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Original Article

Induced frailty and acute sarcopenia are overlapping consequences of hospitalisation in older adults

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Abstract

Objectives: To determine the effects of hospitalisation upon frailty and sarcopenia. **Methods**: Prospective cohort study at single UK hospital including adults ≥70 years-old admitted for elective colorectal surgery, emergency abdominal surgery, or acute infections. Serial assessments for frailty (Fried, Frailty Index, Clinical Frailty Scale [CFS]), and sarcopenia (handgrip strength, ultrasound quadriceps and/or bioelectrical impedance analysis, and gait speed and/or Short Physical Performance Battery) were conducted at baseline, 7 days post-admission/post-operatively, and 13 weeks post-admission/post-operatively. **Results**: Eighty participants were included (mean age 79.2, 38.8% females). Frailty prevalence by all criteria at baseline was higher among medical compared to surgical participants. Median and estimated marginal CFS values and Fried frailty prevalence increased after 7 days, with rates returning towards baseline at 13 weeks. Sarcopenia incidence amongst those who did not have sarcopenia at baseline was 20.0%. However, some participants demonstrated improvements in sarcopenia status, and overall sarcopenia prevalence did not change. There was significant overlap between diagnoses with 37.3% meeting criteria for all four diagnoses at 7 days. **Conclusions**: Induced frailty and acute sarcopenia are overlapping conditions affecting older adults during hospitalisation. Rates of frailty returned towards baseline at 13 weeks, suggesting that induced frailty is reversible.

Keywords: Acute sarcopenia, Frailty, Induced frailty, Sarcopenia

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Introduction

Frailty and sarcopenia are known to be related but distinct conditions. The prevalence of both conditions increases with age[1]. Frailty is a condition of increased vulnerability and susceptibility to the effects of illness[2]. It can be defined phenotypically (Fried frailty)[3] or based on the accumulation of increasing numbers of health deficits (Frailty Index)[4]. Characteristics included within the phenotypic definition are weakness, slowness, self-reported exhaustion, weight loss, and low physical activity[3]. Sarcopenia is defined by skeletal muscle insufficiency, with reduced muscle strength being demonstrated with reduced muscle quantity or quality; additional demonstration of low physical performance defines severe sarcopenia[5]. Sarcopenia has been shown to overlap especially with Fried frailty[6]. However, previous studies have classically considered the prevalence of frailty and/or sarcopenia at a single timepoint, rather than considering the dynamic nature of these conditions, particularly in the context of acute illness. Induced frailty is an increasingly recognised condition of frailty developing acutely by the effects of illness[7]. Similarly, acute sarcopenia is defined by incident sarcopenia within six months, normally following a stressor event[5,8]. This study aimed to characterise dynamic changes in frailty and sarcopenia status following hospitalisation in older adults.

Methods

Study design and setting

The full protocol for this study has been published previously (9). Participants were recruited to this study from the Queen Elizabeth Hospital Birmingham, UK, from May 2019 – April 2021. Recruitment was paused from March 2020 – September 2020 and January 2021 – March 2021 due to the Coronavirus 2019 (COVID-19) pandemic. Three groups of participants were recruited: patients undergoing elective colorectal surgery were recruited from preoperative assessment clinic, patients undergoing emergency abdominal surgery were recruited from general surgery wards, and patients admitted with acute infections were admitted from general medical wards. All participants were aged 70 years and older. Assessments were performed at baseline, 7 (+/-2) days post-admission or post-operatively, and 13 (+/-1) weeks post-admission or post-operatively.

Frailty definitions

Fried frailty phenotype

Fried frailty was defined dichotomously based on the presence of three or more of five characteristics: weight loss, low handgrip strength, low gait speed, self-reported exhaustion, and low physical activity. Low physical activity was defined as per the Frailty Intervention Trial definition[10], and all other characteristics were defined according to the original study definition (Table S1)[3]. During the COVID-19 pandemic, an amendment was made to conduct telephone follow-ups in place of in person review at 13 weeks. It was, therefore, not possible to assess Fried frailty at this timepoint for these participants.

Frailty index

The deficits included within the Frailty Index (FI) were adapted from those included within the UK electronic Frailty Index (eFI) (Table S2)[11]. The presence or absence of each deficit was recorded as a binary variable, and the FI was calculated as the number of variables present, divided by the total number measured. The FI was recorded as a continuous variable, with the presence of frailty specifically defined as a score of 0.25 or greater.

Clinical Frailty Scale

The Clinical Frailty Scale (CFS)[12] was calculated by a single geriatrician based on a Comprehensive Geriatric Assessment, considering activities of daily living, physical and cognitive function, symptomatic burden of morbidities, and perceived vulnerability by the investigator. The CFS was measured on an ordinal scale from 1 – 8 (an additional discrete category of 9 applied to participants who were not otherwise frail but considered to be within the last year of life, but no participants in this study met this criteria) (Figure S1). The CFS was assessed at baseline by considering the participant's overall function and health two weeks prior to admission. In contrast, the CFS was calculated at 7 days and 13 weeks, by considering the participant's function and health at that timepoint. At 7 days, some participants were already discharged and assessed at home, others had discharge plans in place, and others required ongoing care and treatment in hospital. The CFS was assessed at this timepoint as a global assessment of health and function involving the patient, and other members of the multidisciplinary team. The stability and trajectory of function and health during hospitalisation were considered when assessing CFS at the timepoint. When considering overall frailty prevalence, a score of 5 or greater was considered consistent with frailty.

Sarcopenia definition

Probable sarcopenia was defined by the presence of low handgrip strength alone. Definite sarcopenia was defined by the presence of low handgrip strength with low muscle quantity measured using quadriceps ultrasound (Bilateral Anterior Thigh Thickness [BATT])[13] and/or bioelectrical impedance analysis (Sergi equation)[5]. Severe sarcopenia was defined by additional demonstration of reduced gait speed and/or reduced Short Physical Performance Battery (SPPB) score. Participants were categorised as having sarcopenia with unclear severity if they met criteria for definite sarcopenia but it was not possible to measure physical performance. Cut-offs utilised for diagnosis are available online (Table S3). When considering overall prevalence, sarcopenia was defined dichotomously according to those with definite sarcopenia and those without. As per Fried frailty, it was not possible to

		Overall (N=80)	Elective surgery (N=24)	Emergency surgery (N=15)	Medical (N=41)	p value
Age – mean (SD)		79.2 (6.6)	76.4 (5.3)	75.5 (4.2)	82.1 (6.7)	<0.001[a]
Gender – Females % (N)		38.8 (31)	50.0 (12)	33.3 (5)	34.1 (14)	0.400[b]
Ethnicity – % (N)	White British	93.8 (75)	95.8 (23)	100 (15)	90.2 (37)	0.727[b]
	White Irish	2.5 (2)	0 (0)	0 (0)	4.9 (2)	
	Indian	2.5 (2)	4.2 (1)	0 (0)	2.4 (1)	
	Arab	1.3 (1)	0 (0)	0 (0)	2.4 (1)	
Frailty index – mean (SD)		0.27 (0.11)	0.20 (0.09)	0.25 (0.13)	0.32 (0.09)	<0.001[a]
Clinical Frailty Scale – median (IQR)		4 (3 – 5)	3 (3 – 4)	3 (3 – 4)	5 (4 – 5)	<0.001[c]

[a]One-way ANOVA; [b]Chi-squared test; [c]Kruskal-Wallis test

Table 1. Baseline characteristics of participants.

assess sarcopenia status at 13 weeks in participants where only telephone follow-up was made.

