

Investigating the Need for Prehospital Education to Include Sex Differences in the Clinical Presentation of Stroke

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Abstract

Since Congress passed the National Institutes of Health Revitalization Act of 1993, a document that mandates the inclusion of women and minority groups in medical research, sex differences in the clinical presentations of diseases and responses to medication have emerged.¹ It has been found that women and men can present differently when experiencing a stroke, with women more often experiencing “atypical” or “nontraditional” signs and symptoms.^{2–8} Prehospital curriculum standards have not yet included this information for emergency medical technicians (EMTs) or paramedics. Further, prehospital provider education standards do not require competency in sex differences in epidemiology, physiology, pathophysiology, or pharmacology.^{9,10} Patients of EMS providers would likely benefit if their providers were aware of these sex differences, because previous research has found that women experiencing a stroke receive a lower quality of EMS care than men.¹¹ Early identification of stroke and timely notification to the nearest appropriate hospital can affect treatment decisions, and time to treatment can heavily influence functional outcomes.¹² Since there is robust evidence that the clinical presentation, quality of care, and health outcomes of stroke differ between men and women,

EMS education should include and emphasize these topics.

Methodology

This integrative review identified appropriate articles through a PubMed search from June 1, 2024, through August 14, 2024, with the keywords “sex and gender differences,” “sex and gender differences in the clinical presentation of,” “stroke,” “pathophysiology,” “anatomy,” “differences in stroke clinical presentation of transgender individuals,” “EMS recognition of stroke,” and “time to treatment and outcome.” The PubMed search did not include “chromosomal anomalies,” because this information lies outside the scope of EMS provider education standards.⁹ A total of 49 articles were assessed and considered relevant if they were published after the year 2000 and addressed one or more of the following questions:

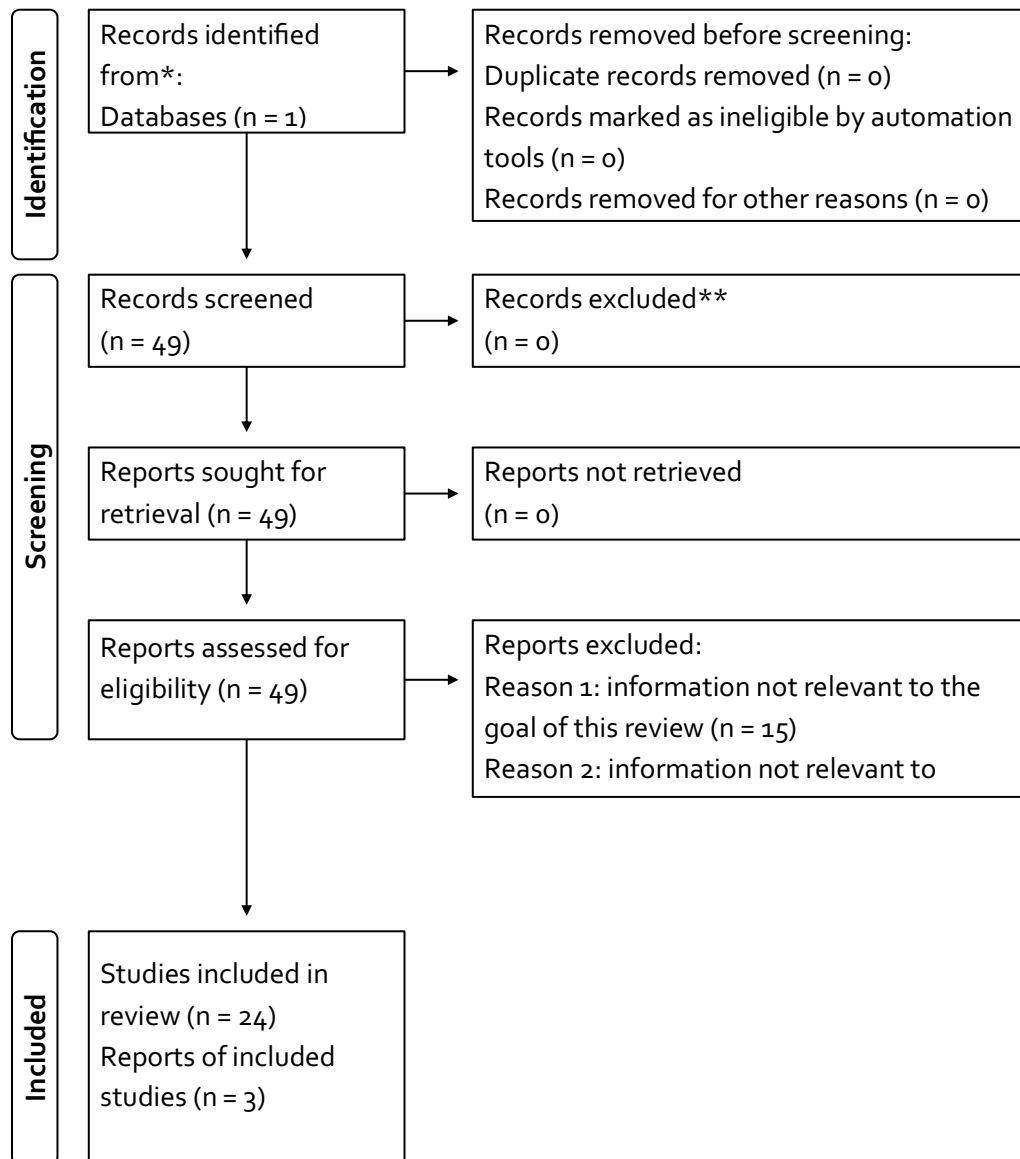
- Are there sex differences in the clinical presentation of stroke? If so, which sexes are included in these studies?
- Do men’s and women’s hormonal differences affect the development of stroke? Do sex differences in anatomy or physiology differ in the pathogenesis of stroke? Are there sex differences in risk factors for stroke?

