ORIGINAl RESEARCH

Association of Nutrition Status at Dialysis Start With Long-Term Survival: A 10-Year Retrospective Study

Sara Blumberg Benyamini, PhD,*†‡ Zvi Barnea, MD,*§ Relu Cernes, MD,*§ Anna Katkov, MD,*§ Anat Levi, MSc,† Alexander Biro, MD,* Zeev Katzir, MD,* and Leonid Feldman, MD,*§

Objective: The objectives of the study are to explore the association between nutritional status at the initiation of dialysis and the improvement or worsening of nutrition status during first 3 months of dialysis and first 5 years of survival on dialysis.

Methods: Two hundred ninety-seven patients who started dialysis between March 2009 and March 2019 were enrolled in the study. The nutritional status of the patients at dialysis commencement was evaluated by the method of The Integrative Clinical Nutrition Dialysis Score (ICNDS). Improvement or worsening of nutrition status was monitored by calculating the ICNDS slope for each patient enrolled in the study from 3 ICNDS values from the first 3 months on dialysis. The baseline ICNDS and the slope of 3 subsequent monthly ICNDS values were tested for correlation with the odds of all-cause mortality for each of the first 5 years on dialysis.

Results: There was a significant difference between the survival odds of patients who started dialysis with an ICNDS at 75 and those who started dialysis with an ICNDS <75 (hazard ratio [HR] 2.505, confidence interval [CI] 1.235-5.079, P = .011 after 1 year on dialysis; HR 1.543, CI 1.083-2.198, P = .016 after 5 years). Deterioration of nutritional status (a negative ICNDS slope) during the first 3 months of dialysis was associated with increased mortality during 1-3 years after dialysis start, compared to a positive ICNDS slope indicating a stable or improved nutritional status (HR 1.732, CI 1.151-2.607, P = .008 after 3 years on dialysis).

Conclusions: Nutritional status at initiation of dialysis is associated with long-term (5 years) survival. Deterioration of nutritional status during the first 3 months on dialysis significantly increases the risk of death during the first 3 years on dialysis.

Keywords: hemodialysis initiation; nutritional status; survival; nutrition assessment

© 2022 by the National Kidney Foundation, Inc. All rights reserved.

Introduction

Nutritional status has been shown to affect the survival of dialysis patients.1-3 However, most previous studies have been conducted on patients undergoing hemodialysis (HD) treatment for at least 8 weeks.1-3 To date, there have been only a limited number of studies that considered the association between clinical outcome and baseline nutritional status at the initiation of dialysis and any changes after dialysis start. McQuillan et al.4 identified malnutrition as a risk factor for early mortality in dialysis. This was supported by the results of Kwon et al.,5 who revealed that the risk of mortality for patients nutritionally assessed as being in subjective global assessment (SGA) B and C categories at baseline, was almost tripled by 12 months, and that the changes in nutritional status during the first year of dialysis were associated with all-cause mortality. Mehrotra et al.6 and Pupim et al.7 reported that initiation of HD was associated with improvement of nutritional markers in the serum (albumin, prealbumin, and an increase in dietary protein intake) over a period of up to 6 months. The extent of improvement was dependent on the nutrition in dialysis. This was supported by the results of Kwon et al.,5 who revealed that the risk of mortality for patients nutritionally assessed as being in subjective global assessment (SGA) B and C categories at baseline, was almost tripled by 12 months, and that the changes in nutritional status during the first year of dialysis were associated with all-cause mortality. Mehrotra et al.6 and Pupim et al.7 reported that initiation of HD was associated with improvement of nutritional markers in the serum (albumin, prealbumin, and an increase in dietary protein intake) over a period of up to 6 months. The extent of improvement was dependent on the nutritional status at the time of initiation of dialysis therapy.8 Nevertheless, transition to dialysis is associated with particularly high mortality rates early after dialysis initiation.9-12 Various clinical and biochemical parameters have been used in clinical practice to assess the nutritional status of dialysis patients. We used the Integrative Clinical Nutrition Dialysis Score (ICNDS),13,14 which is based on biochemical assessment of albumin, creatinine, urea, cholesterol, dialysis adequacy, C-reactive protein (CRP), and post-dialysis weight change. These laboratory parameters are routinely measured monthly before starting each dialysis session, and are known to be associated with morbidity.
Materials and Methods

