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Frailty exists in younger adults admitted as surgical emergency leading to adverse outcomes.

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<u>Abstract</u>

Background: Frailty is prevalent in the older adult population (≥ 65 years of age) and results in adverse outcomes in the emergency general surgical population.

Objective: To determine whether frailty exists in the younger adult emergency surgical population (<65 years) and what influence frailty may have on patient related outcomes.

Design: prospective observational cohort study.

Setting: emergency general surgical admissions.

Participants: all patients \geq 40 years divided into 2 groups: younger adults (40-64.9 years) and older adult comparative group (\geq 65).

Measurements: over a 6-month time frame the following data was collected: demographics; Scottish Index of Multiple Deprivation (SIMD); blood markers; multi-morbidities,poly-pharmacy and cognition. Frailty was assessed by completion of the Canadian Study of Health and Ageing (CSHA). Each patient was followed up for 90 days to allow determination of length of stay, readmission and mortality.

Results: 82 young adults were included and the prevalence of frailty was 16% (versus older adults 38%; p=0.001) and associated with: multi-morbidity; poly-pharmacy; cognitive impairment; and deprivation. Frailty in younger adults resulted in longer hospital stay and had 5 times greater risk of mortality at 30 and 90 days [OR 5.67, 95% CI (0.33-96.89)].

Conclusions: This novel study has found that frailty exists in 16% of younger adults admitted to emergency general surgical units, leading to adverse short and long-term outcomes. Strategies need to be developed that identify and treat frailty in this vulnerable younger adult population. Keywords: frailty; young adults, emergency surgery.

Introduction

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Frailty is a complex concept which has been defined as "a medical syndrome with multiple causes and contributors that is characterised by diminished strength, endurance and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death"[1,2]. It has almost exclusively been studied in the older adult populations (aged 65 years or above), particularly in the medical and community settings, where it has been shown to be associated with impaired cognition, delirium, multi-morbidity and polypharmacy resulting in increased morbidity, mortality and hospital re-admission [3].

In older adult surgical populations, the presence of frailty has been associated with adverse elective and emergency postoperative outcomes, including increased length of hospital stay and three-to-four fold increases in death [4][5][6]. These findings have led to interventions, including the multi-disciplinary approach of the comprehensive geriatric assessment (CGA) that identify and address specific geriatric issues pre-operatively to potentially improve patient outcomes [7].

Despite research that has suggested chronological age does not always reflect biological age, there has been little work assessing the incidence of frailty in younger adults (<65 years of age) in either surgical or non-surgical populations [8]. One group assessed outcomes in cardiac surgical patients finding that the presence of frailty increased the risk of adverse outcomes, an effect that was independent of age suggesting that frailty is not unique to the older population [9].

This study aimed to determine the prevalence of frailty in a younger adult population admitted with emergency general surgical conditions using an older adult cohort as a comparative

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reference group. The secondary aim was to look at the association between frailty and patient related outcomes.

<u>Methods</u>

Patients.

Consecutive patients aged 40 years and upwards were included into this prospective cohort study which was performed in accordance with the STROBE Statement [10]. Each patient had been admitted to the acute general surgical unit of one hospital in the West of Scotland and was identified and data collected during 2 ten-week time frames between October 2014 and March 2015. This study was deemed a service evaluation and was registered with The Clinical Effectiveness Department, Greater Glasgow and Clyde on 24/10/2014. Patients were excluded if they lacked capacity to give verbal consent to completing the questionnaires.

Data Collection.

The following data were collected on admission using the hospital's electronic records system, patient case notes and prescribing charts: age; sex; Scottish Index of Multiple Deprivation (SIMD) quintile (SIMD is an established tool for identifying areas of poverty and inequality across Scotland where 1 -2 indicates the most deprived groups and 3-5 the least deprived) [11], haemoglobin (\leq 129g/L defined as anaemia), albumin (\leq 35g/L defined as hypoalbuminaemia), number of current medications (\geq 5 considered poly-pharmacy).multi-morbidity (defined as \geq 2 co-morbidities) and cognition using the MoCA. The Montreal Cognition Assessment Test or MoCA, is is a 30-point questionnaire that assesses 7 areas of cognitive function where a score of 26 or greater is considered normal. It has been validated in elderly populations, including Alzheimer's disease [13,14] and in older emergency general surgical patients [15]. It was assessed within 24 hours of hospital admission.

It was recorded whether each patient underwent surgery and the maximum level of care each patient received during their admission (ward, High Dependency/ Intensive Care Unit). Length of hospital stay, readmission to hospital within 30 days of discharge, and death within 30 or 90 days of the original acute admission were recorded.

Assessment of Frailty

Within 24 hours of admission and prior to any surgery, patients were assessed for the presence of frailty. To minimise observer bias, four researchers were responsible for identifying patients for the study, including and led by the main author with all receiving formal training in the tools for measuring frailty.

