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Original Article

The impact of musculoskeletal ill health on quality of life and function after critical care: a multicentre prospective cohort study

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Summary

Physical disability is a common component of post-intensive care syndrome, but the importance of musculoskeletal health in this population is currently unknown. We aimed to determine the musculoskeletal health state of intensive care unit survivors and assess its relationship with health-related quality of life; employment; and psychological and physical function. We conducted a multicentre prospective cohort study of adults admitted to intensive care for > 48 h without musculoskeletal trauma or neurological insult. Patients were followed up 6 months after admission where musculoskeletal health state was measured using the validated Musculoskeletal Health Questionnaire score. Of the 254 participants, 150 (59%) had a musculoskeletal problem and only 60 (24%) had received physiotherapy after discharge. Functional Comorbidity Index, Clinical Frailty Scale, duration of intensive care unit stay and prone positioning were all independently associated with worse musculoskeletal health. Musculoskeletal health state moderately correlated with quality of life, r_s = 0.499 (95%CI 0.392–0.589); anxiety, r_s = -0.433 (95%CI -0.538 to -0.315); and depression, r_s = -0.537 (95%CI -0.631 to -0.434) (all $p < 0.001$). Patients with a musculoskeletal problem were less physically active than those without a problem (median (IQR [range]) number of 30 min physical activity sessions per week 1 (0–3.25 [0–7]) vs. 4 (1–7 [0–7]), $p < 0.001$, respectively). This study found that musculoskeletal health problems were common after intensive care unit stay. However, we observed that < 25% of patients received physical rehabilitation after discharge home. Our work has identified potential high-risk groups to target in future interventional studies.

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Introduction

The number of patients who survive after admission to the intensive care unit (ICU) is increasing [1]. Survivors of critical illness frequently experience new or worsening physical, mental and cognitive impairments, collectively termed post-intensive care syndrome, which may persist for years after the acute hospitalisation episode [2]. Resultant socio-economic burden is high, with continued high healthcare utilisation and prolonged periods of unemployment [3, 4].

Musculoskeletal conditions are common and often present alongside other long-term conditions that affect physical and mental health. They are a leading cause of pain, disability and work absence in the general population in the UK [5, 6], and account for 19% of all healthy years of life lost due to disability in low- and middle-income countries [7]. Musculoskeletal conditions may develop, or be exacerbated, after ICU admission. Patients with multi-organ injury typically lose 2% of muscle mass per day of inactivity [8]. This rapid muscle mass loss puts joints at risk of excess movement during patient handling and positioning in ICU, potentially resulting in injury [9].

Group exercise programmes that consist of cardiopulmonary and general strengthening exercises are typically prescribed for the physical disability component of post-intensive care syndrome [10–12] but, to date, these have not been proven to be effective [13]. Musculoskeletal conditions remain under-investigated as a potential cause of long-term disability in ICU survivors. Our scoping review of musculoskeletal complications following critical illness highlighted multiple studies that investigated individual aspects of musculoskeletal health (i.e. range of movement, pain or strength) after hospital discharge [14]. These studies reported a high prevalence of musculoskeletal complications; however, to our knowledge, no studies have evaluated the overall musculoskeletal health state of ICU survivors using specific patient-reported measures and work metrics [15]. Generation of this data would aid characterisation of the population to inform more targeted interventions post-ICU.

We hypothesised that musculoskeletal complications after discharge from ICU are common and significantly contribute to poor physical function; psychological function; and health-related quality of life. Therefore, we conducted a multicentre prospective cohort study to determine the health-related quality of life health state of ICU survivors 6 months following admission and assess its relationship with health-related quality of life, employment, anxiety, depression and physical function. We also aimed to identify prognostic factors for musculoskeletal health after critical illness.

Methods

The study was approved by an ethics committee and all participants provided written informed consent. This manuscript was prepared according to STROBE guidelines [16] and the study protocol was published prospectively [17].

A multicentre prospective cohort study was undertaken across five ICUs at four UK Trusts of varying sizes. Four of the ICUs were general ICUs of between six and 22 beds, accepting both medical and surgical patients. The fifth ICU was an eight-bedded surgical ICU. Adult patients (aged ≥ 18 y) admitted to ICU for > 48 h were eligible for participation and were recruited before hospital discharge. We did not study patients with neurological injury or pathology resulting in weakness, and/or being admitted to the ICU with musculoskeletal complications or trauma. A full list of eligibility criteria is available in online Supporting Information Table S1.

