Research Square

Preprints are preliminary reports that have not undergone peer review. They should not be considered conclusive, used to inform clinical practice, or referenced by the media as validated information.

Could The “Modified 8 D’s of Stroke Care” Improve Sex Disparities in Door-to-Needle Time in Acute Ischemic Stroke?

Meilka Jameie
Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran. https://orcid.org/0000-0002-2028-9935

Mana Jameie
Cardiovascular Diseases Research Institute, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran https://orcid.org/0000-0001-6382-0346

Ghasem Farahmand
Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Saba Ilkhani
Surgery and Vascular Surgery Department, Shahid Beheshti University of Medical Sciences, Tehran, Iran https://orcid.org/0000-0003-1233-1141

Hana Magrouni
Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Zahra Ranjbar
Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Sanaz Heydari
Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Mojtaba Shahbazi
Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Maryam Kaeedi
Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Rosita Amiri
Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Fateme Alizade

Neurology Department, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Pargol Balali

Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran.

Mobina Amanollahi

Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran.

Mahnaz Varedi

Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran.

Bahareh Pourghaz

Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran.

Mojdeh Ghabaee (mojdeh.ghabaee@gmail.com)

Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran. https://orcid.org/0000-0002-1822-389X

Research Article

Keywords: Ischemic Stroke, Thrombolytic Therapy, Tissue Plasminogen Activator, Door-to-Needle time, Health Status Disparities, D's of stroke care

Posted Date: January 12th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1249644/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

---

Abstract

Background and objective

Door-to-needle (DTN) time is an important factor in stroke settings for which studies have reported delays in women, resulting in worse stroke outcomes. We aimed to evaluate whether our modified algorithm could reduce sex disparities, especially in DTN.

Methods

This longitudinal cohort study was conducted between September 1, 2019, and August 31, 2021, at a comprehensive stroke center. Previously we utilized the conventional “D’s of stoke care” for timely management. The “modified 8 D’s of stroke care” was designed by our team in September 2020. Patients were analyzed in two groups: group 1, before, and group 2, after employing the modified algorithm. Sex as the main variable of interest along with other selected covariates were regressed towards the DTN, using univariable and multivariable logistic regressions.

Results

We enrolled 47 and 56 patients who received intravenous thrombolysis (IVT) in groups 1 and 2, respectively. Although there was a significant difference in DTN≤ 1 hour in group 1 (36% of females vs. 52% of males, p= 0.019), it was not significantly different in group 2 anymore (48% of females vs. 48.4% of males, p= 0.97). Furthermore, regression analysis showed being female was a significant predictor of DTN> 1 hour in group 1 (aOR= 6.65, p= 0.02), while after the modified algorithm gender was not a predictor of delayed DTN anymore.

Conclusion

Although we have a long way to achieve performance measures in developed countries, we seem to have succeeded in reducing gender disparities in DTN using the modified algorithm.

Introduction

Gender differences in stroke and especially the sex disparities in the treatment of stroke are emerging as an issue of interest in the past few years [1–8]. Stroke, specifically ischemic stroke, is the second leading cause of mortality and disability in the general population and also in women according to the Global Burden of Disease 2019 (GBD) [9, 10]. Among the Iranian population, stroke accounts for 10.46% of total deaths and 12.5% of female deaths [9], with the incidence rates considerably higher than in Western countries [11]. A recent systematic review along with other studies [11, 12] suggested that generally the risk of stroke in Iran is not affected by gender [13].

It is suggested that women have a higher lifetime risk of stroke [1], emphasizing the importance of reducing possible sex disparities in acute stroke settings for providing equal and timely treatment.

Previous researches have revealed that even after adjusting for confounders, women have poorer outcomes following a stroke [14]. Older age at the time of stroke, worse pre-stroke functional status, and multiple comorbidities in women are some of the suggested reasons for this issue [14–17]. In the past decade, studies have been conducted on the disparities in the quality of care provided to men and women in the stroke care units [4–6, 18, 19]. Pre-hospital and in-hospital delays in diagnostic and treatment procedures, including delays in door-to-needle time (DTN) - a pivotal factor for patients receiving recombinant tissue plasminogen activator (r-tPA)- are possible contributors to worse outcomes in women [15,19–22]. Hence, more attention is drawn to gender disparities in DTN duration recently, albeit their findings are inconsistent [3–5, 18, 19, 23].