Ethical approval

This research was sponsored by the University of Birmingham. Ethical approval was obtained from Wales Research Ethics Committee 4 (19/WA/0036), the Health Research Authority, and the University Hospitals Birmingham NHS Trust Research and Development department. Written informed consent was obtained from all participants who were considered to have capacity to consent for themselves. Written personal or professional consultee declaration was obtained if the participant was considered to lack capacity to consent to participation. The use of both informed consent and consultee declaration was approved by the ethics committee.

Statistical analysis

Unless specified otherwise, statistical analyses were performed using IBM SPSS Statistics Version 26 (IBM Corp). All analyses were calculated overall and separated by patient group, to assess for differences across the three timepoints. The original power calculation was derived to identify changes in patient-reported physical function within groups. Unfortunately, it was not possible to recruit to the original target due to the study being paused during the COVID-19 pandemic, and the power calculation was revised to enable analysis of differences across groups rather than within groups. This study represents analysis of differences in prevalence in frailty and sarcopenia status across timepoints. A post-hoc power calculation specific to this analysis showed that a sample size of 40 participants was able to detect a change in prevalence from 30% to 60% with 80% power and alpha of 0.05. A sample size of 47 participants was able to detect a change in prevalence from 60% to 85% with 80% power and alpha of 0.05.

Estimated marginal means (EMMs) and statistical significance of changes for FIs were calculated from linear mixed models. Statistical significance of change in CFS was calculated considering CFS as an ordinal variable using Skillings-Mack tests using STATA. Skillings-Mack tests are more robust to missing values than Friedman tests, but exclude single measures, with clinical differences across the study population interpreted by median values. To enhance the interpretation of sensitivity to change, EMMs were calculated from Generalized Linear Mixed Methods, considering CFS as a non-parametric continuous variable. Statistical significance of changes in prevalence across the five categories of sarcopenia status were calculated using Skillings-Mack tests. Where ties existed, p values were obtained from a simulated conditional null distribution of Skillings-Mack. Statistical significance of differences in frailty and sarcopenia statuses defined dichotomously between both groups and timepoints were assessed using Chi-squared tests. Change scores between FI, CFS, and sarcopenia categories were calculated for the study population overall. Changes between unclear severity and confirmed or severe sarcopenia were considered as no change. The association of differences in changes between FI, CFS, and sarcopenia were assessed using Spearman's rank correlations. Statistical significance of all analyses was set at $p<0.05$.

Results

Eighty-one participants were recruited to this study. One participant was excluded from analysis as they were recruited in error (elective admission within emergency surgery cohort). Screening, recruitment, and drop-out rates have been published previously[14]. The recruitment flowchart for this analysis is included online (Figure S2). The mean age of participants was 79.2 (6.6) years; 38.8% (31) were female. Baseline characteristics of participants are shown in Table 1.

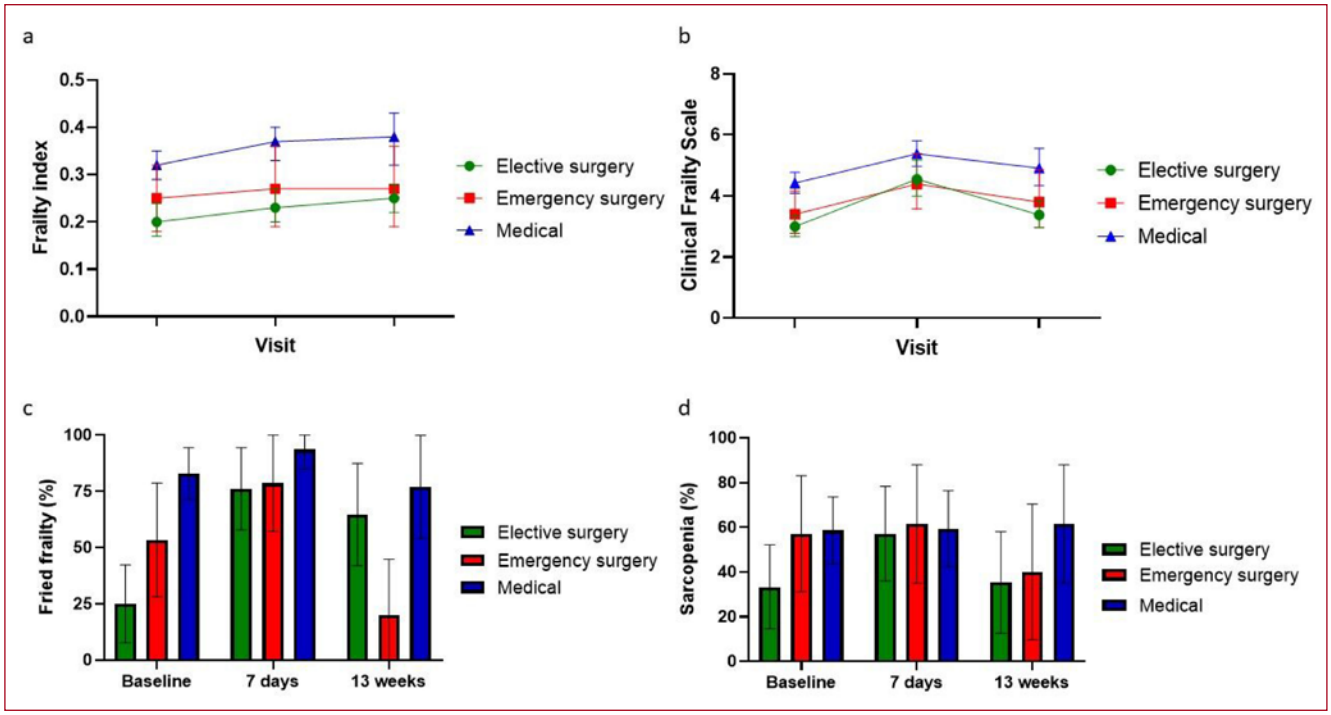

Figure 1. Changes in frailty and sarcopenia status separated by cohort. Clinical Frailty Scale increased from baseline at 7 days post-admission/post-operatively and returned towards baseline at 13 weeks for all groups. The prevalence of Fried frailty increased at 7 days in elective and emergency surgery patients. Frailty index and sarcopenia prevalence did not significantly differ across timepoints.

