Withholding and Withdrawal of Life Support in Mechanically Ventilated Stroke Patients

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Research

Keywords: Ischemic stroke, Intracerebral hemorrhage, Subarachnoid hemorrhage, end-of-life care, mechanical ventilation

Posted Date: August 25th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-62282/v1

Abstract

Background. The determinants of decisions to limit life support (withholding or withdrawal) in ventilated stroke patients have been poorly investigated.

Methods. In a prospective multicenter observational cohort (2005-2016), we evaluated limitation of life support in ventilated stroke patients compared to a non-brain-injured population and identified factors associated with such decisions in stroke patients using Fine and Gray competing risk models.

Results. We identified 373 stroke patients (ischemic, n=167 (45%); hemorrhagic, n=206 (55%)), and 5683 non-brain-injured patients. Decisions to limit life support were taken in 41% of ischemic stroke cases (vs. non-brain-injured patients, sHR 3.59 [95% CI 2.78-4.65]) and in 33% of hemorrhagic stroke cases (vs. non-brain-injured patients, sHR 3.9 [95% CI 2.97-5.11]). Time from ICU admission to the first limitation was longer in ischemic than in hemorrhagic stroke (5 [3 - 9] vs 2 [1 - 6] days, p<0.01). Limitation of life support preceded ICU death in 70% of ischemic strokes and 45% of hemorrhagic strokes (p<0.01). Life support limitation in ischemic stroke was associated with a vertebrobasilar location (vs. anterior circulation, sHR, 1.61 [95% CI 1.01 - 2.59]) and in hemorrhagic stroke, it was associated with an age>70 years (2.29 [1.43 - 3.69]), a Glasgow score<8 (2.15 [1.08 - 4.3]) and a lower non-neurologic admission SOFA score (per point, 0.89 [0.82 - 0.97]).

Conclusions. In ventilated stroke patients, decisions to limit life support are more than 3 times more frequent than in non-brain injured patients, with different timing and associated risk factors between ischemic and hemorrhagic strokes.

Background

The prognosis of mechanically ventilated stroke patients is poor, with 1-year mortality rates ranging from 60–92% [1–5]. In this subset of extremely severe cases with high fatality rates, a high incidence of limitation (withholding or withdrawal) of life support has been reported, ranging from 30 to 40% [6–8] compared to 9–14% in large multicenter observational studies in the general Intensive Care Unit (ICU) population [9–15]. Compared to non-brain-injured critically ill patients, the decision to limit life support in brain-injured patients may have more serious consequences, as the continuation of organ support could result in months or years of life in a state of disability that may be against the patient's wishes [16]. Assessing long-term vital and functional outcomes in these patients is difficult, and current prognostic models do not include treatment restrictions that can affect the outcomes of the populations in which the models were developed [17].

The high incidence of life support limitation in mechanically ventilated stroke patients and the potential confounding impact on prognostication models suggests that determinants of limitation of life support should be thoroughly investigated. In this observational multicenter study, we sought to describe the incidence, timing, and factors associated with life-support limitation in critically ill patients, with either ischemic or hemorrhagic stroke, requiring invasive mechanical ventilation (IMV).

Methods

Patient data source

This observational cohort study was conducted using data from the French prospective multicenter (n = 28 ICUs) OUTCOMEREA database. Patients admitted between 2005 and 2016 were considered for this study. We chose 2005 as the beginning of the study period as important end-of-life legislation was acted in France that year. The OUTCOMEREA database, described in previous publications [18], has been approved by the French Advisory Committee for Data Processing in Health Research and the French Informatics and Liberty Commission (CNIL, registration no. 8999262). The database protocol was submitted to the Institutional Review Board of the Clermont-Ferrand University Hospital (Clermont-Ferrand, France), who waived the need for informed consent (IRB no. 5891). The datasets used during the current study are available from the corresponding author on reasonable request.

Study populations and definitions

The stroke population included all adult patients with acute stroke and requiring IMV within 24 h of ICU admission. ICU stays were considered as related to acute stroke in cases of: 1) direct ICU admission following stroke onset, or 2) ICU admission during the initial acute care hospital stay following stroke onset. We excluded patients without hospitalization reports. From the same ICUs where the stroke population was selected, we defined a non-brain-injured population comprised of non-stroke adult patients requiring IMV within 24 h of ICU admission, and without admission diagnoses associated with brain injury: cardiac arrest, status epilepticus, meningitis/encephalitis, and traumatic brain injury.

