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Comparação de ferramentas de avaliação do risco nutricional em doentes em programa regular de hemodiálise: simple Protein-Energy Wasting Score, Geriatric Nutritional Risk Index, Modified Creatinine Index com o Malnutrition-Inflammation Score.

Leila Brícia Meneses de Oliveira Aguiar

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Comparison of tools for nutritional risk assessment of patients in maintenance hemodialysis: simple Protein-Energy Wasting Score, Geriatric Nutritional Risk Index, modified Creatinine Index with Malnutrition-Inflammation Score.

Leila Brícia Meneses de Oliveira Aguiar, Nutricionista (CP 1254N)

Faculdade de Ciências da Nutrição e Alimentação da Universidade do Porto, Porto

Departamento Médico, Diaverum Portugal

Orientador: Prof. Doutor Edgar de Almeida – Faculdade de Medicina da Universidade de Lisboa

Coorientador: Dr. Fernando Macário – Diaverum AB, Sweden

Coorientador: Prof. Doutor Nuno Borges – Faculdade de Ciências da Nutrição e Alimentação da Universidade do Porto

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Resumo

O estado nutricional tem um grande impacto no prognóstico dos doentes em programa regular de hemodiálise. Por conseguinte, a gestão do estado nutricional deve ser prioritária, a avaliação do risco frequente e a implementação exequível, baseados nos parâmetros já disponíveis e quando a aplicação de ferramentas mais abrangentes não é possível. Algumas ferramentas satisfazem estes critérios, nomeadamente, o *modified creatinine index*, o *geriatric nutritional risk index*, e o *simple protein energy score*, e que estão associados com os riscos de morbilidade e mortalidade em doentes em hemodiálise. O objetivo desta tese é confirmar se estas ferramentas estão significativamente associadas com a mortalidade por todas as causas e compará-las com o *malnutrition-inflammation score*.

Este é um estudo de coorte histórico de doentes em hemodiálise de 25 clínicas. O estado nutricional e inflamatório foi avaliado na *baseline* com o *malnutrition-inflammation score*, o *geriatric nutritional risk index*, o *modified creatinine index*, e o *simple protein-energy wasting score*. Para análise dos dados recorreu-se à análise uni e multivariada com os modelos de regressão de Cox aditivo. Foram utilizados testes de *partial likelihood ratio* para comparar o desempenho dos modelos de Cox *non-nested*.

Foram analisados 2322 doentes, 59% homens, 31.7% diabéticos, com uma mediana de idade de 70 anos (P_{25}=60, P_{75}=79) e uma mediana de *follow-up* de 45 meses (P_{25}=31; P_{75}=45). A mortalidade por todas as causas foi observada em 778 doentes (33.5%).

A mediana do *modified creatinine index* foi 18.3 mg/kg/day (P_{25}=16.8, P_{75}=20.0), e os valores mais elevados foram observados nos doentes sobreviventes ($p<0.001$).

Os resultados da análise multivariada mostraram que valores mais elevados do produto fosfocálcio e de índice de comorbilidade de Charlson, e menores de *modified creatinine index*, de albumina, de fosfatemia, de índice de massa corporal e da taxa de remoção de ureia estavam significativamente associados com o risco de morte.

Relativamente ao *geriatric nutritional risk score*, a mediana foi 106.6 (P_{25}=99.4, P_{75}=114.2), sendo significativamente maior no grupo sobrevivente ($p<0.001$). Nos resultados da análise multivariada, uma maior idade e índice de comorbilidade de Charlson, e um menor *geriatric nutritional risk index*, taxa de catabolismo proteico normalizado, e taxa de remoção de ureia estavam significativamente associados com o risco de morte.

Os resultados menores do *simple protein-energy wasting score* foram mais frequentes no grupo dos doentes que faleceram ($p<0.001$). Nos resultados da análise multivariada, uma maior idade, índice de comorbilidade de Charlson, ganho de peso interdialítico, e um menor *simple protein-energy wasting score*, e uma menor taxa de remoção de ureia, estavam significativamente associados com o risco de morte.

Na avaliação com o *malnutrition-inflammation score*, a mediana foi 6 (P_{25}=4, P_{75}=8), e 50.6% dos doentes tinham um score ≥6, com os resultados mais altos mais frequentes no grupo dos doentes que faleceram ($p<0.001$). Nos resultados da análise multivariada um maior *malnutrition-inflammation score*, idade, índice comorbilidade de Charlson, ganho de peso interdialítico, e um menor Kt/V, taxa de catabolismo proteico normalizado, e albumina, estavam significativamente associados com o risco de morte.

Nos quatro modelos, doentes com cateter venoso central apresentavam maior risco de morte quando comparado com a fistula arteriovenosa.

Os *partial likelihood ratio tests* mostraram que o *malnutrition-inflammation score* se ajustou melhor nos modelos que não incluía o *simple protein-energy wasting score*. Todas as ferramentas apresentaram uma boa performance discriminativa com o *Harrell's C-statistic*, variando entre 0.71-0.74. Os modelos do *malnutrition-inflammation score* e o *modified creatinine index* apresentaram os maiores valores.

Por conseguinte, todas as ferramentas estão significativamente associadas com a mortalidade. O *modified creatinine index* e o *geriatric nutritional risk index* apresentaram uma performance semelhante à do *malnutrition-inflammation score*.

Palavras-Chave: hemodiálise, risco nutricional, malnutrition-inflammation score, geriatric nutritional risk index, simple protein-energy wasting score, modified creatinine index, mortalidade

Abstract

The nutritional status greatly impacts the prognosis of maintenance hemodialysis patients. Therefore, its management should be a priority, and risk screening frequent and easily implemented, based on the biochemical and clinical routine parameters already available, when the use of more comprehensive tools is not possible. Many tools fit these simple criteria, namely the modified creatinine index, geriatric nutritional risk index, and simple protein energy wasting score. These scores are associated with mortality and morbidity risk in hemodialysis patients. This study aims to confirm that these scores are significantly associated with all-cause mortality and to compare them with malnutrition inflammation score.

This is an historical cohort study of hemodialysis patients from 25 outpatient clinics. The nutritional and inflammation status was assessed at baseline with malnutrition-inflammation score, geriatric nutritional risk index, modified creatinine index, and simple protein-energy wasting score. Univariable and multivariable Cox additive regression models were used to analyse data. Partial likelihood ratio tests to compare the performance of non-nested Cox models were used.

We analysed 2322 patients, 59% males, 31.7% diabetic, with a median age of 70 years (P_{25}=60, P_{75}=79), during a median follow-up period of 45 months (P_{25}=31; P_{75}=45). All-cause mortality was observed in 778 patients (33.5%).

The median of the modified creatinine index was 18.3 mg/kg/day (P_{25}=16.8, P_{75}=20.0), and a higher index value was observed for the surviving patients ($p<0.001$). Multivariable analysis results showed that higher phosphocalcium

product, Charlson comorbidity index, lower modified creatinine index, albumin, phosphate, body mass index, and urea removal rate were significantly associated with the risk of death.

Regarding geriatric nutritional risk score, a median of 106.6 (P_{25}=99.4, P_{75}=114.2) was observed, being significantly higher in the survival group ($p<0.001$). In the multivariable analysis results, higher age and Charlson comorbidity index, lower geriatric nutritional risk index, normalized protein catabolic rate, and urea removal rate were significantly associated with the risk of death.

Simple protein-energy wasting score lower scores were more frequent in the group of deceased patients ($p<0.001$). In the multivariable analysis results, higher age, Charlson cormorbidity index, and interdialytic weight gain, lower simple protein-energy wasting score, and urea removal rate, were significantly associated with the risk of death.

For the malnutrition-inflammation score, the median was 6 (P_{25}=4, P_{75}=8), and 50.6% of the patients had a score ≥6, with higher scores being more frequent in the group of deceased ($p<0.001$). In the multivariable analysis results, higher malnutrition-inflammation score, age, Charlson comorbidity index, interdialytic weight gain, and lower Kt/V, normalized protein catabolic rate, and albumin, were significantly associated with the risk of death.

In the four models, central venous catheter had a significantly higher risk of death when compared with fistula.

