

Intradialytic Parenteral Nutrition during In-Center Hemodialysis of Patients Leads to Increase in Albumin without Compromising Safety Retrospective Analysis

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Key Points

- Intradialytic parenteral nutrition (IDPN) is a safe therapy with improvement in serum albumin levels, a marker of morbidity and mortality in patients on hemodialysis.
- Clinically significant improvements in albumin levels can be observed within 2 months of initiation of IDPN use.
- Research on IDPN is needed to identify benefits of its use in subgroups and on important clinical outcomes (*i.e.*, quality of life, hospitalization, and mortality).

Abstract

Background Albumin is an established survival surrogate in dialysis. We evaluated the effect of intradialytic parenteral nutrition (IDPN) on albumin levels in patients with ESKD undergoing in-center hemodialysis and determined characteristics associated with response to IDPN treatment.

Methods We conducted a 5-year (May 2018–April 2023) retrospective chart review of 2270 patients on in-center hemodialysis from 1039 dialysis centers, in 43 states and the District of Columbia, who received concurrent IDPN treatment three times per week. Patients were aged 18 years and older (mean 69.1 years) with albumin levels <4.0 g/dl (mean 3.11 g/dl) and were on hemodialysis for more than 6 months (mean 3.7 years). Other criteria included unintentional weight loss ($\geq 5\%$ /3 months) and/or body mass index below 20 kg/m². The coprimary end points included mean change in albumin levels from baseline to month 6 of IDPN therapy and percentage of patients with a clinically significant change in albumin levels, defined as ≥ 0.2 g/d with a $P < 0.05$. Each patient studied was their own control. We used Kaplan–Meier curves to evaluate the time to positive IDPN response. Two-sample *t* tests for continuous variables and Chi-square tests for categorical variables were used to determine whether certain defined patient characteristics were associated with a positive response to IDPN therapy.

Results One thousand nine hundred forty-six eligible patients consented to being evaluated. Baseline demographics include 50.9% female and 49.1% male with a mean albumin of 3.11 g/dl. Evaluable data at 6 months were available for 73% of patients. Mean change in albumin levels from baseline to 6 months after initiation of IDPN therapy was 0.330 g/dl; 82.0% of patients achieved ≥ 0.2 -g/dl increase in albumin level within those 6 months. Younger age and lower baseline albumin levels were significantly and independently associated with a higher and more rapid significant rise, $P < 0.05$, in albumin levels. While receiving IDPN, fewer than 8% of patients reported minimal and treatable side effects.

Conclusions IDPN is a safe and effective therapy resulting in clinically significant improvement in serum albumin levels. Further research on associated outcomes and quality-of-life data is needed.

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Introduction

It is well established that hypoalbuminemia is associated with increased morbidity, hospitalization, and mortality risk.^{1–3} Even small reductions in albumin levels of 0.1–0.2 g/dl are associated with increased risk of mortality.⁴ According to the United States Renal Data System 2023 Annual Data Report, only 49.2% of patients on initial hemodialysis had a normal albumin level of ≥ 4.0 g/dl.⁵ Such high prevalence of hypoalbuminemia in the other 50.8% of patients on hemodialysis presents potential risk of adverse clinical outcomes and poor quality of life (QoL) in this patient population.^{1–4}

The etiology of hypoalbuminemia and its management in patients on hemodialysis is complex. Although albumin losses during dialysis treatment are the primary contributing factors, significant reduction in albumin synthesis may also be critical as pointed out by others.^{4,6,7} Providing substrate to correct this reduction is an option which merits an evaluation. The problem of hypoalbuminemia in patients on hemodialysis has been identified as a promising area of study^{6,9,10} because its associated risks include mortality and missed hemodialysis treatments.^{2,8,11–13}

It is important for clinicians to have more than one option available to address such challenges. Under most circumstances, first-line treatments that encourage oral nutrition intake counseling by a registered dietitian (RD) and by provision of oral nutrition supplementation (ONS) are sufficient to boost amino acid (AA) availability for albumin and whole-body protein synthesis in the setting of hypoalbuminemia.¹⁴ However, there are limits to a patient's ability and willingness to consume and absorb adequate amounts of protein^{15,16} because of various reasons, including poor appetite, nausea,¹⁰ and even significant impairments in small intestinal protein assimilation in patients on hemodialysis.¹⁶ All these factors contribute to both a limited AA pool needed for adequate protein synthesis and to a reduction of albumin levels with its associated risks.^{4,6}

Intradialytic parenteral nutrition (IDPN) is a dialysis-specific form of parenteral nutrition that is infused during hemodialysis to provide a high dose of a variety of AAs and sufficient dextrose to support protein anabolism. While a premixed 2:1 or 3:1 admixture can be used, it is common practice in the United States for patient-specific formulations to be compounded that allow for, on average, higher provision of protein (85–100 g AA per treatment); it permits the use of lower volume, lower dextrose concentrations and provides the option to add intravenous lipid emulsions (ILEs) as needed to increase total calorie content.

