Risk factors of refeeding syndrome in malnourished older hospitalized patients

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Summary

Background & aims: Despite the high prevalence of malnutrition among older hospitalized persons, it is unknown how many of these malnourished patients are at risk of developing the refeeding syndrome (RFS). In this study, we sought to compare the prevalence and severity of malnutrition among older hospitalized patients with prevalence of known risk factors of RFS.

Methods: This cross-sectional multicenter-study investigated older participants who were consecutively admitted to the geriatric acute care ward. Malnutrition screening was conducted using Nutritional Risk Screening (NRS-2002), Malnutrition Universal Screening Tool (MUST) and Mini Nutritional Assessment-Short Form (MNA-SF). The National Institute for Health and Clinical Excellence (NICE) criteria were applied for assessing patients at risk of RFS. Weight and height were measured. Degree of weight loss (WL) was obtained by interview. Serum phosphate, magnesium, potassium, sodium, calcium, creatinine and urea were analyzed according to standard procedures.

Results: The study group comprised 342 participants (222 females) with a mean age of 83.1 ± 6.8 and BMI range of 14.7–43.6 kg/m². More participants were assessed at risk of malnutrition using NRS-2002 (n = 253, 74.0%) compared to MUST (n = 170, 49.7%) and MNA-SF (n = 191, 55.8%). Of total participants, 239 (69.9%; 157 females) were considered to be at risk of RFS. Based on NRS-2002, 75.9% (n = 192) of patients at risk of malnutrition are at risk of RFS whereas according to MUST and MNA-SF, 85.9% (n = 146) and 69.1% (n = 132) of patients at risk of malnutrition are exposed to high risk of RFS, respectively. In addition, the prevalence of risk of RFS is significantly increased with higher score of NRS-2002 and MUST and lower score of MNA-SF. In a stepwise multiple regression analysis, disease severity (38.2%), WL in 3 months (20.3%) and BMI (33.3%) mainly explained variance in NRS-2002, MUST and MNA-SF scores, respectively, in patients with risk of RFS.

Conclusion: Nearly three-quarters of geriatric hospitalized patients with risk of malnutrition demonstrated significant risk of RFS. Therefore, additional screening for risk of RFS in patients screened for malnutrition appears to be advisable among this population.

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1. Introduction

Refeeding syndrome (RFS) can be defined as a clinical complex which encompasses acute fluid and electrolyte disturbances (i.e. phosphate, potassium, magnesium, sodium) and thiamin deficiency associated with metabolic abnormalities in starved individuals as a consequence of reintroduction of feeding whether...
orally, enterally or parenterally [1]. The symptoms may be various and very unpecific and often occur 2–5 days after the start of refeeding [2,3]. RFS is associated with high mortality; however, it is frequently unrecognized [3,4]. As there is no precise and unique definition of RFS, unsurprisingly the incidence of RFS is unknown. However, the criteria of the National Institute for Health and Clinical Excellence (NICE) guidelines [5] are recognized as a useful tool for identifying and screening patients at high risk of developing RFS.

RFS may occur usually in malnourished patients undergoing refeeding after a period of undernutrition [1,6]. Malnutrition is the most predominant and frequent clinical risk factor among elderly people who are prone for developing RFS due to many underlying comorbidities [4,7]. Results of the previous studies [8,9] reveal the significant possibility for RFS and it is tempting to speculate the link between comorbidity, malnutrition and RFS. Malnutrition is related with high risk of complications such as low quality of life, increased length of hospital stay and higher mortality and morbidity [10,11]. Although, the prevalence of malnutrition is high among hospitalized elderly people, it remains a widely unrecognized and under-treated problem in this population [12,13].

Accordingly, identification and early treatment of older individuals at risk of malnutrition is essential due to minimizing its occurrence and avoiding mortality and morbidity related with this phenomenon [14]. Several screening tools have been established to assess the risk and degree of malnutrition for use in elderly or hospital populations that apply the variables like BMI, recent poor intake and weight loss as well as severity of disease. The Mini-Nutritional Assessment Short Form (MNA-SF) has been proposed as an effective tool for screening the nutritional status of geriatrics across settings [15]. In contrast to MNA-SF, the Malnutrition Universal Screening Tool (MUST) [16] and the Nutritional Risk Screening 2002 (NRS-2002) [17] proposed by the European Society for Clinical Nutrition and Metabolism (ESPEN) for the hospital setting [18,19] are applicable to all hospital patients, irrespective of age.

