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## Original Article

# No Sex Differences in Mechanical Thrombectomy Time Metrics and Outcomes in Saskatchewan

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**ABSTRACT:** ***Background and Purpose:*** Numerous studies have shown longer pre-hospital and in-hospital workflow times and poorer outcomes in women after acute ischemic stroke (AIS) in general and after endovascular treatment (EVT) in particular. We investigated sex differences in acute stroke care of EVT patients over 5 years in a comprehensive Canadian provincial registry. ***Methods:*** Clinical data of all AIS patients who underwent EVT between January 2017 and December 2022 in the province of Saskatchewan were captured in the Canadian OPTIMISE registry and supplemented with patient data from administrative data sources. Patient baseline characteristics, transport time metrics, and technical EVT outcomes between female and male EVT patients were compared. ***Results:*** Three-hundred-three patients underwent EVT between 2017 and 2022: 144 (47.5%) women and 159 (52.5%) men. Women were significantly older (median age 77.5 [interquartile range: 66–85] vs.71 [59–78], $p < 0.001$), while men had more intracranial internal carotid artery occlusions (48/159 [30.2%] vs. 26/142 [18.3%], $p = 0.03$). Last-known-well to comprehensive stroke center (CSC)-arrival time (median 232 min [interquartile range 90–432] in women vs. 230 min [90–352] in men), CSC-arrival-to-reperfusion time (median 108 min [88–149] in women vs. 102 min [77–141] in men), reperfusion status (successful reperfusion 106/142 [74.7%] in women vs. 117/158 [74.1%] in men) as well as modified Rankin score at 90 days did not differ significantly. This held true after adjusting for baseline variables in multivariable analyses. ***Conclusion:*** While women undergoing EVT in the province of Saskatchewan were on average older than men, they were treated just as fast and achieved similar technical and clinical outcomes compared to men.

**Résumé:** **La thrombectomie mécanique : pas de différence entre les sexes en ce qui concerne les indicateurs de temps et les résultats obtenus en Saskatchewan.** ***Contexte et but :*** Dans de nombreuses études, on fait état de flux de travaux prolongés en phase préhospitalière et hospitalière et de résultats moins favorables chez les femmes que chez les hommes après un accident vasculaire cérébral (AVC) ischémique aigu en général, et notamment après un traitement endovasculaire (TEV). L'étude, fondée sur un registre provincial exhaustif au Canada, avait donc pour but d'examiner les différences de soins donnés aux hommes et aux femmes traités par TEV après un accident vasculaire cérébral aigu, sur une période de 5 ans. ***Méthode :*** Des données cliniques recueillies sur tous les patients soumis à un TEV après un AVC ischémique aigu, entre janvier 2017 et décembre 2022, en Saskatchewan, ont été inscrites dans le registre OPTIMISE au Canada, puis complétées par d'autres données sur des patients, provenant de sources administratives. Il y a eu ensuite comparaison des données en ce qui concerne les caractéristiques de base, les mesures du temps de transport et les résultats techniques du TEV, entre les hommes et les femmes. ***Résultats :*** Dans l'ensemble, 303 patients ont subi un TEV entre 2017 et 2022, soit 144 femmes (47,5 %) et 159 hommes (52,5 %). Les femmes étaient significativement plus âgées que les hommes (âge médian : 77,5 ans [intervalle interquartile {II} : 66-85] contre [c.] 71 [59-78]; $p < 0{,}001$), tandis que les hommes souffraient davantage d'occlusions intracrâniennes de la carotide interne (48/159 [30,2 %] c. 26/142 [18,3 %]; $p = 0{,}03$). Les données relatives au temps écoulé entre le dernier moment où la personne avait été vue en bonne santé et l'arrivée au centre de soins intégrés des AVC (temps médian : 232 min [II : 90-432] chez les femmes c. 230 min [90-352] chez les hommes), au temps écoulé entre l'arrivée au centre de soins intégrés et la reperfusion (temps médian : 108 min [88-149] chez les femmes c. 102 min [77-141] chez les hommes), aux résultats de la reperfusion (reperfusion réussie : 106/142 [74,7 %] chez les femmes c. 117/158 [74,1 %] chez les hommes) et au score de Rankin modifié au bout de 90 jours ne présentaient pas de différence significative, et ce, malgré le rajustement des variables de base dans les analyses

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plurifactorielles. ***Conclusion :*** Si les femmes soumises à un TEV en Saskatchewan étaient en moyenne plus âgées que les hommes, le temps écoulé avant le traitement était aussi court que celui enregistré chez les hommes, et les résultats cliniques et techniques obtenus dans les deux groupes étaient comparables.

