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ORIGINAL

Impact of frailty on mortality, functional outcome, and health status after out-of-hospital cardiac arrest: insights from the TTM2-trial

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Abstract

Purpose: To explore the association of frailty with mortality, functional outcome, and health status after out-of-hospital cardiac arrest.

Methods: This is a cohort-based secondary analysis of the Targeted Hypothermia versus Targeted Normothermia after out-of-hospital cardiac arrest (TTM2) trial, an international, prospective, multicentre study. Frailty was assessed using the Clinical Frailty Scale (1–9): fit (1–3), prefrail (4), frail (5), and severely frail (6–9). Main outcomes were mortality and poor functional outcome (modified Rankin Scale 4–6) at 6 and 24 months. Additional outcomes included neuroprognostication, withdrawal-of-life-sustaining-therapies (WLST), functional decline (retrospectively reported pre-arrest versus 6 month Glasgow Outcome Scale Extended score), health status (EQ-5D-5L, EQ-VAS), and life satisfaction at 6 and 24 months.

Results: Of 1861 participants, 240 (13%) were prefrail, and 188 (10%) were frail or severely frail. Mortality and poor functional outcome increased significantly with greater frailty. Compared to fit participants, adjusted ORs (95% CI) for 6 month mortality were: prefrail 2.7 (1.8–3.8), frail 3.7 (1.9–7.1), and severely frail 8.9 (4.2–18.7); and poor functional outcome: prefrail 2.9 (1.9–4.2), frail 3.9 (1.9–8.1), and severely frail 35.4 (8.4–148.8). Severely frail participants underwent neuroprognostication less often ($p < 0.001$), while WLST was more common in the prefrail, frail and severely frail ($p < 0.001$). Prefrail and frail survivors tended to report more frequent functional decline and lower health status, though with individual variation.

Conclusion: Frailty was associated with a significantly increased risk of mortality and poor functional outcome after out-of-hospital cardiac arrest. Findings suggest more frequent functional decline and lower overall health status in frail survivors.

Trial registration: NCT02908308.

Keywords: Frailty, Out-of-hospital cardiac arrest, Mortality, Functional outcome, Patient-reported outcomes

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Introduction

Advanced age is associated with significantly increased mortality following out-of-hospital cardiac arrest [1]. With age, frailty—a syndrome characterized by reduced physical, physiological and cognitive reserve, leading to increased vulnerability to health stressors, even minor illnesses—becomes more prevalent [2]. Frailty affects approximately one-third of adults admitted to critical care and is associated with adverse outcomes in critically ill patients [3].

The focus on clinical frailty in critical illness is evolving [3], but few studies have investigated how frailty may affect outcomes following out-of-hospital cardiac arrest. Some studies report increased mortality [4–6] and lower incidence of favourable neurological outcome [7]. However, a recent meta-analysis did not confirm the association between frailty and increased mortality in out-of-hospital cardiac arrest patients due to a lack of power [7]. Furthermore, pre-arrest neurological impairments may influence post-arrest outcomes, highlighting the need to consider baseline status when evaluating survivors with frailty [8].

Cardiopulmonary resuscitation is an intense intervention [7], with an aging population, there is an increasing need to study outcomes in the frail to minimize harm. This study aimed to explore the association of frailty with mortality, functional outcome, and health status after an out-of-hospital cardiac arrest.

Take-home message

Pre-arrest frailty was associated with higher mortality and poor functional outcome following out-of-hospital cardiac arrest. Survivors with pre-arrest frailty tended to more often experience functional decline and report lower health status. These findings highlight the importance of assessing pre-arrest frailty, as it influences long-term recovery. Notably, survivors reported individual variations, suggesting complex relationships between frailty, outcome, and perceived quality of life.

Methods

Study design, setting and participants

We conducted a cohort-based secondary analysis of all 1861 participants in the Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial, a multicentre randomized clinical trial conducted from November 2017 to January 2020 (ClinicalTrials.gov: NCT02908308). The trial found no differences in mortality or functional outcome between temperature groups [9]. Eligible participants were unconscious adults with return-of-spontaneous-circulation after out-of-hospital cardiac arrest of presumed cardiac or unknown cause, eligible for intensive care without limitations in care. Full eligibility criteria have been published [10]. For this secondary analysis, we performed no separate sample size calculation, as the study size was determined by the available TTM2-population. Written informed consent was obtained, waived, or deferred from participants or legal representatives according to national regulations; all who regained mental capacity provided consent. At 6 and 24 months, a trained, blinded assessor conducted structured follow-up and evaluated outcomes primarily face-to-face, secondarily by telephone or home visits [11].

Frailty

The Clinical Frailty Scale (CFS) is a validated tool assessing frailty in critical illness [12] based on baseline health status two weeks before hospital admission, including physical frailty, cognition, comorbidity, disability, activity, and function [13]. In the TTM2-trial, the physician in charge or study team assessed the CFS score during hospitalization using medical records and, if needed, information from relatives, guided by a visual scale with a short explanatory text describing frailty levels from 1 (very fit) to 9 (terminally ill) [13]. We categorised participants as fit (CFS 1–3), prefrail (CFS 4), and frail (CFS 5) based on prior literature. We combined the higher categories into severely frail (CFS 6–9), due to small group sizes and few survivors.

Outcome and outcome measures

The main outcomes for this study were the associations between frailty and 6- and 24 month mortality and poor functional outcome. Additional outcomes included neuroprognostication, withdrawal-of-life-sustaining-therapies (WLST), functional decline, health status and life satisfaction at 6 and 24 months.

Poor functional outcome

We assessed functional outcome using the modified Rankin Scale (mRS), an ordinal scale from 0–6 where higher scores indicate worse outcome, and mRS 6 denotes death. The mRS, included in the Core Outcome Set for Cardiac Arrest (COSCA), is commonly used after neurological events [14]. We defined poor functional outcome as an mRS score of 4–6. If follow-up was not performed, we classified participants as independent (mRS 0–3) or dependent (mRS 4–6) in basic activities of daily living, using available data from healthcare professionals, relatives or medical records.

Neuroprognostication and WLST

An independent physician performed neuroprognostication after 96 h using the TTM2-trial criteria for a likely poor neurological outcome. Treating physicians made all WLST decisions in collaboration with the participants' relatives or legal surrogates. Neuroprognostication and WLST were managed as separate processes [10].

