Intensive care–treated cardiac arrest: A retrospective study on the impact of extended age on mortality, neurological outcome, received treatments and healthcare-associated costs

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Abstract

Background: Cardiac arrest (CA) is a leading cause of death worldwide. As population ages, the need for research focusing on CA in elderly increases. This study investigated treatment intensity, 12-month neurological outcome, mortality and healthcare-associated costs for patients aged over 75 years treated for CA in an intensive care unit (ICU) of a tertiary hospital.

Methods: This single-centre retrospective study included adult CA patients treated in a Finnish tertiary hospital's ICU between 2005 and 2013. We stratified the study population into two age groups: <75 and 75 years. We compared interventions defined by the median daily therapeutic scoring system (TISS-76) between the age groups to find differences in treatment intensity. We calculated cost-effectiveness by dividing the total one-year healthcare-associated costs of all patients by the number of survivors with a favourable neurological outcome. Favourable outcome was defined as a cerebral performance category (CPC) of 1–2 at 12 months after cardiac arrest. Logistic regression analysis was used to identify independent association between age group, mortality and neurological outcome.

Results: This study included a total of 1,285 patients, of which 212 (16%) were 75 years of age. Treatment intensity was lower for the elderly compared to the younger group, with median TISS scores of 116 and 147, respectively ($p < 0.001$). The effective cost in euros for patients with a good one-year neurological outcome was €168,000 for the elderly and €120,000 for the younger group. At 12 months after CA 24% of the patients in the elderly group and 47% of the patients in the younger group had a CPC of 1-2 ($p < 0.001$). Age was an independent predictor of mortality (multivariate OR = 3.36, 95% CI:2.21-5.11, $p < 0.001$) and neurological outcome (multivariate OR = 3.27, 95% CI: 2.12-5.03, $p < 0.001$).

Conclusions: The elderly ICU-treated CA patients in this study had worse neurological outcomes, higher mortality and lower cost-effectiveness than younger patients. Further efforts are needed to recognize the tools for assessing which elderly patients benefit from a more aggressive treatment approach in order to improve the cost-effectiveness of post-CA management.

Background

CA is one of the leading causes of death in the developed world [1], with over three million patients affected each year worldwide [2]. This, in addition to a clear increase in patient longevity globally, mandates more research efforts towards care of the elderly post CA [3, 4]. Not unexpectedly, cardiopulmonary resuscitation (CPR) is more commonly initiated in younger patients, and younger patients receive more aggressive treatment by mobile medical teams [4, 5]. Although post-CA mortality increases with age, it has been disputed whether this is due to age in itself or other CA characteristics [6–8]. Pre-arrest comorbidity and CA factors still need more research in order to explain the variability of outcome in CA among elderly [9].

Only a few studies have focused on the post CA treatment of the elderly in the intensive care unit (ICU)

 he aim of this study is to explore treatment intensity, outcome and healthcare-associated costs of the ICU-treated elderly CA patients treated in a single centre over a 9-year period. We hypothesise that compared with younger patients, the elderly have higher mortality and worse neurological outcome despite high treatment costs and intensity.

Methods

Study Design And Setting

This retrospective cohort study was conducted at Meilahti Hospital, Helsinki, Finland, which serves as the primary referral centre for CA patients in the Helsinki and Uusimaa region. This region has a population of approximately 1.7 million people (30% of the total Finnish population). Data were extracted from the Finnish Intensive Care Consortium (FICC) database [11] and include adult CA patients ($\geq$ 18 years of age) treated in the hospital's ICU between January 1, 2005 and December 31, 2013. We reviewed Electronic health records (EHR) of individual patients for relevant data. Patients with incomplete or missing data and patients where return of spontaneous circulation (ROSC) was not achieved were excluded from the analyses. The patients were divided into two age groups for descriptive purposes: <75 (young) and >75 years (elderly).

