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Original Article

# Regional differences in mortality among patients with ruptured intracranial aneurysms in Denmark

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## ABSTRACT

**INTRODUCTION.** Intracranial aneurysms are a serious clinical condition. Recent annual reports from the Danish Stroke Registry indicate a 30-day mortality rate of 27%, with notable regional variation ranging from 20% to 36%. This study aimed to examine whether these regional disparities in mortality are attributable to differences in demographic, clinical or treatment-related factors among the four Danish neurosurgical departments.

**METHODS.** This multicentre registry-based cohort study utilised data from DanStroke. Differences in risk factors, mortality and neurological complications are presented as odds ratios with 95% confidence intervals calculated in a logistic regression model.

**RESULTS.** A total of 1,426 patients were registered. The results of this study show that the patient population varies regionally, with patients admitted to Odense University Hospital (OUH) and Aalborg University Hospital (AaUH) generally being older and in a poorer clinical condition than patients admitted to Rigshospitalet (RH), which explains why fewer patients at the OUH and the AaUH received closure of the aneurysm. These regional differences contribute to the observed differences in mortality between the four neurosurgical departments. Importantly, among patients who received closure of the aneurysm, no significant difference in mortality was observed across departments.

**CONCLUSIONS.** The mortality rate following intracranial aneurysmal haemorrhage is high in Denmark. Regional differences in mortality may reflect variations in the patient population and logistical aspects of transport, highlighting the importance of considering these parameters when comparing departments.

**FUNDING.** None.

**TRIAL REGISTRATION.** The study was approved by the Danish Stroke Register and the Data Protection Board of Copenhagen University Hospital (reference number p-2023-14241).

The incidence of intracranial aneurysms in the general population is declining and was approximately 6.1 % in 2010 [1, 2]. There is a risk of rupture leading to aneurysmal subarachnoid haemorrhage (aSAH). If untreated, the mortality rate following aSAH can reach 35%, and surviving patients frequently suffer from persisting symptoms

 

[3-5]. Established risk factors for poor outcome after aSAH include older age, smoking and hypertension [6, 7].

The Danish Stroke Registry (DanStroke) has been collecting clinical data on patients with aSAH since 2017. The most recent annual report from 2023 uncovered a 27% 30-day mortality rate with regional variation in the 20-36% range. Previous reports have identified similar patterns with substantial regional differences. The mortality recorded in DanStroke is high compared with recent international studies, which report in-hospital mortality rates in the 7.1-20.1% range [8-10].

The present study investigated whether these regional differences in mortality reflect demographic, clinical or treatment-related differences among the four Danish neurosurgical departments.

## Methods

This was a multicentre registry-based cohort study. All data were obtained from DanStroke. The study period ran from 1 January 2017 to 31 August 2022. Data were reported via the four neurosurgical departments at: Rigshospitalet (RH), Odense University Hospital (OUH), Aarhus University Hospital (AUH) and Aalborg University Hospital (AaUH).

All Danish patients diagnosed with aSAH are treated at one of these departments, except for cases in which treatment is deemed futile due to poor clinical condition. National clinical guidelines on patient treatment are in place, ensuring consistency across the four centres.

Reporting to the DanStroke registry is compulsory for neurosurgical departments.

### Variables in DanStroke

The collected patient data include gender, age at admission and admitting department. Risk factors include previous acute myocardial infarction (AMI), known atrial fibrillation (AFib), diabetes, hypertension, peripheral arteriosclerosis, previous transient cerebral infarction (TCI), treatment with anticoagulant medication and smoking status. A positive smoking status includes both current and former smokers.

The clinical condition before the haemorrhage is assessed using the Modified Rankin Scale (mRS), which ranges from 0 (no symptoms) to 6 (death) and evaluates neurological function. The World Federation of Neurosurgical Societies (WFNS) grading system is used to assess the clinical severity of aSAH based on GCS and neurological deficits. The severity of the haemorrhage is assessed using the Fisher scale, a radiological grading based on the amount of blood on a CT scan.

A range of neurological complications can occur in association with aSAH. The most common neurological complication associated with aSAH is hydrocephalus. Treatment involves the placement of a temporary external ventricular drain (EVD) for acute pressure relief. Rebleeding may occur until the aneurysm has been secured, and rebleeding significantly increases mortality.

Delayed cerebral ischaemia (DCI) is a specific complication to aSAH, which may lead to infarction with neurological consequences.

Ventriculitis refers to an infection in the ventricular system caused by contamination of the pressure-relieving EVD. Infarction can, in addition to DCI, be caused by an elevated ICP due to the original haemorrhage, rebleeding or occlusion of arterial branches as a complication of aneurysm treatment.