Functional decline

Glasgow Outcome Scale Extended (GOSE) is another assessment of functional status. To evaluate functional decline, we used the question "Was the patient independent at home before the injury?" and retrospectively compared pre-arrest status with GOSE at 6 months [15]. We categorised outcomes as good (GOSE 4–8) or poor (GOSE 2–3) and defined functional decline as a shift from good to poor. If GOSE was missing, we used all available data to assess participants as good or poor based on independency or dependency in basic activities of daily living.

Health status

The EQ-5D-5L is a brief self-reported health status questionnaire recommended by COSCA for health-related quality of life. It includes five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, each rated from 1 (no problems) to 5 (extreme problems or inability) [14]. We dichotomized responses into "no problems" (1) versus "any problems" (2–5) [14]. The EQ-VAS, part of EQ-5D-5L, records overall health, on a visual analogue scale, (range 0–100), with higher scores indicating better general health [14].

Life satisfaction

Assessed by a single question from the World Values Survey; "All things considered, how satisfied are you with your life as a whole these days?" The question reflects a subjective overall satisfaction with life and ranges from 1 (completely dissatisfied) to 10 (completely satisfied) [16].

Statistical analysis

We reported descriptive statistics for binary and categorical variables in counts and percentages and continuous variables as median with interquartile range (IQR). We explored associations between frailty and mortality or poor functional outcome using univariable and multivariable logistic regression models, reporting odds ratio (OR) with 95% confidence intervals (CI). Adjusted models controlled for clinically relevant confounders, including sex, age, Charlson comorbidity index, first monitored rhythm, presumed cause (cardiac vs non-cardiac), circulatory shock on admission, time to return-of-spontaneous-circulation, witnessed cardiac arrest and bystander cardiopulmonary resuscitation, to reduce confounding bias. We assessed multicollinearity among covariates and found no strong correlations. We evaluated model fit using the Hosmer–Lemeshow test, which indicated a good fit when the time to return-of-spontaneous-circulation was dichotomized at the median (<25 vs ≥ 25 min). Age was treated as a continuous variable in all models. Missing data for mortality and poor functional outcome were minimal ($<2\%$ at 6 months; $<4\%$ at 24 months; none for covariates) and handled via complete-case analysis. We used logistic regression to compare rates of neuroprognostication and WLST between groups. Due to few frail survivors and limited follow-up assessments, additional outcomes, including functional decline and health status, were only reported descriptively to avoid overinterpreting unstable results. We performed all analyses in Stata 18 (versions 18.0–18.5; Mac, StataCorp LLC, College Station, TX, USA). This study adheres to STROBE guidelines for observational studies [17].

Results

Of 1861 out-of-hospital cardiac arrest participants included in the TTM2-trial, 240 (13%) were prefrail and 188 (10%) were living with frailty pre-arrest, including 107 (6%) who were severely frail. Participants with frailty were older, had more frequent cardiac arrests at home, and were less likely to have a presumed cardiac cause or shockable first rhythm compared to fit participants (Table 1).

Mortality and poor functional outcome

Participants with greater frailty had higher odds of mortality at both 6 and 24 months in unadjusted and adjusted models. In adjusted analyses, the odds of mortality increased progressively with frailty severity compared to fit participants, beginning with prefrail participants and strongest among the severely frail (Table 2). Table 1 presents mortality rates, and Fig. 1 illustrates these findings alongside functional outcome across frailty categories. No participant with CFS score ≥ 7 survived to 6 months.

Participants with greater frailty had higher odds of poor functional outcome at both 6 and 24 months in unadjusted and adjusted models. In adjusted analysis, the odds of poor functional outcome increased progressively with greater frailty, with the most pronounced associations observed among severely frail participants (Table 2). Table 1 presents poor functional outcome rates, and Fig. 1 illustrates the findings alongside mortality across frailty categories.

Table 1 Patient characteristics and outcomes by CFS category

	Fit *n* = 1433 (77%)	Prefrail *n* = 240 (13%)	Frail *n* = 81 (4%)	Severely frail *n* = 107 (6%)	Total *N* = 1861 (100%)
Pre-arrest variables					
Male	1183 (83)	171 (71)	52 (64)	71 (66)	1477 (79)
Age (years)	63 (53–72)	72 (64–78)	74 (66–79)	74 (66–80)	65 (56–74)
Charlson comorbidity index	2 (1–4)	4 (3–6)	5 (3–6)	5 (4–6)	3 (1–4)
Cardiac arrest related variables					
Location of cardiac arrest, home	702 (49)	142 (59)	61 (75)	73 (68)	978 (53)
Witnessed arrest	1309 (91)	219 (91)	75 (93)	99 (93)	1702 (91)
Bystander CPR	1185 (83)	171 (71)	60 (74)	71 (66)	1487 (80)
First monitored rhythm, shockable	1159 (81)	131 (55)	35 (43)	46 (43)	1371 (74)
Presumed cause, cardiac	1291 (90)	189 (79)	62 (77)	71 (66)	1613 (87)
Circulatory shock on admission	387 (27)	84 (35)	27 (33)	38 (36)	536 (29)
Minutes to ROSC	25 (17–39)	27 (16–42)	26 (18–41)	25 (16–36)	25 (17–40)
Mortality					
Mortality, 30 days	530/1422 (37)	170 (71)	66 (81)	96 (90)	862/1850 (47)
Mortality, 6 months	564/1422 (40)	181 (75)	68 (84)	98 (92)	911/1850 (49)
Mortality, 24 months	608/1386 (44)	188/230 (82)	73/80 (91)	99 (93)	968/1803 (54)
Days to death	5 (2–9)	4 (2–9)	4 (2–6)	4 (1–6)	5 (2–9)
Neuroprognostication performed	704/1432 (49)	112/239 (47)	36 (44)	31/106 (29)	883/1858 (48)
WLST	373 (26)	124 (52)	52 (64)	71 (66)	620 (33)
Hours to WLST	111 (71–165)	95 (51–149)	95 (50–131)	74 (17–107)	100 (60–150)
Reason for WLST					
Poor neurological prognosis	214 (57)	50 (40)	20 (38)	14 (20)	298 (48)
Organ failure	62 (17)	22 (18)	8 (15)	19 (27)	111 (18)
Combination	32 (9)	20 (16)	14 (27)	19 (27)	85 (14)
Comorbidity	7 (2)	9 (7)	2 (4)	10 (14)	28 (5)
Other	55 (15)	20 (16)	7 (13)	8 (11)	90 (15)
Unknown	3 (1)	3 (2)	1(2)	1(1)	8(1)
Cause of death[a]					
Cardiovascular	109 (21)	51 (30)	23 (35)	27 (29)	210 (24)
Cerebral	303 (58)	84 (49)	26 (39)	37 (39)	450 (52)
Multi-organ failure	89 (17)	25 (15)	12 (18)	22 (23)	148 (17)
Other	26 (5)	12 (7)	5 (8)	8 (9)	51 (6)
Functional outcome					
Poor[b], 6 months	622/1404 (44)	191/238 (80)	70/80 (88)	105 (98)	988/1829 (54)
Poor[b], 24 months	708/1373 (52)	206/239 (86)	74/80 (93)	104/106 (98)	1092/1798 (61)
Follow-up assessments					
6 months	769/858 (90)	52/59 (88)	10/13 (77)	5/9 (56)	836/939 (89)
24 months	623/778 (80)	40/42 (95)	4/7 (57)	3/8 (38)	670/835 (80)

