OPEN

Life Support Limitations in Mechanically Ventilated Stroke Patients

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OBJECTIVES: The determinants of decisions to limit life support (withholding or withdrawal) in ventilated stroke patients have been evaluated mainly for patients with intracranial hemorrhages. We aimed to evaluate the frequency of life support limitations in ventilated ischemic and hemorrhagic stroke patients compared with a nonbrain-injured population and to determine factors associated with such decisions.

DESIGN: Multicenter prospective French observational study.

SETTING: Fourteen ICUs of the French OutcomeRea network.

PATIENTS: From 2005 to 2016, we included stroke patients and nonbrain-injured patients requiring invasive ventilation within 24 hours of ICU admission.

INTERVENTION: None.

MEASUREMENTS AND MAIN RESULTS: We identified 373 stroke patients (ischemic, $n = 167$ [45%]; hemorrhagic, $n = 206$ [55%]) and 5,683 nonbrain-injured patients. Decisions to limit life support were taken in 41% of ischemic stroke cases (vs nonbrain-injured patients, subdistribution hazard ratio, 3.59 [95% CI, 2.78–4.65]) and in 33% of hemorrhagic stroke cases (vs nonbrain-injured patients, subdistribution hazard ratio, 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 d [1–6] d; $p < 0.01$). Limitation of life support preceded ICU death in 70% of ischemic strokes and 45% of hemorrhagic strokes ($p < 0.01$). Life support limitations in ischemic stroke were increased by a vertebrobasilar location (vs anterior circulation, subdistribution hazard ratio, 1.61 [95% CI, 1.01–2.59]) and a prestroke modified Rankin score greater than 2 (2.38 [1.27–4.55]). In hemorrhagic stroke, an age greater than 70 years (2.29 [1.43–3.69]) and a Glasgow Coma Scale score less than 8 (2.15 [1.08–4.3]) were associated with an increased risk of limitation, whereas a higher nonneurologic admission Sequential Organ Failure Assessment score was associated with a reduced risk (per point, 0.89 [0.82–0.97]).

CONCLUSIONS: In ventilated stroke patients, decisions to limit life support are more than three times more frequent than in nonbrain-injured patients, with different timing and associated risk factors between ischemic and hemorrhagic strokes.

KEY WORDS: critical care; end-of-life care; intracerebral hemorrhage; ischemic stroke; subarachnoid hemorrhage

The prognosis of mechanically ventilated stroke patients is poor, with 1-year mortality rates ranging from 60% to 92% (1–5). In this subset of extremely severe cases with high fatality rates, a high incidence of

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limitation (withholding or withdrawal) of life support has been reported, ranging from 30% to 40% (6–8) compared with 9–14% in large multicenter observational studies in the general ICU population (9–15). Compared with nonbrain-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 are based on datasets including a significant proportion of patients with treatment restriction. In turn, these life support limitations 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 suggest 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).

MATERIALS AND 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 (18). Per this law, withholding or withdrawal of treatments is authorized when they appear "useless, disproportionate or having no other effect than solely the artificial preservation of life." However, the decision to withdraw or withhold a treatment from a patient unable to express their will has to consider the wishes they might have expressed through advance directives and/or the wishes of a trusted person or, last, of the family. Furthermore, before making any decision, physicians have to respect a collegial medical procedure. Finally, euthanasia in France remains illegal. The OUTCOMEREA database, described in previous publications (19), has been approved by the French Advisory Committee for Data Processing in Health Research and the French Informatics and Liberty Commission (registration number 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 (Institutional Review Board number 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 hours 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 nonbrain-injured population comprised of nonstroke adult patients requiring IMV within 24 hours of ICU admission and without admission diagnoses associated with brain injury: cardiac arrest, status epilepticus, meningitis/encephalitis, and traumatic brain injury. We also chose to exclude subdural hematomas from our analysis, as it was retrospectively difficult to ascertain their nontraumatic nature.

