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Abstract

Objective: To determine the predictive markers for the occurrence of upper limb spasticity in the first 12 months after stroke.

Data Sources: A systematic review was undertaken of the databases MEDLINE, EMBASE, CINAHL and PEDRO to 31st December 2017.

Study Selection: Non-experimental or experimental studies that included a control group with spasticity who did not receive an experimental intervention which investigated at least one variable (explanatory variable) measured at baseline against the development (or not) of spasticity at a future time point within 12 months post-stroke were selected independently by two reviewers. Eleven papers met the selection criteria.

Study Appraisal: Data were extracted into tabular format using predefined data fields by two reviewers. Study quality was evaluated using the modified Downs and Black tool. Data were analysed using a meta-analysis or narrative review.

Results: Ten studies, including 858 participants were analysed. The predictive markers of upper limb spasticity at one month post-stroke were: motor 11.25 (odds ratio, OR); [95% CI:2.48, 51.04] and sensory impairments 4.91 (OR); [1.24,19.46]; haemorrhagic stroke 3.70 (OR); [1.05, 12.98] and age 0.01 (OR) [0.00, 69.89]. Only motor impairment was found as a significant predictor at six months post-stroke 30.68 (OR); [1.60, 587.06].

Limitations: Low number of studies exploring biomechanical and neurophysiological in addition to clinical predictors of spasticity were included.

Conclusion and implications of key findings: Using the results, the identified predictive markers have potential to better inform clinical decision-making and to plan specific

rehabilitation interventions by physiotherapists for stroke survivors with upper limb spasticity.

Introduction

Stroke is the third leading cause of adult disability worldwide [1]. Upper limb deficits are frequent, despite the benefits of rehabilitation, with 33 to 66% of people reporting a lack of upper limb function at six months after stroke [2,3]. Consequentially everyday activity such as picking up a glass of water and fastening zips are difficult if not impossible for many stroke survivors. Key factors associated with poor upper limb recovery are: lesion location, initial severity of motor impairment or function, and changes in muscle tone such as the development of spasticity over time [4,5].

Spasticity is a complex sensori-motor disorder which has been defined as "impaired sensori-motor control from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles" [6]. Alleviation of spasticity is a rehabilitation focus when it limits activity due to contractures and/or pain [7,8]. The cost of healthcare for stroke survivors with spasticity has been estimated as being four-times higher than when spasticity is not a secondary complication [9]. Unfortunately, for many people, upper limb spasticity is common [10,11]. At Day Three post-stroke, spasticity is present in approximately 25% of people who have upper limb paresis and frequency can increase up to 46% at 12 months [12].

A limited understanding of the predictors of developing upper limb spasticity can limit the application of rehabilitation interventions. Enhanced understanding of the predictive markers of upper limb spasticity could enable physiotherapists to identify people at higher risk leading to: more accurate prognosis estimations; adaption of rehabilitation techniques and preventive

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strategies. Prior to commencing this study, a scoping literature search conducted and did not find any high-quality systematic reviews of predictive markers of upper limb spasticity after stroke. Two narrative reviews have explored the predictive markers of the early development of upper limb spasticity after stroke [13,14] although neither used a comprehensive search strategy, assessed the potential risk of bias of included studies, or provided information about the characteristics of included studies. The aim of this systematic review is therefore to determine the predictive markers of upper limb spasticity after stroke.

The systematic review was registered on PROSPERO (ID: CRD42016027642).

Study criteria

Types of study design: (a) non-experimental such as cohort and case control studies, or experimental studies that included a control group with spasticity who did not receive an experimental intervention, (b) which investigated at least one variable (explanatory variable) measured at baseline against the development (or not) of spasticity at a future time point within 12 months post-stroke [5].

Types of participants: (a) had a confirmed clinical diagnosis of a haemorrhagic or ischaemic stroke and (b) upper limb spasticity as measured by the Modified Ashworth Scale (MAS) scored greater than or equal to one point [15]. Participants were excluded if they had an additional neurological condition such as Parkinson's disease, multiple sclerosis or upper limb peripheral neuropathy.

