


# Factors associated with nutritional risk in patients receiving haemodialysis assessed by Nutritional Risk Screening 2002 (NRS2002)

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## Abstract

**Background:** Nutritional Risk Screening 2002 is recommended as a screening tool to identify patients at risk of undernutrition for all patients in hospitals by the European Society of Clinical Nutrition and Metabolism. Nutritional risk is associated with increased morbidity and mortality in patients, and it is common among patients on haemodialysis. Factors associated with nutritional risk that could facilitate the screening/diagnostic procedures are warranted.

**Objectives:** Identification of factors that are associated with nutritional risk in patients with end-stage renal disease treated with haemodialysis.

**Design and Participants:** Single-centre, cross-sectional study in patients receiving haemodialysis ( $n = 53$ ) were screened for nutritional risk using Nutritional Risk Screening 2002. Associations were made with data on dietary intake by 24-h dietary recall, and measurement of body composition, anthropometric measurements and biochemical variables.

**Results:** Nutritional risk was common among patients on haemodialysis (26%), and was associated with low energy and protein intake, and low pre-albumin concentrations also after adjustments for age and sex. Nutritional risk was neither associated with diabetes nor duration of dialysis treatment.

**Conclusion:** Measurement of pre-albumin and dietary assessment using a 24-h dietary recall can support the identification of patients receiving haemodialysis at nutritional risk.

## KEYWORDS

chronic kidney failure, cross-sectional studies, nutrition risk screening

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## INTRODUCTION

Chronic kidney disease affects about 11%–13% of the total population (Hill et al., 2016) and can eventually progress to kidney failure requiring replacement therapy which affects about 5256 patients in Norway (The Norwegian Renal Registry, 2018). Of these, about 1572 are treated with haemodialysis (HD). Kidney failure is associated with profound changes in nutrient metabolism and high rates of protein-energy wasting and other nutritional disturbances (Carrero et al., 2018; Fouque et al., 2008).

## LITERATURE REVIEW

One method to identify patients who are undernourished or at risk of becoming undernourished is the use of a screening tool for this purpose, such as Malnutrition Universal Screening Tool (MUST), Mini Nutritional Assessment (MNA) and Nutritional Risk Screening 2002 (NRS2002) (Cederholm et al., 2017). NRS2002 is recommended to be used in hospitals by the European Society of Clinical Nutrition and Metabolism (Cederholm et al., 2017; Kondrup et al., 2003). The aim of NRS2002 is 'to predict the probability of a better or worse outcome due to nutritional factors, and whether nutritional treatment is likely to influence this' (Kondrup et al., 2003). NRS2002 uses factors such as weight loss, reduced food intake and low body mass index (BMI), disease severity and age for the identification of nutritional risk. In Norway, all patients admitted to hospitals are scheduled to undergo nutritional risk screening (Guttormsen, 2009). About 30% of all hospitalised patients are at nutritional risk (Tangvik et al., 2015), which is associated with increased risk of mortality and morbidity, reduced quality of life, disability and prolonged hospital stay (Tangvik et al., 2014). Of note, it is important to distinguish nutritional risk screening from nutritional assessment. Nutritional assessment should be performed in all patients identified as being at risk by nutritional risk screening (Cederholm et al., 2017). Assessment of nutritional status is a more complex procedure, and should include, among others, information on anthropometry, body composition, biochemical markers, dietary intake and requirements. Predefined assessment tools exist, such as Subjective Global Assessment (SGA) (Jeejeebhoy et al., 2015).

Within the NRS2002 screening procedures, especially the identification of reduced food intake is difficult in clinical practice, as patients do not recognise their food intake or do not remember this and health personal often lack time or competence to judge whether food intake is sufficient or not (Eide et al., 2015). One option for estimating food intake in patients is a 24-h dietary recall, which can give, if done according to standardised procedures (Blanton et al., 2006) and ideally repeated several times (Nutrition Research Council, 1981), sufficient information on dietary intake of patients (Bingham et al., 1994).

In addition to weight and height, other measures of anthropometry and body composition can give additional information about the nutritional status. Among these, waist circumference, mid-upper arm circumference (MUAC) and body composition have been proven

useful in the assessment of nutritional status, with waist circumference closely related to overweight and obesity and associated risks, and MUAC related to both under- and overnutrition (Pischon et al., 2008; Rodrigues et al., 2017; Schaap et al., 2018).