The study was approved by the ethics committee of the Operative Division of Helsinki University Hospital (June 2014: 194/13/03/02/2014 TMK02 § 97), the Finnish National Institute for Health and Welfare (May 2014: THL/713/5.05.01/2014), Statistics Finland (May 2014: TK-53-1047-14), the Social Insurance Institution (September 2015: Kela 55/522/2015) and the Office of the Data Protection Ombudsman (February 2016: 2794/204/2015).

Data Collection And Extracted Variables

The FICC database provided data on hospital survival, preadmission physical status (a modified World Health Organization/Eastern Cooperative Oncology Group (WHO/ECOG) classification implemented by FICC), mean TISS-76 score and its components for the complete ICU stay, and Acute Physiology and Chronic Health Evaluation II (APACHE II) components and scores [12–15]. In this study APACHE II scores were used excluding the points for age. We obtained the confirmed date of death by linking the patients' unique personal identification numbers with the Finnish Population Register Centre database, which registers all deaths of Finnish residents. Detailed information regarding preadmission physical status, time of CA, time to ROSC, initial CA rhythm and location as well as CPC for survivors at one year after CA was collected from the hospital's EHR [16–19]. We determined preadmission functional status by using a simplified WHO/ECOG classification, where "independent" was defined as the patient being independent in self-care and "dependent" was defined as the patient being partly or fully dependent on help in self-care prior to hospital admission. [20]. A favourable neurological outcome was defined as CPC scores of 1–2 and an unfavourable neurological outcome as CPC scores of 3–4 [19].

Healthcare-associated Costs

The ECPSFNO was €168,000 and €120,000 for the elderly and young group, respectively. The effective cost for the elderly patient group was higher than that for the younger patient group in all locations of CA except for ICUCA, where it was €173,000 and €308,000, respectively. The elderly patient group received less median funding from the Social Insurance Institution, €714 compared to €1,670 in the younger age group (Table 3, Fig. 1, Additional file 4). Median rehabilitation costs were higher for the elderly patient group when we only included those with a favourable 12-month neurological outcome, 5,700 compared to 2,000 ($p = 0.012$) (Table 3).

Table 3
Resource use

	Age < 75 (n = 1073)	Age ≥75 (n = 212)	*p*
Cost of treatments in €, median (IQR)			
Hospital costs	29 971 (13 381 – 50 212)	18 356 (9 740 – 37 102)	< 0.001
Rehabilitation	0 (0–6 543)	0 (0–7 574)	0.928
Social Insurance Institution	1 669 (579-6 686)	714 (392-1 760)	< 0.001
Cost of treatment of those with CPC 1–2 after 12 months in €, median (IQR) (57%)			
Hospital	41 194 (27 031–63 709)	34 888 (19 083 – 60 029)	0.071
Rehabilitation	2113 (0–9 603)	6073 (417 – 13 319)	0.012
Social Insurance Institution	4 561 (1 173 – 15 043)	2 049 (1 196-3 509)	< 0.001
Total cost in €, median (IQR)			
Everyone	38 195 (16 505-71680)	22 641 (12 488 – 47 006)	< 0.001
Those with CPC 1–2 after 12 months (57)	54 510 (36 148 – 86 461)	39 482 (24 101 – 93 020)	0.040
Effective cost[1] in €			
Of those with CPC 1–2 after 12 months	119 941	168 416	-
Effective cost in € among those with CPC 1–2 after 12 months			
OHCA	90 499	133 134	-
IHCA	161 670	199 540	-
ICUCA	308 000	172 595	-

[1]Effective cost: The total healthcare-associated costs of all patients within their respective age group divided by the number of survivors with a favourable neurological outcome

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Results

Study Population And Factors At Resuscitation

The study included 1,285 patients, of which 1,073 (84%) were younger than 75 years and 212 (16%) 75 years or older (Table 1). OHCAs were less common among the elderly with an occurrence of 43% compared to 64% in the young group, $p < 0.001$ (Table 1). A number of other differences between the younger and the elderly population were noted: less elderly patients had an independent preadmission functional status (75% vs. 90%, $p < 0.001$), a non-shockable initial CA rhythm was more common (49% vs. 35%, $p < 0.001$), and ROSC was achieved faster among the elderly patients (median of 10 min vs. 16 min, $p < 0.001$).

