Hospital volume and 1-year mortality after treatment of intracranial aneurysms: a study based on patient registries in Scandinavia

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OBJECT The object of this study was to examine the relationship between hospital volume and long-term mortality after treatment of intracranial aneurysms.

METHODS The authors identified patients treated for intracranial aneurysms between 2002 and 2010 from patient registries of Denmark, Norway, and Sweden, and linked to data on 1-year mortality from the population registry of each country. Cox regression models were used to relate hospital volume to the risk of death and adjusted for potential confounders (age, sex, year of treatment, Charlson comorbidity index, country, and surgical treatment).

RESULTS The authors identified 5773 patients with ruptured and 1756 patients with unruptured intracranial aneurysms, treated at 15 hospitals. One-year mortality rates were 15.6% for patients with ruptured aneurysms and 2.7% for patients with unruptured aneurysms. No consistent relationship was found between hospital volume and 1-year mortality for ruptured aneurysms in the unadjusted analyses, but higher hospital volume was associated with increased mortality in the analyses adjusted for potential confounders (hazard ratio [HR] per 10-patient increase 1.04, 95% CI 1.00–1.07). There was a trend toward a lower mortality rate in higher-volume hospitals after treatment for unruptured intracranial aneurysms, but this was not statistically significant after adjustment for potential confounders (HR per 10-patient increase 0.69, 95% CI 0.42–1.10). There were large variations in mortality after treatment for both ruptured and unruptured intracranial aneurysms across hospitals and between the Scandinavian countries ($p < 0.01$).

CONCLUSIONS The findings in this study did not confirm a relationship between higher hospital volume and reduced long-term mortality after treatment of ruptured intracranial aneurysms. Prospective registries for evaluating outcomes after aneurysm treatment are highly warranted.

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KEY WORDS intracranial aneurysm; surgery; endovascular treatment; vascular disorders; rupture; hospital volume; Scandinavia

EVIDENCE that mortality after complex surgical procedures is lower at high-volume centers has led to suggestions that these surgeries should be centralized to high-volume centers.^{5,11} However, there is substantial heterogeneity in the results and hospital volume may not be a valid proxy for quality of care.^{9,10}

Studies of hospital volume and mortality after treatment for ruptured and unruptured intracranial aneurysms indi-

cate a general trend toward better results at higher-volume hospitals.^{1–4,7,8,12–14,16–18} However, all studies except 2 were from US patient administrative databases,^{1–4,7,8,13,14,16,18} and the findings may not be generalizable to health care systems in other countries where specialist neurosurgical services are delivered at tertiary regional hospitals with a defined population and patients are referred from smaller hospitals. Furthermore, most studies have only examined

ABBREVIATIONS CCI = Charlson Comorbidity Index; CI = confidence interval; HR = hazard ratio; ICD-10 = International Classification of Diseases, 10th revision; NCSP = NOMESCO Classification of Surgical Procedures; SAH = subarachnoid hemorrhage.

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death at discharge.^{1–4,7,8,12–14,16,18} Data collection on the relationship between hospital volume and long-term mortality is highly warranted. This topic is of increasing interest as open surgeries for intracranial aneurysms are being replaced by endovascular procedures.

In this study we examined the relationship between hospital volume and 1-year mortality after surgical and endovascular treatment for ruptured and unruptured intracranial aneurysms in hospitals across Denmark, Norway, and Sweden.

Methods

Study Population

Scandinavia consists of the 3 countries Denmark, Norway, and Sweden, with a combined population of 19.5 million inhabitants. All neurosurgical and endovascular treatments of intracranial aneurysms are regionalized to public hospitals with neurosurgical departments. Patients with verified aneurysmal subarachnoid hemorrhage (SAH) are usually accepted for immediate admission to one of the hospitals with neurosurgical service, independent of age and clinical condition. The exceptions are patients considered in a moribund state after exclusion of acute hydrocephalus by CT.