Partial likelihood ratio tests showed that the malnutrition-inflammation score only fitted better than the model including simple protein-energy wasting score. All scores had a good discriminative performance with Harrell's C-statistic ranging

from 0.71-0.74. Malnutrition-inflammation score and modified creatinine index models attained the highest values.

All the tools were significantly associated with mortality. The modified creatinine index and geriatric nutritional risk index were the scores that performed most similarly to the malnutrition-inflammation score.

Keywords: Hemodialysis, Nutritional Risk, Malnutrition-Inflammation Score, Geriatric Nutritional Risk Index, simple Protein-Energy Wasting score, Modified Creatinine Index, Mortality

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List of Abbreviations

Alb – Albumin

AVF – Arterio-Venous Fistula

AVG – Arterio-Venous Graft

BMI – Body Mass Index

CaxP- Phosphocalcium product

CCI – Charlson Comorbidity Index

CI – Confidence Interval

CKD – Chronic Kidney Disease

CVC – Central Venous Catheter

GNRI – Geriatric Nutritional Risk Index

HD – hemodialysis

HR – Hazards Ratio

IDWG – Interdialytic Weight Gain

mCI -modified Creatinine Index

MIS – Malnutrition-Inflammation Score

nPCR –normalized Protein Catabolic Rate

PCreat – Serum Creatinine

PEW – Protein Energy Wasting

P – Phosphorus

PTHi – intact Parathormone

RRT – Renal Replacement Therapy

SGA – Subjective Global Assessment

sPEW – simple Protein-Energy Score

TBIC – Total Binding Iron Capacity

URR – Urea Removal Rate

1.Introduction

Nutritional status management is crucial in all stages of chronic kidney disease (CKD) because of the intricate role of kidney function and its impact on nutritional metabolism homeostasis and other related morbidities in the progression of CKD. [1]

The kidney function decline, failure, and renal replacement therapies (RRT) have a direct influence on nutritional status either through alteration of the nutritional intake or/and by an increment of the catabolic pressure on the homeostatic mechanisms, more notorious on advanced CKD stages and in some RRT, such as maintenance hemodialysis (HD). [2]

Currently, the prevalence of CKD patients with RRT is increasing (in Portugal the prevalence in 2023 was 2072.16 pts/million, 1250.27 of which HD), and the demography has become more challenging, with older and more comorbid patients (a recent large study estimated that 50% of the HD patients had a significant malnutrition-inflammation risk). A prioritized, individual, and consistent medical nutritional therapy for the maintenance of an optimal nutritional status, as part of the global and interdisciplinary therapeutic approach, is pertinent. [1-6]

Therefore, nutritional risk assessment and management should be a part of the definition and implementation of broad clinical strategies and policies that sustain nutritional rehabilitation and diminishes nutritional risk. [4, 7]

Recently, the 2020 KDOQI recommended the Subjective Global Assessment (SGA) for nutritional assessment (Level of Evidence (LOE) 1B) and Malnutrition-Inflammations Score (MIS) (LOE 2C). MIS is a quantitative and comprehensive tool, and its prognostic value was recently confirmed with suggested new cutoffs and an emerging trend. [4, 7]

However, MIS assessment needs specialized and trained human resources, and not all the clinical contexts of HD patients have the means to consistently apply MIS, so other tools that could be automatically determined must be considered, namely the Geriatric Nutritional Risk Index (GNRI), the modified Creatinine Index (mCI) and the Protein-Energy Wasting score (sPEW). These scores have also been associated with mortality and morbidity risk in HD patients. [1-3, 8-10,14,22]

The GNRI is an elderly-specific index, that uses albumin and body mass index (BMI), developed to assess the malnutrition-related risk of morbidity and mortality for hospitalized elderly patients. Since then, its prognosis value has been studied in several chronic diseases, from malignant tumors to cardiovascular mortality. [10-16]

The mCI is a simple nutritional index that considers the complexity of creatinine kinetic modeling and is calculated using age, gender, Kt/V for urea, and pre-dialysis serum creatinine values, reflecting animal protein intake and skeletal muscle mass. Low values of this index have been associated with sarcopenia, handgrip strength, and mortality. [14, 15, 17-20]

Finally, protein-energy wasting (PEW) is defined by the International Society of Renal Nutrition and Metabolism (ISRNM) as "a state of decline in body reserves of protein and energy fuels", and is a critical condition characterized by inadequate nutritional intake, accumulation of uremic toxins, inflammation, catabolism, and is one of the independent risk factors associated with a high mortality rate. [3]

The proposed diagnosis criteria consider 4 categories: altered biochemical indicators; low body weight, decreased body fat reserves, or significant weight loss; decreased muscle mass; and reduced protein and energy consumption. sPEW

is based on these criteria, which can be promptly calculated based on the available clinical and biochemical parameters. [1, 3, 21-23]

So, although the MIS is an important and validated tool, in clinical contexts where trained nutritionists and all clinical data needed are unavailable, other simpler and automatic tools might be interesting.

2. AIMS

The aim of this study was, first to confirm that GNRI, mCI, and sPEW nutritional scores are significantly associated with all-cause mortality, and secondly to compare them with MIS.

3. METHODS AND ANALYSIS

Study Design

This is a historical cohort study performed in a group of patients on maintenance HD from 25 dialysis outpatient clinics, followed up between 2015 and 2019. Patients were submitted to an assessment of the nutritional and inflammation status at baseline with MIS, and GNRI, mCI and sPEW was obtained retrospectively.

Population

The initial exclusion criteria were as follows: age <18 years, HD vintage < 3 months, any disability that would affect data collection or the scores assessment, and the patient's unwillingness to participate in the study.

For this analysis were included the followed up patients that had all the available data that allow us to determine, retrospectively, GNRI, mCI, and sPEW.

Ethics

The study was submitted and approved by the local ethics committee (reference number 2022-04) and follows the principles of the Declaration of Helsinki. All patients have signed an informed consent authorizing the use of clinical data for medical research, and patient data were treated anonymously.

Data Collection

Demographic and Biochemical data

Patients' data were collected retrospectively based on patients' charts and electronic clinical record system treatment records.

The routine biochemical data were obtained from pre and post-dialysis blood samples of the midweek day (Wednesday or Thursday), with all the laboratory analyses performed nationwide by the same methodology and protocol. To consider patients' routine clinical parameters patterns, when possible, a 3-month average was calculated. Serum albumin assessment was made using the bromocresol green method. Instead of using total iron binding capacity (TIBC), we chose to use transferrin values, as originally suggested: ≥200 mg/dL (score 0), 199-170 mg/dL (score 1), 169-140 mg/dL (score 2), and <140 mg/dL (score 3).

Malnutrition-Inflammation Score

The MIS is a comprehensive and quantitative assessment tool of nutritional and inflammation risk that consists of 4 main areas: clinical history (changes in body weight, dietary intake, gastrointestinal symptoms, functional capacity, comorbid conditions), physical assessment (decreased fat stores and signs of muscular atrophy), BMI and laboratory results (albumin and transferrin/TBIC), in a total of 10 items, each scored from 0 (normal) to 3 (severely abnormal), giving a final MIS ranging between 0 and 30. [1,8, 9] The assessment was performed between September 15th, 2015, and January 31st, 2016 in all the prevalent HD patients by a team of trained nutritionists. The physical examination was made according to the SGA criteria.

Current dry weight and measured height were used to determine BMI.