Intracranial hemorrhages and subarachnoid hemorrhages were merged as "hemorrhagic strokes" [19]. Limitations of life support were categorized as either withholding or withdrawing. Withholding of life support was defined as a decision not to start or increase a life-sustaining intervention. Withdrawal of life support was defined as a decision to actively stop a life-sustaining intervention presently underway [20]. If more than one limitation decision occurred for a single patient, the most active limitation (withdrawing > withholding) defined the limitation category. End-of-life outcomes were categorized as follows: 1) death without limitation if death occurred in absence of any decision to limit life support, 2) death following limitation if death occurred after any limitation of life support, and 3) brain death, in cases of documented cessation of cerebral function [20]. The severity of illness was graded at ICU admission with the use of the Simplified Acute Physiology Score (SAPS) II [21] and the sequential organ failure assessment (SOFA) score [22]. The non-neurologic SOFA was defined as the SOFA score without the neurologic component. Coma was defined as a Glasgow coma score (GCS) < 8 [23]. We used the Charlson comorbidities index to assess the burden of comorbid conditions [24].

Data collection

Data were prospectively collected at admission and daily throughout the ICU stay, through an anonymized electronic case report form using Vigirea, Rhea, and e-Rhea software (OutcomeRea, Aulnay-sous-Bois, France). Long term survival after hospital discharge was collected by each local investigator.

We retrospectively collected the following data in medical charts: date of stroke, location and acute phase therapy (*i.e.* thrombolysis or endovascular thrombectomy for ischemic strokes and neurosurgery or embolization for hemorrhagic strokes).

Statistical analysis

Quantitative variables are presented as medians, 1st and 3rd quartiles, and compared between groups with the Wilcoxon test. Qualitative variables are presented as frequencies and corresponding percentages and compared with the Chi-square test or Fisher exact test, as appropriate.

To compare the risk of life support limitation between stroke and non-brain-injured populations, we used an adjusted Fine and Gray sub-distribution competing risk model [25] to estimate the sub-distribution hazard of stroke as a class variable (ischemic stroke/hemorrhagic strokes/no stroke), and considering ICU death without limitation as the competing event. For each stroke subgroup, factors associated with the occurrence of a limitation of life support were evaluated using a Fine and Gray model [25], with the same competing event. All models were adjusted on non-collinear factors associated ($p < 0.1$) with the outcome of interest in univariate analysis using a backward selection procedure. The log-linearity of quantitative variables included in the models was tested. When this was not the case, variables were binarized using the median as the cutoff. To account for variability in practice of life support limitation across ICUs [12, 26], models were stratified on center (centers with less than 10% of the cohort were combined into one stratum). Two-by-two clinically relevant interactions were tested in each model. Missing data were all completely at random with less than 10% missing values per variable, and were handled by simple imputation with the median/most frequent method [27]. For each stroke subgroup, we conducted a sensitivity analysis by forcing in the models the period of study inclusion, arbitrarily divided into 4-year time intervals.

All statistical analyses were carried out with SAS 9.4 (SAS Institute Inc., Cary, NC, USA). A *p-value* of 0.05 and lower was considered statistically significant.

Results

Among 17520 ICU admissions over the study period, we identified 373 acute stroke patients from 14 ICUs where IMV was initiated within 24 h of admission. In the same 14 ICUs, we identified 5683 non-brain-injured patients (**Additional file 1**). Stroke patients were predominantly male (59%), aged 68.7 [58.2–76.5] years, with strokes classified as ischemic (n = 167, 45%) and hemorrhagic (n = 206, 55%). Patients' characteristics according to stroke type or absence of brain injury are presented in Table 1. Ischemic stroke patients were admitted to university hospitals in 92/167 (55%) cases, hospitals with a stroke unit in 160/167 (96%) cases, and with a neurosurgery unit and interventional radiology in 80/167 (48%) cases. Hemorrhagic stroke patients were admitted to university hospitals in 131/206 (64%) cases, hospitals with a stroke unit in 182/206 (88%) cases, and with a neurosurgery unit and interventional radiology in 107/206 (48%) cases.