Intracranial hemorrhages (ICHs) and subarachnoid hemorrhages (SAHs) were merged as "hemorrhagic strokes" (20). 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. Life-sustaining interventions comprised organ support (mechanical ventilation invasive or not, vasopressors and dialysis) and acute phase stroke therapies if there was a theoretical indication for it. Withdrawal of life support was defined as a decision to actively stop a life-sustaining intervention presently underway (21). 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 (21). The severity of illness was graded at ICU admission with the use of the Simplified Acute Physiology Score II (22) and the Sequential Organ Failure Assessment (SOFA) score (23). The nonneurologic SOFA was defined as the SOFA score without the neurologic component. Coma was defined as a Glasgow Coma Scale (GCS) score less than 8 (24). We used the Charlson comorbidities index to assess the burden of comorbid conditions (25).

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, first and third 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 nonbrain-injured populations, we used an adjusted Fine and Gray subdistribution competing risk model (26) to estimate the subdistribution 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 (26), with the same competing event. All models were adjusted on clinically relevant factors or factors associated ($p < 0.2$) with the outcome of interest in univariate analysis. In the presence of collinear variables, the most clinically relevant one was retained. Variables were selected using a backward selection procedure with a threshold of p value of less than 0.1. 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, 27), models were stratified on center (centers with < 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 (28). 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, Cary, NC). A p value of 0.05 and lower was considered statistically significant.

RESULTS

Among 17,520 ICU admissions over the study period, we identified 373 acute stroke patients from 14 ICUs where IMV was initiated within 24 hours of admission. In the same 14 ICUs, we identified 5,683 nonbrain-injured patients (**Supplemental Fig. 1**, Supplemental Digital Content 1 http://links.lww.com/CCX/A505). Stroke patients were predominantly male (59%), age 68.7 years (58.2–76.5 yr) old, with strokes classified as ischemic (n = 167, 45%) and hemorrhagic (n = 206, 55%). The reasons for intubation and mechanical ventilation were coma (n = 271, 73%), respiratory failure (n = 46, 12%), seizures (n = 27, 7%), cardiac arrest (n = 17, 5%), and elective procedure (n = 12, 3%). 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 of 167 cases (55%), hospitals with a stroke unit in 160 of 167 cases (96%), and hospitals with a neurosurgery unit and interventional radiology in 80 of 167 cases (48%). Hemorrhagic stroke patients were admitted to university hospitals in 131 of 206 cases (64%), hospitals with a stroke unit in 182 of 206 cases (88%), and hospitals with a neurosurgery unit and interventional radiology in 107 of 206 cases (48%).

During their ICU stay, 137 of 373 stroke patients (37%) and 695 of 5,683 nonbrain-injured patients (12%) 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 subdistribution multivariable competing risk model

TABLE 1.
Population Characteristics According to Stroke Subtype or Absence of Brain Injury

Variables	Nonbrain-Injured Patients, $n = 5,683$	Ischemic Stroke Patients, $n = 167$	Hemorrhagic Stroke Patients[a], $n = 206$	p[b]
Demographics/history				
Age, yr, median (quartile 1–quartile 3)	62.4 (49.4–74)	69.6 (61.2–77.2)	67 (56.6–76.4)	0.09
Male sex, *n* (%)	3,506 (61.7)	112 (67.1)	109 (52.9)	< 0.01
Charlson comorbidity index ≥ 1, *n* (%)	3,810 (67)	103 (61.7)	97 (47.1)	< 0.01
ICU characteristics				
University affiliated ICU, *n* (%)	3,846 (67.7)	92 (55.1)	131 (63.6)	0.10
Glasgow Coma Scale score at admission, median (quartile 1–quartile 3)	12 (5–15)	6 (3–10)	3 (3–6)	< 0.01
Simplified Acute Physiology Score II, median (quartile 1–quartile 3)	50 (37–64)	56 (45–67)	61 (52–77)	< 0.01
ICU length of stay, d, median (quartile 1–quartile 3)	6 (3–13)	7 (4–13)	3 (2–8)	< 0.01
Life support limitations				
Any life support limitation[c], *n* (%)	695 (12.2)	69 (41.3)	68 (33)	0.10
Limitation categories[c], *n* (%)				< 0.01
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, d, median (quartile 1–quartile 3)	6 (2–15)	5 (3–9)	2 (1–6)	< 0.01
Outcomes, *n* (%)				
ICU mortality	1,322 (23.3)	92 (55.1)	145 (70.4)	< 0.01
End-of-life outcome				< 0.01
Brain death	0	21 (22.8)	68 (46.9)	.
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)	.

