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Clinical paper

Frailty and associated outcomes and resource utilization following in-hospital cardiac arrest

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Abstract

Background: In-hospital cardiac arrest (IHCA) is common and associated with high mortality. Frailty is increasingly recognized as a predictor of worse prognosis among critically ill patients, but its association with outcomes and resource utilization following IHCA is unknown.

Methods: We performed a retrospective analysis (2013–2016) of a prospectively collected registry from two hospitals of consecutive hospitalized adult patients with IHCA occurring on the hospital wards. We defined frailty using the Clinical Frailty Scale (CFS) score ≥5. CFS scores were based on validated medical review criteria. The primary outcome is hospital mortality. Secondary outcomes include return of spontaneous circulation (ROSC), discharge to long-term care, and hospital costs. We used multivariable logistic regression to adjust for known confounders.

Results: We included 477 patients, and 124 (26.0%) had frailty. Frailty was associated with increased odds of hospital death (adjusted odds ratio [aOR]: 2.91 [95% confidence interval [CI]: 2.37–3.48) and discharge to long-term care (aOR 1.94 [95% CI: 1.57–2.32]). Compared with patients without frailty, patients with frailty had decreased odds of ROSC following IHCA (aOR 0.63 [95% CI: 0.41–0.93]). No difference in mean total costs was demonstrated between patients with and without frailty ($50,799 vs. $45,849). Frail patients did have higher cost-per-survivor ($947,546 vs. $161,550).

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Conclusions: Frail individuals who experience an IHCA are more likely to die in hospital or be discharged to long-term care, and less likely to achieve ROSC in comparison with individuals who are not frail. The hospital costs per-survivor of IHCA are increased when frailty is present.
Keywords: Frailty, In-hospital cardiac arrest, Intensive care unit, Hospital costs

Introduction

Q9 In-hospital cardiac arrest (IHCA), defined as the loss of circulation prompting cardiopulmonary resuscitation[1,2] occurs in approximately 1−6 individuals per 1000 hospital admissions.[3] Survival to discharge among patients experiencing IHCA varies between 12−25%, with some improvement in recent years.[4,5] Long-term survival rates are similarly low, with only modest increases over the past decade.[6] Prediction of prognosis following IHCA remains a major area of ongoing research.[1,7] Traditionally, emphasis has been placed on better understanding out-of-hospital cardiac arrest (OHCA), with an attempt to generalize findings to IHCA. However, it is becoming increasingly clear that IHCA represents a distinct event in a distinct population, with unique arrest etiology and epidemiology.[1,8] Understanding prognostic factors not only enables clinicians to guide care following IHCA, but also enables shared decision-making and planning with patients and families regarding the inclusion of cardiopulmonary resuscitation (CPR) in their goals-of-care during hospital admission.[7]

Frailty is a clinical state characterized by reduced physiologic reserve and vulnerability to adverse health outcomes from physiologic stressors resulting from the accumulation of age- and disease-related deficits.[9,10] While frailty is often thought to be a geriatric syndrome, this condition is prevalent among young populations, particularly those with significant comorbidities, such as chronic obstructive pulmonary disease, and liver dysfunction.[11,12] In the intensive care unit (ICU), frailty may be identified using the Clinical Frailty Scale (CFS),[13] a scale assessing frailty from 1 (least frail) to 9 (most frail), which can be applied easily and reliably. Growing evidence demonstrates an association between the CFS score and outcomes following critical illness.[14−20] While the relationship between increasing age and reduced survival from IHCA has been demonstrated,[21] it is unclear if this is due to the higher prevalence of frailty, or due to another factor associated with aging. Therefore, our objective was to estimate the association between frailty and in-hospital mortality (primary outcome), as well as discharge disposition, and ROSC following IHCA. We also investigated the relationship between frailty, resource utilization and health care costs.[22,23]

Methods

We received approval for this study from The Ottawa Health Science Network Research Ethics Board (Protocol 20160570-01 H).