Results are presented in counts (percentages) or in median (interquartile range). Denominators are shown only for variables with missing data; otherwise, the full sample size applies. For follow-up assessments, denominators reflect the number of participants alive at each time point. Participants were categorised as fit (CFS 1–3), prefrail (CFS 4), frail (CFS 5), and severely frail (CFS 6–9)

CFS Clinical frailty scale, *CPR* Cardiopulmonary resuscitation, *ROSC* Return of spontaneous circulation, *WLST* Withdrawal-of-life-sustaining-therapies

[a] Cause of death is only described for participants who died in the hospital

[b] Modified Rankin scale (mRS) 4–6 was considered as poor functional outcome

Table 2 Logistic regression of mortality and poor functional outcome at 6 and 24 months

	N events / N at risk	Odds ratio (95% confidence interval)	
		Univariable model	Multivariable model
Mortality			
6 months			
Fit	564/1422	1	1
Prefrail	181/240	4.7 (3.4–6.4)*	2.7 (1.8–3.8)*
Frail	68/81	8 (4.4–14.5)*	3.7 (1.9–7.1)*
Severely frail	98/107	16.6 (8.3–33.1)*	8.9 (4.2–18.7)*
24 months			
Fit	608/1386	1	1
Prefrail	188/230	5.7 (4–8.1)*	3 (2–4.5)*
Frail	73/80	13.3 (6.1–29.2)*	5.5 (2.4–12.5)*
Severely frail	99/107	15.8 (7.7–32.8)*	7.1 (3.3–15.6)*
Poor functional outcome			
6 months			
Fit	622/1404	1	1
Prefrail	191/238	5.1 (3.7–7.1)*	2.9 (1.9–4.2)*
Frail	70/80	8.8 (4.5–17.2)*	3.9 (1.9–8.1)*
Severely frail	105/107	66 (16.2–268.5)*	35.4 (8.4–148.8)*
24 months			
Fit	708/1373	1	1
Prefrail	206/239	5.9 (4–8.6)*	3.1 (2–4.7)*
Frail	74/80	11.6 (5–26.8)*	4.8 (2–11.6)*
Severely frail	104/106	48.8 (12–198.7)*	21.8 (5.2–91.5)*

Mortality and poor functional outcome by CFS category. Functional outcome was assessed using the mRS, with scores of 4–6 defined as a poor functional outcome. The multivariable logistic regression models were adjusted for sex, age, Charlson comorbidity index, first monitored rhythm, presumed cause (cardiac vs non-cardiac), circulatory shock on admission, time to return-of-spontaneous-circulation, witnessed cardiac arrest, and bystander cardiopulmonary resuscitation. Participants were categorised as fit (CFS 1–3), prefrail (CFS 4), frail (CFS 5), and severely frail (CFS 6–9)

CFS Clinical frailty scale, *mRS* modified rankin scale

* $p < 0.001$

Neuroprognostication and WLST

Severely frail participants received neuroprognostication less often ($p < 0.001$). Additionally, prefrail, frail and severely frail participants underwent WLST more often ($p < 0.001$), with a trend towards shorter time to WLST. While poor neurological prognosis was the main reason for WLST overall, combined reasons were more frequent in prefrail and frail participants, while in severely frail participants, organ failure and combined reasons were most frequent (Table 1).

Survivors

Survivors with frailty participated less frequently in follow-up assessments at both 6 and 24 months (Table 1). At 6 months, 58/840 (7%) of fit, 10/57 (18%) of prefrail, 2/12 (17%) of frail, and 7/9 (78%) of severely frail survivors had a poor functional outcome based on the mRS. Among prefrail, frail and severely frail survivors, 7/75 (9%) reported poor pre-arrest functional status based on the GOSE. Functional decline occurred in 36/767 (5%) of the fit, 5/54 (9%) of the prefrail, 2/12 (17%) of the frail, and 4/9 (44%) of the severely frail survivors (Fig. 2).

At 6 months, mobility problems on the EQ-5D-5L increased with greater frailty. Severely frail survivors reported more frequent problems with self-care and usual activities. Pain/discomfort and anxiety/depression varied slightly between the groups (Fig. 3, Table E1). At 24 months, fit and prefrail survivors' health status was similar to 6 months, while prefrail and severely frail survivors' responses varied (Fig. E1, Table E2). The 6-month overall health on the EQ-VAS was highest in fit survivors, slightly lower in prefrail and frail, and lowest in the severely frail, consistent at both time points (Figs. E2a, E3a).

Few severely frail survivors reported life satisfaction ($n = 4/9$); this group reported the highest median score at 6 months, followed by fit survivors. Prefrail and frail reported slightly lower scores (Fig. E2b). At 24 months, prefrail, frail and severely frail survivors reported lower life satisfaction than fit survivors (Fig. E3b).