Baseline data were collected for all patients including: patient characteristics; admission information; ICU interventions; pre-admission function; and comorbidities including musculoskeletal history. Patients received a telephone follow-up 6 months after admission to ICU, where all outcome data were collected. The primary outcome was musculoskeletal health state, measured using the Musculoskeletal Health Questionnaire (MSK-HQ), a generic patient-reported outcome measure specifically designed to measure musculoskeletal health state [18]. Secondary outcomes included variables recommended as part of the ICU follow-up core outcome set [19], including: health-related quality of life; employment; anxiety and depression; and symptoms of post-traumatic stress disorder. These were measured using the European quality of life five dimensions (EQ-5D-5L) [20] score; John's Hopkins employment questionnaire [4]; hospital anxiety and depression score (HADS) [21]; and impact of events scale-revised (IES-R) score [22] (Box 1). Details on musculoskeletal injuries or treatment after discharge from hospital were also collected. Full details of the measures are available in online Supporting Information Table S2.

The sample size calculation was based on the identification of prognostic factors for musculoskeletal health 6 months after admission to ICU. Even though the aim of the study was not to formally construct a prognostic model, we based the sample size on current recommendations for their development and reporting [23,

Box 1 Outcome measures.

Musculoskeletal Health Questionnaire (MSK-HQ)	A single, short questionnaire developed to assess both musculoskeletal symptoms and health domains, capturing a patients' overall musculoskeletal health without the need for multiple condition-specific outcome measures. Scored out of 56 with a lower score indicating a worse musculoskeletal health state.
European Quality of Life Five Dimensions (EQ-5D-5L)	A brief, standardised tool used as a measure of health outcome. The utility score is scored out of 100 with a lower score indicating a worse overall health.
Hospital Anxiety and Depression Score (HADS)	A self-reported questionnaire designed to identify depression and anxiety. Each subscale is totalled out of 21 with a score of above seven indicating a potentially abnormal score.
Impact of Events Scale-Revised (IES-R)	A self-reported questionnaire designed to measure the subjective distress caused by traumatic events. Total scores are summed with higher scores indicating greater distress with regard to a specific event.

24]. Fifteen baseline prognostic factors potentially associated with a worse musculoskeletal health state were identified prospectively from the literature (online Supporting Information Table S2). Assuming an approximately normal distribution of residuals, the minimum sample size required to estimate a multiplicative margin of error of 0.1 was 249 patients [24]. Allowing for a 25% loss to follow-up, target recruitment was 332 participants.

Statistical analysis was performed using SPSS (version 27; SPSS Inc., Chicago, IL, USA) and a detailed statistical analysis plan has been made publicly available (https://doi.org/10.1186/ISRCTN24998809). Correlation of potential prognostic factors with the MSK-HQ score was analysed using Spearman's ρ for continuous variables and Mann–Whitney U tests for categorical variables. Spearman's ρ was also used to assess the relationships between MSK-HQ and employment, EQ-5D-5L, HADS and IES-R. Multivariable linear regression was used to assess the independent association of the previously identified potential predictors with the MSK-HQ score. Before including variables in the regression model, collinearity between candidate predictors was assessed. A backwards elimination (stepwise) procedure was used to identify which of the pre-specified candidate predictor variables (online Supporting Information Table S2) were included in the final multivariable regression model, with $p < 0.157$ (equivalent to the Akaike's information criterium) taken to warrant inclusion.

Results

Between 18 February 2022 and 2 January 2023, 334 patients were enrolled (Fig. 1). Final follow-up was in June 2023 with a follow-up rate of 76% (n = 254/334) and a mean (SD) follow-up of 190 (16.3) days. All patients completed the primary outcome data collection with 93% (n = 236/254) completing all other secondary outcomes. Baseline data had low levels of missingness with only one variable having > 10% of missing data (Medical Research Council sum score 83/254, 33% missing). These small levels of missingness in baseline and outcome measures meant planned multiple imputation was not warranted.

