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ABSTRACT

Background: The Royal College of Physicians recently introduced the 4AT (Alertness, Abbreviated Mental Test-4, Attention and Acute change or fluctuating course) for screening patient cognitive impairment and delirium. The 4AT and nutritional status are both indicators of health status, but their relationship has not been studied. Here, we examined the association of the 4AT with nutritional status in patients admitted to a single hospital with hip fractures between January 1, 2016 and June 6, 2019.

Methods: Nutritional status was assessed using the Malnutrition Universal Screening Tool (MUST) protocol and the 4AT was assessed within 1-day after hip surgery. Differences between categorical outcome variables were tested with chi-squared tests, and logistic regression was conducted to assess the association of nutritional status (dependent variable) with 4AT scores (independent variable).

Results: From 1082 patients (298 men, 784 women: mean age 83.8 \pm 8.7 (SD) years, range=60-103) categorized into 4AT scores of 0, 1-3 or \geq 4, the prevalence of malnutrition risk was 15.5, 27.3 and 39.6% and for malnourishment were 4.1, 13.2 and 11.3%, respectively. After age and sex adjustment, compared with the 4AT=0 cohort, a 4AT score of 1-3 was associated with an increased malnutrition risk: (odds ratio (OR)=2.3, 95% confidence interval (CI)=1.6-3.1), or malnutrition itself (OR =3.6, 95%CI=2.1-6.3). For a 4AT score \geq 4 corresponding ORs were 4.0 (95%CI=2.8-5.9) and 3.6 (95%CI=1.9-6.8) . These associations persisted with additional adjustments for polypharmacy, anticholinergic burden and co-morbidities including dementia, stroke and Parkinson's disease. Overall, there was a significant positive association, whereby as 4AT scores increased, so also did malnutrition risk.

Conclusions: Among older adults admitted with hip fractures, high 4AT scores, suggestive of cognitive impairment and delirium, identified patients at increased malnutrition risk. These findings lend further support for the use of 4AT as a screening tool to identify patients, who are in an acute setting, at increased health risk.

INTRODUCTION

The 4AT (Alertness, Abbreviated Mental Test-4, Attention and Acute change or fluctuating course) has been designed as a simple and practical tool for screening cognitive impairment and delirium.^{1,2} Recently, the 4AT was introduced by the Royal College of Physicians (RCP) to evaluate its clinical effectiveness among older patients admitted to an emergency department with hip fractures.^{3,4} Between 20 and 28% of older adults admitted to hospital have evidence of delirium, based on the 4AT.^{2,5} In a recent study, we found patients with high 4AT scores had increased risk of adverse outcomes from hip surgery, including: failure to mobilise within 1-day; prolonged length of stay; and mortality in hospital.⁵ The association between the 4AT and poor outcomes will be complex but the underlying health of the patient is likely to be a significant factor. Nutritional status reflects the health of an individual; illnesses often lead to a loss of appetite, whilst a lack of adequate nutrition results in physical and mental impairment and impedes recovery from an acute illness. In older populations, malnutrition plays a key role in them sustaining bone fractures by promoting the risk of osteoporosis, or falls because of frailty,⁶ visual impairment, postural instability,⁷ infections,^{8,9} immobility,¹⁰ and cognitive decline.¹¹

Malnutrition (undernutrition), one of five serious nutritional disorders,¹² is defined as “a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease”.¹³ Malnutrition may arise from starvation, illness or advanced aging, or in combination.¹⁴ It may occur in overweight or obese individuals in the setting of an

illness or injury, or lacking the right nutrients even when consuming high-energy diets, such that malnutrition and over-nutrition may co-exist.¹²

Although modern healthcare services in high income countries have significantly improved the general health of the population over the past century, malnutrition remains highly prevalent in older people, particularly those with neuropsychiatric disorders and ranging between 15 and 65%.^{15,16} Because 4AT is a relatively novel tool, there is a lack of data on its relationship with nutritional status. In this study, we sought to examine the association of malnutrition with cognitive impairment and delirium, based on the 4AT in older adults admitted to hospital with a hip fracture.