Table 1
Population characteristics according to stroke subtype or absence of brain injury

Variable N (%) or median [Q1 - Q3]	Non-brain-injured patients n = 5683	Ischemic stroke patients n = 167	Hemorrhagic stroke patients [a] n = 206	p [b]
Demographics/history				
Age, years	62.4 [49.4–74]	69.6 [61.2–77.2]	67 [56.6–76.4]	0.09
Male sex	3506 (61.7)	112 (67.1)	109 (52.9)	< .01
Charlson comorbidity index ≥ 1	3810 (67)	103 (61.7)	97 (47.1)	< .01
ICU characteristics				
University affiliated ICU	3846 (67.7)	92 (55.1)	131 (63.6)	0.10
GCS at admission	12 [5–15]	6 [3–10]	3 [3–6]	< .01
SAPS II	50 [37–64]	56 [45–67]	61 [52–77]	< .01
ICU length of stay, days	6 [3–13]	7 [4–13]	3 [2–8]	< .01
Life support limitations				
Any life support limitation	695 (12.2)	69 (41.3)	68 (33)	0.10
Limitation categories [c]				< .01
Withholding	504 (8.9)	31 (18.6)	16 (7.8)	.
Withdrawal	314 (5.5)	38 (22.8)	52 (25.2)	.
Time from ICU to first limitation, days	6 [2–15]	5 [3–9]	2 [1–6]	< .01
Outcomes				
ICU mortality	1322 (23.3)	92 (55.1)	145 (70.4)	< .01
End-of-life outcome				< .01
Brain death	0	21 (22.8)	68 (46.9)	.

Abbreviations: ICU, Intensive Care Unit; GCS, Glasgow Coma Scale; SAPS, Simplified Acute Physiology Score.

[a] Intracranial hemorrhage and subarachnoid hemorrhage; [b] Comparison of acute ischemic stroke patients and hemorrhagic stroke patients; [c] If more than one limitation of life support occurred, the most active limitation (withdrawing > withholding) defined the limitation category

Variable N (%) or median [Q1 - Q3]	Non-brain-injured patients n = 5683	Ischemic stroke patients n = 167	Hemorrhagic stroke patients [a] n = 206	p [b]
Death without limitation of life support	755 (57.1)	7 (7.6)	12 (8.3)	.
Death following a limitation of life support	567 (42.9)	64 (69.6)	65 (44.8)	.
Abbreviations: ICU, Intensive Care Unit; GCS, Glasgow Coma Scale; SAPS, Simplified Acute Physiology Score.				
[a] Intracranial hemorrhage and subarachnoid hemorrhage; [b] Comparison of acute ischemic stroke patients and hemorrhagic stroke patients; [c] If more than one limitation of life support occurred, the most active limitation (withdrawing > withholding) defined the limitation category				

During their ICU stay, 137/373 (37%) stroke patients and 695/5683 (12%) non-brain-injured patients underwent a limitation of life support. The frequency of such limitation was 41% (69/167 patients) for ischemic strokes and 33% (68/206 patients) for hemorrhagic strokes ($p = 0.1$). In a Fine and Gray sub-distribution multivariable competing risk model adjusted on age, comorbidities, and severity at ICU admission, we found that having an ICU admission diagnosis of ischemic stroke was associated with a 3.6-fold increased (95% confidence interval (CI) [2.78–4.65]) risk of undergoing a limitation of life support, as compared to the non-brain-injured population. Similarly, having an ICU admission diagnosis of hemorrhagic stroke was associated with a 3.9-fold increased (95% CI [2.97–5.11]) risk of qualifying for limitation of life support, as compared to the non-brain-injured population (**Additional file 2**).

Among patients who underwent life support limitation, withdrawal was the predominant limitation category in the stroke population (ischemic strokes, 38/69 (55%); hemorrhagic strokes, 52/68 (76%)), whereas withholding was the most frequent category in the non-brain-injured population (381/695 (55%)). Time from ICU admission to the first limitation of life support differed between ischemic stroke and hemorrhagic strokes (5 [3–9] vs 2 [1–6] days, $p < 0.01$). The daily ICU incidence rate of life support limitation according to stroke subtype or absence of brain injury is presented in Fig. 1 and shows different time patterns between stroke and non-brain-injured patients.

ICU mortality was 92/167 (55%), 145/206 (70%), and 1322/5683 (23%) for ischemic stroke, hemorrhagic stroke, and non-brain-injured populations respectively (Table 1). In the non-brain injured population, death following life support limitation occurred in 567/1322 (43%) cases (Table 1). In the stroke population, death following a limitation of life support occurred in 129/235 (55%) patients, including 64/90 (70%) ischemic stroke patients and 65/145 (45%) hemorrhagic stroke patients ($p < 0.01$). Brain death occurred in 21/90 (23%) ischemic stroke and 68/145 (47%) hemorrhagic stroke patients ($p < 0.01$). In the stroke population, ICU mortality after a decision to withhold life support was 43/47 (92%) and was 86/90 (96%) after a decision to withdraw life support. 1-year mortality was 100% for both groups (Table 2). End-of-life outcomes according to the time from ICU admission and by stroke subtype are presented in Fig. 2. From the 5th day of ICU stay and beyond, the rate of death following life support limitation exceeded 80% in ischemic stroke patients, and 70% in hemorrhagic stroke patients.