Several studies with a limited number of patients have reported significant improvements in biomarkers and measures of patient nutrition status, including albumin and hemoglobin levels, composite nutrition assessment scores, and spontaneous improved oral intake of protein and calories.^{17–22} However, as pointed out by many other relatively limited, previous studies, there is widespread uncertainty about the value of and indications for IDPN use in a variable and large number of patients on hemodialysis.^{23,24} Of the 23 studies conducted to date, most have been significantly constrained in duration and in population size. This limits their application to a diverse

hemodialysis population, thus leaving the questions of efficacy and safety unanswered. In this study, using a retrospective database analysis, we review and evaluate the largest population to date of patients on in-center hemodialysis (ICHD) who use IDPN therapy, with and without ILEs, to characterize the response of albumin levels and to further clarify new areas of study for this unique form of nutrition support.

Methods

Study Design and Patient Population

This study is a retrospective database review of 2270 patients on ICHD from 1039 dialysis centers located in 43 states and the District of Columbia in the United States. All patients consented to have their electronic medical records used for research, and an Institutional Review Board waiver was obtained. Included patients received concurrent IDPN treatment three times per week. Centers ranged in size, and data are only available on patients who had been treated with IDPN. The breakdown of the number of included patients per state is presented in [Figure 1](#).

Inclusion Criteria

All patients received ICHD three times per week between May 1, 2018, and April 30, 2023; were aged 18 years and older; and carried a diagnosis code of International Classification of Diseases, Tenth Revision (ESKD [N18.6]); they all received IDPN therapy for at least 6 months. [Table 1](#) summarizes in detail the demographics of the study population. Patient selection varied from center to center, but all were older than 18 years (mean 69.1) and had albumin levels lower than 4.0 g/dl, measured three times over 3 months (with a mean of 3.11 g/dl) and were on hemodialysis for at least 6 months (mean of 3.7 years). Other criteria included unintentional weight loss of 5% or greater within 3 months and/or body mass index (BMI) trending below 20 kg/m²; patients were also evaluated for documentation of (1) ongoing nutrition counseling from an RD, (2) poor oral intake, (3) trial of oral nutritional supplement (ONS), and (4) consideration to initiate enteral nutrition (EN).

Exclusion Criteria

Patients were excluded from the study if they were younger than 18 years at IDPN initiation, their dialysis prescription deviated from the standard 3 days per week ICHD treatment, IDPN was initiated outside the research period, or they had previously received intraperitoneal nutrition or IDPN within 6 months of the start of the study. Patients who received concurrent EN or total parenteral nutrition or if they were on IDPN for less than 6 months (180 days) were also excluded. Patients also were excluded if they had a history of liver disease or gastric bypass or were undergoing cancer treatment at any time during IDPN therapy.

Data Collection

Eligible patients who received IDPN therapy within the study period were identified using a dataset compiled from available electronic medical records provided by the