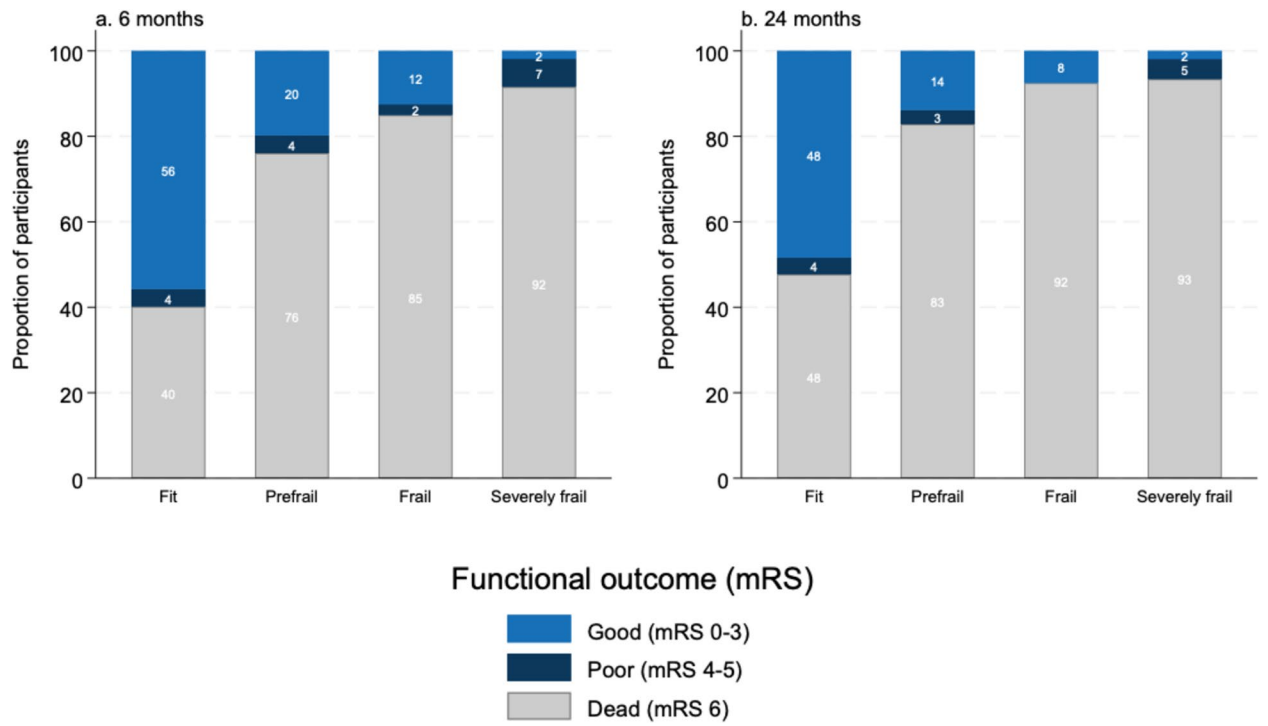

Fig. 1 Mortality and functional outcome based on mRS at 6 and 24 months, grouped by CFS category. At 6 months, among fit participants, 782/1404 (56%) had a good functional outcome, 58/1404 (4%) had a poor functional outcome, and 564/1404 (40%) had died. Among prefrail participants, 47/238 (20%) had a good functional outcome, 10/238 (4%) a poor functional outcome, and 181/238 (76%) had died. Among frail participants, 10/80 (12%) had a good functional outcome, 2/80 (2%) a poor functional outcome, and 68/80 (85%) had died. Among severely frail participants, 2/107 (2%) had a good functional outcome, 7/107 (7%) a poor functional outcome, and 98/107 (92%) had died. At 24 months, among fit participants, 665/1373 (48%) had a good functional outcome, 53/1373 (4%) had a poor functional outcome, and 655/1373 (48%) had died. Among prefrail participants, 33/239 (14%) had a good functional outcome, 8/239 (3%) a poor functional outcome, and 198/239 (83%) had died. Among frail participants, 6/80 (8%) had a good functional outcome, and 74/80 (92%) had died. Among severely frail participants, 2/106 (2%) had a good functional outcome, 5/106 (5%) a poor functional outcome, and 99/106 (93%) had died. Percentages may not sum to 100% due to rounding. Participants were categorised as fit (CFS 1–3), prefrail (CFS 4), frail (CFS 5), and severely frail (CFS 6–9). *CFS* Clinical frailty scale. *mRS* modified rankin scale

Discussion

In this cohort-based secondary analysis of the TTM2-trial, frail participants had higher long-term mortality and poorer functional outcome at 6 and 24 months. Severely frail participants received neuroprognostication less often, while prefrail, frail and severely frail participants underwent WLST more frequently. Functional decline compared to pre-arrest tended to be more frequent with greater frailty. Prefrail and frail survivors reported lower overall health status than fit participants, but with individual variation.

Our finding of higher mortality in frail participants aligns with previous studies on out-of-hospital cardiac arrest [4–6, 18]. The CFS is commonly used in critically ill patients, with ≥5 considered frail [12]. We initially separated CFS categories based on expected outcome differences, except CFS 1–3 due to absence of frailty [19]. However, with few participants in higher categories and none with CFS ≥7 surviving to 6 months, we merged CFS 6–9 into severely frail. While this may have influenced the results, we believe it preserved more clinical nuance than dichotomizing frailty. Severely frail participants showed markedly higher odds of mortality, and the absence of survivors with CFS ≥7 supports findings from McPherson et al. [18]. Our categorisation also revealed higher mortality among prefrail participants, suggesting that binary classifications may obscure important differences, a notion further supported by Hwai et al. [20] who indicated a non-linear increased risk of poor neurological outcome across the frailty scale. Previous studies have used the CFS as either a linear scale [6, 18] or as categories [4, 6, 18], a distinction crucial when interpreting results.

