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ORIGINAL ARTICLE

Service delivery in acute ischemic stroke patients: Does sex matter?

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Abstract

Background and purpose: Women with acute ischemic stroke (AIS) are older and have greater preexisting handicap than men. Given that these factors do not fully explain their poorer long-term outcomes, we sought to investigate potential sex differences in the delivery of acute stroke care in a large cohort of consecutive AIS patients.

Methods: We analyzed all patients from ASTRAL (Acute Stroke Registry and Analysis of Lausanne) from March 2003 to December 2019. Multivariable analyses were performed on acute time metrics, revascularization therapies, ancillary examinations for stroke workup, subacute symptomatic carotid artery revascularization, frequency of change in goals of care (palliative care), and length of hospital stay.

Results: Of the 5347 analyzed patients, 45% were biologically female and the median age was 74.6 years. After multiple adjustments, female sex was significantly associated with higher onset-to-door (adjusted hazard ratio [aHR] = 1.09, 95% confidence interval [CI] = 1.04–1.14) and door-to-endovascular-puncture intervals (aHR = 1.15, 95% CI = 1.05–1.25). Women underwent numerically fewer diagnostic examinations (adjusted odds ratio [aOR] = 0.94, 95% CI = 0.85–1.04) and fewer subacute carotid revascularizations (aOR = 0.69, 95% CI = 0.33–1.18), and had longer hospital stays (aHR = 1.03, 95% CI = 0.99–1.07), but these differences were not statistically significant. We found no differences in the rates of acute revascularization treatments, or in the frequency of change of goals of treatments.

Conclusions: This retrospective analysis of a large, consecutive AIS cohort suggests that female sex is associated with unfavorable pre- and in-hospital time metrics, such as a longer onset-to-door and door-to-endovascular-puncture intervals. Such indicators of less effective stroke care delivery may contribute to the poorer long-term functional outcomes in female patients and require further attention.

KEYWORDS
service delivery, sex differences, stroke

INTRODUCTION

Although there is mounting evidence that women are older and have greater preexisting handicap and comorbidities at stroke onset than men [1–3], this only partially explains the poorer long-term functional outcome in female stroke patients. Possibly, acute stroke care treatment, workup, and secondary prevention could differ between sexes and contribute to these findings, and more data are needed on this latter aspect of stroke management as well as on care delivery in the acute and subacute phases. Considering the expected age-dependent increase in stroke incidence in women in the next decades, this issue becomes even more important. In this quality assurance project, we sought to investigate potential sex differences in care delivery in acute ischemic stroke (AIS) in a large consecutive cohort of patients treated at our institution.

METHODS

Patients and data collection

We reviewed retrospective data from March 2003 to December 2019 of all patients in the prospectively constructed Acute Stroke Registry and Analysis of Lausanne (ASTRAL) [4]. ASTRAL collects data from all AIS patients admitted to the stroke unit and/or intensive care unit of Lausanne University Hospital within 24 h of last known time well. Our center's patient population consists of one third distant referrals from community hospitals and stroke units mainly addressed for acute revascularization treatment, and approximately two thirds patients from the primary catchment area.

We recorded demographic data, vascular risk factors (arterial hypertension, smoking, atrial fibrillation, valve replacements, dyslipidemia, coronary artery disease, and diabetes mellitus), multiple other comorbidities (like a history of renal disease, cancer, dementia, and depression), and previous cerebrovascular events. We collected medications at the time of stroke and the prestroke modified Rankin Scale (mRS). The National Institutes of Health Stroke Scale (NIHSS) was performed or supervised on arrival by NIHSS-certified personnel.

Neuroimaging was computed tomography (CT)-based up to April 2018, after which magnetic resonance imaging (MRI) became the initial imaging modality of choice. CT or magnetic resonance arteriography and perfusion imaging for supratentorial strokes were performed whenever possible.

Stroke mechanism was classified according to TOAST [5]. The rest of the acute stroke management and secondary prevention followed European Stroke Organisation guidelines in use at the time of stroke. Rankin-certified personnel assessed mRS at 7 days, and then at 3 months in the outpatient clinic (or by a structured telephone interview for patients unable to attend the 3-month outpatient clinic).

