LITERATURE REVIEW

Unique Stroke Symptoms in Women: A Review

CE 1.0 ANCC Contact Hour

Renee Colsch, Glenda Lindseth

ABSTRACT

Background: Research suggests that there is a delay in recognizing unique stroke symptoms in women by both healthcare professionals and the general population. The purpose of this review was to identify and summarize the most relevant literature regarding recognition and assessment of unique stroke symptoms in women. **Methods:** Literature review using PubMed, CINAHL, ERIC, MEDLINE, PsycINFO, and Google Scholar was used to search literature describing unique stroke symptoms. **Results:** Unique stroke symptoms, female sex, and race are associated with delayed recognition, treatment, misdiagnosis, and outcomes. Women experience unique symptoms of nausea/vomiting, headache, dizziness, and cognitive dysfunction more often than men. Stroke assessment tools and registries recognize 1 to 4 of the 11 unique stroke symptoms in women, no study directly assesses the sensitivity and specificity of these unique symptoms, and all studies included women and men. **Conclusions and Nursing Implications:** Current assessment tools and registries are not sensitive and specific to measuring unique stroke symptoms in women. Accurately identifying unique stroke symptoms in women may reduce presentation and treatment time, minimizing misdiagnoses and poor patient outcomes.

Keywords: assessment, sex, stroke, unique, women

Stroke is the fifth leading cause of death and remains the leading cause of disability in the United States.[1] Annually, women make up 60% of all stroke deaths in the United States.[1] Women may experience unique stroke symptoms (uSS).[2–17] Furthermore, research suggests there has been a delay in recognizing uSS by both healthcare professionals and the general population.[18] For this study, we have defined uSS as symptoms that are unusual for that individual, regardless of the presence of common stroke symptoms.

It is unclear how uSS in women (uSSw) are described and whether current stroke assessment tools and national stroke registries are sensitive and specific to early recognition of uSS. Therefore, the purpose of this review was to identify and summarize the most relevant literature regarding recognition and assessment of uSS and uSSw. Specific aims for this review were (1) to describe uSSw terminology, (2) to describe uSS recognition by the general population and healthcare professionals, and (3) to identify the sensitivity and specificity of current stroke assessment tools and registries for common stroke symptoms and uSS.

This review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[19] PubMed, CINAHL, ERIC, MEDLINE, PsycINFO, and Google Scholar were used to search stroke assessment tools and registries describing uSSw. Key terms used in this search to identify relevant literature include text words, title, abstract, and medical subject headings. Searches included the terms "stroke" or "cerebral vascular attack." These terms were combined using "and" individually with each of the following: "gender," "difference," "sex," "symptom," "women," "diagnosis," "assessment," "tool," "prehospital," "emergency," "scale," "screen," "unique," "nontraditional," "individual," "presentation," and "recognition." Articles were included if they addressed uSS; were published before July 2017 and less than 5 years old; addressed stroke recognition, tools, or registries; were published in English; were peer-reviewed; addressed ischemic stroke; and compared statistical differences in sex management of adult patients with stroke who were older than 18 years. The references from the included articles were manually searched to identify other relevant literature.

Literature was collected from 2012 to June 2017. Websites were scanned for gray literature. The Cochrane Grading of Recommendations, Assessment, Development,

Questions or comments about this article may be directed to Renee Colsch, MS RN, at renee.colsch@und.edu. She is a PhD Student, University of North Dakota, Grand Forks, ND, and an Assistant Professor, St. Catherine University, St. Paul, MN.

Glenda Lindseth, PhD RN FADA FAAN, is Professor, University of North Dakota, Grand Forks, ND.