- Is there an association between time to treatment for stroke and functional outcomes or mortality? How does EMS play a role in a patient's functional outcome?
- How accurate is EMS recognition of stroke?

- Is there a difference in the quality of EMS care between male and female patients?

Figure 1 describes the screening process for the reviewed articles.

Figure 1. Identification of Studies through Database Searching.



Sex and Gender

A person's chromosomal makeup of XX (female) or XY (male) defines one's sex. Other chromosomal anomalies exist, such as XXY (Klinefelter's syndrome) or X (Turner's syndrome). Gender is defined as a person's chosen identification and how they express themselves. Gender includes categories such as man, woman, transgender man or woman, or nonbinary, as well as others. The reviewed studies placed patients into binary categories of "male" or "female." None of the reviewed studies included individuals with chromosomal anomalies or transgender individuals. Therefore, this paper will focus on the differences between males and females.

Stroke

Signs and Symptoms

EMS providers commonly care for patients with stroke-like signs and symptoms. A stroke can present with focal or nonfocal symptoms, or both. Focal symptoms result from a lesion in the central nervous system, spinal cord, or nerve that then affects a specific area of the body. Examples of focal symptoms include unilateral muscle weakness, vertigo, and dysarthria. Nonfocal symptoms affect the body in a nonspecific manner and do not correspond to a particular area of the brain. Examples of nonfocal symptoms include fatigue, dizziness, and headache. Previous research has found differences in how women and men might present with any type of stroke.⁴⁻⁷ One difference is that women more commonly present with nonfocal

symptoms than men.⁴⁻⁷ Specifically, these nonfocal symptoms include changes in level of consciousness and mental status, headaches or migraines, and pain.⁴⁻⁷ Women also more often present with coma or stupor.⁴ In the prehospital setting, these nonfocal symptoms alone can warrant a long list of differential diagnoses and complicate the prehospital provider's impression of the patient's condition.

