Long-Term Risk of Ischemic Stroke among Elderly Survivors of Non-Traumatic Subarachnoid Hemorrhage

Melvin Parasram Neal S. Parikh Alexander E. Merkler Judy H. Ch'ang
Babak B. Navi Hooman Kamel Cenai Zhang Santosh B. Murthy

Clinical and Translational Neuroscience Unit, Department of Neurology, Feil Family Brain and Mind Research Institute, Weill Cornell Medicine, New York, NY, USA

Keywords

Subarachnoid hemorrhage · Ischemic stroke · Outcomes

Abstract

Introduction: Non-traumatic subarachnoid hemorrhage (SAH) is associated with poor long-term functional outcomes, but the risk of ischemic stroke among SAH survivors is poorly understood. **Objectives:** The aim of this study was to evaluate the risk of ischemic stroke among survivors of SAH. **Methods:** We performed a retrospective cohort study using claims data from Medicare beneficiaries from 2008 to 2015. The exposure was a diagnosis of SAH, while the outcome was an acute ischemic stroke, both identified using previously validated ICD-9-CM diagnosis codes. We used Cox regression analysis adjusting for demographics and stroke risk factors to evaluate the association between SAH and long-term risk of ischemic stroke. **Results:** Among 1.7 million Medicare beneficiaries, 912 were hospitalized with non-traumatic SAH. During a median follow-up of 5.2 years (IQR, 2.7–6.7), the cumulative incidence of ischemic stroke was 22 per 1,000 patients per year among patients with SAH, and 7 per 1,000 patients per year in those without SAH. In adjusted Cox models, SAH was associated with an increased risk of isch-

emic stroke (HR, 2.0; 95% confidence interval, 1.4–2.8) as compared to beneficiaries without SAH. Similar results were obtained in sensitivity analyses, when treating death as a competing risk (sub HR, 3.0; 95% CI, 2.8–3.3) and after excluding ischemic stroke within 30 days of SAH discharge (HR, 1.5; 95% CI, 1.1–2.3). **Conclusions:** In a large, heterogeneous national cohort of elderly patients, survivors of SAH had double the long-term risk of ischemic stroke. SAH survivors should be closely monitored and risk stratified for ischemic stroke.

© 2021 The Author(s).

Published by S. Karger AG, Basel

Introduction

Non-traumatic subarachnoid hemorrhage (SAH) is associated with high in-hospital mortality and morbidity [1, 2]. A significant proportion of patients who survive an SAH admission continue to have long-term functional and cognitive disability [3, 4]. Cerebral infarction, often attributable to procedural complications related to aneurysm treatment, delayed cerebral ischemia, or cardiac complications such as takotsubo car-

diomyopathy [5, 6], and occurring during the initial hospitalization, is one such factor contributing independently to the mortality and poor functional outcomes in SAH patients [7].

The crude global incidence of SAH has declined over 2 decades, while there has been an increase in SAH incidence in patients over 75 years of age, mainly among women [8]. Moreover, the mortality of SAH has also steadily trended down [1, 9], implying these patients are likely to survive longer after SAH. Several prior studies have suggested that within the first year, survivors of SAH are burdened with myocardial infarction and higher cardiovascular mortality, compared to the general population [2, 10–12]. Whether the risk of ischemic stroke is similarly increased after the initial hospitalization for SAH, particularly in the elderly population is poorly understood. We therefore sought to study the long-term risk of ischemic stroke after SAH using a large, nationally representative sample of Medicare beneficiaries.

Methods

Study Design

We performed a retrospective cohort study using data of both inpatient and outpatient claims on a 5% sample of Medicare beneficiaries. The United States (U.S.) CMS provides health insurance information to a majority of U.S. citizens aged 65 years and older [13]. The CMS provides de-identified claim-based datasets submitted by hospitals and providers. Longitudinal analysis of the care of each beneficiary over time was possible due to a unique and anonymous identifier code linking multiple claims for a patient. The Weill Cornell Medicine institutional review board approved this study.

Patient Population

Data were obtained from inpatient and outpatient claims of Medicare beneficiaries between January 2008 and September 2015. We limited our cohort to beneficiaries with continuous coverage in traditional CMS fee-for-service Medicare (Parts A and B) for at least 1 year or until death to keep within the standard practice of analyzing Medicare data. Although Medicare eligibility begins at 65 years of age, only patients aged 66 years or older were included in our study to allow time for beneficiaries to enter medical care and for their providers to document any preexisting medical comorbidities.