[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.

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% CI (CI) [2.78—4.65]) risk of undergoing a limitation of life support, as compared to the nonbrain-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 nonbrain-injured population

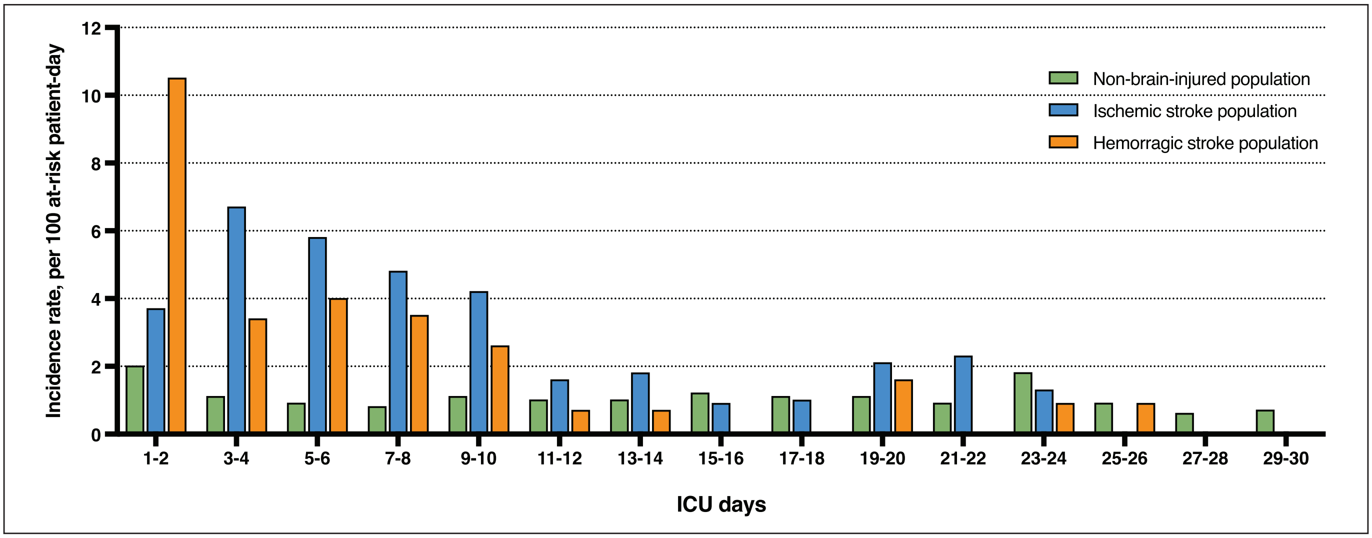

Figure 1. Daily ICU occurence rate of life support limitations according to stroke subtype or absence of brain injury.

(**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCX/A505).

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%]). The daily ICU incidence rate of life support limitation according to stroke subtype or absence of brain injury is presented in **Figure 1** and shows different time patterns between stroke and nonbrain-injured patients. Time from ICU admission to the first limitation of life support was the shortest in hemorrhagic stroke, both compared with ischemic strokes (2 [1–6] vs 5 d [3–9 d]; $p < 0.01$) and non-brain-injured patients (2 [1–6] vs 6 d [2–15 d]; $p < 0.01$). There was no difference in time from ICU admission to the first limitation between ischemic stroke nonbrain-injured patients (5 [3–9] vs 6 d [2–15 d]; $p = 0.67$).

ICU mortality was 92 of 167 (55%), 145 of 206 (70%), and 1,322 of 5,683 (23%) for ischemic stroke, hemorrhagic stroke, and nonbrain-injured populations, respectively (Table 1). In the nonbrain-injured population, death following life support limitation occurred in 567 of 1,322 cases (43%) (Table 1). In the stroke population, death following a limitation of life support occurred in 129 of 237 (54%) patients, including 64 of 92 ischemic stroke patients (70%) and 65 of 145 hemorrhagic stroke patients (45%)($p < 0.01$). Brain death occurred in 21 of 92 ischemic stroke patients (23%) and 68 of 145 hemorrhagic stroke (47%) ($p < 0.01$). End-of-life outcomes according to the time from ICU admission and by stroke subtype are presented in **Figure 2**. From the fifth 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.