Patients had a mean (SD) age of 60 (15.0) y; were predominantly male (142/254, 64%); identified as white British (230/254, 91%); and were an emergency admission to ICU (210/254, 83%). There was a low prevalence of frailty and comorbidity (median (IQR [range]) Clinical Frailty Scale 3 (2–3 [1–7]) and Functional Comorbidity Index 1 (0–2 [0–7]), respectively). There was also a low prevalence of active musculoskeletal problems on admission to ICU (22/254, 9%). Mechanical ventilation was required for 121/254 (48%) patients for a median (IQR [range]) of 80 (34.5–171.5 [12–1008]) h. Almost all patients received active rehabilitation interventions while in ICU (243/254, 96%), but only 60/254 (24%) received physical rehabilitation after discharge from the acute hospital. Full participant characteristics are available in Table 1 and online Supporting Information Table S3.

Most patients lost to follow-up had either been re-admitted to hospital, commenced on palliative care or died (41/80, 51%) (Fig. 1). This sub-population had several differences with the rest of the cohort, including a greater proportion who were admitted with sepsis, received steroids or lived in a more socio-economically deprived area (online Supporting Information Table S3).

Most patients had a new musculoskeletal problem (150/254, 59%). In these patients, the mean (SD) MSK-HQ score was 40.1 (10.44). The most common individual locations for musculoskeletal problems were shoulder (51/150, 34%); lower back (35/150, 23%); and knee (29/150, 19%). However, multisite problems were frequently reported (59/150, 39%). Patients with a musculoskeletal problem achieved a lower level of mobility on ICU

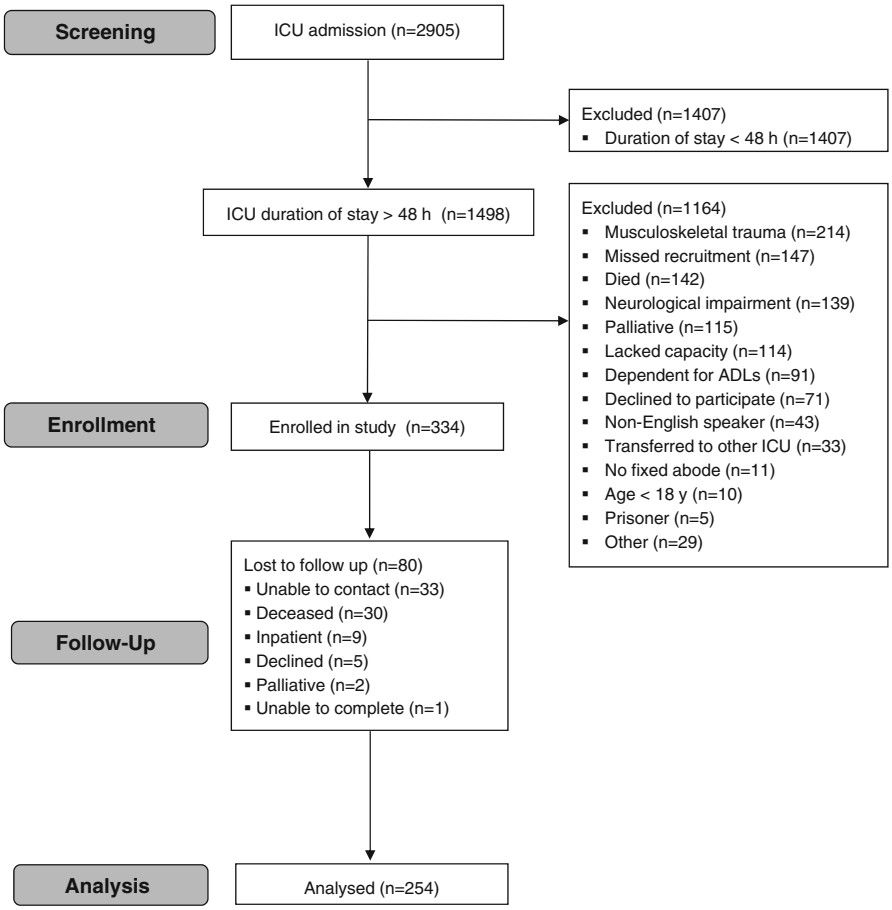

Figure 1 Study flow diagram. ADL, activities of daily living.