Geriatric Nutritional Risk Index

The GNRI was calculated according to the following formula:

GNRI=[14.89 × serum albumin (g/dL)] + [41.7 × (actual body weight/ideal body weight)], where ideal body weight was obtained as follows: ideal body weight (kg) = [height (m)]2 × 22 (kg/m2). [24]

Modified Creatinine Index

The mCI was calculated according to the following formula that considers gender: mCI for men = 16.21+1.12–0.06 × [age (year)] − 0.08 ×(single pool Kt/V)+0.009 ×[serum creatinine (μmol/L)], mCI for women = 16.21–0.06 ×[age (year)] − 0.08 × (single pool Kt/V)+0.009 × [serum creatinine (μmol/L)]. [17]

Protein-Energy Wasting Score

sPEW was calculated according to the diagnostic criteria of the ISRNM for PEW: scoring 0, if below or equal to the cutoff, and 1 if superior in the following items: serum albumin ≤ 3.8 g/dL, BMI ≤ 23 kg/m2, Serum creatinine/Body Surface Area ≤ 380 μmol/L/m2, normalized Protein Net Appearance ≤ 0.8g/kg. The score ranges from 0 – severe wasting, to 4 – normal status.[23]

Statistical Analysis

Categorical data were presented as frequencies (percentages) and quantitative variables as median and inter-quartile range (25th-75th percentile). Mann-Whitney and chi-squared tests were used as appropriate. Survival rate estimates were obtained using the Kaplan-Meier estimator and compared using the log-rank test. Additive Cox regression models were used to decide the coding of the quantitative explanatory variables. After the univariable analysis, four multivariable Cox proportional hazards regression models (one for each nutritional score) were fitted to the data concerning the time until death from all causes. Variables that attained a p-value<0.25 in the univariable analyses were candidates

for the multivariable models. Because serum Alb and BMI values were required for GNRI estimation and the patient's sex, age, urea clearance, and serum creatinine level were required for mCI calculation, these variables were excluded from the respective multivariable models.

Crude and adjusted hazard ratios were estimated with corresponding 95% confidence intervals (CIs). To test the proportional hazards assumption of Cox regression models, plots based on Schoenfeld residuals were used. [25]

To compare the performance of the multivariable models including mCI, GNRI, or sPEW scores with that including MIS, partial likelihood ratio tests for non-nested Cox regression models were used. [26] To assess the discriminative ability of the multivariable survival models, Harrell's C-indexes with corresponding 95% CIs were estimated. [27] A level of significance $\alpha=0.05$ was considered. Data were analysed using the statistical program R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

4. RESULTS

Patient's Demographic, Clinical and Biochemical Characteristics

We analysed 2322 patients, 59% males, 31.7% diabetic, with a median age of 70 years (P_{25}=60, P_{75}=79), during a median follow-up period of 45 months (P_{25}=31; P_{75}=45). All-cause mortality was observed in 778 pts (33.5%). The baseline patients' demographic, clinical, and biochemical parameters are presented in Table 1.

The median of mCI was 18.3 mg/kg/day (P_{25}=16.8, P_{75}=20.0), whereas a higher mCI median of 18.8 mg/kg/day (P_{25}=17.4, P_{75}=20.5) was observed for the survived patients ($p<0.001$). A median of 106.6 was observed for the GNRI (P_{25}=99.4, P_{75}=114.3), being significantly higher in the survival group, 107.5 (P_{25}=101.1, P_{75}=115; $p<0.001$). Regarding sPEW, the frequency of each score from 0 to 4 was 306, 380, 111, 1369, and 156, respectively, with the lower scores (0-1) being more frequent in the group of deceased patients ($p<0.001$).

For MIS the median was 6 (P_{25}=4, P_{75}=8), and 50.6% of the patients had a score ≥6, with higher scores being more frequent in the group of deceased ($p<0.001$).

The group of patients that survived had a lower age, HD vintage, MIS, and serum calcium, and higher albumin, normalized protein catabolic rate (nPCR), serum phosphorus, PxCa, IDWG, PTHi, and BMI ($p<0.001$).

Figure 1 represents the Kaplan-Meier estimates of the survival functions corresponding to the mCI, GNRI, and MIS quartiles, and the sPEW five categories. For each score, the highest risk category differs, with statistical significance, from the remaining ($p<0.001$).

Multivariable Cox Regression Results

The results of the univariable analysis are shown in Supplementary Table S1.

Modified Creatinine Index

Multivariable Cox regression analysis results (Table 2) showed that lower BMI, higher PxCa and Charlson Comorbidity Index (CCI) values were associated with a higher risk of death. On the contrary, higher values of P, BMI, and urea removal rate (URR) were associated with a lower risk. Both arteriovenous graft (AVG) and central venous catheter (CVC) had a higher risk of death when compared with fistula, although only the latter attained statistical significance. Regarding the mCI score, for each unit increase, there is a 26.2% decrease in the risk of death (HR=0.738; 95% CI: 0.675 – 0.807, p<0.001). This multivariable model attained a C-index estimate of 0.734 (95% CI: 0.716-0.752).

Geriatric Nutritional Risk Index

Considering the multivariable model with GNRI (Table 3), results showed that older age, higher CCI values, and lower nPCR values (≤1.05g/kg/d), were risk factors regarding death. On the other hand, higher values of URR were protective. Both AVG and CVC had a higher risk of death when compared with AVF, although only the latter attained statistical significance. Regarding GNRI, for each unit increase, there is a 2.8% decrease in the risk of death (HR=0.972; 95% CI: 0.965 – 0.978, p<0.001). This multivariable model attained a C-index estimate of 0.725 (95% CI: 0.707-0.743).

Protein-Energy Wasting Score

Results of the multivariable Cox regression analysis, depicted in Table 4, showed that higher values of age, CCI, and IDWG were associated with an increased risk of death. Higher values of URR were protective. According to previous results, AVG and CVC were associated with a higher risk of death, when compared with AVF. However, only CVC attained statistical significance. Regarding sPEW, a binary

variable was considered: categories 0 and 1 versus categories 2, 3, and 4, being the last one, the reference category. Adjusted results showed that patients with lower sPEW values have a higher risk of death (HR=1.373; 95% CI:1.184 – 1.593, p<0.001). This multivariable model attained a C-index estimate of 0.712 (95% CI: 0.694-0.730).

Malnutrition-Inflammation Score

Multivariable Cox regression analysis results (Table 5) showed that higher values of age, CCI, IDWG, and lower nPCR values were associated with a higher risk of death. On the contrary, higher values of Kt/V were protective against death. Similar results were found regarding AVG and CVC when compared to AVF.

Regarding the MIS score, for each unit increase, there is a 5.9% increase in the risk of death (HR=1.059; 95% CI: 1.039 – 1.080, p<0.001). This multivariable model attained a C-index estimate of 0.734 (95% CI: 0.715-0.752).

Results of the comparison of the multivariable model including MIS with the remaining models are presented in Table 6.

5. DISCUSSION

There are several challenges in routine clinical nutrition practice in HD patients, one of them is the lack of resources, and the other is trying to define clinical strategies that comprehensively address nutritional risks, knowing that, a priori, a higher rate of nutritionally assessed patients would increase the probability of an adequate management of nutritional status, individually and globally.

The aim of this study comes from the fact that, although the MIS is a comprehensive and validated tool, there are some limitations concerning the availability of trained resources, and biochemical data, and it is a time-consuming tool.

With MIS it is possible to understand which factors have the greatest impact and define strategies to address individual and global risk, and it is also recommended for more longitudinal assessments [4].

Therefore, a tool that would fill this gap, that is simple to implement with the data already available, is needed. Our data shows that GNRI, mCI, and sPEW fit this criteria.

Consistent with previous studies, the GNRI showed a significant association with survival in the models used [14, 26, 28-32]. Older patients, with higher CCI, lower nPCR and URR, and with CVC had a higher risk of death. As found in previous studies, there was no significant difference between patients with AVG compared with the reference category, AVF. Currently, there are several proposals for risk classification based on strata: < 82 - high risk, 82-91 - moderate risk, 92-98 - low risk: 92–98, and > 98 no risk; and on cutoffs that range from 86.0 (Güneş, 2022) to 96 (Nakagawa, 2015). [4, 14, 28-32]

However, most of these findings are in an age-mixed population, which might impact this value when we compare it with a much older and homogenous population. [29] Some authors suggest that cutoffs, such as 91.2 (Yamada, 2008) should be used in all ages (middle+elderly), while other cutoffs should be considered for patients older than 65 years. [29]

Population heterogeneity (age, genetics, and other demography variables) and also the exposure and frequency of distinct nutritional management approaches (from less frequent to intensive nutritional therapy and highly focused nutritional status rehabilitation) must be considered when comparing the results of the different studies, for example, most of these studies are in younger and Asian patients, while our population is older and mainly southwest European Caucasians. Other confounders and limitations should also be considered such as the changes in body composition and progression of hypoalbuminemia that occur with aging. Some authors, even propose a cutoff revision for every decade of age (which adds some practical complexities), or even a GNRI formula revision incorporating age. [33]

Concerning mCI, a useful tool that reflects protein and lean body mass dynamic, we found a significant association with survival in the models used. [17] Several studies with HD patients also reported that mCI was significantly associated with survival, heart disease, and all-cause mortality (both in males and females), adverse outcomes related to sarcopenia, and long-term infection, although many studies used arbitrary and non-consistent cutoff points derived from their cohorts [17-19, 34].