The “D’s of stroke care” is a mnemonic device to facilitate the diagnosis and treatment of acute ischemic stroke (AIS) in patients who are eligible for receiving intravenous thrombolysis (IVT) [24, 25]. This study is designed to evaluate the implications of a modified form of this algorithm, called the “modified 8 D’s of stroke care”, which is discussed in detail elsewhere [26], on possible sex disparities, especially focusing on DTN time.

Materials And Methods

Study Setting

This single-center longitudinal cohort study was conducted in two equal periods between September 1, 2019, and August 31, 2021, at a certified comprehensive stroke center affiliated with Tehran University of Medical Sciences (TUMS), Tehran, Iran. Our stroke team includes attending neurologists, nurse practitioners, stroke fellows, and neurology residents. Consecutive data of the patients were gathered prospectively and the analyses were conducted retrospectively. Our specialized stroke care team provided the patients with full diagnostic and therapeutic measures.

The “D’s of stoke care” describes 8 major steps in diagnosis and treatment of stroke to improve obstacles in IVT with r-tPA [24, 25]: detection (D1), dispatch (D2), delivery (D3), door (D4), data (D5), decision (D6), drug (D7), and disposition (D8). Our stroke care team designed a modified form of this algorithm in September 2020 called the “modified 8 D’s of stroke care” with the primary aim of overcoming some of the obstacles in timely treatment in our center [26]. This modified algorithm was developed with a special focus on splitting D4 and D6 steps into the following times: patients’ arrival to the emergency room (D4-A), early assessment by the neurologist (D4-B), neurologist decision on patient’s eligibility to receive r-tPA (D6-A), and patient’s transfer to the stroke care unit (D6-B). In this study, patients were classified into two separate groups to evaluate the possible effect of the modified algorithm on sex disparities, particularly on DTN. Group 1 included patients managed with the conventional “D’s of stroke care” between September 1, 2019, and August 31, 2020. Group 2 included patients managed with the “modified 8 D’s of stroke care” between September 1, 2020, and August 31, 2021. Patients’ data were collected from the hospital web-based registry [27].

During the first and second periods, the respective total number of patients who presented to the emergency room with stroke-related symptoms initiated in less than 24 hours were 359 and 412. Of the 217 and 251 patients diagnosed with AIS, 47 and 56 patients eligible for receiving r-tPA with symptom onset less than 4.5 hours were included in this study. Patients who underwent bridging therapy (the combination of r-tPA and mechanical thrombectomy) were excluded.

Study measures

The patient's eligibility to receive r-tPA was defined according to the American Heart Association/American Stroke Association (AHA/ASA) guidelines and evaluated by the neurology team [28]. Patients' stroke severity was assessed using the NIHSS score (National Institute for Health Stroke Scale), and categorized as follow: minor stroke (1 ≤ NIHSS ≤ 4), moderate stroke (5 ≤ NIHSS ≤ 15), moderate to severe stroke (16 ≤ NIHSS ≤ 20), and severe stroke (21 ≤ NIHSS ≤ 42). Considering the mode of arrival to the hospital, patients were as follow: patients who used the emergency medical services with pre-notification (EMS group), those who were brought to the hospital with personal vehicle (private group), and those who had a stroke during their hospitalization for other reasons (in-hospital group). DTN time was defined as the difference between the door-time and the needle-time and reported by neurology residents. Door-time is defined as the time at which the patient presented at the emergency room (D4 in the conventional algorithm and D4-A in the modified algorithm). For hospitalized patients, the time of examination by the neurologist (D4-B) was considered as the door-time [23]. Needle-time is defined as the time of r-tPA administration (D7). DTN was categorized as less than 1 hour and more than 1 hour (delayed DTN) according to recommended DTN by AHA/ASA guidelines [28]. Patients who were admitted to the hospital between 3:00 pm to 7:00 am were defined as out-of-hour admissions (OOHA).