discharge and had a longer duration of hospital stay compared with those who did not have a musculoskeletal problem (median (IQR [range]) ICU mobility scale 5 (5–8 [0–10]) vs. 8 (5–10 [0–10]) and 17.5 (12–32 [5–116]) vs. 14 (10–22.75 [4–116]) days, respectively) (Table 1). There was a statistically significant correlation between the MSK-HQ score and Functional Comorbidity Index (r_s = -0.208 (95%CI -0.347 to -0.042); p = 0.008) and ICU duration of stay (r_s = -0.222 (95%CI -0.354 to -0.071); p = 0.005) (online Supporting Information Table S4). All patients who were positioned prone while their lungs were mechanically ventilated reported a musculoskeletal problem, and we found a negative relationship with lower MSK-HQ scores (U = 278.50, p = 0.002) in this cohort (Table 1 and online Supporting Information Table S5).

Fifteen variables were entered into the multivariable regression model after confirmation that collinearity was not present (online Supporting Information Tables S6 and S7). The multivariable linear regression model explained 17% of the variation in the MSK-HQ scores (F (5, 223) = 8.988, p < 0.001). The contribution of each variable to the final model is displayed in Table 2. Age; Clinical Frailty Scale; Functional Comorbidity Index; prone positioning; and ICU duration of stay were independently associated with the MSK-HQ score.

Patients with a musculoskeletal problem had significantly lower EQ-5D utility scores and higher anxiety and depression scores (Table 3). The MSK-HQ score was moderately correlated with EQ-5D utility score (r_s = 0.499 (95%CI 0.392–0.589), p < 0.001); HADS anxiety (r_s = -0.433 (95% CI -0.538 to -0.315), p < 0.001); and HADS depression (r_s = -0.537 (95%CI -0.631 to -0.434), p < 0.001). There were no differences in new unemployment or a reduction in working hours between patients with and without a musculoskeletal problem (Table 3). Patients without a musculoskeletal problem reported undertaking 30 min of physical activity four times more often per week than those with a musculoskeletal problem (median (IQR [range]) 4 (1–7 [0–7]) vs. 1 (0–3 [0–7]), p < 0.001). Three times as many patients with a musculoskeletal problem experienced falls

Table 1 Patient baseline and clinical characteristics. Values are mean (SD), number (proportion) or median (IQR [range]).

	Total n = 254	Musculoskeletal problem* n = 150	No musculoskeletal problem n = 104
Age; y	60 (15.0)	61 (14.4)	59 (15.8)
Sex; female	112 (44%)	67 (45%)	45 (43%)
Derived IMD	8 (6–9 [1–10])	8 (6–9 [1–10])	8 (6–10 [2–10])
Clinical Frailty Scale	3 (2–3 [1–7])	3 (2–4 [1–6])	3 (2–3 [1–7])
Functional Comorbidity Index	1 (0–2 [0–7])	1 (0.75–3 [0–7])	1 (0–2 [0–6])
Pre-existing musculoskeletal problem	22 (9%)	15 (10%)	7 (7%)
APACHE 2	17 (5.1)	17 (5.1)	16 (5.0)
Admission diagnosis			
Surgical	145 (57%)	86 (57%)	59 (57%)
Medical	109 (43%)	64 (43%)	45 (43%)
Mechanical ventilation	121 (48%)	79 (53%)	42 (40%)
Neuromuscular blocking drug	32 (13%)	24 (16%)	8 (8%)
Steroids	46 (18%)	24 (16%)	22 (21%)
Sepsis	101 (40%)	58 (39%)	43 (41%)
Prone position	7 (3%)	7 (5%)	0
Medical Research Council sum score; n = 171	52 (44–59 [8–60])	52 (40–57 [8–60])	54 (48–60 [12–60])
First day rehabilitation	2 (1–4 [0–35])	2 (1–4 [0–35])	2 (1–3 [1–24])
ICU mobility scale	6 (5–8 [0–10])	5 (5–8 [0–10])	8 (5–10 [0–10])
ICU duration of stay; d	5 (4–9.25 [2–54])	6 (4–11 [2–54])	5 (4–8 [2–28])
Hospital duration of stay; d	16 (11–29 [4–116])	17.5 (12–32 [5–116])	14 (10–22.75 [4–116])

IMD, Index of multiple deprivation.
*Musculoskeletal problem defined as participant-reported joint, back, neck, bone or muscle symptom such as ache, pain and/or stiffness.