METHODS

Design, participants and setting

The present study is part of a large study and participates in the National Hip Fracture Database.^{3,5,17} In this study, we analysed a total of 1082 patients over the age of 60 years, admitted with hip fractures between January 1, 2016 and June 6, 2019 to the orthogeriatric ward in a National Health Service (NHS) hospital, serving a population of more than 400,000 people.

Data collection

Data were prospectively collected by a Trauma Coordinator for every patient admitted with a hip fracture from the point of admission to discharge. The data comprised patients' clinical characteristics including demographic factors, nutritional and mental health status, medical and drug history, as well as care quality including outcome measures such as length of stay in hospital, nosocomial complications,

discharge destination, disability and mortality. Co-morbidities including dementia, Parkinson's disease and stroke were identified from electronic record databases by the disease codes classified by the International Classification of Diseases.¹⁸ The data were managed and updated regularly into a database by the orthogeriatrician.

Nutritional status assessment

Nutritional status was assessed using the Malnutrition Universal Screening Tool (MUST) protocol,¹⁹ whereby the overall phenotypic and etiologic scores of 0, 1 and ≥ 2 indicate low, medium and high risk of malnutrition, respectively. Malnourishment was also assessed according to the National Institute for Health and Care Excellence (NICE) guideline²⁰ (**Table 1**) as: a body mass index (BMI) below 18.5 kg/m²; an unintentional weight loss of more than 10% within the last 3–6 months; or a BMI below 20 kg/m² and an unintentional weight loss of more than 5% within the last 3–6 months.²⁰ Nutritional status was classified into three groups: well-nourished (patients without evidence of malnutrition or malnourishment); high risk of malnutrition for patients with MUST score ≥ 2 ; or malnourishment for those who met the NICE criteria.

4AT assessment

The 4AT was measured within one day after hip surgery including 'Alertness', 'AMT4', 'Attention', and 'Acute change or fluctuating course' (**Table 2**).¹ The scores obtained from the components of the 4AT were summated to produce a composite score; (0: unlikely to have delirium or severe cognitive impairment; 1-3: possible cognitive impairment and does not exclude the possibility of delirium; ≥ 4 : possible delirium \pm cognitive impairment).¹

Medications and alcohol consumption

Polypharmacy was defined for patients who were regularly taking four or more different types of medications a day. The anticholinergic burden (ACB) scale was assessed using scores based on the drugs listed by the Aging Brain Program.²¹ Consumption of more than 14 units of alcohol a week, on a regular basis, was considered to be excessive.²²

Statistical analysis

Continuous data are presented as mean and standard deviation (SD). Chi-squared tests tested for differences between categorical outcome variables; logistic regression examined the association of nutritional status (dependent variable) with 4AT scores (independent variable). Four models were presented: *model 1*, unadjusted; *model 2*, adjusted for sex and age; *model 3*, further adjustment to model 2 for alcohol consumption, medications (polypharmacy and ACB) and co-morbidities (stroke, Parkinson's disease, ischaemic heart disease, diabetes); *model 4*, repeat of model 3 with additional adjustment for dementia. Analyses were performed using IBM SPSS Statistics, v25.0 (IBM Corp., Armonk, NY).