Univariate analysis of factors associated with any life support limitation is presented in **Table 2** (for univariate analysis by stroke subset see **Supplemental Tables 2** and **3**, Supplemental Digital Content 1, http://links.lww.com/CCX/A505). In the subset of ischemic stroke patients, variables significantly associated with a decision to limit life support in multivariate analysis were stroke location (vertebrobasilar vs anterior circulation location, subdistribution hazard ratio [sHR], 1.61 [1.01–2.59]) and a modified Rankin score greater than 2 before stroke onset (sHR, 2.38 [1.27–4.55]) (**Fig. 3**). In the subset of hemorrhagic stroke patients, variables independently associated with a decision to limit life support in multivariate analysis were age greater than 70 years (sHR, 2.29 [1.43–3.69]), a GCS score less than 8 at ICU admission (sHR, 2.15 [1.08–4.3]), and the nonneurologic 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 (**Supplemental Tables 4** and **5**, Supplemental Digital Content 1, http://links.lww.com/CCX/A505). Among the 137 patients with a limitation of life support, univariate analysis of factors associated with a choice of withholding rather than withdrawal of life support is presented in the **Supplemental Table 6** (Supplemental Digital Content 1, http://links.lww.com/CCX/A505).

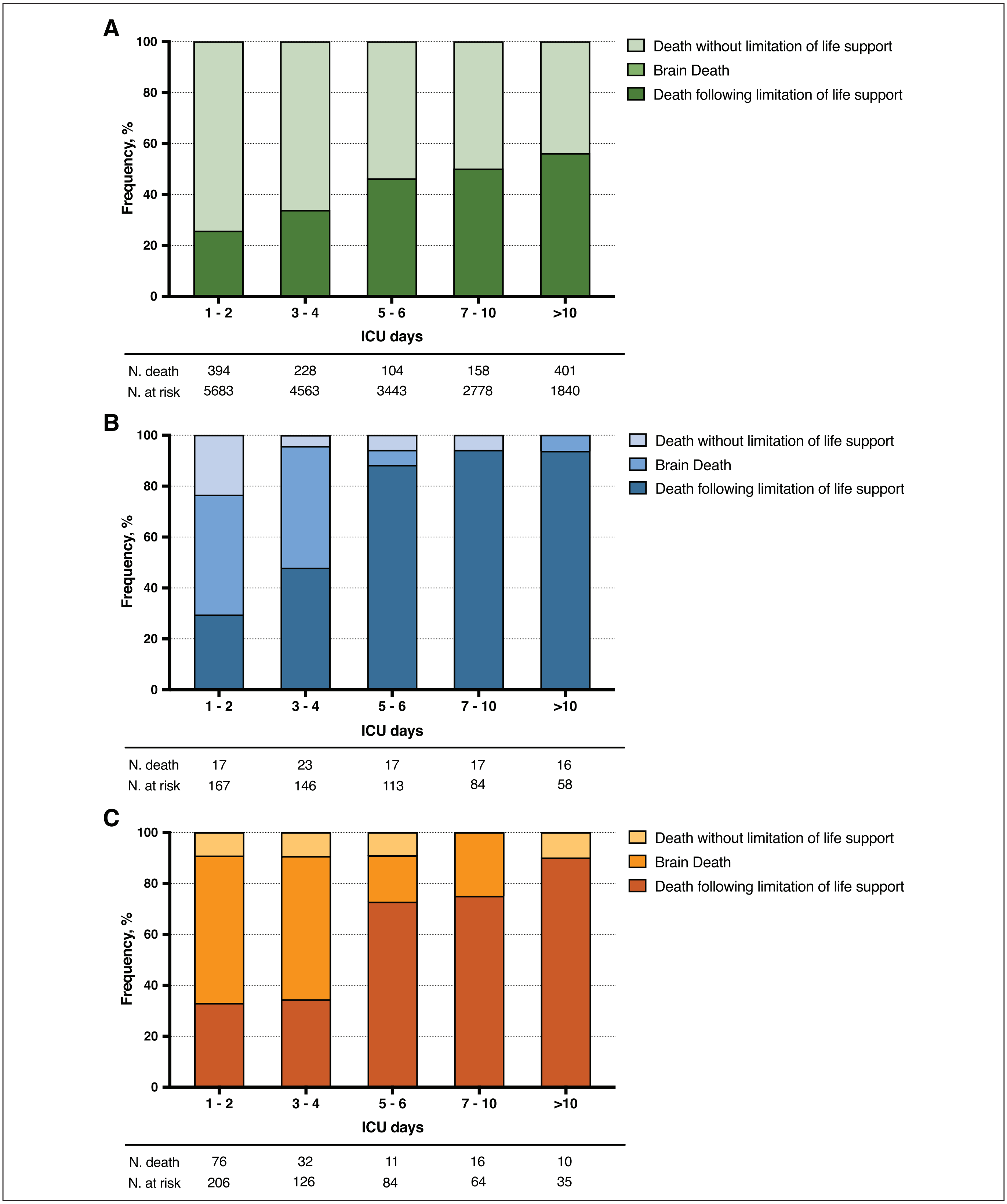

Figure 2. End-of-life outcome according to length of ICU stay (d): comparison between nonbrain-injured patients and stroke subtypes. **A**, Nonbrain-injured patients. **B**, Ischemic stroke patients. **C**, Hemorrhagic stroke patients.

TABLE 2.
Stroke Population Characteristics, With or Without Limitation of Life Support (n = 373)

Variables	Limitation of Life Support		p
	No Limitation, n = 236	Any Limitation, n = 137	
Demographics/history			
Age, yr, median (quartile 1–quartile 3)	65.5 (56.3–74.1)	72.8 (62.6–79.6)	< 0.01
Male sex, n (%)	134 (56.8)	87 (63.5)	0.20
Charlson comorbidity index ≥ 1, n (%)	120 (50.8)	80 (58.4)	0.16
Hospital characteristics, n (%)			