Also, biochemical markers, mostly albumin and pre-albumin concentrations, have been used to characterise nutritional status in patients receiving HD. Albumin concentrations have been shown to be associated to nutritional status in some studies (Tan et al., 2016), but not in all (Yang et al., 2020), and low albumin concentrations are related to increased mortality in this patient group (Dierkes et al., 2000). Albumin is, however, strongly influenced by inflammation which limits the use to measure nutritional status (Pifer et al., 2002; Takata et al., 2010). In contrast to albumin, pre-albumin is not routinely measured in many hospitals, but may work as a nutritional marker in patients receiving HD (Chertow et al., 2000, 2005; Rambod et al., 2008), although it is also affected by inflammation. It has, however, not been linked to nutritional risk in these patients.

As it is known that nutritional risk is a problem in patients receiving HD, the aim of the study was to identify factors that are associated with nutritional risk and that may facilitate the identification and thus treatment of nutritional risk.

## PATIENTS AND METHODS

This is a cross-sectional study in patients with kidney failure treated with HD at Haukeland University Hospital, Bergen, Norway. Patients were eligible if clinically stable with HD for at least 3 months, aged older than 18 years and capable of understanding Norwegian or English. Patients were excluded if they had an expected living time of <6 months.

All patients were screened by NRS2002. The initial screening consists of four questions, and if one is answered with yes, the procedure is continued to the main screening which consists of a point scoring system regarding the nutrition status and severity of the disease. These are separately graded with a score from 0 to 3. Patients get an additional age point if older than 70 years (Kondrup et al., 2003). A patient is at nutritional risk if the total score is >3 points.

Food intake was estimated by a single 24-h dietary recall conducted by a trained interviewer using the multiple pass method (Blanton et al., 2006). Other data collected than food and drink consumption were food preparations methods, brand names and ingredients used in mixed meals. Data were analysed using the online tool *Kostholdsplanleggeren.no* which is based on the Norwegian food composition tables. Low energy intake was defined as  $\leq 25$  kcal/kg body weight and low protein intake as  $\leq 0.80$  g/kg body weight (Fouque et al., 2008). For these calculations, measured body weight after dialysis was used with no further adjustments.

Anthropometric measurements included weight and height, waist circumference and MUAC. For these measurements, a portable weight (Seca 877) and stadiometer (Seca model 217) was used and a nonelastic, flexible tape (SECA), using standard procedures. From weight and height, BMI was calculated.

For the biochemical measurements, one blood sample per patient was taken before dialysis and usually after the weekend. Albumin, C-reactive protein (CRP), haemoglobin and lipids were measured at the Central Laboratory at Haukeland University Hospital using standard automated methods (details provided at [www.analyseoversikten.no](http://www.analyseoversikten.no)). Pre-albumin was measured using a nephelometric method (BN-II method; Siemens Healthineers Global). Dialysis quality was expressed as  $Kt/V$ , information on residual function and comorbidities (diabetes mellitus, hypertension) were derived from the electronic patients' records.

For all data analyses conducted, IBM SPSS Statistics Software version 25 (IBM Corp., released 2017, IBM SPSS Statistics for Windows; IBM Corp.) was used. A comparison between those at nutritional risk and those not at nutritional risk was made by Wilcoxon tests or  $\chi^2$  tests, followed by logistic regression analyses with NR/no-NR as a binary outcome for those variables that had  $p < 0.10$  in the Wilcoxon's test. Age and sex were always included in the logistic regression. Prealbumin was additionally adjusted for CRP. To receive meaningful estimates from the logistic regression analysis, the unit for energy intake was transformed to 100 kcal instead of 1 kcal, and the unit for pre-albumin was transformed to g/dL instead of g/L.

The study has been approved by the regional ethics committee for the Health Trust of Western Norway. All patients received oral and written information about the study and gave their written informed consent.

## RESULTS

This analysis includes 53 patients out of our total population of 101 potentially eligible patients on HD, 74% men ( $n = 39$ ) and 26% women ( $n = 14$ ), with an average age of 62 years. The average time on dialysis was 691 days (1.89 years). Diabetic or hypertensive nephropathy was the most common cause of kidney disease (42%), and both diabetes and hypertension were common comorbidities (40% and 83%, respectively).

Energy intake was 1363 kcal/day in women and 1709 kcal/day in men, and protein intake was 54 and 68 g/day, respectively. Low energy intake ( $<25$  kcal/kg BW) was observed in 58% of patients and low protein intake ( $<0.8$  g/kg BW) was observed in 30% of patients, and 56% had lower intake than 1.0 g/kg BW. Protein and energy intake were strongly correlated ( $r = 0.83$ ;  $p < 0.001$ ). The average concentration of C-reactive protein (CRP) was  $<5$  mg/L, however, 10 patients had CRP levels exceeding 15 mg/L. Median albumin concentration was 41 g/L and median prealbumin was 0.34 g/L. Other data from the anthropometric, biochemical, clinical and dietary assessment are provided in Table 1.