Measurements

The exposure was non-traumatic SAH, which is identified by the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis code 430.x in any diagnostic position. The code for SAH has a sensitivity of over 90% and a specificity of 96%, when compared with medical record review [14, 15]. Patients with any diagnosis code for trauma were excluded. To identify the underlying cause of non-traumatic SAH, we used ICD-9-CM diagnosis codes to delineate the etiology. These included

intracranial aneurysm (437.3), arteriovenous malformation (747.81), and Moyamoya disease (735.5) [16, 17]. We also excluded patients with prevalent SAH or ischemic stroke at the time of enrollment into the Medicare registry, to prevent misclassification of chronic events. Additionally, we did not include patients who had an ischemic stroke concurrently with the SAH hospitalization, given difficulty in establishing which occurred earlier, and consequently, to prevent inclusion of patients who had SAH as a complication of thrombolysis or mechanical thrombectomy for stroke. Furthermore, we only counted the first admission for SAH, since some patients with multiple intracranial aneurysms may experience repeated SAH episodes.

Information on cardiovascular risk factors and relevant comorbidities were collected using previous ICD-9-CM code algorithms: hypertension, diabetes, tobacco use, alcohol use, atrial fibrillation, cardiac valve disease, chronic kidney disease, and peripheral vascular disease. The burden of comorbidities was quantified using the Charlson Comorbidity Index [18, 19], which is a weighted score of 17 comorbidities identified through ICD-9-CM codes, has been used in previous studies using administrative data to adjust for illness burden [20, 21]. The cardiovascular comorbidities have been shown to have good agreement compared with chart review, and are accurate in assessing the risk of stroke [22, 23]. The primary outcome was an incident acute ischemic stroke, which was identified using the ICD-9-CM code 430, 433.x1, 434.x1, and 436. The diagnosis codes for ischemic stroke have a sensitivity of 86% and specificity of 95% [14, 24].

Statistical Analysis

Baseline characteristics were analyzed using Pearson χ^2 test for categorical variables, and the Student's *t* test for continuous variables. We used Cox regression analysis to estimate the hazard ratio (HR) and 95% confidence interval (CI) for the association between SAH and ischemic stroke. To ensure that the proportional hazards assumption was met, we performed visual inspection using log-log plots. Participants were followed through until death, outcome, or the last available follow-up. The covariates in the Cox models were chosen a priori, and they included age, sex, race, vascular risk factors including hypertension, diabetes mellitus, atrial fibrillation, valvular heart disease, chronic kidney disease, alcohol and tobacco use, and Charlson comorbidities. These covariates were chosen regardless of their significance level in univariate analyses, as has been done in prior studies [25, 26]. We performed 3 sensitivity analyses. First, we performed a survival analysis treating death as a competing risk. In the second analysis, we excluded all ischemic strokes that occurred in the first 30 days after discharge for an index SAH hospitalization. This conservative step was done to decrease errors from carrying forward any ischemic strokes that occurred due to procedural complications or vasospasm during the index hospitalization for SAH. Third, we excluded beneficiaries with atrial fibrillation and valvular heart disease since these conditions are independent stroke risk factors and this subset of patients are likely to be on antithrombotic therapy, which was not available in the dataset. The covariates in the sensitivity analyses were similar to those in the primary analysis. Statistical analyses were performed using Stata (StataCorp, Statistical Software, Release 15, College Station, TX, USA, StataCorp 2019). The threshold for statistical significance was $p < 0.05$.

Results

Study Population

There were a total of 1.8 million Medicare beneficiaries, of whom we excluded 68,292 (3.8%) with prevalent stroke. Among the 1.7 million beneficiaries, 912 (0.05%) were hospitalized with SAH. The causes of SAH were intracranial aneurysms ($n = 606$, 66.5%), arteriovenous malformations ($n = 37$, 4.1%), and Moyamoya disease ($n = 2$, 0.2%). Patients with SAH were older (77.2 vs. 73.3 years), predominantly women (61%), and had higher prevalent vascular comorbidities such as hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, valvular heart disease, alcohol use, tobacco use, and chronic kidney disease (Table 1).