Dynamic changes in frailty status

Frailty index did not change significantly across timepoints (Figure 1a; Table S4). However, medical patients had higher FIs at baseline compared to patients within the surgical groups. There were significant differences in CFS across visits considering both changes in median values (Table S5) and EMMs (Figure 1b; Table S6). Similar to FI, CFS was higher for medical patients at baseline. The prevalence of Fried frailty significantly increased at 7 days post-operatively in the elective and emergency surgery groups (Figure 1c; Table 2). The prevalence of Fried frailty did not differ significantly across visits in the medical group, although the prevalence of Fried frailty was high at baseline in this group.

Dynamic changes in sarcopenia status

The prevalence of sarcopenia did not significantly differ across timepoints or between groups when considering sarcopenia as a binary construct (Figure 1d; Table 2). There were significant differences in ordinal categories of severity across timepoints for the study population overall; these differences were statistically significant when using a simulated Skillings-Mack model to account for ties (Table S7). However, these differences were accounted for by participants meeting criteria for severe criteria at 7 days, where this had been unclear at baseline.

Figure 2 demonstrates changes in sarcopenia status across timepoints. Of those who did not meet criteria for sarcopenia at baseline, 20.0% (5/25) (excluding drop-outs) met criteria for sarcopenia at 7 days, and a further 8.0% (2/25) had probable sarcopenia. Whilst some participants moved from lower sarcopenia status/severity to higher severity, others showed improvements in status to lesser severity. Four participants changed from severe sarcopenia to no sarcopenia at 7 days; two of these experienced a 1 kg increase in handgrip strength, whereas the other two experienced 6kg and 10 kg increases respectively. Individual change scores in components included within sarcopenia criteria from baseline to 7 days, and 7 days to 13 weeks are shown in Figure S3. Mean BATT and gait speed declined from baseline to 7 days, with a mean improvement/recovery from 7 days to 13 weeks. However, with all variables, there was considerable variation, with some participants experiencing declines in measurements between timepoints, and others experiencing improvements.

Changes in overlapping frailty and sarcopenia prevalence across timepoints

Figure 3 shows changes in frailty and sarcopenia prevalence across timepoints. Of all diagnostic criteria, CFS appeared the most discriminatory, with few participants

	Baseline – % (N)	7 days – % (N)	13 weeks – % (N)	p value
Frailty Index				
Overall	61.3 (49/80)	75.0 (51/68)	67.9 (36/53)	0.204
Elective	33.3 (8/24)	54.5 (12/22)	52.4 (11/21)	0.281
Emergency	53.3 (8/15)	69.2 (9/13)	50.0 (5/10)	0.586
Medical	80.5 (33/41)	90.9 (30/33)	90.9 (20/22)	0.336
p value	0.001*	0.008*	0.010*	
Clinical Frailty Scale				
Overall	31.3 (25/80)	60.9 (42/69)	36.2 (21/58)	0.001*
Elective	4.2 (1/24)	50.0 (11/22)	14.3 (3/21)	0.001*
Emergency	13.3 (2/15)	53.8 (7/13)	40.0 (4/10)	0.071
Medical	53.7 (22/41)	70.6 (24/34)	51.9 (14/27)	0.230
p value	<0.001*	0.258	0.026*	
Fried Frailty				
Overall	60.0 (48/80)	84.8 (56/66)	57.5 (23/40)	0.001*
Elective	25.0 (6/24)	76.2 (16/21)	64.7 (11/17)	0.001*
Emergency	53.3 (8/15)	78.6 (11/14)	20.0 (2/10)	0.018
Medical	82.9 (34/41)	93.5 (29/31)	76.9 (10/13)	0.240
p value	<0.001*	0.176	0.017*	
Sarcopenia				
Overall	50.6 (40/79)	59.1 (39/66)	45.0 (18/40)	0.339
Elective	33.3 (8/24)	57.1 (12/21)	35.3 (6/17)	0.220
Emergency	57.1 (8/14)	61.5 (8/13)	40.0 (4/10)	0.565
Medical	58.5 (24/41)	59.4 (19/32)	61.5 (8/13)	0.982
p value	0.126	0.967	0.335	

*p values were derived from chi-squared tests; p<0.05 are denoted with *.*

Table 2. Frailty and sarcopenia prevalence separated by group and timepoint.

meeting criteria for CFS alone at any timepoint. The least discriminatory was FI frailty. The proportion of participants meeting criteria for all frailty diagnoses and sarcopenia was greatest at the 7 day timepoint. Change in FI moderately correlated with change in CFS between baseline and 7 days (r_s=0.43; p<0.001), and 7 days and 13 weeks (r_s=0.37; p=0.018). Change in sarcopenia status did not correlate with change in FI or CFS between timepoints (Table S8 and Table S9).

Discussion

Our results demonstrate that hospitalisation is associated with induced frailty in medical and surgical patients, where frailty is defined by Fried criteria or CFS. This effect was more marked in surgical patients, as medical patients already had higher rates of frailty at baseline. Importantly, this effect appears to be potentially reversible, with rates and severity of frailty returning towards baseline after 13 weeks. Dynamic changes in FI were less significant. This is to some extent unsurprising when considering the deficits that were included within the FI. The deficits that were included were validated from large community populations, and predominantly represent deficits that are chronic and acquired over time[11]. Dynamic changes may be more marked if deficits are modelled from a secondary care population, where risk is more likely to be affected by acutely evolving factors. Induced frailty is considered different to age-related frailty that progresses over time. Specifically, it occurs secondary to an insult, and our results are promising in demonstrating that this state is more likely to be temporary and reversible. However, even accepting this reversibility, it is potentially associated with equivalent individual risk in the short-term[7]. Frailty has been shown to be associated with impairments in the immune system[15]. This will lead to a state