Outcome measures of potential predictors: (a) age (< or ≥65 years); (b) gender (female, male); (c) behavioural habits such as smoking (>5 cigarettes/day) [23]; (d) handedness (right, left); (e) upper limb motor impairment defined as score >2 on item 5 on the National Institutes of Health Stroke Scale (NIHSS) [10, 16]; (f) upper limb somatosensory impairment as defined as score ≥1 on item 8 on the NIHSS [10, 16]; (g) side of stroke (left versus right); (h) location of

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stroke (cortical, subcortical, mixed); (i) type of stroke (ischemic, haemorrhagic); (j) muscle activity measured by electromyography; and (k) biomarkers measured by brain imaging or non-invasive brain stimulation.

Search Strategy

A search of the databases MEDLINE, EMBASE (Excerpta Medica Database), CINAHL (Cumulated Index of Nursing and Allied Health Literature) and PEDRO (Physiotherapy Evidence Database) was conducted from database inception to 31st December 2017. A summary of the search strategy is presented in the Appendix (Table A). A hand search of the reference lists of each included article and the identified literature reviews were also screened for relevant publications.

The titles and/or abstract from the search results were independently screened against the pre-determined inclusion criteria by two reviewers. The full-text version of all papers which were potentially eligible were obtained and independently reviewed by the same two reviewers. Papers which satisfied the eligibility criteria at this stage were included in the review. Disagreement in eligibility judgment between the reviewers was resolved through consultation of the full-text article and discussion.

Risk of potential bias appraisal and Data Extraction

Two review authors independently critically appraised the included studies for risk of potential bias using the modified Downs and Black assessment [17,18]. This modified version of the tool has been previously reported [19]. The assessment contains 27 'yes'-or-'no' questions across five sections. To make it specific to the research question, items related to randomisation and intervention were removed. This process left 17 items exploring: (1) study quality (seven items) – the overall quality of the study; (2) external validity (three items) – the ability to generalise findings of the study; (3) study bias (five items) – assesses bias in the outcome

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measure(s); and (4) confounding and selection bias (two items) – determines bias from sampling or group assignment. Disagreements were resolved through consultation of the full-text publication and discussion. Papers achieving at least 65% of the maximum possible score was classified as having 'substantial' quality [19].

Data extracted were: number of participants, gender, side of stroke, type and location of stroke, time since stroke and any predictor characteristics that were identified, for example clinical assessment of spasticity, upper limb strength. Data extraction was carried independently by two reviewers into a table proforma developed by authors. Disagreements were resolved by including a third reviewer.

Data Synthesis

Demographic characteristics of mean age, frequency of males/females, type of stroke and characteristics of pre- and post-stroke presentation were calculated. Between-study heterogeneity was evaluated through visual analysis of the completed dataset. Where substantial between-study heterogeneity was evident (for participant characteristics and method of assessing development of upper limb spasticity), a narrative analysis of the data was performed.

When there was low study heterogeneity, a meta-analysis comparing probabilities of incident spasticity occurring at one and six months post-baseline assessment for each of the variables was undertaken. Statistical heterogeneity was assessed by using the I^2 and Chi^2 tests. Where I^2 equated to 50% or more and $Chi^2 = p<0.10$, a random-effects statistical model was used. When this was not the case, a fixed-effects statistical model was employed [20]. Data for categorical predictive markers were assessed to using odd ratios (OR) and 95% confidence intervals (CI) to determine the probability of spasticity occurring at the follow-up assessment. All analyses

were conducted on Revman version 5.3 (The Cochrane Collaboration Statistical Software, Copenhagen, 2016).

Results

From the thorough search process, 11 papers were eligible for qualitative analysis. After discussion between all reviewers, one paper [21] was excluded due to not clearly exploring predictors of spasticity (Appendix Table B). Therefore 10 papers were included in the analyses (Figure 1).

Insert Figure 1 about here

Participant Characteristics

A summary of the characteristics of the included papers is presented in Table 1. In total 856 participants were included in the analysis; 518 (60.5%) were males and 338 (39.5%) were females. Side of stroke was reported in seven papers; 254 (48.9%) of participants having a left-sided stroke and 265 (51.5%) had a right-sided stroke [21-26]. Six papers reported that 304 (84.0%) had ischaemic stroke and 58 (16.0%) had haemorrhagic stroke [10,22-26,28]. From four studies, eight (2.5%) participants had cortical stroke, 12 (3.4%) had sub-cortical stroke and 19 (5.3%) had sub-cortical/cortical stroke [20]. The remaining studies presented the type of stroke according to the Oxford classification; 73 (20.5%) had a total anterior circulation stroke, 34 (9.6%) had a Lacunar stroke, 79 (22.2%) had a Partial anterior circulation stoke, 31 (8.7%) had a Posterior circulation stroke [22,25], 85 (23.9%) had supratentorial stroke and 15 (4.2%) had a infratentorial stroke [28].

