

1 **Original Research Paper**

2 **Title: The Relationship between Malnutrition Risk and Clinical Outcomes in a**
3 **Cohort of Frail Older Hospital Patients**

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22 **Abstract**

23 **Background & Aims:** Malnutrition has an adverse effect on clinical outcomes and
24 frail older people may be at greater risk of malnutrition. The purpose and aims of this
25 study was to investigate the relationship between markers of malnutrition risk and
26 clinical outcomes in a cohort of frail older hospital patients.

27 **Methods:** 78 frail older hospital patients had the following measurements recorded;
28 length of stay (LOS), time to medical fitness for discharge (TMFFD), body mass
29 index (BMI), malnutrition universal screening tool (MUST) and mini-nutritional
30 assessment short-form (MNA-SF) scores, blood urea, C-reactive protein (CRP),
31 albumin, CRP-albumin ratio; and bioelectrical impedance assessment (BIA)
32 measurements (n=66). Patients were grouped by mortality status 12 months post
33 hospital admission. Grouping by albumin classification was performed (n=66)
34 whereby, <30 g/l indicated severe malnutrition, 30-34.9, moderate and >35, low.
35 Receiver-operating characteristic (ROC) curve analysis was performed on variables
36 as potential predictors of mortality.

37 **Results:** After 12 months, 31% (n=24) of patients died. LOS was significantly greater
38 in this group (25.0±22.9 vs 15.4±12.7d, P<0.05). BMI (23.8±4.9 vs 26.4±5.5kg/m²);
39 fat mass (FM) (17.2±9.9 vs 25.5±10.5kg), fat mass index (FMI) (9.3±4.1 vs
40 17.9±2.4kg/m²); and MNA-SF score (6.6±2.4 vs 8.6±2.7) were significantly lower
41 (P<0.05), and urea significantly higher (11.4±8.7 vs 8.8±4.4mmols/l, P=0.05).
42 Albumin was typically low across the entire group (30.5±5.9 g/l) and a potential
43 relationship was identified between albumin and MNA-SF score. MNA-SF, FM, and
44 FMI were significant predictors of mortality outcome by ROC curve analysis,
45 whereas MUST was a poor predictor.

46 **Conclusion:** This study highlights a potential relationship between indicators of
47 malnutrition risk and clinical outcomes in frail older hospital patients which should be
48 studied in larger cohorts with an aim to improve patient care.

49 (275 words)

50

51 **Keywords:** *malnutrition, frailty, cachexia, malnutrition universal screening tool*
52 *(MUST), mini nutritional assessment (MNA), bioelectrical impedance assessment.*

53

54 **Introduction**

55 Frail older people may be admitted to hospital wards suffering from a range of acute
56 and chronic disease/s, with signs and symptoms of physical and/or cognitive frailty
57 and be on multiple medications. Identifying possible nutritional risk/malnutrition is
58 important and may affect trajectory of health, morbidity, and mortality¹⁻⁴. Different
59 screening methods exist including the '*malnutrition universal screening tool*'
60 (MUST)^{1,5}, the '*mini-nutritional assessment*' (MNA)^{1,6-8} and the '*geriatric nutritional*
61 *risk index*', (GNRI)⁹. In the United Kingdom (UK), the MUST is the standard routine
62 method of screening in all hospital wards and care homes, although in reality there is
63 no universal gold standard tool⁴. We showed recently in a cohort of frail older
64 hospital patients that there is a significant discordance between MUST and 'MNA-
65 short form' (MNA-SF) malnutrition screening categorisation¹⁰. The MUST
66 predominantly categorized patients as 'low risk' (77%) and MNA-SF predominantly
67 as 'at risk' (46%) and 'malnourished' (45%). Reliability assessment found poor
68 reliability between the screening tools and bioelectrical impedance assessment (BIA)

69 assessment was in general agreement with MNA-SF scoring patterns, especially in
70 male patients. A potential body mass index (BMI) paradox was also highlighted
71 whereby some patients who were 'at risk' or 'malnourished' by MNA-SF scores had
72 normal BMI and depleted/borderline BIA measurements of fat free mass (FFM) / fat
73 mass (FM) and specifically indices (FFMI and FMI, in kg/m²). Potential reasons for
74 the observed MUST-MNA-SF discordance include: the MUST uses World Health
75 Organization (WHO) BMI grading criteria, and there maybe difficulty in obtaining
76 accurate weight loss information in this patient group. Further, the MNA-SF has
77 additional screening questions on 'mobility' and 'neuropsychological problems' which
78 would create a tendency to score worse in a frail older patient group.