Data regarding aneurysms include the number of aneurysms along with the size and location of the aneurysm that caused the haemorrhage. For the present analyses, the location was divided into the anterior circulation (anterior communicating artery, middle cerebral artery, internal carotid artery) and posterior circulation

 

(posterior communicating artery, basilar artery). Entries marked as “other” were classified as “NA” in the analyses.

### Statistical methods

Differences in risk factors, mortality and neurological complications between the four neurosurgical departments were analysed using logistic regression models, with results presented as OR with 95% CI. Adjusted and unadjusted analyses were performed on variables related to neurological complications and vital status. In the adjusted analyses, adjustments were made for age and the GCS at admission, as these parameters influence patient outcomes after aSAH. Since RH receives and treats the most patients, it was chosen as the reference for all analyses. $p < 0.05$ was considered statistically significant.

Missing data were addressed using the multiple imputation method from the Multivariate Imputation by Chained Equations (MICE) package. Data analyses were performed in R-Studio version 4.3.2.

### Ethics

The study was approved by the Danish Stroke Register and the Data Protection Board of Copenhagen University Hospital (reference number p-2023-14241). The requirement for individual patient consent was waived. The data were pseudo-anonymised and handled and stored in accordance with the provisions of the Danish Data Protection Agency and the General Data Protection Regulations.

*Trial registration:* The study was approved by the Danish Stroke Register and the Data Protection Board of Copenhagen University Hospital (reference number p-2023-14241).

## Results

A total of 1,426 patients were registered with aSAH in DanStroke during the study period, of whom 39.2% were admitted to RH, 25.3% to OUH, 24.0% to AUH and 11.4% to AaUH.

### National baseline data

**Table 1** presents demographic and clinical patient data for all aSAH patients in Denmark. The average age was 59 years, and 69.4% were women. The most common risk factor was smoking, followed by hypertension and anticoagulant therapy. The patients had an average GCS of 11 and a WFNS score of 2.7. Most aneurysms were located in the anterior circulation, and most patients had only one aneurysm.

**TABLE 1** Baseline data for all Danish patients admitted with aneurysmal subarachnoid haemorrhage. The table shows figures for the entire country as well as for each of the four neurosurgical departments.