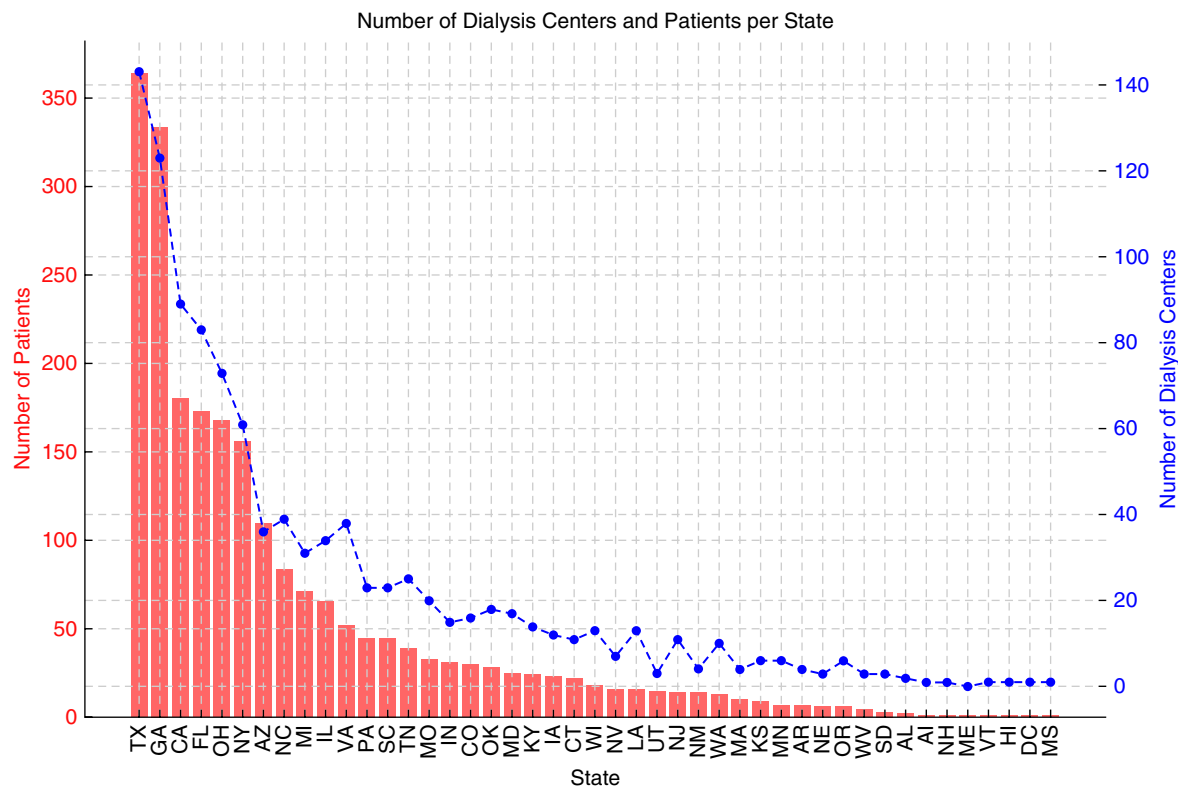


Figure 1. Number of dialysis centers and patients per state.

referring dialysis clinics. This dataset includes history and physical examinations or current problem lists, patient demographics, chart notes from the RD, and laboratory results. Patient weights from the 2–3 months before the referral for IDPN were also recorded and included. Demographic and medical information that could not be directly extracted from patient records through an automated report generation process was manually entered by data entry specialists.

Laboratory results and weight data for 3 months before starting IDPN (mean of three-monthly measurements) were collected and summarized to establish baseline values. Monthly albumin results were obtained over a 15-month period after initiation of IDPN therapy.

Intervention

The compounded IDPN contained a combination of dextrose (D70%) and AAs (prosol 20%, clinisol 15%, or plenamine 15%); there was also the option of adding ILEs in all patients who were on or started IDPN. Due to a formulary change, patients prescribed lipids prior to August 1, 2020 received Intralipid 20%, Fresenius Kabi AB, and after August 1, 2020 they received Clinolipid, Baxter Healthcare Corporation. IDPN was administered to patients during their thrice-weekly dialysis sessions. Patients had individualized prescriptions for IDPN on the basis of their height, weight, and other nutrition considerations, including but not limited to the presence of wounds, recent hospitalizations, and electrolyte imbalance. Prescriptions were modified as required to increase or decrease goal infusion rate, adjust protein levels, and/or add or remove

lipids. Lipids were selectively prescribed upon physician orders for patients who needed additional calories because of unintentional weight loss of 5% or greater within a prior 3-month period and/or low BMI ($<20 \text{ kg/m}^2$).

While each IDPN formulation was tailored to the individual, the formula was developed using the following guidelines: 1.2–1.4 g protein/kg per day, 3–8 mg/kg per minute glucose infusion rate, and lipids (if included); on average 476–570 kcal and 85–100 g of AA was provided per patient per treatment. Patients were followed from the time of IDPN initiation through 15 months of treatment or until discontinuation of therapy, whichever occurred first.

Assessment

The coprimary end points were (1) mean change in albumin levels from baseline to month 6 of IDPN therapy and (2) percentage of responders (*i.e.*, patients who achieved $\geq 0.2 \text{ g/dl}$ increase in albumin levels at month 6 after initiation of IDPN). Secondary end points included (1) time to IDPN response (albumin level increase $\geq 0.2 \text{ g/dl}$ at month 2–6), (2) mean change in albumin levels from baseline to month 12, and (3) percentage of responders at month 12. Other observations included (1) factors that differentiated IDPN responders from nonresponders, (2) factors predictive of IDPN response, and (3) time to IDPN response between patients who did and did not receive lipids with their IDPN therapy.

Statistical Analyses

The study was sufficiently powered for the primary and secondary objectives (NCSS, LLC, Kayville, UT).