79 An important area to address which overlaps malnutrition is 'cachexia'/'cachexia-
80 risk', as acute and chronic illness has a typical effect upon food intake (anorexia) and
81 metabolism (e.g. hypermetabolism and raised protein breakdown), principally
82 through actions of circulating proinflammatory cytokines^{11,12}. Other measurable
83 domains of nutritional status which are sensitive to malnutrition and inflammation
84 include important blood markers such as albumin, which is utilised in the GNRI⁹, and
85 is a well known prognostic marker¹³⁻¹⁶. C-reactive protein (CRP) is another routine
86 blood marker indicating inflammatory status and has known prognostic potential^{17,18}.
87 Recently, the CRP/albumin ratio has been used to better predict mortality risk in
88 septic patients¹⁹.

89 A better understanding of the relationship between malnutrition risk screening, body
90 composition assessment and blood markers in heterogeneous groups of frail older
91 hospital patients on clinical outcomes may improve coordinated hospital nutritional
92 care in the UK.

93 This study was undertaken in a heterogeneous group of frail older adults admitted to
94 wards specialising in elder care in the UK. We examined outcome of hospital
95 admission, length of stay (LOS), time to medical fitness to discharge (TMFFD) and
96 mortality at 12 months post admission and related them to inpatient measurements
97 of MUST, MNA-SF and BIA. Further, examination was made of routine blood
98 markers, urea, albumin, CRP, and the CRP/albumin ratio to investigate their
99 importance in relation to malnutrition risk and outcomes.

100 (497 words)

101

102 **Methods**

103 ***Participants and study design***

104 This cohort study was undertaken between September 2012 and May 2013 and
105 recruits were from a purposive sampling from admissions to two hospital wards in
106 Lincoln, UK specializing in care of frail older patients¹⁰. Full ethical approval was
107 obtained from NHS Leicester, East Midlands Research Ethics Committee (ref:
108 12/EM/0186) prior to study commencement, ethical guidelines followed and informed
109 consent sought from all patients. Exclusion criteria from the study were: patients
110 unable or unwilling to give informed consent and patients who were nil by mouth or
111 tube fed. BIA measures were contraindicated in patients with defibrillation or cardiac
112 pacemaker devices. The aim was to recruit 100-150 patients in-line with other similar
113 studies; however the exclusion criterion of ability to consent and designated study
114 time restraints dictated the current number. Patients were followed from admission to
115 12 months post admission with outcomes recorded including: TMFFD, LOS in

116 hospital (days), and deaths at 12 months. Blood measurements were also recorded
117 where available.

118 **Nutritional assessment**

119 ***MUST tool and MNA-SF[®] screening***

120 MUST and MNA-SF[®] screening was performed as described previously¹⁰, whereby
121 screening scores were converted into categories for nutritional status using MUST
122 and MNA-SF[®] scoring criteria either 'low risk'/'normal'(0 points-MUST, 12-14 MNA-
123 SF), 'medium risk/at risk' (1 point-MUST, 8-11 MNA-SF) and 'high
124 risk'/'malnourished' (≥ 2 points-MUST, 0-7 MNA-SF).

125 ***Anthropometric measurements***

126 Height (m) and weight (kg) measurements were performed as described
127 previously¹⁰.

128 ***Bioelectrical impedance measurements***

129 BIA measurements were performed as described previously¹⁰, using the Kyle et al²⁰
130 equation for estimation of FFM (kg) and FM (kg) and index values, FFMI (kg/m²) and
131 FMI (kg/m²), and compared to reference values²¹.

132 ***Blood markers***

133 Routine blood markers were collected and measured in-line with normal patient care
134 in hospital. Ethical clearance was obtained to utilise these as part of the research
135 study. Markers utilised and analysed included; urea, albumin, C-reactive protein
136 (CRP) and the CRP-albumin ratio. Patients were also classified according to albumin

137 level and 'malnutrition severity', using an adapted method from paper by Bouillanne
138 et al⁹, i.e. <30 g/l: severe; 30-34.9 g/l: moderate; and >35 g/l low+absent combined.