| | Denmark ($N_{DK}$ = 1,426) | Rigshospitalet ($N_{RH}$ = 559) | Odense University Hospital ($N_{OUH}$ = 361) | Aarhus University Hospital ($N_{AUH}$ = 343) | Aalborg University Hospital ($N_{AaUH}$ = 163) |
|---|---|---|---|---|---|
| *Patient characteristics* | | | | | |
| Sex, n/N (%): | | | | | |
| Woman | 990/1,426 (69.4) | 387/559 (69.2) | 254/361 (70.4) | 239/343 (69.7) | 110/163 (67.5) |
| Man | 436/1,426 (30.6) | 172/559 (30.8) | 107/361 (29.6) | 104/343 (30.3) | 53/163 (32.5) |
| Age, mean (range), yrs | 59 (18-97) | 58.6 (25-86) | 60.5 (22-94) | 58.6 (22-97) | 61.5 (18-89) |
| Not available, n/N (%) | 6/1,426 (0.4) | - | 2/361 (0.6) | 1/343 (0.3) | 3/163 (1.8) |
| *Risk factors?, n/N (%)* | | | | | |
| Smoking?: | | | | | |
| Yes | 733/1,426 (51.4) | 329/559 (58.9) | 145/361 (40.2) | 140/343 (40.8 | 65/163 (39.9) |
| No | 309/1,426 (21.7) | 131/559 (23.4) | 42/361 (11.6) | 92/343 (26.8) | 44/163 (27.0) |
| Not available | 384/1,426 (26.9) | 99/559 (17.7) | 174/361 (48.2 | 111/343 (32.4) | 54/163 (33.1) |
| Diabetes?: | | | | | |
| Yes | 67/1,426 (4.7) | 19/559 (3.4) | 14/361 (3.9) | 23/343 (6.7) | 11/163 (6.7) |
| No | 1,317/1,426 (92.4) | 529/559 (94.6) | 331/361 (91.7) | 320/343 (93.3) | 137/163 (84.1) |
| Not available | 42/1,426 (2.9) | 11/559 (2.0) | 16/361 (4.4) | - | 15/163 (9.2) |
| Hypertension?: | | | | | |
| Yes | 502/1,426 (35.2) | 191/559 (34.2) | 127/361 (35.2) | 122/343 (35.6) | 62/163 (38.0) |
| No | 869/1,426 (60.9) | 350/559 (62.6) | 217/361 (60.1) | 221/343 (64.4) | 81/163 (49.7) |
| Not available | 55/1,426 (3.9) | 18/559 (3.2) | 17/361 (4.7) | - | 20/163 12.3) |
| AMI?: | | | | | |
| Yes | 61/1,426 (4.3) | 15/559 (2.7) | 19/361 (5.3) | 17/343 (5.0) | 10/163 (6.1) |
| No | 1,320/1,426 (92.6) | 534/559 (95.5) | 325/361 (90.2) | 325/343 (94.7) | 136/163 (83.4) |
| Not available | 55/1,426 (3.9) | 10/559 (1.8) | 17/361 (4.7) | 1/343 (0.3) | 17/163 (10.4) |
| AFib?: | | | | | |
| Yes | 54/1,426 (3.8) | 20/559 (3.6) | 14/361 (3.9) | 10/343 (2.9) | 10/163 (6.1) |
| No | 1,331/1,426 (93.3) | 529/559 (94.6) | 333/361 (92.2) | 333/343(97.1) | 136/163 (83.4) |
| Not available | 41/1,426 (2.9) | 10/559 (1.8) | 14/361 (3.9) | - | 17/163 (10.4) |
| Peripheral arteriosclerosis?: | | | | | |
| Yes | 34/1,426 (2.9) | 12/559 (2.1) | 7/361 (1.9) | 9/343 (2.6) | 6/163 (3.7) |
| No | 1,337/1,426 (93.8) | 529/559 (94.6) | 334/361 (92.5) | 333/343 (97.1) | 141/163 (86.5) |
| Not available | 55/1,426 (3.9) | 18/559 (3.2) | 20/361 (5.5) | 1/343 (0.3) | 16/163 (9.8) |
| Anticoagulant medication?: | | | | | |
| Yes | 225/1,426 (15.8) | 80/559 (14.3) | 60/361 (16.6) | 61/343 (17.8) | 24/163 (14.7) |
| No | 1,124/1,426 (78.8) | 464/559 (83.0) | 278/361 (77.0) | 279/343 (81.3) | 103/163 (63.2) |
| Not available | 77/1,426 (5.4) | 15/559 (2.7) | 23/361 (6.4) | 3/343 (0.9) | 36/163 (22.1) |
| TCI?: | | | | | |
| Yes | 24/1,426 (1.7) | 9/559 (1.6) | 6/361 (1.7) | 7/343 (2.0) | 2/163 (1.2) |
| No | 1,341/1,426 (94.0) | 533/559 (95.4) | 331/361 (91.7) | 334/343 (97.4) | 143/163 (87.7) |
| Not available | 61/1,426 (4.3) | 17/559 (3.0) | 24/361 (6.6) | 2/343 (0.6) | 18/163 (11.1) |
| *Clinical status at admission* | | | | | |
| GCS: | | | | | |
| Score, mean (range) | 11 (3-15) | 11.5 (3-15) | 10.3 (3-15) | 11.4 (3-15) | 9.9 (3-15) |
| Not available, n/N (%) | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |
| WFNS: | | | | | |
| Grade, mean | 2.7 | 2.6 | 3.0 | 2.5 | 2.9 |
| Not available, n/N (%) | 52/1,426(3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |
| Fisher scale: | | | | | |
| Score, mean | 3.3 | 3.3 | 3.4 | 3.3 | 3.2 |
| Not available, n/N (%) | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |
| mRS ad debut: | | | | | |
| Score, mean (range) | 0.44 (0-5) | 0.42 (0-5) | 0.40 (0-4) | 0.37 (0-4) | 0.9 (0-5) |
| Not available, n/N (%) | 224/1,426 (15.7) | 94/559 (16.8) | 35/361 (9.7) | 39/343 (11.4) | 56/163 (34.4) |

Continues >

**TABLE 1 (CONTINUED)** Baseline data for all Danish patients admitted with aneurysmal subarachnoid haemorrhage. The table shows figures for the entire country as well as for each of the four neurosurgical departments.