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and Evaluation approach was used to assess studies for quality, study design, data reporting, and risk of bias. Included studies with tools or registries were rated as "high" or "low" based on the 6 domains of possible risk: selection, performance, detection, attrition, reporting, and other bias (Table 1).[25] Full-text articles were assessed for methodological quality (Figure 1). The number of extracted articles totaled 1378 with 438 duplicates. Google Scholar articles were removed for not meeting inclusion/exclusion criteria and totaled 687. The remaining titles and abstracts were scanned for relevance, related terms, and study purpose, with 225 studies excluded. After a manual review, 3 studies lacked data on uSS and were excluded. Twenty-five total articles met the review criteria.

Fifteen included articles described stroke assessment using several assessment tools and registries: Emergency Severity Index (ESI), National Institutes of Health Stroke Scale (NIHSS), Los Angeles Prehospital Stroke Screen (LAPSS), Cincinnati Prehospital Stroke Scale (CPSS), Face Arm Speech Test (FAST), Melbourne Ambulance Stroke Screen, Medic Prehospital Assessment for Code Stroke, Ontario Prehospital Stroke Screening Tool, and Recognition of Stroke in the Emergency Room. Stroke registries included multiethnic clinical registry, National Neurology Registry, Ontario Stroke Registry, China National Stroke Registry, Greater Cincinnati/Northern Kentucky Stroke Study, and Healthcare Cost and Utilization Project stroke risk questionnaire. A summary of 10 studies that assessed sensitivity and specificity is presented in Table 1, and a list of the 25 articles included in this review is presented as a document, Supplemental Digital Content 1 (available at http://links.lww.com/JNN/A144).

Terminology

Symptoms of stroke depend on where and how much of the brain tissue is deprived of blood supply and can be different depending on age, sex, and risk factors.[1,2] Common stroke symptoms are the hallmark signs of stroke.[1,2] However, a stroke can disrupt any nervous system function leading to uSS—symptoms that are unusual or different than the common stroke symptoms.[1–3,11] Although women and men can experience uSS, women experience these uSS more often, and these symptoms can be sudden, persistent, subtle, or general.[1–3,11] Using current literature and the National Stroke Association, the uSSw for this review included loss of consciousness or fainting, general weakness, difficulty breathing or shortness of breath, confusion, unresponsiveness or disorientation, sudden behavioral change, agitation, hallucination, nausea or vomiting, pain, seizures, and hiccups.[1,2,6,10,16,18,20–22,27] Common stroke symptoms include "sudden numbness or weakness of face, arm or leg, especially on one side of the body, sudden confusion, trouble speaking, or understanding, sudden trouble seeing in one or both eyes, sudden trouble walking, dizziness, loss of balance or coordination, and sudden severe headache with no known cause."[1,2]

In other studies, uSS have been described in terms such as "atypical," "nonspecific," "nontraditional," or "other." Some studies have addressed stroke symptoms as "sex differences" or "sex disparities." For example, 1 study listed "other" symptoms and then defined them as nausea/vomiting, pain, and ataxia.[3] Another study referred to "atypical" symptoms as symptoms associated with posterior circulation strokes.[4] These studies highlight the variations in terminology for describing uSS. Therefore, for this review, the term "unique" reflecting the National Stroke Association terminology was used.[2]

uSS and the General Population and Healthcare Professionals

Studies specifically addressing uSSw within the general population and healthcare professionals included men and were limited and few. Therefore, studies that included men and women were included in this review. In a literature review about sex differences in stroke, women presented with more uSS and delayed seeking treatment for both uSS and common stroke symptoms up to 3 times longer than men.[5] In 1 study, uSS and common stroke symptoms were poorly recognized among a nationally representative sample of women (N = 1205). The sample included 54% white, 17% Hispanic, 17% black, and 12% other ethnic races.[6]