**Keywords:** Thrombectomy; ischemic stroke; sex

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## Introduction

Patient sex plays an important role not only in acute ischemic stroke (AIS) pathophysiology but also in acute stroke care.[1,2] Women are on average older[3] and show a higher degree of pre-stroke disability at the time of their first stroke.[4–8] Women are also more likely to live alone at the time of stroke onset, and thus strokes in women may occur more often unwitnessed, get discovered later, and are associated with problems when obtaining consent to treatment.[2,6] Delays in hospital admission, diagnosis, and treatment may be more pronounced in female stroke patients as compared to their male counterparts.[9,10] This may lead to worse outcomes in female stroke patients undergoing endovascular treatment (EVT) compared to their male counterparts,[2,11,12] although the literature is controversial in this regard.[1,2]

We used a comprehensive Canadian provincial dataset to compare sex differences with regard to patient baseline characteristics, treatment time metrics, and clinical outcomes in AIS patients undergoing EVT over a 5-year time period, between January 2017 and December 2022.

## Methods

*Patient Study Population:* This study included all patients who underwent EVT between January 2017 and December 2022 in the province of Saskatchewan, Canada, with a population of 1.2 million.[13] All EVT procedures in the province occur at one comprehensive stroke center (CSC) (Royal University Hospital) because this is the only EVT-capable center in the province.

*Data collection and Curation:* Clinical data of all AIS patients who underwent EVT in the 5-year period in the province of Saskatchewan are captured in the Canadian OPTIMISE registry, a national registry supported by the Canadian Stroke Consortium to ensure quality control for endovascular therapy and intravenous thrombolysis among patients with AIS.[14] Data for the OPTIMISE registry are captured using a web-based electronic data capture and reporting system and housed on a secure server at the Population Health Research Institute at McMaster University. These data included patient age, sex, baseline National Institutes of Health Stroke Scale, baseline Alberta Stroke Program Early CT Score, occlusion location, collateral score, time of stroke onset, witnessed vs. unwitnessed stroke onset, transport mode (direct to CSC vs. transfer from primary stroke center [PSC] vs. in-hospital stroke), intravenous thrombolysis, and detailed procedural EVT data (arterial access time, reperfusion time, final expanded Thrombolysis in Cerebral Infarction score as assessed by the operator). OPTIMISE data were supplemented with patient data from administrative data sources (patient homes' postal code, which were derived from patients' electronic medical records and used as a proxy for patient location at the time of stroke onset), time of imaging at the primary stroke center, and CSC and last intracranial run time [used as a surrogate for reperfusion time in case no expanded Thrombolysis in Cerebral Infarction Score 2b/3 reperfusion was achieved/documented]).

### Outcomes of Interest

The co-primary outcomes of interest were

a) the time from last known well (LKW) to CSC arrival (capturing the entire pre-hospital and transfer phase prior to CSC arrival), derived from the OPTIMISE database

b) the time from CSC arrival to reperfusion (capturing the entire CSC in-hospital phase), CSC arrival time, reperfusion time (or last intracranial run time in case no reperfusion was achieved/documented) derived from the local Picture Archiving and Communications System

c) final expanded Thrombolysis in Cerebral Infarction score (capturing technical EVT success).

The secondary outcome was modified Rankin Score.

*Statistical analysis*: Patient baseline characteristics, workflow times, and technical and clinical outcomes for the overall patient sample and for women and men were reported using medians and interquartile ranges for continuous data and counts and frequencies for categorical data. Univariable comparisons of the above variables between female and male stroke patients were made using Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables. Multivariable linear regression (LKW to CSC arrival time, CSC arrival to reperfusion time) or ordinal logistic regression (final expanded Thrombolysis in Cerebral Infarction Score, 90-day modified Rankin Score) with adjustment for age, baseline National Institutes of Health Stroke Scale and baseline Alberta Stroke Program CT Score was used to obtain adjusted effect size estimates with respective 95% confidence intervals for patient sex on outcomes. For linear regression, normal distribution of residuals was assessed visually and tested with the Shapiro–Francia–Wilk test. In case the residuals of dependent variables in linear regression were not normally distributed, logarithmic transformation of variables was attempted. The parallel regression assumption for proportional odds (i.e., ordinal logistic) regression was tested with the Brant test. Since missing data were few and balanced between sexes, and because we could not assume with certainty that data were completely missing at random, we decided against imputation for missing data.