Primary Outcome

During a median follow-up of 5.2 years (interquartile range [IQR], 2.7–6.7), the cumulative incidence of ischemic stroke was 22 per 1,000 patients per year among patients with SAH, and 7 per 1,000 patients per year in those without SAH. In the unadjusted Cox regression analysis, SAH was associated with an increased risk of ischemic stroke (HR, 3.4; 95% CI, 2.5–4.8) (Fig. 1). After adjustment for demographics, vascular risk factors, and Charlson comorbidity index, SAH was associated with an increased risk of ischemic stroke (HR, 2.0; 95% CI, 1.4–2.8) as compared to beneficiaries without SAH (Table 2). We also noted an increased risk of subsequent hemorrhagic stroke after SAH (HR, 6.8; 95% CI, 4.6–10.2).

Sensitivity Analysis

In prespecified sensitivity analyses, SAH was associated with an increased risk of ischemic stroke when treating death as a competing risk (sub HR, 3.0; 95% CI, 2.8–3.3), when excluding SAH patients who had an ischemic stroke in the first 30 days after SAH discharge (HR, 1.5; 95% CI, 1.1–2.3), and after the exclusion of beneficiaries with atrial fibrillation and valvular heart disease, a subset likely to be on antithrombotic therapy (HR, 1.7; 95% CI, 1.1–3.0).

Post hoc Analysis

Given the differences in baseline characteristics of beneficiaries with and without SAH, we performed a propensity score analysis, where participants were matched on age, sex, race, hypertension, diabetes mellitus, and atrial fibrillation. All 912 patients with SAH were matched with controls based on the propensity

Table 1. Characteristics of patients stratified by presence of subarachnoid hemorrhage

Characteristic	SAH (N = 912)	No SAH (N = 1,751,791)
Age, mean (SD), years	77.2 (7.7)	73.3 (7.7)
Female	554 (61)	998,807 (57)
Race		
White	764 (84)	1,507,729 (86)
Black	76 (8)	137,363 (8)
Other	72 (8)	106,699 (6)
Atrial fibrillation/flutter	256 (28)	135,810 (8)
Hypertension	831 (91)	973,048 (56)
Diabetes mellitus	411 (45)	406,282 (23)
Peripheral vascular disease	269 (30)	122,315 (7)
Chronic kidney disease	197 (22)	95,844 (5)
Chronic obstructive pulmonary disease	293 (32)	205,654 (12)
Valvular heart disease	222 (24)	124,981 (7)

SAH, subarachnoid hemorrhage; SD, standard deviation. Data are presented as n (%) unless otherwise specified.

Fig. 1. Kaplan-Meier survival analysis showing the risk of an ischemic stroke after subarachnoid hemorrhage. SAH, subarachnoid hemorrhage.

score using 1:1 matching. A univariate Cox proportional hazards model was then fitted using the matched sample. Robust variance estimator was used to account for the clustering within matched sets. In the final analytical cohort, SAH was independently associated with an increased risk of ischemic stroke (HR, 2.0; 95% CI, 1.3–3.0).

Table 2. Cox regression analyses showing the relationship between SAH and risk of ischemic stroke

Cox regression models	HR (95% CI)	<i>p</i> value
Primary unadjusted analysis ¹ (entire cohort)	3.4 (2.5–4.8)	<0.001
Primary adjusted analysis ¹ (entire cohort)	2.0 (1.4–2.8)	<0.001
Sensitivity analyses		
Competing risk analysis ²	3.0 (2.8–3.3)	<0.001
Exclusion of events in first 30 days ¹	1.5 (1.1–2.3)	<0.001
Exclusion of beneficiaries with atrial fibrillation and valvular heart disease ¹	1.7 (1.1–3.0)	<0.02
Propensity score analysis ³	2.0 (1.3–3.0)	<0.001

A *p* value <0.05 was considered significant. CI, confidence interval; HR, hazard ratio; SAH, subarachnoid hemorrhage. ¹ Models adjusted for age, sex, race, hypertension, diabetes mellitus, atrial fibrillation, valvular heart disease, chronic kidney disease, alcohol use, tobacco use, and Charlson comorbidities. ² Death was treated as competing risk. Sub-hazard ratios were calculated. ³ Propensity score analysis where subjects were matched on age, sex, race, hypertension, diabetes mellitus, and atrial fibrillation.