Although women more often present with nonfocal symptoms, focal symptoms, in general, affect women and men at comparable rates. Certain focal symptoms, such as lightheadedness, gait disturbance, imbalance, ataxia, and aphasia, affect women and men similarly.⁴ In contrast, other symptoms disproportionately affect one sex over the other. Women more commonly present with dysarthria and vertigo, and men more commonly present with paresis or hemiparesis, diplopia, and focal visual disturbances.⁴ Figure 2 displays the similarities and differences among these signs and symptoms. Last, women and men tend to experience a similar number of symptoms, because a systematic review and meta-analysis by Ali et al. found that both sexes experienced a mean of three symptoms.⁴ These differences highlight that, although women and men both display nonfocal and focal symptoms, certain symptoms may be more common in one sex than the other. EMS providers should receive up-to-date information on these trends in clinical presentation, with an emphasis on women's more common presentation with nonfocal symptoms and appropriate management.

Figure 2. Signs and Symptoms Categorized According to Sex.

Signs and Symptoms Categorized by Sex

Signs/symptoms more common in males	Similar signs/symptoms in males and females	Signs/symptoms more common in females
Focal – Paresis – Hemiparesis – Diplopia – Focal visual disturbances	Focal – Lightheadedness – Gait disturbance – Ataxia – Aphasia	Nonfocal – Change in level of consciousness – Fatigue – Dizziness – Headache Focal – Dysarthria – Vertigo

Pathophysiology

There are several underlying differences in stroke risks and pathophysiology between women and men. Annually, more women have strokes than men.^{13,14} It is thought that women’s longer life span partially contributes to the discrepancy in incidence.¹³ In addition, it has been shown that female sex is a risk factor for stroke in patients with atrial fibrillation.¹⁴ Proposed reasoning for this increased risk in women with atrial fibrillation is that they have more coexisting conditions than men.¹⁵ However, more research is needed to determine whether female sex alone presents an increased risk or whether increased age and coexisting conditions fully account for this discrepancy.

Women and men also tend to experience different types of strokes. Women more commonly experience either subarachnoid hemorrhage (SAH), cardioembolic stroke, or a larger territorial infarct.^{4,16} Since a greater proportion of women have atrial fibrillation, it makes sense that women

also have an increased risk of cardioembolic stroke. Meanwhile, men more often experience a stroke due to small-vessel disease or lacunar infarcts.^{8,16} Differences in risk factors and the types of infarcts may partly account for the differences in clinical presentation. However, more research is needed to explore the relationship between symptoms and stroke types. Nonfocal symptoms can arise from injury to any area of the brain, so it is unclear why women more often present with these symptoms. Nonetheless, including pathophysiologic differences in the prehospital curriculum could bolster prehospital providers’ understanding of the clinical differences they may encounter.

Clinical Assessment and Implications

To assess whether a patient is experiencing a stroke, prehospital providers are taught one or more nationally recognized prehospital stroke scales. These include the Cincinnati and FAST-ED stroke scales. The Cincinnati Prehospital Stroke Scale assesses facial asymmetry, arm drift, and