Data Source

The patient registries of Denmark, Norway, and Sweden contain data on all inpatient care in each respective country. We collected data from the patient registries on all patients ≥ 18 years old with a national identity number who were admitted to hospitals in Denmark, Norway, and Sweden. We included patients admitted from January 1, 2002, to December 31, 2010, in Denmark and Sweden. For Norway, we included patients admitted from January 1, 2008, to December 31, 2010. This difference in dates was because the Norwegian hospital discharge registry only included person-identifiable data from 2008 onwards. The study was approved by the Regional Committee for Medical and Health Research Ethics North in Norway, and by the patient registries of Denmark, Norway, and Sweden.

Inclusion Criteria for Ruptured Intracranial Aneurysm

We included 5773 patients ≥ 18 years of age with an emergency admission, a discharge diagnosis of SAH (International Classification of Diseases, 10th revision [ICD-10] codes I60.0–I60.7 and I60.9), and a procedure code for surgical or endovascular treatment of an intracranial aneurysm (NOMESCO Classification of Surgical Procedures [NCSP] codes AAC00–AAC15 [surgery] and AAL00 [endovascular]).

Inclusion Criteria for Unruptured Intracranial Aneurysm

We included 1807 patients ≥ 18 years of age with a planned admission, a discharge diagnosis of unruptured intracranial aneurysm (ICD-10 code I67.1), and a procedure code for surgical or endovascular treatment of an intracranial aneurysm (NCSP codes AAC00–AAC15 [surgery] and AAL00 [endovascular]). We excluded 51 patients with prior SAH (secondary discharge diagnosis of sequelae of

SAH, ICD-10 code I69.1, or prior admission for ruptured intracranial aneurysm in our dataset) to reduce the possibility that recovery from previous SAH would affect the results. This left 1756 patients with unruptured intracranial aneurysms available for analysis.

Data Collection

For each patient we collected the following data: age, sex, dates of admission and discharge, primary and secondary diagnosis codes, procedure codes, and hospital. Based on the secondary diagnoses, we calculated the Charlson Comorbidity Index (CCI), a widely used measure for classifying comorbid conditions that alter the risk of death.⁶ For patients with repeat admissions, we used the data from the first admission.

We obtained data on date of death for each patient up to December 31, 2011, by linkage of the hospital discharge registry and the population registry in each respective country, using the patient's unique personal identification number. Record linkage was conducted at each patient registry. Follow-up duration was set at 12 months after the date of admission or until death occurred within the 12-month follow-up period.

Statistical Analysis

We calculated descriptive statistics for patients with ruptured and unruptured intracranial aneurysms separately. For each hospital, we calculated average annual volume of patients and 1-year mortality rates. We used the Kruskal-Wallis test to examine whether mortality differed across year of admission, hospital, and country. We used Poisson regression to calculate age-adjusted 1-year mortality for each hospital and plotted the age-adjusted 1-year mortality for each hospital against the average annual volume of patients in the corresponding hospital.

We used Cox regression analysis to calculate hazard ratios (HRs) and 95% confidence intervals (CIs), with time until death as the dependent variable. We assessed hospital volume as a continuous variable and as a categorical variable in 3 tertile groups. For ruptured intracranial aneurysms, the 3 tertile groups were: 5 hospitals in the lowest tertile (6.2–36.0 patients per year); 5 hospitals in the intermediate tertile (43.8–62.4 patients per year); and 5 hospitals in the highest tertile (63.1–118.0 patients per year). For unruptured intracranial aneurysms, the 3 tertile groups were: 5 hospitals in the lowest tertile (2.9–10.9 patients per year); 5 hospitals in the intermediate tertile (14.3–19.7 patients per year); and 5 hospitals in the highest tertile (21.9–45.6 patients per year). The *p* value for trend was calculated by entering the categorical variable of hospital volume as a continuous variable in the regression models. The analyses were performed unadjusted and adjusted for age, sex, surgical treatment, CCI, year of treatment, and country. We fitted age as a continuous variable, sex and surgical treatment as dichotomous variables, and CCI (0, 1, or 2), country (Denmark, Norway, and Sweden), and year of treatment as categorical variables. The proportional hazards assumption was verified using Schönfeld's residuals and by inspection of log-log plots.

