

The nutrition impact symptoms (NIS) score detects malnutrition risk in patients admitted to nephrology wards

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1 **The Nutrition Impact Symptoms (NIS) score detects malnutrition risk in patients admitted to**
2 **nephrology wards.**

3
4 **Abstract**

5 **Background:** Nutritional screening tools recommended for the general hospitalised population do not
6 always adequately detect malnutrition risk in patients with kidney disease. This study assessed the
7 validity and reliability of the Nutrition Impact Symptoms (NIS) score as a nutrition screening tool for
8 hospitalised inpatients in nephrology wards.

9
10 **Methods:** Nutritional status was classified using Subjective Global Assessment (SGA). NIS scores
11 were calculated from the total score of responses to questions assessing symptoms impacting upon
12 nutritional status from the patient-generated SGA. Concurrent validity of NIS score was assessed using
13 a receiver operating characteristics curve to predict malnutrition risk against SGA. Predictive validity
14 was examined against length of hospital stay (LOS) and 30-day readmission using Poisson and logistic
15 regression respectively. Inter-rater reliability of NIS scoring between assessors was determined using
16 intra-class correlation.

17
18 **Results:** In 143 patients (90M; mean (SD) age 57.8 (15.8) years), malnutrition prevalence was 38%
19 (54/143) using SGA (rating B/C). Predicting malnutrition risk with an NIS score of ≥ 3 had a
20 sensitivity of 0.89 and a specificity of 0.65 (area under the curve = 0.81 [95% confidence interval (CI),
21 0.74 - 0.88]). For each 1-point increase in NIS score, the model predicted a 1.9% rise in the risk of an
22 increased LOS ($p=0.002$). 30-day readmission was not associated with NIS score. Inter-rater reliability
23 was moderate (mean difference =0.53; intra-class correlation coefficient = 0.74; 95% CI 0.57-0.85).

24
25 **Conclusions:** NIS score is a valid stand-alone nutrition screening tool to identify malnutrition risk in
26 nephrology inpatients, and is associated with length of hospital stay.

27

28

29 **Introduction**

30 Malnutrition is a common complication of renal disease, particularly in the later stages of chronic
31 kidney disease (CKD) (stages 3-5) (KDIGO, 2013). Studies demonstrate that over 50% of patients
32 admitted to nephrology wards are malnourished (1, 2), and uraemia, acidosis, dialysis and comorbidities
33 all impact upon food intake and nutritional status in patients with kidney disease (3, 4). Impaired
34 nutritional status is associated with poor clinical outcomes, including increased morbidity, longer
35 hospital stay, readmission, reduced quality of life and poorer survival (5-9).

36
37 Nutritional screening is simple and efficient method of identifying those at risk of malnutrition, and
38 screening in the hospital setting helps ensure that patients receive timely and effective treatment where
39 needed (10, 11). In the UK, the Malnutrition Universal Screening Tool (MUST), identifies between 19-
40 60% of hospitalised patients as at risk of malnutrition (10). However, evidence suggests that MUST
41 lacks sensitivity and identifies only those at the highest malnutrition risk in patients with kidney disease
42 when compared to nutrition assessment with Subjective Global Assessment (SGA) (12). Fluctuations
43 in weight due to fluid retention masking undetected loss of tissue, may make detection or assessment of
44 weight loss difficult; a factor which is essential for the accurate completion of MUST, and any other
45 tool using BMI as a screening criteria (2). Other nutrition screening tools such as the Mini Nutrition
46 Assessment and Malnutrition Screening Tool (MST) have also demonstrated little promise for use in
47 patients with kidney damage (Afsar et al., 2006; Lawson et al., 2012). These findings are in agreement
48 with the results of a systematic review reporting no single screening tool is appropriate for use in all
49 hospitalised patients, and that future research should focus on trying to identify the most suitable
50 screening tools for specific patient groups (13). Research on renal specific nutrition screening tools has
51 continued. The renal nutrition screening toll (R-NST) was recently developed and tested for validity
52 and feasibility (1). The R-NST demonstrated high sensitivity and specificity against SGA, however,
53 when introduced into clinical practice there was low uptake when used by nurses, attributed to the need
54 to access information from electronic clinical information systems, and poor agreement for scoring
55 between researchers and nurses (1). Therefore, the need for a user friendly and valid nutrition
56 screening tool for renal patients remains evident.