University hospital	137 (58.1)	86 (62.8)	0.37
Stroke unit on-site	220 (93.2)	122 (89.1)	0.16
Neurosurgery unit on-site	119 (50.4)	68 (49.6)	0.88
ICU type			0.64
Medical	129 (54.7)	79 (57.7)	
Mixed	104 (44.1)	55 (40.1)	
Surgical	3 (1.3)	3 (2.2)	
ICU authorized for organ donation	161 (68.2)	84 (61.3)	0.18
Ischemic stroke characteristics (n = 167)			
Location, n (%)			0.11
Anterior circulation	67/98 (68.4)	38/69 (55.1)	
Vertebrobasilar circulation	31/98 (31.6)	31/69 (44.9)	
Acute phase therapy[a], n (%)	26/98 (26.5)	8/69 (11.6)	0.02
Time from stroke to ICU admission, d, median (quartile 1–quartile 3)	2 (1–7)	1 (1–2)	0.02
Hemorrhagic stroke [b] characteristics (n = 206)			
Location, n (%)			0.62
Deep	32/138 (23.2)	14/68 (20.9)	
Lobar	85/138 (61.6)	40/68 (58.8)	
Infratentorial	21/138 (15.2)	14/68 (20.6)	
Acute phase therapy[c], n (%)	27/138 (19.6)	7/68 (10.3)	0.09
Time from stroke to ICU admission, d, median (quartile 1–quartile 3)	1 (1–2)	1 (1–1)	0.09

(*Continued*)

TABLE 2. (*Continued*).
Stroke Population Characteristics, With or Without Limitation of Life Support ($n = 373$)

	Limitation of Life Support		
Variables	No Limitation, $n = 236$	Any Limitation, $n = 137$	p
ICU characteristics			
Glasgow Coma Scale score at admission, median (quartile 1–quartile 3)	5 (3–9)	3 (3–6)	< 0.01
Simplified Acute Physiology Score II, median (quartile 1–quartile 3)	56 (45–68.5)	65 (53–77)	< 0.01
Duration of mechanical ventilation, d, median (quartile 1–quartile 3)	3 (2–8)	5 (2–8)	0.02
Vasopressor support, *n* (%)	127 (53.8)	52 (38)	< 0.01
ICU length of stay, d, median (quartile 1–quartile 3)	4 (2–11)	6 (3–9)	0.24
Outcomes, *n* (%)			
ICU mortality	108 (45.8)	129 (94.2)	< 0.01
Hospital mortality	126 (53.4)	134 (97.8)	< 0.01
1 yr mortality[d]	138/215 (64.2)	136/136 (100)	< 0.01

[a]Thrombolysis or endovascular thrombectomy. [b]Intracranial hemorrhage and subarachnoid hemorrhage. [c]Neurosurgery or embolization.
[d]Twenty-two of 373 stroke patients (6%) were lost to follow-up and censored at 47 d (23–153 d).