All analyses were conducted using Stata 17.0 (Stata, LLC Corp.), and p-values $< 0.05$ were considered statistically significant. Visualizations were generated using Microsoft PowerBI (Version 2.91).

This study was approved by the ethics committee of the Royal University Hospital, Saskatoon (REB 23-06). The data that were used for analysis will be made available by the corresponding author upon reasonable request.

## Results

Between January 2017 and December 2022, 303 patients underwent EVT in the province of Saskatchewan at the Royal University Hospital of Saskatchewan in Saskatoon, of which 144 (47.5%) were women and 159 (52.5%) were men (Fig. 1). Baseline characteristics


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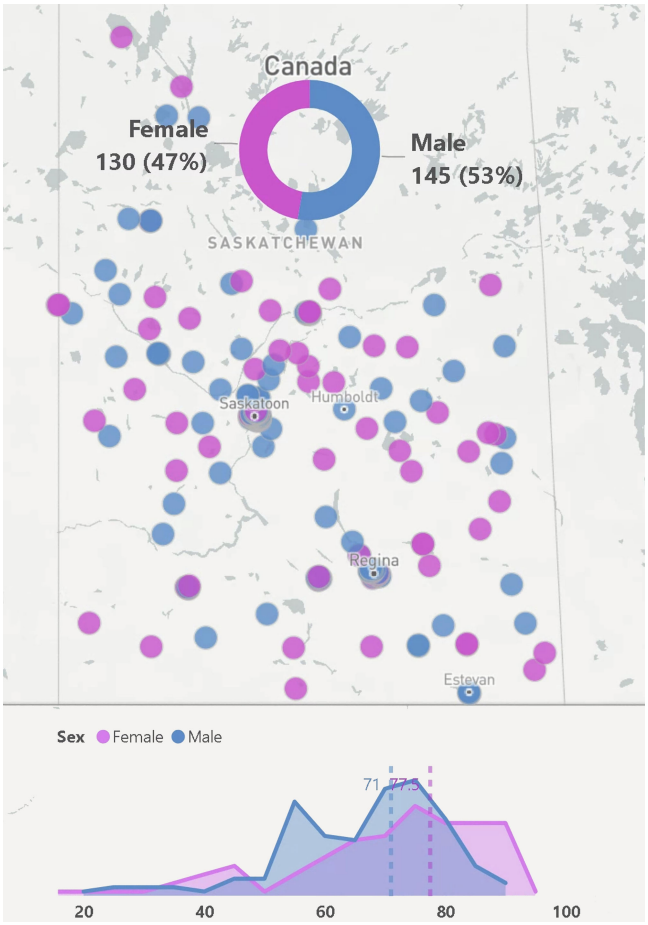


**Figure 1:** Distribution of women and men with acute ischemic stroke across the province who underwent EVT between January 2017 and December 2022. Graph at the bottom illustrates patient age by sex, with a median age of 71 in men and 77.5 in women who underwent EVT. Note that not all dots may be seen individually since they may overlap.

of women and men did not differ significantly, except for age at stroke onset, which was higher in women, and intracranial occlusion location on baseline imaging, whereby intracranial internal carotid artery occlusions occurred more commonly in men and M1 segment occlusions were more frequent in women (Table 1).

### *Comparison of Co-primary Outcomes in Female vs. Male Stroke Patients*

In unadjusted analyses, LKW to CSC arrival times, CSC arrival to reperfusion times, and final expanded Thrombolysis in Cerebral Infarction Score did not differ between women and men (Table 2, Fig. 2).

For the adjusted analysis, time from LKW to CSC arrival and time from CSC arrival to reperfusion were log-transformed to achieve a normal distribution of residuals. Log-transformed time variables resembled a normal distribution more closely compared to the non-log-transformed time variables (Suppl. Figures I–III). While the Shapiro–Francia–Wilk test indicated that the normality distribution assumption was still violated for time from LKW to CSC arrival ($p < 0.001$), there was no evidence that the normality distribution assumption for CSC arrival to reperfusion time was violated ($p = 0.156$).