Table 2 Final multivariable linear regression model.

Predictors	B*	95%CI	p Value
Age	0.102	0.004 to 0.199	0.041
Clinical Frailty Scale	−1.490	−2.896 to −0.083	0.038
Functional Comorbidity Index	−1.810	−2.851 to −0.770	0.001
Prone position	−12.172	−20.313 to −4.660	0.004
ICU duration of stay	−0.277	−0.466 to −0.087	0.004

*Change in the MSK-HQ score per unit of increase in the predictor variables.
Candidate predictor variables included in the multivariable regression model that was eliminated were: derived Index of Multiple Deprivation; presence of an active musculoskeletal problem on admission to ICU; admission diagnosis; APACHE 2 score; mechanical ventilation; neuromuscular blocking drugs; steroids; ICU mobility score; day to first rehabilitation intervention; and hospital duration of stay.

at home compared with those without (27/150, 18% vs. 6/104, 6%; p = 0.004) (Table 3).

Discussion

In this UK-based multicentre prospective cohort study, 59% of patients developed a new musculoskeletal problem 6 months after ICU admission, whereas only 24% received physical rehabilitation in the period after hospital discharge. Pre-admission frailty and comorbidity; prone positioning; and ICU duration of stay were independently associated with a worse musculoskeletal health state at follow-up. Furthermore, musculoskeletal health state was correlated with health-related quality of life, anxiety and depression. Our study identifies an important potential source of disability in ICU survivors that has not previously been thoroughly investigated. Further work is required to establish interventions to improve musculoskeletal health before critical illness. Current or future post-ICU

Table 3 Physical and psychological function. Values are mean (SD), median (IQR [range]) or number (proportion).

	Total n = 254	Musculoskeletal problem* n = 150	No musculoskeletal problem n = 104	p Value
EQ-5D-5L	64 (21.3)	57 (21.4)	73 (17.3)	< 0.001
HADS				
Depression	3 (1–6.75 [0–18])	5 (2–8.75 [0–18])	1.5 (0–4 [0–12])	< 0.001
Anxiety	3 (1–7 [0–21])	4 (2–9 [0–21])	2.5 (1–5 [0–18])	< 0.001
IES-R	0 (0–2 [0–62])	0 (0–4 [0–62])	0 (0–0 [0–39])	0.087
Employment				
New off work	32 (13%)	22 (15%)	10 (10%)	0.271
New part-time	7 (13%)	4 (3%)	3 (9%)	0.409
Fall	33 (13%)	27 (18%)	6 (6%)	0.004
Received physiotherapy	60 (24%)	46 (31%)	14 (14%)	0.002
Physical activity**	2 (0–5 [0–7])	1 (0–3.25 [0–7])	4 (1–7 [0–7])	< 0.001

EQ-5D 5l, European Quality of Life 5 Dimensions; HADS, Hospital Anxiety and Depression Score; IES-R, Impact of Events Scale-Revised.
*Musculoskeletal problem defined as participant-reported joint, back, neck, bone or muscle symptom such as aches, pain and/or stiffness.
**Number of sessions of physical activity per week lasting ≥ 30 min.

rehabilitation interventions should consider the contribution of poor musculoskeletal health to impaired physical function.

Physical disability is common following an ICU admission [25], with specific musculoskeletal problems a potential underlying cause [14]. Our study is the first to specifically evaluate musculoskeletal health in an unselected population of ICU patients and found that specific musculoskeletal problems are common and a significant burden of patient-reported disability after an ICU admission. These findings are consistent with previous studies evaluating single components of musculoskeletal health which have reported similarly high rates of pain [26–28]; weakness [29, 30]; and loss of joint range of movement [9]. Previous studies have identified the shoulder as the most common location for pain with decreased range of movement after admission to ICU [9, 27, 31, 32], consistent with our findings. The limited investigation of physical activity levels of ICU survivors after discharge from hospital to date suggests low levels of activity [33]. Patients with a musculoskeletal problem reported undertaking a physical activity session lasting at least 30 min only once per week, which was significantly less than those without a problem. Similarly, falls after critical illness is also a relatively under-investigated area [34]. We found patients who reported a musculoskeletal problem experienced more falls after discharge.