Outcomes

We chose eight outcomes to assess potential differences in care delivery between female and male stroke patients:

- Onset-to-door (OTD) time analyzed as a continuous variable, that is, the time between the reported symptom onset (or last proof of good health in unknown and sleep-onset patients) and arrival at our tertiary hospital.
- Proportion of acute revascularization treatments (intravenous thrombolysis [IVT] and/or endovascular treatment [EVT]) in the first 24 h. The decision to perform acute revascularization treatment followed the written multidisciplinary hospital guidelines that mirror Swiss [6] and European recommendations [7].
- Times to acute revascularization treatment, analyzed as continuous variables:
  - Door-to-needle time in IVT; and/or
  - Door-to-puncture (DTP) time in EVT.
- Diagnostic examination score. We attributed 1 point for each of the following eight ancillary diagnostic examinations performed during the subacute hospital phase at our stroke center: neurovascular ultrasound (cervical arteries with transcranial Doppler whenever a bone window was present), subacute cranial CT, subacute cranial MRI, subacute cerebral CT angiography or magnetic resonance angiography (MRA; with or without cervical arteries), transthoracic echocardiography (TTE) and/or transesophageal echocardiography (TEE), and patent foramen ovale detection by TTE and/or TEE with microbubble injection. The decision to perform these examinations was taken by the treating physician in the stroke unit.
- Carotid revascularization treatments (carotid endarterectomy [CEA] and/or carotid artery stenting [CAS]) within 1 month for a symptomatic stenosis ≥50%. The decision to perform these treatments was based on our published multidisciplinary hospital guidelines that are subject to Swiss [8] and European [9] recommendations at the time of the intervention. In summary, the preferred intervention was CEA; CAS was offered to patients with anatomical situations unsuitable for CEA, restenosis after previous revascularizations, and postradiation stenosis, and on demand from patients aged <70 years.
- Change in goals of care (CGC) toward a palliative care attitude during the hospitalization for the index stroke. Patients or their legal representatives and the neurologist in charge addressed a CGC based on clinical variables such as initial course, comorbid conditions, prestroke disability, prior patient directives, or presumed wishes of the patient. Any CGC decision was registered in the patient's medical record and in ASTRAL, including the time from stroke onset.
- Length of hospital stay, analyzed as a continuous variable. The onset of the hospital stay was defined as the time of arrival at the hospital of patients admitted thereafter to the stroke unit and/or intensive care unit of our institution (for in-hospital stroke, it was defined as the last proof of good health). The end of the hospital stay coincided

with discharge from the stroke unit and/or intensive care unit either to another institution or to another in-house acute medical service.

We applied the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) method [10].

Ethical considerations

ASTRAL is registered in our institution as a clinical and research databank and follows the institutional regulations on clinical and research registries. Patients received a written document from the hospital that their routinely collected clinical data may be used for quality and scientific purposes, and we did not consider a patient's decision to opt out from data analysis, as this was a quality assurance project of the treatment practice in our institution. This type of analysis, which aims to evaluate treatment efficiency and safety for quality purposes, falls outside of the Swiss Human Research Act of 2011.

Statistical analyses

Study participants' data were analyzed according to sex classification, as shown in Figure S1. We assessed demographic, clinical, and radiological variables from the acute phase of stroke (<24 h) recorded in the ASTRAL database. Continuous variables were summarized as median with interquartile range and categorical variables as percentages and numbers.

Initially, univariate comparisons were performed according to sex and the unadjusted odds ratios (ORs) were evaluated. Subsequently, multiple regression analyses of the aforementioned eight main outcomes were conducted to identify independent associations with sex, after adjusting for the following 23 covariates: age, ethnicity (Caucasian vs. all others), prehospital referral pattern (patients coming from primary vs. secondary hospital catchment areas), time of symptom onset to hospital admission, history of prior cerebrovascular events, stroke severity, prehospital admission mRS, cerebrovascular risk factors (hypertension, diabetes, hyperlipidemia, smoking, atrial fibrillation, alcohol abuse, body mass index [BMI]), peripheral artery disease, coronary artery disease, cardiac heart valves, cardiac ejection fraction, migraine, active cancer, depression, and psychosis. Additional adjustments were made for specific analyses: OTD time to assess the proportion of acute revascularization treatment (IVT and/or EVT), OTD time and carotid stenosis grade to evaluate carotid revascularization treatments, and OTD time to assess length of hospital stay and a CGC.