RESULTS

A total of 1082 patients admitted with hip fractures (298 men, 784 women), with a mean age 83.8 years (SD = 8.7, range 60-103), were analysed. The proportions of patients who were well-nourished, at risk of malnutrition and with actual malnutrition were 67.8, 23.9 and 8.2%, respectively. Likewise, the proportions of patients with 4AT scores of 0, 1-3 and 4 were 50.0, 29.5 and 20.5%, respectively. The proportion

of those with polypharmacy was 76.2%; those with an ACB score ≥ 1 was 39.8% and score ≥ 2 was 10.0%. There were 4.8% of patients consuming >14 units of alcohol per week, 28.5% of patients with dementia, 4.1% with Parkinson's disease, 15.9% with stroke, 9.7% with ischaemic heart disease and 12.3% with diabetes (**Table 3**). For patients with respective 4AT scores of 0, 1-3 or ≥ 4 , the prevalences of malnutrition risk were 15.5, 27.3 and 39.6% and for actual malnutrition were 4.1, 13.2 and 11.3% (**Figure 1**).

After adjustments for age and sex (model 2) and compared to patients with a 4AT score = 0, a 4AT score of 1-3 was associated with an increased malnutrition risk: odds ratio (OR) = 2.3 (95% confidence interval (CI) = 1.6-3.1), or malnutrition itself: OR = 3.6 (95%CI = 2.1-6.3), and a 4AT score ≥ 4 was also associated with an increased malnutrition risk: ORs = 4.0 (95%CI = 2.8-5.9) or malnutrition itself: OR = 3.6 (95%CI = 1.9-6.8) (**Table 4**). These significant associations were maintained with additional adjustments for polypharmacy, ACB and co-morbidities (model 3) and further inclusion of dementia data (model 4).

DISCUSSION

In this study of adults over 60 years old admitted with hip fractures, those with evidence of cognitive impairment and delirium based on 4AT assessment had increased risk of malnutrition and malnourishment by two- to three-fold, independent of age and sex, medications and co-morbidities (stroke, Parkinson's disease and dementia). In a recent study,⁵ we reported similar findings to those of Rosted et al,²³ that those with 4AT scores ≥ 4 (suggestive of delirium) were at increased risk of

failure to mobilise within one day of hip surgery, had prolonged hospital stay and mortality, independent of malnutrition and malnourishment.

Cognitive impairment/delirium and malnutrition are both important determinants of health outcomes in patients admitted to hospital. Malnutrition remains a challenging aspect of clinical management in older and vulnerable individuals, even in western countries. Previous studies in European countries and Japan have reported variable rates of malnutrition risk (44-48%) and malnourishment (7-37%) in patients admitted to hospital with hip fractures.²⁴⁻³¹ Of interest, in a similar cohort of patients, we have also shown that the incidence of acquiring a new hospital-acquired pressure ulcer was 1% for well-nourished patients, 1.7% for patients with a risk of malnutrition and 5% for malnourished patients (group differences: $\chi^2 = 10.4$, $p = 0.006$).³²

A previous study by Rosted et al showed that compared to patients without evidence of delirium or malnutrition, those with both conditions had four times the risk of mortality in one month follow-up, a seven-fold risk of discharge to nursing homes, and stayed three days longer in hospital.²³ However, due to its relative novelty there exist no previous studies examining the association of cognitive impairment/delirium, based on the 4AT, with nutrition status.

The association between cognitive impairment/delirium (indicated by the 4AT) and malnutrition is complex and likely to be bidirectional, resulting in a vicious cycle. On the one hand, the lack of adequate nutritional intake, especially superimposed by co-existing infections, co-morbidities and a number of drugs, often leads to delirium.³³ On the other hand, patients with cognitive impairment or delirium are at high risk of

malnutrition due to a lack of appetite or dysphagia.¹⁵ There are a number of other factors in play, for example older people with cognitive impairment may have difficulties in expressing their wishes and needs for eating, leading to weight loss,³⁴ while such group of individuals may inadvertently overeat, leading to obesity.³⁵

Overall, evidence from existing studies^{5,23} indicates that attention should be directed to patients with high 4AT scores to identify reversible underlying causes of delirium and other adverse outcomes, with a focus on early and appropriate nutritional support. Prospective studies have shown that oral nutritional supplement helps reduce both the length-of-stay in hospital by 2.3 days and early hospital readmission by 2.3%.³⁶ Among critically-ill patients, enteral nutrition reduces mortality by 56%,³⁷ Furthermore, a delay in a dysphagia screen (thus a delay in nutrition support) for patients admitted with an acute stroke is associated with a longer length of stay on hyperacute stroke units, as well as increased risk of urinary tract infection and pneumonia within seven days of admission and greater in-patient mortality.³⁸