Patients

This retrospective observational study was approved by the Ethics Committee of E. Wolfson Medical Center, Ethics Committee approval code: 0067–20–WOMC. Baseline demographic and clinical data of the study population are presented in Table 1. A total of 299 patients started HD at the Nephrology and Hypertension Department, in E. Wolfson Medical Center between March 1, 2009 and March 1, 2019. Four percent of patients died during the first month in dialysis, so that their first ICNDS was not available, and they were excluded from study. Another 1.74% underwent kidney transplantation, while 2% were transferred to other dialysis units, and 3.1% were refugees who were transferred abroad for transplantation by “Medecins Sans Frontieres.” A flow chart of the study is presented in Figure 1.

Determination of Nutritional Status of Hemodialysis Patients

The ICNDS was evaluated at dialysis commencement as described previously.13 All the blood samples were drawn prior to dialysis session. Each component of the score reflects a single feature of the nutritional status, and is generally accepted as an indicator of that status, contributing to the survival odds of dialysis patients. We followed the Kidney Disease Outcomes Quality Initiative recommendations, which point out that isolated nutrition markers should be used as part of a comprehensive and inclusive nutrition assessment.14 Each parameter is ranked between 1 and 5, with the higher rank derived from the recommended National Kidney Foundation Kidney Disease/Dialysis Outcomes and Quality Initiative values, and the lower rank indicating any deviation from those values.13 The final ICNDS is the sum of the ranks of the 7 parameters (albumin, creatinine, urea, cholesterol, CRP, dialysis adequacy, and weight change). Weight change and albumin levels were given greater weight corresponding to their profound effect on the outcome of HD patients (25% each and 10% for the other 5 components). Scoring results for all parameters were summed, and a final result was given for each patient.

Each parameter is ranked between 1 and 5, with the higher rank derived from the recommended National Kidney Foundation Kidney Disease/Dialysis Outcomes and Quality Initiative values, and the lower rank indicating any deviation from those values. The final ICNDS is the sum of the ranks of the 7 parameters (albumin, creatinine, urea, cholesterol, CRP, dialysis adequacy, and weight change). Weight change and albumin levels were given greater weight corresponding to their profound effect on the outcome of HD patients (25% each and 10% for the other 5 components). Scoring results for all parameters were summed, and a final result was given for each patient.

Determination of Integrative Clinical Nutrition Dialysis Score Slope

The ICNDS slope was calculated for each patient enrolled in the study, from 3 consecutive monthly ICNDS values, starting from the start of dialysis. A positive slope was previously shown to be associated with reduced mortality.13
Statistical Analyses

**Baseline, Clinical, and Nutritional Characteristics of Patients Enrolled in the Study**

We have assessed clinical characteristics and demographic data at baseline of patients enrolled in study, including gender, age at dialysis start, and comorbidities before dialysis commencement: presence of diabetes mellitus (DM), cardiovascular disease (CVD), and history of malignancy or stroke. Nutritional status at dialysis initiation was assessed by ICNDS\(^{13}\) and the 7 components of the ICNDS, together with the slope of the first 3 monthly ICNDS values for each patient.

Data are expressed as means ± standard deviations for normally distributed data, medians and interquartile ranges (quartiles 1-3) for variables that did not follow a normal distribution, and frequencies for categorical variables.

We used the 2-sided \(t\)-test to compare baseline normally distributed continuous variables of patients with an initial ICNDS ≥75 and patients with an initial ICNDS < 75. Non-normally distributed continuous variables were compared between the 2 groups (patients with an initial ICNDS ≥75 and patients with an initial ICNDS <75) by nonparametric Mann-Whitney \(U\)-tests. Chi-squared tests were used to assess the differences between categorical variables of the 2 groups.