57
58 The Nutrition Impact Symptoms (NIS) score (Table 1) is part of the patient-generated SGA (PG-SGA),
59 a validated nutrition assessment tool initially developed for use in oncology and also validated in
60 haemodialysis (14, 15). Based on recent evidence supporting the efficacy of the NIS score as a
61 nutrition screening tool for haemodialysis outpatients (16), and the high level of malnutrition with
62 multiple aetiologies in patients admitted to nephrology wards, it is hypothesised that the NIS score may
63 be a valid and reliable nutrition screening tool for renal inpatients on nephrology wards.

64

65 **Methods**

66 A cross-sectional and observational validation study was conducted. Patients over 18 years were
67 considered eligible for inclusion in the study if they were admitted for a planned or unplanned/
68 emergency admission, under the care of a consultant nephrologist, to an acute renal unit consisting of
69 two wards, and had been an inpatient for <4 days. All patients meeting the inclusion criteria were
70 approached to participate in the study, during 3 separate recruitment periods of 4-8 weeks, between
71 July 2014 and April 2015, with different assessors for each period. Patients were introduced to the
72 researcher by members of the clinical care team - either the patient's nurses, doctors or dietitian
73 approached the patient to request permission for the researcher to inform the patient about the study.
74 To maintain consistency, all researchers were trained in the study methods by the same trainer (HM),
75 and reached competency standards for NIS score and SGA assessment prior to data collection.
76 Patients were excluded if their total hospital stay was less than 24 hours, or were unable to provide
77 informed consent.

78

79 Ethical approval was granted by the National Research Ethics Service Committee London - City &
80 East (reference number 15/LO/0204), and permission to use the PG-SGA (2015, v3.22.15; metric
81 and non-metric version) was obtained from pt-global.org. Patients who met the inclusion criteria
82 were given verbal and written information about the study prior to providing written informed consent.
83 Confidentiality was maintained by coding patient identifiable details on paper records and in secure
84 password protected electronic documentation.

85

86 *Concurrent Validity*

87 To calculate the NIS score, patients were asked “Have you had any of the following problems that have
88 kept you from eating enough during the past two weeks?”, followed by listing each NIS symptom in turn.
89 The total NIS score was calculated by adding the scores for all symptoms identified positively by
90 patients (Table 1). Individual NIS were only scored positively if they affected food intake (14). The
91 SGA was completed at the same time using the standard method (12) and SGA global classifications
92 were used to categorise nutritional status (A – well nourished, B - moderately malnourished and C -
93 severely malnourished). Patients identified as malnourished, with an SGA rating on B or C, were
94 referred directly to the responsible clinical renal dietitian for further assessment and intervention.

95 The ability of the NIS score to identify malnutrition risk was assessed against the SGA global
 96 classification of nutritional status as the reference standard. Specificity (true negative cases / [(true
 97 negative + false positive] cases), and sensitivity (true positive cases / [true positive + false negative]
 98 cases), of a range of NIS scores to detect malnutrition risk were determined.

99
 100 Table 1. Nutrition Impact Symptoms (NIS) score for symptoms impacting on food intake*.

Score = 1	Score = 2	Score = 3
<ul style="list-style-type: none"> • nausea • constipation • things taste funny or have no taste • dry mouth • smells bother me • feel full quickly • fatigue • other (e.g. depression, finances, dental issues) 	<ul style="list-style-type: none"> • mouth sores • problems swallowing 	<ul style="list-style-type: none"> • no appetite, just did not feel like eating • vomiting • diarrhoea • Pain: where? _____

101 *Adapted from the PG-SGA (2015, v3.22.15; metric and non-metric version) <http://pt-global.org>

102
 103 *Predictive and Clinical Validity*

104 Predictive validity was evaluated against length of stay (LOS) and readmission to any ward in the same
 105 hospital within 30 days of discharge. LOS was defined as the total number of days spent as an
 106 inpatient during the admission, calculated by subtracting the hospital admission date from the date of
 107 discharge. Serum albumin and C-reactive protein (CRP) concentrations on admission were recorded
 108 for each patient and the Charlson Comorbidity Index score (17) was calculated using clinical history
 109 and demographic data from electronic patient records.

