip strength, biceps and triceps skinfold thickness, and total cholesterol, were normally distributed. Statistical analysis utilized paired t-tests. Following the administration of IDPN therapy for 3 months, there were no significant differences observed in UAC (mean difference =

0.13;  $p = 0.69$ ), BMI (mean difference = 0.13;  $p = 0.50$ ), hand grip strength (mean difference = -0.96;  $p = 0.282$ ), biceps skinfold thickness (mean difference = 0.13;  $p = 0.69$ ), triceps skinfold thickness (mean difference = 0.59;  $p = 0.134$ ), and total cholesterol (mean difference = -1.5;  $p = 0.71$ ) (Table 2 and Figure 1).

**Table 2.** Differences in pre and post-anthropometric status 3 months after IDPN nutritional therapy

Parameter	Mean Difference	Std. Deviation	p-value
UAC 3rd month (cm) - UAC early(cm)	0,13	1,51	0,69
BMI 3rd month - BMI early	0,13	0,92	0,50
Handgrip strength 3rd month (kg) - Handgrip strength early (kg)	-0,96	4,26	0,28
SfT tricep 3rd month (mm) - SfT tricep early (mm)	0,59	1,85	0,13
SfT bicep 3rd month (mm) - SfT bicep early (mm)	0,13	1,51	0,69
Cholesterol 3rd month (mg/dl) - Cholesterol early (mg/dl)	-1,50	19,59	0,71

UAC: upper arm circumference; SfT: skinfold thickness; BMI: body mass index



**Figure 1.** Changes in anthropometric status after giving IDPN therapy for 3 months

## Discussion

Nearly 400,000 individuals in the United States with stage 5 CKD undergo chronic HD, facing a high annual mortality risk of 20-25%. Although cardiovascular disease is the leading cause of mortality in CKD patients, traditional cardiovascular risk factors like hypertension or hypercholesterolemia do not seem to significantly influence their mortality. Instead, insufficient protein intake, low serum albumin, weight loss, or a low BMI serve as significant indicators of high mortality risk in chronic HD patients.<sup>12</sup>

CKD patients often experience malnutrition, known as protein-energy wasting (PEW), due to various factors. To prevent uremia, CKD patients are typically advised to follow a low-protein diet, consuming around 0.8 grams per kilogram of body weight. Additionally, chronic inflammation present in CKD patients further contributes to PEW. During chronic HD, there is a loss of albumin and amino acids during the intradialytic process.<sup>13, 14</sup>

Due to its association with increased mortality risk in CKD patients, interventions aimed at improving nutritional status have the potential to enhance survival rates.

Hypoalbuminemia is commonly used as a marker for PEW in dialysis patients and is strongly correlated with mortality. IDPN, a recognized intervention for providing parenteral nutritional support during HD sessions, emerges as a potential strategy for addressing PEW conditions, particularly intradialytic hypoalbuminemia.<sup>12</sup>

A study by Goldstein et al. illustrated the effectiveness of IDPN in addressing organic causes of PEW among young adult and adolescent patients undergoing chronic HD. The advantage of using IDPN lies in its significant protein content, supplying 37%-42% of protein intake compared to the recommended 10% of protein from the total weekly calorie intake.<sup>13</sup> Research by Capelli et al. in 1994 demonstrated that the therapy group, compared to the control group, exhibited an increase in body weight. During 8 months of nutritional therapy, the therapy group showed a weight increase to  $157.3 \pm 40$  lbs, which further continued to rise to  $168.7 \pm 44$  lbs by the 12th month.<sup>15,16</sup>

Different findings emerged when comparing the effectiveness of IDPN, oral supplementation, and counseling nutritional

interventions. Compared to oral supplementation, IDPN did not show a positive impact on patient quality of life or nutrition. The French Intradialytic Nutrition Evaluation Study (FineS), a randomized controlled trial involving 186 malnourished chronic HD patients, found that one year of IDPN administration did not increase mortality rates, hospitalization rates, or reduce quality of life. In two randomized controlled trials (RCTs) examining IDPN, no significant differences were observed in improvements in BMI, serum prealbumin, serum albumin, or subjective global assessment (SGA) scores compared to oral supplementation. However, the results of these studies were limited by small sample sizes and non-compliance, with discontinuation rates ranging from 19% to 26% for oral supplements and 24% for IDPN. Additionally, there were differences in participant numbers between groups, with 17% discontinuation in the control group compared to 0% in the IDPN group. The only significant improvement in nutritional markers was observed in a small prospective cohort study (N = 20) conducted in Turkey, which reported a substantial increase in serum albumin after 4 months among patients receiving IDPN instead of oral supplements. However, this study did not directly compare intervention and control groups and was limited by lack of compliance (40% of patients switched from oral supplements to IDPN due to noncompliance) and no statistical adjustment for bias variables.<sup>17</sup>