Table 1. Baseline demographics and clinical characteristics

| Characteristic | Patients (N=1946) |
|--|-------------------|
| Age (yr) | |
| Mean±SD | 69.1±13.5 |
| Median (range) | 70 (18–102) |
| Sex, n (%) | |
| Female | 991 (50.9) |
| Male | 955 (49.1) |
| Weight (kg) | |
| Mean±SD | 70.7±20.7 |
| Median (range) | 67.4 (32.5–208.3) |
| Race, n (%) | |
| Black | 583 (30.0) |
| Other ^a /unstated | 841 (43.2) |
| White | 522 (26.8) |
| Ethnicity, n (%) | |
| Hispanic | 232 (11.9) |
| Non-Hispanic | 907 (46.6) |
| Unstated | 807 (41.5) |
| Diabetes, n (%) | 1349 (69.3) |
| Missing ^b | 42 (2.2) |
| Anemia, n (%) | 1254 (64.4) |
| Hypertension, n (%) | 1457 (74.9) |
| RKF/proteinuria, n (%) | 50 (2.6) |
| Therapy holds, n (%) | 1010 (51.9) |
| Mean±SD | 1.01±1.38 |
| Median (range) | 1 (0–9) |
| IDPN duration (mo)^c | |
| Mean±SD | 13.9±8.0 |
| Median (range) | 11 (0.9–63) |
| Dialysis duration (yr)^d | 3.74 (4.08) |
| Mean±SD | 3.74±4.08 |
| Median (range) | 2 (0.005–27) |
| Albumin (g/dl) (pre-IDPN SOC)^d | |
| Mean±SD | 3.11±0.42 |
| Median (range) | 3.13 (1.53–4.60) |
| Reason for referral, n (%)^e | |
| Albumin | 907 (46.6) |
| Albumin/weight loss | 523 (26.9) |
| Weight loss | 153 (7.9) |
| Albumin/BMI | 114 (5.9) |
| Albumin/weight loss/BMI | 115 (5.9) |
| BMI | 61 (3.1) |
| Weight loss/BMI | 70 (3.6) |
| Other | 3 (0.2) |
| ONS program, n (%) | 1932 (99.3) |
| Lipids, n (%) | 329 (16.9) |
| Lipid type, n (%) | |
| Clinolipid | 269 (13.8) |
| Intralipid | 31 (1.6) |
| Intralipid before January 8, 2020, and Clinolipid after January 8, 2020 | 29 (1.5) |

BMI, body mass index; IDPN, intradialytic parenteral nutrition; ONS, oral nutrition supplementation; RKF, residual kidney function; SOC, start of care.

^aOther encompasses Afro-Caribbeans, American Indians, Asians, Native Hawaiians, and Pacific Islanders.

^bMissing data.

^cSummary statistics exclude missing values ($n=199$).

^dSummary statistics exclude missing values (albumin=315).

^eAt the time of referral, patients are evaluated for IDPN eligibility which requires patients to have trialed ≥ 2 months of ONS and nutrition counseling and meet one or more of the following criteria: albumin averaging < 3.5 g/dl for 3 months, BMI < 20 kg/m², and weight loss $\geq 5\%$ within 3 months.

Baseline demographic and clinical characteristics (including missing data) are reported descriptively as means with SDs and medians with ranges for continuous variables and as frequencies and percentages for categorical variables. Missing data were not imputed for the primary or secondary end points.

For the coprimary end points, all patients with baseline and 6-month measurements of albumin levels ($N=1631$) were included in the analysis. We used paired t tests to determine if the mean change from baseline to month 6 was ≥ 0.2 g/dl. Likewise, all patients with baseline and 12-month measurements of albumin levels ($N=1631$) were included in the analysis of the change in albumin level from baseline to month 12, and paired t tests were used to determine if the change was ≥ 0.2 g/dl. We used Kaplan–Meier curves to evaluate the time to IDPN response.

To assess whether certain patient characteristics were associated with a response to IDPN therapy (*i.e.*, ≥ 0.2 g/dl increase in albumin level from baseline to month 6), we used two-sample t tests (or Mann–Whitney–Wilcoxon tests if normality assumptions were not met by Shapiro–Wilk tests) for continuous variables and Chi-square tests (or Fisher's exact tests for sample sizes < 5) for categorical variables. On the basis of the findings, a logistic regression model was used to identify independent variables (*e.g.*, age, sex, and duration of dialysis) significantly associated with a treatment response. Results are reported as odds ratios with corresponding 95% confidence intervals (CIs).

To assess the response to IDPN therapy among the three subgroups of patients who received lipids (Clinolipid, Intralipid) and those who did not receive lipids (no lipids), we used descriptive statistics to summarize baseline demographic and clinical characteristics. We used Kaplan–Meier curves to evaluate the time to IDPN response over an interval of 12 months. We used log-rank tests to evaluate potential differences in the time to IDPN response among these three subgroups and a Cox proportional hazards model to determine the effects of relevant covariates (*e.g.*, lipid/no lipid subgroup, baseline albumin levels, and other patient characteristics) on the time to IDPN response. Results are reported as hazard ratios (HRs) with corresponding 95% CIs.

All statistical analyses were conducted using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). P values < 0.05 were considered to be statistically significant. Practical significance (*i.e.*, an increase in albumin level of ≥ 0.2 g/dl¹⁷) was considered in the interpretation of the results.

This study followed the Declaration of Helsinki and was exempt under code 45 code of federal regulations §46.104(d)(4) with respect to central Institutional Review Board requirements. The research was conducted under the ethics compliance standard operating procedures of our respective affiliations.