While frailty was strongly associated with mortality, this relationship is complex. Frailty may reflect underlying biological vulnerability, but it may also influence clinical decision-making, including WLST, which was more common in frail participants and not always based solely

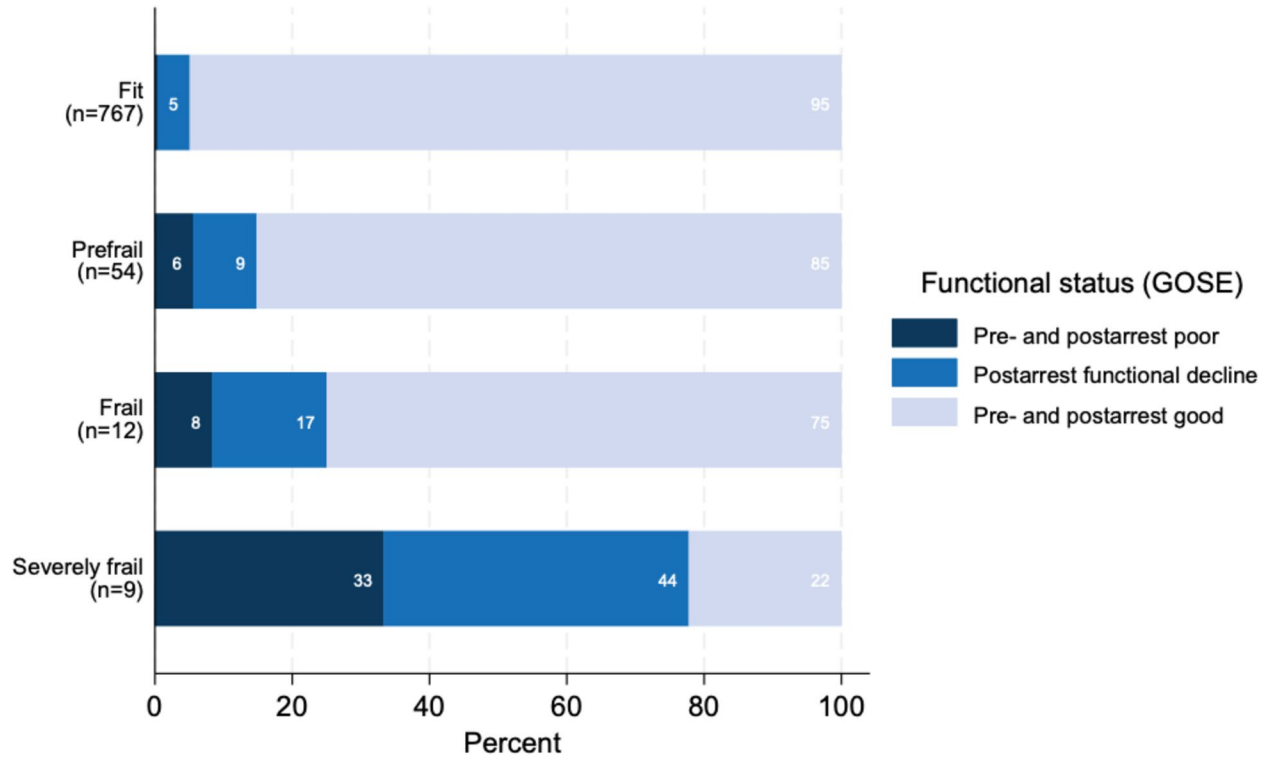

Fig. 2 Functional decline at 6 months according to GOSE, compared to pre-arrest functional status, and shown by CFS category. GOSE scores of 2–3 were considered poor functional status, scores of 4–8 were considered good functional status, and a shift from good to poor was defined as functional decline. Results are reported descriptively without statistical comparison. Participants were categorised as fit (CFS 1–3), prefrail (CFS 4), frail (CFS 5), and severely frail (CFS 6–9). *GOSE* Glasgow outcome scale extended, *CFS* Clinical frailty scale

on neurological prognosis. This finding should not be interpreted as evidence of a causal relationship. Although poor neurological prognosis precedes most deaths after cardiac arrest, guidelines recommend considering age, comorbidities, and overall organ function in WLST decisions. Thus, WLST may be ethically considered even in cases with uncertain or favourable neurological prognoses [21]. Despite higher mortality and WLST rates, one in ten frail participants survived to 6 months. Our findings do not justify withholding cardiopulmonary resuscitation based on frailty alone, but rather guide treatment to avoid potential harm and ensure fit older patients receive appropriate and beneficial care [2]. Preferences for cardiopulmonary resuscitation vary and some elderly express unrealistic expectations [22], underscoring the need for clear communication about prognosis and treatment goals.

Frail participants were less likely to achieve a good functional outcome after out-of-hospital cardiac arrest, consistent with previous findings [7]. While increased mortality largely explained this, we assumed that pre-arrest dependency in daily activities, central to both frailty and poor functional outcome, also contributed. Although there was a trend towards impaired pre-arrest function, most prefrail and frail survivors reported independence before their cardiac arrest. Instead, we found a more pronounced functional decline among survivors with greater frailty. Similarly, Mowbray et al. [6] reported that 67% of home care patients classified as frail by the Frailty Index [23, 24] experienced a decline in functional independence following out-of-hospital cardiac arrest. We acknowledge the risk of recall bias in retrospectively assessing pre-arrest functional status, especially when based on survivors' or relatives' reports. The use of a single, non-validated question limits the precision and reliability of this baseline measure. However, involving relatives in follow-up assessments may have mitigated some of this bias. This exploratory approach nonetheless provides valuable insight into functional changes over time and highlights that some impairments may have been present before the cardiac arrest. Supporting this, prior research found both fit and frail in-hospital survivors had impaired pre-arrest neurological status, with most experiencing stable or improved outcome at discharge [8]. Ohbe et al. [25] similarly reported no significant change in care needs from before cardiopulmonary