Table 1
Patients characteristics

	Age < 75 (n = 1073)	Age ≥75 (n = 212)	*p*
Women, % (no.)	281 (26)	70 (33)	0.041
Location of arrest, % (no.)			< 0.001
OHCA	64 (691)	43 (92)	
IHCA	27 (286)	46 (97)	
ICUCA	9 (96)	11 (23)	
Women, % (no.)	281 (26)	70 (33)	0.041
Witnessed arrest, % (no.) [1]	935 (87)	193 (91)	0.130
Initial cardiac-arrest rhythm, % (no.)			< 0.001
Shockable (VT or VF)	641 (60)	94 (44)	
Non-Shockable (all other rhythms)	378 (35)	104 (49)	
Unknown	54 (5)	14 (6.6)	
Time to ROSC in minutes, median (IQR) [2]	16 (10–23)	10 (5–18)	< 0.001
Independent preadmission functional status % (no.)[3]	90 (960)	75 (158)	< 0.001
[1] 2% of patients are missing this information			
[2] 9,5% of patients are missing this information			
[3] 4.7% of patients are missing this information			

Treatment Intensity & ICU Factors

No difference was observed in the APACHE II scores between the elderly and younger patients when points for age where excluded (Table 2). Treatment intensity was lower in the elderly than in the younger age group, with median daily average TISS scores of 34 and 37 for the elderly and younger patients, respectively, $p < 0.001$. The total amount of TISS points was also lower for the elderly (116 vs. 147, $p < 0.001$) (Table 2). In-hospital as well as in-ICU mortality was higher for the elderly group (ICU mortality 33%

 . 33%, $p < 0.001$). The ICU LOS was shorter for the elderly than for the younger patients (Table 2). The ICU LOS among the survivors was however not different. Table 2 details the ICU factors, in-hospital mortality, TISS-point distribution and the difference in the selected treatments received at the hospital. TISS-point distribution can be viewed in more detail in the supplementary material (Additional file 1–3).

Table 2
Intensive care unit-factors

	Age < 75 (n = 1073)	Age ≥75 (n = 212)	*p*
APACHE II-score excluding age points, median (IQR)	20 (15–27)	22 (15–27)	0.181
TISS-Score, median (IQR)			
Daily average	37 (31–43)	34 (28–41)	< 0.001
Total TISS-score	147 (93–227)	116 (65–192)	< 0.001
Treatments received, no. (%)			
Controlled ventilation with or without PEEP	1055 (98)	197 (93)	< 0.001
Induced hypothermia	450 (42)	34 (16)	< 0.001
Vasoactive drug infusion (> 1 drug)	503 (47)	80 (38)	0.015
Continous antiarrhythmia infusions	212 (20)	35 (17)	0.273
Rx of seizures	140 (13)	13 (6)	0.004
Hemodialysis in unstable patient	18 (2)	8 (4)	0.048
Arterial line	1071 (100)	211 (100)	0.432
In-hospital mortality %(no.)			
Dead in ICU	18 (194)	33 (69)	< 0.001
Dead in hospital	33 (357)	49(104)	< 0.001
Length of stay in days, median (IQR)			
ICU	3 (2–5)	2 (1–4)	< 0.001
Hospital	10 (4–20)	8 (3–16)	0.003
Length of stay in days among patients discharged alive, median (IQR)			
ICU	3 (2–6)	3 (2–6)	0.085
Hospital	14 (8–24)	14 (8–23)	0.654

Neurological Outcome And Mortality

Neurological outcome was worse for the elderly group, with only 24% (50/212 patients) having CPC scores of 1–2 after 12 months, compared with 47% (507/1073 patients) of the younger age group, $p < 0.001$. Long-term mortality was higher for the elderly group compared to the younger group; 70% of the elderly (vs. 44%) had died within two years, $p < 0.001$. Mortality in the elderly versus the younger age group during the first year is shown in Fig. 2. Separate Kaplan Meier curves illustrating mortality during the whole follow-up period for all patients, patients based on location of arrest (OHCA, IHCA and ICUCA) as well as based on initial rhythm (shockable and non-shockable) can be found in the supplementary material (Additional file 5–6). The median follow-up time was 1.6 years per patient.