To assess frailty, we used a 7-point clinical frailty scale derived from the Canadian Study of Health and Ageing (CSHA) [15]. The scale is derived from a deficit-based Frailty Index and has been widely validated across a range of populations [16]. Participants were classified as frail if they scored 5 or greater [15]. **Statistical Analysis.**

Descriptive statistics were generated to compare demographic and clinical case-mix of the patients, by age group (younger adults: 40-64.9 versus older adult reference group 65 and older). Unless otherwise stated, for continuous data two sample Student t-tests were used unless the residuals breached the assumptions of normality and then a Mann Whitney-U test was used, and for categorical data Chi-squared test were used. In cases where the assumptions of the Chi-squared were violated, the Fisher's exact test was used. In the younger age group a crude logistic regression was used to test for associations between clinical outcome (mortality at 30 days, and length of hospital stay) and frailty. All statistical analysis was conducted using SPSS version 22[17].

<u>Results</u>

Patient Demographics.

A total of 169 patients were admitted to the emergency surgical unit during the study time frame with 82 younger adults and 87 in the older adult reference group. All questionnaires and assessments were completed except for 9 patients who were unable to complete the MoCA.

Comparison of the two groups found the younger adults had: lower multi-morbidity (41% vs 74%, P<0.001), lower poly-pharmacy (38% vs 82%, P<0.001), and fewer patients with anaemia (30% vs 51%, P=0.003) and hypoalbuminaemia (33% vs 59%, P<0.001). There were no differences between groups in the number of patients that underwent surgery, however younger adults had a significantly shorter length of hospital stay (median 3 days vs 4, p=0.046) and were more likely to be clinically managed on the general surgical ward (95% vs 78%, p=0.001). Re-admission rates and 30 and 90-day mortality did not differ between the younger and older adult groups [Table 1], but caution is needed when interpreting these findings as they were under powered.

Frailty in younger adults.

Frailty was recorded in 16% of the younger adults (versus 38% of older adults; p=0.001). Table 2 displays the comparison of frail versus non-frail younger adults finding the presence of frailty to be associated with: cognitive impairment [OR 12.31 (2.51-60.49); P=0.002]; multi-morbidity [OR 25.64 (3.13 -209.75); P=0.002]; poly-pharmacy [OR 7.62 (1.90-30.54); P=0.004] and higher levels of deprivation [OR 4.60 (1.16-18.20); P=0.030]. In addition, there was evidence of a prolonged hospital stay in frail younger patients [less than 3 days versus 1 week stay; OR 3.31 (0.93-44.9); P=0.06].

At 90-days, only one patient had died in frail and non-frail groups. Frailty resulted in 5times greater risk of mortality at 30 and 90 days [OR 5.67, 95% CI (0.33-96.89)].

Discussion

This study is the first to document that frailty exists in 1a significant proportion (16% in this cohort) of younger adults admitted as a surgical emergency and is associated with longer hospital stays and carries a higher risk of mortality. This study supports the concept that frailty is not unique to the older adult population and that early identification and management strategies need to be developed that improve outcomes for these vulnerable young adults. Indeed, it may be that the strategies being developed for older adults, including Cognitive Geriatric Assessment should be transferred to the frail younger adults [7].

Why frailty exists in younger adults appears to be associated with similar factors that influence frailty in the older adult population: multi-morbidity, poly-pharmacy and cognitive impairment. If frailty is a clinical expression about a patient's vulnerability, both physiologically and psychologically, to recover from an acute illness, then it is not unexpected that these 3 factors also influence frailty in younger adults [2,5,6,9]. This could be reflecting a disconnection between chronological and biological ageing, leading to the idea that frailty in younger adults could reflect 'accelerated ageing'. Mitnitski et al (2013) stated that ageing develops gradually and starts from small changes in health, which accumulate across adult life [18]. Theses changes result in deficits in health and an increase in recovery time with each new health issue, which in the older adult population leads to an increased level of care on hospital discharge. These findings were consistent in this population of frail younger adults where evidence of health deficits (multimorbidity, poly-pharmacy and cognitive impairment) led to a significantly longer time to inhospital recovery.

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Deprivation was also associated with frailty in the younger adults and this is of particular interest in Greater Glasgow, where premature mortality rates consistently exceed the UK average across all categories of deprivation [19]. There is currently no explanation for this phenomenon, which is often referred to as the "Glasgow Effect" as other post-industrial cities in the UK with similar profiles of deprivation do not have similarly high mortality rates [19,20,21]. If deprivation is linked to frailty then comparison of this cohort to another in the U.K. could provide more insight.

Although the presence of frailty in younger adults did not significantly influence re-admission and mortality rates, it is worth highlighting that those frail, younger patients were 5 times more likely to die at 30 and 90 days post-admission. However it is a limitation of this study that there are small numbers in each group and that it was not powered. Future multi-centred work, including a focus on frail patients undergoing emergency laparotomy, is planned to increase patient numbers, allowing improved analysis of these patient outcomes.

Conclusions

Frailty is not unique to the older adult population, existing in 16% of the younger adult emergency surgical population. Frail young adult patients have a significantly prolonged hospital stay and have a higher risk of mortality at 30 and 90 days. Frailty is influenced by multi-morbidity, poly-pharmacy, cognitive impairment and deprivation and early recognition and management of this condition could lead to improved patient outcomes.