All patients completed the MSK-HQ score in full. Given that multisite musculoskeletal problems were common, the MSK-HQ score provides clinicians with an efficient and evidence-based method of evaluating change in musculoskeletal condition following an ICU admission. The mean MSK-HQ score of 40.1 in our study was higher than in other musculoskeletal populations, indicating better musculoskeletal health than, for example, pre-operative orthopaedic knee patients (mean 33.5 [18]). However, the wide range of MSK-HQ scores (5–55) indicates that the severity of problems varies greatly among the post-ICU population. The MSK-HQ score is correlated with EQ-5D-5L in other musculoskeletal populations [18] and was moderately correlated with HADS anxiety, HADS depression and EQ-5D-5L in our study. This supports our hypothesis that there is a relationship between musculoskeletal health, physical function, psychological function and health-related quality of life.

Previous studies have reported risk factors for continued pain after critical illness inconsistently [26–28, 32]. Reported risk factors have included sepsis; surgical admission; female sex; duration of stay; and being prone positioned. In our study, pre-admission comorbidity and frailty; being prone positioned; and duration of time in ICU were all identified as potential risk factors for a worse musculoskeletal health state. The decision to prone position is the only potentially modifiable risk factor identified in this study; clinicians should therefore consider longer-term musculoskeletal consequences when implementing this intervention. A recent review of rehabilitation trials suggests that patients with two or more comorbidities are more likely to respond to rehabilitation interventions, supporting the potential for improving pain and health-related quality of life in this group [35].

Our study has several strengths. First, the study protocol was prospectively registered and published [17]. Second, the

study reached its pre-specified recruitment and follow-up targets and had high outcome measure completion rates. Third, this is the only study to our knowledge to comprehensively evaluate musculoskeletal health following an ICU admission, and assess its relationship with physical, psychological and participation outcomes. A limitation of the study is that outcomes were measured using patient-reported outcome measures, which although considered useful as screening tools, should not be used as diagnostic tools [36]. Variables included in the linear regression model were not transformed to assess for non-linear relationships, so the strength of association with the MSK-HQ score should be interpreted with caution, alongside the relatively low explanatory power of the model. Further studies are required to confirm their potential predictive ability for musculoskeletal health state. Finally, our study population was predominantly from south-east England, which may reduce the external validity of the study due to a lack of participant diversity.

In summary, 6 months after admission to ICU, 59% of survivors had experienced a new musculoskeletal problem, with the shoulder most affected. Patients with a musculoskeletal problem were four times less physically active and experienced three times more falls than those without a problem. Despite this, few patients received physical rehabilitation after discharge from hospital. The musculoskeletal health state of ICU survivors was successfully measured using the MSK-HQ score and correlated with health-related quality of life, anxiety and depression. Several non-modifiable potential predictors of worse musculoskeletal health were identified, which should be further investigated and could be used to highlight high-risk groups for future studies of targeted therapeutic interventions.

Further research into targeted musculoskeletal rehabilitation interventions for this population is required. Given the high prevalence of problematic musculoskeletal health after ICU admission, a musculoskeletal assessment should form part of the physical evaluation used to determine personalised rehabilitation interventions following an ICU admission. Post-ICU rehabilitation programmes should ensure upper limb function is addressed and considered when measuring physical function. Future investigation research should explore the potential for musculoskeletal interventions to increase physical activity and decrease falls following critical illness.

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Supporting Information

Additional supporting information may be found online via the journal website.

Table S1. Inclusion and exclusion criteria.

Table S2. Variables and outcomes.

Table S3. Responder and non-responder characteristics.

Table S4. Continuous and ordinal correlation with MSK-HQ.

Table S5. Nominal variable association with MSK-HQ.

Table S6. Correlations of variables included in the multivariable regression.

Table S7. Multicollinearity assessment of final multivariable regression model.