**Association Between Baseline Nutritional Status and Survival**

The Cox proportional hazard model was used to present differences in mortality hazard ratio (HR) following 12, 24, 36, 48, and 60 months on dialysis between patients whose first ICNDS value was ≥75, and those with an initial score

---

**Figure 1.** Flow diagram of the study.
<75, after controlling for the relevant covariates (age, gender, DM, CVD, history of malignancy, history of stroke). Similarly, Cox survival curves were also used to present differences in HR between patients whose first 3-month slope was ≥0 and patients whose first slope was negative. Cox regression analyses are presented as HRs and 95% confidence intervals (CIs).

Statistical analyses were performed using SPSS software, version 25.0 (SPSS Inc, Chicago, IL).

**Results**

**Patients’ Demographic and Clinical Data According to Baseline Threshold**

The baseline demographic and clinical data of the 287 patients who started HD treatment between 2009 and 2019 at the Nephrology and Hypertension Department, E. Wolfson Medical Center, and whose initial nutritional score and 3 first months slope of nutritional score, were available, are presented in Table 1.

The majority of patients who started dialysis (70.7%) had an ICNDS ≥75. DM, CVD, and a history of malignancy were significantly more prevalent in patients with an initial ICNDS ≥75 (DM: 55.6% in patients with an initial ICNDS ≥75 and 70.7% in patients with initial ICNDS <75, P = .022; CVD: 55.1% in patients with an initial ICNDS ≥75 and 68.3% in patients with initial ICNDS <75, P = .046; history of malignancy: 19% in patients with ICNDS ≥75 and 30.5% in patients with ICNDS <75, P = .021). Patients with an initial ICNDS <75 were also significantly older (70.6 ± 13.1 years in patients with initial ICNDS ≥75, 66.5 ± 14.2 years in patients with initial ICNDS <75, P = .025). There were no differences in gender or history of stroke between patients with ICNDS ≥75 or those with ICNDS <75.

Table 1 also presents the score components for dialysis patients with initial ICNDS ≥75, and those whose first score was <75. The results for albumin, creatinine, urea, and cholesterol were significantly higher in patients with an initial ICNDS <75. In contrast, the level of CRP was significantly higher in patients whose initial score was <75. There was no significant difference between the ICNDS score groups with respect to Kt/V or percent weight change.

**Baseline Integrative Clinical Nutrition Dialysis Score Is Associated to All-Cause Mortality Hazard Ratio During 5 years on Dialysis**

Table 2 presents prognostic factors for all-cause mortality for the first 12–60 months on dialysis. The association between ICNDS and mortality was tested by the baseline ICNDS and the mortality HR for each of first 5 years on dialysis. The results indicated that an ICNDS value <75 at dialysis initiation was significantly associated with increased mortality hazard compared to an
ICNDS ≥75 (HR 2.505, CI 1.235–5.079, \( P = .011 \) after 1 year; HR 1.798, CI 1.053–3.069, \( P = .032 \) after 2 years; HR 1.838, CI 1.200–2.813, \( P = .005 \) after 3 years; HR 1.489, CI 1.027–2.159, \( P = .066 \) after 4 years; and HR 1.543, CI 1.083–2.198, \( P = .016 \) after 5 years of dialysis.)

Changes in Nutritional Status Over First 3 First Months in Dialysis Is Associated With Risk of Death During First 3 Years in Dialysis

Table 2 presents the association of the deterioration in nutrition status during first 3 months in dialysis with all-cause mortality for the first 12–60 months on dialysis. A negative slope for the monthly ICNDS values over the first 3 months of dialysis was also associated with increased mortality during the 1–3 years after dialysis start: HR 2.792, CI 1.372–5.681, \( P = .005 \) after 1 year; HR 2.194, CI 1.311–3.672, \( P = .003 \) after 2 years; and HR 1.732, CI 1.151–2.607, \( P = .008 \) after 3 years. A negative slope for the 3 first months was not associated with increased mortality after 4 or 5 years of dialysis.