110
 111 *Inter-Rater Reliability*

112 The reliability of the NIS score was determined by repeating the NIS score in a subgroup of study
 113 participants (n=43) using a second measurer (a dietitian, nurse or healthcare assistant), blinded to the
 114 initial scoring, to assess NIS score only. The NIS score was repeated on the same day to ensure that
 115 conditions were comparable.

116

117 *Data Analysis*

118 Statistical analysis was carried out using SPSS version 22 (IBM). Sample size calculations were based
119 on findings from pilot testing of the NIS tool. With an expected prevalence of malnutrition at 50%,
120 88% specificity and 80% sensitivity for NIS, and precision within 10% and type-1 error of 5%, 125
121 patients were required in the study. Normality of the data was assessed using histograms and the
122 Shapiro–Wilk test of normality. Results were considered significant at $p < 0.05$ and 95% confidence
123 intervals (CIs) were computed where applicable. Baseline characteristics between malnourished (SGA B
124 or C) and well nourished (SGA A) patients were compared with chi-squared tests - or Fisher's Exact
125 test when needed - for categorical variables, and independent t-tests or Mann Whitney U tests for
126 parametric and non-parametric continuous variables, respectively.

127

128 To establish the optimal NIS cut off score maximising the sensitivity and specificity of the tool in
129 determining malnutrition risk, a receiver operating characteristic (ROC) curve and contingency table
130 was produced comparing the NIS score with the SGA global rating of nutritional status as the
131 reference standard (where SGA A = well-nourished and SGA B or C = malnourished). With the
132 finalised risk categories, concurrent validity of the NIS score was examined against the SGA global
133 rating of nutritional status to determine the sensitivity and specificity of the NIS score in identifying
134 malnutrition risk using the contingency table. The associations between NIS score and clinical
135 morbidity indicators, CRP, albumin and Charlson score, were assessed with Spearman rank correlations.
136 The relationship between all 4 indicators and LOS or 30-day readmission were examined using Poisson
137 linear regression analysis and forward, stepwise logistic regression analysis, respectively. Intra-class
138 correlation tested the inter-rater reliability of the NIS score.

139

140 **Results**

141 Of the 178 potentially eligible patients, 143 patients were recruited to the study. Baseline characteristics
142 are outlined in Table 2. 38% of patients were malnourished when classified by SGA (33% as SGA
143 rating B and 5% classified as SGA rating C). Albumin, CRP and NIS score were significantly different
144 between well-nourished and malnourished patients, and malnourished patients had a greater proportion
145 of emergency/ unplanned admissions, compared to those who were well nourished.

146

147 *Concurrent Validity*

148 Examination of the contingency table indicated that the concurrent validity of the NIS score was
149 greatest at a score of ≥ 3 , classifying 55% (79/143) of patients as at risk of malnutrition. The area under
150 the ROC curve (AUC) was 0.81 (95% CI 0.74 - 0.88), indicating good concurrent validity (13).

151 Sensitivity was 89% (true risk of malnutrition identified) and specificity was 65% (true no risk of
 152 malnutrition identified), compared to SGA.

153

154 Table 2. Baseline characteristics of patients admitted to acute renal inpatient wards by nutritional status

Variable	Well-Nourished	Malnourished	p
	SGA ¹ A	SGA B or C	
N (%)	89 (62%)	54 (38%)	
Age (years), mean \pm SD ²	57.4 \pm 15.7	58.3 \pm 16.0	0.8 ⁸
Gender, n (%)			
Male	55 (62%)	35 (65%)	0.7
Female	34 (38%)	19 (35%)	
Ethnicity, n (%)			
White	33 (37%)	27 (50%)	0.2
Black	33 (37%)	12 (22%)	
Other	23 (26%)	15 (28%)	
Albumin (g/L) mean \pm SD	38.3 \pm 5.5	35.7 \pm 6.3	0.009 ⁸
CRP ³ (mg/L), median (IQR)	9.7 (3.8 – 28.8)	25.1 (8.0 – 93.5)	0.014 ⁷
Charlson Score, mean \pm SD	5.1 \pm 2.3	5.2 \pm 2.5	0.6 ⁸
Admission type, n (%)			
Elective	37 (42%)	11 (20%)	0.01
Unplanned	52 (58%)	43 (80%)	
Kidney Damage, n (%)			
CKD ⁴ stages 1-2	7 (8%)	2 (4%)	0.2 ⁹
CKD stages 3-4	22 (60%)	12 (22%)	
CKD stage 5	53 (24%)	30 (56%)	
Acute Kidney Injury	7 (8%)	10 (18%)	
Length of stay (days), median	4 (2 - 8)	5 (3 - 11)	0.1 ⁷
(IQR) ⁵	1.0 (0 - 4)	7.0 (4 - 10)	<0.001 ⁷
NIS ⁶ score, median (IQR)			