Nutritional risk using NRS2002 was recognised in 14 patients (10 men and 4 women,  $p < 0.05$ ). Patients with nutritional risk were older, had lower energy and protein intake and lower pre-albumin values (Table 2).

The logistic regression analysis showed an association of energy intake, protein intake and pre-albumin with nutritional risk, after controlling for sex and age (Table 3). The RR for pre-albumin was 0.33 (95% confidence interval, 0.14–0.80) per g/dl increase of pre-albumin and was

substantially attenuated to 0.90 after further adjustment for CRP (Table 3).

## DISCUSSION

This cross-sectional study shows that nutritional risk is common among patients with kidney failure receiving HD. This is alarming as nutritional risk is associated with increased morbidity and mortality. Indeed, clinical nutrition screening scores, among them NRS2002, predicted all-cause mortality better than biochemical variables (Dai et al., 2017; Fiedler et al., 2009). Several other studies have found similar or even higher rates of nutritional risk in this patient group, either by using NRS2002 (Tan et al., 2016), or other assessment tools like SGA or malnutrition inflammation score (MIS) (Fiedler, 2009; Dai, 2017), thus supporting our findings. However, despite these high rates, there is a lack of standard nutritional counselling and nutritional treatment in patients with kidney disease in many countries (Sabbatini et al., 2019).

In the present study, we measured several anthropometric and biochemical variables that have been associated with nutritional risk in previous studies. In addition, we measured dietary intake by a standardised 24-h dietary recall. After adjusting for age and sex, only energy and protein intake and pre-albumin concentrations were significantly associated with nutritional risk.

The screening for nutritional risk is nowadays routinely done in many hospitals, however, several challenges remain, including the assessment of food intake. Food intake is difficult to measure in an objective way, and ideally the assessment covers several days, including dialysis and non-dialysis days (Stark et al., 2011). Due to the limited availability of dietitians in hospitals, data on food intake are often estimated in non-standardised ways and thus of low quality (Mowe et al., 2008; Phillips, 2015; Thoresen et al., 2008). Ideally, food intake is measured by frequent standardised 24-h dietary recalls, which could also identify changes in dietary intake over time (Ikizler, 2020).

In the present study, patients at nutritional risk had indeed low energy and protein intake, which was, independently from age and sex, associated with nutritional risk. An increase in energy intake of 100 kcal/day was associated with a 12% lower risk for nutritional risk. This amount is, for example, equivalent to one slice of whole-grain bread or a glass of milk. This result shows that it is important to monitor the energy intake in patients receiving HD and encourage sufficient energy intake. This is also important in light that there is a strong correlation between energy and protein intake, thus it will be likely that those who are not meeting their energy intakes will also have low protein intakes. This will lead to a catabolic situation with the loss of muscle mass and fat mass, and eventually lead to sarcopenia or protein-energy wasting (Hara et al., 2018; Moorthi & Avin, 2017). Indeed, low protein intake was associated with a higher risk of nutritional risk. In general, patients on HD have difficulties meeting their protein requirement, due to lack of appetite, or dietary restrictions especially on phosphorus (Bossola et al., 2005; Ikizler et al., 2020; Stark et al., 2011). Additionally, patients receiving HD frequently have restrictions on potassium, sodium and fluids, which