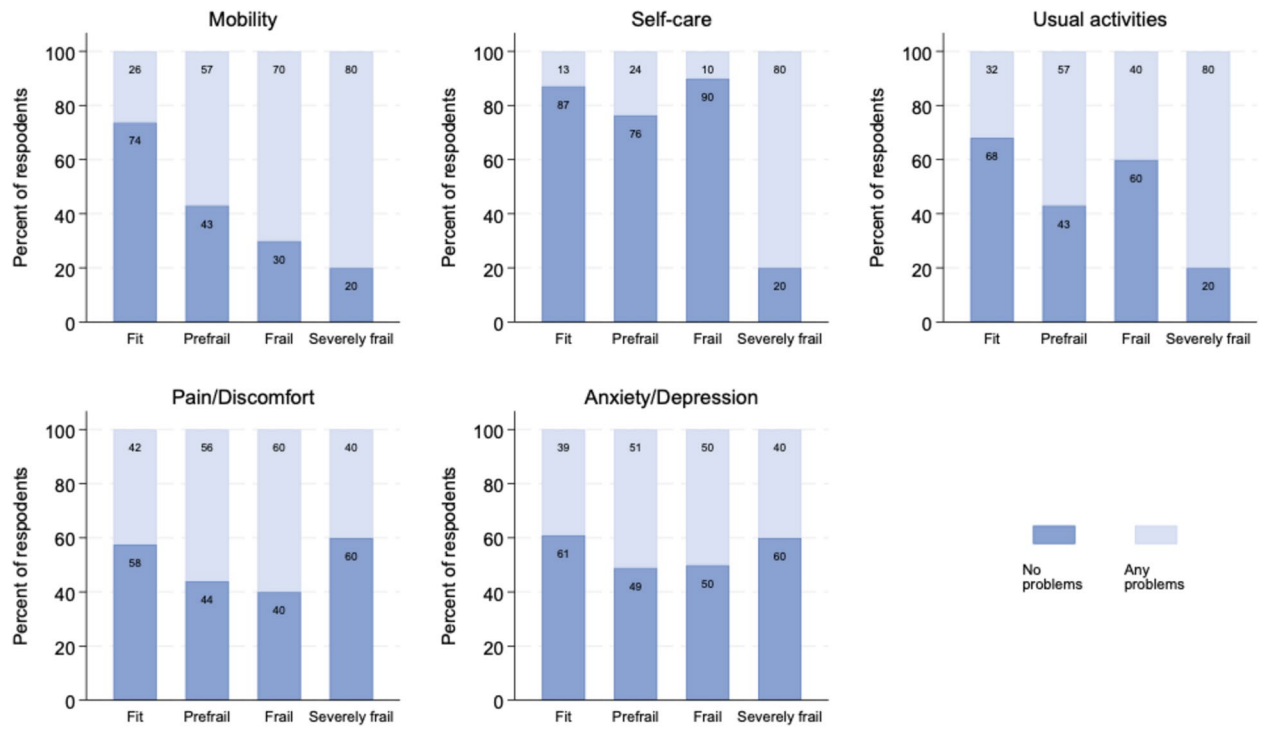

Fig. 3 Patient-reported health status at 6 months based on EQ-5D-5L, dichotomized into "no problems" versus "any problems", and presented by CFS category. In total, 750/858 (87%) of fit survivors, 51/59 (86%) of prefrail survivors, 10/13 (77%) of frail survivors, and 5/9 (56%) of severely frail survivors completed the questionnaire. Results are reported descriptively without statistical comparison. Participants were categorised as fit (CFS 1–3), prefrail (CFS 4), frail (CFS 5), and severely frail (CFS 6–9). *EQ-5D-5L* EuroQol 5-dimensions 5-levels, *CFS* Clinical frailty scale

resuscitation to one year after, in both in-hospital and out-of-hospital cardiac arrest cases, emphasizing the importance of accounting for pre-arrest status. Given the risk of post-arrest functional decline, especially in frail individuals, comprehensive geriatric assessment and specialist multidisciplinary care may be essential, as they can reduce cognitive and functional decline, lower in-hospital mortality, and increase the chances of returning home [2].

To our knowledge, no previous study has explored patient-reported outcomes by frailty in out-of-hospital cardiac arrest survivors. Frail survivors participated less frequently in follow-up assessments, likely due to poorer health, which may underestimate the 'true' problems in our results. Therefore, our descriptive exploratory findings should be interpreted cautiously.

At 6 months, EQ-5D-5L responses suggested tendencies towards more problems with mobility, self-care, and usual activities among severely frail survivors, which is expected since the CFS partly reflects these aspects of everyday function. Reports of pain/discomfort and anxiety/depression appeared similar across frailty categories. This result contrasts with a study of in-hospital cardiac arrest survivors where frail survivors reported more frequent problems in these dimensions [8]. Differences in health status and comorbidity burden between out-of-hospital and in-hospital survivors may partly explain this contrast [26]. At 24 months, frail and severely frail survivors rated their health status differently compared to 6 months, though low responses limit interpretation.

Overall health, based on EQ-VAS at both 6 and 24 months, was slightly lower in prefrail and frail survivors, consistent with findings in frail in-hospital survivors [8]. Due to varying CFS categorisations, we observed the largest reduction among severely frail survivors. Poor self-assessed health is relevant to frailty and may reflect accurate self-awareness [27]. While prefrail and frail survivors showed a declining trend in life satisfaction, severely frail survivors reported the highest median score. Given the very small number of severely frail survivors reporting life satisfaction, this finding should be interpreted with great caution. Frailty is strongly associated with cognitive impairment and dementia [2], which may have influenced responses. Although frailty correlates with lower quality of life [28], qualitative studies suggest some survivors view their survival as a second chance at life [29]. Our findings may align with Vanleerberghe et al. [30], who report that some frail individuals

experience a high quality of life and argue that coping and resilience can influence how individuals perceive quality of life. Further research is needed to understand these outcomes better and demonstrates the necessity of including patient-reported and qualitative data in frail cardiac arrest survivors.

Strengths and limitations

The primary strength of this study lies in the use of a validated frailty instrument and a large, international, prospective sample with minimal missing data. Additional strengths include blinded follow-up assessments, patient-reported outcomes, and a retrospective measure to control for pre-arrest function. We applied extensive efforts to include all survivors in follow-up assessments, offering home visits when feasible, though some may still have been missed.

