Review

Evaluation of Post-stroke Spasticity and Its Relationship with Age, Gender, Type of Stroke, and Lesion Location: A Systematic Review

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Abstract

Introduction: This was a systematic review of the literature on the prevalence and development mechanism of post-stroke spasticity (PSS) over time and the relationship of spasticity with age, gender, type of stroke, and cerebral lesion location to establish whether these variables are effective factors in prognosis and treatment of PSS.

Methods: This PRIZMA-based systematic review searched all papers in different databases (Google Scholar, Springer, ScienceDirect, PubMed, and Scopus), published between 2000-2020, using the following keywords: spasticity, hypertonicity, stroke, cerebrovascular accident, epidemiology, hemorrhagic, ischemic, location, gender, and age.

Results: In all, 769 papers were found in the initial search, out of which 42 papers were selected after reviewing their topic and abstract. Finally, only 16 papers were included after reading their full texts.

Conclusion: PSS is not correlated with age, gender, type of stroke, and lesion location. Nevertheless, the results of the current study should be used cautiously and more studies are needed.

Keywords: Stroke, Spasticity, Epidemiology, Systematic review

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Introduction

Stroke is defined as an abrupt neurological deficit of local vascular origin. Each year, about 795,000 people in the United States suffer from a new or recurrent stroke [1]. In Iran, 139 per 100,000 people suffer from stroke every year, which is higher than the majority of western countries [2]. Stroke has various clinical manifestations, which can be attributed to the complex anatomy of the brain and cerebral arteries. Approximately one-third of patients develop permanent disability after a stroke, which accounts for 63 million disabilities by age in the world [3, 4].

Spasticity is a post-stroke complication in some of these patients. Lance (1980) defined spasticity as a "motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper-excitability of the

stretch reflex." PSS can adversely affect patients' ability and life quality and increase the risk of falls and bone fractures [5, 6].

Studies have shown that direct treatment costs of patients with PSS (PSS+) are four times higher than those of patients without PSS (PSS-). hyper-excitability peaks 1-3-month after onset of spasticity; in addition, when spasticity stabilizes after a year or more, hyper-excitability decreases [7].

Therefore, PSS is expected to change over time. Due to age- and gender-dependent differences in neuromuscular properties and internal muscle characteristics, differences in prevalence and severity of PSS are likely to be observed [8, 9]. Although patients with hemorrhagic stroke suffer more from dysfunction than those with ischemic stroke, the former group often shows greater improvement. On the other hand, PSS+ patients suffer more from dysfunction than PSS-, which can be attributed to a possible relationship between type of stroke and spasticity [10]. Lesions in different anatomical areas and different cerebral arteries are accompanied by muscle relaxation and declines in motor control following stroke. It has been found that patients with more severe muscle weakness are more prone to spasticity in the first few days after a stroke. As a result, the involved area is also probably correlated with PSS. Knowing factors related to PSS (including time, age, gender, type of stroke, and lesion location) and the effects of these variables on severity of and changes in spasticity contribute to early detection of patients prone to PSS, particularly severe and permanent spasticity, and can substantially help the treatment team, the patients and their families in preventing and reducing the associated problems [11, 12]. This was a systematic review of the literature on the prevalence and mechanism of PSS over time. It also investigated the relationship of spasticity with age, gender, type of stroke, and lesion location on the brain to establish whether these variables are effective factors in the prognosis and treatment of PSS.

Methods

To review the literature on PSS and problems associated with it, Google Scholar, Springer, ScienceDirect, PubMed, and Scopus were searched for English papers published between 2000-2020, based on the PRISMA Flowchart. The searched keywords were: Spasticity, Hypertonicity, Stroke, Cerebrovascular accident, Epidemiology, Hemorrhagic, Ischemic, Location, Gender, and Age (selected based on mesh). The search strategy in PubMed is briefly described as follows:

1. Spasticity AND Hemorrhagic / Epidemiology AND Spasticity / Spasticity AND Location / Spasticity AND Gender / Spasticity AND Cerebrovascular accident / Spasticity AND Stroke / Stroke AND Epidemiology / Stroke AND Hemorrhagic / Stroke AND Ischemic / Stroke AND Location / Stroke AND Gender / Stroke AND Age.

The inclusion criteria were:

1. Evaluation of spasticity at a certain time after stroke
2. Relationship of PSS with at least one of the following factors: Time, age, gender, type of stroke, and stroke location
3. Full text articles

Only English papers were included. There was no relevant paper in Persian. Based on the inclusion and exclusion criteria, 769 papers were extracted, out of which only 16 papers were finally reviewed based on Flowchart 1 [13-28].