For continuous response variables (OTD time, door-to-needle time, door-to-puncture time, and length of hospital stay), a Cox proportional hazards model, fitted using the partial likelihood approach, was employed to associate covariates with the response. This method has the advantage that no distributional assumptions are made for the continuous response. For any covariate where the proportional odds assumption is not met, the reported hazard ratio (HR) can be interpreted as the average risk of this covariate on the response.

For categorical outcomes, with limited values, a proportional odds model was used to identify important links between response and background information.

For continuous response variables, a Cox proportional hazards model was employed to associate covariates with the response. This approach has the advantage that no distributional assumptions are made for the continuous response. For categorical outcomes, with limited values, a proportional odds model was used to identify important links between response and background information. The above models are examples of multivariate statistical approaches fitted by optimizing a likelihood function (or an appropriately modified version of it), whereas the impact of a covariate on the response is assessed by the likelihood ratio test approach, in which the effect of other important covariates on the response is allowed.

Missing data were imputed using multivariate imputation by chained equations methodology. All variables had <5% missing values except for BMI (15.2%), mRS at 3 months (6.7%), and further cerebrovascular events over 3 months (19.2%; see Table S11). Five imputed datasets were generated. Stepwise selection methods were employed to identify significant associations of the selected covariates with the specific outcome on each imputed dataset. Results of the five imputed analyses were combined appropriately to formulate the final analysis results, which are given as adjusted odds ratios (aORs) with confidence intervals (CIs) for categorical and ordinal outcomes, and adjusted HRs (aHRs) with CIs for continuous outcomes. All statistical analyses were conducted using the R statistical software version 4.4.2 (R Core Team 2017).

RESULTS

Retrospective data from 5347 patients who fulfilled the inclusion criteria were analyzed (Figure S1). Of these patients, 45% were female, 3.8% were of non-Caucasian ethnicity, and the median age was 74.6 years. The proportion of women in the population referred from the secondary catchment area was 30.4%, lower than the proportion of men (34.7%). Detailed sex-specific description of the cohort is described in Tables 1 and S1; it resembles closely our previous sex-specific analysis concentrating on clinical presentations and long-term outcomes [2].

Unadjusted comparisons (see Tables 1 and S1) showed a significantly higher OTD time (205 min vs. 177 min, HR per hour = 1.02), a slightly lower proportion of IVT (22.7% vs. 24.6%), and a similar proportion of EVT treatments (15.2% vs. 15.1%) for women compared to men. Furthermore, women had longer door-to-imaging times (72 min vs. 48 min) and DTP times (98 min vs 92 min, HR per hour = 1.01), fewer diagnostic examinations despite equal median numbers (3 vs. 3, OR = 0.9, 95% CI = 1.01), fewer subacute carotid revascularization treatments (1.7% vs. 4.4%), longer lengths of hospital stay (9 vs. 8 days), and a higher proportion of CGC (12.3% vs. 9.1%) compared to men.

In the adjusted multivariate analysis (see Table 2), female sex remained significantly associated with higher OTD (aHR = 1.09,

TABLE 1 Overall and sex-specific unadjusted baseline characteristics of the population.