Study design, setting and subjects

We included patients from two hospitals within The Ottawa Hospital network (Ottawa, ON). Combined, these hospitals have approximately 1200 hospital beds and 64 ICU beds, with 60,000 total hospital admissions and 2500 total ICU admissions per year. We retrospectively examined prospectively collected data from The Ottawa Hospital Data Warehouse, a health administrative database used in previous studies.[24−26] Data is gathered daily from each admitted patient and stored in The Ottawa Hospital Data Warehouse. Data quality assessments are executed routinely, and quality-assurance initiatives are conducted regularly to ensure completeness and accuracy.

We included all patients ≥18 years of age, admitted to the hospital wards between 2013−2016, who experienced IHCA, defined as all of the following: (A) absence of palpable pulse; (B) absence of spontaneous breathing; and (C) Glasgow coma scale of 3; and initiation of chest compressions. Similar to other IHCA database studies,[27] IHCA occurring in the ICU or operating room were not included. We further excluded patients with a "Do-Not-Resuscitate" order, and those with missing data related to baseline function prior to admission. ROSC was defined as both presence of palpable pulse and measurable blood pressure following IHCA, and had to be sustained ≥ 20 min, as described previously.[2] In cases with more than one cardiac arrest during the admission, ROSC was defined on the basis of the first cardiac arrest. "Monitored" arrest was defined by presence of continuous telemetry monitoring, which exists both within the ICU and in other units outside of the ICU. "Witnessed" arrest was defined as an arrest witnessed by healthcare providers. Patients with cardiac arrest occurring out-of-hospital were excluded.

Data collection

We obtained all data from The Ottawa Hospital Data Warehouse. We abstracted basic demographic data, comorbidities, Elixhauser Comorbidity Score,[28] and multiple organ dysfunction score (MODS).[29] As part of the database, outcome data were collected from admission until either the point of discharge from hospital, or hospital death.

Patient costs during hospital admission were determined using the case-costing system of The Ottawa Hospital Data Warehouse, as performed previously.[18,30] Total hospital costs include both direct and indirect sources. Direct costs are all expenses to the hospital with fee codes linked to a patient identifier. Indirect costs refer to any overhead operational fees associated with provided services. The Ottawa Hospital uses as a standardized case-costing methodology, developed by the Ontario Case Costing Initiative, and based upon the Canadian Institute for Health Information Management guidelines.[31] Costs were indexed to 2018 Canadian Dollars using consumer price indices.[18,30] The cost-per-survivor is determined by dividing the total hospital costs of a group by the number of survivors to discharge, as demonstrated previously.[25] The nine equivalents of nursing manpower score (NEMS), an indicator of nursing requirements, was also calculated daily for ICU patients.[32]

The primary outcome was hospital mortality, as indicated in the Data Warehouse. Secondary outcomes included discharge directly from hospital to long-term care (among survivors to hospital discharge originally from home), ICU length of stay (LOS), hospital LOS, resource utilization, and total costs.

Identifying frailty

We used the CFS to identify the presence of frailty. This is a 9-point global frailty scale that evaluates baseline mobility, energy, physical activity, and function (prior to hospital admission).[13] We applied the CFS for each study patient as described previously.[18,19] Briefly, we evaluated patient pre-admission mobility and function assessments (prior to the acute illness), as completed by clinical staff, nursing staff or occupational therapy within 24 h of hospital admission. We used these staff assessments to retrospectively score each patient on the CFS, using a standardized abstraction tool (Supplemental Fig. S1). This method has been used previously in critically ill patients, and been shown to have comparable reliability to prospective assessment.[18,33] Data were abstracted from charts according to accepted standards.[34] To evaluate reproducibility in abstraction, two independent investigators (SMF, CD), blinded to each other's scores, individually evaluated a random sample of 20% of patient records. As inter-rater reliability was excellent ($\kappa = 0.94$), a single investigator (SMF) completed the remaining records. Consistent with previous research, a CFS $\geq$ 5 was used to identify the presence of frailty.[15,16]