Female sex was associated neither with log-transformed LKW to CSC arrival time (beta-coefficient 0.11 [95% CI −0.13–0.35]) nor with CSC arrival to reperfusion time (beta-coefficient 0.01 [95% CI −0.10–0.13]).

Female sex was not associated with final expanded Thrombolysis in Cerebral Infarction Score (adjusted common odds ratio 1.15 [95% CI 0.74–1.81]). The Brant test indicated that the proportional odds assumption was not violated ($p = 0.184$).

### *Comparison of Secondary Outcomes in Female vs. Male Stroke Patients*

In univariable analysis, mRS at 90 days did not differ significantly between women and men (Suppl. Table I, $p = 0.715$). In multivariable analysis (after adjustment for age, baseline National Institutes of Health Stroke Scale and baseline Alberta Stroke Program Early CT Score), female sex was not associated with 90-day modified Rankin Score (adjusted common odds ratio 1.15 [95%CI 0.75–1.77], p[Brant] = 0.768).

## Discussion

In this Canadian province-wide study that included patients undergoing EVT over a 5-year time period, female EVT patients were on average older at the time of stroke onset, but no sex differences in EVT time metrics in the pre-hospital and in-hospital phase, reperfusion quality, or clinical outcomes were seen.

Numerous studies have found that women are on average 4–5 years older than men when they suffer their first stroke,[3] and our study confirmed this "age discrepancy." Prior research has also shown that women are more commonly disabled at the time of their first stroke, are more likely to be widowed, and live alone more often.[4–8] Furthermore, strokes in women may occur more often unwitnessed, and by the time the patient's symptoms are discovered and emergency services are called, the window of opportunity for intravenous thrombolysis and/or EVT may have already passed.[6]

Prior studies on the topic show conflicting results on whether sex differences in post-EVT outcomes exist or not: many studies did not find any sex differences in functional outcomes after EVT.[15,16] As an example, similar to our study, Sheth et al. report that women, despite being on average older at stroke onset and having higher rates of atrial fibrillation, achieve similar functional outcomes compared to men.[17] On the other hand, one large meta-analysis by Dmytriw et al.[12] and a nationwide registry study from Germany[11] found worse post-EVT outcomes in women, whereby the latter study showed that this discrepancy is mostly, if not completely, explained by confounding factors such as older age at stroke onset.

However, stroke care often does differ between women and men: in some studies, women were 13% less likely to receive intravenous thrombolysis than men in Western countries,[2,18] particularly in hospitals without specialized stroke unit care.[19] With regard to EVT, some studies reported undertreatment of women in the acute phase, while others suggested the opposite.[6,7,20] Due to their worse pre-stroke functional status, female AIS patients may also be at a greater risk of "withdrawal bias" during the acute and post-acute phase of stroke, which may aggravate undertreatment even further in a vicious cycle. It is currently not entirely clear to what extent outcomes in female EVT patients can attributed to their baseline status vs. undertreatment and delayed treatment.[21]

One reason for the similar outcomes between women and men undergoing EVT in Saskatoon, despite the slightly older age of


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**Table 1:** Baseline characteristics of the entire patient sample and of women vs. men

| Variable | Entire patient sample (n = 303) | Women (n = 144) | Men (n = 159) | P-value* |
|---|---|---|---|---|
| Age (years) – median (IQR) | 73 (62–81), n = 303 | 77.5 (66–85), n = 144 | 71 (59–78) n = 159 | <0.001 |
| NIHSS at baseline – median (IQR) | 17 (11–20), n = 281 | 16 (11-20), n = 135 | 17 (12–20), n = 146 | 0.273 |
| Witnessed stroke onset – n (%) | 219/303 (72.3) | 104/144 (72.2) | 115/159 (72.3) | 1.000 |
| Occlusion location – n (%) | | | | 0.026 |
| Intracranial ICA | 74/301 (24.6) | 26/142 (18.3) | 48/159 (30.2) | |
| M1 segment | 182/301 (60.5) | 92/142 (64.8) | 90/159 (56.6) | |
| M2 segment | 19/301 (6.3) | 13/142 (9.2) | 6/159 (3.8) | |
| Basilar artery | 25/301 (8.3) | 10/142 (7.0) | 15/159 (9.4) | |
| Other posterior circulation | 1/301 (0.3) | 1/142 (0.7) | 0 (0) | |
| Baseline ASPECTS – median (IQR) | 8 (7–10), n = 303 | 8 (8–10), n = 144 | 8 (7–10), n = 159 | 0.423 |
| Collateral score – n (%) | | | | 0.633 |
| Poor | 28/303 (9.2) | 12/144 (8.3) | 16/159 (10.1) | |
| Intermediate | 60/303 (19.8) | 26/144 (18.1) | 34/159 (21.4) | |
| Good | 215/303 (71.0) | 106/144 (73.6) | 109/159 (68.6) | |
| Transport mode – n (%) | | | | 0.926 |
| Direct-to-CSC | 167/303 (55.1) | 80/144 (55.6) | 87/159 (54.7) | |
| PSC-to-CSC transfer | 108/303 (35.6) | 50/144 (34.7) | 58/159 (36.5) | |
| In-hospital stroke | 28/303 (9.2) | 14/144 (9.7) | 14/159 (8.8) | |

