

Decompressive hemicraniectomy for space-occupying brain infarction: Nationwide population-based registry study

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Objective: We analyzed data from the Norwegian Stroke Registry (NSR) to study access to and outcomes of decompressive hemicraniectomy for brain infarction in a nationwide routine clinical setting. We also discretionary assessed whether the outcomes were comparable with those achieved in randomized controlled trials (RCTs), and whether the use was in accordance with guidelines. **Methods:** The NSR is a nationwide (population 5.3 million) clinical quality registry. We included all stroke-cases operated in 2017 through 2019, and retrieved data on baseline characteristics, treatment and functional outcome after three months (dichotomized modified Rankin Scale score; favorable (0-3) or unfavorable (4-6)). Crude treatment rates and the expected proportion of patients transferred from a local hospital to a stroke-center for the operation were estimated, based on the total population's distribution of residency. **Results:** The 68 cases were 17 (25%) women and 51 (75%) men with a median National Institute of Health Stroke Scale (NIHSS) score on admission

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of 14.0 (inter-quartile range (IQR) 11.0) and a median time from onset to hemicraniectomy of 34.3 (IQR 40.9) hours. The crude treatment rate varied between regions from 0.29 to 1.40 operations per 100,000 population per year, and the proportion transferred from a local hospital (50%) was lower than expected (68%). A favorable outcome was achieved in 20/52 (38.5%) cases. **Conclusions:** The findings indicate gender- and geographic-inequalities in access. Among operated cases, outcomes were comparable with those reported from RCTs, and the use in accordance with recommendations in the current guidelines from the American Stroke Association.

Keywords: Acute stroke—Brain edema—Decompressive surgery—Registry—Outcome

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Introduction

Middle cerebral artery thrombosis can cause space-occupying brain infarction, progressive neurologic deterioration, herniation and death. Eight prospective randomized controlled trials (RCTs) show that decompressive hemicraniectomy within 48 hours after symptom onset reduce mortality and improve outcomes.¹⁻⁸ Accordingly, it is recommended by current guidelines, e.g. the guideline from the American Stroke Association.⁹

Registry data can be used to evaluate the external validity of RCTs and the applicability of recommendations in guidelines. We therefore aimed to analyze data from the Norwegian Stroke Registry (NSR) to study access to and outcomes of hemicraniectomy in a nationwide routine clinical setting. We also discretionary assessed whether the outcomes were comparable with those achieved in the RCTs, and the use is in accordance with recommendations in guidelines.

Methods

Setting, study design, participants and data source

This is a population-based retrospective analysis of prospectively collected register data. The NSR is a nationwide (population 5.3 million, 2018) clinical quality registry with adherence from all hospitals (100 %). The coverage rate for individuals was 87 %, and the case completeness at follow-up after three months 77 % in 2018.¹⁰ Hospital staff recorded data during admissions and trained raters (mainly certified nurses) collected outcome data by

Table 1. Baseline characteristics and treatments.

Variable	Missing, n (%)	All n=68	Favorable outcome (mRS score 0-3) n=20	Unfavorable outcome (mRS score 4-6) n=32	p-value
mRS-score before stroke-onset, n (%)	2 (2.9)				0.241
0		54 (79.4)	19 (95.0)	24 (75.0)	
1		8 (11.8)	1 (5.0)	4 (12.5)	
2		4 (5.9)	0	3 (9.4)	
NIHSS-score on admission, median (IQR)	14 (20.6)	14.0 (11.0)	12.0 (13.0)	15.0 (9.0)	0.064
Hours from onset to decompressive hemicraniectomy, median (IQR)	16 (23.5)	34.3 (40.9)	34.2 (43.7)	34.3 (39.8)	0.855
Thrombolysis, n (%)	0	32 (47.1)	4 (20.0)	20 (62.5)	0.004
Thrombectomy, n (%)	0	31 (45.6)	12 (60.0)	14 (43.8)	0.393

mRS; modified Rankin scale, IQR; interquartile range.

standardized telephone interviews at follow-up. Decompressive hemicraniectomy is provided by neurosurgical units at five regional stroke-centers. Registration of the operation in the NSR commenced in 2017. We included all registered cases operated in 2017 through 2019.