| | Denmark ($N_{DK}$ = 1,426) | Rigshospitalet ($N_{RH}$ = 559) | Odense University Hospital ($N_{OUH}$ = 361) | Aarhus University Hospital ($N_{AUH}$ = 343) | Aalborg University Hospital ($N_{AaUH}$ = 163) |
|---|---|---|---|---|---|
| *Aneurysm characteristics* | | | | | |
| Localisation, n/N (%): | | | | | |
| A. communicans anterior | 516/1,426 (36.2) | 202/559 (36.1) | 127/361 (35.2) | 140/343 (40.8) | 47/163 (28.8) |
| A. cerebralis media | 292/1,426 (20.5) | 112/559 (20.0) | 75/361 (20.8) | 69/343 (20.1) | 35/163 (21.5) |
| A. communicans posterior | 198/1,426 (13.9) | 89/559 (15.9) | 43/361 (11.9) | 47/343 (13.7) | 19/163 (11.7) |
| A. basilaris | 112/1,426 (7.9) | 47/559 (8.4) | 31/361 (8.6) | 21/343 (6.1) | 13/163 (8.0) |
| A. carotis interna | 65/1,426 (4.6) | 23/559 (4.1) | 16/361 (4.4) | 20/343 (5.8) | 7/163 (4.3) |
| Other | 191/1,426 (13.4) | 74/559 (13.2) | 55/361 (15.2) | 43/343 (12.5) | 18/163 (11.4) |
| Not available | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |
| Multiple aneurysms?, n/N (%): | | | | | |
| Yes | 283/1,426 (19.8) | 126/559 (22.5) | 43/361 (11.9) | 83/343 (24.2) | 31/163 (19.0) |
| No | 1,091/1,426 (76.5) | 421/229 (75.3) | 305/361 (84.5) | 257/343 (74.9) | 108/163 (66.3) |
| Not available | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |
| Size of aneurysm, n/N (%): | | | | | |
| > 25 mm | 20/1,426 (1.4) | 3/559 (0.5) | 10/361 (2.8) | 4/343 (1.2) | 3/163 (1.8) |
| 12-25 mm | 169/1,426 (11.9) | 75/559 (13.5) | 36/361 (9.9) | 42/343 (12.2) | 16/163 (9.8) |
| 7-12 mm | 422/1,426 (40.0) | 170/559 (30.4) | 115/361(31.9) | 103/343 (30.0) | 34/163 (20.9) |
| < 7 mm | 763/1,426 (53.5) | 299/559 (53.5) | 187/361(51.8) | 191/343 (55.7) | 86/163 (52.8) |
| Not available | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/16 (14.7) |
| *Time and treatment* | | | | | |
| Time from onset to admission at neurosurgical department[a], median (range), h | 3.6 (0.02-1,735) | 5.1 (0.1-1,735) | 3.9 (0.08-1,227) | 1.4 (0.016-1,445) | 3.0 (0.47-379) |
| Time from onset to treatment[b]: | | | | | |
| Median (range), h | 19.7 (1.2-5,435.8) | 22.5 (1.2-1,777.5) | 18.8 (1.33-5,435.8) | 17.4 (2.00-2,257.5) | 68.6 (3.1-2,168.5) |
| Not available, n | 16 | 8 | 6 | - | 2 |
| Time from onset to treatment[b], n /N (%): | | | | | |
| ≤ 24 h | 710/1,197 (59.3) | 265/500 (53.3) | 169/278 (60.8) | 209/309 (67.6) | 67/110 (60.9) |
| > 24 h | 471/1,197 (40.0) | 227/500 (45.5) | 103/278 (37.1) | 100/309 (32.4) | 41/110 (37.3) |
| Not available | 16/1,197 (1.3) | 8/500 (1.6) | 6/278 (2.2) | - | 2/110 (1.8) |
| Treatment modality, n /N (%): | | | | | |
| No treatment | 173/1,426 (12.1) | 47/559 (8.4) | 67/361 (18.6) | 31/343 (9.0) | 28/163 (17.2) |
| Endovascular | 793/1,426 (55.6) | 290/559 (51.9) | 216/361 (59.8) | 232/343 (67.6) | 55/163 (33.7) |
| Surgical | 408/1,426 (28.6) | 210/559 (37.6) | 65/361 (18.0) | 77/343 (22.4) | 56/163 (34.4) |
| Not available | 52/1,426 (3.9) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |
| *Mortality and neurological complications, n/N (%)* | | | | | |
| In-hospital mortality?: | | | | | |
| Yes | 302/1,426 (21.2) | 95/559 (17.0) | 103/361 (28.5) | 60/343 (17.5) | 44/163 (27.0) |
| No | 1,072/1,426 (75.2) | 452/559 (80.9) | 245/261 (67.9) | 280/343 (81.6) | 95/163 (58.3) |
| Not available | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |
| Rebleeding?: | | | | | |
| Yes | 155/1,426 (10.9) | 53/559 (9.5) | 53/361 (14.7) | 39/343 (11.4) | 10/163 (6.1) |
| No | 1,206/1,426 (84.6) | 489/559 (87.5) | 292/361 (80.9) | 301/343 (87.8) | 124/163 (76.1) |
| Not available | 65/1,426 (4.6) | 17/559 (3.0) | 16/361 (6.1) | 3/343 (0.9) | 29/163 (17.8) |
| DCI?: | | | | | |
| Yes | 319/1,426 (22.4) | 126/559 (22.5) | 43/361 (11.9) | 106/343 (30.9) | 44/163 (27.0) |
| No | 1,025/1,426 (71.9) | 415/559 (74.2) | 289/361 (80.1) | 234/343 (68.2) | 87/163 (53.4) |
| Not available | 82/1,426 (5.8) | 18/559 (3.2) | 29/361 (8.0) | 3/342 (0.9) | 32/163 (19.6) |
| Infractions?: | | | | | |
| Yes | 315/1,426 (22.1) | 122/559 (21.8) | 75/361 (20.8) | 86/343 (25.1) | 32/163 (19.6) |
| No | 1,059/1,426 (74.3) | 425/559 (76.0) | 273/361 (75.6) | 254/343 (74.1) | 107/163 (65.6) |
| Not available | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |

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**TABLE 1 (CONTINUED)** Baseline data for all Danish patients admitted with aneurysmal subarachnoid haemorrhage. The table shows figures for the entire country as well as for each of the four neurosurgical departments.

| | Denmark ($N_{DK}$ = 1,426) | Rigshospitalet ($N_{RH}$ = 559) | Odense University Hospital ($N_{OUH}$ = 361) | Aarhus University Hospital ($N_{AUH}$ = 343) | Aalborg University Hospital ($N_{AaUH}$ = 163) |
|---|---|---|---|---|---|
| Hydrocephalus?: | | | | | |
| Yes | 578/1,426 (40.5) | 340/559 (60.8) | 215/361 (59.6) | 216/343 (63.0) | 77/163 (47.2) |
| No | 848/1,426 (59.5) | 219/559 (39.2) | 146/261 (40.4) | 127/343 (37.0) | 86/163 (52.8) |
| Ventriculitis?: | | | | | |
| Yes | 68/1,426 (4.8) | 37/559 (6.6) | 6/361 (1.7) | 22/343 (6.4) | 3/163 (1.8) |
| No | 1,306/1,426 (91.6) | 510/559 (91.2) | 342/361 (94.7) | 318/343 (92.7) | 136/163 (83.4) |
| Not available | 52/1,426 (3.6) | 12/559 (2.1) | 13/361 (3.6) | 3/343 (0.9) | 24/163 (14.7) |

AFib = atrial fibrillation; AMI = acute myocardial infarction; DCI = delayed cerebral ischaemia; GCS = Glasgow Coma Scale; mRS = Modified Rankin Scale; TCI = transient cerebral infarction; WFNS = World Federation of Neurosurgical Societies.
a) Time from onset to admission is calculated for patients where the time was > 0 h.
b) Time from onset to treatment is only calculated for patients who received active treatment of their aneurysm and for whom accurate data reporting was available.

The time from onset of aSAH to admission to the neurosurgical department was calculated for 1,333 patients after excluding 99 patients with incorrectly recorded travel time. The median time from onset of aSAH to admission to a neurosurgical department was 3.6 hours. The time from onset of aSAH to treatment was calculated for 1,197 patients, whereas 52 patients were excluded due to missing treatment modality data, 173 because they did not receive active aneurysm occlusion, and an additional four due to negative time values, reflecting reporting error. The median time from onset of aSAH to treatment was 19.7 hours. A total of 59.3% of all patients received aneurysm treatment within 24 hours.

Most patients were treated endovascularly. A total of 12.1% of the patients did not receive aneurysm occlusion. This was primarily due to very poor clinical condition, making further treatment futile; in a few cases, treatment was withheld because of the aneurysm's anatomical location and structure.

The most common neurological complication was hydrocephalus, followed by DCI and infarction. The in-hospital mortality was 21.1%.

### Regional differences in demographics and comorbidities

**Table 2** presents regional differences in demographics and risk factors, as well as variations in haemorrhage severity, aneurysm location and size.

**TABLE 2** Unadjusted odds ratios for demographic risk factors, aneurysm characteristics and treatment modality across the four neurosurgical departments, including 95% confidence intervals and p values.