Age at baseline had a significant effect on survival from the second to the fifth year on dialysis: HR 1.039, CI 1.014–1.065, \( P = .002 \) after 2 years; HR 1.029, CI 1.010–1.049, \( P = .003 \) after 3 years; HR 1.041, CI 1.023–1.059, \( P = .001 \) after 4 years; and HR 1.041, CI 1.024–1.058, \( P = .001 \) after 5 years.

Diabetes had a significantly worsening effect on survival: after the second year in dialysis, at the limit of significance, HR 1.716, CI 0.996–2.958, \( P = .052 \) after 2 years; HR 1.660, CI 1.074–2.568, \( P = .023 \) after 3 years; HR 1.901, CI 1.309–2.759, \( P = .001 \) after 4 years; and HR 1.925, CI 1.350–2.745, \( P = .001 \) after 5 years.

A history of stroke emerged as having a worsening effect on survival after 3 years on dialysis: HR 1.878, CI 1.193–2.955, \( P = .006 \) after 3 years; HR 1.635, CI 1.076–2.485, \( P = .021 \) after 4 years; and HR 1.597, CI 1.062–2.401, \( P = .024 \) after 5 years.

CVD emerged as a worsening effect on survival after 4 and 5 years in dialysis, although at the limit of significance: HR 1.411, CI 0.982–2.027, \( P = .063 \) after 4 years and HR 1.407, CI 0.996–1.987, \( P = .053 \) after 5 years.

Figure 2. Cox survival curves over time by nutritional score at dialysis start, for patients with ICNDS ≥75 or <75 threshold. Cox survival curves for patients with baseline ICNDS ≥75 or <75 threshold. Over (A) 12 months, (B) 36 months, and (C) 60 months following dialysis initiation. Patients who started dialysis with ICNDS ≥75 are represented by a solid line and patients who started dialysis with ICNDS <75 by a dashed line. ICNDS, Integrative Clinical Nutrition Dialysis Score.
Gender and history of malignancy (before dialysis initiation) did not predict mortality.

Figure 2 shows the 12, 36, and 60 months survival curves for all-cause mortality of patients with initial ICNDS ≥75, compared to those whose first score was <75.

Figure 3 presents the 12, 36, and 60 months survival curves for all-cause mortality of patients whose first 3-month slope of ICNDS was ≥0, and patients whose first 3-month score was negative.

Figure 4 presents (1) mortality HR over 60 months for patients whose first score was <75 compared to patients whose first score was ≥75. (2) Mortality HR >60 months for patients with a negative compared to a positive ICNDS 3 first months slope. Notably, while the relationship of mortality HR remains significantly associated with first ICNDS <75 compared to ICNDS ≥75 over 5 years of dialysis, the association with a negative compared to positive first ICNDS slope remains significant for only 3 years following dialysis start.

Although mortality HR remains significantly related to initial ICNDS score over 5 years following dialysis start, a negative ICNDS slope compared to those with a positive first slope remains significant for 3 years following dialysis start.

Discussion

The main finding of this research is that the nutritional status at the start of dialysis is associated with long-term 5-year survival on RRT. In addition, a decline in nutritional status over the first 3 months of dialysis significantly increases the risk of death during the first 3 years in dialysis.

The results revealed a significant difference in the mortality HR of patients who started dialysis with an ICNDS ≥75, and those who started RRT with an ICNDS <75.