In the multivariable analysis, patients with higher CCI and PxCa, lower BMI, and with CVC had a higher risk of death, while patients with higher URR, had a lower

risk. There was also no significant difference for patients with AVG compared to the reference category AVF.

Concerning mCI, several authors propose different cutoffs: 20.8 mg/kg/day (Yamada et al, 2020), 22 mg/kg/day (Yamamoto et al, 2021), 21.07 mg/kg/day for males, and 19.57 mg/kg/day for female (Tian et al, 2022), 20.16 mg/kg/day (Yajima et al, 2022), found in younger, mainly male (>60%) and East Asian HD patients. In 2020 Canaud et al., in a large study of the European population, suggested a cutoff of 20.5 mg/kg/day. They also found that mCI tends to be higher in male and younger HD patients, declining months before death (both in male and female patients). Older patients can have less than 26-27% of lean body mass than the younger ones. [35]

Several factors can contribute to different values found in these studies: demography, genetic pool, limitations inherent to creatinine level fluctuation in these patients (the impact of catabolic processes, food intake, residual kidney function, HD efficacy, and prescription, etc.), and also the fact that all these patients were exposed to a regular and protocoled nutrition intervention focused on protein intake and metabolic goals which can have an impact when comparing with other populations. [7, 36, 37]

The sPEW, a score developed to reflect each major group that generally interferes with a patient's nutritional status, was also significantly associated with survival. The best model found for score categorization was: scores 0 and 1 vs scores 2, 3, and 4, similar to the findings of Moreau-Gaudry et al and Kobayashi et al., but different from others.[22, 23, 38, 39] Considering the last as the reference category, patients in the lower category had a 37.3% higher mortality risk. In the

multivariable analysis older age, higher CCI, IDWG, and CVC increased the risk, while a higher URR had a protective effect.

Finally, MIS also was significantly associated with mortality risk, as also found in our previous study.[4]

An increment of one unit increased the risk of death by 5.9%. Older patients, with CVC, higher CCI and IDWG, and lower nPCR had higher death risk. A higher Kt/V and albumin had a protective effect.

Literature that compares various nutritional scores is scarce.

In our sample, similar Harrell's C statistics (values ranged from 0.71-0.74) were estimated, having all good performance in discriminating death, particularly compared with previous studies.[32] The mCI and MIS had the highest value (0.734), followed by GNRI (0.725), while sPEW had the lowest value, 0.712, but still satisfactory.

Comparing the three models' performance with that of the MIS model using the partial likelihood ratio test (Table 6), mCI is the one that performed most similarly to the MIS (P=0.529), followed by GNRI (p=0.451), and lastly by SPEW (p<0.001).

Overall strengths

This is a large-scale study (n=2322) with a wide range of inclusion criteria, a high number of deaths (n=778), and a long period of follow-up (median 45 months). Therefore, it is expected to reflect the risk for clinical outcomes, and to the better of our knowledge one of the largest in the southern European population.

Overall limitations

Although we rigorously adjusted for baseline confounding factors, known and unknown residual confounding factors might have an impact. Only MIS was assessed at the baseline, the other scores were calculated retrospectively. We

measured mCI, GNRI, and sPEW only once at the baseline, so an eventual misclassification bias cannot be excluded because of changes during the observation period. Other scores could have been added to this analysis, such as BMI, however since the findings in the literature were weak or the data needed to complete them was unavailable, we chose these three scores.

Considering it is a large nationwide cohort, the reproducibility to other populations in other countries can be limited. The endpoint all-cause mortality might not perfectly reflect PEW, and other end-points that have influence, such as quality of life, cause-specific mortality, and hospital admission, should be considered in further studies.

Despite these limitations, we believe the current study will provide a better understanding of the decision-making when choosing the nutrition score.

6. CONCLUSION

All the tools were significantly associated with mortality. The mCI and GNRI are the ones that performed most similarly to the MIS.

Practical application

Nutritional assessment should be frequent, feasible, promptly available, with good intra/interobserver reproducibility, inexpensive, and less time-consuming, to contribute to a more efficient management of the nutritional status. If it is impossible to use MIS, due to his performance in this analysis, mCI or GNRI may stand as a valid option.

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A. FIGURES

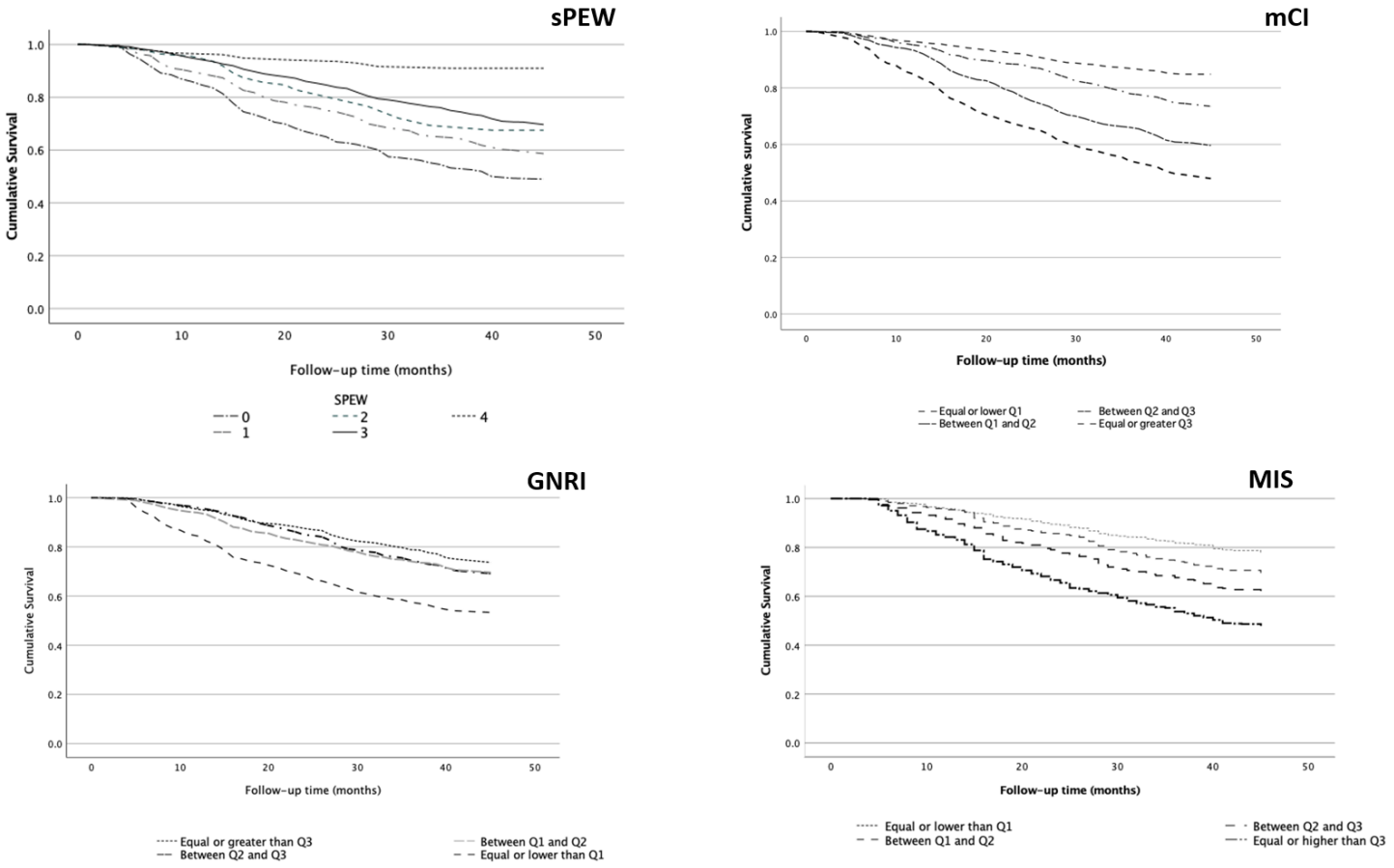

Figure 1. All-cause mortality Kaplan-Meier survival curves estimates considering mCI, GNRI and MIS quartiles, and PEW in five categories.