Limitations and strengths

The present study has certain limitations due to the nature of its design. Although risk of malnutrition was identified on admission and routinely treated in our centre, we did not have information on their subsequent nutritional status. However, all those with evidence for risk of malnutrition were referred to dietitians. Our study is based on a Caucasian population in a developed country and therefore may not be applicable to other populations. In high income countries, inadequate nutrition may co-exist with, or be a consequence of, underlying chronic conditions, especially among older patients with neuropsychiatric disorders.³⁹⁻⁴¹ However, in low income

nations malnutrition is often the primary cause of poor health and diseases among all ages.⁴²

The strengths of the study include its relatively large sample, with precise and detailed data collected according to the national guidelines.⁴ This enabled comprehensive adjustment for potential confounding factors, including co-existing morbidities and medications, particularly polypharmacy and ACB. Although the 4AT is a relatively novel screening tool, it has been extensively studied and well-validated in a wide range of conditions and in many countries.⁴³⁻⁴⁷

In conclusion, among older adults admitted with hip fractures high 4AT scores, suggestive of cognitive impairment and delirium, identified patients at increased risk of malnutrition. These findings lend further support for the use of 4AT as a screening tool for identifying patients at increased health risk in an acute setting.

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LEGENDS

Figure 1. Prevalence of malnutrition risk (open bars) or of malnutrition itself (black bars) in different categories of 4AT for patients admitted with a hip fracture.

Comment [CF1]: See above

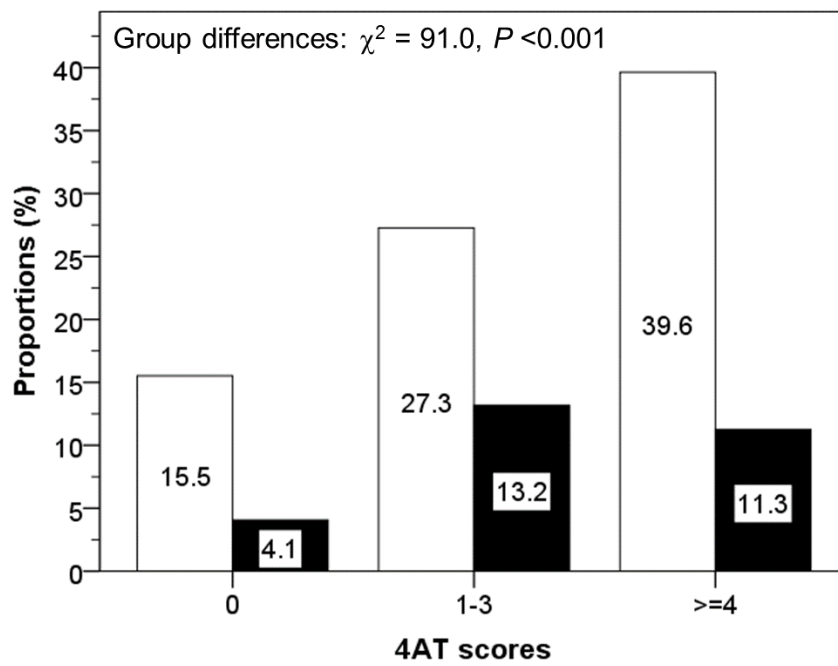


Table 1. Classification of nutrition status adopted from MUST screening tool¹⁹ and NICE guideline.²⁰