Due to the limited number of studies, the difference in study design, and the lack of adequate data in the texts, we could not include the results from the relationship of spasticity with age, type of stroke, and stroke location in the systematic review. Since studies on the prevalence of spasticity were conducted at different times, their results could not be combined. Therefore, only the results of three studies, which reported the incidence rate of

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spasticity throughout their study period, were combined. Four of the nine studies on the relationship of gender with spasticity met the inclusion criteria. Data analysis was done using the R software. The homogeneity of the data was investigated using the chi-square homogeneity test. The combined results were analyzed using the model of stochastic effects.

Results

Using the keywords and excluding replicated papers, 769 papers were obtained. After reviewing the topics and abstracts, 42 papers were selected, and finally, after reading the texts of the 42 articles, 16 of them that met the inclusion criteria entered the research. A summary of the data derived from these papers is presented in Table 1. According to this table, these papers investigated different factors. However, this review study only considered the sections related to onset of spasticity and the correlation of spasticity with age, gender, type of stroke, and lesion location. To investigate the effect of time on PSS, several muscle groups in the upper and lower limbs should be investigated. Moreover, sampling should be hospital-centered so that the samples can properly represent the population of stroke patients. Additionally, the time for precise evaluation after stroke onset should be determined. Nine of the sixteen studies (Table 1) investigated the prevalence of and changes in PSS in a prospective and hospital-centered manner. Seven studies that investigated the muscle groups of the upper and lower limbs are presented in Table 2 by evaluation time. Moreover, two studies investigated a smaller number of muscle groups in the upper limbs only. Therefore, these studies are separately presented in Table 1. Of the 16 studies nine investigated the relationship between PSS and age and nine studied the relationship between PSS and gender. The results of these studies are listed in Table 1. Since sampling from outpatients does not represent the stroke patient population, hospital-centered studies are more valuable. Five of the sixteen studies investigated the relationship of PSS with type of stroke (hemorrhagic or ischemic). The results are presented in Table 1. Six of the sixteen studies investigated the relationship between stroke location and PSS (Table 1).

Discussion

Concerning the relationship of PSS with time, the investigated muscle groups included shoulder and hip adductors, as well as elbow, wrist, finger, knee, and ankle flexors. Lundström et al. (2010) evaluated spasticity at 2-10 days, one month, and six months after stroke using the Modified Ashworth Scale and found that the prevalence rates of spasticity were 4%, 23%, and 27%, respectively [22]. Based on the observations, the majority of the patients who had spasticity in the first month after stroke still had it sixth months post stroke (n = 7), three patients had spasticity only sixth months post stroke (n = 3), and five patients with first-month spasticity had normal muscle tone sixth months post stroke. Moreover, disabling spasticity (patients in need of drug therapy, intensive physiotherapy, or orthosis) was observed in only one patient one month after stroke and in 13% of the patients sixth months post stroke. Therefore, spasticity develops in the first month after stroke while disabling spasticity needs more than one month to develop. However, the sample size in this study was relatively limited and a precise method for the evaluation of the disabling spasticity was not employed. Sommerfeld et al. (2004) showed that the prevalence rates of spasticity in the first week and the third month after stroke were 21% and 19%, respectively, indicating that the onset of spasticity in the majority of patients was in the first week after stroke [14].

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Table 1: Summary of all articles reviewed