Results

Patient Disposition and Baseline Characteristics

Of the 2270 screened patients, 324 patients were excluded because of the presence of comorbid conditions described in the exclusion criteria (Figure 2). There were

an additional 315 patients with missing baseline and/or inadequate follow-up albumin levels who were not included in the primary and secondary analyses. In totality, 1631 patients were analyzed.

Baseline demographic and clinical characteristics are summarized in [Table 1](#). Of evaluable patients, the mean (SD) duration of dialysis was 3.7 (4.1) years, and the mean (SD) duration of IDPN was 13.9 (8.0) months. Fifty-two percent of patients had ≥ 1 IDPN therapy holds; the mean (SD) number of IDPN holds was 1.0 (1.4). We could not determine the reason for the number and duration of the IDPN therapy holds because of the variation among patients for uncertain reasons with only incomplete data available. Most (85.3%) of the patients had been referred for IDPN because of low albumin levels (average albumin level < 3.5 g/dl over a 3-month interval) or low albumin combined with a weight loss of 5% or greater within a 3-month period and/or BMI trending to < 20 kg/m². Nearly all (99.3%) patients were initially placed on an ONS program, and only 8% experienced minor adverse events during IDPN therapy. Only 17% of patients received ILEs as part of their IDPN therapy; 14% received Clinolipid, 2% received Intralipid, and 2% transitioned from Intralipid to Clinolipid in August 2020. When evaluating patients and creating the IDPN recommended formula, the AA regimen was based on approximately 1.2–1.4 g protein/kg of patient weight, dextrose was 3–9 mg/kg per minute (glucose infusion rate) midrange for patients with diabetes, and lipids were 0–4 mg/kg per minute. The amount of time that the patient was dialyzed influenced the amount of dextrose and lipids.

Coprimary End Points

Among evaluable patients ($N = 1631$), the mean change in albumin level from baseline to month 6 of IDPN therapy was 0.330 (95% CI, 0.305 to 0.356) g/dl ($P < 0.001$). The percentage of patients who achieved a response to IDPN therapy (*i.e.*, ≥ 0.2 -g/dl increase in albumin level between baseline and month 6) was 82.0% (95% CI, 80.0% to 83.8%).

Secondary End Points

The mean change in albumin level from baseline to month 12 of IDPN therapy was 0.366 (95% CI, 0.323 to 0.408) g/dl ($P < 0.001$). The percentage of patients who achieved a ≥ 0.2 -g/dl increase in albumin level between baseline and month 12 was 85.8% (95% CI, 84.0% to 87.4%).

Baseline demographic and clinical characteristics associated with a response to IDPN therapy within 6 months included younger age (68.6 versus 71.0; $P = 0.006$), lower mean baseline albumin level (3.06 versus 3.34; $P < 0.001$), and IDPN without lipids (15.6% versus 27.6%; $P < 0.001$; [Supplemental Table 1](#)). Results of the logistic regression analysis confirmed these findings at month 6; the logistic regression results for month 12 were similar for age and baseline albumin level; however, the results for IDPN without lipids did not reach statistical significance ([Table 2](#)).

The time to IDPN response (≥ 0.2 -g/dl increase in albumin level) from baseline through month 12 is depicted in the Kaplan–Meier curve in [Figure 3](#), which illustrates that the median probability (marked at 0.50) of achieving an IDPN response occurred approximately 1.35 months after

the start of IDPN therapy. Approximately 50% of patients reached the threshold after < 2 months of therapy.

Results from the Cox proportional hazards regression model confirmed that patients with comorbid diabetes mellitus (DM, type 1 and 2) were 16.4% more likely to achieve a positive IDPN response as compared with those without DM (HR, 1.16 [95% CI, 1.02 to 1.33]; $P = 0.022$) while patients with residual kidney function (RKF) were 46.2% less likely than those without residual kidney function to achieve a positive IDPN response (HR, 0.54 [95% CI, 0.36 to 0.80]; $P = 0.002$). For every unit increase in baseline albumin level, patients were 35.9% less likely to achieve an IDPN response (HR, 0.64 [95% CI, 0.56 to 0.74]; $P < 0.001$; [Supplemental Table 2](#)).

Discussion

Hypoalbuminemia is common in patients on hemodialysis and is associated with many complications and adverse outcomes.^{1–3,5} Although malnutrition may not be the root cause of low albumin, increasing protein availability through nutrition support has been shown to increase albumin and whole-body protein synthesis in patients on hemodialysis.^{11,17}

In our retrospective study, we have analyzed albumin response to IDPN therapy in 1631 patients, which is the largest cohort to date in a study of IDPN. Patients on hemodialysis were referred for IDPN therapy on the basis of individual dialysis clinic-specific criteria related to albumin levels, unintentional weight loss of 5% or greater within 3 months, and/or BMI trending below 20 kg/m²; patients were further evaluated for documentation of (1) ongoing nutrition counseling from a RD, (2) poor oral intake, (3) trial of ONS, and (4) consideration to initiate EN. In this retrospective review, selected patients served as their own controls by comparing changes in albumin after treatment with their baseline albumin values; no placebo control was possible for ethical reasons because previous studies suggested that some intervention to raise or normalize albumin levels in patients on hemodialysis is beneficial to the patients' outcomes.