Variable	Overall, $N=5347$	Female sex, $n=2395$	Male sex, $n=2952$	p
Demographics and major vascular risk factors				
Age	74.6 (19.7)	78.1 (17.0)	71.2 (19.9)	<0.01
Hypertension	3944 (73.8)	1802 (75.3)	2142 (72.6)	0.02
Diabetes	1057 (19.8)	387 (16.2)	670 (22.7)	<0.01
Hyperlipidemia	4068 (76.2)	1768 (73.9)	2300 (78.0)	<0.01
Smoking [current or stopped <2 years]	1219 (23)	418 (17.6)	801 (27.4)	<0.01
Atrial fibrillation	1621 (30.3)	846 (35.4)	775 (26.3)	<0.01
Prehospital and admission data				
Known time of stroke onset	3623 (67.8)	1543 (64.5)	2080 (70.5)	<0.01
Stroke present at wake-up	1313 (24.6)	602 (25.1)	711 (24.1)	<0.01
mRS prestroke = 3–5	685 (12.8)	397 (16.6)	288 (9.8)	<0.01
Previous ischemic cerebral event	951 (17.8)	387 (16.2)	564 (19.1)	<0.01
OTD time, min	188.5 (519.2)	205 (592.0)	177 (459.5)	<0.01
Patient referred from outside the primary catchment area	1751 (32.8)	727 (30.4)	1024 (34.7)	<0.01
NIHSS on admission	6 (11)	7 (12)	6 (10)	<0.01
Acute treatment				
IVT [with or without EVT]	1268 (23.7)	543 (22.7)	725 (24.6)	ns
EVT [with or without preceding IVT]	812 (15.2)	365 (15.2)	447 (15.1)	ns
Door-to-IVT time, min	44 (42)	43 (41)	44 (43)	ns
Door-to-puncture time, min	95 (63.5)	98 (57)	92 (68)	ns
Symptomatic extracranial carotid stenosis 50%–99%	795 (17.4)	279 (13.9)	516 (20.2)	<0.01
Other outcome measures				
Subacute carotid revascularization procedure at 12 months	168 (3.2)	39 (1.7)	129 (4.4)	<0.01
Number of subacute diagnostic exams, diagnostic exam score	3.0 (2.0)	3.0 (2.0)	3.0 (2.0)	<0.01
Length of hospital stay, days	8 (8.0)	9 (8.0)	8. (8.0)	0.6
Change in goals of care during acute hospitalization	561 (10.5)	294 (12.3)	267 (9.1)	<0.01

Note: Values are expressed as median (interquartile range) for continuous variables, and absolute count (percentage) for categorical variables unless otherwise stated. The number and proportion of missing data are reported in the Table S11.

Abbreviations: EVT, endovascular treatment; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; ns, not significant; OTD, onset-to-door.

95% CI = 1.04–1.14, $p<0.01$) and DTP times (aHR = 1.15, 95% CI = 1.05–1.25, $p<0.01$). Although not statistically significant, we observed a lower number of diagnostic examinations (aOR = 0.94, 95% CI = 0.85–1.04, $p=0.21$), fewer subacute carotid revascularization treatments (aOR = 0.69 95% CI = 0.33–1.18, $p=0.147$), and longer hospital durations (aHR = 1.03, 95% CI = 0.99–1.07, $p=0.19$) in women. Furthermore, in the multivariate analysis, we no longer saw trends in the proportions of IVT and/or EVT or changes in goals of treatments between male and female patients.

DISCUSSION

In this retrospective study of 5347 consecutive AIS patients admitted to a comprehensive stroke center, we found that female sex was significantly associated with longer OTD and DTP times. Additionally, we noted numerically fewer diagnostic examinations in women during the acute hospital stay, fewer subacute carotid revascularization treatments, and longer hospital durations, but these differences did not reach statistical significance. Altogether, these indicators of less effective stroke care delivery may contribute to the poorer long-term functional outcomes in female patients [2, 11] and warrant further attention.

Existing literature focusing on sex differences in acute stroke care and service delivery is limited and yields inconsistent results. An older analysis from the GWTG Stroke program [12] showed that women received poorer quality of acute stroke care than men, whereas a recent large retrospective study in China [1] did not show significant sex differences in acute management and intrahospital and discharge performance measures. A pooled analysis of five randomized controlled trials found that women were more likely to be admitted to an acute stroke unit [13], whereas other studies

TABLE 2 Results of the univariate and multivariate analysis for each of the eight sex-specific outcomes (reference = male sex).