DISCUSSION

In this reanalysis of a prospective database, including 6,056 critically ill patients requiring mechanical ventilation within 24 hours of admission, we showed that 37% of stroke patients (n = 373) underwent life support limitation, representing more than a three-fold increase in the risk of receiving a decision to limit life support compared with nonbrain-injured patients (n = 5683). Although there was no difference in the global risk of limitation of life support between ischemic and hemorrhagic strokes, limitations occurred earlier in hemorrhagic stroke patients. Factors associated with life support limitation differed between stroke types, including mainly stroke location and prestroke modified Rankin score for ischemic strokes and mainly age and organ failure for hemorrhagic strokes.

The 37% rate of life support limitation observed in our cohort is consistent with rates reported in previous studies conducted in ICH 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 (26, 29). 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, 30). A prospective multicenter study investigating 1-year outcomes, ethical issues, and care pathways of acute stroke patients requiring IMV in the ICU is ongoing (NCT 03335995) (31).

We found that 54% of stroke patient ICU deaths and 43% of those of nonbrain-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% to 53% (10, 15, 32). 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

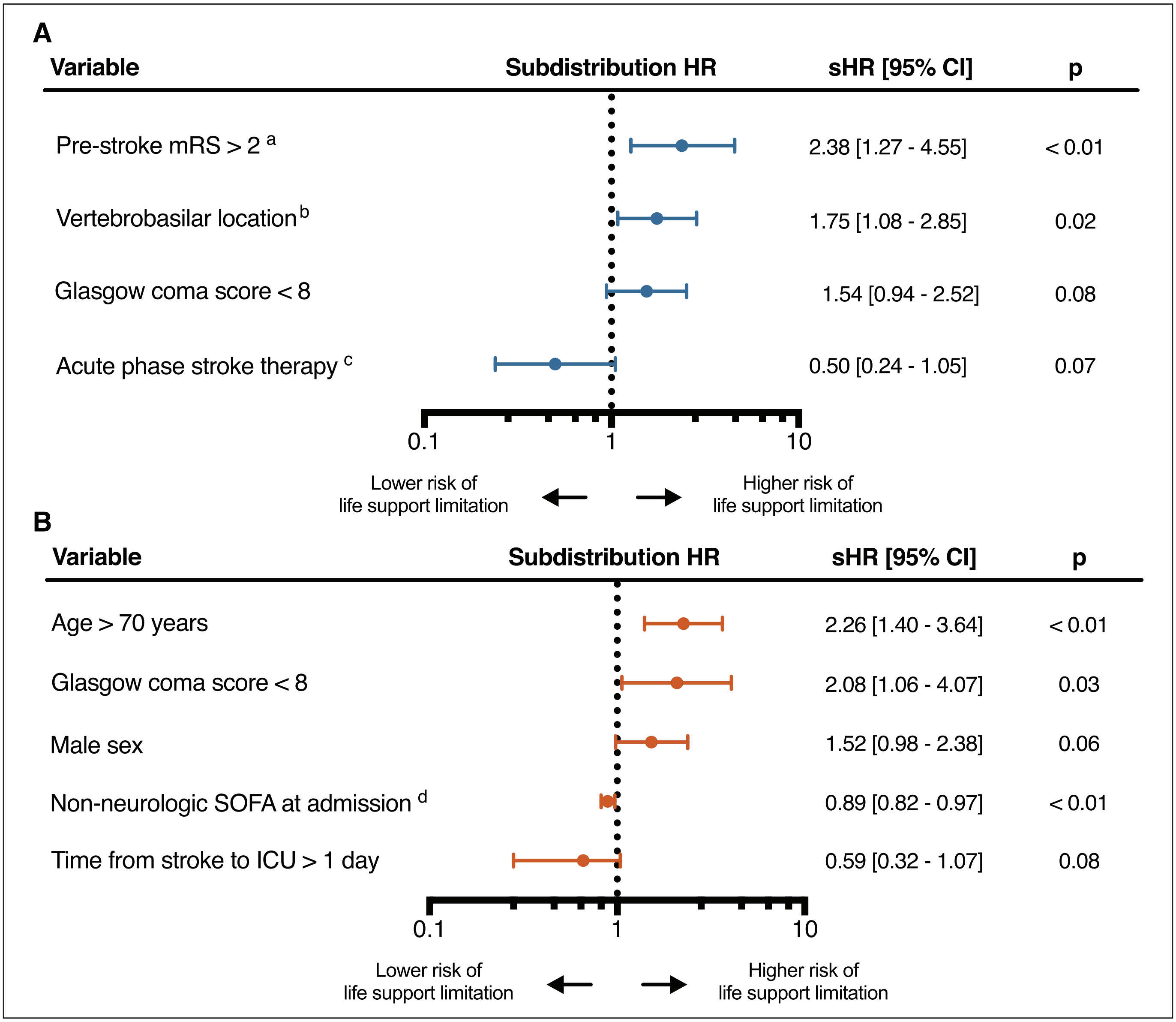

Figure 3. Fine and Gray subdistribution hazard analysis for the occurrence of life support limitations, and death without such limitation as the competing event. **A**, Ischemic stroke patients. **B**, Hemorrhagic stroke patients. [a]modified Rankin Score, [b]versus anterior circulation location, [c]thrombolysis or endovascular thrombectomy, [d]per SOFA point. HR = hazard ratio, sHR = subdistribution hazard ratio, SOFA = Sequential Organ Failure Assessment.

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 hours following ICU admission, with a more than two-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, 33). Inappropriate prognostic pessimism and premature limitations of life support define the mechanism by which self-fulfilling prophecies occur (34). Unfortunately, the design of our study and available data did not allow us to neither quantify the effect of self-fulfilling prophecies nor explore further this issue. Currently, life support limitation within 48 hours of ICU admission is not recommended in ICH patients (35), and time-limited ICU trials should be proposed in severe stroke patients. Bias that may result in underuse of life support in severe stroke patients include erroneous prognostic estimates (36–38), misunderstanding patient's values and expectation (39) and undervaluing the future patient's health state (disability paradox) (30, 40). The influence of cognitive bias in the decision-making process must also be acknowledged and may be as important as patient factors (41).