All analyses were preplanned and conducted separately.

ly for patients with ruptured and unruptured intracranial aneurysms. We had also planned to use propensity-score matching to compare mortality rates between patients treated at low- and high-volume hospitals, but the low number of patients treated at low-volume hospitals precluded these analyses. As data from Norwegian hospitals were first available from 2008, we performed additional analyses restricted to patients admitted between 2008 and 2010. We used a 5%, 2-sided level of significance and analyzed the data with STATA (version 12, StataCorp).

Results

We included 5773 patients treated for ruptured intracranial aneurysms and 1756 patients treated for unruptured intracranial aneurysms from a total of 15 hospitals in Denmark, Norway, and Sweden between 2002 and 2010. Baseline characteristics of the patients are given in Table 1. The average annual volume for each hospital is given in Fig. 1. The average annual number of treatments varied from 6.2 to 118 patients per year for ruptured intracranial aneurysms and from 2.9 to 45.6 patients per year for unruptured intracranial aneurysms.

Ruptured Intracranial Aneurysms

For patients with ruptured intracranial aneurysms, 1-year mortality across all hospitals was 15.6%, and varied from 4.7% to 21.4% among the hospitals ($p < 0.01$, Kruskal-Wallis test). Mortality did not change across year of admission ($p = 0.21$, Kruskal-Wallis test). One-year mortality by mean hospital volume, adjusted for age, is shown in Fig. 2 upper.

Hazard ratios for 1-year mortality by hospital volume are given in Table 2. No clear relationship between hospital volume and mortality was observed in the unadjusted analyses. In the analyses adjusted for potential confounders, we observed a small statistically significant relationship between increasing hospital volumes and higher

FIG. 1. Average annual volume of patients treated for intracranial aneurysms in Scandinavia from 2002 to 2010, according to hospital. Letters on the y-axis represent individual hospitals.

1-year mortality ($p = 0.04$). Figure 3 upper shows age-adjusted cumulative mortality by hospital volume tertile.

Unruptured Intracranial Aneurysm

For patients with unruptured intracranial aneurysms, 1-year mortality across all hospitals was 2.7%, and varied from 0% to 5.6% between the hospitals ($p < 0.01$, Kruskal-Wallis test). Mortality did not change across year of admission ($p = 0.98$, Kruskal-Wallis test). One-year mortality by mean hospital volume, adjusted for age, is given in Fig. 2 lower.

Hazard ratios for 1-year mortality by hospital volume are given in Table 2. We found an inverse relationship between hospital case volume and 1-year mortality in the unadjusted analyses. Similar HRs were observed after adjustment for potential confounders, but the association between hospital volume and 1-year mortality was no longer

TABLE 1. Patient characteristics according to hospital volume tertile

Characteristic	Hospital Volume Tertile*			p Value†
	Low	Intermediate	High	
Ruptured intracranial aneurysms				
Patients	510	2417	2846	
Mean age in yrs (± SD)	55.3 ± 11.9	56.2 ± 11.9	55.2 ± 12.5	0.01
Female sex (%)	321 (63)	1663 (69)	1919 (67)	0.04
Mean CCI (± SD)	0.25 ± 0.49	0.20 ± 0.46	0.21 ± 0.49	0.15
Surgically treated (%)	371 (73)	1104 (46)	1059 (37)	<0.01
Unruptured intracranial aneurysms				
Patients	349	588	819	
Mean age in yrs (± SD)	56.2 ± 10.5	54.4 ± 10.1	54.4 ± 10.4	0.02
Female sex (%)	253 (72)	416 (71)	616 (75)	0.17
Mean CCI (± SD)	0.22 ± 0.49	0.14 ± 0.40	0.19 ± 0.45	0.01
Surgically treated (%)	181 (52)	231 (39)	405 (49)	<0.01

* Ruptured intracranial aneurysms: low-volume tertile = 6.2–36.0 patients per year, intermediate-volume tertile = 43.8–62.4 patients per year, high-volume tertile = 63.1–118.0 patients per year. Unruptured intracranial aneurysms: low-volume tertile = 2.9–10.9 patients per year, intermediate-volume tertile = 14.3–19.7 patients per year, high-volume tertile = 21.9–45.6 patients per year.