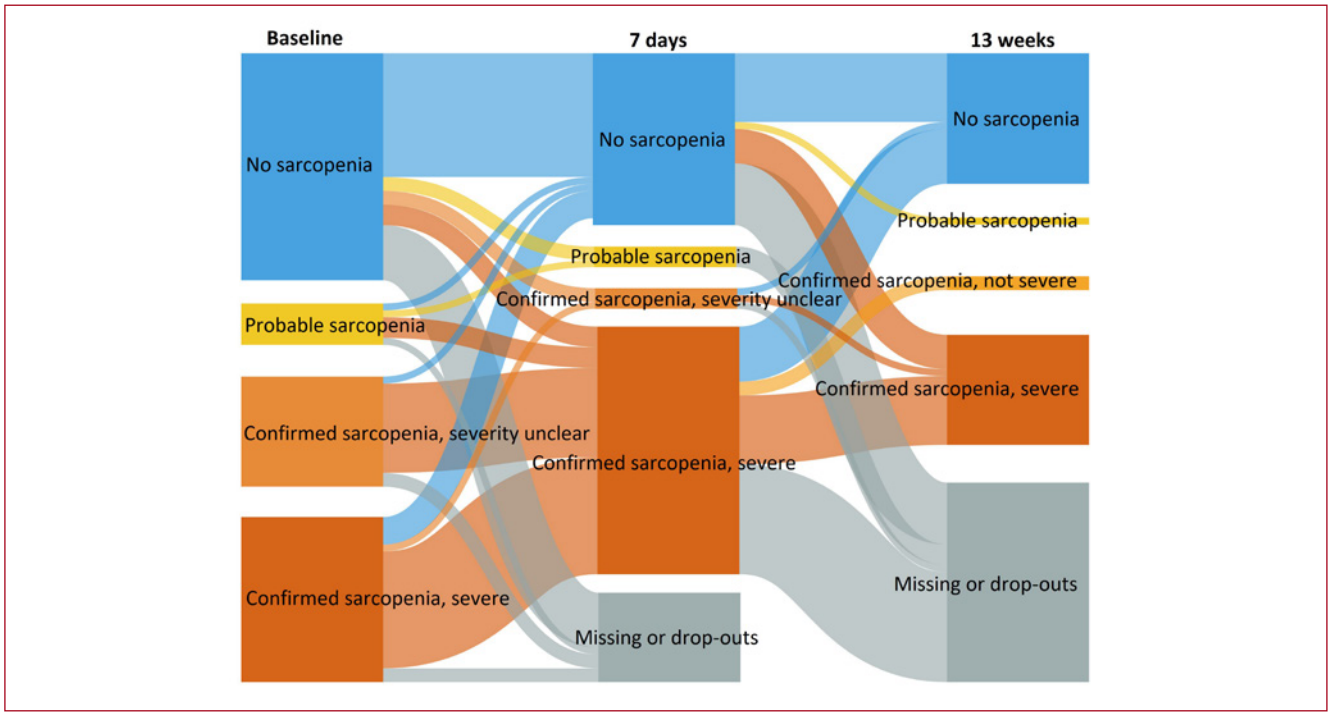

Figure 2. Prevalence of sarcopenia status across timepoints. The individual sections shown are proportional to the number of participants at each stage. Some participants experienced improvements in sarcopenia status, whereas others experienced worsening.

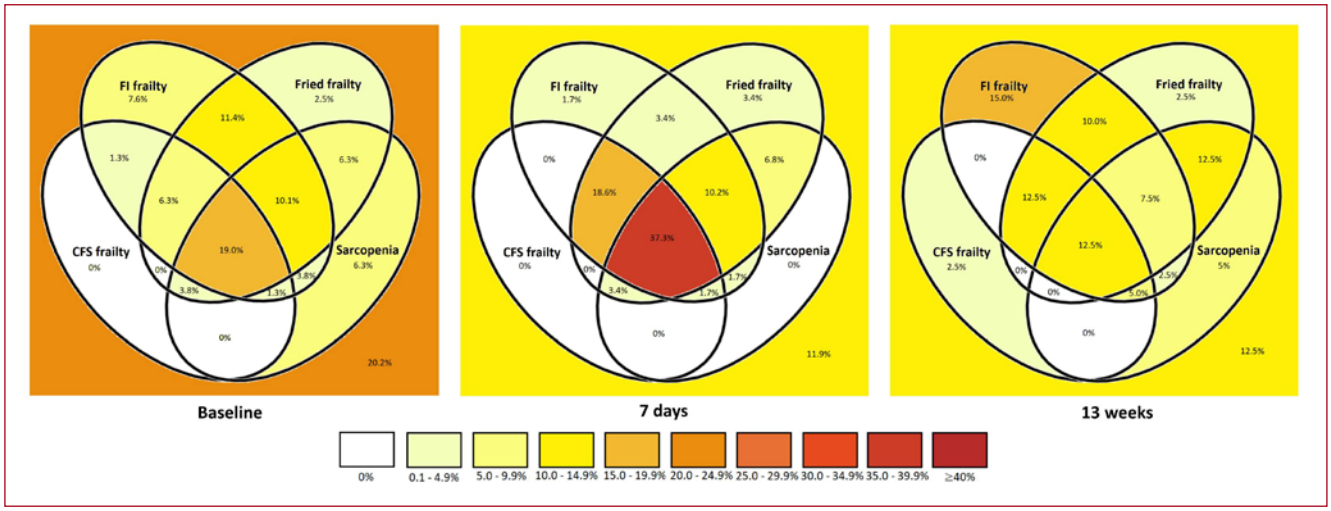

Figure 3. Overlapping frailty and sarcopenia prevalence at each timepoint. Areas of overlap with higher prevalence are colour-coded more red, with lower prevalent areas appearing yellow or lighter. Participants were included if all four criteria were available at the particular timepoint.

of increased vulnerability, and increased likelihood of further deterioration in the event of secondary insults, potentially leading to a vicious cycle of heightened risk. This may be associated with increased risk of organ insufficiency, such as the risk of acute sarcopenia and muscle dysfunction through ineffective repair mechanisms[8].

Conversely, the prevalence of sarcopenia did not clearly change over time. However, examining individual

trajectories demonstrated that some participants experienced improvements in their sarcopenia status, whereas others experienced declines. The significant overlap between sarcopenia and frailty at 7 days suggests that most participants who experienced acute sarcopenia also met criteria for frailty at this timepoint. Overall, significant overlap between diagnoses was demonstrated. Few people met criteria for just one frailty or sarcopenia diagnosis at any one time. The greatest overlap was observed at 7 days, with over a third of participants meeting criteria for all diagnoses. Considering the individual diagnoses, CFS was shown to be the most discriminatory, with few or no participants meeting criteria for frailty based on CFS alone at this timepoint. This suggests that if only one tool is to be used to assess vulnerability in clinical practice, then CFS may be the most pragmatic. The CFS is not specific to deficits in muscle or physical function, but similar to FI, encompasses a broader picture including cognition and other deficits[4]. The differences in overlap may also relate to the cut-offs that were used in defining frailty and sarcopenia. It is recognised that frailty forms a spectrum of increasing risk and vulnerability. Although a score of 5 or greater was selected, a CFS score of 4 is now considered to represent living with very mild frailty[16]. Similarly, two participants changed from severe sarcopenia to no sarcopenia at 7 days, due to a 1 kg improvement in handgrip strength, which is unlikely to represent clinically meaningful improvement.