(Insert Table 1 about here)

Risk of potential bias appraisal

The Down's and Black scores for each paper are presented in Table B. From the included studies, six presented with substantial quality (>65%) and four presented with low quality (<65%) (Appendix Table B) [18]. Strengths included that all: studies reported the aims of the study, provided estimates of the random variability in the data for the main outcomes, reported actual probability values and used appropriate statistical tests. Nine papers (90%) reported the accuracy of outcome measures chosen, description of the main findings and participants who were representative of the entire population from which they were recruited. Only two papers (20%) contained items about adjustment in the analysis [10,26]. One paper (10%) described the recruitment process and blinding [27] and another reported time to follow-up [10].

Meta-Analysis: Predictors of Upper Limb Spasticity

Upper limb motor, somatosensory impairments and haemorrhagic stroke were statistical significant predictors of upper limb spasticity. Overall, there was a significant increase in the probability of spasticity at one-month and six-months post-stroke when measured by motor (OR:15.20, 95% confidence intervals (CI): 4.01 to 57.64; N=95; I^2: 0%; p=0.54), somatosensory (OR: 3.56; 95% CI: 1.19 to 10.60, N=95; I^2: 0%; p=0.46) upper limb impairments and haemorrhagic stroke (OR: 3.47; 95% CI: 1.22 to 9.89, N=116; I^2: 0%; p=0.57) (Figures 2,3 and 4).

(Insert Figures 2,3,4 about here)

When analysed by period following baseline assessment (one month versus six months), at one-month post-stroke, all factors remained statistically significant (motor; OR: 11.25; 95% CI: 2.48 to 51.04, N=48, I^2: 0%; p=0.55, somatosensory; OR: 4.91; 95% CI: 1.24 to 19.46; N=48; I^2: 0%; p=0.46, haemorrhagic; OR: 3.70; 95% CI: 1.05 to 12.98; N=69; I^2: 0%; p=0.57). Upper limb motor impairments were also significant predictors of spasticity at six months post—stroke OR: 30.68; 95% CI: 1.60 to 587.06, N=47, I^2: 0%; p=0.55); however,

somatosensory upper limb impairments nor haemorrhagic stroke were not significant (OR: 2.10; 95% CI: 0.35 to 12.76; N=47; I^2: 0%; p=0.46, OR: 2.92; CI: 0.43 to 19.61; N=47; I^2: 0%; p= 0.57 respectively) (Table 2). Age was also a significant predictor (OR: 0.01; 95% CI: 0.00, 69.89; N=96; I^2: 94%; p<0.0001). There was no statistically significant association between upper limb spasticity, ischemic stroke, side of stroke, level of smoking and gender (Table 2).

(Insert Table 2 about here)

Behavioural, biomechanical and neurophysiological predictors of upper limb spasticity

Studies that explored the association between upper limb spasticity and behavioural measures showed that there was moderate quality evidence to indicate that severity of upper limb motor impairments when measured with instruments such as Birgitta Lindmark Motor Assessment, Upper Extremity Motricity Index and Fugl-Meyer Assessment were significant predictors of upper limb spasticity during the first six months post-stroke (r=0.51; p<.001) [28], (OR: 0.94; 95% CI: 0.92-0.96; p<0.001) [24] and (OR 0.45; 95% CI:0.31-0.65,p=<0.001) [21]. As a result, people with moderate paresis (OR=0.23; 95% CI, 0.10 to 0.54; p=0.001) and mild paresis (OR=0.15; 95% CI, 0.07 to 0.35; p≤0.001) showed a decreased risk of developing spasticity compared with severe paresis [30]. Low scores of activities of daily living outcome measures such as Barthel Index or the modified version were also identified as predictors of upper limb spasticity at admission, at three (OR=1.03; 95% CI: 1.01-1.01, p=0.012) [24], (p<0.001) [29], four (p=0.002) [27] and six months post-stroke (p=<0.001) [29]. Finally, lower quality of life scores were associated with upper limb spasticity at six months post-stroke (p=0.001) [30].