Study/ year	Sample size	Main Purpose	Result
Watkins / 2002	106	Prevalence of PSS and its relationship with functional ability 12 months after stroke	The prevalence of this complication is 27 to 36%
Sommerfeld/ 2004	95	Prevalence of PSS and its association with disability (movement impairment and activity limitation) at the beginning and 3 months after stroke	The prevalence of this complication was 21% in the first week and 19% in the first three months
Welmer/ 2006	66	Prevalence of PSS and its relationship with postoperative function	Patients without PSS are more active
Van Kujik / 2007	43	Determination of risk factors for ischemic stroke hypertoniazel in the supratentorial region	There was a weak relationship between PSS and disability and the number of patients with severe disability was equal in both spastic and non-spastic groups.
Lundstrom/2008	140	DS one year after stroke	The prevalence of this disease was 20%
Moura Rde / 2009	146	Determining the predictors of PSS	Patients without PSS perform better
Kong / 2010	140	Prevalence of PSS and factors affecting organ function	Patients without PSS have a better quality of life
Lundstrom / 2010	49	Identification of PSS brucellosis six months after stroke	The prevalence of this complication is 63%
Ryu / 2010	245	Determining the Prevalence and Predictors of PSS in Patients During Rehabilitation	PSS was relatively dynamic, appearing in three modes: early, transient, and late
Urnan / 2010	211	Prevalence of spasticity after ischemic stroke and its relationship with initial clinical findings following stroke and its effects on daily activities and quality of life	None of the clinical features were significantly associated with hypertension
Wissel / 2010	93	Prevalence of PSS and its risk factors	The prevalence of PSS was 17%
De Jong / 2011	50	Prevalence and incidence of hypertonic reflexes of the elbow and the effect of stroke	Patients with PSS have a Modified ranking scale and Barthel Index compared to other patients.
Kong / 2012	153	Changes in upper limb spasticity over time and related and predictive factors in stroke patients referred for rehabilitation	DS was more prevalent in the upper extremities and was inversely related to age.
Picelli / 2014	39	Association between myocardial infarction site and severe upper extremity spasticity following stroke	The prevalence of the complication was 25%
Wallmark / 2014	87	Prevalence of PSS and its risk factors	PSS was significantly associated with the extent of the lesion, pre-stroke and pre-stroke manual labor.

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Wissel et al. (2010) evaluated spasticity at 2, 6, and 16 weeks after the stroke and reported the prevalence rates of 24%, 26%, and 21%, respectively [15]. They observed that the majority of patients with onset of spasticity six weeks after stroke (n =16) still suffered from it 16 weeks post stroke. However, a few participants had regained normal muscle tone in the 16th week after stroke. Moreover, in a few participants (n = 2) who did not have spasticity in the sixth week after stroke, spasticity was observed in the 16th week post stroke. Moreover, all patients with severe spasticity in the 16th week after stroke exhibited less severe spasticity in the 6th week post stroke. The prevalence of spasticity was 42% six months after stroke (Urban et al., 2010) [23]. This prevalence rate was much higher compared to other studies, which can be attributed to its restrictive inclusion criteria (only patients with ischemic stroke who suffered from muscle weakness in a limb or half of the body entered the research) and to the fact that muscle weakness is a risk factor for PSS. In this study, the prevalence of PSS was higher than in other studies. Wallmark et al. (2014) reported a 22% prevalence of spasticity six months after aneurysmal subarachnoid hemorrhage [27]. Despite differences in the inclusion criteria, their results are consistent with those of other studies.

The studies presented in Table 3 only investigated the muscles in the upper limbs and considered different criteria for the evaluation of spasticity and used more restrictive inclusion criteria. As a result, the comparison of their results with those of the studies in Table 2 was not possible and they were presented separately. Van Kuijk et al. (2007) investigated the prevalence of PSS in the elbow flexor muscles in the 1st, 2nd, 3rd, 6th, and 12th weeks after stroke in patients who lacked voluntary upper extremity movement on the first day after stroke [18]. The incidence rates of spasticity (number of new patients) were 25% over three weeks, 50% over six weeks, and 63% over 26 weeks. In addition, 25% of the patients had early tone increase (in three weeks), 10% had transient tone increase, and 15% had delayed tone increase. The emphasis of this study was more on the number of new patients with spasticity (contrary to the majority of studies that investigated the prevalence). Moreover, in this study, AS $\geq$ 2 was considered tone increase. De Jong et al. (2011) investigated the spasticity of elbow flexors in patients with weak upper limbs following stroke [24]. The prevalence of spasticity was 10% over 48 hours, 20% over 10-12 days, 42% over three months, and 42% over six months after stroke. Moreover, the number of new patients with spasticity until the 3rd month after stroke peaked at 30% and then started to decrease. Transient spasticity was observed only in 8% of the patients.