Results in context of wider literature

Induced frailty is a relatively new concept. Previous studies have often evaluated frailty at a single timepoint, rather than as a dynamic construct. Where dynamic changes have been measured, this has normally been as part of a longitudinal study, rather than in the context of hospitalisation. However, longitudinal studies in community-dwelling older adults have shown that whilst some individuals will experience deteriorations in frailty status, some will not change, and others will experience improvement in frailty status[17]. A previous prospective study in Italy showed that of those without sarcopenia at admission, 14.7% of the sample developed sarcopenia during admission[18]. These findings are not inconsistent with our study findings, as the incidence of sarcopenia at 7 days was 20.0% for those who did not have sarcopenia at baseline. However, we also showed that changes were bidirectional, to the extent that the overall prevalence did not change significantly between timepoints. Previous studies have demonstrated that there is overlap between Fried frailty and sarcopenia[6], and Fried frailty and FI, with differences in overlap dependent on cut-offs and definitions used[19]. The CFS is known to correlate with FIs, and was validated from the original study population[4]. The CFS is now the most common tool utilised in frailty assessment embedded into clinical practice. It has shown wide utility across a number of different clinical settings in predicting adverse outcomes and enabling holistic decision-making[20,21]. At present, CFS is routinely measured for hospitalised older adults at the point of admission, based on function two weeks prior to this, but is not recorded dynamically during hospitalisation, or at the point of discharge. The Hierarchical Assessment of Balance and Mobility is a tool that can be used to monitor progress and changes in in-bed mobility, transfers, and ambulation, in a similar manner to vital signs. Embedding of such tools into clinical practice could enable the identification of at risk individuals by monitoring trends over time[22].

Strengths and limitations

This study represents the first of its kind, prospectively characterising rates of frailty and sarcopenia across multiple timepoints in medical and surgical patients. We used recognised, validated diagnostic criteria in this process. Importantly, all recruitment and follow-up assessments were performed by clinicians with geriatric medicine expertise. However, there are a number of limitations that should be considered. Firstly, although the assessor did not refer back to assessments at earlier timepoints when performing frailty and sarcopenia assessments, they were not truly blinded to these readings. Secondly, considering sarcopenia diagnosis, we did not include measurements of muscle quality. Low muscle quality without low muscle quantity is now recognised as sufficient to meet criteria for sarcopenia. Echogenicity was recorded as part of this study, and we previously demonstrated that changes over 13 weeks correlated with change in handgrip strength and gait speed. However, at present there are no recognised cut-off values for sarcopenia that could be utilised. As echogenicity is known to vary between ultrasound devices, cut-offs would need to be validated from a reference population using the same device.

Thirdly, due to the COVID-19 pandemic, the sample size was smaller than that originally stated in the protocol. Our post-hoc power calculation demonstrates that the sample size achieved was sufficient to detect statistically significant differences in CFS frailty and Fried frailty prevalence at 7 days. However, we acknowledge that this sample size may have been insufficient to detect statistically significant differences in smaller changes in prevalence across timepoints. The rates of missing data were high, particularly at the 13 week timepoint, where it was not possible to perform in person assessments. It is unclear how this might have affected the results, but it will have reduced the overall power given the relatively small sample size. Lastly, importantly, this study is the first of its kind and provides proof of concept results that will need to be validated in a larger study across multiple settings. Frailty (measured by CFS[23], FI[24], and Fried[24]), and sarcopenia[18,25] status have been measured with widespread use in hospitalised patients, although the FI variables used within this study were validated from a community population[11]. It is increasingly recognised that dynamic assessments are important, and studies have individually

utilised these assessments both at admission to[18,23,25], and discharge[18,24] from hospital.

Recommendations for future research and clinical practice

We consider that further research is warranted to determine what factors are predictive of changes in muscle quantity and function, and, importantly, the significance of such changes, before these assessments are in embedded into clinical practice. Research should focus on determining what is different about those who experienced improvements in muscle quantity and function compared to those who experienced declines. Assessment of frailty status should occur at baseline for hospitalised patients; assessment of baseline CFS is normally recommended to consider function two weeks prior to admission to hospital to account for the effects of acute illness[16]. However, frailty should be recognised and considered as a dynamic process. For instance, in patients with prolonged lengths of hospital stay, it may be appropriate to reassess frailty status, as it is likely that their vulnerability will have changed. This may have implications upon their overall management and goal-setting. Further research that aims to understand the effects of induced frailty upon immune dysregulation is strongly encouraged. The broad dynamic changes encountered in this study beyond changes in muscle and physical function alone have implications on how rehabilitation and interventional strategies are designed and implemented. Further research should address the benefits of multi-modal programmes e.g. targeting cognition as well as physical function.

Conclusion

Induced frailty and acute sarcopenia are overlapping conditions affecting older adults during hospitalisation. Induced frailty is likely to be reversible, but will be associated with increased vulnerability. Clinicians should be aware of the dynamic nature of frailty and sarcopenia, and should consider reassessing prior to discharge, and throughout admission in patients with prolonged lengths of stay. Further research should aim to stratify changes to enable targeted interventions.

Authors' contributions

CW designed the research question and study protocol. TAJ, CAG, TM, and TP all contributed towards design of the study protocol. CW, ZM, and HM all significantly contributed towards recruitment and follow-up assessments of participants in the study. CW analysed and interpreted the results, and was responsible for manuscript preparation. All authors significantly contributed towards the writing of the manuscript and approved the final submitted version.

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Supplement

Shrinking (Score 1 if either yes)	4.5 kg weight loss over last year?		Yes	No
	Over 5% loss of previous year's body weight on examination with scales		Yes	No
Weakness (score 1 if below or equal to cut-offs)	BMI – Male	Cut-off (kg)	BMI - Female	Cut-off (kg)
	≤24	≤29	≤24	≤17
	24-26	≤30	24-26	≤17.3
	26-28	≤30	26-28	≤18
	>28	≤32	>28	≤21
Self-reported exhaustion (score 1 if answers most or all of the time to either question)	How often over the last week have you felt that the following statements were true?			
	I felt that everything I did was an effort		None of the time	
			Some of the time	
			Most of the time	
			All of the time	
	I could not get going		None of the time	
			Some of the time	
			Most of the time	
			All of the time	
Gait speed (score 1 if below or equal to cut-offs)	Height (cm) – Male	Cut-off (m/s)	Height (cm) –Female	Cut-off (m/s)
	≤173	≤0.65	≤159	≤0.65
	>173	≤0.76	>159	≤0.76
Low physical activity (score 1 if answers yes to any questions)	In the last three months, have you:			
	Performed no weight-bearing physical activity		Yes	No
	Spent more than 4 hours/ day sitting		Yes	No
	Been for a short walk once/ month or less frequently		Yes	No

Table S1. Fried frailty definition. A score of 3 or more out of 5 was considered indicative of frailty. Low physical activity definition was adapted from the Frailty Intervention Trial[10]. All other definitions were taken from original study population definition[3].