Table 2
Characteristics of the stroke population according to limitation of life support category

Variable **N (%) or median [Q1 - Q3]**	**Limitation of life support [a]**			**p**
	No limitation **n = 236**	**Withholding** **n = 47**	**Withdrawal** **n = 90**	
Demographics/history				
Age, years	65.5 [56.3–74.1]	72.5 [62.4–77.6]	73.8 [62.7–81.3]	< .01
Male sex	134 (56.8)	33 (70.2)	54 (60)	0.23
Charlson comorbidity index ≥ 1	120 (50.8)	28 (59.6)	52 (57.8)	0.36
Hospital characteristics				
University hospital	137 (58.1)	25 (53.2)	61 (67.8)	0.17
Stroke unit on-site	220 (93.2)	42 (89.4)	80 (88.9)	0.37
Neurosurgery unit on-site	119 (50.4)	18 (38.3)	50 (55.6)	0.16
ICU type				0.2
Medical	129 (54.7)	21 (44.7)	58 (64.4)	.
Mixed	104 (44.1)	25 (53.2)	30 (33.3)	.
Surgical	3 (1.3)	1 (2.1)	2 (2.2)	.
ICU authorized for organ donation	161 (68.2)	30 (63.8)	54 (60)	0.36
Ischemic stroke characteristics (n = 167)				
Location				0.18
Anterior circulation	67/98 (68.4)	17/30 (56.7)	20/38 (52.6)	.
Vertebrobasilar circulation	31/98 (31.6)	13/30 (43.3)	18/38 (47.4)	.
Acute phase therapy [b]	26/98 (26.5)	2 (6.5)	6 (15.8)	0.04

Abbreviations: ICU, Intensive Care Unit; GCS, Glasgow Coma Scale; SAPS, Simplified Acute Physiology Score.

[a] If more than one limitation of life support occurred, the most active limitation (withdrawing > withholding) defined the limitation category; [b] Thrombolysis or endovascular thrombectomy; [c] Intracranial hemorrhage and subarachnoid hemorrhage; [d] Neurosurgery or embolization; [e] 22/373 (6%) stroke patients were lost to follow-up and censored at 47 [23; 153] days

Variable N (%) or median [Q1 - Q3]	Limitation of life support [a]			p
	No limitation n = 236	Withholding n = 47	Withdrawal n = 90	
Time from stroke to ICU admission, days	2 [1–7]	1 [1–6]	1 [1–2]	0.05
Hemorrhagic stroke [c] characteristics (n = 206)				
Location				< .01
Deep	32/138 (23.2)	9/16 (56.3)	5/52 (9.6)	.
Lobar	85/138 (61.6)	6/16 (37.5)	34/52 (65.4)	.
Infratentorial	21/138 (15.2)	1/16 (6.3)	13/52 (25)	.
Acute phase therapy [d]	27/138 (19.6)	0	7/52 (13.5)	0.11
Time from stroke to ICU admission, days	1 [1–2]	1 [1–1.5]	1 [1–1]	0.13
ICU characteristics				
GCS at admission	5 [3–9]	4 [3–8]	3 [3–6]	< .01
SAPS II	56 [45–68.5]	66 [54–78]	62.5 [53–74]	< .01
Duration of mechanical ventilation, days	3 [2–8]	5 [2–9]	5 [2–8]	0.07
Vasopressor support	127 (53.8)	18 (38.3)	34 (37.8)	0.01
ICU length of stay, days	4 [2–11]	6 [2–11]	6 [3–9]	0.49
Outcomes				
ICU mortality	108 (45.8)	43 (91.5)	86 (95.6)	< .01
Hospital mortality	126 (53.4)	45 (95.7)	89 (98.9)	< .01
1-year mortality [e]	138 (64.2)	46 (100)	90 (100)	< .01

Abbreviations: ICU, Intensive Care Unit; GCS, Glasgow Coma Scale; SAPS, Simplified Acute Physiology Score.