| | | OR (95%CI) p value | | |
|---|---|---|---|---|
| | Rigshospitalet | Odense University Hospital | Aarhus University Hospital | Aalborg University Hospital |
| *Patient characteristics* | | | | |
| Sex: men | Ref. | 0.97 (0.72; 1.29) 0.82 | 0.99 (0.72; 1.29) 0.92 | 1.1 (0.74; 1.64) 0.62 |
| Age | Ref. | 1.70 (–0.07; 3.47) 0.06 | –0.007 (–1.79; 1.78) 0.99 | 2.21 (–0.24; 4.66) 0.077 |
| *Risk factors* | | | | |
| Smoking | Ref. | 1.27 (0.96; 1.69) 0.096 | 0.86 (0.65; 1.13) 0.27 | 0.70 (0.48; 1.02) 0.065 |
| Diabetes | Ref. | 1.13 (0.57; 2.21) 0.72 | 1.82 (0.99; 3.34) 0.054 | 1.75 (0.75; 3.79) 0.174 |
| Hypertension | Ref. | 1.13 (0.85; 1.49) 0.39 | 1.03 (0.78; 1.37) 0.84 | 1.57 (1.07; 2.28) 0.020 |
| AMI | Ref. | 2.05 (1.03; 4.16) 0.041 | 1.87 (0.92; 3.83) 0.084 | 2.18 (0.86; 5.14) 0.0819 |
| AFib | Ref. | 1.19 (0.59; 2.35) 0.617 | 0.80 (0.35; 1.69) 0.57 | 1.41 (0.54; 3.25) 0.45 |
| Peripheral arteriosclerosis | Ref. | 0.78 (0.29; 1.90) 0.603 | 1.04 (0.427; 2.39) 0.936 | 1.73 (0.603; 4.40) 0.27 |
| Anticoagulant medication | Ref. | 0.81 (0.57; 1.18) 0.27 | 0.80 (0.55; 1.15) 0.22 | 0.69 (0.43; 1.12) 0.13 |
| TCI | Ref. | 1.59 (0.62; 4.12) 0.33 | 1.44 (0.54; 3.80) 0.46 | 1.78 (0.48; 5.57) 0.34 |
| *Clinical status ad admission* | | | | |
| GCS score | Ref. | –1.20 (–1.84; –0.56) 0.0003 | –0.04 (–0.69; 0.60) 0.99 | –1.58 (–2.47; –0.69)) 0.0005 |
| WFNS grade | Ref. | 0.35 (0.13; 0.57) 0.0021 | –0.06 (–0.28; 0.16) 0.60 | 0.30 (–0.008; 0.60) 0.056 |
| Fisher scale score | Ref. | 0.18 (0.07; 0.29) 0.002 | 0.09 (–0.02; 0.20) 0.11 | –0.03 (–0.18; 0.12) 0.69 |
| mRS ad debut | Ref. | –0.02 (–0.14; 0.09) 0.69 | –0.03 (–0.15; 0.08) 0.55 | 0.47 (0.31; 0.63) < 0.0001 |
| *Aneurysm characteristics* | | | | |
| Localisation: anterior | Ref. | 0.86 (0.64; 1.16) 0.34 | 0.76 (0.56; 1.02) 0.074 | 0.84 (0.55; 1.26) 0.42 |
| Multiple aneurysms | Ref. | 0.47 (0.32; 0.68) 0.00009 | 1.08 (0.78; 1.48) 0.64 | 0.96 (0.61; 1.48) 0.85 |
| Size of aneurysm: > 12 mm | Ref. | 0.92 (0.62; 1.35) 0.66 | 0.94 (0.63; 1.39) 0.76 | 0.95 (0.54; 1.60) 0.86 |
| *Time and treatment* | | | | |
| Treatment later than 24 h from onset | Ref. | 0.71 (0.53; 0.96) 0.027 | 0.56 (0.42; 0.75) 0.0001 | 0.71 (0.46; 1.09) 0.123 |
| Active treatment | Ref. | 0.39 (0.26; 0.59) 0.000005 | 0.94 (0.56; 1.52) 0.79 | 0.37 (0.23; 0.63) 0.00015 |
| Endovascular treatment[a] | Ref. | 2.41 (1.74; 3.36) < 0.0001 | 2.18 (1.60; 3.00) < 0.0001 | 0.71 (0.47; 1.07) 0.11 |

AFib = atrial fibrillation; AMI = acute myocardial infarction; GCS = Glasgow Coma Scale; mRS = Modified Rankin Scale; ref. = reference; TCI = transient cerebral infarction; WFNS = World Federation of Neurosurgical Societies.
a) Includes stents and/or coils.

Gender distribution was consistent across the four neurosurgical departments. OUH and AaUH had older patients than RH. The most common risk factor, smoking, was not significantly different between the four departments. Hypertension was significantly higher in AaUH. OUH had a significantly higher proportion of patients with previous AMI.

No significant differences were observed among the four neurosurgical departments regarding the following premorbid comorbidities: diabetes, atrial fibrillation, peripheral arteriosclerosis, previous TCI and anticoagulant therapy.

### Differences related to aneurysm and severity of bleeding

A significantly higher proportion of patients at OUH had only one aneurysm. There were no significant differences in the location or size of the aneurysms between the hospitals.

Patients at OUH and AaUH arrived at the neurosurgical department with significantly lower GCS scores than patients admitted to RH. This was also reflected in the WFNS score, with patients admitted to OUH having a significantly higher score. Patients admitted to OUH had a significantly higher Fisher score. Moreover, the functional level of patients before the bleeding was significantly poorer among those admitted to AaUH than to RH.

The proportion of patients who received aneurysm treatment was significantly lower at OUH and AaUH than at RH. A significantly larger proportion of patients were treated endovascularly at OUH and AUH than at RH.

Finally, AUH andOUH had a significantly higher proportion of patients treated within 24 hours from SAH onset than RH.

### Differences in neurological complications and mortality

**Table 3** presents differences in neurological complications and mortality among the four neurosurgical departments in Denmark. After adjusting for age and GCS, there was a significantly higher risk of in-hospital mortality among patients at OUH than at RH.