Deficit	Definition
Activity limitation	Positive Fried physical activity score
Anaemia and haematinic deficiency	As per local reference ranges (female Hb<115, male Hb<135) or on medication for haematinic deficiency
Arthritis	Patient reported (includes osteoarthritis and inflammatory arthritis)
Atrial fibrillation	Any history – paroxysmal, temporary, or permanent
Cerebrovascular disease	Vascular dementia or stroke disease
Chronic kidney disease	eGFR <60
Diabetes mellitus	Known history/ confirmed diagnosis
Dizziness	Patient reported
Dyspnoea	Patient reported
Falls	Two or more over previous year
Foot problems	Patient reported
Fragility fracture	Previous history
Hearing impairment	Need for hearing aids
Heart failure	Known history/ confirmed diagnosis
Heart valve disease	Known history
Housebound	Lawton instrumental ADLs
Hypertension	On treatment or recorded
Presyncope/ syncope	Patient reported (altered from "hypotension" in original eFI)
Ischaemic heart disease	Known history
Memory and cognitive problems	Any cognitive spectrum disorder including mild cognitive impairment, delirium, and dementia
Osteoporosis	On treatment or known history
Parkinsonism and tremor	Includes tremor of any cause – known history or on treatment
Peptic ulcer	Known history
Peripheral vascular disease	Known history
Polypharmacy	≥5 prescribed medications
Requirement for care	Formal carers
Respiratory disease	Any history of chronic disease e.g. asthma, COPD
Skin ulcer	Present history as per Mini Nutritional Assessment (MNA) – patient reported
Sleep disturbance	Patient reported
Social vulnerability	Lives alone
Thyroid disease	Known history
Urinary or faecal incontinence	Katz ADLs
Urinary system disease	Known history
Visual impairment	Wears glasses/ visual aids or on treatment for eye condition(s)
Weight loss and anorexia	Fried weight loss OR MNA weight loss OR MNA intake decline

Table S2. Variables included within frailty index. Variables were adapted from those validated within the electronic Frailty Index (eFI)[11] for utilisation within a secondary care population.

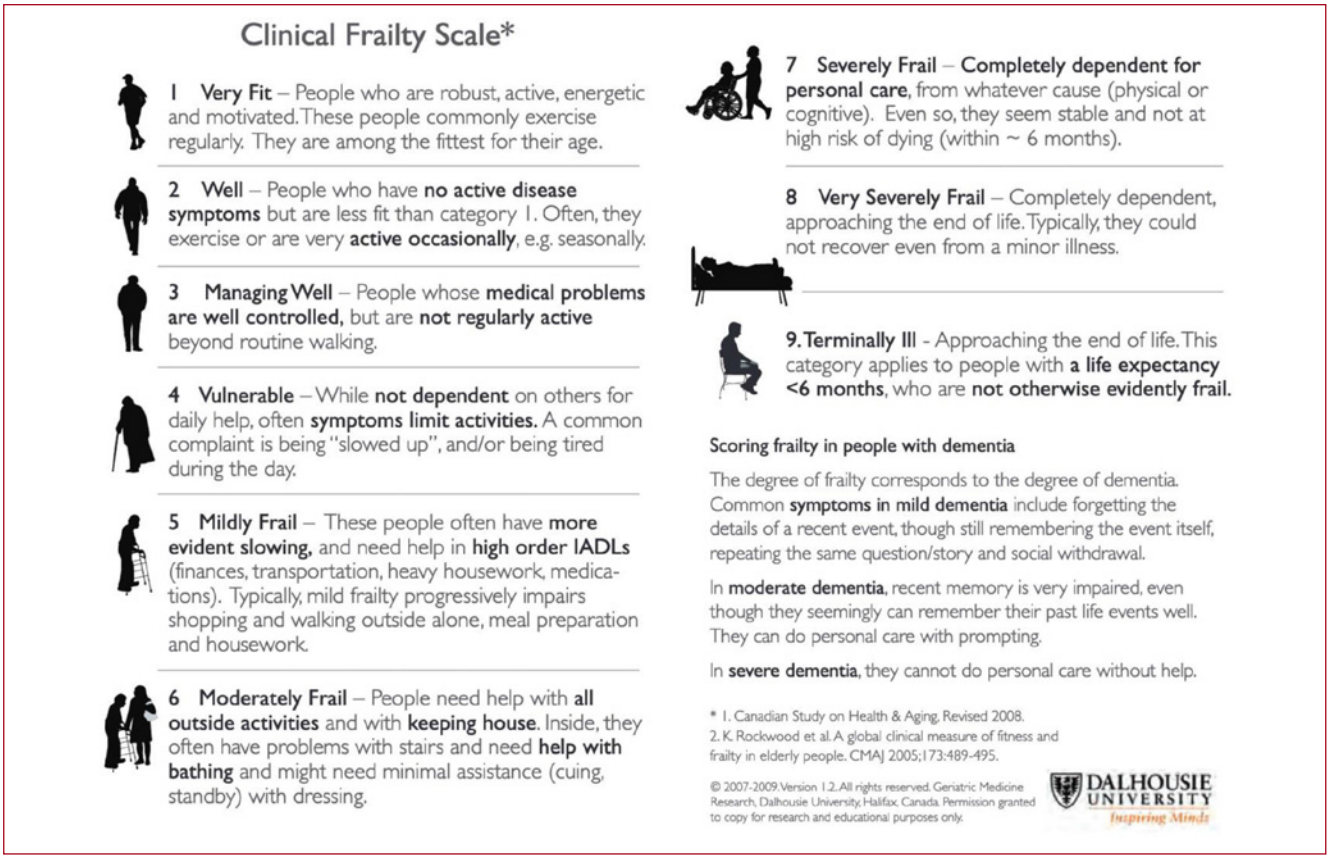

Figure S1. Clinical Frailty Scale (2008) (4, 12-Reproduced with permission).