ASPECTS = Alberta stroke program early CT score; CSC = comprehensive stroke center; IQR = interquartile range; ICA = internal carotid artery; NIHSS = national institutes of health stroke scale; PSC = primary stroke center.
Note that "n" in each cell indicates the overall number of patients for which a particular variable was available.
*P-values for comparison of women vs. men derived from Wilcoxon rank sum test (continuous variables)/ Fisher's exact test (categorical variables).

**Table 2:** Unadjusted comparison of LKW to CSC arrival times, CSC arrival to reperfusion times, and final eTICI between women and men

| Outcome variable | Women (n = 144) | Men (n = 159) | p-value* |
|---|---|---|---|
| LKW to CSC arrival time (min) – median (IQR) | 232 (90–432), n = 130 | 230 (90–352), n = 145 | 0.575 |
| CSC arrival to reperfusion time** (min) – median (IQR) | 108 (80–149), n = 144 | 102 (77–141), n = 159 | 0.528 |
| Final eTICI score – n (%) | | | 0.800 |
| eTICI 0 | 3/142 (2.1) | 6/158 (3.8) | |
| eTICI 1 | 1/142 (0.7) | 1/158 (0.6) | |
| eTICI 2a | 6/142 (4.2) | 4/158 (2.5) | |
| eTICI 2b | 26/142 (18.3) | 30/158 (19.0) | |
| eTICI 2c | 33/142 (23.2) | 44/158 (27.9) | |
| eTICI 3 | 73/142 (51.4) | 73/158 (46.2) | |

CSC = comprehensive stroke center; eTICI = expanded thrombolysis in cerebral infarction; IQR = interquartile range; LKW = last known well.
Note that "n" in each cell indicates the overall number of patients for which a particular variable was available.
*P-values for comparison of women vs. men derived from Wilcoxon rank sum test (time variables)/ Fisher's exact test (final eTICI).
**In case no reperfusion could be achieved (eTICI 0-2a), the last intracranial run time was used as a surrogate for reperfusion time.

women, may be that Saskatchewan has a uniform acute stroke pathway, whereby patients are directly triaged to stroke centers (PSC or CSC) if an acute stroke is suspected by the pre-hospital team, and hospitals that neither provide thrombolysis nor EVT are bypassed. Although one would intuitively think that this is the case in most jurisdictions, this workflow is not explicitly established in some geographies.

Additionally, some studies in which women suffered worse 90-day functional post-EVT outcomes than men were conducted in jurisdictions with private healthcare systems,[22,23] where access to stroke rehabilitation programs depends on the individual patient's financial situation and employment. Since women may work more often part-time, and women's wages are on average lower[24] in almost any country, one may hypothesize that many women simply cannot afford stroke care, which may, in part, explain the observed discrepancies. Canada, on the other hand, has a publicly funded healthcare system where access to acute stroke care and post-stroke rehabilitation is, at least in theory, relatively equal for both sexes irrespective of the patient's financial situation. That being said, few studies that reported inferior post-EVT outcomes in women were conducted in countries with publicly funded healthcare systems such as Germany.[11]

In the current study, women did have a higher age at stroke onset and thus a poorer baseline functional status. However, the NIHSS scores were similar to male patients, and none of the time metrics captured in the pre-hospital an in-hospital phase differed between women and men, neither did technical EVT success rates or clinical outcomes at 90 days. It seems that the timely high-quality stroke care provided to female EVT patients could "offset" the higher age at stroke onset. Thus, EVT should be provided to female EVT patients even if their baseline characteristics are more unfavorable compared to their male counterparts, since it seems that they can nevertheless achieve similar good outcomes compared to men. This also means that sex-specific


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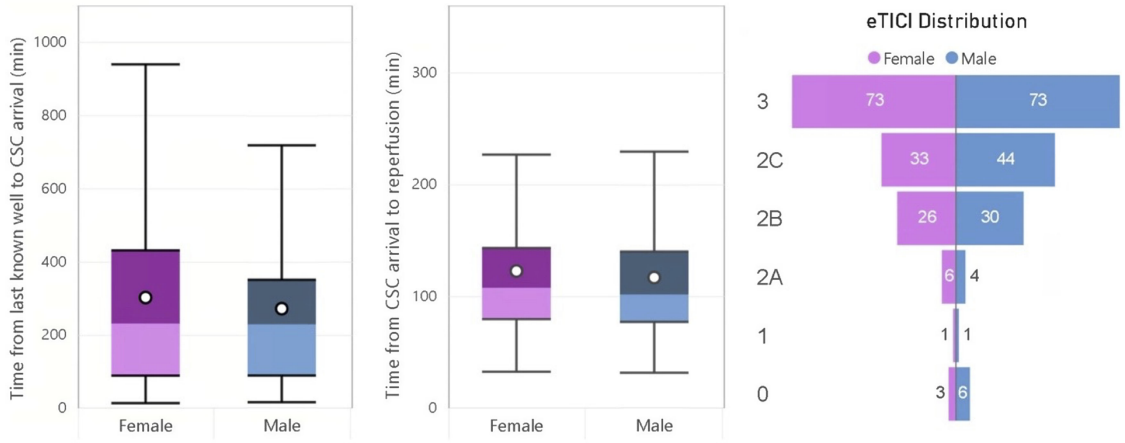


**Figure 2:** Time from last known well to CSC arrival in min (A), time from CSC arrival to reperfusion in min (B), and final expanded thrombolysis in cerebral infarction score (C) in women vs. men who underwent EVT. White dots in the box plots represent means. Numbers in the bars in (C) represent patient numbers.

undertreatment and withdrawal bias should be investigated and addressed whenever such sex discrepancies are identified.

### *Limitations*

This study has several limitations. First, only patients undergoing EVT were included, and we were therefore unable to investigate potential biases with regard to patient selection for EVT. In other words, we could not exclude the possibility that EVT selection criteria for women were more stringent or lenient compared to men. It is also possible that the time of presentation/time since LKW differed between women and men in such a way that women presented later and were thus more often excluded from EVT, or vice versa. Therefore, we will aim to investigate sex differences a more inclusive patient sample that included both patients treated and not treated with EVT in a future study. Second, we performed analyses stratified by patient sex rather than gender. While sex refers to biological factors, the term gender encompasses social roles, behaviors, and expressions[25] and is arguably the more important concept in the setting acute stroke care. In older generations, which account for the majority of EVT patients, however, the number of transgender individuals is thought to be low (although it is unclear if there are generational differences in disclosure/self-identification) and sex can likely be reasonably used as a proxy for gender.[26] Third, our data are a from a single Canadian province with a single CSC and the results may therefore not be generalizable to other geographic regions or countries. Lastly, we are limited by data availability; our patient sample included all patients treated with EVT, but we cannot reliably report the total number of strokes having occurred in the province during this timeframe. As such, we cannot definitively comment on the percentage of male and female patients undergoing EVT among all eligible patients.

## Conclusion

Women undergoing EVT in the province of Saskatchewan between 2017 and 2022 were on average older compared to men at the time of their stroke onset. However, despite this age discrepancy, women were treated just as fast and achieved similar technical and clinical EVT outcomes compared to male patients.

**Supplementary material.** The supplementary material for this article can be found at https://doi.org/10.1017/cjn.2023.286.

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**Author contribution.** Nima Kashani and Johanna M. Ospel are contributed equally.

JO, NK, GH, RW, MK, LP: data curation, data analysis and interpretation, drafting, and critical revision of the manuscript and figures. Remaining authors: data interpretation and critical revision of the manuscript.

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