In general, patients who started RRT with an ICNDS <75 threshold were significantly older, with a higher prevalence of background diseases, DM, CVD, and history of malignancy than those with a higher ICNDS. In addition, they had significantly lower values for albumin, creatinine, urea, and cholesterol, which are biochemical parameters used in the score that are known for their association with nutritional status, but significantly higher values of CRP, a marker of inflammation. The pathogenesis of inflammation present at the start of dialysis is multifactorial, and can be attributed to comorbidities related to CKD: the uremic state, heart failure, oxidative stress, and infections. There were no differences between the groups with high or low ICNDS with respect to kt/V or percent weight change.
In this context, an initial change in body weight is thought to reflect a decrease in extracellular volume due to the removal of excess fluid by ultrafiltration. We conclude that protein energy wasting and inflammation, together known as malnutrition-inflammation complex syndrome, underlines the differences in biochemical parameters and comorbidities between patients who started dialysis with ICNDS above or below the threshold value. The results of our research call for special attention for predialysis care. We suggest a multidisciplinary approach that includes attention to diet and provision of adequate treatment for comorbidities in the period before initiation of dialysis, with the aim of increasing the ICNDS during the transition to RTT. This then might improve survival odds after dialysis initiation.

The first 3-month slope of nutritional status, which is a parameter unique to our study, enables the identification of the first indications of nutritional deterioration, even for patients with adequate nutritional status. Theoretically, the initiation of dialysis should have positive effects on the nutritional state, the increased removal of uremic toxins which cause a reduction in food intake, the correction of acidosis, and the possibility for an increased protein consumption, when compared with the predialysis stage. Nevertheless, the ICNDS slope for the first 3 months in dialysis was negative in 40% of the patients in our study. This phenomenon probably derives from the burden of starting RRT, and highlights the importance of improving the nutritional status during the first months in dialysis. Importantly, a negative ICNDS slope for the first 3 months on dialysis significantly increased the risk of death during the first 3 years in dialysis, compared to patients with a positive slope. Dietary, medical, and social intervention at this time might achieve a change from a negative to positive slope and thereby increase the odds of survival.

The findings of our study suggest that ICNDS indicates not only the nutritional status of patients, but is also a measure of the patients’ baseline inflammatory situation derived from parameters such as baseline medical condition.

The strengths of this study include a 10-year careful collection of monthly biochemical data and detailed baseline information on HD patients over a long follow-up period.

We recognize some limitations in our study. The first is that the study is based on a relatively small sample size and represents a single dialysis center, thereby limiting the possibility of generalizing these findings. Second, this study employed an exclusively observational approach, without handling of risk factors and therefore, no specific cause-and-effect associations can be derived for any of the risk factors analyzed. Third, the study includes patients who received pre–end-stage renal disease care as well as patients who started dialysis as an emergency treatment. Patients who have received pre–end-stage renal disease care are likely to start dialysis in a better clinical condition and to have a better prognosis. Nevertheless, we consider the impact on our results to be minimal, as this study was designed to investigate the effect of baseline clinical situation on long-term survival.

In summary, the results of our study confirm that the nutritional status at commencement of HD and the change in nutritional status over the first 3 months on dialysis are major prognostic long-term survival factors. Further research is needed to explore the possible survival implications of transition between nutritional scores and slopes while on dialysis.

**Practical Application**

The main finding of our study is that the nutritional status at dialysis initiation is associated with long-term survival, for up to 5 years following RRT commencement. This calls for special attention to be paid to diet and adequate treatment of comorbidities as patients approach dialysis, in order to optimize survival after dialysis start.

Our study also suggests the importance of improving the nutritional status during the first months in dialysis. Dietary intervention at this time, during the first 3 months on dialysis, might improve survival during the 3 years following RRT commencement.
CRediT authorship contribution statement

Sara Blumberg Benyamini: Conceptualization, Software, Formal analysis, Writing – original draft, Writing – review & editing.
Zvi Barnea: Conceptualization, Software, Formal analysis, Writing – original draft, Writing – review & editing.
Relu Cernes: Conceptualization, Investigation, Validation.
Anna Katkov: Conceptualization, Investigation, Validation.
Anat Levi: Methodology, Data curation, Visualization.
Alexander Biro: Conceptualization, Writing – review & editing.
Zeev Katzir: Writing – review & editing.
Leonid Feldman: Formal analysis, Writing – review & editing.
Supervision, Project administration.

References