Variables

We received data on baseline characteristics, treatment and functional outcome. The National Institute of Health Stroke Scale (NIHSS) score on admission was used to assess severity. The primary outcome was the modified Rankin Scale (mRS) score after three months, dichotomized as favorable (0-3) or unfavorable (4-6).

Statistical analysis

Statistical analysis was done with the Statistical Package for the Social Sciences (SPSS; version 27, IBM Corp). Continuous data were not normally distributed, and we report medians and interquartile ranges (IQR). Category data are reported as proportions (%). Differences between groups were compared with the Mann-Whitney U-test for continuous, and the chi-square or Fisher's exact test ($n < 5$ in one or more cells) for category variables. Cases with missing values were excluded from estimation of p-values (significance level < 0.05). We calculated crude treatment rates by dividing the mean annual number of hemicraniectomies with the mean population (2017-2019). The expected proportion of patients transferred from a local

hospital was estimated from the total population's distribution of residency, under assumption of ignorable geographic differences in the incidence of ischemic stroke.

Ethics

We received anonymous individual data from the NSR. To avoid indirect identification, the registry calculated age distributions, detained individual data about age, and restricted information about residency to health regions. The data protection officer at the University Hospital of North Norway (file 02593) and the Regional Committee for Medical and Health Research Ethics North (file 184357) approved the study.

Results

68 cases (17 (25 %) women) with median age 57.5 (IQR 17.7) years underwent a decompressive hemicraniectomy (table 1). Most had a high functional level (mRS-scores 0-1) (62/68, 91.2 %) and lived at home without assistance (66/68, 97.1 %), and 29/68 (42.6 %) were employed before the stroke. The median NIHSS-score on admission was 14.0 (IQR 11.0). Computed tomography or magnetic resonance imaging verified a space-occupying brain infarction in all cases. Median time from onset to hemicraniectomy was 34.3 (IQR 40.9) hours. Imaging also showed a large vessel occlusion in 44/68 (64.7 %) cases, and 31/68 (45.6 %) cases underwent a thrombectomy in addition to the craniectomy.

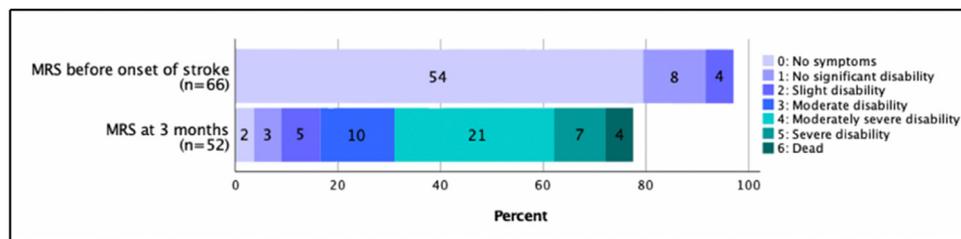


Fig. 1. Stacked-bar chart showing modified Rankin Scale (mRS) score before stroke onset and at three months follow-up. Numbers on bars are the number of cases. The differences between the lengths of the bars and the full scale are caused by missing data.

The crude treatment rate was 0.43 per 100,000 population per year, with five-fold variation between the health regions: South-East 0.29, West 0.36, Middle 0.37 and North-Norway 1.40 per 100,000 population per year. The proportion transferred from a local hospital to one of the five stroke-centers providing hemicraniectomy was lower (50 %) than expected (68 %) from the geographic distribution of residency.

Outcome data were missing for 16 (23.5 %) cases. Fig. 1 shows outcomes for the 52 (76.5 %) followed-up cases. The proportion with a favorable outcome was 20/52 (38.5 %). They all lived at home, 13/20 (65 %) without assistance. Among 28 (61.5 %) cases with an unfavorable outcome, 14 (43.8 %) were in a rehabilitation-unit and 9 (28.1 %) in a nursing home, while 4/52 (7.7 %) were dead.

Table 2 compares this cohort with the cases who underwent decompressive hemicraniectomy in the RCTs. The only noticeable difference was the lower NIHSS-score at baseline.