Outcome	Unadjusted ratio[a]	95% CI	*p* unadjusted	Adjusted ratio[a]	95% CI	*p* adjusted
Onset-to-door time (hours)	1.02	1.01–1.03	<0.01	1.09	1.04–1.14	<0.01
Diagnostic exam score (0–8)	0.91	0.88–0.94	<0.01	0.85	0.85–1.04	0.21
Acute revascularization treatment, i.e., IVT and/or EVT (%)	1.09	0.91–1.3	0.26	1.05	0.91–1.22	0.48
Door-to-needle time for IVT (hours)	0.99	0.97–1.01	0.28	0.95	0.86–1.05	0.34
Door-to-puncture time for EVT (hours)	1.01	0.95–1.07	0.75	1.15	1.05–1.25	<0.01
Subacute revascularization for symptomatic carotid stenosis (50%–99%)	0.36	0.25–0.52	<0.01	0.63	0.33–1.18	0.15
Length of hospital stay (days)	1.01	1.00–1.01	0.6	1.03	0.99–1.07	0.19
Change in goals of care	1.4	1.18–1.67	<0.01	0.99	0.8–1.23	0.92

Note: For detailed results of each outcome, see Tables S1–S11. For factors used for adjustment, see Methods section.
Abbreviations: CI, confidence interval; EVT, endovascular treatment; IVT, intravenous thrombolysis.
[a]Odds ratio for categorical and ordinal outcomes, and hazard ratio for continuous outcomes.

from France and Canada did not confirm significant sex disparities in rates of stroke unit admission [14] or showed the contrary [15]. This same adjusted pooled analysis did not demonstrate that women were less likely to benefit from intensive care treatment and acute interventions such as intubation [13], nasogastric feeding [13], and treatment for fever [13]. On the contrary, a recent nationwide study from Canada showed that women and older patients (≥80 years) had lower odds of receiving life-sustaining care, but disparities in intensive care unit admission narrowed over time [16].

Regarding prehospital timing, several other studies reported longer onset-to-hospital times for women [17–22] whereas others did not find a sex-related difference [23, 24]. One plausible reason for increased prehospital times is that women are more often widowed and living alone [25], leading to a later activation of emergency medical services [21]. Measures to minimize loneliness by reinforcing social contacts and networks may reduce this risk. Additionally, persons living alone can be equipped with electronic alert systems connected with significant others or a service provider. Another explanation might be more nonfocal, atypical, and nontraditional symptoms in acute stroke presentations in women, leading to underrecognition of stroke and nonactivation of stroke alert pathways [26, 27].

Multiple studies have shown that longer prehospital delays are associated with longer intrahospital treatment time [28] and poorer long-term functional outcome, both in revascularized [29] and in nonrevascularized patients [30].

Regarding intravenous thrombolysis, our results confirmed those of other studies showing comparable treatment rates and time metrics for both sexes [1, 22, 23, 31, 32]. However, one study of Danish public registries [21] and a recent meta-analysis of 17 studies showed 13% lower unadjusted odds of receiving intravenous recombinant tissue plasminogen activator (rt-PA) in women [33]. Reassuringly, such differences seem to decrease toward more sex equity over time; a recent nationwide analysis in the United States showed that in the past decade, utilization of rt-PA increased at a faster pace in women compared to men [34]. This trend was confirmed by epidemiological data from France [15] and by the aforementioned meta-analysis by Strong and coworkers [33]. Recent data from Catalonia for the period from 2016 to 2019 showed even a higher proportion of acute reperfusion therapies in women [24].

Regarding the rate of EVT, we found no differences between sexes after adjusting for several factors, whereas other studies showed higher EVT rates in women [14, 31, 33, 35]. Given that several of these other studies [14, 35] adjusted their comparisons with multiple covariates, there is no simple explanation for these findings, such as higher admission NIHSS scores or rates of atrial fibrillation [2].

We found longer DTP times in women treated with endovascular therapies, despite adjusting for prehospital delays. This contrasts with other studies that found similar intrahospital times for EVT [24, 36, 37]. Our finding does not have an obvious explanation, but a possible explanation is a cognitive sex bias. Although the absolute difference of 6 min for the DTP time seems minor compared to 28 min for the OTD time, Saver et al. have well demonstrated that any intrahospital delay to EVT is associated with a poorer functional long-term outcome [29]. Therefore, particular efforts should be undertaken by acute stroke teams and emergency departments to identify female patients as EVT candidates through education and awareness training.