Within the first 6 months of IDPN therapy, 82% of patients experienced a clinically significant improvement in albumin levels with an average increase of 0.330 g/dl. This is relevant based on published findings that concluded that if albumin levels could be increased by 0.3 g/dl within 6 months in patients experiencing hypoalbuminemia, the risk of death could be reduced by 22% for the following 18 months.⁸ Eighty-two percent patients in our study showed a significant rise in albumin levels (0.2 g/dl) after IDPN therapy. Lacson *et al.* showed a 75% improvement for the same albumin level increase, which they projected could potentially save 2800 lives, avert 14,450 hospitalizations, and save \$88 million in annual costs.² Owing to improvements in the formulation of IDPN to provide a higher amount of protein with a lower amount of dextrose and lower total volume content per treatment, it is difficult to compare our results with those from previous studies that provided lower amounts of AAs than 1.2–1.4 g/kg per day of AAs calculated for formulation in this study.^{25–28} Our findings are consistent with other more recently completed prospective studies of IDPN using

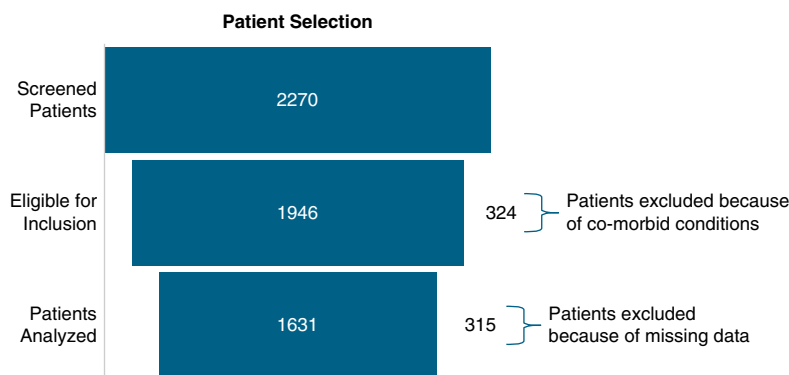


Figure 2. Patient selection funnel.

higher AA concentrations; albumin improved by an average of 0.3 g/dl and were sustained at 6 months, and the patients receiving IDPN had significant improvement in spontaneous calorie and protein intake.¹⁸ Gurlek-Demirci *et al.*, in their prospective observational study, found that counseling alone (group 1) resulted in a decline in albumin and normalized protein catabolic ratio levels, as well as increased malnutrition inflammation scores while ONS alone (group 2) did not show significant improvements in albumin levels; only the IDPN and IDPN with ONS groups (groups 3 and 4) showed significant improvements in all measures, except inflammation, as measured by high sensitivity C-reactive protein.²⁰

In this study, by being able to analyze a large population database containing patients with diverse demographics and comorbid conditions, despite the inconsistencies and

limitations that this presents, we have identified a possible time line variability for response to therapy among select patients. This suggests a potential area for further studies. While half of our study patients displayed measurable clinically significant improvements in albumin levels within 2 months of initiation of treatment, further improvement with continued use of IDPN beyond that time frame is expected given the average improvement in this study of 0.330 g/dl at 6 months and 0.366 g/dl at 12 months.

Our patients with comorbid DM were 16.4% more likely to achieve a clinically significant improvement in albumin levels after IDPN treatment than those without DM. As previously described by Cano *et al.*, and also found in this study, patients on hemodialysis with DM had generally lower levels of albumin than those without DM (3.06 versus 3.34 g/dl).²⁹ It is likely that this was a contributing

Table 2. Logistic regression models evaluating factors related to reaching the albumin threshold (≥ 0.2 g/dl change from baseline) within 6 and 12 months of intradialytic parenteral nutrition therapy (N=1472)