Evidence in the literature indicates that a percentage of patients with stroke are initially misdiagnosed because of either uSS or stroke mimics—nonvascular conditions that present with strokelike symptoms. In 1 study, healthcare professionals were unable to regularly identify uSS in both women and men.[3] Stroke identification failure was greater with younger patients and those experiencing a decreased level of consciousness.[3] Of 2027 patients, 283 stroke cases were misdiagnosed initially for a different diagnosis when brain imaging revealed acute stroke later during the hospital stay.[3] The top 5 incorrect diagnoses included altered mental status (100, 35%), cardiac conditions other than myocardial infarction (33, 11%), myocardial infarction (19, 6%), infections (19, 6%), and other neurologic diagnoses (17, 6%) (n = 283).[3] In another study, 29 of 189 patients (15.3%) were not identified as having a stroke when first admitted to the hospital.[7] However, these patients were later discharged from a hospital with a confirmed diagnosis of stroke.[7] In a study of 29 patients, 64% (23) of the patients were initially misdiagnosed because of uSS.[8] Nurses' expertise

TABLE 1. Stroke Symptoms: Assessment Tools, Registries, and Differences

Author/Year	Subjects (Women and Men)	Grade	Assessment Tool/Registry	Stroke Symptom Sensitivity and Specificity, Range		Findings: 1 = Terminology; 2 = Number out of 11 Unique Symptoms in Women; 3 = Main Findings
				Common (95% CI)	Unique (95% CI)	
Madsen et al[11]/2015	N = 537	Low	ESI NIHSS	0.29–1.31 0.23–0.48	1.36–6.82 1.03–3.81	1. Unique symptoms referred to as ''atypical''2. 3/11 (SOB, n/v, ''generalized'' weakness)3. Unique symptoms had higher odds of being triaged to a non–critical care bed.
Arch et al[4]/2016	N = 465	Low	NIHSS	0.007–0.994	1.60–10.1	1. No reference to term ''unique''2. 1/11 (n/v)3. Misdiagnosed strokes contributed to nausea/vomiting, dizziness, and posterior strokes.
Wang et al[16]/2013	N = 6263	Low	CNSR	1.002–1.359	0.406–0.768	1. No reference to term ''unique''2. 1/11 (cognitive dysfunction)3. Delayed treatment associated with female sex, cognitive dysfunction, and headache or vertigo.
Fothergill et al[20]/2013	N = 2528	Low	FAST ROSIER	1.03–1.19 1.08–1.28	Not assessed or reported	1. No reference to term ''unique''2. 1/11 (LOC/syncope)3. Incorrect diagnoses included altered mental status, syncope, hypertensive emergency, systemic infection, and suspected acute coronary syndrome.
Brandler et al[21]/2014	Literature review	Low	CPSS LAPSS MASS Med PACS OPSS ROSIER FAST	0.93–4.87 2.16–13.46 1.83–7.2 0.97–1.24 4.64–8.68 1.07–1.28 1.02–1.19	Not assessed or reported	1. No reference to term ''unique'' 2. 4/11 (LOC, fainting, unresponsiveness/disorientation, seizures) 3. Prehospital stroke scales varied in their accuracy and missed up to 30% of acute strokes in the field.
Asimos et al[22]/2014	N = 2442	Low	CPSS LAPSS	77%–83% Sen. 44%–52% Sp. 71%–77% Sen. 43%–53% Sp.	Not assessed or reported	1. No reference to term ''unique''2. 4/11 (LOC, fainting, unresponsiveness or disorientation, seizures)3. The CPSS had a higher sensitivity; CPSS and LAPSS each had a specificity of 48%.
Chen et al[23]/2013	N = 1130	Low	LAPSS	75%–80% Sen. 85%–95% Sp.	Not assessed or reported	1. No reference to term ''unique''2. 4/11 (LOC, fainting, unresponsiveness or disorientation, seizures)3. 997/1130 patients clinically diagnosed with stroke