Regarding the in-hospital stroke workup in the subacute phase, our results showed that we performed numerically fewer diagnostic examinations in women, but this did not reach statistical significance.

Again, prior literature is divided when reporting on sex differences in diagnostic evaluation of stroke, with evidence for less extracranial MRA [23], echocardiography, and carotid evaluation in women [38, 39], whereas older populations [40] and multicentric studies in the United States and Canada did not demonstrate significant sex inequities for these examinations [41, 42].

A further main result of our study was that after adjusting for age and stenosis grade, we observed numerically fewer subacute carotid vascularization procedures in women, not reaching statistical significance. This result may be explained by evolving sex-specific treatment recommendations for symptomatic carotid stenosis [43, 44]. Some studies show a higher stroke risk in male carotid stenosis patients compared to women, probably due to higher plaque instability [45], but endarterectomy risk seems similar [46], and the meta-analysis of randomized trial data does not show a differential effect of carotid revascularization depending on biological sex [44].

As for the lengths of hospital stay, the longer hospital duration for women was numerically present but not significant after adjusting for the known greater stroke severity and prestroke handicap [2]. Longer hospitalization in women has been reported by Somerford et al. [47], possibly related to the more frequent absence of a spouse at home who could participate in the care.

Finally, regarding the complex question of sex disparities in CGC in AIS, we did not observe a significant difference in CGC decisions in our adjusted analysis. This confirms what we found in our recent analysis that identified several powerful predictors of GCS, but not sex [48].

Limitations of our work are its retrospective, nonrandomized design in a tertiary stroke center with approximately one third of patients being referred from other hospitals or stroke units. As a quality assurance project in a single institution, it may not be applicable to other populations, in particular, non-Caucasian and younger populations. We did not measure several variables that may have confounded our main outcomes, such as educational level, extent of social networks, isolation and loneliness, and socioeconomic and sociocultural status. Finally, the inclusion criteria for ASTRAL with its 24-h limit since stroke onset, or (a few) stroke patients not being admitted to the stroke unit, may create a sex selection bias that we cannot measure or account for.

The strengths of our work are the consecutive nature of the collected data over a long period with prespecified and standardized data collection, and rigorous adjustment of multiple confounders for the eight main outcome analyses.

In conclusion, this study suggests that female patients with AIS arriving at a comprehensive stroke center have longer OTD and DTP times, whereas other indicators for care delivery are not statistically different. Some of these observations may contribute to the explanation of poorer long-term functional outcomes in female patients and require further attention.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

The raw, anonymized data that support the findings of this study are available from the corresponding author upon reasonable request and after signing a data transfer and use agreement (DTUA). If such data are then used for a publication, the publication methods should be communicated, and internationally recognized authorship rules should be applied.

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REFERENCES

1. Gu HQ, Wang CJ, Yang X, et al. Sex differences in vascular risk factors, in-hospital management and outcomes of patients with acute ischemic stroke in China. *Eur J Neurol*. 2022;29(1):188-198.
2. Medlin F, Amiguet A, Eskandari A, Michel P. Sex differences in consecutive acute ischemic strokes:causes, clinical presentation and outcomes. *Eur J Neurol*. 2020;27(8):1680-1688.
3. Hoyer C, Schlenker J, Sandikci V, et al. Sex-specific differences in pre-stroke characteristics reveal vulnerability of elderly women. *J Pers Med*. 2022;12:344.
4. Michel P, Odier C, Rutgers M, et al. The Acute STroke Registry and Analysis of Lausanne (ASTRAL): design and baseline analysis of an ischemic stroke registry including acute multimodal imaging. *Stroke*. 2010;41:2491-2498.
5. Adams HP Jr, Bendixen BH, Kappelle LJ, et al. 3rd classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. trial of ORG 10172 in acute stroke treatment. *Stroke*. 1993;24:35-41.
6. Michel P, Diepers M, Mordasini P, et al. Acute revascularization in ischemic stroke: updated Swiss Guidelines. *Clin Transl Neurosci*. 2021;5(1):9.
7. Fiehler J, Cognard C, Gallitelli M, et al. European recommendations on organisation of interventional care in acute stroke (EROICAS). *Eur Stroke J*. 2016;1(3):155-170.
8. Déglise S, Dubuis C, Mosimann P, et al. Prise en charge des sténoses carotidiennes [management of the carotid artery stenosis]. *Rev Med Suisse*. 2013;9(391):1305-1311.
9. Naylor AR, Ricco JB, de Borst GJ, et al. Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 clinical practice Guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg*. 2018;55(1):3-81.
10. Von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Epidemiology*. 2007;18:800-804.
11. Xu M, Amarilla Vallejo A, Cantalapiedra Calvete C, et al. Stroke outcomes in women: a population-based cohort study. *Stroke*. 2022;53(10):3072-3081.
12. Reeves MJ, Fonarow GC, Zhao X, Smith EE, Schwamm LH, Get With The Guidelines-Stroke Steering Committee & Investigators.