Concerning PSS relationship with age and gender, Wallmark et al. (2014) conducted a hospital-centered study and compared the gender and mean age of the PSS+ and PSS- patients six months after stroke induced by aneurysmal subarachnoid hemorrhage, and did not find a relationship between PSS and patients' age and gender [27]. In this study, the relationship between these variables and severity of PSS was not investigated. Welmer et al. (2006) compared the younger patients (< 65 years) with older ones (> 65 years) for the prevalence of spasticity and showed a higher prevalence of spasticity in younger patients in the third month after stroke [16]. However, they did not find any significant relationship between age and spasticity 18 months after stroke. In this study, sample attrition was considerable between the 3rd month (n = 9) to the 18th month (n = 66) after stroke, which could have affected the results. On the other hand, the relationship of age and gender with the severity of PSS was not studied. Wissel et

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al. (2010) did not observe any relationship of PSS with age and gender 6 weeks and 16 weeks after stroke; In addition, the relationship of these variables with the severity of spasticity was not expressed [15]. Lundström et al. (2010) showed that there was no difference between gender and mean age of the PSS+ and PSS- patients 1 month after stroke [22]. Moreover, there was no relationship of age and gender with the prevalence of disabling spasticity 6 months after stroke. In this study, no precise criterion was used for evaluating disabling spasticity; in addition, the small sample size could have affected the results. Van Kuijk et al. (2007) did not find any relationship between severity of PSS in the upper limbs and gender 6, 12, and 26 weeks after stroke [18]. In this study, plasticity of lower limbs was not evaluated, the sample size was small, and the relationship between age and spasticity was not investigated.

Picelli et al. (2014) investigated patients who had unilateral ischemic stroke 3-6 months earlier and MRI images within the first 7 days after stroke [26]. They determined the relationship of severe PSS in the upper limbs and lesion location by using brain voxel-based lesion-symptom mapping (VLSM) procedures and showed that the number of MRI voxels involved by the stroke lesion was significantly higher in PSS+ patients than in the PSS- patients. Moreover, lesions in the insula, thalamus, basal ganglia, internal capsule, corona radiata, and external capsule were significantly correlated with severe upper limbs PSS. In this study, only severe plasticity of upper limbs was investigated and the sample size was relatively small. Wallmark et al. (2014) determined the lesion location in patients with aneurysmal subarachnoid hemorrhage based on the aneurysm location in the anterior and posterior cerebral circulations with the prevalence of 85% and 19%, respectively [27]. They also showed that there was no relationship between the lesion location and PSS prevalence.

Time has an important role in increasing muscle tone following stroke. The prevalence of severe PSS increases with the passage of time after stroke. As compared to mild PSS patients, patients with moderate PSS in the acute phase are more likely to develop severe PSS in the chronic phase. The majority of previous studies did not find any relationship between age and the prevalence of PSS, except one study that showed PSS was more prevalent among younger patients in the 3rd month after stroke; however, such a relationship was not observed in the 18th month after stroke [8, 9, 29, and 30]. The difference between the results of this research and those of other studies may be due to the higher mean age of the participants. In addition, contrary to the majority of other studies, which compared the mean age of PSS+ and PSS- patients, this study compared the patients < 65 years to those > 65 years. Most studies on more chronic phases (over three months after stroke) investigated the relationship of PSS with age and did not observe any relationship between them in the chronic stages of stroke. However, there is little and weak evidence on the relationship of PSS with age in its acute phase (< 3 months). Therefore, given that reflexes slow with age, its relationship in acute phases (< 3 months) needs further studies because a higher prevalence of spasticity is expected in the acute stroke phase where spasticity has a central origin. Finally, it should be said that no relationship was observed between gender and PSS. The meta-analysis results showed that the incidence rates of spasticity among men and women were not significantly different. Weaker evidence also showed that there was no association between gender and the severity of PSS. The majority of these studies investigated only the upper limbs or did not provide a precise measure for the evaluation of disabling spasticity. Therefore, more precise and comprehensive studies are needed on the relationship between gender and the severity of PSS.

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There was no relationship between type of stroke (ischemic and hemorrhagic) and prevalence of PSS. There is weak evidence on the lack of relationship between type of stroke and severity of PSS. Therefore, the relationship between type of stroke and PSS requires more accurate and comprehensive research. Only one study investigated the relationship between lesion location in sub-cortical areas and the severity of PSS. Its results showed a correlation between severe upper limbs PSS and lesion in the insula, thalamus, basal ganglia, internal capsule, corona radiata, external capsule, and superior longitudinal fasciculus. Other studies investigated lesion location based on the involved area of the circulatory system or the involved lobe; however, they did not find any relationship between the lesion location and PSS or between lesion location and severity of upper limb PSS. It was also found that the lesion size and involvement of more than one lobe were correlated with spasticity.

Conclusion:

PSS is not correlated with age, gender, type of stroke, and lesion location. Nevertheless, the results of the current study should be used cautiously and more studies are needed

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