RFS in not usually considered as a common condition to investigate in older people presenting with undernourishment. Namely, the risk of RFS is mostly not measured among hospitalized or institutionalized elderly persons even if malnutrition is evident. Thus, it remains unclear how many of older individuals with malnutrition have to be considered at risk of RFS. As malnutrition is the main risk factor for RFS, routine malnutrition screening should also screen for risk of RFS [20]. Unfortunately, the criteria of malnutrition screening tools and the NICE criteria for risk of RFS differ substantially. In addition, screening for malnutrition and screening for risk of RFS with different tools and criteria appears to be unpractical and somehow redundant. In this study, we sought to compare the prevalence and severity of malnutrition among older hospitalized patients with prevalence of known risk factors of RFS.

2. Subjects and methods

2.1. Study design and subjects

This prospective cross-sectional study was undertaken between July 2015 and February 2016 at six acute geriatric hospital departments in Germany. The study population comprised 342 consecutive hospitalized elderly participants (222 females) with aged between 60 and 100 years. The study protocol had been approved by the ethical committee of Friedrich-Alexander-University, Erlangen-Nürnberg. Exclusion criteria from the study were: age < 60 years, missing or withdrawn consent of the patients, hypercalcemia, primary hyperparathyroidism and inability to cooperate.

2.2. Anthropometric measurements

Weight was measured in the morning, in light clothing with an empty bladder on a chair scale (Seca Chair Scale 956, Hamburg, Germany).

Body weight was assessed in light clothing with an accuracy of 0.1 kg, and height was measured to the nearest 0.5 cm with a stadiometer in first day after admission to hospital. The degree of unintentional weight loss (WL) was obtained either by interviewing the patients and their relatives, if competent, or asking their proxy, where necessary. Calf circumference was measured as part of the MNA-SF in a sub-group of 308 patients. Patient’s medication histories were obtained at least within 24 h after hospital admission either through interview or from the medication lists of the general practitioner. All information including malnutrition screening was recorded by attending physician.

2.3. Malnutrition screening tools

The risk of malnutrition was evaluated using NRS-2002, MUST and MNA-SF on the day after hospital admission.

2.3.1. NRS-2002

According to the developing authors [17], the initial screening of NRS-2002 was skipped, because of the high prevalence of malnutrition in the geriatric hospital patients. The final screening of the NRS-2002 consists of two criteria: impaired nutritional status based on WL, food intake and BMI (1–3 points) and severity of disease (1–3 points). Further, for older patients > 70 years, one point to the total score was added. Patients were grouped as no risk (<3 points) or at risk (≥3 points).

2.3.2. MUST

The MUST [16] includes/considers information on BMI, unintentional WL in the last 3–6 months (0–2 points), presence of acute disease (0–2 points) and absence of food intake > 5 days (0 or 2 points). Participants are stratified as low risk (0 points), medium risk (1 point) and high risk (≥2 points).

2.3.3. MNA-SF

The MNA-SF [15] is a revised screening tool] reduced version of the Mini-Nutritional Assessment (MNA) which assesses reduction in food intake, WL during last 3 months, mobility, psychological stress and acute diseases, neuropsychological problems and BMI. Patients are classified as having normal nutritional status (12–14 points), at risk of malnutrition (8–11 points) and malnourished (0–7 points).

2.4. Refeeding syndrome

NICE criteria [5] have been applied for assessing patients at risk of RFS. Subjects with at least one of the following major parameters (BMI < 16 kg/m², unintended WL > 15% in last 3–6 months, no nutrition intake > 10 days, low concentration of plasma magnesium, potassium or phosphate before feeding) or with two of the following minor features (BMI < 18.5 kg/m², unintended WL > 10% in last 3–6 months, no nutrition intake > 5 days, medical history of alcohol or drug abuse) of NICE criteria were considered to be at high risk of RFS.

2.5. Laboratory methods

Blood tests were performed on the day of admission at each hospital clinical chemistry laboratory and serum phosphate, magnesium, potassium, sodium, calcium, creatinine and urea were
analyzed according to local standard procedures. Serum phosphate level < 0.8 mmol/l was defined as hypophosphatemia. In addition, serum magnesium and potassium levels < 0.70 mmol/l and 3.5 mmol/l were considered as hypomagnesemia and hypokalemia, respectively.