Statistical analysis

All statistical analyses were performed with R (Version 3.3.3) and IBM SPSS (Version 24.0). We present data as mean values, with standard deviation (SD), or medians, with interquartile range (IQR), where appropriate. We performed the Student's *t*-test (parametric values), Mann–Whitney test (non-parametric values), and χ^2 (for categorical values) to determine between-group baseline differences. As recommended for observational studies in the critically ill,[35] we determined confounders *a priori*, on the basis of their likelihood of influencing both the presence of frailty and associated outcomes, informed by clinical knowledge and existing studies evaluating the association between frailty and outcomes in critically ill patients.[14,18,20] In accordance with the existing recommendations,[35] we used multivariable logistic regression modeling to adjust for important continuous (age, illness severity [MODS], and Elixhauser comorbidity index) and categorical (sex, comorbidities, arrest in monitored setting, witnessed arrest, shockable rhythm, post-IHCA therapeutic hypothermia, and post-IHCA coronary angiography) variables. In our primary analysis, frailty was coded using a categorical variable, based on presence or absence (i.e. CFS $\geq$ 5). We also performed a secondary analysis, coding frailty as a continuous variable. We present adjusted odds ratios (aOR) with 95% confidence intervals. A *P* value of $\leq$0.05 was considered statistically significant.

Results

We identified 489 patients who experienced IHCA from the Data Warehouse (Supplemental Fig. S2). Of these, 8 patients were excluded (1.6%) as no resuscitation was attempted (following clarification of goals-of-care), and 4 patients were excluded (0.8%) because there was insufficient data for CFS scoring. In total, we included 477 patients in the analyses. Of these patients, 124 (26.0%) had frailty (CFS $\geq$ 5). Baseline characteristics of patients with and without frailty are shown in Table 1. Patients with frailty were older

Table 1 – Characteristics of non-frail and frail patients experiencing in-hospital cardiac arrest (*n* = 477). Q1

Characteristic	No frailty (*n* = 353)	Frailty (*n* = 124)	*P* value
Age, years, mean (SD)	56.1 (18.1)	65.7 (12.1)	<0.001
Male, n (%)	196 (55.5)	67 (54.0)	0.77
MODS, mean (SD)	3.1 (2.4)	4.2 (2.3)	<0.001
Comorbidities			
Congestive heart failure	13 (3.7)	20 (16.1)	<0.001
Atrial fibrillation	34 (9.6)	24 (19.4)	<0.001
Peripheral vascular disease	13 (3.7)	13 (10.5)	<0.01
Hypertension	93 (26.3)	36 (29.0)	0.56
Chronic obstructive pulmonary disease	9 (2.5)	39 (31.5)	<0.001
Diabetes mellitus	87 (24.6)	44 (35.5)	0.02
Chronic kidney disease	12 (3.4)	10 (8.0)	0.03
Liver disease	19 (5.4)	18 (14.5)	<0.001
Malignancy	30 (8.5)	28 (22.6)	<0.001
Alcohol misuse	22 (6.2)	9 (7.3)	0.69
Psychosis	4 (1.1)	1 (0.8)	0.76
Depression	12 (3.4)	2 (1.6)	0.31
Elixhauser comorbidity score, mean (SD)	3.3 (5.1)	9.0 (7.1)	<0.001
Arrest in monitored setting, *n* (%)	136 (38.5)	50 (40.3)	0.72
Witnessed arrest, *n* (%)	193 (54.7)	64 (51.6)	0.54
Initial rhythm, *n* (%)			0.80
Ventricular fibrillation	93 (26.3)	30 (24.2)	
Ventricular tachycardia	19 (5.4)	5 (4.0)	
Pulseless electrical activity	144 (40.8)	50 (40.3)	
Asystole	97 (27.5)	39 (31.4)	
Previous ED visits, mean (SD)[a]	2.3 (2.6)	2.2 (2.0)	0.36
Previous ICU admissions, mean (SD)[a]	0.3 (0.6)	0.3 (0.9)	0.28
Previous ICU days, mean (SD)[a]	1.2 (5.1)	1.6 (6.7)	0.11

Abbreviations: CPR = cardiopulmonary resuscitation; ED = Emergency Department; ICU = intensive care unit; MODS = multi-organ dysfunction score; SD = standard deviation.
[a] Only including patients with previous visits to The Ottawa Hospital.

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Table 2 – Outcomes of non-frail and frail patients following in-hospital cardiac arrest (*n* = 477).