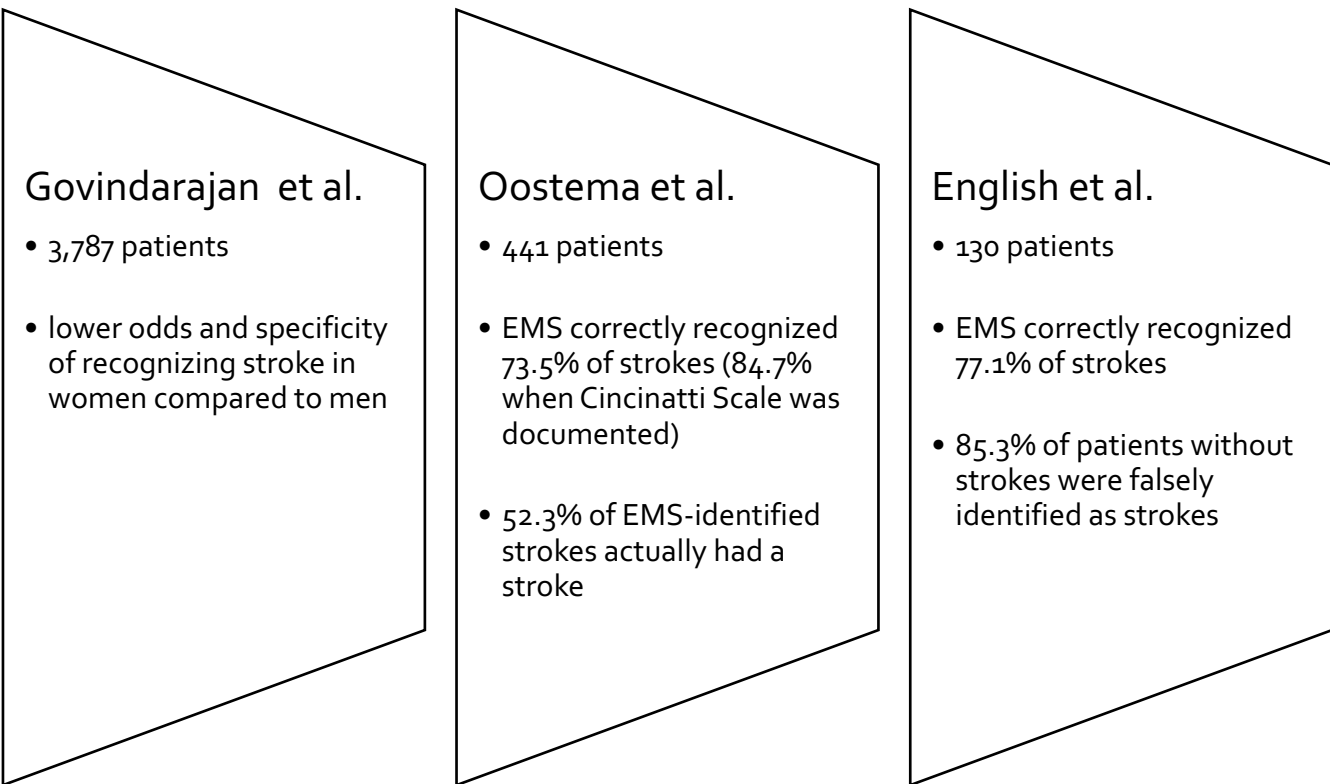
speech, and the FAST-ED Prehospital Stroke Scale assesses facial asymmetry, arm weakness, speech, time when the patient was last seen normal, eye deviation, and whether the patient recognizes weakness in the upper extremity.^{17,18} When a patient has a positive stroke scale, EMS providers are taught to call in a stroke alert and transport the patient to the nearest stroke center. Notably, these stroke scales assess focal symptoms. Since more women have nonfocal symptoms, it is possible that more women may be experiencing a stroke but may not have a positive stroke scale. Subsequently, more women may not be transported with appropriate priority or to an appropriate stroke center. It is worth educating prehospital providers that both women and men may not have a positive stroke scale because of the possibility of a stroke manifesting with nonfocal symptoms. On the basis of the severity of nonfocal symptoms, the scene where the patient was found, and the patient's history, the provider should assign appropriate priority so that the patient arrives at the emergency department with the necessary resources already prepared.

Recognition of stroke in the prehospital setting is important because previous research has found that, after a stroke, time to treatment can affect functional outcomes. A patient's functional outcome tends to decrease as time to endovascular therapy, a common stroke treatment, increases.¹² Further, longer times from symptom onset to reperfusion are associated with increased mortality.^{12,19} Multiple studies have found that women have worse functional outcomes and greater mortality than men.^{11,16} However, the demographics between women and men differ. At stroke onset, women are typically older and live alone.²⁰ It is thought that older age and living alone

greatly contribute to women experiencing longer delays to treatment and more severe symptoms.²⁰ EMS providers should be aware of these social factors so that they may remain suspicious of stroke or other life-threatening conditions for patients with these demographics and presentation.