Our study has several limitations. First, the TTM2-trial likely excluded the frailest patients, resulting in lower (10%) frailty prevalence than in other out-of-hospital cardiac arrest studies [4, 18]. Therefore, our findings likely underestimate the true prevalences and should be interpreted with caution given the limited generalisability of this cohort. Second, the CFS lacks objective measures and has not been validated in younger populations [13], though it is widely used in critical care [12] and cardiac arrest studies [4, 6, 18]. Since frailty is multidimensional [28], it may have been underestimated, compared to assessments by geriatricians who may better capture its complexity; moreover we also relied on unblinded evaluations. Third, our observational design prevented us from distinguishing biological effects of frailty from care decisions such as WLST, limiting causal interpretation and introducing the risk of self-fulfilling prophecy bias. Future studies using advanced causal methods are needed to clarify these relationships. Fourth, dichotomizing mRS and GOSE reduced granularity, and the small number of frail survivors limited statistical analysis of follow-up data, but their reported outcomes still offer valuable insight into this vulnerable group. Although the total sample was large, few participants were severely frail, resulting in wide confidence intervals and imprecise estimates. Still, frailty was clearly associated with higher mortality and poor functional outcome.

Conclusion

This study adds to the limited research on frailty in out-of-hospital cardiac arrest. Participants with frailty had higher odds of mortality and poor functional outcomes. Our findings suggest more frequent functional decline and lower overall health status in frail survivors, but with individual variations.

Supplementary Information

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Authors contributions

Concept and design: SGA, SU, AWE, NN, GL. Acquisition, analysis, or interpretation of data: All authors. Statistical analysis: SGA, SU. Drafting the manuscript: SGA, SU, AWE, NN, GL. Critical revision of manuscript for important intellectual content and approval of final version for publishing: All authors. Supervision: SU, AWE, NN, GL. Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: All authors.

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Data availability statement

Data are available upon reasonable request.

Declarations

Conflicts of interest

SGA, AWE, SU, TC, HF, JCJ, EBN, KH, AC, MH, JH, CRy, FST, PJY, NN, GL report no conflicts of interest. CRo received fees as a speaker from BD. MPW has served on advisory boards for DRW Diagnostics and the Clinical Expert NICE Advice Service. CR is Deputy Editor for Intensive Care Medicine. She has not taken part in the review or selection process of this article.

Ethical approval

The study was approved by the Regional Ethics Committee at Lund University (2015/228) and in all participating countries. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

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References

1. Zanders R, Druwé P, Van Den Noortgate N, Piers R (2021) The outcome of in- and out-hospital cardiopulmonary arrest in the older population: a scoping review. Eur Geriatr Med 12:695–723. https://doi.org/10.1007/s41999-021-00454-y
2. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K (2013) Frailty in elderly people. Lancet 381:752–762. https://doi.org/10.1016/S0140-6736(12)62167-9
3. Gordon JI, Brummel NE (2024) Implications of frailty before and after intensive care unit admission. Curr Opin Crit Care 30:472–478. https://doi.org/10.1097/mcc.0000000000001197
4. Yamamoto R, Tamura T, Haiden A, Yoshizawa J, Homma K, Kitamura N, Sugiyama K, Tagami T, Yasunaga H, Aso S, Takeda M, Sasaki J, Group S-KS (2023) Frailty and neurologic outcomes of patients resuscitated from nontraumatic out-of-hospital cardiac arrest: a prospective observational study. Ann Emerg Med 82:84–93. https://doi.org/10.1016/j.annemergmed.2023.02.009
5. Sulzgruber P, Sterz F, Poppe M, Schober A, Lobmeyr E, Datler P, Keferböck M, Zeiner S, Nürnberger A, Hubner P, Stratil P, Wallmueller C, Weiser C, Warenits AM, van Tulder R, Zajicek A, Buchinger A, Testori C (2017) Age-specific prognostication after out-of-hospital cardiac arrest - the ethical dilemma between "life-sustaining treatment" and "the right to die" in the elderly. Eur Heart J Acute Cardiovasc Care 6:112–120. https://doi.org/10.1177/2048872616672076
6. Mowbray FI, Turcotte L, Strum RP, de Wit K, Griffith LE, Worster A, Foroutan F, Heckman G, Hebert P, Schumacher C, Jones A, Mercier E, Gayowsky A, Costa AP (2023) Prognostic association between frailty and post-arrest health outcomes in patients receiving home care: a population-based retrospective cohort study. Resuscitation 187:109766. https://doi.org/10.1016/j.resuscitation.2023.109766
7. Zhang H, Wang A, Zhou M (2024) Impact of frailty on survival and neurological outcomes after cardiac arrest: a systematic review and meta-analysis. Cardiol Rev. https://doi.org/10.1097/CRD.0000000000000702
8. Jonsson H, Piscator E, Israelsson J, Lilja G, Djarv T (2022) Is frailty associated with long-term survival, neurological function and patient-reported outcomes after in-hospital cardiac arrest? - a Swedish cohort study. Resuscitation 179:233–242. https://doi.org/10.1016/j.resuscitation.2022.07.013
9. Dankiewicz J, Cronberg T, Lilja G, Jakobsen JC, Levin H, Ullén S, Rylander C, Wise MP, Oddo M, Cariou A, Bělohlávek J, Hovdenes J, Saxena M, Kirkegaard H, Young PJ, Pelosi P, Storm C, Taccone FS, Joannidis M, Callaway C, Eastwood GM, Morgan MPG, Nordberg P, Erlinge D, Nichol AD, Chew MS, Hollenberg J, Thomas M, Bewley J, Sweet K, Grejs AM, Christensen S, Haenggi M, Levis A, Lundin A, Düring J, Schmidbauer S, Keeble TR, Karamasis GV, Schrag C, Faessler E, Smid O, Otáhal M, Maggiorini M, Wendel Garcia PD, Jaubert P, Cole JM, Solar M, Borgquist O, Leithner C, Abed-Maillard S, Navarra L, Annborn M, Undén J, Brunetti I, Awad A, McGuigan P, Bjørkholt Olsen R, Cassina T, Vignon P, Langeland H, Lange T, Friberg H, Nielsen N (2021) Hypothermia versus normothermia after out-of-hospital cardiac arrest. N Engl J Med 384:2283–2294. https://doi.org/10.1056/NEJMoa2100591
10. Dankiewicz J, Cronberg T, Lilja G, Jakobsen JC, Belohlavek J, Callaway C, Cariou A, Eastwood G, Erlinge D, Hovdenes J, Joannidis M, Kirkegaard H, Kuiper M, Levin H, Morgan MPG, Nichol AD, Nordberg P, Oddo M, Pelosi P, Rylander C, Saxena M, Storm C, Taccone F, Ullen S, Wise MP, Young P, Friberg H, Nielsen N (2019) Targeted hypothermia versus targeted normothermia after out-of-hospital cardiac arrest (TTM2): a randomized clinical trial-rationale and design. Am Heart J 217:23–31. https://doi.org/10.1016/j.ahj.2019.06.012
11. Lilja G, Nielsen N, Ullen S, Blennow Nordstrom E, Dankiewicz J, Friberg H, Heimburg K, Jakobsen JC, Levin H, Callaway C, Cariou A, Eastwood GM, Helbok R, Hovdenes J, Kirkegaard H, Leithner C, Morgan MPG, Nordberg P, Oddo M, Pelosi P, Rylander C, Saxena M, Taccone FS, Siranec M, Wise MP, Young PJ, Cronberg T (2020) Protocol for outcome reporting and follow-up in the targeted hypothermia versus targeted normothermia after out-of-hospital cardiac arrest trial (TTM2). Resuscitation 150:104–112. https://doi.org/10.1016/j.resuscitation.2020.03.004
12. Bertschi D, Waskowski J, Schilling M, Donatsch C, Schefold JC, Pfortmueller CA (2022) Methods of assessing frailty in the critically Ill: a systematic review of the current literature. Gerontology 68:1321–1349. https://doi.org/10.1159/000523674
13. Rockwood K, Theou O (2020) Using the clinical frailty scale in allocating scarce health care resources. Can Geriatr J 23:210–215. https://doi.org/10.5770/cgj.23.463
14. Haywood K, Whitehead L, Nadkarni VM, Achana F, Beesems S, Bottiger BW, Brooks A, Castren M, Ong ME, Hazinski MF, Koster RW, Lilja G, Long J, Monsieurs KG, Morley PT, Morrison L, Nichol G, Oriolo V, Saposnik G, Smyth M, Spearpoint K, Williams B, Perkins GD, Collaborators C (2018) COSCA (core outcome set for cardiac arrest) in adults: an advisory statement from the international liaison committee on resuscitation. Circulation 137:e783–e801. https://doi.org/10.1161/CIR.0000000000000562
15. Wilson L, Boase K, Nelson LD, Temkin NR, Giacino JT, Markowitz AJ, Maas A, Menon DK, Teasdale G, Manley GT (2021) A manual for the glasgow outcome scale-extended interview. J Neurotrauma 38:2435–2446. https://doi.org/10.1089/neu.2020.7527
16. Haerpfer C, Inglehart R, Moreno A, Welzel C, Kizilova K, Diez-Medrano J, Lagos M, Norris P, Ponarin E, Puranen B (2022). World values survey: round seven - country-pooled datafile version 6.0. JD Systems Institute & WVSA Secretariat. https://doi.org/10.14281/18241.18. Accessed 2 Nov 2022
17. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S (2014) The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 12:1495–1499. https://doi.org/10.1016/j.ijsu.2014.07.013
18. McPherson SJ, Juniper M, Smith N (2023) Frailty is a better predictor than age for shockable rhythm and survival in out-of-hospital cardiac arrest in