[a] If more than one limitation of life support occurred, the most active limitation (withdrawing > withholding) defined the limitation category; [b] Thrombolysis or endovascular thrombectomy; [c] Intracranial hemorrhage and subarachnoid hemorrhage; [d] Neurosurgery or embolization; [e] 22/373 (6%) stroke patients were lost to follow-up and censored at 47 [23; 153] days

Univariate analysis of factors associated with life support limitation is presented in Table 2. In the subset of ischemic stroke patients, the only variable significantly associated with a decision to limit life support was the location of stroke (vertebrobasilar vs. anterior circulation location, sHR 1.61 [1.01–2.59]) (Fig. 3). In the subset of hemorrhagic stroke patients, variables associated with a decision to limit life support were age > 70 years (sHR 2.29 [1.43; 3.69]), a GCS < 8 at ICU admission (sHR 2.15 [1.08–4.3]) and the non-neurologic SOFA score at ICU admission (sHR 0.89 [0.82; 0.97]) (Fig. 3). The period of inclusion in the study, when forced into each model, was not significantly associated with a decision to limit life support (**Additional files 3 and 4**).

Discussion

The 37% rate of life support limitation observed in our cohort is consistent with rates reported in previous studies conducted in intracranial hemorrhage patients, ranging from 34 to 43% [7, 8]. Of note, our study provides unique data regarding the limitation rate in the specific population of ischemic stroke patients requiring IMV. Furthermore, we present accurate estimates, as they integrate the competitive risk of dying without receiving a decision of limitation. These models are particularly relevant in populations with very high case-fatality rates where death precludes the occurrence of the outcome of interest [25, 28]. Our results confirm that stroke patients under IMV are a population submitted to a high incidence of end-of-life decisions, and thus deserve a more thorough evaluation [16, 29]. A prospective multicentre study investigating 1-year outcomes, ethical issues, and care pathways of acute stroke patients requiring IMV in the ICU, is ongoing (NCT 03335995) [30].

We found that 54% of stroke patient ICU deaths and 43% of those of non-brain-injured patients were preceded by a decision to limit life support. These rates are consistent with those reported in the general ICU population, ranging from 47–53% [10, 15, 31]. When evaluating end-of-life outcomes by stroke subtype, it is interesting to note that ischemic stroke patients had a higher proportion of death following a decision to limit life support than hemorrhagic stroke patients, probably because hemorrhagic stroke patients had a higher proportion of brain death.

The highest incidence of life support limitation during ICU stay occurred during the first 4 days. For hemorrhagic strokes in particular, the incidence of limitation was highest within the 48 h following ICU admission, with a more than 2-fold incidence than any other period of the ICU stay. This result could notably be explained by a higher rate of direct ICU admission from home or the emergency department in hemorrhagic stroke patients, where physicians might initiate IMV without knowing neither the patient's medical history nor the extent of brain injury. Early decisions of life support limitation have been associated with a higher risk of short-term mortality independently of patient factors, suggesting that some of these decisions may be undue [7, 8, 32]. Bias that may result in underuse of life support in severe stroke patients include erroneous prognostic estimates [33–35], misunderstanding patient's values and expectation [36], and undervaluing the future patient's health state (disability paradox) [29, 37]. The influence of cognitive bias in the decision-making process must also be acknowledged, and may be as important as patient factors [38]. Inappropriate prognostic pessimism and premature limitations of life support define the mechanism by which self-fulfilling prophecies occur [39]. As such, life support limitation within 48 h of ICU admission is not recommended in intracranial hemorrhage patients [40], and time-limited ICU trials should be proposed in severe stroke patients.

The most commonly described risk factors for receiving a decision to limit life support in the general ICU population are age, the presence of chronic diseases, and clinical severity at ICU admission [11–13, 41, 42]. In critically ill brain-injured patients, age and a low GCS are the most frequently reported [6, 43]. It is interesting to note that in our study, risk factors appear to differ between ischemic and hemorrhagic stroke patients. For the latter, the usual patient-related risk factors were found (*i.e.* age and neurological severity), with the notable addition of non-neurological organ failure that appeared to play a protective role. We hypothesize that intensivists would be more inclined to continue aggressive care in these patients because non-neurologic organ failure may be more reversible and without obvious impact on functional outcome, as compared to neurological failure. For ischemic stroke patients, however, neither age nor comorbidities were associated with life support limitation. We hypothesize that there was an important left censoring in our study (*i.e.* patients having undergone life support limitation before ICU admission) that might have mitigated the effect of age and comorbidities [44, 45].