2.6. Data analysis

The statistical analysis was completed using SPSS statistical software (SPSS Statistics for Windows, IBM Corp, Version 23.0, Armonk, NY, USA). Continuous variables are reported by means and standard deviations (SDs). Categorical variables have shown as n (%). In order to compare the nutritional screening tools, the results of each tool were classified into two groups: malnourished or at risk of malnutrition (NRS-2002, risk of malnutrition with score ≥ 3; MUST, from medium to high risk of malnutrition with score 1 and more; and MNA-SF, at risk of malnutrition and malnourished with 0–11 points) and not at risk of malnutrition (NRS-2002, no risk of malnutrition with score < 3; MUST, low risk of malnutrition with score 0; and MNA-SF, normal nutritional status with scores 12–14). Differences between females and males and between malnourished patients at risk of RFS and not at refeeding risk were analyzed by using an unpaired t test in normally distributed variables. Categorical variables were compared by the Chi square test. Pearson’s correlation was applied for normally distributed variables whereas Spearman’s correlation was used for nonparametric data. Stepwise multiple regression analysis was performed to explain the effect of individual screening tools’ questions such as BMI, WL in last 3 months, no food intake, calf circumference and disease severity (as independent variables) on the variance of each screening tools’ scores (as dependent variable). P < 0.05 was determined as the limit of significance.

3. Results

Baseline characteristics and laboratory data of study participants stratified by gender are presented in Table 1. The study group comprised 342 participants (222 females) with a mean age of 83.1 ± 6.8 (age range between 60 and 100 years). According to the respective MNA-SF items, 45.3% of the study participants (155 subjects) have displayed mild degree of dementia, 42% had no prevalence of risk of RFS is higher in severe malnourished patients (MUST, of 170 older individuals at medium and high risk of malnutrition, 146 patients (85.9%) are at risk of RFS whereas all patients with MUST score 3 or more are exposed to high risk of RFS. Moreover, based on MNA-SF, of 191 older subjects at risk or malnourished, 132 patients (69.1%) are at risk of RFS while the prevalence of risk of RFS is higher in severe malnourished patients with lower score (score < 5; Table 2). In addition, the prevalence of hypophosphatemia is excessively raised in malnourished patients ranged from 13.3% at score of 7–44.4% at score of 5.

Further, in order to compare the results, participants were stratified into two groups, subjects at risk of malnutrition and subjects not at risk of malnutrition. Figure 1a demonstrates the frequency of nutritional status categorization for subjects using MUST, NRS-2002 and MNA-SF. More participants were assessed at risk of malnutrition using NRS-2002 (74%) compared to MUST (49.7%) and MNA-SF (55.8%). In addition, using these nutritional screening tools, the prevalence of risk of RFS is considerably higher compared to not at risk of RFS in malnourished older patients (Fig. 1b).

There were significant differences in actual body weight, BMI, calf circumference and magnitude of WL (% in last 6 months) showed a wide BMI range from 14.7 to 43.6 kg/m² with no sex differences (P = 0.916). Compared with males, females had significantly lower actual body weight, height, calf circumference and WL during last six months. There were no significant differences in all laboratory data between sexes, except for creatinine with lower values in females than males (P < 0.01). According to the guidelines of the NICE criteria, 69.9% of total study population (239 subjects) was considered to be at risk of RFS. In addition, 51 participants (14.9%) had hypophosphatemia as a hallmark of RFS.

The performance of each screening tool to identify malnutrition determined by NRS-2002, MUST and MNA-SF in total population and refeeding risk group are given in Table 2. In total study population, based on NRS-2002, 89 patients (26%) had no risk of malnutrition and 253 subjects (74%) were at risk of malnutrition. Of these 253 malnourished participants, 192 patients (75.9%) are at risk of RFS. The incidence of risk of RFS significantly increased with higher risk score.

In addition, the prevalence of patients at nutritional risk according to MUST and MNA-SF tools in total population was as follows: MUST (at medium risk, 17 patients, 5%; at high risk, 153 patients, 44.7%), MNA-SF (at risk of malnutrition, 153 patients, 44.7%; malnourished, 38 patients, 11.1%; Table 2). According to MUST, of 170 older individuals at medium and high risk of malnutrition, 146 patients (85.9%) are at risk of RFS whereas all patients with MUST score 3 or more are exposed to high risk of RFS. Furthermore, based on MNA-SF, of 191 older subjects at risk or malnourished, 132 patients (69.1%) are at risk of RFS while the prevalence of risk of RFS is higher in severe malnourished patients with lower score (score < 5; Table 2). In addition, the prevalence of hypophosphatemia is excessively raised in malnourished patients ranged from 13.3% at score of 7–44.4% at score of 5.

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There were significant differences in actual body weight, BMI, calf circumference and magnitude of WL (% in last 6 months)
Table 2
Nutritional status categorization (n; %) in total study population (n = 342) and according to the NICE criteria.