over 16-year-olds. Resusc Plus 16:100456. https://doi.org/10.1016/j.resplu.2023.100456
19. Kim DH, Rockwood K (2024) Frailty in older adults. N Engl J Med 391:538–548. https://doi.org/10.1056/NEJMra2301292
20. Hwai H, Wu CK, Chi CY, Tsai MS, Huang CH (2025) Association between the clinical frailty scale and neurological outcomes in out-of-hospital cardiac arrest: a retrospective study. Rev Cardiovasc Med 26:26333. https://doi.org/10.31083/RCM26333
21. Nolan JP, Sandroni C, Böttiger BW, Cariou A, Cronberg T, Friberg H, Genbrugge C, Haywood K, Lilja G, Moulaert VRM, Nikolaou N, Olasveengen TM, Skrifvars MB, Taccone F, Soar J (2021) European resuscitation council and European society of intensive care medicine guidelines 2021: post-resuscitation care. Intensive Care Med 47:369–421. https://doi.org/10.1007/s00134-021-06368-4
22. Armour D, Boyiazis D, Delardes B (2024) Perspectives on cardiopulmonary resuscitation in the frail population: a scoping review. Monash Bioeth Rev. https://doi.org/10.1007/s40592-024-00220-3
23. Mitnitski AB, Mogilner AJ, Rockwood K (2001) Accumulation of deficits as a proxy measure of aging. Sci World J 1:323–336. https://doi.org/10.1100/tsw.2001.58
24. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K (2008) A standard procedure for creating a frailty index. BMC Geriatr 8:24. https://doi.org/10.1186/1471-2318-8-24
25. Ohbe H, Nakajima M, Miyamoto Y, Shibahashi K, Matsui H, Yasunaga H, Sasabuchi Y (2023) 1-year functional outcomes after cardiopulmonary resuscitation for older adults with pre-existing long-term care needs. Age Ageing. https://doi.org/10.1093/ageing/afad072
26. Djarv T, Bremer A, Herlitz J, Israelsson J, Cronberg T, Lilja G, Rawshani A, Arestedt K (2020) Health-related quality of life after surviving an out-of-hospital compared to an in-hospital cardiac arrest: a Swedish population-based registry study. Resuscitation 151:77–84. https://doi.org/10.1016/j.resuscitation.2020.04.002
27. Liu J, Zhu Y, Tan JK, Ismail AH, Ibrahim R, Hassan NH (2024) Factors associated with frailty in older adults in community and nursing home settings: a systematic review with a meta-analysis. J Clin Med 13:2382. https://doi.org/10.3390/jcm13082382
28. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP (2019) Frailty: implications for clinical practice and public health. Lancet 394:1365–1375. https://doi.org/10.1016/s0140-6736(19)31786-6
29. Forslund AS, Jansson JH, Lundblad D, Soderberg S (2017) A second chance at life: people's lived experiences of surviving out-of-hospital cardiac arrest. Scand J Caring Sci 31:878–886. https://doi.org/10.1111/scs.12409
30. Vanleerberghe P, De Witte N, Claes C, Verté D (2019) The association between frailty and quality of life when aging in place. Arch Gerontol Geriatr 85:103915. https://doi.org/10.1016/j.archger.2019.103915