† Analysis of variance for continuous variables, chi-square test for categorical variables.

FIG. 2. Graphs of age-adjusted 1-year mortality after surgical and endovascular treatment for ruptured (**upper**) and unruptured (**lower**) intracranial aneurysms in Scandinavia from 2002 to 2010, according to average annual hospital volume. Whisker bars show 95% CIs.

statistically significant. Figure 3 lower shows age-adjusted cumulative mortality by hospital volume tertile.

Between-Country Differences in Mortality

Hazard ratios for 1-year mortality by country are given in Table 3. Mortality for both ruptured and unruptured aneurysms varied significantly between patients from Denmark, Norway, and Sweden. The between-country differences remained statistically significant after adjustment for potential confounders.

Additional Analyses

Analyses restricted to patients admitted between 2008 and 2010 provided similar directions of the effect size for the relationship between hospital volume and mortality after treatment compared with the original analyses. For ruptured intracranial aneurysms, the HR per 10-patient increase was 1.02 (95% CI 0.98–1.06). For unruptured intracranial aneurysms, the HR per 10-patient increase was 0.48 (95% CI 0.31–0.85).

Analyses stratified by treatment modality (endovascular and surgical) found similar directions in the effect size for the relationship between hospital volume and mortality after treatment of both ruptured intracranial aneurysms

(HR per 10-patient increase in the surgical group was 1.04 [95% CI 0.99–1.09] and in the endovascular group 1.02 [95% CI 0.98–1.07]) and unruptured intracranial aneurysms (HR per 10-patient increase in the surgical group was 0.59 [95% CI 0.29–1.23] and in the endovascular group 0.79 [95% CI 0.42–1.50]).

Discussion

The main findings of the present study are that hospital volume was not consistently associated with 1-year mortality after treatment for ruptured intracranial aneurysms, whereas there was a trend toward lower mortality after treatment for unruptured intracranial aneurysms in high-volume hospitals. Furthermore, there were large differences in long-term (1-year) mortality across hospitals and between the 3 Scandinavian countries.

Our study adds to the literature by being the first to examine the relationship between hospital volume and long-term mortality after treatment of intracranial aneurysms. Most previous studies of hospital volume and mortality after treatment for unruptured and ruptured intracranial aneurysms have found lower mortality in high-volume compared with low-volume hospitals, but different definitions of “low-volume hospital” make direct comparison with our study difficult.^{1–4,7,8,13,14,16–18} All previous studies except 1 have reported mortality at discharge. The lower mortality in high-volume hospitals may therefore have been confounded, for instance, by differences in length of stay and discharge routines.^{1–4,7,8,12–14,16,18} Furthermore, all previous studies except 2 originated in the US and the analyses include data from hospitals where multidisciplinary neurosurgical care is likely to be less available or absent.^{1–4,7,8,13,14,16,18} Results from these studies may not be generalizable to health care systems in other countries where specialist neurosurgical services are centralized to tertiary regional hospitals with a defined population and patients are referred from smaller hospitals. A possible explanation for the differences between our results and those published from the US is that all treatments of intracranial aneurysms in Scandinavia are performed at academic hospitals by specialized cerebrovascular surgeons and interventional neuroradiologists, whereas neurosurgeons working in low-volume hospitals in the US may be more likely to be general neurosurgeons than specialized cerebrovascular surgeons.

Two previous studies have examined the relationship between hospital volume and outcome after aneurysm treatment in a health care system where specialist neurosurgical services are delivered at tertiary regional hospitals with a defined population.^{12,17} One study from Japan found no relationship between hospital volume and functional outcome (Glasgow Outcome Scale score) at discharge after treatment of ruptured and unruptured intracranial aneurysms.¹² One study from the United Kingdom examined the relationship between hospital volume and 6-month mortality after (aneurysmal and nonaneurysmal) SAH.¹⁷ This study found a relationship between hospital volume and mortality, but the use of aggregated data, lack of adjustment for age or other prognostic factors, and inclusion of patients with nonaneurysmal SAH limit the generalizability of the results.