The strengths of our study include a multicenter population from a high-quality prospective database. The relatively small number of patients included, considering the study period and the 14 ICUs, is due to the fact that several ICUs did not contribute throughout the 12 years, and some used only a fraction of their beds to feed the database. Our study also has limitations. First, the OUTCOMEREA database was not built specifically for stroke studies, and all data regarding stroke are retrospective, collected from hospitalization records. As a result, some data, such as the stroke volume, are lacking. Furthermore, data regarding the modality of treatments withheld or withdrawn, and the reason for undertaking a life support limitation was not available. Second, end-of-life decision-making is a complex process, and we did not explore all the determinants that lead to a limitation of life support, which may include patient- or surrogate-centered determinants, and physicians' personal beliefs [16, 29]. Third, our study population excluded stroke patients that were critically ill, but were not referred to the ICU because of care-limiting decisions made by the neurologist or the emergency physician in charge. Fourth, our results and conclusion may apply only for the setting and culture we recruited the patients from, as this is an exclusively French cohort including only medical and mixed ICUs. As only 50% of the cohort were treated with on-site neurosurgery and interventional radiology, we may have selected a population with a high proportion of patients not eligible for acute phase stroke therapy. However, as all multivariate models were stratified on centers of inclusion, we believe that this effect was accounted for. Fifth, data on functional outcomes in survivors could not be reported.

Conclusions

In this secondary data use of a prospective multicenter cohort study of critically ill patients requiring IMV, we showed that life support limitation was more than 3 times more frequent in stroke patients than in non-brain injured patients. There were significant differences in timing and risk factors for limitation of life support between ischemic and hemorrhagic strokes. In ventilated stroke patients, early decisions to limit life support are frequent and a high proportion of deaths follow such decisions. These findings warrant further investigations to clarify the impact of life support limitation on prognostication models.

List Of Abbreviations

95% CI: 95% Confidence Interval

GCS: Glasgow Coma Score

ICU: Intensive Care Unit

IMV: Invasive Mechanical Ventilation

SAPS: Simplified Acute Physiology Score

sHR: subdistribution Hazard Ratio

SOFA: Sequential Organ Failure Assessment

Declarations

Ethics approval and consent to participate

The OUTCOMEREA database has been approved by the French Advisory Committee for Data Processing in Health Research (CCTIRS) and the French Informatics and Liberty Commission (CNIL, registration no. 8999262). The database protocol was submitted to the Institutional Review Board of the Clermont-Ferrand University hospital (Clermont-Ferrand, France), who waived the need for informed consent (IRB no. 5891).

Consent to participate

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Work Under Consideration for Publication: no competing interest.

Relevant financial activities outside the submitted work: Guillaume Thiéry (Gilead-Kite).

Funding

None.

Authors' contributions

Conception and design of the study: EDM, SR, RS, JFT.

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Figures

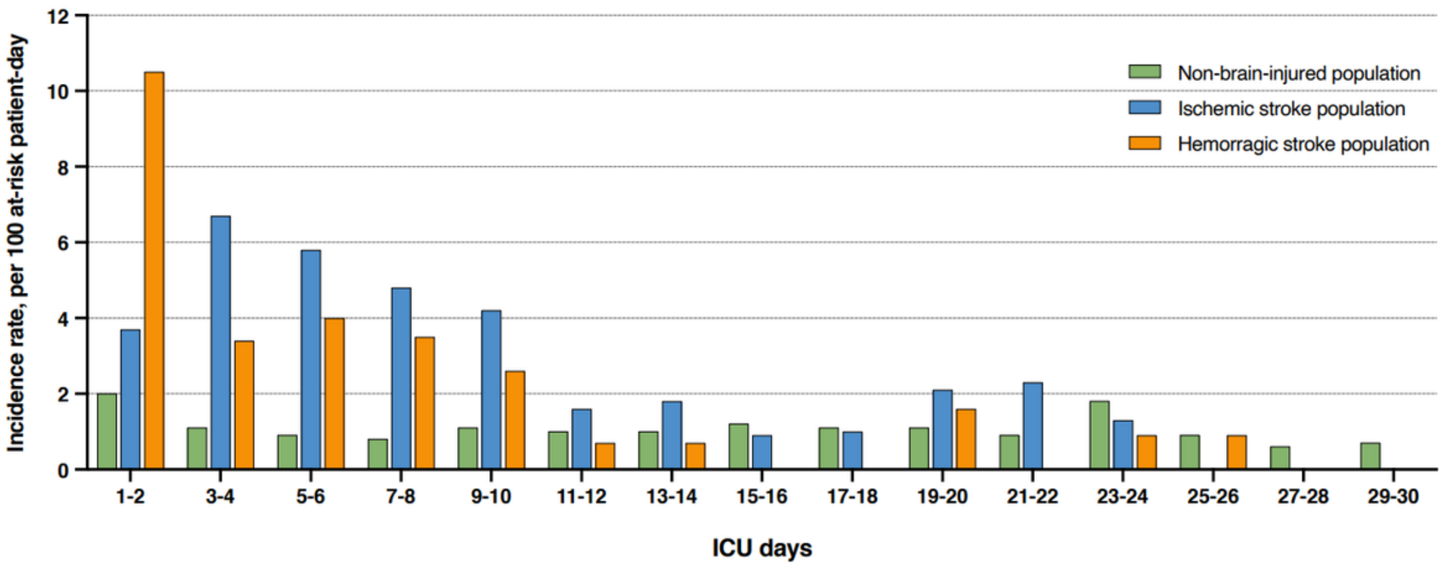

Figure 1

Daily ICU incidence rate of life support limitations according to stroke subtype or absence of brain-injury