	Male	Female
No sarcopenia	1. Handgrip strength ≥27kg	1. Handgrip strength ≥16kg
Probable sarcopenia	1. Handgrip strength <27kg	1. Handgrip strength <16kg
	2. BATT ≥5.44cm AND SMMSergi ≥20kg	2. BATT ≥3.85cm AND SMMSergi ≥20kg
Definite sarcopenia, not severe	1. Handgrip strength <27kg	1. Handgrip strength <16kg
	2. BATT <5.44cm AND/OR SMMSergi <20kg	2. BATT <3.85cm AND/OR SMMSergi <15kg
	3. Gait speed >0.8m/s AND SPPB >8	3. Gait speed >0.8m/s AND SPPB >8
Definite sarcopenia, severity unclear	1. Handgrip strength <27kg	1. Handgrip strength <16kg
	2. BATT <5.44cm AND/OR SMMSergi <20kg	2. BATT <3.85cm AND/OR SMMSergi <15kg
	3. Gait speed not measured AND SPPB not measured	3. Gait speed not measured AND SPPB not measured
Definite sarcopenia, severe	1. Handgrip strength <27kg	1. Handgrip strength <16kg
	2. BATT <5.44cm AND/OR SMMSergi <20kg	2. BATT <3.85cm AND/OR SMMSergi <15kg
	3. Gait speed ≤0.8m/s AND SPPB ≤8	3. Gait speed ≤0.8m/s AND SPPB ≤8

Table S3. Cut-off values used for sarcopenia diagnosis. Cut-off values for handgrip strength, SMMSergi, gait speed, and SPPB are taken from those recommended by the European Working Group in Older People 2[5]. Cut-off values for BATT are taken from those recommended by Wilson et al[13]. *BATT=Bilateral Anterior Thigh Thickness; SMMSergi=Skeletal Muscle Mass (Sergi equation).*

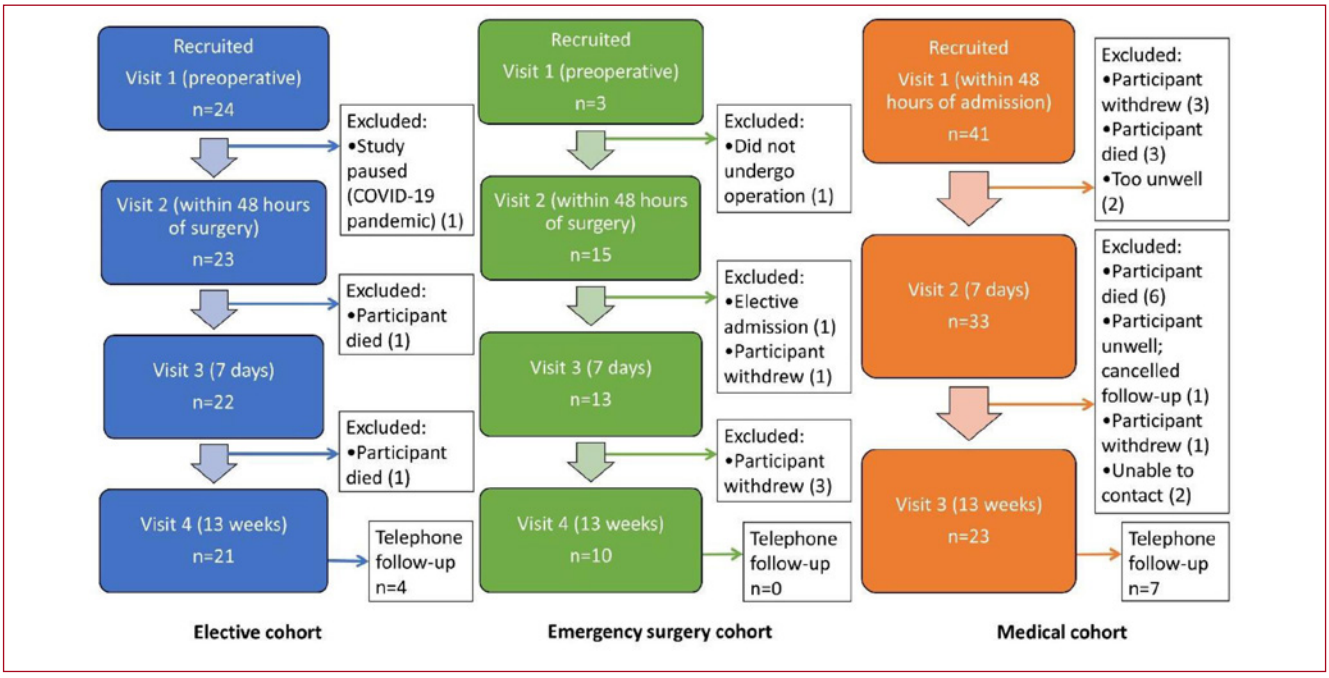

Figure S2. Recruitment flowchart.