Discussion

In a large, heterogeneous cohort of Medicare beneficiaries, we observed a 2-fold heightened long-term risk of ischemic stroke after SAH compared to those without. The risk was similarly elevated after excluding SAH patients who had an ischemic stroke in the first 30 days after SAH discharge.

Several prior studies have evaluated the risk of major cardiovascular complications after SAH. In a Danish nationwide cohort study, a higher incidence of cardiovascular disease and death was observed in SAH patients than in the general population [11]. However, little is known about the cerebrovascular complications after SAH discharge. In this context, our study provides a novel finding of an elevated risk of ischemic stroke among SAH survivors.

From a pathophysiologic standpoint, the risk of ischemic stroke after SAH may be attributed to shared vascular risk factors, mainly hypertension and smoking, and other mechanisms such as cessation of antithrombotic medications or a systemic inflammatory response that occurs after SAH [8, 27, 28]. In fact, troponin elevation in the acute phase of SAH predicts cardiovascular events in the first year, suggesting a potential underlying role of myocardial injury [29, 30]. Additionally, takotsubo or stress cardiomyopathy, an acute complication of SAH is independently associated with ischemic stroke, myocardial infarction, and vascular death, as late as 10 years after diagnosis, further bolstering the early myocardial injury hypothesis [5, 31]. A noteworthy finding in our study was the heightened risk of subsequent hemorrhagic stroke af-

ter SAH, highlighting the need to carefully assess the risk-benefit ratio of secondary stroke prevention therapies. Since many patients with SAH have multiple aneurysms, these may play a role in future hemorrhagic stroke events. Larger prospective studies are therefore needed to further explore mechanisms of ischemic stroke after SAH, and potential prevention strategies.

Our study has several important limitations. First, our study may have been subject to surveillance bias as patients with SAH are more likely to undergo serial work up and neuroimaging resulting in a higher incidence of ischemic stroke. Second, inclusion of patients over 66 years likely limited the generalizability of our results to the general population. Third, the use of claims data is subject to errors in misclassification of events and diagnostic codes. For example, SAH may have been misclassified as “stroke” in subsequent hospitalizations. However, the ICD-9-CM codes for SAH and ischemic stroke used in this study have been validated to have high sensitivity and specificity [24]. Furthermore, our results were similar after a 30-day washout period that ensured that only new ischemic stroke events were captured in the analysis. Fourth, while we did not obtain information on aneurysm treatment procedures such as clipping or endovascular coiling; this likely did not influence our findings particularly because these procedures tend to increase the risk of stroke intra- or perioperatively, and not long-term after the index SAH [32, 33]. Information on medications often used for secondary stroke prevention such as antithrombotic, lipid lowering, and antihypertensive therapy were not available. Nevertheless, these medications are known to reduce the risk of ischemic stroke, and this risk was there-

fore presumably underestimated in our analysis. Finally, we did not have information on SAH severity like the Hunt-Hess score or the modified Fisher Scale score.

Conclusion

In a large, heterogeneous sample of Medicare beneficiaries, SAH was independently associated with an increased risk of ischemic stroke. This finding warrants further study to better delineate the risk and identify optimal prevention strategies in this high-risk group of SAH patients.

Acknowledgment

The authors are grateful to Kelsey Lansdale for her editing and clerical assistance.

Statement of Ethics

The Center for Medicare Services CMS provides de-identified claim-based datasets submitted by hospitals and providers. The Weill Cornell Medicine institutional review board approved the study and waived the requirement for informed consent (reference number: 1507016424).

Conflict of Interest Statement

A.M. is supported by the NIH (grant KL2TR002385), the American Heart Association (18CDA34110419), and the Leon Levy Foundation. Bard reports grants from Hyperfine, Biogen, and Astrocyte unrelated to this work. B.B.N. is supported by the NIH (K23NS091395) and the Florence Gould Endowment for Discovery in Stroke. H.K. is supported by the NIH (U01NS095869 and R01NS097443) and the Michael Goldberg Research Fund; serves

as a member of the data and safety monitoring board for the Patient-Centered Outcomes Research Institute (PCORI)-funded Transeptal versus Retrograde Aortic Ventricular Entry to Reduce Systemic Emboli (TRAVERSE) trial; and has received personal fees for medicolegal consulting on stroke. HK reports serving as co-PI for the NIH-funded ARCADIA trial (NINDS U01NS095869) which receives in-kind study drug from the BMS-Pfizer Alliance for Eliquis® and ancillary study support from Roche Diagnostics, serving as Deputy Editor for JAMA Neurology, serving as a steering committee member of Medtronic's Stroke AF trial (uncompensated), serving on an end point adjudication committee for a trial of empagliflozin for Boehringer-Ingelheim, and having served on an advisory board for Roivant Sciences related to Factor XI inhibition. All remaining authors declare no competing interests.