mCI, modified Creatinine Index; GNRI, geriatric nutritional risk; sPEW, proten-energy wasting score; MIS, malnutrition-inflammations score

mCI quartiles: Q1≤16,8; Q2]16,8-18,3]; Q3]18,3-20[; Q4≥20

GNRI quartiles: Q1≤99,4; Q2]99,4-106,6]; Q3]106,6-114,2[; Q4≥114,2

MIS quartiles: Q1≤4; Q2]4-6]; Q3]6-8[; Q4≥8

B. TABLES

Table 1. Patient´s Demographic, Clinical and Biochemical Parameters by Group (Survived/Deceased)

	Total n=2322	**Survived n=1544**	**Deceased n=778**	**p-value**
Male	1369(59.0%)	899(58.2%)	470(60.4%)	0.312
Diabetes	736(31.7%)	434(28.1%)	302(38.8%)	**<0.001**
MIS≥5	1485(64.0%)	892(57.8%)	593(76.2%)	**<0.001**
MIS≥6	1176(50.6%)	672(43.5%)	504(64.8%)	**<0.001**
Age (years)				
≤ 65	853(36.7%)	696(45.1%)	157(20.2%)	**<0.001**
66-74	586(25.2%)	413(26.7%)	173(22.2%)	
≥75	883(38.0%)	435(28.2%)	448(57.6%)	
Vascular access				
AVF	1862(80.2%)	1286(83.3%)	576(74.0%)	**<0.001**
AVG	266(11.5%)	128(8.3%)	138(17.7%)	
CVC	194(8.4%)	130(8.4%)	64(8.2%)	
Percentiles	**P_{50} (P_{25}-P_{75})**	**P_{50} (P_{25}-P_{75})**	**P_{50} (P_{25}-P_{75})**	
Age (years)	70 (60-79)	67 (56-76)	77 (68-82)	**<0.001***
HD vintage (months)	65 (52-74)	62 (48-71)	70 (61-78)	**<0.001***
Albumin (g/dL)	4.0 (3.8-4.2)	4.0 (3.9-4.2)	3.9 (3.7-4.1)	**<0.001***
nPCR(g/kg/d)	1.1 (0.92-1.3)	1.1 (0.95-1.3)	1.0 (0.84-1.2)	**<0.001***
Calcium (mg/dL) †•	9.3 (8.9-9.6)	9.2 (8.9-9.6)	9.4 (9.1-9.8)	**<0.001***
P (mg/dL)†	4.1 (3.4-4.9)	4.2 (3.6-4.9)	3.9 (3.2-4.7)	**<0.001***
PxCa (mg^2/dL^2)†	38 (32-45)	39 (33-46)	37 (30-44)	**<0.001***
Pcreat (mg/dL)	7.2(5.9-8.7)	7.6 (6.4-9.1)	6.4 (5.4-7.7)	**<0.001***
IDWG(%)†	3.0(2.4-3.7)	3.0 (2.4-3.7)	2.9 (2.3-3.6)	**0.018***
Htc(%)†	34 (32-36)	34 (32-36)	34 (32-36)	0.308*
Kt/V†	1.9 (1.7-2.1)	1.9 (1.7-2.1)	1.9 (1.7-2.1)	0.092*
PTHi (pg/dL)†	359 (233-520)	365 (242-532)	339 (215-495)	**0.013***
URR(%)†	0.8 (0.76-0.83)	0.8 (0.76-0.83)	0.8 (0.76-0.83)	0.203*
BMI (kg/m^2)	25.0(22.0-28.0)	25.1 (22.2-28.5)	24.6 (21.4-27.8)	**0.001***
MIS	6 (4-8)	5 (3-7)	7 (5-10)	**<0.001***
GNRI	106.6 (99.4-114.3)	107.5 (101.1-115)	104.2 (96.4-112.3)	**<0.001***
mCI	18.3 (16.8-20.0)	18.8 (17.4-20.5)	17.3 (16.2-18.7)	**<0.001***
sPEW				
Score 0	306 (13.2%)	150 (9.7%)	156 (20.1%)	**<0.001**
Score 1	380 (16.4%)	223 (14.4%)	157 (20.2)	
Score 2	111 (4.8%)	75 (4.9%)	36 (4.6%)	
Score 3	1369 (59.0%)	954 (61.8%)	415 (53.3%)	
Score 4	156 (6.7%)	142 (9.2%)	14 (1.8%)	

AVF, arteriovenous fistula; AVG, arteriovenous graft; CI, confidence interval; mCI, modified Creatine Index; CVC, central venous catheter; PxCa, phosphocalcium product; GNRI, geriatric nutritional risk index; IDWG, interdialytic weight gain; Htc, hematocrit; MIS, malnutrition-inflammation score; nPCR, normalized protein catabolic rate; P, inorganic phosphorus; Pcreat, serum creatinine; PTHi, parathormone intact; sPEW, protein-energy wasting score; URR, urea removal rate.
*Mann-Whitney test *P*-value; the remaining P-values were obtained by chi-square test.

• Albumin.
† Three months´ average.

Table 2. Multivariable Cox regression model considering mCI score.

	Hazard Ratio Estimate	95% CI		p-values
		Lower limit	Upper Limit	
mCI	0.738	0.675	0.807	**<.001**
Albumin (g/dL)	0.500	0.413	0.605	**<.001**
CCI	1.194	1.158	1.230	**<.001**
URR (%)*	0.125	0.037	0.418	**<.001**
PxCa*	1.075	1.045	1.106	**<.001**
P (mg/dL)	0.489	0.366	0.653	**<.001**
BMI ≤23 (kg/m^2)**	1.357	1.166	1.579	**<.001**
Vascular access***				
AVG	1.105	0.853	1.432	0.449
CVC	1.532	1.268	1.853	**<.001**

AVG, arteriovenous graft; CCI, Charlson comorbidity index; CI, confidence interval; mCI , modified creatinine index; CaxPi, phosphocalcium product; CVC, central venous catheter; URR, urea removal rate.

* Three months average.

** Reference category: BMI >23kg/m^2 (Fouque et al, 2008)

*** Reference category: vascular access by arteriovenous fistula.

Table 3 . Multivariable Cox regression model considering GNRI score.

		95% CI		
	Hazard Ratio Estimate	Lower limit	Upper Limit	p-values
GNRI	0.972	0.965	0.978	**<.001**
Age (years)	1.028	1.020	1.036	**<.001**
CCI	1.184	1.147	1.222	**<.001**
nPCR cat (g/kg/d) *	1.297	1.120	1.501	**<.001**
URR (%)†	0.101	0.030	0.337	**<.001**
Vascular access**				
AVG	1.124	0.868	1.456	0.377
CVC	1.567	1.296	1.893	**<.001**

AVG, arteriovenous graft; CCI, Charlson comorbidity index; CI, confidence interval; CVC, central venous catheter; GNRI, geriatric nutritional risk index; nPCR cat, normalized protein catabolic rate categorized; URR, urea removal rate.

* Reference category nPCR>1.05g/kg/d (Sá Martins et al, 2021)

**Reference category: vascular access by arteriovenous fistula.

† 3 months average

Table 4. Multivariable Cox regression model considering SPEW score.