Quality of care in women with ischemic stroke in the GWTG program. *Stroke*. 2009;40(4):1127-1133.
13. Carcel C, Wang X, Sandset EC, et al. Sex differences in treatment and outcome after stroke: pooled analysis including 19,000 participants. *Neurology*. 2019;93(24):e2170-e2180.
14. Yu AYX, Austin PC, Rashid M, et al. Sex differences in intensity of care and outcomes after acute ischemic stroke across the age continuum. *Neurology*. 2023;100(2):e163-e171.
15. Olié V, Grave C, Tuppin P, Duloquin G, Béjot Y, Gabet A. Patients hospitalized for ischemic stroke and intracerebral hemorrhage in France: time trends (2008-2019), in-hospital outcomes, age and sex differences. *J Clin Med*. 2022;11(6):1669.
16. Joundi RA, Smith EE, Yu AYX, Rashid M, Fang J, Kapral MK. Age-specific and sex-specific trends in life-sustaining care after acute stroke. *J Am Heart Assoc*. 2021;10(18):e021499.
17. Menon SC, Pandey DK, Morgenstern LB. Critical factors determining access to acute stroke care. *Neurology*. 1998;51:427-432.
18. Barr J, McKinley S, O'Brien E, Herkes G. Patient recognition of and response to symptoms of TIA or stroke. *Neuroepidemiology*. 2006;26:168-175.
19. Mandelzweig L, Goldbourt U, Boyko V, Tanne D. Preceptual, social, and behavioral factors associated with delays in seeking medical care in patients with symptoms of acute care. *Stroke*. 2006;37:1248-1253.
20. Foerch C, Misselwitz B, Humpich M, Steinmetz H, Neumann-Haefelin T, Sitzer M. Sex disparity in the access of elderly patients to acute stroke care. *Stroke*. 2007;38:2123-2126.
21. Mainz J, Andersen G, Valentin JB, Gude MF, Johnsen SP. Disentangling sex differences in use of reperfusion therapy in patients with acute ischemic stroke. *Stroke*. 2020;51(8):2332-2338.
22. de Ridder I, Dirks M, Niessen L, Dippel D, Investigators PRACTISE. Unequal access to treatment with intravenous alteplase for women with acute ischemic stroke. *Stroke*. 2013;44(9):2610-2612.
23. Gattringer T, Ferrari J, Knoflach M, et al. Sex-related differences of acute stroke unit care. Results from the Austrian stroke unit registry. *Stroke*. 2014;45:1632-1638.
24. Silva Y, Sánchez-Cirera L, Terceño M, et al. Sex and gender differences in acute stroke care: metrics, access to treatment and outcome. A territorial analysis of the stroke code system of Catalonia. *Eur Stroke J*. 2023;8(2):557-565.
25. Reeves MJ, Prager M, Fang J, Stamplecoski M, Kapral MK. Impact of living alone on the care and outcomes of patients with acute stroke. *Stroke*. 2014;45:3083-3085.
26. Bushnell C, Howard VJ, Lisabeth L, et al. Sex differences in the evaluation and treatment of acute ischaemic stroke. *Lancet Neurol*. 2018;17(7):641-650.
27. Ali M, van Os HJA, van der Weerd N, et al. Sex differences in presentation of stroke: a systematic review and meta-analysis. *Stroke*. 2022;53(2):345-354.
28. Strbian D, Ringleb P, Michel P, et al. Ultra-early intravenous stroke thrombolysis: do all patients benefit similarly? *Stroke*. 2013;44(10):2913-2916.
29. Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316(12):1279-1288.
30. Ntaios G, Faouzi M, Ferrari J, Lang W, Vemmos K, Michel P. An integer-based score to predict functional outcome in acute ischemic stroke: the ASTRAL score. *Neurology*. 2012;78(24):1916-1922.