TABLE 2. Hazard ratios for 1-year mortality after surgical and endovascular treatment for ruptured and unruptured intracranial aneurysms, according to annual volume of patients

Variable	No. of Hospitals	No. of Deaths/ Patients	1-Yr Mortality (%)	HR (95% CI)	
				Unadjusted	Adjusted†
Ruptured intracranial aneurysms					
Hospital volume tertile*					
Low	5	71/510	13.9	Reference	Reference
Intermediate	5	397/2417	16.4	1.19 (0.92–1.53)	1.57 (1.19–2.10)
High	5	431/2846	15.1	1.10 (0.85–1.41)	1.24 (1.05–1.81)
p value for trend				0.88	0.57
Hospital volume (continuous variable), per 10-patient increase	15	899/5773	15.6	1.02 (0.99–1.05)	1.04 (1.00–1.07)
Unruptured intracranial aneurysms*					
Hospital volume tertile					
Low	5	16/349	4.6	Reference	Reference
Intermediate	5	17/588	2.9	0.62 (0.32–1.24)	0.59 (0.28–1.25)
High	5	15/819	1.8	0.39 (0.19–0.80)	0.49 (0.23–1.04)
p value for trend				0.01	0.07
Hospital volume (continuous variable), per 10-patient increase	15	48/1756	2.7	0.59 (0.40–0.88)	0.69 (0.42–1.10)

* See Table 1 for tertile breakdowns.

† Adjusted for patient age, patient sex, year of treatment, country, CCI, and surgical treatment.

We found no consistent relationship in our study between hospital volume and mortality after treatment for ruptured intracranial aneurysms, but there was a trend toward lower mortality after treatment for unruptured intracranial aneurysms in high-volume hospitals. We believe a plausible explanation for this finding is that surgical experience is more directly associated with outcome after treatment for unruptured intracranial aneurysms because these patients are otherwise healthy and undergo planned surgery. In comparison, other factors that are not related to the surgical experience (such as severity of the SAH, prehospital care, and rehabilitation) may be more important contributors to outcome after treatment for ruptured intracranial aneurysms than hospital volume.

Our findings do not support centralization of treatment for ruptured intracranial aneurysms to high-volume centers. However, we found large between-hospital and between-country variations in mortality after surgical and endovascular treatment of both ruptured and unruptured intracranial aneurysms. The cause for this is unknown. Although the variations in mortality may reflect differences in quality of care, an equally possible explanation is differences in unmeasured prognostic factors (confounding by indication).¹⁵ For instance, some hospitals may have a more aggressive treatment approach for severe SAH (which has a poor prognosis) or for small, unruptured intracranial aneurysms (which has an excellent prognosis). Appropriate selection criteria for treatment are important, especially for unruptured intracranial aneurysms in which the decision to treat involves a tradeoff between the immediate surgical risk and the long-term risk of rupture. Studies from patient registries are unable to adjust for differences in selection to treatment as they lack data on

important prognostic factors such as disease severity and aneurysm morphology. Prospective registries for evaluating patient outcomes after treatment for intracranial aneurysms are therefore highly warranted. Such a registry is currently being established in Norway.

The differences in mortality between hospitals should be interpreted with caution as some hospitals' samples were small and extreme outcomes (both high and low) are likely to occur randomly in small samples.²⁰ From the patient's perspective, this may be of importance and favor undergoing treatment at larger-volume hospitals, as small sample sizes make it more difficult to determine the quality and safety of surgery in low-volume compared with high-volume hospitals. We also observed a large difference in the use of surgical treatment for ruptured intracranial aneurysms between high- and low-volume hospitals, which may reflect differences in the availability of interventional neuroradiology services 24 hours a day.