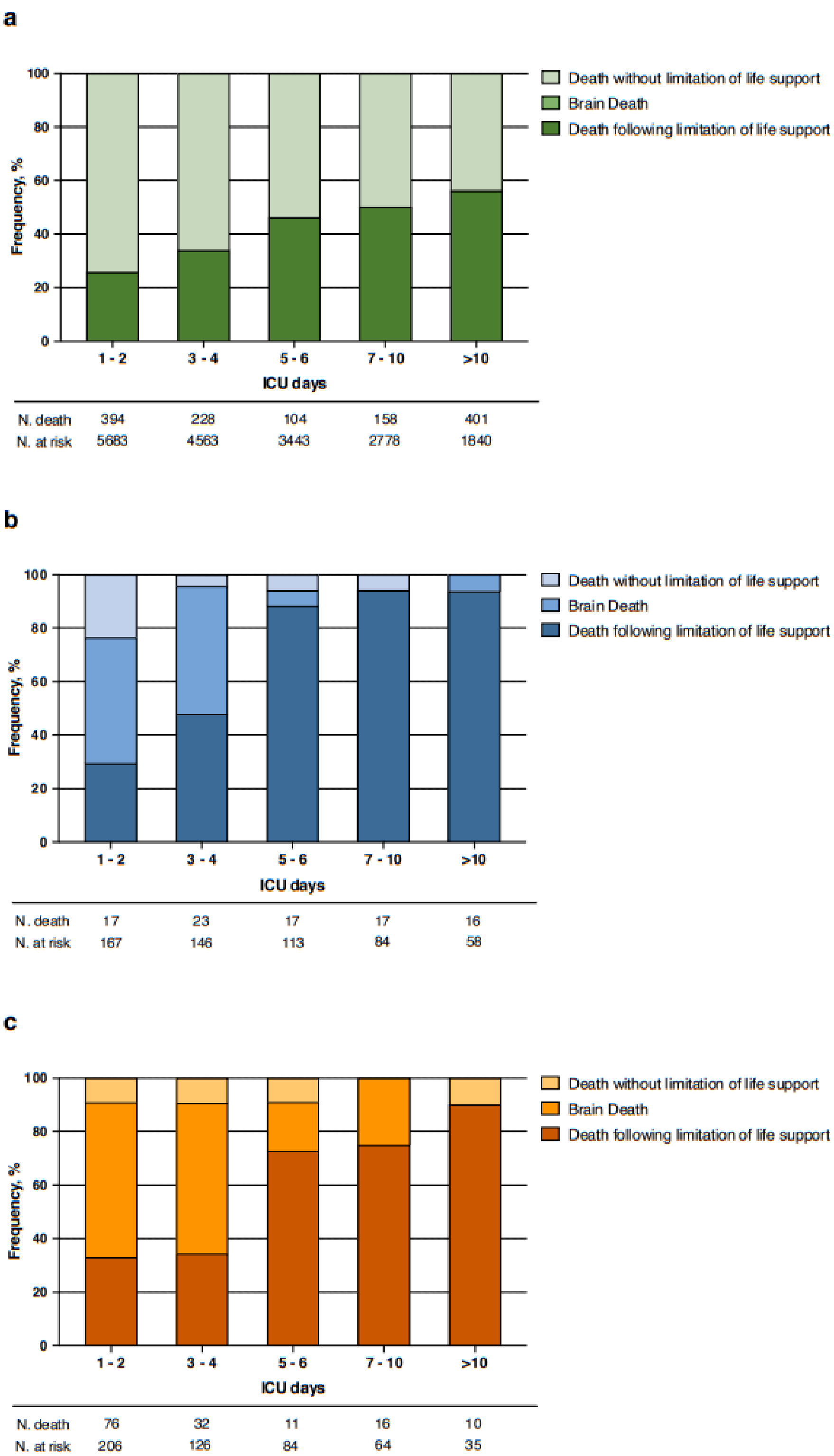

Figure 2

End-of-life outcome according to length of ICU stay (days): comparison between non-brain-injured patients and stroke subtypes. a. Non-brain-injured patients; b. Ischemic stroke patients; c. Hemorrhagic stroke patients.