Statistical Analysis

Continuous variables are presented in mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Categorical variables were compared using the chi-squared test. Continuous variables were compared using independent t-test (for normally distributed variables) or Mann-Whitney U test (for non-normally distributed variables). To evaluate the relationship between gender and DTN time> 1 hour, univariable and multivariable binary logistic regressions were performed separately for both conventional and modified groups and the results are presented with odds ratio (OR), 95 % confidence interval (CI), and p-value. Covariates included in the multivariable regression were chosen based on the existing literature and our medical knowledge, including age, admission NIHSS, out-of-hour admission, and mode of arrival [3,23,29,30]. Data were analyzed using SPSS software, version 20. P-values less than 0.05 were considered significant.

Results

Baseline characteristics of female and male patients in both conventional (group 1) and modified algorithm (group 2) groups are shown in table 1. The mean age of females was 73.5 in group 1 and 75.64 in group 2. Female patients were significantly older at the time of stroke than men in group 1 (p-

value: 0.004). However, no significant difference was observed in this regard in group 2. Stroke severity based on categorized NIHSS was significantly different between men and women in group 2, with a higher proportion of females presented with moderate and moderate-to-severe stroke than men (100% of females versus 74% of males presented with at least moderate severity, p-value= 0.019). During the whole study period, more than 80% of both genders were transferred to the hospital with pre-notification by emergency medical services (EMS). Apart from smoking status, no significant differences were seen between men and women considering cardiovascular risk factors in neither of the groups. Additionally, in-hospital mortality was not significantly different between men and women during the whole study period (table 1).

After employing the modified algorithm, in women, median DTN was decreased from 75 to 65 minutes and the 75th percentile from 90 to 74 minutes which is clinically considerable, however, the difference was not statistically significant (p-value for medians: 0.11 and for means: 0.36). Furthermore, women significantly had DTN≤ 1 hour less often compared to men in the conventional group (36% versus 52%, p-value=0.019), while after employing the modified algorithm, DNT time was not significantly different between them anymore (48% of females versus 48.4% of males, p-value = 0.97) (table 1).

Binary logistic regression findings in the conventional and modified algorithm groups are shown in table 2. Variables such as age, mode of arrival, NIHSS at admission, and out-of-hour admissions, were not significantly related to DTN> 1 hour, in both groups, neither in univariable nor multivariable analyses. Univariable regression showed a significant relationship between gender and having DTN> 1 hour in the conventional group: females' odds for having DTN> 1 hour was 3.72 times that of males (p-value= 0.03). After adjusting for possible confounders, being female was still a significant predictor for having DTN> 1 hour in this group, with the odds ratio increasing to 6.65 (p-value= 0.02). Interestingly, after employing the modified algorithm, female gender was not a significant predictor of having DTN> 1 hour, even after adjusting for other covariates (p-value in univariable model= 0.98, p-value in multivariable model= 0.77) (table 2).

Discussion

Regarding the sex disparities between men and women, we found that female patients were significantly older at the time of stroke than men in the first group, although this was not the case with the second group. The age difference in the first period is consistent with previous findings that reported women were significantly older at the time of stroke [7,31–34]. While no significant difference was observed in the severity of stroke between men and women during the first period, the pattern of presentation has changed in the second group, with a higher proportion of women presenting with moderate and moderate-to-severe stroke compared to men. This finding aligns with previous claims that women had a higher stroke severity at admission [4, 7, 34]. There were no sex differences considering the mode of arrival and in-hospital mortality between men and women during the whole study period. Remarkably, we found that although DTN was previously affected by gender using the conventional algorithm (females had almost 4 times odds for delayed DTN as males, which increased almost to 6.5 times after adjusting for

age, NIHSS at admission, mode of arrival, and time of admission), after employing the modified algorithm, being female was no longer associated with DTN> 1h, even after adjusting for important covariates. This interesting finding implies that using the modified algorithm with a special focus on D4 and D6 is plausible to alleviate sex disparities in DTN time, thereby improving females' stroke outcomes. This result is consistent with findings from GWTG-Stroke (Get with The Guidelines-Stroke) study that showed adhering to a stroke performance program could narrow the gap in performance measures between men and women [4].