**TABLE 1** Characteristics of the study population

	Total (n = 53)	Female (n = 14)	Male (n = 39)
<b>General characteristics</b>			
Age, years	62 (48–75)	60 (49–75)	62 (47–77)
Time on dialysis, days	691 (431–1389)	452 (320–1123)	828 (492–1537)
BMI, kg/m <sup>2</sup>	24 (20–27)	22 (21–28)	25 (21–27)
<b>Clinical data</b>			
Kt/V <sup>a</sup>	1.20 (0.92, 1.50)	1.70 (0.95, 1.90)	1.2 (0.90, 1.40)
Diabetes mellitus	21 (40%)	6 (43%)	15 (39%)
Hypertension	44 (83%)	12 (86%)	32 (82%)
<b>Cause of CKD</b>			
–Diabetes or hypertension	22 (42%)	6 (43%)	16 (41%)
–Glomerular disease	6 (11%)	2 (14%)	4 (10%)
–Polycystic kidney disease	5 (9%)	1 (7%)	4 (10%)
–Neoplastic disease	4 (8%)	1 (7%)	3 (8%)
–Other defined causes	10 (19%)	3 (21%)	7 (18%)
–Unknown	6 (11%)	1 (7%)	5 (13%)
<b>Anthropometric data</b>			
Weight, kg <sup>a</sup>	69.8 (61.4–79.7)	64.5 (53.8–70.0)	72.8 (63.2–81.7)
Height, m	1.71 (1.64–1.77)	1.60 (1.56–1.66)	1.73 (1.69–1.80)
MUAC, cm	29.0 (26.2–31.8)	27.0 (25.1–32.1)	29.0 (26.3–31.7)
WC, cm	94.5 (83.8–102.3)	84.7 (79.4–98.6)	95.0 (86.5–104.3)
<b>Biochemical data</b>			
Haemoglobin, g/dl	11.1 (10.3–12.1)	10.1 (9.9–11.9)	11.2 (10.4–12.2)
Pre-albumin, g/L	0.340 (0.280–0.400)	0.375 (0.315–0.423)	0.330 (0.260–0.400)
Albumin, g/L	41 (38–43)	40 (38–43)	41 (39–43)
CRP, mg/L	3 (1–9)	3 (0–14)	3 (1–9)
Total cholesterol, mmol/L	3.4 (2.7–4.3)	3.9 (2.7–4.5)	3.2 (2.7–4.1)
<b>Dietary intake</b>			
Energy, kcal	1594 (1154–1956)	1363 (973–1582)	1709 (1315–2462)
Energy, kcal/kg BW	22 (17–29)	21 (15–28)	24 (17–30)
Protein, g/day	66 (47–84)	54 (40–75)	68 (54–94)
Protein, g/kg BW	0.93 (0.72–1.24)	0.95 (0.35–1.24)	0.93 (0.74–1.26)
Protein, E%	16 (14–19)	17 (15–19)	16 (14–19)
Fat, g	67 (41–86)	55 (31–67)	71 (50–90)
Fat, E%	38 (30–43)	37 (27–42)	38 (30–44)
Carbohydrate, g	187 (134–254)	145 (126–175)	201 (148–262)
Carbohydrate, E%	48 (41–53)	47 (38–57)	48 (41–52)
Fibre, g	14 (10–21)	13 (10–14)	16 (9–24)

Note: Continuous data are given as median with interquartile range in parentheses, and frequencies are provided as *n* and % in parentheses.

Abbreviations: CRP, C-reactive protein; E%, energy percent; kg BW, kilogram per body weight; MUAC, mid-upper arm circumference; WC, waist circumference.

<sup>a</sup>Weight is given as weight after dialysis. Measurements of two patients were missing for pre-albumin. Measurements of three patients were missing for energy and protein intake. Kt/V information was available in 36 patients.

**TABLE 2** Biochemical and anthropometric measurements and dietary intake in dialysis patients with and without NR

	NR, Yes	NR, No	p value
Female/male	4/10	10/29	<b>0.046</b>
Age, years	58 (46, 80)	62 (49, 75)	0.739
Time on dialysis	603 (389, 1655)	828 (461, 1325)	0.716
Diabetes, %	6/14 (43%)	15/39 (38%)	0.773
Weight, kg	68.6 (54.8, 80.2)	70.1 (62.8, 80.2)	0.215
BMI, kg/m <sup>2</sup>	23 (20, 28)	24 (22, 27)	0.572
MUAC, cm	27.0 (24.8, 30.4)	29.0 (26.3, 32.0)	0.140
WC, cm	92.5 (77.2, 108.9)	94.5 (85.0, 101.3)	0.716
Energy, kcal	1186 (898, 1747)	1623 (1378, 2433)	<b>0.045</b>
Energy, kcal/kg BW	18 (14, 29)	24 (19, 30)	0.083
Protein, g/day	52.4 (35.9, 69.3)	68.4 (54.1, 92.5)	<b>0.043</b>
Protein, g/kg BW	0.74 (0.57, 1.14)	0.99 (0.81, 1.26)	0.075
Protein, E%	15 (13, 20)	16 (14, 19)	0.368
Albumin, g/L	39.5 (36.5, 43)	42.0 (39.0, 43.0)	0.123
Pre-albumin, g/dl	0.310 (0.220, 0.330)	0.385 (0.307, 0.403)	<b>0.013</b>
Haemoglobin, g/dl	10.7 (10.2, 11.2)	11.2 (10.3, 12.5)	0.332
CRP, mg/L	3 (0, 21)	3 (1, 7)	0.976

Note: Data are presented as median and IQR. Nutritional risk was diagnosed according to NRS2002. Bold values statistically significant at  $p < 0.05$ . Abbreviations: CRP, C-reactive protein; E%, energy percent; IQR, interquartile range; kg BW, kilogram per body weight; MUAC, mid-upper arm circumference; NR, nutritional risk; NRS2002, Nutritional Risk Screening 2002; PAL, physical activity level; WC, waist circumference.

makes it even more challenging to meet the dietary recommendations and demonstrate the importance of dietary counselling.