| Variable (Reference) | Model 1: within 6 mo | | | Model 2: within 12 mo | | |
|---|----------------------|---------------|---------|-----------------------|---------------|---------|
| | OR | 95% CI | P Value | OR | 95% CI | P Value |
| Age | 0.98 | 0.97 to 1.00 | 0.01 | 0.98 | 0.97 to 1.00 | 0.01 |
| Female sex (male) | 1.02 | 0.77 to 1.35 | 0.90 | 1.04 | 0.76 to 1.42 | 0.80 |
| Race (White) | | | | | | |
| Black | 0.95 | 0.63 to 1.45 | 0.83 | 0.96 | 0.60 to 1.52 | 0.85 |
| Other ^a /unstated | 0.98 | 0.67 to 1.42 | 0.90 | 0.84 | 0.56 to 1.27 | 0.41 |
| Hispanic (not Hispanic) | 0.8 | 0.47 to 1.35 | 0.40 | 0.74 | 0.42 to 1.31 | 0.31 |
| Unstated | 0.87 | 0.60 to 1.27 | 0.48 | 0.85 | 0.56 to 1.28 | 0.44 |
| Diabetes (no diabetes) | 0.96 | 0.70 to 1.32 | 0.82 | 0.85 | 0.60 to 1.21 | 0.36 |
| Unknown | 2.21 | 0.73 to 6.70 | 0.16 | 3.13 | 0.71 to 13.77 | 0.13 |
| Anemia (not anemic) | 1.10 | 0.82 to 1.49 | 0.51 | 1.06 | 0.76 to 1.47 | 0.74 |
| RKF/proteinuria (none) | 1.59 | 0.53 to 4.78 | 0.41 | 1.50 | 0.43 to 5.17 | 0.52 |
| Baseline albumin | 0.20 | 0.14 to 0.30 | <0.001 | 0.21 | 0.14 to 0.32 | <0.001 |
| Therapy holds | 1.05 | 0.94 to 1.18 | 0.36 | 1.12 | 0.99 to 1.28 | 0.08 |
| ONS program (no) | 1.03 | 0.20 to 5.19 | 0.98 | 1.44 | 0.28 to 7.33 | 0.66 |
| Lipid type (Clinolipid) | | | | | | |
| Intralipid | 0.56 | 0.22 to 1.45 | 0.23 | 0.89 | 0.29 to 2.68 | 0.83 |
| Intralipid before January 8, 2020, and Clinolipid after January 8, 2020 | 2.72 | 0.32 to 23.08 | 0.36 | 1.57 | 0.18 to 13.63 | 0.68 |
| No lipids | 1.68 | 1.17 to 2.41 | 0.005 | 1.45 | 0.97 to 2.16 | 0.07 |

CI, confidence interval; ONS, oral nutrition supplementation; OR, odds ratio; RKF, residual kidney function.

^aOther encompasses Afro-Caribbeans, American Indians, Asians, Native Hawaiians, and Pacific Islanders.

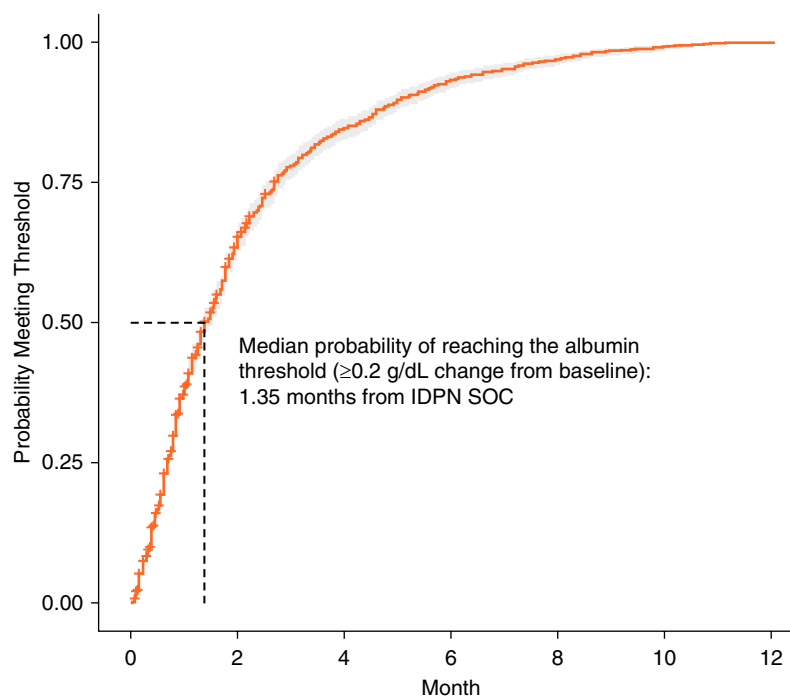


Figure 3. Kaplan–Meier curve for albumin levels within 12 months of IDPN therapy. IDPN, intradialytic parenteral nutrition; SOC, start of care.

factor in patients with DM (both types 1 and 2) experiencing the significantly increased improvement in albumin levels after IDPN treatment.

Conversely, because patients with RKF experience increased proteinuria when protein intake is increased through oral or other means,³⁰ treatment with IDPN may result in more AAs lost by proteinuria and no apparent improvement. Our study did not reach significance, likely because of only a small percentage of patients, 2.6%, with documented RKF. We believe further studies are needed for both these patient groups, DM and RKF, as well as other small subgroups to provide guidance on IDPN usage in patients on hemodialysis with DM, RKF, and other less frequent comorbidities. The subgroup analysis in these retrospective studies was complicated by both relatively small number of patients and missing information, mostly baseline. This will be corrected in the future prospective studies in these subgroups as we have suggested.