	Hazard Ratio Estimate	95% CI		p-values
		Lower limit	Upper Limit	
sPEW cat‡	1.373	1.184	1.593	**<.001**
Age (years)	1.034	1.026	1.042	**<.001**
CCI	1.173	1.136	1.211	**<.001**
URR(%)*	0.222	0.059	0.836	**0.026**
IDWG*	1.093	1.024	1.166	**<.001**
Vascular access**				
AVG	1.056	0.854	1.369	0.677
CVC	1.635	1.353	1.976	**<.001**

AVG, arteriovenous graft; CCI, Charlson comorbidity index; CI, confidence interval; Cr Index, creatinine index; CaxPi, phosphocalcium product; CVC, central venous catheter; IDWG, interdialytic weight gain; URR, urea removal rate.
*Three months average
**Reference category: vascular access by arteriovenous fistula.
‡ Reference category: SPEW scores 2, 3 and 4.

Table 5. Multivariable Cox regression model considering MIS.

		95% CI		
	Hazard Ratio Estimate	Lower	Upper	p-value
MIS	1.059	1.039	1.080	**<.001**
Age (years)	1.029	1.021	1.037	**<.001**
Kt/V*	0.862	0.767	0.969	**0.013**
CCI	1.157	1.120	1.195	**<.001**
nPCR (g/kg/d)**	1.205	1.039	1.401	**<.001**
IDWG*	1.094	1.027	1.165	**0.005**
Albumin*	0.550	0.447	0.675	**<.001**
Vascular access***				
AVG	1.119	0.864	1.450	0.394
CVC	1.495	1.237	1.808	**<.001**

AVG, arteriovenous graft; CCI, comorbidity index; CI, confidence interval; CVC, central venous catheter; IDWG, interdialytic weight gain; MIS, malnutrition-inflammation score; nPCR, normalized protein catabolic rate.

* three months average

**Reference category nPCR>1.05g/kg/d (Sá Martins et al, 2021)

***Reference category: vascular access by arteriovenous fistula.

Table 6. Models' performance comparison: non-nested likelihood ratio test.

Nutritional Score	p-value*
MIS vs mCI	**0.529**
MIS vs GNRI	**0.451**
MIS vs sPEW	<.001**

mCI, modified creatinine index; GNRI, geriatric nutritional risk index; sPEW, protein-energy wasting score; MIS, malnutrition-inflammation score.
*p-values regarding the comparison of mCI, GNRI, and sPEW with MIS multivariable models.
** The multivariable model including MIS fits better than the model including sPEW (one-tailed test).

C. SUPPLEMENTARY TABLE

Table S1. Univariable analysis with Cox regression model: time to death.

		95% CI		
	Hazard Ratio Estimate	Lower limit	Upper Limit	p-values
Age (years)	1.053	1.046	1.060	**<.001**
HD vintage (months)	1.033	1.028	1.038	**<.001**
Diabetes	1.489	1.271	1.696	**<.001**
Albumin (g/dL)*	0.301	0.255	0.355	**<.001**
CCI	1.273	1.240	1.307	**<.001**
BMI (kg/m^2)	0.968	0.954	0.983	**<.001**
nPCR (g/kg/d)**	0.751	0.708	0.795	**<.001**
nPCR cat (g/kg/d)***	1.775	1.540	2.047	**<.001**
P (mg/dL)$^{+\bullet}$	0.811	0.759	0.866	**<.001**
P cat (mg/dL)$^+$	1.419	1.233	1.634	**<.001**
PxCa (mg^2/dL^2)$^+$	0.985	0.978	0.991	**<.001**
IDWG (%)$^+$	0.940	0.883	0.999	**0.049**
Kt/V$^{+\bullet\bullet}$	0.896	0.802	1.001	0.052
HTC (%)$^+$	1.009	0.988	1.029	0.409
URR (%)$^+$	0.328	0.094	1.142	0.080
PTHi (pg/mL)$^+$	0.999	0.999	1	0.107
Vascular access				
AVG	1.095	0.856	1.418	0.489
CVC	2.075	1.723	2.499	**<.001**
MIS	1.125	1.107	1.144	**<.001**
mCI	0.543	0.503	0.585	**<.001**
GNRI†	0.969	0.963	0.976	**<.001**
sPEW‡				
Score 1	0.725	0.581	0.905	**0.004**
Score 2	0.533	0.371	0.766	**<.001**
Score 3	0.480	0.399	0.587	**<.001**
Score 4	0.129	0.074	0.222	**<.001**

BMI, body mass index; CCI, Charlson comorbidity index; CI, confidence interval; mCI, modified Creatine Index; CVC, central venous catheter; GNRI, geriatric nutritional risk index; HD vintage, hemodialysis vintage; HTC, hematocrit; IDWG, interdialytic weight gain; MIS, malnutrition-inflammation score; nPCR, normalized protein catabolic; nPCR cat, normalized protein catabolic rate categorized; P, inorganic serum phosphorus; P cat, inorganic serum phosphorus categorized; PxCa, phosphocalcium product; sPEW, protein-energy wasting score; URR, urea removal rate.

* Albumin, three months' average.

** value per each 0.2 units increment.

*** Reference category: nPCR>1.05g/kg/d (Sá Martins et al, 2021)

\+ three months average.

• Reference category: P >4mg/dL (Sá Martins et al, 2021)

•• value per each 0.5 units increment.

† value per each unit increment.

‡ reference category SPEW score=0.

Annexes

Remark: during this study and the several exploratory analysis and preliminary results, two abstracts were prepared and submitted to 2 congresses, one international (Annex 1) and the other national (Annex 2), both accepted to oral and mini-oral communication, respectively.

The current study was submitted to an indexed scientific journal, Clinical Nutrition ESPEN, and it is currently in peer revision (Annex 3).

Annex 1

Abstract:
MALNUTRITION RISK IN HEMODIALYSIS PATIENTS AND SCREENING TOOLS PROGNOSIS: GNRI, CREATININE INDEX AND SPEW.

Oral Communication – 60th ERA Congress – Milan (15-18th June 2023)

Presentation: facsimile

Journal: Nephrology Dialysis Transplantation

Impact Factor: 4.6

Reference: **Aguiar L**, Martins VS, Pinto I, Papoila AL, Dias C, Figueiredo R, Pascoal T, Pereira J, Ramião I, Velez B, Adragao T, Borges N, Almeida E, Garrido J, Macário F, #3846 MALNUTRITION RISK IN HEMODIALYSIS PATIENTS AND SCREENING TOOLS PROGNOSIS: GNRI, CREATININE INDEX AND SPEW, *Nephrology Dialysis Transplantation*, Volume 38, Issue Supplement_1, June 2023, gfad063c_3846, https://doi.org/10.1093/ndt/gfad063c_3846

#3846

MALNUTRITION RISK IN HEMODIALYSIS PATIENTS AND SCREENING TOOLS PROGNOSIS: GNRI, CREATININE INDEX AND SPEW

Leila Aguiar[1,2], Vitor Sá Martins[1,3,4], Iola Pinto[5,6], Ana Luisa Papoila[3,7], Catarina Dias[1], Rita Figueiredo[1], Tania Pascoal[1], Juliana Pereira[1], Inês Ramião[1], Brígida Velez[1], Teresa Adragao[8], Nuno Borges[2,4], Edgar Almeida[1,9,10], Jesus Garrido[1] and Fernando Macário[11]

[1]Diaverum Investimentos e Serviços, Lda., Medical Department, Sintra, Portugal, [2]Faculdade de Ciências da Nutrição e Alimentação da Universidade do Porto| FCNAUP, Porto, Portugal, [3]Nova Medical School, Lisboa, Portugal, [4]CINTESIS - Centro de Investigação em Tecnologias e Serviços de Saúde, Faculty of Medicine, University of Porto, Cintesis@RISE, MEDCIDS, Porto, Portugal, [5]NOVA School of Science and Technology, CMA, Caparica, Portugal, [6]Instituto Superior de Engenharia de Lisboa, ISEL, Lisboa, Portugal, [7]Centro de Estatística e Aplicações da Universidade de Lisboa, CEAUL, Portugal, [8]Hospital Santa Cruz, Serviço de Nefrologia, Carnaxide, Portugal, [9]Hospital Beatriz Ângelo, Serviço de Nefrologia, Loures, Portugal, [10]Faculty of Medicine, University of Lisbon, Centro de Cardiologia, Lisboa, Portugal and [11]Diaverum Corporate, Medical Department, Sweden

Background and Aims: nutritional status clearly has a great impact on the prognosis of maintenance hemodialysis patients. Therefore, its management should be a priority and risk screening frequent and easily implemented, based on the biochemical and clinical routine parameters already available. Many tools fit these simple criteria, namely simple Protein Energy Wasting score (sPEW), Geriatric Nutritional Risk Index (GNRI) and Creatinine Index (Cr Index). These scores are associated with a high mortality and morbidity risk in hemodialysis (HD) patients. The objective of this study was to assess the performance of these tools regarding the estimation of all-cause mortality, in a 45-months follow-up of a large patient cohort.