**TABLE 3** Both unadjusted and adjusted analyses of mortality and neurological complications across the four neurosurgical departments. The analyses are adjusted for age and Glasgow Coma Scale score at admission.

| | | OR (95%CI) p value | | | Adjusted OR (95%CI) p value | | |
|---|---|---|---|---|---|---|---|
| | Rigshospitalet | Odense University Hospital | Aarhus University Hospital | Aalborg University Hospital | Odense University Hospital | Aarhus University Hospital | Aalborg University Hospital |
| In-hospital mortality | Ref. | 2.00 (1.45; 2.76) 0.000021 | 1.02 (0.71; 1.45) 0.92 | 2.20 (1.44; 3.34) 0.00023 | 1.65 (1.13; 2.41) 0.0096 | 0.99 (0.66; 1.50) 0.98 | 1.67 (0.98; 2.78) 0.050 |
| Rebleeding | Ref. | 1.68 (1.12; 2.51) 0.011 | 1.16 (0.75; 1.78) 0.51 | 0.77 (0.37; 1.46) 0.45 | 1.63 (1.09; 2.45) 0.018 | 1.16 (0.75; 1.79) 0.501 | 0.75 (0.36; 1.43) 0.40 |
| Hydrocephalus | Ref. | 0.98 (0.75; 1.30) 0.91 | 1.06 (0.80; 1.41) 0.68 | 0.76 (0.52; 1.10) 0.85 | 0.86 (0.65; 1.15) 0.31 | 1.05 (0.79; 1.41) 0.72 | 0.64 (0.43; 0.96) 0.030 |
| Ventriculitis | Ref. | 0.24 (0.09; 0.54) 0.0014 | 0.95 (0.55; 1.63) 0.87 | 0.30 (0.07; 0.86) 0.050 | 0.26 (0.10; 0.57) 0.0023 | 0.96 (0.55; 1.64) 0.87 | 0.33 (0.08; 0.95) 0.072 |
| DCI | Ref. | 0.49 (0.34; 0.71) 0.00021 | 1.51 (1.12; 2.05) 0.0075 | 1.60 (1.06; 2.39) 0.024 | 0.52 (0.35; 0.74) 0.0005 | 1.53 (1.12; 2.08) 0.0067 | 1.71 (1.12; 2.59) 0.012 |
| Infarctions | Ref. | 1.0 (0.71; 1.42) 0.98 | 1.24 (0.90; 1.72) 0.19 | 1.27 (0.79; 2.00) 0.32 | 0.92 (0.66; 1.27) 0.61 | 1.18 (0.86; 1.63) 0.30 | 1.01 (0.64; 1.57) 0.97 |

DCI = delayed cerebral ischaemia; ref. = reference.

Patients at OUH had a higher risk of rebleeding than patients at RH. There was a significantly lower risk of ventriculitis at OUH and AaUH than at RH. The risk of DCI was significantly higher among patients admitted to AUH and AaUH, while it was lower for OUH, compared with patients admitted to RH.

### Subanalyses of treated patients

Subanalyses were performed exclusively in patients who underwent active aneurysm closure to address potential regional differences in outcome after treatment.

**Table 4** presents differences in neurological complications and mortality among the four neurosurgical departments for patients who received active treatment for their aneurysm.

After adjustment, the risk of rebleeding was higher at OUH than RH, whereas the risk of DCI and ventriculitis was significantly lower.

**TABLE 4** Subgroup analyses of patients who received aneurysm occlusion. The table includes both unadjusted and adjusted analyses. Adjustments were made for age and Glasgow Coma Scale score at admission.

| | | OR (95%CI) p value | | | Adjusted OR (95%CI) p value | | |
|---|---|---|---|---|---|---|---|
| | Rigshospitalet | Odense University Hospital | Aarhus University Hospital | Aalborg University Hospital | Odense University Hospital | Aarhus University Hospital | Aalborg University Hospital |
| In-hospital mortality | Ref. | 1.29 (0.82; 2.01) 0.26 | 0.92 (0.57; 1.46) 0.73 | 1.82 (1.02; 3.14) 0.037 | 1.14 (0.70; 1.82) 0.59 | 0.95 (0.56; 1.50) 0.76 | 0.51 (0.84; 2.86) 0.15 |
| Rebleeding | Ref. | 1.65 (1.02; 2.66) 0.042 | 1.42 (0.87; 2.29) 0.15 | 0.66 (0.25; 1.49) 0.36 | 1.64 (1.01;2.65) 0.044 | 1.43 (0.88; 2.31) 0.15 | 0.97 (0.93; 1.01) 0.36 |
| Hydrocephalus | Ref. | 1.33 (0.98; 1.82) 0.070 | 1.18 (0.88; 1.59) 0.27 | 0.96 (0.63; 1.47) 0.85 | 1.26 (0.89; 1.77) 0.19 | 1.24 (0.90; 1.72) 0.19 | 0.83 (0.51; 1.36) 0.46 |
| Ventriculitis | Ref. | 0.23 (0.08; 0.55) 0.0026 | 0.99 (0.56;1.70) 0.97 | 0.36 (0.09; 1.02) 0.092 | 0.24 (0.08; 0.56) 0.00330 | 0.99 (0.56; 1.71) 0.98 | 0.38 (0.09; 1.07) 0.11 |
| DCI | Ref. | 0.56 (0.38; 0.82) 0.0030 | 1.55 (1.14; 2.11) 0.0056 | 2.01 (1.30; 3.09) 0.0016 | 0.57 (0.38; 0.83) 0.0040 | 1.58 (1.15; 2.15) 0.0043 | 2.04 (1.31; 3.17) 0.0067 |
| Infarctions | Ref. | 1.00 (0.71; 1.42) 0.98 | 1.24 (0.90; 1.72) 0.19 | 1.27 (0.79; 2.00) 0.32 | 0.97 (0.68; 1.38) 0.88 | 1.27 (0.91; 1.77) 0.15 | 1.23 (0.75; 1.96) 0.40 |