There is a discrepancy between study findings on gender disparities in DTN duration. The FL-PR CReSD Study (Florida-Puerto Rico Collaboration to Reduce Stroke Disparities) suggested after adjusting for multiple covariates, including the ones that we accounted for, being female is an independent predictor for having DTN≤ 1 hour (OR: 0.81, CI: 0.72-0.92) [3]. Similarly, large registry-based longitudinal studies from GWTG-Stroke also found that women had significantly less odds for having DTN within 1 hour (OR:0.83) [4]. A study among Dutch patients also revealed a significant relationship between female gender and having severely extended DTN (OR 1.17, 95% CI 1.05–1.31) [23]. In contrast, according to European studies, the average DTN for men and women are almost identical or differ only for a few minutes (2013; DTN in women: 67 [48-92] versus 66 [47-90] in men (P-value: 0.002), 2014; DTN: 49 [34-70] in women versus 48 [35-68] in men) [5, 18].

Generally, delayed diagnosis and the inability to determine eligibility are some of the most important reasons for DTN delay [19]. Various reasons are suggested for longer DTN in women, although these reasons are not clear yet [20]. Some of these factors are related to physicians' decisions on patients' eligibility and some others are patient-related factors. Regarding the former factors, studies suggested that physicians may be more reluctant to use r-tPA in women because they tend to be older or present with more severe stroke than men [33–35]. Additionally, several studies have revealed an increased prevalence in stroke mimics as well as non-traditional stroke manifestations in women which could affect physicians' decisions considering the patients' eligibility for receiving r-tPA [7,36–38]. Moreover, previous studies suggested women are less likely to receive timely neuroimaging which could lead to longer DTN [35, 39], although some other studies found no disparity in this regard [32]. Considering the patient-related factors, some researches showed that women are less likely to consent to thrombolysis [4, 40]. Another possible rationale is that women are more likely to be widowed or living alone, resulting in delayed symptoms recognition, later hospital arrival, difficulty in obtaining the time of symptom onset from a family member, and ultimately eventuating in difficulty with physicians' decision on the patient's eligibility to receive r-tPA [17, 33].

Limitations and Strengths

This study was conducted at a single certified comprehensive stroke center, limiting its generalizability especially to the population who does not have access to specialized stroke care. However, our results were in line with large multicenter studies. We attempted to consider every possible factor that could

affect the association between gender and DTN, though there might be some residual undetected confounding factors. We will gather more data in the following years and make every effort to treat both men and women as fast as possible.

Conclusion

The DTN difference between men and women was reduced during the second period of our investigation and being female was not a significant predictor of delayed DNT anymore. It can thus be suggested that the implementation of the modified algorithm in which more emphasis is placed on the patient's arrival time to the emergency room (D4-A) and timing of visit by a neurologist (D4-B), as well as the time of neurologist decision on patient’s eligibility to receive r-tPA (D6-A) and the time of patient’s transfer to the stroke care unit (D6-B), could help reduce DTN difference between men and women. However, the reasons for sex disparities in stroke care are numerous, necessitating further development of quality improvement programs with a special focus on interventions to reduce such disparities.

Declarations

Statements and Declarations:

Authors disclose no financial or non-financial interests that are directly or indirectly related to the work submitted for publication.

Acknowledgment

This study has been funded and supported by the Tehran University of Medical Sciences (TUMS, Grant No. 99.2.118.48888). Research Ethics Committees of School of Medicine-Tehran University of Medical Sciences approved the algorithm (identification code: IR.TUMS.MEDICINE.REC.1399.382). We thank all the patients and staff in our center for making this study possible.