EMS recognition of strokes is not completely accurate. The sensitivity of EMS recognition of stroke varies. Govindarajan et al. found that EMS had lower odds of correctly recognizing stroke in women than in men; one study from southwestern Michigan found that EMS correctly suspected 73.5% of strokes; and English et al. found that their EMS system at the Mayo Clinic correctly identified 77.1% of strokes.²¹⁻²³ EMS sensitivity for stroke recognition likely varies because of study differences and EMS provider education, training, and experience. However, conducting a proper prehospital stroke scale may be associated with correctly identifying strokes, because Oostema et al. found that EMS stroke recognition was highest when the Cincinnati Prehospital Stroke Scale was documented.²² Details of these studies can be found in Figure 3. Among the missed strokes, EMS commonly listed general weakness and altered mental status as their clinical impression.²² Since these nonfocal symptoms have many causes, it is difficult for providers to identify a stroke that presents in this fashion in the absence of focal symptoms. In addition, research has shown that EMS recognition of stroke improves after a stroke training module.²⁴ Therefore, a continuing education course that covers focal and nonfocal symptoms, trends seen in men's and women's stroke presentations, and proper stroke protocols may help improve the sensitivity of EMS stroke recognition.

Figure 3. EMS Recognition of Stroke Among Three Studies.



Care Disparities

There is a discrepancy in EMS providers' delivery of appropriate care to women and men, which should be provided equally. Using national EMS data from 2019 and 2020, Dylla et al. assessed Advanced Life Support providers' compliance with American Stroke Association recommendations; criteria for compliance included eight metrics: documenting stroke scale, hospital prenotification, obtaining blood glucose level, giving oxygen only when oxygen saturation fell below 94%, obtaining a 12-lead electrocardiogram, documenting last known well since symptom onset, having a less than 90-second call-to-dispatch time, and having a less than 15-minute on-scene time.¹¹ These actions play an important role in caring for and transporting a

patient with stroke-like symptoms. Dylla et al. found that EMS providers met all eight criteria in 0.39% of cases.¹¹ A significant proportion of providers caring for male patients met six or more criteria and therefore had greater compliance than providers who cared for female patients.¹¹ Dylla et al.'s study exposes the need to improve EMS training and reduce provider bias nationwide.¹¹ It seems appropriate to structure a continuing education course that refreshes providers on stroke symptoms and protocols and brings awareness to statistics showing sex bias. In addition, current EMS certification classes should consider sharing the statistics regarding gender bias. However, deep-rooted gender bias poses a challenge that will likely take years or generations to resolve. Education could serve as a platform to promote a culture within EMS that frowns on sex bias.

Conclusion

On the basis of evidence of sex disparities in functional outcomes and quality of care, sex differences in the clinical presentation of stroke should be incorporated into the EMS curriculum. The goal of this education is to improve understanding that stroke can present in lesser-known ways and potentially improve EMS stroke recognition. Current providers may be educated through continuing education classes, and future EMS providers could obtain this knowledge through their initial certification. The curriculum should include an overview of stroke pathophysiology, sex differences related to anatomy and physiology, and evidence-based sex differences in the clinical presentation of stroke. History taking should also be reviewed, because certain information, such as the last time the patient was asymptomatic, can help hospital clinicians make treatment decisions. In addition, the curriculum should review the various nationally recognized stroke scales, because there is evidence that documenting these scales helps improve EMS recognition of stroke patients. The education should emphasize that strokes can present with focal or nonfocal symptoms, or both, and that it is important to include stroke in the differential diagnosis when gathering information from the scene.

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More research is needed to explore the relationship among sex differences in anatomy, physiology, risk factors for stroke, and sex differences in clinical presentation. Since women more commonly present with nonfocal symptoms, one future direction could investigate whether these symptoms correlate with the specific types of strokes these women experience. If there are trends in nonfocal symptom presentation and type of stroke, then providers may arrive at a stroke diagnosis more quickly and improve functional outcomes.

Although current research focuses on sex differences related to biological males and females, more research is needed to address whether there are differences in clinical presentations among individuals receiving hormone-replacement therapy, those identifying as transgender, or those with chromosomal disorders. This type of research would broaden providers' awareness if there were differences in clinical presentation among various sexes and genders. With increased awareness of how stroke can present differently across sexes, this education could decrease knowledge gaps and potentially improve quality-of-care discrepancies for all patient populations.

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