139

140 **Data analysis**

141 Data is presented as mean average measurements \pm standard deviation (SD) with a
142 range (minimum-maximum) and [median] values. Data has been grouped into 'alive'
143 and 'deceased' at 12 months post admission and where relevant into nutritional
144 screening categories by albumin. Statistical analysis was performed using IBM
145 SPSS Statistics, version 21, New York, USA. T-tests and Pearson correlations were
146 used for normally distributed data and Mann-Whitney-U and Spearman correlations
147 test for nonparametric data. ANOVA and Bonferroni post-hoc test were performed
148 on more than two groups of data. Categorical differences were analysed using Chi-
149 squared testing. Receiver-operator characteristic (ROC) curve analysis methods
150 were performed on raw data of variables to evaluate their predictive performance on
151 the prediction of mortality outcome in patients²². A P value of < 0.05 was considered
152 statistically significant.

153

154 **Results**

155 Data was recorded for 78 patients and followed up 12 months post admission. Within
156 patient medical notes, blood markers were available for the following: albumin (n=66
157 patients), urea (n=76), CRP (n=73), and CRP/albumin ratio (n=65). Patients were
158 grouped according to mortality status at 12 months and data is presented in Table 1.
159 LOS and urea measurements were significantly higher in the deceased group; and

160 BMI and MNA-SF score significantly lower. Patients had BIA measured (n=66) as
 161 completed previously¹⁰ and grouped by mortality status (Table 2). FM and FMI by
 162 BIA were found to be significantly lower in patients who died.

163

164 **Table 1.** Table to show differences in patients grouped by mortality status, 12
 165 months after hospital admission. Mean \pm SD is presented with (minimum-maximum)
 166 and [median] values for comparison.

	Alive	Deceased
N	54 (69%)	24 (31%)
Males/females	30/24 (56%/44%)	19/5 (79%/21%)
Age, y	81.7 \pm 7.4 (65-93) [83]	83.0 \pm 8.8 (62-96) [84]
TMFFD, d	8.5 \pm 7.6 (0-37) [7]	10.4 \pm 13.8 (0-66) [6]
LOS, d	15.4 \pm 12.7 (2-68) [10]	25.0 \pm 22.9 (6-102) [19]*
BMI, kg/m²	26.4 \pm 5.5 (17.2-45.1) [26.3]	23.8 \pm 4.9 (16.6-37.2) [23.3]*
MUST score	0.4 \pm 0.8 (0-4) [0]	0.6 \pm 1.1 (0-4) [0]
MUST – ‘Low risk’	43 (80%)	17 (71%)
MUST – ‘Medium risk’	5 (9%)	2 (8%)
MUST – ‘High risk’	6 (11%)	5 (21%)
MNA-SF score	8.6 \pm 2.7 (3-14) [8.5]	6.6 \pm 2.4 (2-11) [7]*
MNA-SF – ‘Normal’	7 (13%)	0 (0%)
MNA-SF – ‘At risk’	26 (50%)	9 (46%)
MNA-SF – ‘Malnourished’	21 (37%)	15 (54%)
Urea (mmols/l)	8.9 \pm 4.3 (3.1-21.1) [7.8]	11.4 \pm 8.7 (1.7-43.9) [10]*
CRP (mg/l)	56.1 \pm 67.4 (0.6-287) [25]	78.6 \pm 73.6 (2.1-221) [44.5]
Albumin (g/l)	31.0 \pm 6.1 (15-43) [31]	29.4 \pm 5.2 (20-39) [29]
CRP-albumin ratio	2.1 \pm 2.6 (0.05-11.04) [1]	3.1 \pm 2.7 (0.06-9.39) [2.4]

167 *significantly different compared to patients alive at 12 months: LOS, (P=0.018); BMI, (P=0.018); MNA-SF,
 168 (P=0.001); Urea, (P=0.05).

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170

171 **Table 2.** Comparison of BIA data for FFM and FM and index values (FFMI and FMI
172 in kg/m²) for patient mortality status, 12 months after hospital admission. Mean ± SD
173 is presented with (minimum-maximum) and [median] values for comparison.

	Alive (n = 48)	Deceased (n = 18)
Males/Females	27/21 (56%/44%)	15/3 (83%/17%)
FFM, kg	49.4±9.2 (31.7-72.0) [49.6]	51.5±9.7 (37.5-72.7) [50.7]
FFMI, kg/m²	17.5±2.5 (13.2-23.5) [17.5]	17.9±2.4 (13.5-22.2) [17.8]
FM, kg	25.5±10.5 (3.4-50.6) [22.5]	17.2±9.9 (3.1-42) [18.1]*
FMI, kg/m²	9.3±4.1 (1.1-22.5) [8.1]	6.1±3.8 (1.3-16.8) [6.4]*

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175 *significantly different compared to patient group alive at 12 months: FM, (P=0.005); FMI, (P=0.006).

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177

178 ***Classification by albumin level***

179 Grouping patients by albumin level as a potential indicator of nutritional status is
180 shown in Table 3. The relationship of albumin level against MNA-SF score is
181 depicted in Figure 1 with cut-off points shown. The nonparametric correlation
182 between albumin and MNA-SF was statistical significant (r=0.025, P=0.046).

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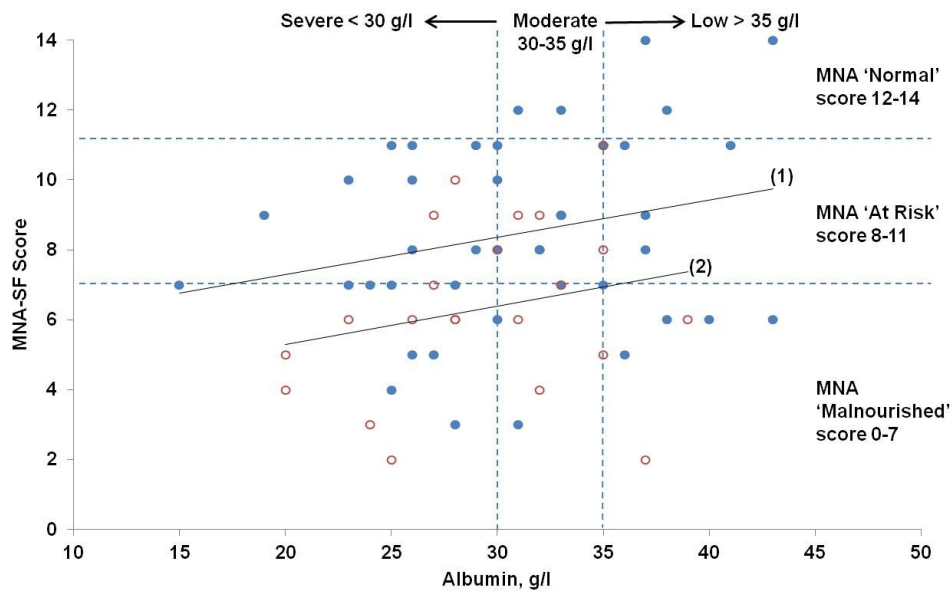
187 **Table 3.** Patients grouped by albumin classification of malnutrition status. Mean \pm
 188 SD is presented with (minimum-maximum) and [median] values for comparison.

	Plasma albumin & malnutrition status		
	<30 g/l – severe	30-34.9 g/l - moderate	>35 g/l – low/absent
Albumin, g/l	25 \pm 3.3 (15-29) [26]*	31.6 \pm 1.2 (30-33) [32]	37.5 \pm 2.6 (35-43) [37]
N (%)	28 (42%)	19 (29%)	19 (29%)
Deaths, N (%)	11 (39%)	6 (32%)	5 (26%)
TMFFD, d	12.4 \pm 13.7 (0-66) [8]*†	8.3 \pm 6.2 (1-22) [6.5]	6.5 \pm 6.6 (0-26) [4]
LOS, d	25 \pm 21.6 (4-102) [19]*†	17.6 \pm 15.4 (2-68) [16]	14.1 \pm 9.5 (2-33) [12]
BMI, kg/m²	24.8 \pm 5.2 (17-35.2) [23.2]	27.1 \pm 6.2 (18.6-45.1) [26.1]	25.4 \pm 5.2 (16.6-33.3) [25.6]
MUST- ‘Low risk’	23 (82%)	16 (84%)	14 (74%)
MUST – ‘Medium risk’	2 (7%)	2 (11%)	1 (5%)
MUST – ‘High risk’	3 (11%)	1 (5%)	4 (21%)
MNA-SF score	7.0 \pm 2.5 (2-11) [7]	8.2 \pm 2.4 (3-12) [8]	8.6 \pm 3.3 (2-14) [8]
MNA-SF – ‘Normal’	0 (0%)	2 (10%)	3 (16%)
MNA-SF – ‘At risk’	11 (39%)	11 (58%)	8 (42%)
MNA-SF – ‘Malnourished’	17 (61%)	6 (32%)	8 (42%)
Urea, mmols/l	10.7 \pm 8.6 (1.7-43.9) [8.0]	9.8 \pm 4.4 (3.1-18.5) [9.4]	8.7 \pm 4.6 (3.2-19.1) [7.6]
CRP, mg/l	96.7 \pm 80.6 (4-287) [86]*	65.6 \pm 71.8 (1.6-232) [45]	29.2 \pm 38.1 (2.5-172) [17]

189 *†: raw uncorrected data significantly different to >35 g/l albumin group (P<0.05), although after Bonferroni
 190 correction no statistical significance remained. *: Bonferroni corrected data <30 g/l albumin significantly different
 191 to >35 g/l albumin group (P=0.005); and CRP significantly different between all groups (P<0.001).

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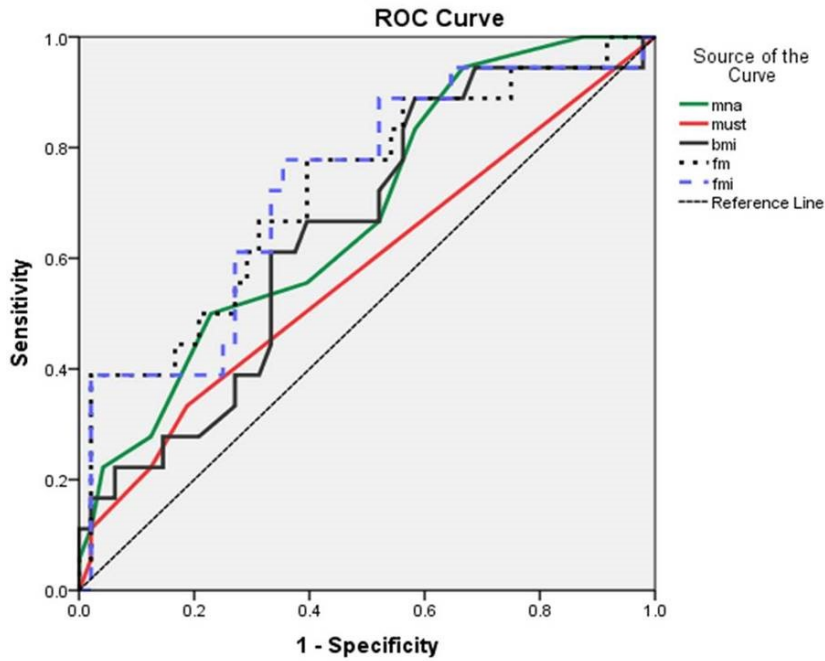
194

195 **Figure 1.** The relationship between plasma albumin (g/l) and MNA-SF score in
 196 patients where albumin data was available (n=66). Relevant cut-points indicating
 197 malnutrition are shown for both MNA-SF and albumin. Patients alive at 12 months
 198 depicted with closed circles (n=44) and deceased open circles (n=22). Note overall
 199 group correlation was statistically significant (Spearman's, $r = 0.25$, $P=0.046$). In
 200 addition, trend-lines are visible for (1): patients alive and (2): deceased.

201

202 **ROC curve analysis**

203 ROC curve analysis was performed on data variables evaluating their relative
 204 performance as mortality predictors and is presented as follows: MNA-SF and MUST
 205 scores, BMI, FM and FMI, Figure 2; and blood markers, urea, CRP, albumin and
 206 CRP-albumin ratio, in Figure 3.



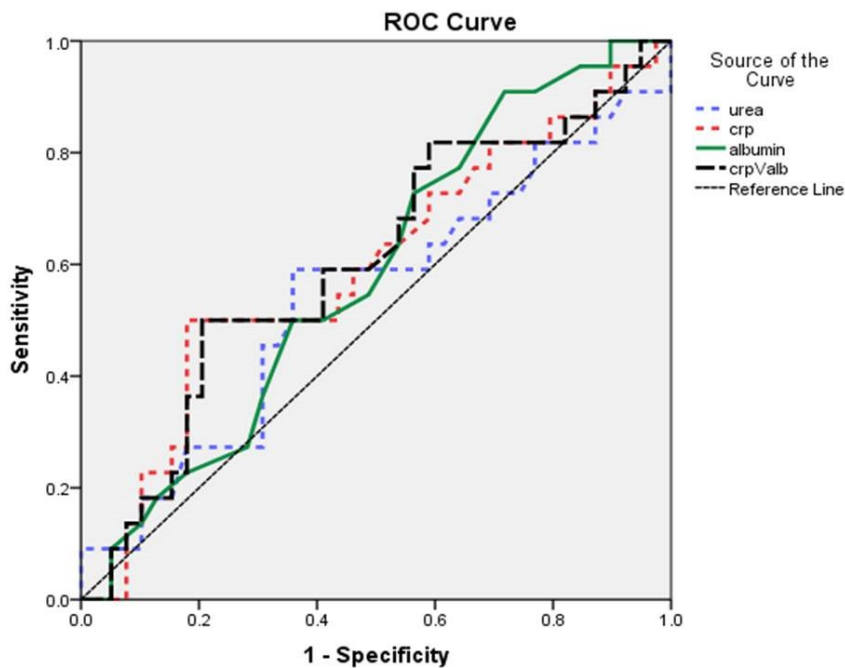
Area Under the Curve

Variable	Area	Std. Error	Sig.	95% Confidence Interval	
				Lower	Upper
fm	0.726	0.072	0.005	0.584	0.867
fmi	0.728	0.071	0.005	0.588	0.868
bmi	0.650	0.074	0.062	0.505	0.795
mna	0.679	0.072	0.026	0.539	0.820
must	0.577	0.083	0.338	0.415	0.739

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209 **Figure 2.** ROC curves for variables: MNA-SF, MUST, BMI, FM and FMI; Statistical
 210 data for area under the curve is presented in Table below graph. Standard error is
 211 under nonparametric assumption and asymptotic significance and 95% confidence
 212 intervals (lower and upper bound) are shown. Null hypothesis: true area = 0.5.



Area Under the Curve

Variable	Area	Std. Error	Sig.	95% Confidence Interval	
				Lower	Upper
urea	0.543	0.080	0.578	0.386	0.700
crp	0.594	0.078	0.224	0.442	0.747
albumin	0.582	0.074	0.290	0.437	0.727
crpValb	0.603	0.077	0.186	0.452	0.753

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214

215 **Figure 3.** ROC curves for variables: urea, CRP, albumin and the CRP-albumin ratio
 216 (crpValb). Statistical data for area under the curve is presented in Table below
 217 graph. Standard error is under nonparametric assumption and asymptotic
 218 significance and 95% confidence intervals (lower and upper bound) are shown. Null
 219 hypothesis: true area = 0.5.

220

221 Variables found to be significantly different from the reference line indicating that
 222 they are significant predictors of mortality were MNA-SF score, FM, and FMI. BMI
 223 had a trend to significance (P=0.062). MUST was not found to be a significant
 224 predictor of mortality outcome. FFM and FFMI were not included in the presentation

225 of data as there was no statistical significance. Blood markers were analysed and
226 have been presented in Figure 3 as a comparison. None were significantly different
227 to the reference line however, the CRP-albumin ratio performed numerically better.
228 However, note the confidence intervals (lower and upper bound) would suggest for
229 all variables relatively high sampling error which is most likely due to the low patient
230 number and data set, and high variability in the blood markers.

231

232 **Discussion**

233 Previously, we showed a potential discordance between MUST and MNA-SF scoring
234 in frail older hospital patients¹⁰. In this report, we show that 12 months after hospital
235 admission a total of 31% of the participants had died. Those patients who died had a
236 significantly longer hospital LOS ($P=0.018$) and a trend for an increase in TMFFD
237 (Table 1). The mortality group had a significantly lower MNA-SF score ($P=0.001$) and
238 there was a visible discordance in relative balance of MUST, MNA-SF categorisation
239 between the alive and deceased patients. ROC curve analysis (Figure 2) found that
240 the MNA-SF was a significant predictor of mortality outcome, whereas MUST was
241 not. Rasheed and Woods also found that the MNA-SF categorised more people
242 admitted to hospital as malnourished/at risk of malnutrition than MUST²³. They noted
243 that both tools have relative ability to predict mortality, but MNA-SF was better at
244 predicting LOS. Van Bokhorst-de van der Schueren et al discussed in a recent
245 systematic review of current nutrition screening tools for the hospital setting, that the
246 MNA generally fairs better in older patients compared to the MUST, and that MUST
247 is a not a good predictor of outcome in older patients⁴. Further, Soderstrom et al,
248 showed in a large cohort of older people ($n=1767$) that the MNA is predictive of

249 mortality (a 50 month follow-up period) after taking into account confounding
250 factors³. However, Vischer et al, failed to show a predictive effect of MNA-SF in
251 hospitalised older patients with a heavy disease burden²⁴. This is interesting as the
252 patient group studied here also had a high disease burden (although this was not
253 recorded as a 'comorbidity/severity index'). The Vischer et al study was performed in
254 a larger patient group (n=444), over a longer 4 year period²⁴. They also observed
255 that BMI was a significant predictor of mortality. In the data presented here BMI was
256 found to be significantly lower in the mortality group, despite still being within a
257 'normal weight' BMI category (by WHO and MUST). Estimation of FM and FMI by
258 BIA was found to be significantly lower, whilst FFMI was similar (17 kg/m²). ROC
259 curve analysis (Figure 2) found that both FM and FMI were significant predictors of
260 mortality outcome (P=0.005), whereas BMI had a trend towards significance
261 (P=0.062). This data may be supportive of a potential BMI or obesity paradox²⁵, and
262 is in-line with a study by Bouillanne et al, which showed a protective effect of FM as
263 opposed to FFM with mortality in older hospital patients²⁶. This may be viewed as
264 unexpected as it has been assumed that FFM has a more important role. For
265 example, the breakdown of FFM body protein tissue to fuel the acute phase stress
266 response to illness and infection and the concomitant production of circulating acute
267 phase proteins and glucose etc. We previously showed that high proportions of male
268 patients had low/depleted FFMI values (and also skeletal muscle index-unpublished
269 data), whilst having a normal BMI (e.g. 20-24.9 kg/m²)¹⁰. The low FFMI values may
270 be due to the effects of complicated overlapping malnutrition, sarcopenia and
271 cachexia states common in the frail older hospitalised patient. This is important to
272 adequately address in clinical practice, however, the relationship of FM with clinical
273 outcomes and mortality in this group requires further study and may relate to other

274 factors. Possible reasons for the observed phenomena may relate to the diverse
275 function of the FM/adipose tissue organ, for example, acting as an energy resource
276 during illness and potentially acting in a protein sparing manner; and/or due to other
277 endocrine and immune functions of the tissue.

278 Routine blood markers have been previously shown to indicate changes in relative
279 nutritional status, inflammation and have prognostic abilities. In this study, albumin,
280 CRP, the CRP-albumin ratio and urea were measured and related to clinical
281 outcomes in patients. Albumin levels were found to be typically low across all
282 patients (30.5 ± 5.9 g/l), potentially indicating a combination of malnutrition and
283 inflammation burden. However, there was no significant difference with patients
284 grouped by mortality at 12 months (Table 1), or significant predictive ability by ROC
285 curve analysis (Figure 3). Grouping patients by albumin classification of malnutrition
286 (Table 3) showed that there were a greater proportion of people who died with lower
287 albumin scores, with a trend for TMFFD and LOS to be higher and a highly
288 significant relationship with CRP (lower albumin, higher CRP). There was also a
289 significant correlation relationship between albumin and MNA-SF score (Figure 1).

290 Furthermore, there were 7 patient deaths in hospital of which 6 had albumin data
291 available (24.5 ± 3.7 g/l), and was found to be significantly lower ($P < 0.05$) than the
292 patients who were alive at 12 months or those that died post hospital discharge. This
293 is in-line with other observations that albumin is a known predictor of mortality¹⁴⁻¹⁶.

294 Albumin may be an important measurable nutritional domain which should be
295 considered in relation to inflammation burden and weight loss, despite recently being
296 observed to not be related to body composition-related nutritional status²⁷. Albumin
297 levels are also utilised within clinically determining cachexia presence (along with
298 weight loss, BMI, presence of inflammation etc.), and is a key component of the

299 GNRI^{9,12}. In particular, the GNRI has been shown to have good prognostic abilities
300 including within a recent Egyptian study which found that the GNRI had better
301 prognostic ability than the MNA²⁸.

302 CRP is another known prognostic indicator and CRP data was collected and
303 assessed in patients (Table 1) as an indicator of inflammatory stress. Levels were
304 clinically significant across the group indicating effects of illness, but there was no
305 significant difference between patients grouped by mortality at 12 months. ROC
306 curve analysis confirmed that neither CRP nor the CRP-albumin albumin were
307 significant predictors of mortality in this group.

308 Finally, urea was significantly higher in the patients who died at 12 months (Table 1),
309 but was found not to be a significant predictor of mortality outcome by ROC curve
310 analysis. Increases in urea may be predictable in this setting indicating higher whole
311 body protein catabolism, due to illness and associated inflammatory stress, and
312 alterations in kidney function. Blood urea nitrogen has been observed to be an
313 independent predictor of mortality outcome in different patient groups including in
314 cardiovascular diseases and acute coronary syndromes²⁹. Pan et al showed recently
315 in older ICU patients that both albumin and urea act as independent and synergistic
316 predictors of mortality³⁰.

317 Study limitations include the patient number which may have meant that some
318 analyses were underpowered (e.g. ROC curve analysis of mortality prediction). The
319 lack of significant relationships with the specific blood markers (e.g. ROC curve
320 analysis, Figure 3) is not surprising as circulating concentrations are highly variable
321 (e.g. albumin and CRP) with many factors affecting them^{14-18,28}. In addition, this was
322 a single sample collection. The use of BIA and the Kyle equation for FFM estimation
323 is discussed elsewhere as a potential limitation¹⁰. Furthermore, another criticism may

324 be the high heterogeneity of frail older people, but this study reflects ‘real-world’
325 medicine and chosen screening and assessment tools must be practically effective
326 in this population.

327 In conclusion, we previously showed discordance between MUST and MNA-SF risk
328 categorisation in frail older hospital patients¹⁰. This paper suggests that discordance
329 is not only theoretical but may have practical implications for outcome in this group.
330 The MNA-SF is a simple tool and in combination with body composition
331 measurements and blood markers may better categorise frail older patients with
332 respects to their nutritional status and possible clinical outcomes, including mortality
333 risk. Further research is necessary in larger patient cohorts as there are potential
334 healthcare, clinical outcome and economic factors implicated.

335

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338

339 **Statement of Authorship**

340 Adrian Slee was the lead author and designated study Chief Investigator, David
341 Stokoe was the designated clinical Principal Investigator; Deborah Birch was a
342 clinical co-investigator involved in data collection and critical input into both the study
343 and manuscript preparation.

344

345

346 **Conflict of Interest**

347 The authors declare that there are no conflicts of interest.

348

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461 **Highlights**

- 462 • The standard routine tool used for malnutrition risk screening in the United
463 Kingdom, the 'MUST', may lack diagnostic accuracy and predictive ability in
464 determining mortality risk in frail older hospital patients.
- 465 • The MNA-SF tool appears to be a more accurate tool in determining malnutrition
466 risk and prediction of mortality risk in this patient group.
- 467 • A potential BMI paradox is highlighted whereby mortality is greater in patients
468 who have a normal range BMI compared to overweight.
- 469 • The fat mass and fat mass index measurements may be predictive of mortality
470 risk in this patient group and requires further study.
- 471 • A combination of methods (e.g. the MNA-SF, body composition assessment and
472 blood markers) may be clinically useful in determining nutritional
473 status/malnutrition risk in this patient group and possible clinical outcomes, such
474 as mortality.

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