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, 42, 43). In critically ill brain-injured patients, age and a low GCS are the most frequently reported (6, 44). 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 neurologic severity), with the notable addition of nonneurologic 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 nonneurologic organ failure may be more reversible and without obvious impact on functional outcome, as compared to neurologic failure. For ischemic stroke patients, however, neither age nor comorbidities were associated with life support limitation. We hypothesize that age and comorbidities are variables strongly associated with a decision of life support limitation even before referring the patients to an ICU (i.e., left censoring) and that this phenomenon may have mitigated the effect of these variables in our dataset (45, 46).

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, specific severity scores are lacking: National Institutes of Health Stroke Scale (47) for ischemic strokes, ICH score for ICHs (48), and World Federation of Neurosurgical Societies or Hunt and Hess scores (49, 50) for SAH. For the same reason, data regarding the modality of treatments withheld or withdrawn, the reason for undertaking a life support limitation, and the presence or absence of advanced directives were 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' determinants (personal beliefs, religion, medical specialty, etc.) (16, 30). 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, when analyzing hemorrhagic strokes, we decided to merge ICH and SAH patients for analytical purposes. Although merging these two clinical entities has previously been done in the literature (20), a separate analysis of ICH and SAH could have brought additional information. Fifth, 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. Sixth, due to the recent rise of mechanical thrombectomy following the publication of important randomized controlled trials (51–53), the current proportion of stroke patients intubated for an elective procedure is likely to be higher than reported in our study, thus limiting the generalizability of our results. Seventh, data on functional outcomes in survivors could not be reported despite being a more relevant endpoint than mortality for stroke studies.

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 three times more frequent in stroke patients than in nonbrain-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.

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