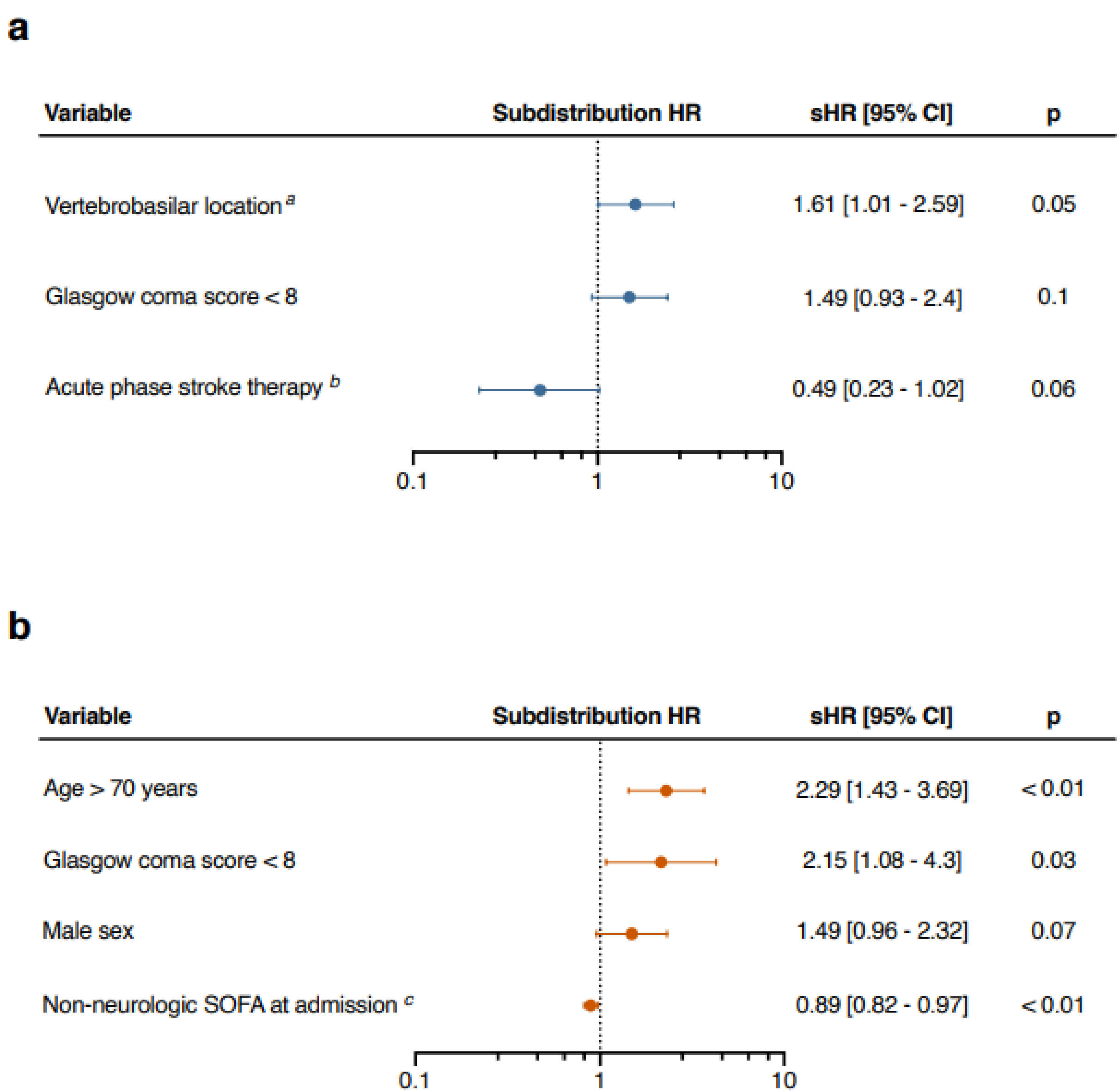

Figure 3

Fine and Gray sub-distribution hazard analysis for the occurrence of life support limitations, and death without such limitation as the competing event a. Ischemic stroke patients; b. Hemorrhagic stroke patients. Abbreviations: ICU, Intensive Care Unit; sHR, subdistribution Hazard Ratio; CI, Confidence Interval; SOFA, Sequential Organ Failure Assessment. a versus anterior circulation location; b Thrombolysis or endovascular thrombectomy; c Per SOFA point

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