Funding Sources

This study is supported by the National Institutes of Health (NIH) (K23NS105948) awarded to S.B.M. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Author Contributions

M.P. and S.B.M. researched the literature and conceived the study. S.B.M. was involved in obtaining ethical approval and C.Z. performed the statistical analyses. M.P. wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Data Availability Statement

The claims data used in this analysis are restricted per the terms of Medicare's data use agreement and therefore cannot be shared directly with other investigators. However, investigators can obtain access to these data by application to the Centers of Medicare and Medicaid Services (CMS).

References

- 1 Chan V, Lindsay P, McQuiggan J, Zagorski B, Hill MD, O'Kelly C. Declining admission and mortality rates for subarachnoid hemorrhage in Canada between 2004 and 2015. *Stroke*. 2018;STROKEAHA118022332.
- 2 Huhtakangas J, Lehto H, Seppä K, Kivisaari R, Niemelä M, Hernesniemi J, et al. Long-term excess mortality after aneurysmal subarachnoid hemorrhage: patients with multiple aneurysms at risk. *Stroke*. 2015;46:1813–8.
- 3 Witsch J, Frey HP, Patel S, Park S, Lahiri S, Schmidt JM, et al. Prognostication of long-term outcomes after subarachnoid hemorrhage: the FRESH score. *Ann Neurol*. 2016;80:46–58.
- 4 Lindberg M, Angquist KA, Fodstad H, Fugl-Meyer K, Fugl-Meyer AR. Self-reported prevalence of disability after subarachnoid haemorrhage, with special emphasis on return to leisure and work. *Br J Neurosurg*. 1992;6:297–304.
- 5 Murthy SB, Shah S, Rao CP, Bershad EM, Suarez JL. Neurogenic stunned myocardium following acute subarachnoid hemorrhage: pathophysiology and practical considerations. *J Intensive Care Med*. 2015;30:318–25.
- 6 Sposato LA, Hilz MJ, Asperg S, Murthy SB, Bahit MC, Hsieh CY, et al. Post-stroke cardiovascular complications and neurogenic cardiac injury: JACC state-of-the-art review. *J Am Coll Cardiol*. 2020;76:2768–85.
- 7 Francoeur CL, Mayer SA. Management of delayed cerebral ischemia after subarachnoid hemorrhage. *Crit Care*. 2016;20:277.
- 8 Etminan N, Chang HS, Hackenberg K, de Rooij NK, Vergouwen MDI, Rinkel GJE, et al. Worldwide incidence of aneurysmal subarachnoid hemorrhage according to region, time period, blood pressure, and smoking prevalence in the population: a systematic review and meta-analysis. *JAMA Neurol*. 2019;76:588–97.