A single RCT involving 107 chronic HD patients compared 16 weeks of IDPN with patients receiving 'regular dietary behavior' consultations. All patients received nutritional consultation at baseline. However, the study found that IDPN did not consistently lead to improvements in patient health or nutrition. At 4 weeks, patients receiving IDPN showed a 15% increase in serum prealbumin compared to controls (41% IDPN vs. 20.5% controls,  $P = 0.0415$ ). Nevertheless, the significance of this finding is uncertain since, when considering its relation to clinical outcomes, a 15% increase remains relatively insignificant. The mean increase in serum prealbumin (26.31 mg/L) at 16

weeks did not meet the >30 mg/L threshold associated with reduced mortality, as found in Cano 2007 (48.7% vs. 31.8%,  $P = 0.1164$ ). IDPN did not improve clinical outcomes regarding death (26.4% vs. 12.9%,  $P = 0.09$ ), hospitalization (hospitalization rate: 59% vs. 43.2%,  $P = 0.15$ ), or quality of life (change SF-12 score: -2.74 vs. 0.34,  $P = 1.1175$ ). Additionally, this study has significant limitations due to its small sample size, indirect results, and lack of information about the types of interventions received by the control and potential co-intervention groups.<sup>17</sup>

In general, IDPN has shown to reduce mortality risk and improve mean scores on nutritional outcomes compared to the standard of care (SOC) for CKD patients. In the largest non-randomized study, the effect of IDPN on 1-year mortality was found to depend on baseline serum albumin levels. Patients with lower baseline serum albumin ( $\leq 3.3$  g/dL) exhibited a decreased mortality rate when receiving IDPN (OR 0.61-0.72;  $P < 0.01$ ). Conversely, patients with higher baseline serum albumin ( $>3.3$  g/dL) showed either the same or increased odds of death compared to controls (OR 0.85;  $P = 0.10 - 2.6$ ;  $P < 0.005$ ). A smaller non-randomized study (N = 81) with a baseline serum albumin of 3.02 g/dL reported improved survival with IDPN. However, a single RCT involving 40 chronic HD patients with refractory anemia found no improvement in nutrition-related functional capacity with IDPN treatment compared to usual care. While many studies have reported improvements in mean scores across various nutritional outcomes compared to usual care, none have provided data on the proportion of patients achieving clinically significant improvements in nutritional outcomes. These studies were limited by small sample sizes (all but one with  $N < 100$ ), lacked information on intervention adherence, and did not perform statistical adjustments for variable bias.<sup>17</sup>

A study conducted in Taiwan by Tsai et al. involving approximately 10,000 CKD patients found that changes in body composition in peritoneal dialysis (PKG) patients influenced hs-

CRP levels. CKD patients with a BMI < 23 or BMI > 23 subgroups with lower eGFR values exhibited higher hs-CRP levels compared to those with higher eGFR values. These findings suggest that improving the nutrition of CKD patients can influence body composition and potentially reduce the chronic inflammatory process.<sup>18</sup>

Providing nutritional therapy to HD patients can supply adequate protein and energy to enhance their nutritional status. Increases in bicep and tricep fold thickness are indicative of improved muscle mass, suggesting enhanced activity status and quality of life for HD patients. However, Demirci et al. reported no change in muscle mass following IDPN administration. It's worth noting that the response to nutritional intervention may also be influenced by the patient's inflammatory status and age.<sup>19</sup>

Our study's results indicated that within 3 months, IDPN did not lead to improvements in the participants' anthropometric status. However, our study was limited by the small sample size and focused solely on evaluating the anthropometric status improvement among IDPN chronic HD patients without comparison to other nutritional therapies. Future research should consider extending the observation period to at least 6 months and examining mortality rates following various nutritional interventions.

## Conclusion

IDPN did not improve the anthropometric status of HD patients with malnutrition after 3 months of administration.

## Limitations of the Study

The limitation of this study is that the observational period of IDPN therapy is short, only three months. Therefore, further research on nutritional therapy to improve the anthropometric status of hemodialysis patients within six months is necessary. Second, IDPN therapy in hemodialysis patients must be matched

to make the comparison between groups more equal.

## Declarations

### Ethics approval and consent to participate

All patients in this study signed informed consent before being given nutritional therapy. This study follows Dr. Soetomo (No: 0090/KEPK/XI/2020).

## Competing interests

There is no conflict of interest.

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## Author's Contribution

Idea/concept: SDS, MT, W, NM. Control/supervision: MT, W, NM. Data collection/processing: SDS, AT, AP. Extraction/Analysis/interpretation: SDS, AT, AP, NM. Literature review: MT, W. Writing the article: SDS, AT, NM. Critical review: MT, W. 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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