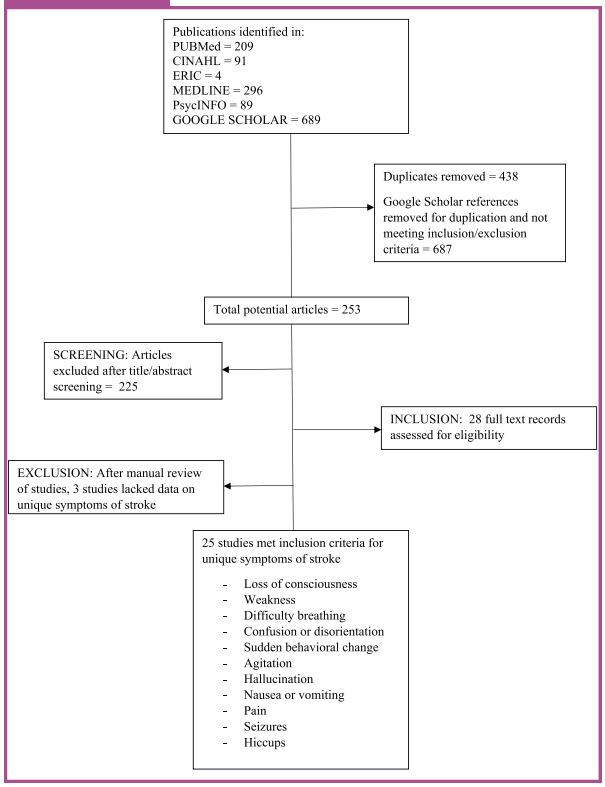
(continues)

TABLE 1. Stroke Symptoms: Assessment Tools, Registries, and Differences, Continued

Author/Year	Subjects (Women and Men)	Grade	Assessment Tool/Registry	Stroke Symptom Sensitivity and Specificity, Range		Findings: 1 = Terminology; 2 = Number out of 11 Unique Symptoms in Women; 3 = Main Findings
				Common (95% CI)	Unique (95% CI)	
Madsen et al[3]/2016	N = 2027	Low	GCNKSS and NIHSS	0.31–0.99	0.31–4.84	1. No reference to term "unique"2. 1/11 (LOC)3. Altered mental status was the most common diagnosis among those with missed stroke.
Kes et al[13]/2016	N = 396	Low	NIHSS	1.08–1.16	Not assessed or reported	1. No reference to term "unique"2. 1/11 (seizure)3. Stroke in younger patients presented with sudden-onset headache or seizure.
Rudd et al[24]/2016	Literature review	Low	LAPSS	73–98	Not assessed or reported	1. No reference to term "unique"2. 4/11 (LOC, fainting, unresponsiveness or disorientation, seizures)3. Studies' cohorts varied between 50 and 1225. Both CPSS and FAST report the highest sensitivity; LAPSS reports higher specificity but lower detection rates.
			MASS	64–90		
			Med PACS	47		
			OPSS	90		
			ROSIER	62–94		
			CPSS	40–88		
			FAST	62–89		

Abbreviations: CNSR, China National Stroke Registry; CPSS, Cincinnati Prehospital Stroke Scale; ESI, Emergency Severity Index; FAST, Face Arm Speech Test; GCNKSS, Greater Cincinnati/Northern Kentucky Stroke Study; LAPSS, Los Angeles Prehospital Stroke Screen; LOC, loss of consciousness; MASS, Melbourne Ambulance Stroke Screen; Med PACS, Medic Prehospital Assessment for Code Stroke; NIHSS, National Institutes of Health Stroke Scale; n/v, nausea or vomiting; OPSS, Ontario Prehospital Stroke Screening Tool; ROSIER, Recognition of Stroke in the Emergency Room; SOB, shortness of breath.

FIGURE 1 Flowchart for Search and Selection Strategy



and competence facilitated the identification of stroke when obtaining and responding to the patients' emergency call for help (n = 29). Patients with uSS were less likely to be diagnosed with a stroke.[9] Stroke symptoms were also recognized as being often missed by emergency personnel because of diversity, drugs, alcohol, audiovisual symptoms, and a lack of educational feedback from hospital professionals.[10] Combined, these studies recognize that a percentage of women and men are initially misdiagnosed when presenting with altered mental status or a decreased level of consciousness as top contributors.[3,7–10,20]