Factors independently associated with unfavourable neurological outcome was age above 75 years (OR = 3.27, 95% CI: 2.12–5.03, $p < 0.001$), dependent pre-admission functional status (OR = 3.13, 95% CI: 1.69–5.79, $p < 0.001$), non-shockable initial CA rhythm (OR shockable rhythm = 0.43, 95% CI: 0.30–0.60, $p < 0.001$), time to ROSC in 10 minutes (OR = 1.61, 95% CI: 1.34–1.93, $p < 0.001$) and APACHE II score excluding points for age (OR = 1.96, 95% CI: 1.61–2.39, $p < 0.001$).

Factors independently associated with mortality were age above 75 years (OR = 3.36, 95% CI: 2.21–5.11, $p < 0.001$), dependent pre-admission functional status (OR = 2.96, 95% CI: 1.60–5.50, $p < 0.001$), initial CA rhythm (OR shockable rhythm = 0.56, 95% CI: 0.40–0.77, $p < 0.001$), location of CA (ICUCA OR = 2.27, 95% CI: 1.26–4.08, $p = 0.006$), time to ROSC (OR = 1.36, 95% CI: 1.16–1.60, $p < 0.001$) and APACHE II score excluding age (OR = 2.06, 95% CI: 1.70–2.50, $p < 0.001$). Table 4 details the independent predictors of an unfavourable neurological outcome and Table 5 the independent predictors of mortality.

Table 4
Univariate models and multivariate models for risk factors predicting 12-month unfavourable cerebral performance status

	Univariate model		**Multivariate model**	
Variable	OR (95% CI)	*p*	OR (95% CI)	*p*
Age				
Young (< 75y)	1		1	
Elderly (> = 75)	3.09 (2.19–4.36)	< 0.001	3.27 (2.12–5.03)	< 0.001
Pre-admission functional status				
Independent	1		1	
Dependent	4.07 (2.48–6.67)	< 0.001	3.13 (1.69–5.79)	< 0.001
Initial CA-rhythm				
Non-shockable	1		1	
Shockable	0.32 (0.25–0.41)	< 0.001	0.43 (0.30–0.60)	< 0.001
Location of arrest				
OHCA	1		1	
IHCA	1.78 (1.37–2.30)	< 0.001	1.46 (0.98–2.18))	0.065
ICUCA	2.24 (1.47–3.41)	< 0.001	2.24(1.21–4.16)	0.010
Witnessed arrest (not witnessed = 1)	0.47 (0.31–0.70)	< 0.001	0.70(0.43–1.12)	0.134
Time to ROSC in 10 minutes	1.15 (1.02–1.29)	0.020	1.61 (1.34–1.93)	< 0.001
APACHE II-score excluding age points[1]	2.51 (2.13–2.95)	< 0.001	1.96 (1.61–2.39)	< 0.001

A total of 980 patients were included. 94 patients had missing CPC, 60 patients had missing functional status, 68 patients had missing initial rhythm, 24 patients had missing if the arrest was witnessed, 118 patients had missing time to ROSC, 1 patient had missing APACHE II-score.

[1] Each step increases the variable by 10

Table 5
Univariate models and multivariate models for risk factors predicting 12-month mortality.