155 1. SGA, Subjective Global Assessment; 2. SD, standard deviation; 3. CRP, C-reactive protein; 4. CKD, chronic kidney
 156 disease; 5. IQR, interquartile range; 6. NIS, Nutrition Impact Symptoms; 7. Mann Whitney *U* test; 8. Independent t-test; 9.
 157 Fisher's Exact test.

158

159 *Predictive and Clinical Validity*

160 Using rank correlation, NIS score was associated with CRP ($p = 0.22$, $p = 0.011$), but not albumin or
 161 Charlson score. In the Poisson regression model, all factors predicted an increased risk of longer LOS;
 162 lower serum albumin concentration on admission, higher CRP, higher NIS score and lower Charlson
 163 score (Table 3). For each 1-point increase in NIS score, the model predicted a 1.9% rise in the risk of
 164 an increased LOS ($p = 0.002$). Using the median NIS score of 7 for malnourished patients, the risk of
 165 a longer LOS increased by 13.3%. 31 (22%) patients were readmitted to the same hospital within 30-
 166 days of discharge; 5 planned and 26 unplanned admissions. Factors associated with 30-day readmission
 167 were initial unplanned admission, LOS and albumin (Table 4). NIS score, Charlson score and CRP
 168 were not associated with readmission to hospital within 30 days, and these results did not change when
 169 the analysis was limited to unplanned readmissions only (data not shown).

170

171 Table 3. Impact of variables on risk of increasing the length of hospital admission (length of stay, LOS)

Predictor variables	Regression co-efficient (β)	Incident rate ratio (e^{β}) and 95% confidence interval	p
Albumin concentration (g/L)	-0.72	0.93 (0.92 – 0.94)	<0.001
C reactive protein (mg/L)	0.002	1.002 (1.001 – 1.002)	<0.001
Nutrition Impact Symptoms (NIS) score	0.019	1.019 (1.007 – 1.031)	0.002
Charlson Comorbidity Index	-0.05	0.95 (0.93 – 0.98)	<0.001

172

173 Table 4 – Multivariable logistic regression for factors related to hospital readmission within 30 days

Predictor variables	Odds ratio (β)	95% Confidence Interval	p
Unplanned admission	4.97	1.36 – 18.05	0.02
Serum albumin	1.09	1.01 – 1.19	0.04
Length of stay (LOS)	1.05	1.01 – 1.09	0.02

174

175 *Inter-Rater Reliability*

176 There was no difference in the total NIS score between measurers in 37% of cases. The mean
 177 difference between repeated NIS scores was 0.53 ± 2.81 (mean \pm SD). The Intra-class correlation
 178 coefficient was 0.74 (95% CI 0.57 - 0.85), indicating moderate reliability between users.

179

180 **Discussion**

181 This study established that the NIS score is a valid nutrition screening tool to assess malnutrition risk in
182 patients admitted to nephrology wards. Concurrent, clinical and predictive validity were demonstrated
183 through comparison to the SGA global rating of nutritional status, and by association with CRP, and
184 increased risk of longer LOS, respectively.

185

186 Compared with SGA, the concurrent validity was deemed to be at its highest with an NIS score of ≥ 3 .
187 This NIS score cut-off is higher than that selected in a previous investigation involving 213
188 haemodialysis outpatients, which found that a NIS score of ≥ 2 was most effective at detecting
189 malnutrition risk (16). Median NIS scores in the well-nourished and malnourished groups were 1.0 and
190 3.5 points lower, respectively, than the median scores in the present study, and less than a quarter of
191 patients were classified as malnourished, indicating that when malnutrition risk is lower, the threshold
192 for detection with a nutrition screening tool is also lower, in order to maximise sensitivity. Together,
193 these studies demonstrate the flexibility of the NIS score as a screening tool across different setting in
194 patients with CKD, and also the importance of validating nutrition screening tools within the intended
195 patient population.