ILEs were selectively prescribed upon physician orders for patients who needed additional calories because of unintentional weight loss of 5% or greater within a prior 3-month period and/or BMI <20 kg/m². Patients who were prescribed ILEs were generally sicker and were more protein depleted than those who did not receive ILEs and although they responded with a rise in albumin, it was lower and more delayed.

Patients who received IDPN without ILEs were 68% more likely to respond to IDPN therapy and reach the albumin threshold compared with those who received IDPN compounded with ILEs (odds ratio, 1.68). Because the mean time from the start of IDPN to the inclusion of

ILEs was 4.7 months, these patients had nearly 5 months of IDPN treatment alone that could have led to improvement in albumin levels. We believe that the addition of ILEs to the IDPN prescription was likely an indicator of the severity of inadequate oral intake because lipids are usually added when both protein and higher calorie content are required. The relatively small number of patients studied did not permit a valid statistical comparison of the group receiving or not receiving ILEs in their IDPN formulation. Comparison was further complicated using two different preparations of lipids, Intralipid and Clinolipid, at different time periods. Any type of comparison will require in the future a prospective study with one preparation of ILEs and similarly selected patients.

Although our retrospective study is distinguished by having a large and diverse population of patients on hemodialysis and is consistent with many other studies of IDPN, it has some significant limitations. As is true of all retrospective observational studies, (1) causative conclusions can be reached only rarely, (2) other factors than those detected may influence the findings, and (3) the selection of patients on hemodialysis for referral to therapy was beyond these investigators' control. Because recommendation for IDPN therapy is a two-step process with the first step initiated at the dialysis clinic by the patient's health care providers, there is great variability in the selection of patients who are to receive IDPN. Each clinic or dialysis company sets their own criteria for IDPN usage, and initiation of therapy is ultimately determined by the individual patient's prescribing nephrologists. We have tried to partially overcome this variability by the large number of patients studied, knowing that this may be

insufficient. The other significant limitation of this study was the frequency of incomplete records that were reviewed for documentation of a minimum of 2 months of (1) ongoing nutrition counseling, (2) trial and failure of ONS, and (3) consideration and rejection of use of EN support. These required exclusions of some patients from the study, as previously indicated, added to the limitations of this study of included patients. As part of the problem with record reviews, we were also limited by gaps in our data because of the inconsistencies in the data made available to us by the individual dialysis clinics and by their reporting differences (different data collection systems). This limited our analysis of baseline and follow-up albumin levels for a small subset of patients. For the 99.3% of patients who were provided 90–120 days of concurrent ONS with their IDPN therapy, there was no documentation or confirmation that patients received or consumed the ONS. Future prospective studies should focus on expanding the work of previous studies^{18,20} to determine the benefits associated with the combination of IDPN with concurrent ONS given the observed improvements of spontaneous calorie and protein intake while patients received IDPN infusions.

Although albumin is a strong predictor of morbidity, hospitalizations, and mortality, we were unable in this retrospective study to analyze critical patient data such as reductions in hospitalizations, changes in QoL, composite nutrition scores, or reduced mortality risk.^{1–3} Further prospective studies with precisely defined and selected patients on hemodialysis are needed to evaluate these important outcomes.

IDPN is a safe and effective therapy associated with clinically significant improvement in serum albumin levels, a key measure for predicting morbidity and mortality in patients on ICHD who have not responded to nutrition counseling and ONSes.^{1–3} Clinically significant response was detected in half of patients within 1.35 months and in 82% of patients within 6 months of initiation of therapy with IDPN. More prospective studies are needed to identify benefits of use of IDPN in subgroups of patients including those with DM, RKF, and inflammatory bowel disease and to correlate important clinical outcomes including composite nutrition scores, QoL, and hospitalization and mortality rates with IDPN treatments in patients on ICHD.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at <http://links.lww.com/KN9/A999>.

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Data Sharing Statement

Original data created for the study are or will be available in a persistent repository upon publication. All data are included in the manuscript and/or supporting information. Anonymized data created for the study are or will be available in a persistent repository upon publication. Clinical Study Report. Aggregated Data . Compiled Data. Observational Data. Recorded Data. Statistical Analysis Plan. Dryad.

Supplemental Material

This article contains the following supplemental material online at <http://links.lww.com/KN9/A1000>.

Supplemental Table 1. Distinguishing characteristics among patients who responded to IDPN therapy (reached 0.2 g/dl change in albumin from baseline) compared with those who did not respond to IDPN therapy.

Supplemental Table 2. Effect of key factors on time until the threshold is reached (Cox proportion hazards model results; N=1475).

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