	Univariate model		**Multivariate model**	
Variable	OR (95% CI)	*p*	OR (95% CI)	*p*
Age				
Young (< 75y)	1		1	
Elderly (> = 75)	3.44 (2.44–4.84)	< 0.001	3.36 (2.21–5.11)	< 0.001
Pre-admission functional status				
Independent	1		1	
Dependent	4.20 (2.55–6.92)	< 0.001	2.96 (1.60–5.50)	< 0.001
Initial CA-rhythm				
Non-shockable	1		1	
Shockable	0.33 (0.26–0.42)	< 0.001	0.56 (0.40–0.77)	< 0.001
Location of arrest				
OHCA	1		1	
IHCA	2.07 (1.61–2.67)	< 0.001	1.61 (1.11–2.34)	0.12
ICUCA	2.29 (1.52–3.449	< 0.001	2.27 (1.26–4.08)	0.006
Witnessed arrest (not witnessed = 1)	0.59 (0.40–0.86)	< 0.006	0.80 (0.51–1.27)	0.353
Time to ROSC in 10 minutes	1.04 (0.93–1.16)	0.520	1.36 (1.16–1.60)	< 0.001
APACHE II-score excluding age points[1]	2.34 (2.01–2.73)	< 0.001	2.06 (1.70–2.50)	< 0.001

A total of 1055 patients were included. 60 patients had missing functional status, 68 patients had missing initial rhythm, 24 patients had missing if the arrest was witnessed, 118 patients had missing time to ROSC, 1 patient had missing APACHE II-score.

Discussion

This current study presents a comprehensive estimation of CA-associated costs including hospital costs, rehabilitation costs and social insurance costs at a tertiary university hospital. Long-term survival and functional outcome was as expected significantly lower among the elderly. In addition they received less intensive ICU treatment and had a shorter ICU LOS overall. Cost effectiveness was lower for the elderly patient group than for the younger patient group in most cases except ICUCAs.

Given our ageing population, our study highlights the need to individually assess the cost effectiveness of care post CA.
Both TISS-point distribution and the median total cost are lower for the elderly group. This in combination with an even APACHE-score distribution between the age groups (indicating roughly the same comorbidity pre-CA) indicates that age seems to have been a factor affecting treatment intensity. The difference in total TISS-point-distribution can be affected by the LOS, but the LOS does not explain the difference in average daily TISS-points. We speculate that initial treatment intensity was high for both age groups, but that some treatments were stopped earlier in the elderly group due to a perceived poor prognosis, thus decreasing the average daily TISS-score. This indicates that an active daily evaluation of patients was in use in order to allocate resources in a more beneficial way. Recent studies demonstrate that ROSC rates, one-year survival and favourable neurological outcome at one month among elderly CA patients have increased over time with increase in the proportion of advanced in-hospital treatments (i.e. extracorporeal membrane oxygenation, therapeutic hypothermia and/or percutaneous coronary angiogram/intervention) provided [23]. In our study, in-hospital costs of the total provided treatments were lower for the elderly, even when excluding those with a poor one-year neurological outcome. One could argue that the elderly may not benefit from more aggressive treatment, but age in itself should not affect the administered treatments even if it affects mortality, as neurological outcome seems to remain good for survivors [3]. In this study, the ECPSFNO was higher for the elderly group in all locations of CA except ICUCA. Thus, although fewer resources were used by the elderly, the cost per survivor remained higher than the younger age group owing to the high mortality in the elderly group.

Due to marked differences in healthcare funding, direct comparisons of our results with other studies are difficult. Our results also indicate a clear inter-patient variation. Costs in the range of €20,000–40,000 for ICU-treated CA survivors have been determined in previous studies [24, 25]. Nonetheless, several studies and meta-analyses have shown that age negatively affects post-CA mortality [26]. Long-term survival among elderly CA patients is generally lower than that among younger age groups in the case of OHCA [27, 28].