Characteristic	No frailty (*n* = 353)	Frailty (*n* = 124)	Adjusted odds ratio[b] (95% CI)	*P* value
ROSC, *n* (%)	169 (47.9)	44 (35.5)	0.63 (0.41–0.93)	<0.01
In-hospital mortality, *n* (%)	242 (68.6)	118 (95.2)	2.91 (2.37–3.48)	<0.001
Disposition, *n* (%)[a]			1.94 (1.57–2.32)	<0.001
Home	44 (39.6)	1 (16.7)		
Long-term care centre	67 (60.4)	5 (83.3)		
Post-IHCA therapeutic hypothermia, *n* (%)	23 (6.5)	5 (4.0)		0.31
Post-IHCA coronary angiography, *n* (%)	17 (4.9)	4 (3.2)		0.46
ICU length of stay following ROSC, days, median (IQR)	4 (1–4)	3 (1–4)		0.09
Hospital length of stay following ROSC, days, median (IQR)	7 (4–9)	6 (4–8)		<0.01
Readmission to hospital within 30 days from discharge, *n* (%)[a]	24 (21.6)	2 (33.3)		0.50

Abbreviations: ICU = intensive care unit; IHCA = in-hospital cardic arrest; IQR = interquartile range; MODS = multi-organ dysfunction score; SD = standard deviation.
[a] Only includes patients surviving to discharge.
[b] Ratio of frail patients to non-frail patients.

(mean age 65.7 years vs. 56.1 years, $P < 0.001$), had higher severity of illness (mean MODS 4.2 vs. 3.1, $P < 0.001$), and higher prevalence of comorbidities. There were no differences in the proportion of arrests in monitored settings, witnessed arrests, or initial rhythm.

Patient outcomes between groups by frailty status are shown in Table 2. Hospital mortality among patients without frailty was 68.6%, as compared to 95.2% among patients with frailty. Among the 6 patients with frailty who survived to discharge, the mean age was 60.4 years. 4 of these patients had a CFS of 5, while one had a CFS of 6, and one had a CFS of 7. Multivariable logistic regression analyses examining in-hospital mortality and ROSC are displayed in the appendix (Supplemental Tables S1–2, respectively) as suggested by existing recommendations.[35] Frailty was independently associated with lower odds of ROSC (adjusted OR 0.63 [95% CI: 0.41–0.93]), and higher odds of hospital mortality (adjusted OR 2.91 [95% CI: 2.37–3.48]). Only 6 of the 124 patients (5%) with frailty survived to hospital discharge, of which only 1 was discharged to a home setting. A similarly significant effect was found when evaluating the CFS as a continuous variable in logistic regression analyses (Supplemental Tables S3–4). In comparison with patients without frailty, those with frailty had a higher likelihood of discharge to a long-term care facility (adjusted OR 1.93 [95% CI: 1.57–2.32]).

Resource utilization among patients with and without frailty is demonstrated in Table 3. Patients who died prior to ICU admission are not included. Overall, there were no significant differences between groups in the use of invasive mechanical ventilation, non-invasive mechanical ventilation, vasoactive medications, arterial line use, renal replacement therapy, or NEMS. Patient costs are displayed n Table 4. Mean total costs did not differ between patients with and without frailty ($45,849 vs. $50,799, $P = 0.14$). There were no differences in components of cost, namely nursing, pharmacy, or laboratory costs. When accounting for mortality, cost-per-survivor among non-frail patients was $161,550, while cost-per-survivor among frail patients was $947,546. Among patients achieving ROSC, ICU costs-per-survivor were $62,261 for patients without frailty, compared with $ 251,893 for patients with frailty.

Discussion

We found that the presence of pre-admission frailty among ward patients with IHCA was associated with increased odds of in-hospital mortality, decreased odds of ROSC and more frequent discharge to long-term care among survivors. 95% of patients with frailty died in-hospital following IHCA, and only 1 survivor was able to be discharged home from hospital. While no differences in resource utilization and total hospital costs were found between patients with and without frailty, the low survival rate among patients with frailty translated into

Table 3 – Intensive care unit resource utilization among non-frail and frail patients with return of spontaneous circulation following in-hospital cardiac arrest (*n* = 213).