196

197 A nutrition screening tool should have a high level of sensitivity to detect malnutrition, to reduce the
198 risk of failing to detect malnutrition risk in a malnourished patient (false negative result) (10). An NIS
199 score ≥ 3 had a sensitivity of 89%, demonstrating a far superior ability to detect malnutrition risk in
200 patients with kidney disease than the MUST and MST tools; which were shown to have sensitivities of
201 54% and 49% compared to SGA respectively (2). With a specificity of 65%, the NIS score at a cut-off
202 of ≥ 3 was relatively effective at identifying well-nourished patients, with similar specificity to the MST
203 (18), although it does carry a reasonably high rate of false positive results. More recently, another
204 nutrition screening tool, the R-NST was developed specifically for renal inpatients (1). The R-NST is
205 more complex than the NIS score, and includes biochemical parameters alongside nutrition impact
206 symptoms and weight loss history. The R-NST demonstrated high sensitivity (97%) and moderately
207 high specificity (74.4%), compared to SGA. However in the reliability and feasibility phase of the study,
208 the R-NST tool had low levels of completion by clinical staff due to the time taken to calculate 6-
209 month weight change, and extract the clinical data from the electronic medical records. Reliability was
210 difficult to measure due to the very low completion rate for nursing staff (1), **Together these results**
211 **indicate that the R-NST may have limited translational capacity for use in clinical practice.**

212

213 This study is the first investigation to show that the NIS score is associated with LOS, an indicator of
214 morbidity in patients with kidney disease (19), thus demonstrating a degree of predictive validity of the
215 NIS score. The NIS score has also previously been shown to predict long term clinical outcomes in
216 patients on maintenance haemodialysis, as an NIS score of ≥ 2 was associated with a higher risk of
217 mortality, whereas the SGA global rating was not (16).

218
219 The NIS score had moderate inter-rater reliability, with an ICC of 0.74, and identical NIS scores were
220 reported between assessors in 37% of patients. Whilst this is less than ideal, it is significantly higher
221 than the agreement between assessors using the R-NST, where the same score was achieved in the
222 repeated measure in only 8% of cases (1). Reliability of nutritional assessment using SGA can also be
223 limited, with only fair inter-rater reliability between assessors following completion of an online training
224 package (20). The research team provided brief training to clinical assessors before determining the
225 NIS score. Between-user differences might be minimised by introducing more in-depth training for all
226 assessors, where measurers would be expected to demonstrate competency before using the NIS score
227 in practice.

228
229 The limitations of this study are also acknowledged. In each assessment, the NIS and the SGA were
230 undertaken by the same researcher in a single session, so blinding the researchers to the outcomes of
231 the individual components was not possible. However, as the study was conducted in three different
232 time periods with different researchers, the robustness of the tool across users and over time is
233 demonstrated. There are several advantages of using the NIS score as a nutrition screening tool in
234 preference to other tools. The NIS score does not require measurement of body weight, knowledge of
235 oedema free weight or previous weight loss. The NIS score also has no biochemical parameters
236 included, so it can be quickly and easily completed at the bedside. Furthermore, the NIS score can
237 identify the main factors impacting on food intake early during hospitalisation and can thus inform
238 subsequent interventions to improve nutritional status (16). As the NIS score identifies specific factors
239 relating to malnutrition risk, it guides the choice of clinical intervention. Symptoms such as dry mouth,
240 taste changes, nausea, vomiting and constipation can all be treated clinically, whilst swallowing
241 problems, feeling full quickly and fatigue require specific nutritional interventions.

242
243 The outcomes of this study support the use of the NIS score as a nutrition screening tool for
244 hospitalised patients on nephrology wards, adding to previous findings supporting its use in
245 haemodialysis outpatients. Concurrent, predictive and clinical validity were demonstrated against the
246 SGA global rating of nutritional status, and the reliability between users was moderate. Future research
247 into the use of the NIS as a nutrition screening tool should focus on the effect of training and nursing

248 involvement in clinical implementation and the effect on longer-term clinical outcomes such as mortality, and
249 patient focused outcomes such as quality of life, and discharge with maintained or improved functional capacity.
250

251 Transparency Declaration

252 The lead author affirms that this manuscript is an honest, accurate, and transparent account of the
253 study being reported. The lead author affirms that no important aspects of the study have been omitted
254 and that any discrepancies from the study as planned have been explained.
255

256

257

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