We also looked at the distribution of costs in three separate categories (hospital costs, rehabilitation costs and social insurance costs) among different age groups. Costs were higher for the younger patient group in all categories except rehabilitation. The difference in hospital costs could be attributable to the elderly receiving less aggressive treatment and having to be in a better initial condition in order to survive CA and be taken to the ICU. Less intensive treatment is needed to attain a favourable outcome if the pre-arrest comorbidities are lower, which also decreases hospital costs. The younger age group probably received more funding from the Social Insurance Institution because they got a paid sick-leave from work. Patients over 68 years of age receive pension, which does not alter if the patient is severely ill and therefore isn't included in these calculations. The higher risk of early post-CA mortality in elderly patients might also have decreased social insurance reimbursements as compared to the younger patients. We noticed that median rehabilitation costs were higher among the elderly when only including those with a favourable 12-month neurological outcome. This could be an indicator for the elderly having more long-

Loading [MathJax]/jax/output/CommonHTML/jax.js t see the same difference in rehabilitation costs when taking into account all patients as the early mortality among elderly decreases the median rehabilitation costs. The effect of less aggressive treatment on the need for rehabilitation among elderly is something further research could focus on.

Additionally, we demonstrated worse long-term outcome in elderly compared to younger patients following care in the ICU after CA. This difference was the most pronounced in OHCAs but was evident in patients with IHCA as well. Interestingly, this study shows that the same percentage of patients in both age groups had a CPC of 3–4 12 months post CA, but our multivariable model still indicates that age affects neurological outcome. It is debatable how much old age correlates with worse neurological outcome as the high mortality probably affects the statistics. Previous studies also indicate that there isn't a difference in neurological outcome among elderly compared to younger CA survivors[3, 28]. It is worth noting that age does not always correlate with outcome and is not in itself an adequate prognostic factor, as two elderly persons of the same age can have very different medical conditions [29]. High frailty and a low performance status have been connected with higher ECPSFNO and mortality in previous studies [30–33]. The increased mortality related to age in this study is indeed partially explained by the pre-admission functional status of the elderly patients; thus, this in combination with age seems to better predict both mortality and neurological outcome. Performance status could be a more precise tool when deciding which patients benefit the most from intensive care and more advanced treatment options.

Another possible tool for risk assessment among the elderly seems to be the initial rhythm, as an initially shockable rhythm predicts a better outcome even among the very elderly, where other prognostic factors seem to fail [34]. Supporting the results of previous studies, initial rhythm was one of the factors with the strongest association with outcome among both the younger and elderly patients in this study as well. Interestingly, in our study the elderly had lower incidences of ventricular fibrillation (VF) and ventricular tachycardia (VT) than the younger age group. This could be related to a difference in the aetiology of the arrests or to mechanisms such as faster conversion of VF/VT to asystole owing to the faster depletion of energy in the aged heart. Such an abnormality has been described in mitochondrial metabolism with ageing in the muscle cells [35]. Previous studies have also shown that bradyarrhythmia-related CA patients were generally older than those with tachyarrhythmia-related CA [36]. The significant difference in location of arrest is also something that affects mortality and neurological outcome as CA aetiology differs depending on where the CA occurred [37]. We may speculate that as the elderly had a higher percentage of IHCAs, they also had a higher amount of unfavourable pre-arrest comorbidities, which increases mortality as these comorbidities affect CA-aetiology and initial rhythm in an unfavourable manner [38]. Factors in IHCA that may decrease mortality compared to OHCAs are shorter times to response and more available treatments, but these do probably not affect mortality as much as the pre-arrest comorbidities seem to do.

A major strength of this study is its minimal selection bias owing to socioeconomic factors and personal insurance, as this study was conducted in a setting of government-funded healthcare. A limitation and factor affecting the outcome of this study is that the studied population only included patients with ROSC

 y excludes patients in such a bad initial state that they did not survive until admission to the ICU and patients with low chances of benefiting from intensive treatment. This leads to a selection bias especially among the elderly, with those surviving to the ICU having a higher probability of surviving altogether and being in a better initial condition compared to the mean population with the same age.

Conclusion

The interpretation of this study is that treatment intensity for the elderly is lower as a group, the mortality, the risk for a poor neurological outcome is higher and the cost-effectiveness is lower compared to the younger age group. Further studies should focus on the tools for identification of patients who can benefit from a more aggressive treatment approach, enabling an improvement in the resource distribution in post-CA ICU care in the elderly.