Characteristic	No frailty (*n* = 169)	Frailty (*n* = 44)	*P* value
Invasive mechanical ventilation, n (%)	167 (98.8)	44 (100.0)	0.47
Invasive mechanical ventilation days, median (IQR)	3 (2–5)	3 (2–4)	0.16
Non-invasive mechanical ventilation, n (%)	27 (16.0)	8 (18.2)	0.73
Non-invasive mechanical ventilation days, median (IQR)	1 (1–2)	1 (1–2)	0.39
Vasoactive medication, n (%)	153 (90.5)	41 (93.2)	0.58
Vasoactive medication days, median (IQR)	2 (1–4)	2 (1–3)	0.09
Arterial line, n (%)	160 (94.7)	40 (90.9)	0.35
Arterial line days, median (IQR)	3 (1–4)	3 (1–4)	0.29
Renal replacement therapy, n (%)	75 ()	15 ()	0.18
Renal replacement therapy days, median (IQR)	3 (1–5)	3 (1–5)	0.56
NEMS/day, mean (SD)	26.4 (7.1)	25.8 (7.9)	0.41

Abbreviations: IQR = interquartile range; NEMS = nine equivalents of nursing manpower scale; SD = standard deviation.

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Table 4 – Mean costs of non-frail and frail patients experiencing in-hospital cardiac arrest (*n* = 477).

Characteristic	No frailty (*n* = 353)	Frailty (*n* = 124)	*P* value
Total costs, \$, mean (SD)	50,799 (38,348)	45,849 (38,349)	0.14
Total direct costs, \$, mean (SD)	38.348 (30,382)	31,389 (32,393)	0.03
Total cost per survivor, \$	161,550	947,546	
Post-ROSC ICU cost per survivor, \$	62,261	251,893	
Attributable costs, \$, mean (SD)			
Food services	1282 (1139)	983 (1320)	0.38
Health professionals (non-physician or nursing)	2726 (2,029)	2394 (2.290)	0.31
Laboratory	1837 (1832)	1762 (1392)	0.55
Medical imaging	1493 (1230)	1392 (1259)	0.62
Pharmacy	3223 (3001)	2945 (3032)	0.22
Respiratory therapy	3844 (6923)	3013 (6831)	0.27
Nursing	36,349 (33,349)	31,349 (30,832)	0.09
ICU costs, \$, mean (SD)			
Total costs	40,893 (35,349)	34,349 (40,737)	0.11
Direct costs	32,329 (30,923)	25,293 (21,939)	0.15
Indirect costs	8239 (8020)	7949 (7.848)	0.12

Abbreviations: ICU = intensive care unit; SD = standard deviation.

Q2

much higher costs per survivor. Taken together, these findings provide important information regarding outcomes and resource use following IHCA, and therefore may assist in discussions surrounding patient goals-of-care at the time of hospital admission.

Survival following IHCA is poor, however, the evidence informing prognosis from IHCA has largely been extrapolated from out-of-hospital cardiac arrest.[1] Therefore, a growing need exists to identify factors that are associated with changes in survival following IHCA. Previous evidence has strongly linked age with IHCA outcomes. Older patients are less likely to survive from IHCA,[36] and a dose-response relationship has been shown, with increasing age associated with decreasing survival.[37] Similarly, the presence of increased comorbidity burden has also been associated with poor survival following IHCA. For example, patients with active malignancy have higher adjusted odds of mortality following IHCA.[38] The potential link between these various prognostic factors may be frailty, which describes a state of physiological decline and vulnerability. Given emerging evidence that frailty can be feasibly and reliably ascertained in hospitalized and critically ill patients, understanding the association between frailty and outcomes after IHCA can provide patients and clinicians with important information when creating care plans and deciding upon goals of care.