Stroke Assessment Tools: Sensitivity and Specificity to Common Stroke Symptoms and uSS

Current stroke assessment tools recognize only 1 to 4 of the 11 uSSw (Table 1), and no study directly assessed the sensitivity and specificity of uSS. Furthermore, all of the studies included women and men. Therefore, the sensitivity and specificity of common stroke symptoms and uSS were included in this review. The prehospital CPSS stroke tool had a stroke recognition sensitivity rate of 75% (n = 186).[26] Similarly, using the LAPSS, stroke recognition rates were 88.2% (n = 1130) after correction of 215 false negatives.[23] In comparison, the CPSS had a sensitivity of 80% versus LAPSS's sensitivity of 74%. Both tools had a specificity of 48%.[22] Similarly, another study concluded that the CPSS had a sensitivity of 80% and the LAPSS had a sensitivity of 74%. Both had a specificity of 48% to 68% and encompassed comparable screening features, with each having partial specificity.[27] In contrast, a different study found that the CPSS had 83% sensitivity and 68% specificity. The LAPSS missed 29% to 56% of the stroke cases and had a 92% to 98% specificity (n = 689).[28]

In a review article, studies that included FAST, Recognition of Stroke in the Emergency Room, LAPSS, Melbourne Ambulance Stroke Screen, Ontario Prehospital Stroke Screening Tool, Medic Prehospital Assessment for Code Stroke, and CPSS varied in quality.[24] The CPSS and FAST study had the highest level of sensitivity, and the LAPSS study had the highest specificity rates but lower detection rates.[24] A previous review of the 7 stroke tools included studies with variable sample sizes ranging from 100 to 11 296 participants. Sex, race, age, and ethnicity of the participants also varied across the studies. It was concluded that each stroke tool varied in accuracy with an average of 30% acute stroke identifications missed before hospital admission.[21] None of the previously mentioned studies assessed or reported on the sensitivity and specificity of uSS.

Using the ESI, 92.1% of women were triaged at ESI level 1 or 2, in contrast to 93.6% of men (n = 537). Unique stroke symptoms had higher odds of being triaged to a non–critical care bed and 3.04 times higher odds of being triaged as ESI 3 versus ESI 1 or 2.[11] The modified Rankin Scale (MRS) score increased in women (67.8%) when compared with men (P = .021) (N = 6635).[12] Studies using the NIHSS found that greater odds for missed stroke diagnosis were associated with nausea/vomiting and dizziness and 37% of posterior strokes were initially misdiagnosed compared with 16% of anterior strokes (P < .001).[4] Using the stroke risk questionnaire, sudden-onset headache was indicated in 20.16% of the older age group and almost half of the younger age group (n = 396).[13]

Overall, stroke assessment tool studies varied in quality, sensitivity, and specificity. The tools identified 1 to 4 of the 11 uSSw, with only 4 of the studies reporting on some of the uSS, and the tools had a nonidentification error rate of 30% for strokes.[21–24,26–28] Nausea/vomiting, dizziness, and posterior strokes were the top contributors for misdiagnosis, with women having higher odds for an ESI (3 or 2 vs 1) and an increased MRS score in comparison with men.[4,12,13]

Stroke Registries: Sensitivity and Specificity to Common Stroke Symptoms and uSS

Current stroke registries recognize only 1 to 4 of the 11 uSSw (Table 1), no study directly assessed the sensitivity and specificity of uSS, and all studies included women