31. Weber R, Krogias C, Eyding J, et al. Age and sex differences in ischemic stroke treatment in a nationwide analysis of 1.11 million hospitalized cases. *Stroke*. 2019;50(12):3494-3502.
32. Nagaraja N, Olasoji EB, Patel UK. Sex and racial disparity in utilization and outcomes of t-PA and thrombectomy in acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2020;29(9):104954.
33. Strong B, Lisabeth LD, Reeves M. Sex differences in IV thrombolysis treatment for acute ischemic stroke: a systematic review and meta-analysis. *Neurology*. 2020;95(1):e11-e22.
34. Otite FO, Saini V, Sur NB, et al. Ten-year trend in age, sex, and racial disparity in tPA (alteplase) and thrombectomy use following stroke in the United States. *Stroke*. 2021;52(8):2562-2570.
35. Bonkhoff AK, Karch A, Weber R, Wellmann J, Berger K. Female stroke: sex differences in acute treatment and early outcomes of acute ischemic stroke. *Stroke*. 2021;52(2):406-415.
36. Momen AI, Francis T, Schaafsma JD, et al. Sex differences in functional outcomes following endovascular treatment for acute ischemic stroke. *Can J Neurol Sci*. 2023;50:174-181. doi:10.1017/cjn.2022.22
37. Bala F, Casetta I, Nannoni S, et al. Sex-related differences in outcomes after endovascular treatment of patients with late-window stroke. *Stroke*. 2022;53(2):311-318.
38. Smith MA, Lisabeth LD, Brown DL, Morgenstern LB. Gender comparisons of diagnostic evaluation for ischemic stroke patients. *Neurology*. 2005;65(6):855-858.
39. Turaj W, Slowik A, Wnuk M, Szczudlik A. Gender-related differences in diagnostic evaluation and outcome of ischemic stroke in Poland. *Stroke*. 2009;40(3):980-982.
40. Gall SL, Donnan G, Dewey HM, et al. Sex differences in presentation, severity, and management of stroke in a population-based study. *Neurology*. 2010;74:975-981.
41. Watanabe E, Allen NB, Dostal J, et al. Diagnostic evaluation for patients with ischemic stroke: are there sex differences? *Cerebrovasc Dis*. 2009;27:450-455.
42. Kapral MK, Ben-Yakov M, Fang J, et al. Gender differences in carotid imaging and revascularization following stroke. *Neurology*. 2009;73:1969-1974.
43. The European Stroke Organisation (ESO) Executive Committee and the ESO Writing Committee: Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis*. 2008;25:457-507.
44. Bonati LH, Kakkos S, Berkefeld J, et al. European stroke organisation guideline on endarterectomy and stenting for carotid artery stenosis. *Eur Stroke J*. 2021;6:I-XLVII.
45. van Dam-Nolen DHK, van Egmond NCM, Dilba K, et al. Sex differences in plaque composition and morphology among symptomatic patients with mild-to-moderate carotid artery stenosis. *Stroke*. 2022;53(2):370-378.
46. Dansey KD, Pothof AB, Zettervall SL, et al. Clinical impact of sex on carotid revascularization. *J Vasc Surg*. 2020;71:1587-1594.
47. Somerford PJ, Lee AH, Yau KK. Ischemic stroke hospital stay and discharge destination. *Ann Epidemiol*. 2004;14(10):773-777.
48. Hausammann R, Maslias E, Amiguet M, Jox RJ, Borasio GD, Michel P. Goals of care changes after acute ischaemic stroke: decision frequency and predictors. *BMJ Support Palliat Care*. 2022. doi:10.1136/spcare-2022-003531

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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