Method: Historical cohort study of HD pts from 25 outpatient clinics. sPEW, GNRI and Cr Index were estimated. Kaplan-Meier estimator and univariable Cox regression models to analyze time until death were used. To compare survival curves the log-rank test or Tarone test were used, as appropriate. The level of significance $\alpha = .05$ was considered. All data were analyzed using SPSS 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows. Armonk, NY, USA: IBM Corp).

Results: We analyzed 2322 pts, 59% males, 31.7% diabetic, with a median age of 70 years ($P_{25} = 60$, $P_{75} = 79$) followed up for a maximum of 45-month ($P_{25} = 31$; $P_{75} = 45$). All-cause mortality was observed in 778 pts (33.5%). To assess the mortality risk, the exposures GNRI and CR Index, were discretized using quartiles.

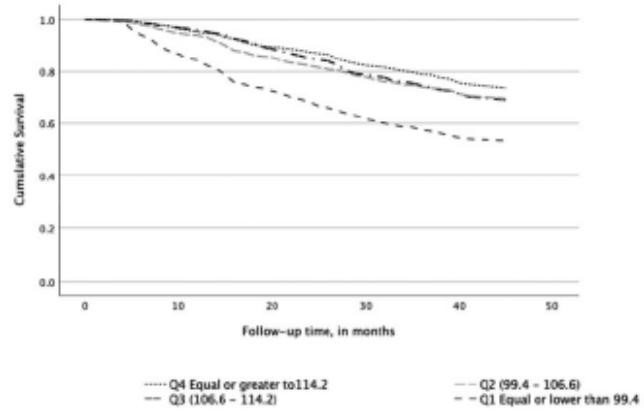

Figure 1: Kaplan-Meier survival curves for all-cause mortality estimated by quartiles of GNRI.

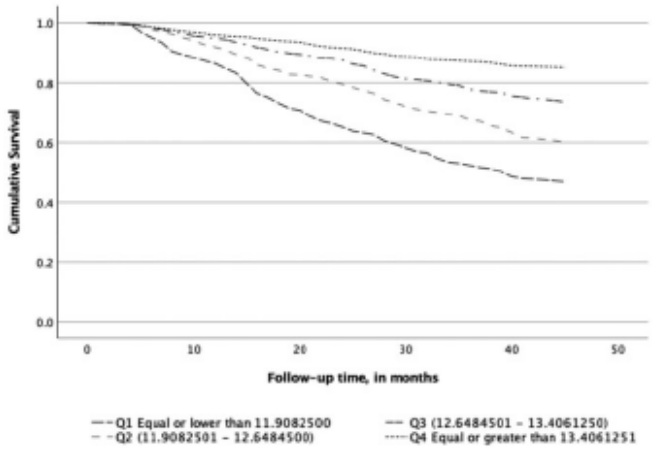

Figure 2: Kaplan-Meier survival curves for all-cause mortality estimated by quartiles of CR Index.

GNRI

The median was 106.6 (P_{25} = 99.4, P_{75} = 114.2). The log-rank test results showed a significantly lower survival for patients in GNRI Q1 category (GNRI ≤ 99.4). A p-value <0.001 was obtained when comparing patients in Q4, Q3 and Q2 with patients in Q1. The univariable Cox regression model showed that patients in Q1 had a 2-fold increased risk of death, when compared with Q4 (HR = 2.1, 95% CI: 1.7-2.6, p<0.001).

Creatinine Index

The median was 12.648 (P_{25} = 11.908, P_{75} = 13.406). The log-rank test for the equality of survival functions for the different levels was considered statistically significant and showed a significantly lower survival for patients in CR Index Q1 category, when compared with the remaining categories (p<0.001). The univariable Cox regression model showed that comparatively with Q4, patients in Q1 had a 5-fold increased risk of death (HR = 4.8, 95% CI: 3.7-6.0, p<0.001), patients in Q2 a 3-fold increased risk of death (HR = 3.1, 95% CI:2.4– 3.9, p<0.001), and patients in Q3 a 2-fold increased risk of death (HR = 1.9, 95% CI: 1.4 – 2.4, p<0.001).

sPEW

The frequency of each score from 0 to 4 was 306, 380, 111, 1369 and 156, respectively. The log-rank test for the equality of survival functions corresponding to the different levels showed a significantly higher survival for patients with a sPEW score of 4 when comparing with the remaining levels (p<0.001). The univariable Cox regression model showed that comparatively with a score of 4, patients with a: score of 0 had an 8-fold increased risk of death (HR = 7.7, 95% CI: 4.5-13.3, p<0.001), score of 1 a 6-fold increase risk of death (HR = 5.6, 95% CI: 3.3– 9.7, p<0.001), score of 2 a 4-fold increase risk of death (HR = 4.1, 95% CI: 2.2– 7.7, p<0.001), and a score of 3, almost a 4-fold increased risk of death (HR = 3.7, 95% CI: 2.2– 6.3, p<0.001).

Conclusion: In this exploratory analysis, the three tools showed a significant association with mortality during follow-up. These tools, if adequately validated in future studies, may select patients for further intervention to modify the outcome.

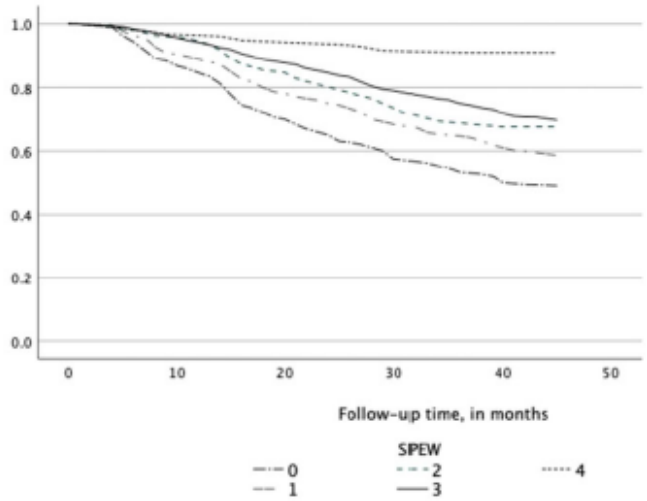

Figure 3: Kaplan-Meier survival curves for all-cause mortality estimated by all categories of sPEW score.

Annex 2

Abstract title:
#92 – MO-SEX-012 A SIMPLE NUTRITIONAL RISK SCREENING TOOL: HOW DOES GERIATRIC NUTRITIONAL RISK INDEX PERFORMS IN A LARGE MAINTENANCE HEMODIALYSIS COHORT?

Authors:
Aguiar L, Martins VS, Pinto I, Papoila AL, Dias C, Figueiredo R, Pascoal T, Pereira J, Ramião I, Velez B, Adragao T, Borges N, Almeida E, Garrido J, Macário F.

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Abstract Nº 98

A SIMPLE NUTRITIONAL RISK SCREENING TOOL: HOW DOES GERIATRIC NUTRITIONAL RISK INDEX PERFORMS IN A LARGE MAINTENANCE HEMODIALYSIS COHORT?