Discussion

Key results

Stroke-cases treated with decompressive hemicraniectomy in routine practice in Norway were comparable to those included in the RCTs with respect to age, timing of the operation and outcomes. The NIHSS-score at admission was lower than the score at randomization in the RCTs. Treatment rates varied five-fold between regions, the proportion transferred from a local hospital was lower than expected, and the proportion of females was low.

Interpretation

The current guideline from the American Stroke Association recommends decompressive hemicraniectomy for patients ≤ 60 years with middle cerebral artery infarction who deteriorate neurologically within 48 hours from brain swelling.⁹ This has been incorporated in the national Norwegian guideline. Our findings suggest that hemicraniectomy has been implemented in routine clinical practice in accordance. The low NIHSS-score (median 14) could indicate a lower threshold for the operation than in the RCTs (≥ 20). However, the score increases in patients who deteriorate. Six of the RCTs recorded the score at randomization, which could be hours after admission, while the NSR records the score on admission. Deterioration before randomization could thus explain the difference, and also why lower NIHSS-scores did not correspond with more favorable outcomes in the present study. This suggests the external validity of the RCTs is good.

We found a low proportion of females (25 %), as in two of the RCTs.^{4,8} Women constituted 45 % of the cases in the NSR in the study period.¹⁰ Inequality in women's disfavor is a general concern. The low proportion transferred from a local hospital raises concern about inequality in access

Table 2. Comparison of outcomes of decompressive hemicraniectomy in eight randomized prospective trials and the present cohort study.

Study	Cases, n	Age, years	Women, %	Time from symptom onset to DHC, hours	NIHSS-score, points	Registration of NIHSS score, time point	Favorable outcome (mRS score ≤ 3), %
DECIMAL trial ¹	20	43.4 (mean)	52.6	20.5 (mean)	22.5 (mean)	Randomization	25 % (6 months)
DESTINY trial ²	17	44.6 (mean)	53.1	24.0 (median)	21.0 (median)	Admission	47 % (6 months)
HAMLET trial ³	32	48.7 (mean)	40.6	41.0 (median)	23.0 (median)	Randomization	25 % (12 months)
Zhao et al ⁴	24	64.0 (median)	27.7	23.6 (mean)	n.a.	n.a.	21 % (6 months)
Slezins et al ⁵	11	61.5 (mean)	42.9	21.0 (mean)	21.2 (mean)	Randomization	45 % (12 months)
DESTINY II trial ⁶	49	70.0 (median)	50.0	28.0 (median)	20.0 (median)	Randomization	14 % (6 months)
HeADDFIRST trial ⁷	26	55.1 (median)	30.8	53.8 (median)	23.0 (median)	Randomization	29 % (3 months)
HeMMI trial ⁸	15	50.2 (mean)	13.8	36.6 (mean)	22.8 (mean)	Randomization	27 % (6 months)
Norwegian Stroke Registry cohort	68	57.5 (median)	25.0	34.3 (median)	14.0 (median)	Admission	29 % (3 months)

DHC; decompressive hemicraniectomy, NIHSS; National Institute of Health Stroke Scale, mRS; modified Rankin scale

for rural populations, despite Norway's comprehensive air-ambulance system, which aims to compensate large geographic distances' influence on access to emergency care.

Limitations

Hemicraniectomy is recommended for a small proportion of strokes, and therefore the number of cases was low, although higher than in the RCTs, despite use of nationwide register data. This implies a risk for random variation, and the study should be repeated, e.g. 10 years after registrations commenced. The lack of repeated NIHSS-scores in patients who deteriorate and follow-up after three (and not six months) are weaknesses for comparisons with the RCTs, and for assessment of guideline-adherence. The NSR does not register whether patients fulfill the criteria for hemicraniectomy, irrespectively of whether the procedure is provided or not, implying we do not know the number of eligible patients who did not get access to the operation. Finally, 23.5 % were lost to follow-up. This is comparable to the follow-up rate in the NSR in general, but could cause selection bias in reporting of outcomes.

Conclusions

The low proportion of women, low proportion transferred from a local hospital and geographic variation in treatment rates indicate inequalities in access to decompressive hemicraniectomy. For cases undergoing the operation, the use was in accordance with current guidelines, and the outcomes comparable with those reported from RCTs. This suggests good external validity of the RCTs and that current guidelines are applicable to routine clinical practice.

Declaration of Competing Interest

None

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