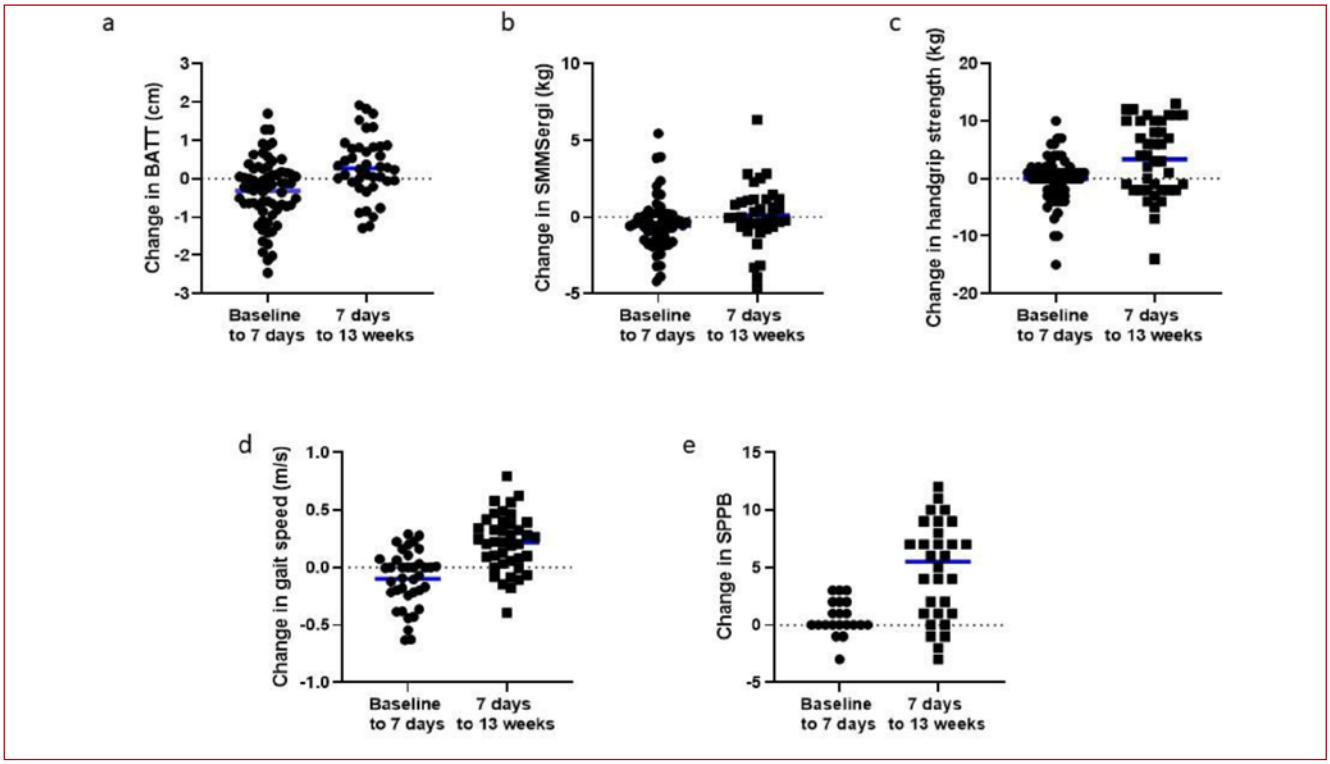

Figure S3. Raw change scores between individual component variables between timepoints.

	Baseline	7 days	13 weeks	p value
Overall	0.27 (0.25 – 0.30)	0.31 (0.28 – 0.33)	0.30 (0.27 – 0.34)	0.150
Elective	0.20 (0.17 – 0.24)	0.23 (0.20 – 0.27)	0.25 (0.22 – 0.28)	0.129
Emergency	0.25 (0.18 – 0.32)	0.27 (0.19 – 0.36)	0.25 (0.13 – 0.38)	0.902
Medical	0.32 (0.29 – 0.35)	0.37 (0.33 – 0.40)	0.38 (0.32 – 0.43)	0.057

Table S4. Estimated marginal means for frailty indices derived from linear mixed models.

	Baseline	7 days	13 weeks	p value
Overall	4 (3 – 5)	5 (4 – 6)	4 (3 – 5)	<0.001
Elective	3 (3 – 3)	4.5 (3 – 6)	3 (3 – 4)	<0.001
Emergency	3 (3 – 4)	5 (3 – 6)	3 (3 – 5)	0.007
Medical	5 (4 – 5)	5 (4.25 – 6)	5 (4 – 6)	0.001

Table S5. Median Clinical Frailty Scale scores across timepoints. Skillings-Mack and p-values are shown in the far right column. Twelve participants (2 elective, 2 emergency surgery, 8 medical) were excluded from analysis as only single baseline scores were available.

	Baseline	7 days	13 weeks	p value
Overall	3.80 (3.54 – 4.08)	4.91 (4.59 – 5.25)	4.11 (3.74 – 4.51)	<0.001
Elective	3.00 (2.67 – 3.37)	4.55 (3.99 – 5.18)	3.38 (2.97 – 3.85)	<0.001
Emergency	3.40 (2.78 – 4.16)	4.39 (3.57 – 5.39)	3.80 (2.97 – 4.87)	0.190
Medical	4.42 (4.08 – 4.77)	5.38 (4.97 – 5.81)	4.91 (4.34 – 5.56)	0.003

Table S6. Estimated marginal means for Clinical Frailty Scale scores as derived from generalized linear mixed models.

		Baseline	7 days	13 weeks	p value
Overall	No sarcopenia	41.8 (33)	36.4 (24)	50.0 (20)	0.148 Simulated: 0.023
	Probable sarcopenia	7.6 (6)	4.5 (3)	5.0 (2)	
	Confirmed sarcopenia, not severe	0 (0)	0 (0)	5.0 (2)	
	Confirmed sarcopenia, severity unclear	20.3 (16)	4.5 (3)	0 (0)	
	Confirmed sarcopenia, severe	30.4 (24)	54.5 (36)	40.0 (16)	
Elective	No sarcopenia	58.3 (14)	42.9 (9)	64.7 (11)	0.396 Simulated: 0.144
	Probable sarcopenia	8.3 (2)	0 (0)	0 (0)	
	Confirmed sarcopenia, not severe	0 (0)	0 (0)	0 (0)	
	Confirmed sarcopenia, severity unclear	0 (0)	9.5 (2)	0 (0)	
	Confirmed sarcopenia, severe	33.3 (8)	47.6 (10)	35.3 (6)	
Emergency	No sarcopenia	35.7 (5)	38.5 (5)	60.0 (6)	0.117 Simulated: 0.021
	Probable sarcopenia	7.1 (1)	0 (0)	0 (0)	
	Confirmed sarcopenia, not severe	0 (0)	0 (0)	20.0 (2)	
	Confirmed sarcopenia, severity unclear	57.1 (8)	0 (0)	0 (0)	
	Confirmed sarcopenia, severe	0 (0)	61.5 (8)	20.0 (2)	
Medical	No sarcopenia	34.1 (14)	31.3 (10)	23.1 (3)	0.949 Simulated: 0.782
	Probable sarcopenia	7.3 (3)	9.4 (3)	15.4 (2)	
	Confirmed sarcopenia, not severe	0 (0)	0 (0)	0 (0)	
	Confirmed sarcopenia, severity unclear	19.5 (8)	3.1 (1)	0 (0)	
	Confirmed sarcopenia, severe	39.0 (16)	56.2 (18)	61.5 (8)	

Table S7. Sarcopenia prevalence separated by severity across groups and timepoints.

	Δ Frailty index	Δ Clinical Frailty Scale	Δ Sarcopenia status
Δ Frailty index	r_s=1.00	r_s=0.43 p<0.001*	r_s=0.09 p=0.477
Δ Clinical Frailty Scale	r_s=0.43 p<0.001*	r_s=1.00	r_s=0.16 p=0.217
Δ Sarcopenia status	r_s=0.09 p=0.477	rs=0.16 p=0.217	r_s=1.00

Table S8. Spearman's correlation between changes in frailty and sarcopenia status between baseline and 7 days.

	Δ Frailty index	Δ Clinical Frailty Scale	Δ Sarcopenia status
Δ Frailty index	r_s=1.00	r_s=0.37 p=0.018*	r_s=0.09 p=0.569
Δ Clinical Frailty Scale	r_s=0.37 p=0.018*	r_s=1.00	r_s=0.25 p=0.126
Δ Sarcopenia status	r_s=0.09 p=0.596	r_s=0.25 p=0.126	r_ss=1.00

Table S9. Spearman's correlation between changes in frailty and sarcopenia status between 7 days and 13 weeks.