<table>
<thead>
<tr>
<th>Malnutrition screening tools</th>
<th>Total population (n = 342; F = 222)</th>
<th>NICE&lt;sup&gt;a&lt;/sup&gt;</th>
<th>At risk of RFS</th>
<th>Not at risk of RFS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 239; F = 156)</td>
<td>(n = 103; F = 66)</td>
<td></td>
<td></td>
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<tr>
<td><strong>NRS-2002 (n; %)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No risk of malnutrition (score &lt; 3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Score 2</td>
<td>89; 26.0</td>
<td>47; 52.8</td>
<td>42; 47.2</td>
<td></td>
</tr>
<tr>
<td>At risk of malnutrition (score ≥ 7)</td>
<td>253; 74.0</td>
<td>192; 75.9</td>
<td>61; 24.1</td>
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<tr>
<td>Score 3</td>
<td>101; 29.5</td>
<td>69; 68.3</td>
<td>32; 31.7</td>
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<td>Score 4</td>
<td>74; 21.6</td>
<td>57; 77.0</td>
<td>17; 23.0</td>
<td></td>
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<tr>
<td>Score 5</td>
<td>56; 16.4</td>
<td>45; 80.4</td>
<td>11; 19.6</td>
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<tr>
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<td>50; 15.0</td>
<td>19; 85.0</td>
<td>1; 99.0</td>
<td></td>
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<tr>
<td>Score 7</td>
<td>2; 0.6</td>
<td>2; 100</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td><strong>MUST (n; %)</strong></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Low risk (score 0)</td>
<td>172; 50.3</td>
<td>93; 54.1</td>
<td>79; 45.9</td>
<td></td>
</tr>
<tr>
<td>Medium risk (score 1)</td>
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<td>9; 52.9</td>
<td>8; 47.1</td>
<td></td>
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<tr>
<td>High risk (score 2 or more)</td>
<td>153; 44.7</td>
<td>137; 89.5</td>
<td>16; 10.5</td>
<td></td>
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<tr>
<td>Score 2</td>
<td>113; 33.0</td>
<td>97; 85.8</td>
<td>16; 14.2</td>
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<tr>
<td>Score 3</td>
<td>24; 7.0</td>
<td>24; 100</td>
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<td>3; 100</td>
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<tr>
<td>Score 6</td>
<td>1; 0.3</td>
<td>1; 100</td>
<td>–</td>
<td></td>
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<tr>
<td><strong>MNA-SF (n; %)</strong></td>
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<td></td>
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<tr>
<td>Normal nutritional status</td>
<td>151; 44.2</td>
<td>107; 70.9</td>
<td>44; 29.1</td>
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<tr>
<td>(Score 12–14)</td>
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<td>Score 14</td>
<td>31; 9.1</td>
<td>20; 64.5</td>
<td>11; 35.5</td>
<td></td>
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<tr>
<td>Score 13</td>
<td>61; 17.8</td>
<td>44; 72.1</td>
<td>17; 27.9</td>
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<tr>
<td>Score 12</td>
<td>49; 14.3</td>
<td>34; 69.4</td>
<td>15; 30.6</td>
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<tr>
<td>At risk of malnutrition</td>
<td>153; 44.7</td>
<td>104; 68.0</td>
<td>49; 32.0</td>
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<tr>
<td>(Score 8–11)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score 11</td>
<td>52; 15.2</td>
<td>34; 65.4</td>
<td>18; 34.6</td>
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<td>Score 10</td>
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<td>26; 66.7</td>
<td>13; 33.3</td>
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<td>31; 9.1</td>
<td>20; 64.5</td>
<td>11; 35.5</td>
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<tr>
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<td>31; 9.1</td>
<td>24; 77.4</td>
<td>7; 22.6</td>
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<tr>
<td>Malnourished (Score 0–7)</td>
<td>38; 11.1</td>
<td>28; 73.7</td>
<td>10; 26.3</td>
<td></td>
</tr>
<tr>
<td>Score 7</td>
<td>21; 6.1</td>
<td>15; 71.4</td>
<td>6; 28.6</td>
<td></td>
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<td>9; 2.6</td>
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<td>Score 4</td>
<td>2; 0.6</td>
<td>2; 100</td>
<td>–</td>
<td></td>
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<tr>
<td>Score 3</td>
<td>1; 0.3</td>
<td>1; 100</td>
<td>–</td>
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</tbody>
</table>

Total patients (n; %) for each category are indicated in bold print.

<sup>a</sup> According to the guidelines of NICE criteria, F; females.

Fig. 1. a) Prevalence of risk of malnutrition according to NRS-2002, MUST and MNA-SF in total study population (n = 342) and b) Prevalence of risk of refeeding syndrome (RFS) in malnourished older patients using NRS-2002 (n = 192 at risk of RFS, n = 61 not at risk of RFS), MUST (n = 146 at risk of RFS, n = 24 not at risk of RFS) and MNA-SF (n = 132 at risk of RFS, n = 59 not at risk of RFS). ***P < 0.001 difference between at risk of RFS and Not at risk RFS within groups (unpaired t test).