DCI = delayed cerebral ischaemia; ref. = reference.

## Discussion

The results of this study show that patient population and patient admittance vary regionally, with patients admitted to OUH and AaUH generally being older and in a poorer clinical condition than patients admitted toRH, which may help explain why fewer patients were offered active treatment. These regional differences contribute to the observed differences in mortality between the four neurosurgical departments. In line with this, no significant difference in mortality was observed between the four neurosurgical departments among patients who received active treatment for their aneurysm.

### Premorbid comorbidities and time factors

Smoking status was missing for 48.2% of patients admitted to OUH, potentially leading to misleading results. Nationwide, 35.2% of patients had known hypertension. From our data, it is not possible to determine whether hypertension was well-controlled.

In the latest Danish study, 7.3% of patients treated for aSAH at RH were transferred from Greenland [11], which may have contributed to the longer transport time observed. During the initial part of the study period, AaUH had no access to endovascular treatment, and patients had to be transferred to AUH. This may have contributed to the longer median time from onset to treatment observed at AaUH.

### Mortality

The overall national mortality rate was 21.1% (Table 1). After adjustment, OUH showed a significantly higher mortality than RH (Table 3). This higher mortality is partly attributable to the lower treatment rate observed atAaUH and OUH. This lower treatment rate is likely a consequence of patients presenting with higher mortality-related risk factors and poorer clinical status upon arrival.

Additionally, OUH had the highest risk of rebleeding, which increases the mortality rate. OUH had the second-longest time from the onset of SAH to admission to the neurosurgical department, which could increase the risk of rebleeding [12]. The geographical uptake area of OUH includes a large rural area and several islands, which may result in challenges with infrastructure and thus prolonged transport time. However, lack of consensus on reporting to DanStroke may also explain part of the higher incidence of rebleeding among patients at OUH. OUH recorded all rebleeding episodes from the time of the SAH to the aneurysm was treated. In contrast, the three other departments reported episodes only from the patient's arrival at the neurosurgical department to aneurysm treatment.

It is important to note that there was no significant difference in mortality among the four neurosurgical departments in the subanalyses, which included only patients who received treatment for their aneurysm (Table 4). However, patients at OUH still had a higher risk of rebleeding. A meta-analysis found that the risk of rebleeding increases with the size of the aneurysm [13]. OUH had the highest proportion of patients with aneurysms exceeding 25 mm, which may also help explain the higher rebleeding risk observed there.

### Strengths and limitations

One limitation of the study is missing data, which could lead to selection bias and limit the variables suitable for adjustment.

Regional variation in the reporting of rebleeding episodes is another limitation. An additional limitation of this study is the lack of data on patients who die from aSAH before hospital admission and are therefore not transferred to a neurosurgical department.

The inclusion criteria of DanStroke of only aSAH admitted to the neurosurgical department may cause a selection bias, as there might be regional differences in the admission pattern of acute intracerebral bleedings. Another limitation of this study is the lack of data on patients who die from aSAH before hospital admission and are therefore not transferred to a neurosurgical department. The study's observational design means that causality cannot be definitively established, and residual confounding factors may influence the results.

Despite its limitations, the study has several strengths. One of the main strengths of this study lies in its large, nationwide scope, which provides a broad and diverse dataset encompassing patients from all neurosurgical departments in Denmark. Additionally, the study benefits from the use of national clinical guidelines for patient treatment, ensuring consistency across the included centres.

## Conclusions

The mortality rate following intracranial aneurysmal haemorrhage is high in Denmark. The regional differences in mortality may reflect variations in the patient population and logistical aspects of transport, underscoring the importance of accounting for these factors when comparing departments.

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