Abbreviations

CA: Cardiac arrest; ICU: intensive care unit; TISS: Therapeutic scoring system; CPC: cerebral performance category; CPR: cardiopulmonary resuscitation; FICC: Finnish Intensive Care Consortium; EHR: electronic health records; ROSC: return of spontaneous circulation; WHO/ECOG: World Health Organization/Eastern Cooperative Oncology Group, APACHE: Acute Physiology and Chronic Health Evaluation; LOS: length of stay; ECPSFNO: Effective cost per survivor with favourable neurological outcome; OHCA: out-of-hospital cardiac arrest; IHCA: in-hospital cardiac arrest; ICUCA: in-intensive-care-unit cardiac arrest

Declarations

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Authors contribution

EH and MBS planned and conceived the study and wrote the first draft. RR assisted with the statistical analysis. All other authors revised the manuscript for intellectual content. All authors approve the submission. EH and MBS take intellectual responsibility for the study findings.

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Availability of data and materials

Legal restrictions prevent us from making the data publicly available, as it is based on patient registers. The data included in this study are obtained from several databases (The Finnish Intensive Care Consortium, Kela, the Finnish National Institute for Health and Welfare, Statistics of Finland and the five university hospitals in Finland). With appropriate research approval, data can be directly requested from the sources.

Ethics approval and consent to participate

The study was approved by the Finnish National Institute for Health and Welfare (December 2017: THL/2034/5.05.00/2017) and the board of the Hospital District of Helsinki and Uusimaa (March 2018: HUS/26/2018).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