The majority of the patients in our cohort had low concentrations of CRP, indicating limited inflammation. This is a prerequisite that serum albumin and pre-albumin concentrations, which are negative acute phase reactants, can be used for the diagnosis of

**TABLE 3** Logistic regression for risk factors for NRS risk, controlled for age and sex

	RR	95% CI
MUAC, cm	0.88	0.74–1.05
Energy, 100 kcal	0.88	0.78–0.99
Energy, kcal/kg BW	0.94	0.86–1.02
Protein, g/day	0.97	0.94–1.00
Protein, g/kg BW	0.20	0.03–1.28
Protein, E%	0.92	0.78–1.09
Pre-albumin, g/dl <sup>a</sup>	0.90	0.82–0.98

Note: PAL calculated by dividing energy intake with resting metabolic rate.

Abbreviations: CI, confidence interval; CRP, C-reactive protein; E %, energy percent; kg BW, per kilogram body weight; NRS, nutritional risk screening; PAL, physical activity level; RR, relative risk.

<sup>a</sup>Adjusted for age, sex and CRP.

malnutrition (Dellièrè & Cynober, 2017). While albumin was not associated to nutritional risk, pre-albumin was significantly associated to nutritional risk, and each increase of 0.1 g/L (1 g/dl) was associated to a 10% reduction of nutritional risk, after adjustment for CRP. This is even more remarkable as almost no patient had very low pre-albumin concentrations (<0.1 g/L). Pre-albumin has been suggested by several authors as a marker for nutritional risk, assuming that the serum concentrations are responsive to dietary intake below the requirements (Devoto et al., 2006; Zhang et al., 2017). Pre-albumin was also a predictor of mortality and hospitalisation in a prospective study with patients receiving HD and follow up for 3 years (Fiedler, 2009). Thus, the results support including pre-albumin measurements into the routine biochemical assessment of patients on HD, to ease the identification of nutritional risk.

Our study has several strengths and limitations. First, this is a cross-sectional study without patient follow-up. Thus, we can only speculate on the impact of nutritional risk for further prognosis. It should be also mentioned that due to the limited sample size, the study should be regarded as a pilot study that should be confirmed in larger studies. Also, the dietary assessment was limited to a single 24-h dietary recall. Ideally, either a dietary record for several days, including dialysis and non-dialysis days (Burrowes et al., 2003), or multiple 24-h dietary recalls should be used for dietary assessment to increase the reliability and validity of the data. Among the



strengths of the study, it is worth mentioning the standardised and comprehensive assessment of nutritional status, nutritional risk and biochemical measurements.

## IMPLICATIONS FOR CLINICAL PRACTICE

Nutritional risk was a common finding in patients receiving HD and was observed in one of four patients. Nutritional risk screening should use a validated screening tool such as NRS2002, and should be repeated weekly, or at least monthly (Guttormsen, 2009). Patients at nutritional risk should receive a more thorough nutritional assessment and a nutritional treatment plan.

Our study showed that both assessment of energy and protein intake and measurement of pre-albumin are useful additions to the nutritional risk screening. Therefore, regular nutritional risk screening, followed by assessment of energy and protein intake and measurement of pre-albumin, is recommended in patients receiving HD.

## CONCLUSION

In conclusion, a dietary assessment by a single 24-h dietary recall can identify patients at nutritional risk who may benefit from nutritional therapy. Dietary intake was overall insufficient in this population, and more attention should be paid to dietary counselling and treatment. Pre-albumin was strongly associated with nutritional risk in this cohort and should be included in the routine biochemical assessment.

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## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

## AUTHOR CONTRIBUTIONS

Jutta Dierkes and Hans-Peter Marti conceived the study, participated in design and coordination, read and approved the final manuscript. Helene Dahl, Natasha L. Welland and Iselin Arnesen participated in design and coordination, undertook interviews, helped to draft manuscript, read and approved the final manuscript. Helene Dahl and Sina-Isabel Warz analysed the data, helped to draft manuscript and approved the final manuscript.

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