References

Table 1. Baseline demographic data and descriptive statistics of Younger Adults with comparisonto older adult reference population.

	Younger adults (40 - 64.9) n=82	Older adults (≥65) n=87	P value
Mean Age in years (range)	51.2 (40-64)	76.8 (65-93)	<0.001*
Female: Male	49: 33	48: 39	0.547
Deprived Yes: No	39: 43	32: 55	0.156
Operation Yes: No	14:68	23: 64	0.141
Length of Stay: Median days (range)	3 (1-28)	4 (1-100)	0.046*&
Level of Care Ward: HDU/ ITU	78:4	68:19	0.001†
Multi-morbidity Yes: No	34: 48	65: 22	<0.001*
Poly-pharmacy Yes: No	31: 51	71: 16	<0.001*
Anaemic Yes: No	25: 57	44: 43	0.003*
‡Hypoalbuminaemic Yes: No	27: 54	51: 36	<0.001*
‡MoCA Pass: Fail	49:32 (60%: 40%)	18: 61 (23%:77%)	<0.001*
Frail Yes: No	13:69 (16%:84%)	33:54 (38%:62%)	0.001*
Readmission 30 day Yes: No	15:67	26: 61	0.079
Mortality 30 day Yes: No	1: 81	5: 82	0.212†
Mortality 90 day Yes: No	2: 80	8:79	0.063†

* denotes P<0.050

*†*Fisher's Exact test for associations used.

‡missing data n=1 albumin younger adults.; n=1 MOCA younger adults, n=8 MOCA older adults.

§ Chi-Square test

& Mann Whitney test was conducted

	Frail	Not Frail	OR	95% CI	P-value
	n=13	n=69			
Mean Age in years (range)	50.1 (40-61)	52.0 (41-64)		NA	0.340&
Female: Male	9:4	40: 29	1.17	(0.49-2.80)	0.450
Deprived Yes: No	10: 3	29:40	4.60	(1.16-18.20)	0.030*
Operation Yes: No	3: 10	11: 58	1.58	(0.37-6.69)	0.530
Length of stay: Less than 3 days Up to 1 week More than 1 week	5 7 1	45 19 5	3.31 1.81	Reference (0.93-44.9) (0.17-42.1)	0.06* 0.62
Level of Care Ward: HDU/ITU	12:1	66:3	0.72	(0.24- 2.07)	0.520
Multi-morbidity Yes: No	12:1	22:47	25.64	(3.13- 209.75)	0.002*
Poly-pharmacy Yes: No	10:3	21:48	7.62	(1.90-30.54)	0.004*
Anaemic Yes: No	4:9	21:48	1.36	(0.39-4.55)	0.640
Hypoalbuminaemia Yes: No	5:8	22:46	1.31	(0.38- 4.46)	0.669
MoCA Pass: Fail	2:11	47:21	12.31	(2.51-60.49)	0.002*
Readmission 30 day Yes: No	1: 12	14: 55	0.33	(0.04-2.73)	0.300
Mortality 30 day Yes: No	1: 12	0:69	5.67	(0.33-96.89)	0.230
Mortality 90 Day Yes: No	1: 12	1:68	5.67	(0.33-96.89)	0.230

Table 2. The effect of frailty and associated outcomes in Younger Adults.

In analysis where there were <8 cases, Fisher's Exact test for associations was used. Chi-square test used in remaining cases.

* denotes P<0.05

&Mann-Whitney Test

	Frail	Not Frail	OR	95% CI	P-value
	n=33	n=54			
Mean Age in years (range)	79.1 (66-92)	75.3 (65-93)		NA	0.001&
Female: Male	19:14	29: 25	1.17	(0.49-2.80)	0.725
Deprived Yes: No	14:19	36:18	1.47	(0.60-3.60)	0.85
Operation Yes: No	8:25	15:38	0.83	(0.31-2.24)	0.717
Length of stay: Less than 3 days Up to 1 week More than 1 week	11 7 14	23 16 14	0.91 2.09	Reference (0.29-2.87) (0.74-5.87)	0.879 0.161
Level of Care Ward: HDU/ITU	27:6	41:13	0.52	(0.48- 4.21)	0.610
Multi-morbidity Yes: No	27:6	38:16	1.89	(0.66- 5.47)	0.237
Poly-pharmacy Yes: No	29:4	42:12	2.07	(0.61-7.06)	0.245
Anaemic Yes: No Hypoalbuminaemia Yes: No	12:21 22:11	14:40 29:25	1.63 1.72	(0.64-4.16) (0.70-4.24)	0.304 0.236
MoCA Pass: Fail	3:23	15:38	3.02	(0.89-11.60)	0.106
Readmission 30 day Yes: No	12:21	40:14	1.63	(0.64-4.16)	0.304
Mortality 30 day Yes: No	2: 31	1:53	3.42	(0.30-39.3)	0.324
Mortality 90 Day Yes: No	5: 28	3:51	3.04	(0.67-13.66)	0.148

In analysis where there were <8 cases, Fisher's Exact test for associations was used. Chi-square test used in remaining cases.

* denotes P<0.05

&Mann-Whitney Test