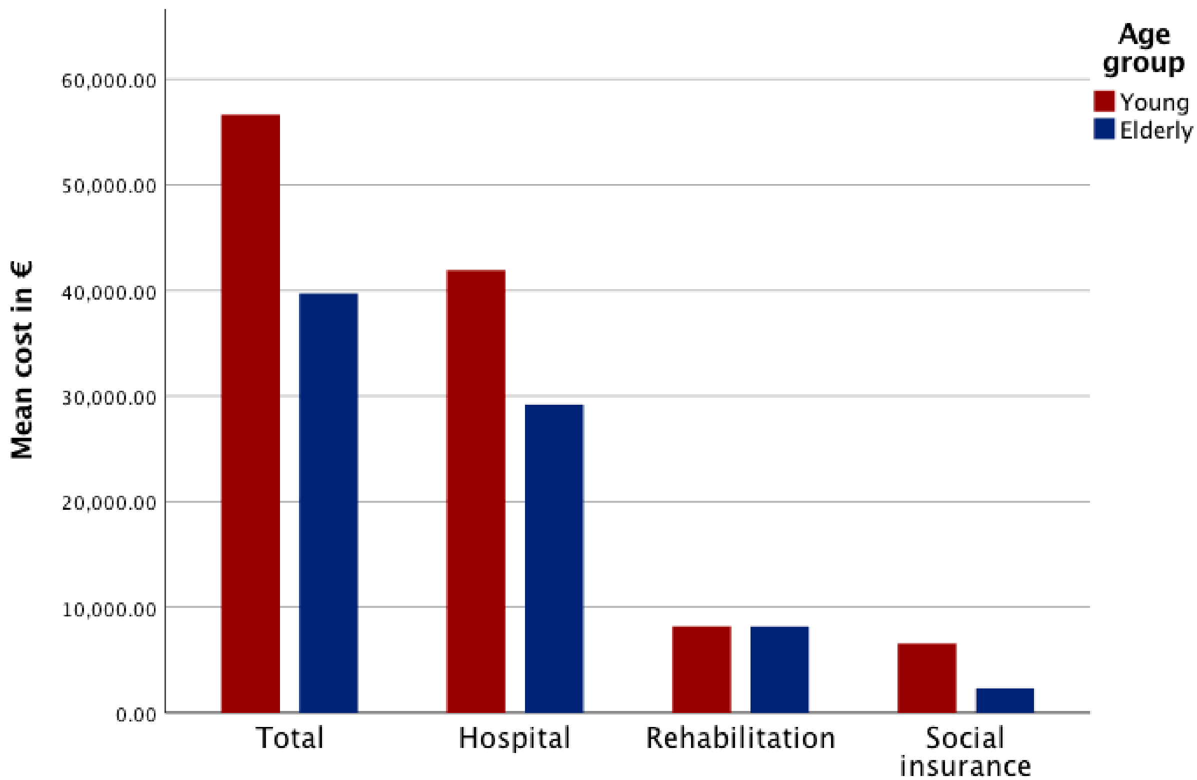

Figure 1

Mean cost distribution in 2021 euros

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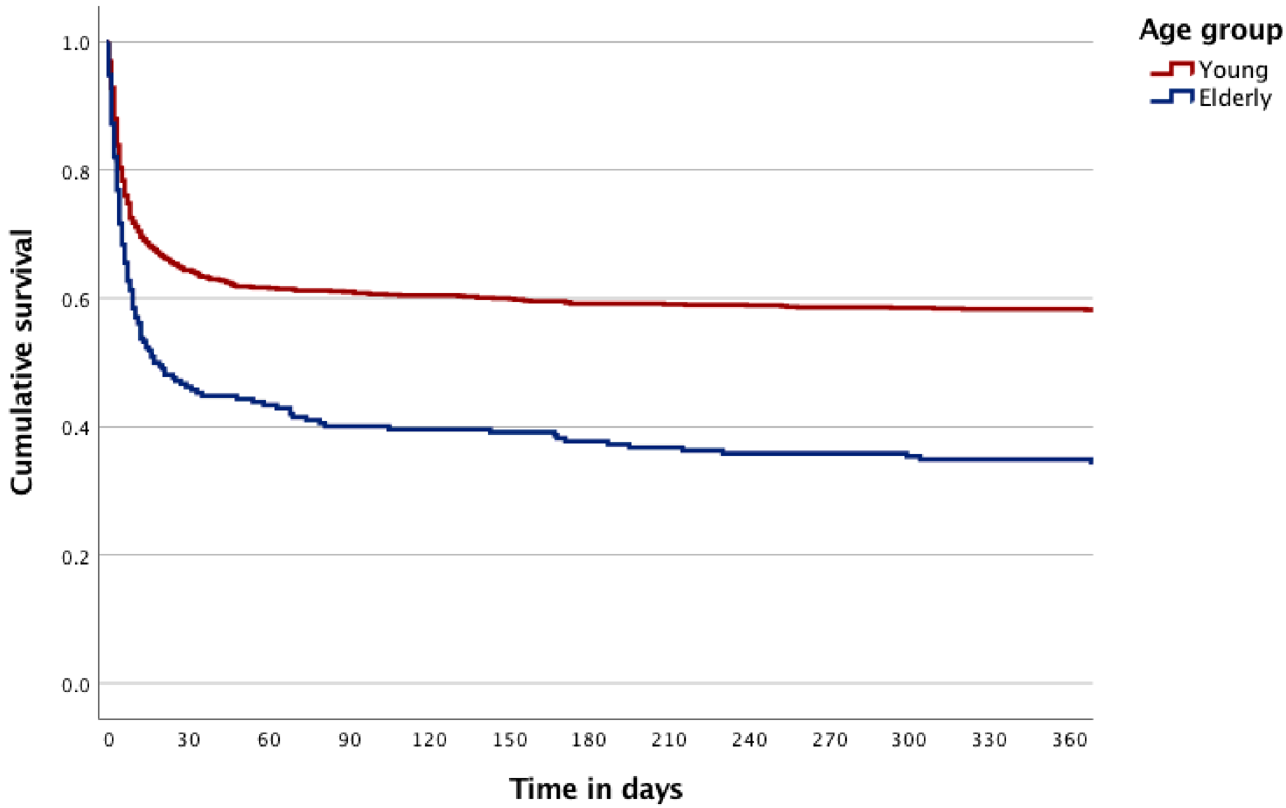

Figure 2

Kaplan-Meier survival curve of all cases during the first year, Log Rank p < 0.001

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