- 9 Stegmayr B, Eriksson M, Asplund K. Declining mortality from subarachnoid hemorrhage: changes in incidence and case fatality from 1985 through 2000. *Stroke*. 2004;35:2059–63.
- 10 Nieuwkamp DJ, Algra A, Blomqvist P, Adami J, Buskens E, Koffijberg H, et al. Excess mortality and cardiovascular events in patients surviving subarachnoid hemorrhage: a nationwide study in Sweden. *Stroke*. 2011;42:902–7.
- 11 Nieuwkamp DJ, Vaartjes I, Algra A, Rinkel GJ, Bots ML. Risk of cardiovascular events and death in the life after aneurysmal subarachnoid haemorrhage: a nationwide study. *Int J Stroke*. 2014;9:1090–6.
- 12 Akkermans A, Peelen LM, van Waes JA, Rinkel GJ, van Klei WA. Cardiac events within one year after a subarachnoid haemorrhage: the predictive value of troponin elevation after aneurysm occlusion. *Eur J Prev Cardiol*. 2019;26:420–8.
- 13 Centers for Medicare & Medicaid Services, Limited Data Set (LDS) Files. Available from: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/Limited-DataSets/>.
- 14 Tirschwell DL, Longstreth WT Jr. Validating administrative data in stroke research. *Stroke*. 2002;33:2465–70.
- 15 Orso M, Cozzolino F, Amici S, De Giorgi M, Franchini D, Eusebi P, et al. Validity of cerebrovascular ICD-9-CM codes in healthcare administrative databases. the Umbria data-value project. *PLoS One*. 2020;15:e0227653.
- 16 Murthy SB, Merkler AE, Omran SS, Gialdini G, Gusdon A, Hartley B, et al. Outcomes after intracerebral hemorrhage from arteriovenous malformations. *Neurology*. 2017;88:1882–8.
- 17 Washington CW, Derdeyn CP, Dacey RG Jr, Dhar R, Zipfel GJ. Analysis of subarachnoid hemorrhage using the nationwide inpatient sample: the NIS-SAH severity score and outcome measure. *J Neurosurg*. 2014;121:482–9.
- 18 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–83.
- 19 Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45:613–9.
- 20 Bar B, Hemphill JC 3rd. Charlson comorbidity index adjustment in intracerebral hemorrhage. *Stroke*. 2011;42:2944–6.
- 21 Jimenez Caballero PE, Lopez Espuela F, Portilla Cuenca JC, Ramirez Moreno JM, Pedrera Zamorano JD, Casado Naranjo I. Charlson comorbidity index in ischemic stroke and intracerebral hemorrhage as predictor of mortality and functional outcome after 6 months. *J Stroke Cerebrovasc Dis*. 2013;22:e214–218.
- 22 Tang J, Wan JY, Bailey JE. Performance of comorbidity measures to predict stroke and death in a community-dwelling, hypertensive Medicaid population. *Stroke*. 2008;39:1938–44.
- 23 Stavem K, Hoel H, Skjaker SA, Haagenen R. Charlson comorbidity index derived from chart review or administrative data: agreement and prediction of mortality in intensive care patients. *Clin Epidemiol*. 2017;9:311–20.
- 24 McCormick N, Bhole V, Lacaille D, Avina-Zubieta JA. Validity of diagnostic codes for acute stroke in administrative databases: a systematic review. *PLoS One*. 2015;10:e0135834.
- 25 Murthy SB, Wu X, Diaz I, Parasram M, Parikh NS, Iadecola C, et al. Non-traumatic subdural hemorrhage and risk of arterial ischemic events. *Stroke*. 2020;51:1464–9.
- 26 Murthy SB, Diaz I, Wu X, Merkler AE, Iadecola C, Safford MM, et al. Risk of arterial ischemic events after intracerebral hemorrhage. *Stroke*. 2020;51:137–42.
- 27 Yoshimoto Y, Tanaka Y, Hoya K. Acute systemic inflammatory response syndrome in subarachnoid hemorrhage. *Stroke*. 2001;32:1989–93.
- 28 Naredi S, Lambert G, Edén E, Zäll S, Runnerstam M, Rydenhag B, et al. Increased sympathetic nervous activity in patients with non-traumatic subarachnoid hemorrhage. *Stroke*. 2000;31:901–6.
- 29 Bustamante A, Díaz-Fernández B, Pagola J, Blanco-Grau A, Rubiera M, Penalba A, et al. Admission troponin-I predicts subsequent cardiac complications and mortality in acute stroke patients. *Eur Stroke J*. 2016;1:205–12.
- 30 Akkermans A, van Waes JA, Peelen LM, Rinkel GJ, van Klei WA. Blood pressure and end-tidal carbon dioxide ranges during aneurysm occlusion and neurologic outcome after an aneurysmal subarachnoid hemorrhage. *Anesthesiology*. 2019;130:92–105.
- 31 Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. *N Engl J Med*. 2015;373:929–38.
- 32 McLaughlin N, Bojanowski MW. Early surgery-related complications after aneurysm clip placement: an analysis of causes and patient outcomes. *J Neurosurg*. 2004;101:600–6.
- 33 Kameda-Smith MM, Klurfan P, van Adel BA, Larrazabal R, Farrokhhyar F, Bennardo M, et al. Timing of complications during and after elective endovascular intracranial aneurysm coiling. *J Neurointerv Surg*. 2018;10:374–9.