4. Discussion

Malnutrition in elderly people is a serious concern and is related with high risk of complications such as increased infection risk, low quality of life and increased mortality and morbidity [10,11]. Previous studies have shown that up to 50% of hospitalized older people [21,22] and 30% of elderly nursing home residents [21] have some degree of malnutrition. In a multi-center prospective study in 13 German hospitals, Pirlich et al. reported that of all consecutively admitted patients (mean age 62.2 ± 17.4), every fourth patient is malnourished at admission or has a risk of becoming malnourished during hospital stay [23]. In that study 43% of all patients > 70 years and 56% of all patients in the geriatric department were considered to be malnourished.

Numerous studies and guidelines have suggested that nutritional screening is fundamental to identify patients at risk of malnutrition or who are malnourished and to manage nutritional determining patients at high risk of malnutrition and RFS concurrently are given in Table 3. According to each nutritional screening tool, subjects at risk of malnutrition and RFS had significantly higher WL during the last 6 months (P < 0.001) and lower magnesium and potassium levels than the malnourished patients not at risk of RFS, with no differences in age and BMI.

Associations of each screening tool questions to total scores in malnourished older patients at risk of RFS are shown in Table 4. Significant correlations were observed between each screening tool question to total scores except for mobility and neuropsychological problems. Further, there were no significant differences between MUST scores and disease severity and between MNA-SF scores and no food intake for >5 days.

In a stepwise multiple regression analysis on malnourished older patients at risk of RFS, the effects of individual screening tools’ questions such as BMI, WL in last 3 months, no food intake, calf circumference and disease severity (as independent variables) on the variance of each screening tools’ scores (as dependent variable) were tested (Table 5). According to NRS-2002, disease severity and no food intake explained 38.2% and 24.5% of the variance in NRS-2002 scores, respectively whereas BMI and WL in 3 months explained additional 14%. Based on MUST, WL in 3 months explained 20.3% of the variance in MUST scores and no food intake for >5 days and BMI explained additional 13% and 11.6%, respectively. In MNA-SF, 33.3% of the variance in MNA-SF scores explained mainly by BMI and 8.5% of the variance explained by WL in 3 months and calf circumference (Table 5).

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Table 3
Characteristics and laboratory data of the study population (n = 342) stratified by three different nutritional screening tools (Mean ± SD).

Table 4
Correlations of each malnutrition screening tool questions to total malnutrition screening scores in malnourished older patients at risk of refeeding syndrome.

Table 5
Results of multiple regression analysis with malnutrition screening tools’ scores as dependent variable and malnutrition screening tools’ questions as independent variables in patients at risk of refeeding syndrome (n = 239).

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acceptable to assume the substantial probability of RFS among frail and malnourished older patients [29]. RFS is a potentially fatal condition and is considered to be a serious clinical problem, particularly, in the population of hospitalized older patients [6]. In the current study, according all three screening tools, three-quarters or more of geriatric hospitalized patients with risk of malnutrition demonstrated significant risk of RFS (see Fig. 1b). Indeed, if MUST-score is above 1, the risk of RFS is 89.5%. Therefore, additional screening for RFS in patients screened for malnutrition appears to be abdicable among this population. However, it would be worthwhile to mention that based on NICE guidelines [5], older subjects at high risk of RFS should be closely monitored for their vital functions [3], electrolytes (i.e. phosphate, magnesium, potassium, sodium) and thiamine while energy supplementation should start with half of demands, and can then be constantly increased to provide adequate nutrition needs after four to seven days [3].

Some limitations of the current study should be discussed. We did not demonstrate the real occurrence of RFS and therefore it remains unclear how severe the risk of RFS really was. Moreover, development of electrolyte disturbances over time and any type of nutritional therapy have not been addressed in this research. Consequently, more research data are required to provide detailed information about occurrence of RFS in older patients to develop the best preventative strategies.

5. Conclusion

This study indicates a high prevalence of malnutrition in older patients with different established nutritional screening tools used. Approximately three-quarters of geriatric hospitalized patients with risk of malnutrition demonstrated significant risk of RFS. Accordingly, further screening for risk factors of RFS in patients screened for malnutrition appears to be abdicable among this population.

Statement of authorship

The study was designed by all authors. Data were obtained by RW, IC, IG, CM, MKM and PHW. Statistical analysis was performed by MP, MP, DV and RW prepared the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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