Limited data already suggest that frailty may be associated with outcomes following IHCA. However, these data have some limitations and have not been generalized. An Australian study using the Hospital Frailty Risk Score (HFRS), a frailty instrument based on diagnostic codes in administrative data, found that higher frailty scores were associated with reduced likelihood of discharge home.[39] In the United Kingdom, a retrospective study of 179 cases of IHCA found that survival to discharge among patients with frailty (using a CFS threshold $\geq$6) was 1.8%, compared with 31.7% in patients without frailty.[40] Our study, which used a clinically-oriented frailty instrument in a multi-hospital network with a larger sample size, supports the generalizability of these findings. Specifically, frailty is a clinically available (although often un-assessed) risk factor for mortality following IHCA. and At the time of hospital admission, clinicians are tasked with discussing goals-of-care with patients, whether to include CPR in an individual's treatment plan. Unfortunately, patients often have limited understanding of outcomes following IHCA,[41] and believe the unrealistic rates of survival that are depicted in popular media.[42] However, data related to prognosis following IHCA may influence patient decisions related to CPR, and older patients frequently decide against CPR when odds of survival are presented.[41] Frailty represents a novel but powerful predictor of outcome, suggesting that it should be assessed and discussed with all patients, particularly those who may be younger but who have significant comorbidities. Assessing frailty with the CFS is quick,[43] and can provide information to patients that can enable them to decide upon the inclusion of CPR in their goals-of-care.

We also analyzed the association between frailty and resource use and costs among patients with IHCA. Understanding resource use is a major focus of healthcare, particularly critical care, and there is a growing need to understand the amount of resource directed toward care that provides little benefit.[23,44] While the prevalence of resource use and costs did not differ significantly between patients with and without frailty, the higher mortality among patients with frailty resulted in a cost per survivor of almost \$1 million (CDN). This cost is much higher than that of typical high-cost ICU populations, such as patients with subarachnoid hemorrhage, or those receiving extracorporeal life support.[25,45] This cost is particularly striking when one considers that only one-third of the patients with frailty surviving to discharge were discharged to a home setting. Understanding these values is important in identifying the resources and cost that are provided to the care of these patients.

We used a multicentre database to identify patients who had IHCA, and were able to identify important associations between frailty, outcomes, and resource utilization. We closely followed existing recommendations for the control of confounding in observational research.[35] However, our study has several limitations. First, and most importantly, while our primary outcome was survival to hospital discharge, we were unable to determine neurological outcome at discharge, which is a high-priority and patient-important outcome following cardiac arrest.[46] The cause of death or withdrawal of life-sustaining therapy among deceased patients was unknown, and if it was secondary to poor neurological outcome, this has the potential to guide discussions with patients prior to IHCA. Future research should identify the impact of frailty on neurological outcome following IHCA, which will provide further prognostic information to patients. Also,

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while all patients had no limitations on care at the time of IHCA, we do not have data related to how goals-of-care changed over the course of ICU admission. This has the potential to bias results, as patients with frailty may be guided toward less aggressive interventions. Secondly, we screened for frailty retrospectively using the CFS, but this tool was designed for prospective application.[13] While this has the potential to introduce bias, we followed previously described methods,[34] and this methodology has been shown to have strong concordance with prospective measurement in ICU populations.[18,33] Third, a significant proportion of costs in our cohort were incurred prior to IHCA, though we were able to provide ICU costs following IHCA separately. Fourth, we did not have data related to long-term outcomes among survivors. Whether frailty is associated with long-term survival and disability among survivors of IHCA is unknown and serves as an important avenue for future work. Understanding long-term costs would also be of interest. Finally, while our data were gathered from two hospitals, they exist within the same network and city, and therefore may be susceptible to bias related to local practice.

Conclusions

We found that pre-admission frailty was associated with increased odds of hospital mortality and discharge to long-term care; and decreased odds of ROSC following IHCA occurring on hospital wards. These findings will inform conversations between clinicians and patients related to the inclusion of CPR in goals-of-care. While resource use and total hospital costs did not differ between patients with and without frailty, patients with frailty had markedly higher costs per survivor.

Conflicts of interest

Dr. Daniel I. McIsaac is supported by the Canadian Anesthesiologists' Society Career Scientist Award and The Ottawa Hospital Anesthesia Alternate Funds Association. Dr. Sean M. Bagshaw is supported by a Canada Research Chair in Critical Care Nephrology. Dr. John Muscedere is the Scientific Director of the Canadian Frailty Network. Dr. Deborah J. Cook is supported by a Canada Research Chair in Critical Care Knowledge Translation. None of the other authors report any conflict of interest.

Author contributions

SMF, DIM, BR, and KK designed the study. SMF, CD, and KK gathered the data. All authors analyzed and interpreted the data. All authors wrote the manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.11.011.

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