MUST screening tool					
Phenotypic criteria				Etiologic criteria	
BMI (kg/m ²)	Score	Unintentional weight loss (%)	Score		Score
>20 (>30)	0	<5	0	If patient is acutely ill and there has been or is likely to be no nutritional intake for >5 days	2
18.5-20	1	5-10	1		
<18.5	2	>10	2		
Overall score = 0 indicates low risk of malnutrition					
Overall score = 1 indicates medium risk of malnutrition					
Overall score ≥2 indicates high risk of malnutrition					
NICE definition for identification of malnourished patients if any of the following factors present					
BMI <18.5 kg/m ²					
Unintentional weight loss >10% within the last 3–6 months					
BMI <20 kg/m ² and unintentional weight loss >5% within the last 3–6 months					

Table 2. The 4AT for screening of cognitive impairment and delirium (adopted from McLullich).¹

4AT components	Score
'Alertness'	0: normal 0: mild sleepiness for <10 seconds after waking 4: abnormal
'AMT4' tests for recall of age, date of birth, place (name of hospital or building) and current year	0: no mistakes 1: one mistake 2: two or more mistakes or untestable
'Attention' tested by instructing the patient to list names of the months in reverse order, starting from December	0: reciting ≥ 7 months backwards correctly 1: starts but lists <7 months or refuses to start 2: untestable
'Acute change or fluctuating course' is the evidence of significant change or fluctuation in mental status within the last 2 weeks and persisting in the last 24 hours	0: no 4: yes

Table 3. Characteristics of 1082 patients admitted with a hip fracture with mean age 83.8 years (SD = 8.7).

	n	%
Sex distribution		
Men	298	27.5
women	784	72.5
Nutritional status		
Well nourished	734	67.8
Risk of malnutrition	259	23.9
Malnourished	89	8.2
4AT categories		
4AT = 0	541	50.0
4AT = 1-3	319	29.5
4AT \geq 4	222	20.5
Alcohol and drug history		
Alcohol consumption >14 units per week	52	4.8
Polypharmacy (\geq 4 medications/day)	824	76.2
Anticholinergic burden score \geq 1	430	39.8
Anticholinergic burden score \geq 2	108	10.0
Co-morbidities		
Dementia	308	28.5
Stroke	172	15.9
Parkinson's disease	44	4.1
Ischaemic heart disease	105	9.7
Diabetes	133	12.3

Table 4. Association of risk of malnutrition or malnourishment with 4AT in patients admitted with a hip fracture.

	At risk of malnutrition			Malnourishment		
	OR	95% CI	<i>P</i>	OR	95% CI	<i>P</i>
Model 1: Unadjusted						
4AT = 0 (reference group)	1	--	--	1	--	--
4AT = 1-3	2.37	1.68-3.35	<0.001	4.37	2.54-7.53	<0.001
4AT ≥4	4.18	2.90-6.03	<0.001	4.54	2.46-8.35	<0.001
Model 2: Adjusted for age and sex						
4AT = 0 (reference group)	1	--	--	1	--	--
4AT = 1-3	2.28	1.60-3.05	<0.001	3.63	2.08-6.31	<0.001
4AT ≥4	4.04	2.78-5.88	<0.001	3.63	1.94-6.78	<0.001
Model 3: Adjusted for age, sex, alcohol consumption, polypharmacy, ACB and co-morbidities*						
4AT = 0 (reference group)	1	--	--	1	--	--
4AT = 1-3	2.22	1.55-3.18	<0.001	3.68	2.09-6.48	<0.001
4AT ≥4	3.82	2.60-5.60	<0.001	3.65	1.92-6.93	<0.001
Model 4: As in model 3 and also dementia						
4AT = 0 (reference group)	1	--	--	1	--	--
4AT = 1-3	1.78	1.21-2.61	0.003	3.29	1.82-5.96	<0.001
4AT ≥4	2.66	1.72-4.12	<0.001	3.07	1.53-6.16	0.002

ACB, anticholinergic burden; *Co-morbidities: Stroke, Parkinson's disease, ischaemic heart disease and diabetes.