References

1. Collaborators GLRoS. Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. *New England Journal of Medicine*. 2018;379(25):2429–2437.
2. Bushnell C, Howard VJ, Lisabeth L, et al. Sex differences in the evaluation and treatment of acute ischaemic stroke. *The Lancet Neurology*. 2018;17(7):641–650.
3. Oluwole SA, Wang K, Dong C, et al. Disparities and Trends in Door-to-Needle Time: The FL-PR CReSD Study (Florida-Puerto Rico Collaboration to Reduce Stroke Disparities). *Stroke*. 2017;48(8):2192–2197. doi:10.1161/STROKEAHA.116.016183
4. Asdaghi N, Romano JG, Wang K, et al. Sex disparities in ischemic stroke care: FL-PR CReSD study (Florida–Puerto Rico Collaboration to Reduce Stroke Disparities). *Stroke*. 2016;47(10):2618–2626.

5. Lorenzano S, Ahmed N, Falcou A, et al. Does sex influence the response to intravenous thrombolysis in ischemic stroke? Answers from safe implementation of treatments in Stroke-International Stroke Thrombolysis Register. *Stroke*. 2013;44(12):3401–3406.
6. De Ridder I, Dirks M, Niessen L, Dippel D. Unequal access to treatment with intravenous alteplase for women with acute ischemic stroke. *Stroke*. 2013;44(9):2610–2612.
7. Gall S, Donnan G, Dewey H, et al. Sex differences in presentation, severity, and management of stroke in a population-based study. *Neurology*. 2010;74(12):975–981.
8. Reeves M, Bhatt A, Jajou P, Brown M, Lisabeth L. Sex differences in the use of intravenous rt-PA thrombolysis treatment for acute ischemic stroke: a meta-analysis. *Stroke*. 2009;40(5):1743–1749.
9. Network GBoDC. Global Burden of Disease Study 2019 (GBD 2019) Reference Life Table. Institute for Health Metrics and Evaluation (IHME). 2021.
10. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics—2021 update: a report from the American Heart Association. *Circulation*. 2021;143(8):e254-e743.
11. Azarpazhooh MR, Etemadi MM, Donnan GA, et al. Excessive incidence of stroke in Iran: evidence from the Mashhad Stroke Incidence Study (MSIS), a population-based study of stroke in the Middle East. *Stroke*. 2010;41(1):e3-e10.
12. Amiri A, Kapral MK, Thrift AG, et al. The incidence and characteristics of stroke in urban-dwelling Iranian women. *Journal of Stroke and Cerebrovascular Diseases*. 2018;27(3):547–554.
13. Tabrizi R, Lankarani KB, Kardeh B, Akbari H, Azarpazhooh MR, Borhani-Haghighi A. A Comprehensive Systematic Review and Meta-analysis on the Risk Factors of Stroke in Iranian Population. *Archives of Iranian Medicine*. 2021;24(1):64–77.
14. Lisabeth LD, Reeves MJ, Baek J, et al. Factors influencing sex differences in poststroke functional outcome. *Stroke*. 2015;46(3):860–863.
15. Maestroni A, Mandelli C, Manganaro D, et al. Factors influencing delay in presentation for acute stroke in an emergency department in Milan, Italy. *Emergency Medicine Journal*. 2008;25(6):340–345.
16. Reid JM, Dai D, Gubitz GJ, Kapral MK, Christian C, Phillips SJ. Gender differences in stroke examined in a 10-year cohort of patients admitted to a Canadian teaching hospital. *Stroke*. 2008;39(4):1090–1095.
17. Kapral MK, Fang J, Hill MD, et al. Sex differences in stroke care and outcomes: results from the Registry of the Canadian Stroke Network. *Stroke*. 2005;36(4):809–814.
18. 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(6):1632–1638.
19. Kamal N, Sheng S, Xian Y, et al. Delays in door-to-needle times and their impact on treatment time and outcomes in get with the guidelines-stroke. *Stroke*. 2017;48(4):946–954.
20. Lisabeth LD, Brown DL, Morgenstern LB. Barriers to intravenous tissue plasminogen activator for acute stroke therapy in women. *Gender medicine*. 2006;3(4):270–278.

21. Reeves MJ, Bushnell CD, Howard G, et al. Sex differences in stroke: epidemiology, clinical presentation, medical care, and outcomes. *The Lancet Neurology*. 2008;7(10):915–926.
22. Fonarow GC, Zhao X, Smith EE, et al. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. *Jama*. 2014;311(16):1632–1640.
23. Kuhrij LS, Marang-van de Mheen PJ, van den Berg-Vos RM, de Leeuw F-E, Nederkoorn PJ. Determinants of extended door-to-needle time in acute ischemic stroke and its influence on in-hospital mortality: results of a nationwide Dutch clinical audit. *BMC neurology*. 2019;19(1):1–8.
24. Jauch EC, Cucchiara B, Adeoye O, et al. Part 11: adult stroke: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(18_suppl_3):S818-S828.
25. Hazinski M. Demystifying recognition and management of stroke. *Curr Emerg Cardiac Care*. 1996;7:8.
26. Ghabaee Mojdeh BP, Pourghaz Bahareh. Stroke Patient Workflow: Optimizing and Simplifying of the 8Ds in Acute Stroke Care. *Journal of Registry Management*. 2021;48(2):72–74.
27. Shahraki AD, Safdari R, Shahmoradi L, Malak JS, Pourghaz B, Ghabaee M. Acute Stroke Registry Planning Experiences. *Journal of registry management*. 2018;45(1):37–42.
28. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. Dec 2019;50(12):e344-e418. doi:10.1161/str.0000000000000211
29. McVerry F, Hunter A, Dynan K, et al. Country-wide analysis of systemic factors associated with acute ischemic stroke door to needle time. *Frontiers in neurology*. 2019;10:676.
30. Davis NW, Bailey M, Buchwald N, Farooqui A, Khanna A. Factors that Influence Door-to-Needle Administration for Acute Stroke Patients in the Emergency Department. *Journal of Neuroscience Nursing*. 2021;53(3):134–139.
31. Appelros P, Stegmayr B, Terént A. Sex differences in stroke epidemiology: a systematic review. *Stroke*. 2009;40(4):1082–1090.
32. Madsen TE, Choo EK, Seigel TA, Palms D, Silver B. Lack of gender disparities in emergency department triage of acute stroke patients. *Western Journal of Emergency Medicine*. 2015;16(1):203.
33. Glader E-L, Stegmayr B, Norrving B, et al. Sex differences in management and outcome after stroke: a Swedish national perspective. *Stroke*. 2003;34(8):1970–1975.
34. Roquer J, Campello AR, Gomis M. Sex differences in first-ever acute stroke. *Stroke*. 2003;34(7):1581–1585.
35. Smith MA, Lisabeth LD, Brown DL, Morgenstern LB. Gender comparisons of diagnostic evaluation for ischemic stroke patients. *Neurology*. 2005;65(6):855–858.

36. Lisabeth LD, Brown DL, Hughes R, Majersik JJ, Morgenstern LB. Acute stroke symptoms: comparing women and men. *Stroke*. 2009;40(6):2031–2036.
37. Jerath NU, Reddy C, Freeman WD, Jerath AU, Brown RD. Gender differences in presenting signs and symptoms of acute ischemic stroke: a population-based study. *Gender Medicine*. 2011;8(5):312–319.
38. Merino JG, Luby M, Benson RT, et al. Predictors of acute stroke mimics in 8187 patients referred to a stroke service. *Journal of Stroke and Cerebrovascular Diseases*. 2013;22(8):e397-e403.
39. Burton KR, Kapral MK, Li S, et al. Predictors of diagnostic neuroimaging delays among adults presenting with symptoms suggestive of acute stroke in Ontario: a prospective cohort study. *CMAJ open*. 2016;4(2):E331.
40. Kapral MK, Devon J, Winter A-L, Wang J, Peters A, Bondy SJ. Gender differences in stroke care decision-making. *Medical care*. 2006:70–80.

Tables

Table 1. Baseline characteristics of patients in the conventional and modified algorithm groups

Variable	Conventional algorithm (n=47)			Modified algorithm (n=56)		
	Male (n=25)	Female (n=22)	P-value	Male (n=31)	Female (n=25)	P-value
Age (year), mean ± SD	63.28± 11.98	73.5 ± 11.14	0.004*	71.74 ± 15.77	75.64 ± 15.77	0.27
Past medical history, n (%)						
Diabetes	9 (36)	9 (40.9)	0.41	12 (38.7)	11 (44)	0.32
Hypertension	19 (76)	15 (68)	0.56	24 (77.4)	18 (72)	0.64
Previous stroke	5 (20)	4 (18)	0.73	6 (19.4)	6 (24)	0.67
AF	7 (28)	5 (22.7)	0.54	8 (25.8)	5 (20.8)	0.67
Dyslipidemia	19 (76)	16 (72.7)	0.76	24 (77.4)	19 (76)	0.9
Current smoking, n (%)	8 (32)	1 (4.5)	0.001*	11 (28.2)	1 (2.5)	0.001*
Arrival, n (%)			0.35			0.64
EMS	21 (84.0)	18 (81.8)		26 (83.9)	23 (92.0)	
Private	1 (4.0)	3 (13.6)		2 (6.5)	1 (4.0)	
In-hospital	3 (12.0)	1 (4.5)		3 (9.7)	1 (4.0)	
OOHA ⊠, n (%)	15 (60)	15 (68.2)	0.56	19 (61.3)	16 (64)	0.83
Admission NIHSS, mean ± SD	10.56 ± 6.03	11.36 ± 5.43	0.63	9.7 ± 4.9	11.3 ± 4.0	0.18
Stroke severity, n (%)			0.61			0.019*
1≤ NIHSS ≤4	2 (8)	3 (13.6)		8 (25.8)	0	
5≤ NIHSS ≤15	17 (78)	14 (63.8)		20 (64.5)	20 (80)	
16≤ NIHSS ≤20	4 (16)	4 (18.2)		3 (9.7)	5 (20)	
21≤ NIHSS ≤42	2 (8)	1 (4.5)		0	0	
DTN (minute), median [IQR]	60 [45 - 90]	75[47.5 - 92.5]	0.08	62 [54 - 75]	65 [55 - 74]	0.72
DTN≤ 1h, n (%)	13 (52)	8 (36.4)	0.019*	15 (48.4)	12 (48)	0.97
In-hospital mortality, n (%)	3 (12)	1 (4.5)	0.36	4 (12.9)	5 (20)	0.47

Table 1. SD: standard devotion, NIHSS: National Institute for Health Stroke Scale, DTN: door-to-needle time.

 Out-of-hour admission

*significant at p-value <0.05

Table 2. Binary logistic regression results in the conventional and modified algorithm groups

	Conventional algorithm (n=47)				**Modified algorithm (n=56)**			
	Univariable		**Multivariable**		**Univariable**		**Multivariable**	
	OR (CI)	P-value	OR (CI)	P-value	OR (CI)	P-value	OR (CI)	P-value
Female	3.72 (1.11 - 12.45)	0.03*	6.65 (1.29 - 34.46)	0.02*	1.02 (0.35 - 2.91)	0.98	0.84 (0.26 - 2.66)	0.77
Age	1.02 (0.97 - 1.07)	0.32	0.96 (0.89 - 1.03)	0.25	1.02 (0.97 - 1.06)	0.34	1.03 (0.99 - 1.09)	0.16
Arrival								
EMS, ref	-	0.42	-	0.27	-	0.93	-	0.95
Private	0.38 (0.03 - 3.32)	0.34	0.20 (0.012 - 3.45)	0.76	1.63 (0.14 - 19.18)	0.69	1.53 (0.12 - 19.48)	0.74
In-hospital	0.38 (0.03 - 3.32)	0.34	0.67 (0.05 - 8.18)	0.07	0.00	0.99	0.00	0.99
OOHA	3.13 (0.88 - 11.16)	0.08	4.05 (0.90 - 18.20)	.068	0.96 (0.33 - 2.84)	0.94	1.15 (0.35 - 3.75)	0.81
Admission NIHSS	1.36 (0.59 - 3.128)	0.46	1.11 (0.97 - 1.26)	0.14	1.01 (0.9 - 1.13)	0.85	0.95 (0.35 - 3.76)	0.48

Table 2. The odds ratio is reported for having a door-to-needle time of more than 1 hour.

NIHSS: National Institute for Health Stroke Scale, EMS: emergency medical service.

*significant at p-value <0.05

- Out-of-hour admission