Our study has important limitations. First, all hospital discharge registries are prone to errors in coding. To reduce the risk of erroneous classification of cases, we used diagnosis codes, procedure codes, and whether the patient was admitted as an emergency to classify the cases as ruptured or unruptured intracranial aneurysms. Second, because of this approach, we did not include patients with intracranial aneurysms who did not undergo surgical or endovascular treatment. Selection criteria for treatment may vary across hospitals and could have influenced the results. Third, we calculated the CCI based on the secondary discharge diagnoses. These diagnoses likely do not fully reflect the patients' comorbidities. Fourth, we did not have data on functional outcome. Functional outcome may be of more interest than mortality, especially for patients

FIG. 3. Graphs of cumulative mortality in patients with ruptured (**upper**) and unruptured (**lower**) intracranial aneurysms, according to hospital volume tertile.

with unruptured intracranial aneurysms. Fifth, we used all-cause mortality and not disease-specific mortality as the outcome of interest. Although this may have attenuated the results, we believe all-cause mortality is of more interest than disease-specific mortality because it puts the magnitude into perspective for prospective decision making. Sixth, we did not have data on prognostic factors such as aneurysm location, size, morphology, and severity of the SAH (for instance, Hunt and Hess and Fisher grades).

Seventh, data on individual surgeons' volumes were not available. Eighth, we only had data available from Norway from 2008 onwards. However, analyses restricted to patients treated between 2008 and 2010 found similar effect size directions as the main analyses. Lastly, we did not have data on patients who emigrated from each country, but this is unlikely to have affected the results as less than 0.5% of the population emigrates annually.¹⁹

The limitations of our study are numerous, but similar limitations (use of hospital discharge data, lack of adjustment for prognostic factors such as aneurysm morphology and disease severity, and lack of data on functional outcome) pertain to all prior studies that examined the relationship between hospital case volume and mortality after aneurysm treatment,^{1–4,7,8,13,14,16–18} except one.¹² Furthermore, although it is possible that more complex aneurysms are transferred to higher-volume centers, we believe this selection bias is less likely to affect the results from Scandinavia than those from the US because each hospital in Scandinavia treats a population in a defined geographic region. Although our findings may be controversial, they are consistent with the only previous study that has adjusted for disease severity.¹² This study did not find a statistically significant relationship between hospital volume and outcome after treatment for ruptured intracranial aneurysms.¹²

Compared with previous studies, our study has important strengths, including a large, population-based sample with long-term follow-up through linkage with population registries. Furthermore, we used individual patient data and adjusted for age, sex, year of treatment, treatment type, and the CCI.

Conclusions

Our findings did not confirm a relationship between higher hospital volume and reduced long-term mortality after treatment of ruptured intracranial aneurysms. Furthermore, we observed significant differences in between-hospital and between-country mortality rates. Prospective registries for evaluating patient outcomes after treatment for intracranial aneurysms are highly warranted.

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TABLE 3. Hazard ratios for 1-year mortality after surgical and endovascular treatment for ruptured and unruptured intracranial aneurysms, according to country

Country	No. of Hospitals	No. of Deaths/Patients	1-Yr Mortality (%)	Unadjusted HR	Adjusted HR*
Ruptured aneurysms					
Sweden	6	347/2736	12.7	Reference	Reference
Norway	4	98/612	16.0	1.29 (1.03–1.61)	1.52 (1.15–1.99)
Denmark	5	454/2425	18.7	1.57 (1.36–1.80)	1.92 (1.66–2.22)
Unruptured aneurysms					
Sweden	6	17/827	2.1	Reference	Reference
Norway	4	2/297	0.7	0.32 (0.08–1.41)	0.41 (0.09–1.89)
Denmark	5	29/603	4.8	2.27 (1.25–4.13)	2.89 (1.53–5.40)

* Adjusted for hospital volume, patient age, patient sex, year of treatment, CCI, and surgical treatment.

and concept of the study. Anne-Marie Andersen at Sundhedsstyrelsen (Denmark), Inger Johanne Bakken at Helsedirektoratet (Norway), and Julius Collin at Socialstyrelsen (Sweden) extracted data from the patient registries and performed the linkage to the population registries.

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Author Contributions

Conception and design: all authors. Acquisition of data: Lindekleiv. Analysis and interpretation of data: Lindekleiv, Førde. Drafting the article: Lindekleiv. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Lindekleiv. Statistical analysis: Lindekleiv. Study supervision: Mathiesen, Førde, Wilsaard, Ingebrigtsen.

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