and men. Therefore, the sensitivity and specificity of common stroke symptoms and uSS were included in this review. Using the National Neurology Registry, higher nausea incidence was found in female patients with stroke in comparison with male patients (17.2% vs 15%, respectively; $P = .048$) (N = 4762).[14] The Ontario Stroke Registry has sensitivity to headaches. Headaches were more frequent in women (n = 2912) than men (n = 2979) ($P = .001$) (N = 5991), and women were less likely than men to have carotid imaging/endarterectomy or have received lipid-lowering therapy.[15] With the China National Stroke Registry, 55.36% of stroke cases (n = 3467) were identified as being associated with delayed arrival (>24 hours) to the hospital; contributing factors included female sex ($P = .0029$), cognitive dysfunction ($P = .0052$), and headache or vertigo ($P < .0001$).[16] The Healthcare Cost and Utilization Project State Inpatient Databases and State ED Databases have sensitivity to headache and dizziness; across 9 US states (N = 23 809), missed stroke cases (n = 1435) were linked to headache or dizziness.[17] The odds of misdiagnosis were lower among men and higher among African Americans, Asian/Pacific Islanders, and Hispanics. These were also higher in nonteaching hospitals and low-volume hospitals.[17] Combined, the data from registry studies indicate that 1 to 4 of the 11 uSSw are tracked; women present to the emergency department more often with nausea, cognitive dysfunction, headache, and dizziness than men.[14–17]

Discussion

Because of the paucity of research on uSS, a comparison of study results on uSSw is limited. However, several gaps in the literature have been identified. First, studies varied in terminology, included both women and men, and were inconsistent when addressing uSS. Most studies referred to sex differences in stroke presentations.[3,4,11]

Second, women delayed seeking care for stroke more often than men.[5,9,16,18] The delay in seeking treatment for stroke was greater in minority groups.[6] In addition, higher percentages of women were initially misdiagnosed in comparison with men.[3,4,7–10,12–17,20] In 3 studies, decreased levels of consciousness were the top contributors for misdiagnoses.[3,12,20] When using the NIHSS, nausea/vomiting, dizziness, and posterior strokes were the top contributors for misdiagnosis.[4] Interestingly, data from the registry studies also recognized that women present more often with nausea, cognitive dysfunction, headache, and dizziness than men, and these symptoms are also top contributors to misdiagnosis.[14–17] In addition, some studies have found that misdiagnosis leads to longer hospital stays and that women had higher odds for less severe ESI and an increased MRS score than men.[3,12,13] However, these studies varied in the percentage of misdiagnoses (ranging from 14% to 64%), and most studies did not separate women versus men's rate of misdiagnosis[3,12,13]

Finally, current stroke assessment tools and registries are not sensitive and specific to women and uSS. The data from these studies failed to specifically examine uSSw when evidence indicates that women present with uSS, nausea/vomiting, and cognitive dysfunction more often than men do.[5,14–17,21–24,26–28] Stroke assessment tools varied with 17 different tools and registries used in the 15 included studies. Seven prehospital stroke tool studies found variations in quality, sensitivity, and specificity, thus resulting in a potential stroke identification error rate of up to 30%, which results in delayed stroke treatment.[21–24,26–28] If the terminology, tools, and registries measuring uSS are standardized and specific to women, it will become easier to compare and generalize conclusions.

Conclusions

Evidence suggests that uSS, female sex, and race are associated with delayed stroke recognition, treatment, misdiagnosis, and poor patient outcomes.[14–17] Variations in terminology for describing uSS and uSSw exist within the literature. Studies that specifically addressed uSS and uSSw are limited and few.[5,6] In addition, the results of this review indicate that current stroke assessment tools and registries are a disservice to women because they only recognize 1 to 4 of the 11 uSSw. Current stroke assessment tools are designed specifically to recognize common stroke symptoms; they are not sensitive to guiding the recognition of uSS and uSSw.[4,12,13,21–24,26–28] Accurately identifying uSSw may reduce presentation and treatment time, minimizing misdiagnoses and poor patient outcomes.

Nursing Implications

Nurses play a key role in facilitating early identification of stroke. A 2-pronged educational strategy for emphasizing uSSw within the general and healthcare professional populations should be considered. Women should be educated that they potentially could experience uSS. Likewise, healthcare professionals should be able to recognize the symptoms that are the top contributors for misdiagnosis and that women present with uSS more often than men do. Researchers and educators should consider having a standardized terminology, assessment tools, and registries that are sensitive and specific to uSSw.

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