Leila Aguiar (1); Vitor Martins (1); Iola Pinto (6); Ana Luisa Papoila (3); Catarina Dias (1); Rita Figueiredo (1); Juliana Pereira (1); Inês Ramião (1); Brigida Velez (1); Teresa Adragão (5); Nuno Borges (2); Edgar Almeida (1); Jesus Garrido (1); Fernando Macário (1);

(1) - Diaverum Portugal, Departamento Médico, Sintra, Portugal;
(2) - Universidade do Porto, Faculdade de Ciências da Nutrição e Alimentação, Porto, Portugal;
(3) - Universidade Nova de Lisboa, Faculdade de Ciências Médicas, Lisboa, Portugal;
(4) - Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, CMA, Lisboa, Portugal;
(5) - Hospital de Santa Cruz, Serviço de Nefrologia, Carnaxide, Portugal;
(6) - Universidade Nova de Lisboa, Nova Math, FCT, Lisboa, Portugal;

Background and Aims: nutritional status management and nutritional risk screening should be a pivotal part of maintenance hemodialysis (HD) treatment. However, some limitations can be referred such as lack of dedicated human resources and available information, for a routine management and screening. The Geriatric Nutritional Risk Index (GNRI) is a simple screening tool to predict the risk of nutrition-related morbidity and mortality in elderly patients, namely in maintenance hemodialysis patients (Yamada et al, 2020), and it can be frequently and easily implemented based on the biochemical and clinical routine parameters already available.
The objective of this study was to assess performance of GNRI in predicting all-cause mortality in a large cohort of patients.

Methods: Historical cohort study of HD patients from 25 outpatient clinics with GNRI calculated retrospectively. GNRI is based on serum albumin levels, current body weight, and ideal body weight. Cox regression models were applied to analyze time until death. The proportional hazards assumption was checked using scaled Schoenfeld residuals. Because this assumption was violated for GNRI, a model with time varying coefficients was fitted to the data. The level of significance alfa=0.05 was considered.

Results: We analyzed 2322 pts, 59% males, 31.7% diabetic, with a median age of 70 years (P25=60, P75=79), followed up for a maximum of 45 months (P25=31; P75=45). The median of GNRI was 106.6 (P25=99.4, P75=114.2). All-cause mortality was observed in 778 patients (33.5%).
Multivariable Cox regression analysis results (Table 1) showed that older patients, lower nPCR values (<=1.05g/kg/d), and a higher Charlson comorbidity index were risk factors regarding death. At the contrary, higher values of three months average of urea removal rate were protective. Both arteriovenous graft and central venous catheter accesses had a higher risk of death when comparing with fistula, although only the latter attained statistical significance (p<0.001). Regarding GNRI, the protection that characterizes this variable decreased with time with a lack of statistical significance in the last period (p=0.216).

Table 1. Multivariable Cox regression analysis results.

		95% CI	95% CI	
	Hazard Ratio Estimate	Lower limit	Upper Limit	p-value
Age (years)	1.028	1.020	1.036	<.001
nPCR cat (g/kg/d)*	1.287	1.112	1.489	<.001
URR 3M (%) **	0.109	0.033	0.362	<.001
CCI	1.180	1.143	1.218	<.001
Vascular Access				
AVG	1.107	0.854	1.434	0.443
CVC	1.539	1.273	1.861	<.001
GNRI***				
P1 (0-16 months)	0.954	0.945	0.964	<.001
P2 (16-30 months)	0.979	0.979	0.989	<.001
P3 (>30 months)	0.992	0.979	1.005	0.216

AVG, arteriovenous graft; CCI, Charlson comorbidity index; CI, confidence interval; CVC, central venous catheter; GNRI, geriatric nutritional risk index; nPCR cat, normalized protein catabolic rate categorized; URR, urea removal rate.
* reference category nPCR>1.05g/kg/d (Sá Martins et al, 2021)
** 3 months average
***continuous GNRI analysed in 0-16 ; 16-30, and > 30 months time intervals

Regarding the discriminative ability of the final multivariable survival model, the C-index was 0.73 (95%CI: 0.71, 0.75).

Conclusions: In this analysis, GNRI is significantly associated with mortality until 30 months of follow up.

Annex 3

Manuscript title:

NUTRITIONAL RISK ASSESSMENT IN HEMODIALYSIS PATIENTS: A COMPARATIVE ANALYSIS OF MODIFIED CREATININE INDEX, GERIATRIC NUTRITIONAL RISK INDEX AND SIMPLE PROTEIN-ENERGY WASTING WITH MALNUTRITION-INFLAMMATION SCORE.

Authors:
Aguiar L, Martins VS, Pinto I, Papoila AL, Dias C, Figueiredo R, Pascoal T, Pereira J, Ramião I, Velez B, Adragao T, Borges N, Almeida E, Garrido J, Macário F.

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Nutritional Risk Assessment in Hemodialysis Patients: A Comparative Analysis of the Modified Creatinine Index, Geriatric Nutritional Index and simple Protein-Energy Wasting Score with Malnutrition-Inflammation Score

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Corresponding Author:	Leila Oliveira Aguiar, RD Diaverum Portugal Sintra, PORTUGAL
First Author:	Leila Oliveira Aguiar, RD
Order of Authors:	Leila Oliveira Aguiar, RD
	Vítor Sá Martins, PhD
	Iola Pinto, PhD
	Ana Luisa Papoila, PhD
	Catarina Dias, RD
	Rita Figueiredo, RD
	Juliana Pereira, RD
	Ines Ramião, RD
	Brigida Velez, RD
	Teresa Adragão, PhD
	Nuno Borges, PhD
	Edgar Almeida, PhD
	Jesus Garrido, MD
	Fernando Macário, MD
Abstract:	Background and Aims: nutritional status has a great impact on the prognosis of maintenance hemodialysis patients. Therefore, its management should be a priority, and risk screening frequent and easily implemented, based on the biochemical and clinical routine parameters already available, when the use of more comprehensive tools is not possible. Many tools fit these simple criteria, namely the modified creatinine index, geriatric nutritional risk index, and simple protein energy wasting score. These scores are associated with mortality and morbidity risk in hemodialysis patients. This study aims to confirm that these scores are significantly associated with all-cause mortality, and to compare them with malnutrition inflammation score. Methods: Historical cohort study of hemodialysis patients from 25 outpatient clinics. The nutritional and inflammation status was assessed at baseline with malnutrition-inflammation score, geriatric nutritional risk index, modified creatinine index, and simple protein-energy wasting score. Univariable and multivariable Cox additive regression models were used to analyse data. Partial likelihood ratio tests to compare the performance of non-nested Cox models were used. Results: We analysed 2322 patients, 59% males, 31.7% diabetic, with a median age of 70 years (P25=60, P75=79), during a median follow-up period of 45 months (P25=31; P75=45). All-cause mortality was observed in 778 patients (33.5%). The median of modified creatinine index was 12.6 mg/kg/day (P25=11.9, P75=13.4), and higher index value was observed for the surviving patients (p<0.001). Multivariable analysis results showed that higher phosphocalcium produt, Charlson comorbidity index, lower modified creatinine index, albumin, phosphate, body mass index and urea

	removal rate were significantly associated with the risk of death. Regarding geriatric nutritional risk score, a median of 106.6 (P25=99.4, P75=114.2) was observed, being significantly higher in the survival group (p<0.001). In the multivariable analysis results, higher age and Charlson comorbidity index, lower geriatric nutritional risk index, normalized protein catabolic rate, and urea removal rate were significantly associated with the risk of death. Simple protein-energy wasting score lower scores were more frequent in the group of deceased patients (p<0.001). In the multivariable analysis results, higher age, Charlson cormorbidity, and interdialytic weight gain, lower simple protein-energy wasting score and urea removal rate, were significantly associated with the risk of death. For malnutrition-inflammation score, the median was 6 (P25=4, P75=8), 50.6% of the patients had a score ≥6, with higher scores being more frequent in the group of deceased (p<0.001). In the multivariable analysis results, higher malnutrition-inflammation score, age, Charlson comorbidity index, interdialytic weight gain, and lower kt/V, normalized protein catabolic rate, and albumin, were significantly associated with the risk of death. In the three models, central venous catheter had a significantly higher risk of death when compared with fistula. Partial likelihood ratio tests showed that malnutrition-inflammation score only fitted better than the model including simple protein-energy wasting score. All scores had a good discriminative performance with Harrell's C-statistic ranging from 0.71-0.74. Malnutrition-inflammation score and modified creatinine index models attained the highest values. Conclusion: All the tools were significantly associated with mortality. The modified creatinine index and geriatric nutritional risk index were the scores that performed most similarly to the malnutrition-inflammation score.
Opposed Reviewers: