

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 ( $25.0 \pm 22.9$  vs  $15.4 \pm 12.7$ d,  $P < 0.05$ ). BMI ( $23.8 \pm 4.9$  vs  $26.4 \pm 5.5$ kg/m<sup>2</sup>);  
39 fat mass (FM) ( $17.2 \pm 9.9$  vs  $25.5 \pm 10.5$ kg), fat mass index (FMI) ( $9.3 \pm 4.1$  vs  
40  $17.9 \pm 2.4$ kg/m<sup>2</sup>); and MNA-SF score ( $6.6 \pm 2.4$  vs  $8.6 \pm 2.7$ ) were significantly lower  
41 ( $P < 0.05$ ), and urea significantly higher ( $11.4 \pm 8.7$  vs  $8.8 \pm 4.4$ mmols/l,  $P = 0.05$ ).  
42 Albumin was typically low across the entire group ( $30.5 \pm 5.9$  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)

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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 mortality<sup>1-4</sup>. Different  
59 screening methods exist including the '*malnutrition universal screening tool*'  
60 (MUST)<sup>1,5</sup>, the '*mini-nutritional assessment*' (MNA)<sup>1,6-8</sup> and the '*geriatric nutritional*  
61 *risk index*', (GNRI)<sup>9</sup>. 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 tool<sup>4</sup>. 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 categorisation<sup>10</sup>. 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/m<sup>2</sup>). 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<sup>11,12</sup>. 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 GNRI<sup>9</sup>, and  
85 is a well known prognostic marker<sup>13-16</sup>. C-reactive protein (CRP) is another routine  
86 blood marker indicating inflammatory status and has known prognostic potential<sup>17,18</sup>.  
87 Recently, the CRP/albumin ratio has been used to better predict mortality risk in  
88 septic patients<sup>19</sup>.

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 patients<sup>10</sup>. 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 previously<sup>10</sup>, 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 previously<sup>10</sup>.

### 128 ***Bioelectrical impedance measurements***

129 BIA measurements were performed as described previously<sup>10</sup>, using the Kyle et al<sup>20</sup>  
130 equation for estimation of FFM (kg) and FM (kg) and index values, FFMI (kg/m<sup>2</sup>) and  
131 FMI (kg/m<sup>2</sup>), and compared to reference values<sup>21</sup>.

### 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 al<sup>9</sup>, 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 patients<sup>22</sup>. 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 previously<sup>10</sup> 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
<b>N</b>	54 (69%)	24 (31%)
<b>Males/females</b>	30/24 (56%/44%)	19/5 (79%/21%)
<b>Age, y</b>	81.7 $\pm$ 7.4 (65-93) [83]	83.0 $\pm$ 8.8 (62-96) [84]
<b>TMFFD, d</b>	8.5 $\pm$ 7.6 (0-37) [7]	10.4 $\pm$ 13.8 (0-66) [6]
<b>LOS, d</b>	15.4 $\pm$ 12.7 (2-68) [10]	25.0 $\pm$ 22.9 (6-102) [19]*
<b>BMI, kg/m<sup>2</sup></b>	26.4 $\pm$ 5.5 (17.2-45.1) [26.3]	23.8 $\pm$ 4.9 (16.6-37.2) [23.3]*
<b>MUST score</b>	0.4 $\pm$ 0.8 (0-4) [0]	0.6 $\pm$ 1.1 (0-4) [0]
<b>MUST – ‘Low risk’</b>	43 (80%)	17 (71%)
<b>MUST – ‘Medium risk’</b>	5 (9%)	2 (8%)
<b>MUST – ‘High risk’</b>	6 (11%)	5 (21%)
<b>MNA-SF score</b>	8.6 $\pm$ 2.7 (3-14) [8.5]	6.6 $\pm$ 2.4 (2-11) [7]*
<b>MNA-SF – ‘Normal’</b>	7 (13%)	0 (0%)
<b>MNA-SF – ‘At risk’</b>	26 (50%)	9 (46%)
<b>MNA-SF – ‘Malnourished’</b>	21 (37%)	15 (54%)
<b>Urea (mmols/l)</b>	8.9 $\pm$ 4.3 (3.1-21.1) [7.8]	11.4 $\pm$ 8.7 (1.7-43.9) [10]*
<b>CRP (mg/l)</b>	56.1 $\pm$ 67.4 (0.6-287) [25]	78.6 $\pm$ 73.6 (2.1-221) [44.5]
<b>Albumin (g/l)</b>	31.0 $\pm$ 6.1 (15-43) [31]	29.4 $\pm$ 5.2 (20-39) [29]
<b>CRP-albumin ratio</b>	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).

169

170

171 **Table 2.** Comparison of BIA data for FFM and FM and index values (FFMI and FMI  
172 in kg/m<sup>2</sup>) 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)
<b>Males/Females</b>	27/21 (56%/44%)	15/3 (83%/17%)
<b>FFM, kg</b>	49.4±9.2 (31.7-72.0) [49.6]	51.5±9.7 (37.5-72.7) [50.7]
<b>FFMI, kg/m<sup>2</sup></b>	17.5±2.5 (13.2-23.5) [17.5]	17.9±2.4 (13.5-22.2) [17.8]
<b>FM, kg</b>	25.5±10.5 (3.4-50.6) [22.5]	17.2±9.9 (3.1-42) [18.1]*
<b>FMI, kg/m<sup>2</sup></b>	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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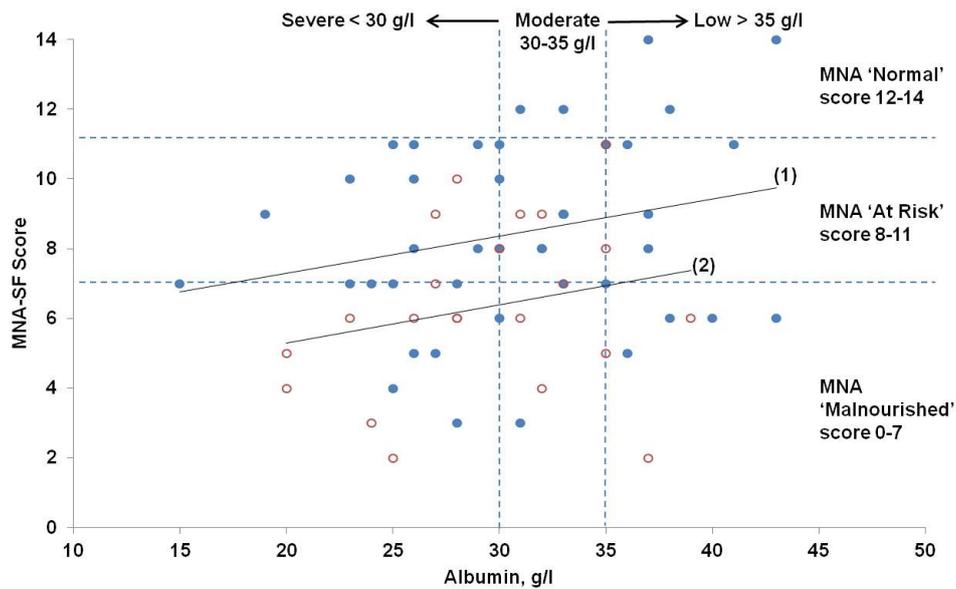
187 **Table 3.** Patients grouped by albumin classification of malnutrition status. Mean  $\pm$   
 188 SD is presented with (minimum-maximum) and [median] values for comparison.

	Plasma albumin & malnutrition status		
	<30 g/l – severe	30-34.9 g/l - moderate	>35 g/l – low/absent
<b>Albumin, g/l</b>	25 $\pm$ 3.3 (15-29) [26]*	31.6 $\pm$ 1.2 (30-33) [32]	37.5 $\pm$ 2.6 (35-43) [37]
<b>N (%)</b>	28 (42%)	19 (29%)	19 (29%)
<b>Deaths, N (%)</b>	11 (39%)	6 (32%)	5 (26%)
<b>TMFFD, d</b>	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]
<b>LOS, d</b>	25 $\pm$ 21.6 (4-102) [19]*†	17.6 $\pm$ 15.4 (2-68) [16]	14.1 $\pm$ 9.5 (2-33) [12]
<b>BMI, kg/m<sup>2</sup></b>	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]
<b>MUST- ‘Low risk’</b>	23 (82%)	16 (84%)	14 (74%)
<b>MUST – ‘Medium risk’</b>	2 (7%)	2 (11%)	1 (5%)
<b>MUST – ‘High risk’</b>	3 (11%)	1 (5%)	4 (21%)
<b>MNA-SF score</b>	7.0 $\pm$ 2.5 (2-11) [7]	8.2 $\pm$ 2.4 (3-12) [8]	8.6 $\pm$ 3.3 (2-14) [8]
<b>MNA-SF – ‘Normal’</b>	0 (0%)	2 (10%)	3 (16%)
<b>MNA-SF – ‘At risk’</b>	11 (39%)	11 (58%)	8 (42%)
<b>MNA-SF – ‘Malnourished’</b>	17 (61%)	6 (32%)	8 (42%)
<b>Urea, mmols/l</b>	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]
<b>CRP, mg/l</b>	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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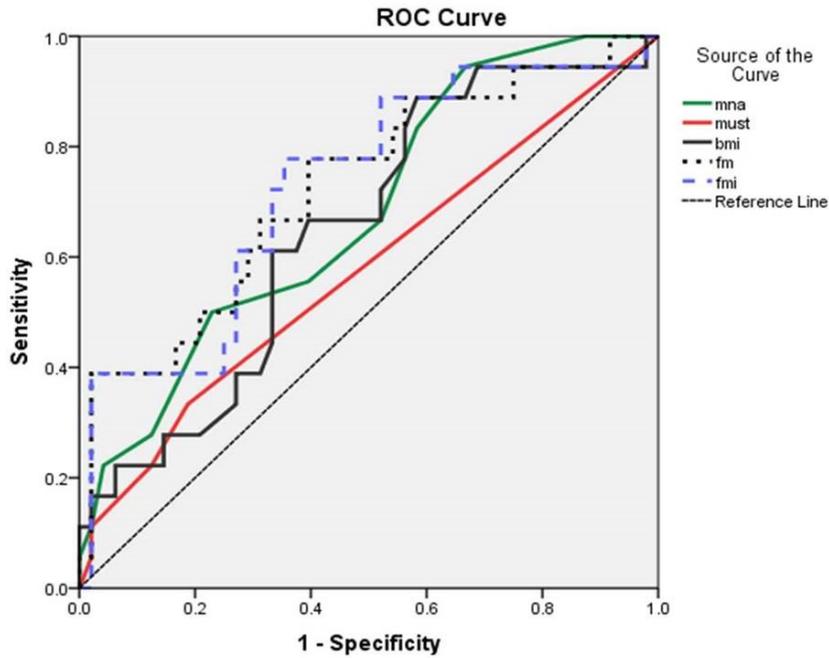
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195 **Figure 1.** The relationship between plasma albumin (g/l) and MNA-SF score in  
 196 patients where albumin data was available (n=66). Relevant cut-points indicating  
 197 malnutrition are shown for both MNA-SF and albumin. Patients alive at 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.



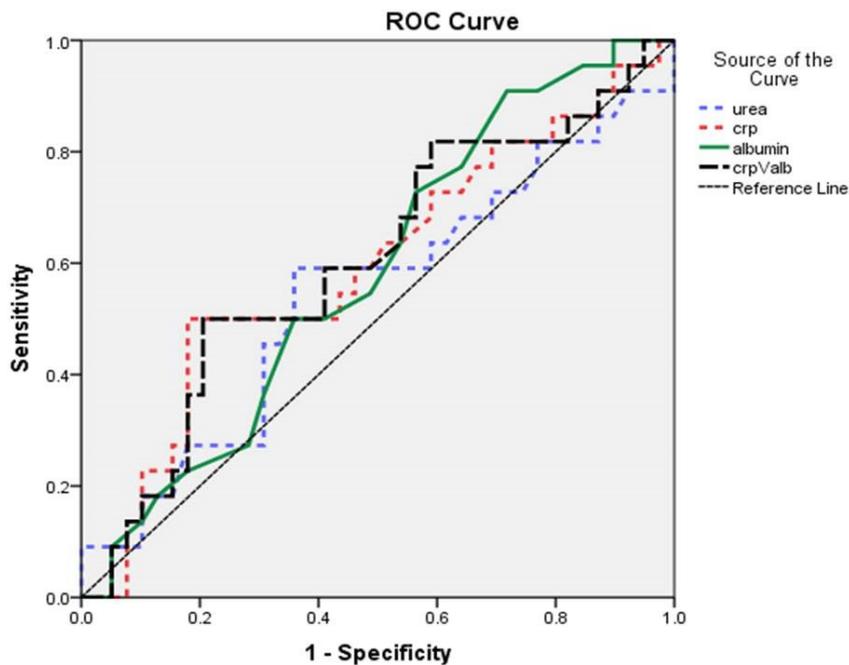
Area Under the Curve

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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208

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

213

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 patients<sup>10</sup>. 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 MUST<sup>23</sup>. 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 patients<sup>4</sup>. 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 factors<sup>3</sup>. However, Vischer et al, failed to show a predictive effect of MNA-SF in  
251 hospitalised older patients with a heavy disease burden<sup>24</sup>. 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 period<sup>24</sup>. 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/m<sup>2</sup>). 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 paradox<sup>25</sup>, 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 patients<sup>26</sup>. 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/m<sup>2</sup>)<sup>10</sup>. 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 ( $30.5\pm 5.9$  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 ( $24.5\pm 3.7$  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 mortality<sup>14-16</sup>.

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 status<sup>27</sup>. 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<sup>9,12</sup>. 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 MNA<sup>28</sup>.

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 syndromes<sup>29</sup>. Pan et al showed recently  
315 in older ICU patients that both albumin and urea act as independent and synergistic  
316 predictors of mortality<sup>30</sup>.

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<sup>14-18,28</sup>. 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 limitation<sup>10</sup>. 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 patients<sup>10</sup>. 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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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.

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346 **Conflict of Interest**

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

348

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- 460

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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