Two studies explored the association between biomechanical properties including contracture and stiffness and upper limb spasticity [26, 27]. Multiple linear regression that spasticity in addition with strength and contracture contributed to upper limb activity during the whole year after stroke (mean r^2_{total} = 0.50, range 0.24-0.68, p= 0.0001-0.008) [26]. Additionally,

measurement of motor impairments by Fugl Meyer Assessment (>18 score) at one month post-stroke was a significant predictor of reflex stiffness gain measured by the elbow joint stretching motor device with force and position sensors (Coefficient: -4.42; p<0.001) [27].

One study reported the association between severe upper limb spasticity and brain lesion location in stroke patients using MRI derived voxel lesion mapping [23]. This reported that a significant greater number of MRI voxels relating to the stroke lesion were associated with upper limb spasticity (p=0.001) [23]. The main brain areas affected by upper limb spasticity from the first week to six months post-stroke were the basal ganglia, thalamus, anterior and posterior limbs of the retrolenticular part of the internal capsule, the anterior, superior, and posterior corona radiate, the external capsule and the superior longitudinal fasciculus.

Discussion

This systematic review identified that motor impairments and age was a significant predictor of upper limb spasticity during the first six months post-stroke. Somatosensory upper limb disturbance and haemorrhagic stroke also were also found as potential predictors at one month post-stroke; however not at six months. Narrative synthesis showed that severity of motor impairments, limitations in activities of daily living and low quality of life were also predictors of upper limb spasticity in the first six months post-stroke.

The profile of the included participants in the review match the study population in that they had an equal amount of left and right sided strokes and cortical, sub-cortical and mixed strokes. Additionally, as expected, ischaemic stroke was more common [31] and the mean age of all the studies was above 60 years. The results of the meta-analysis indicated that age was a significant predictor of upper limb spasticity following stroke. The relationship between age and spasticity has never been specifically explored in stroke, but has been in paediatric populations with cerebral palsy [32]. Age has been identified as a significant predictor of stroke

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severity, aetiology, performance of thrombolysis, gender, risk factors, and stroke complications. In light of the increase in ageing population could have an impact on higher incidence of upper limb spasticity [33]. This suggests that older adults, due to their increased risk of spasticity, may be less likely to achieve a good functional outcome than younger adults [34]. Haemorrhagic stroke presentations were also a significant predictor of upper limb spasticity, but only within the first month post-stroke. The relationship between haemorrhagic stroke and spasticity needs to be further using neurophysiological tools such as electroencephalography and functional Magnetic Resonance imaging through longitudinal studies involving people with stroke from the hyper acute to the chronic stage.

Narrative analyses also showed that severity of upper limb motor impairments can predict upper limb spasticity and this was also reported in similar systematic reviews [13,14]. The meta-analyses results, also showed that level of motor and somatosensory upper limb impairments could predict spasticity. The association between motor impairments and spasticity comes as no surprise. However, when treating spasticity, it did not show any improvement in voluntary motor control [35]. Suggesting that hypertonia is more a cause of contracture than reflex hyperexcitability [36]. Upper limb somatosensory impairments have been reported as being ignored in stroke rehabilitation [37]. This review indicates sensory upper limb deficits may be predictor of upper limb spasticity, this is supported by a previous narrative review Sunnerhagen (2016). In the early stages post-stroke, patients with somatosensory upper limb impairments are more likely to have spasticity. Only one study explored and fully explained the clinical relationship between somatosensory upper limb impairments and spasticity and did not include a detailed somatosensory assessment [21]. Nearly 50% of stroke survivors with upper limb impairment experience somatosensory impairments such as exteroception, proprioception and higher cortical somatosensation, during the first six months

post-stroke [38,39]. Future cross-sectional or longitudinal research in the acute and sub-acute stages could further explore this association.

Future research undertaking greater biomechanical assessment to investigate the motor control reactions may help better understand the underlying neural mechanisms of spasticity [6]. In one of the included studies, measurements of contracture, reflex stiffness and weakness were identified as the major biomechanical contributors measured using electromyography to upper limb spasticity over 12 months post-stroke [24]. This a potential reason for botulinum toxin to be an effective treatment in reducing tone and managing spasticity post stroke [40,41]. Further research exploring both neurophysiological and biomechanical predictors of upper limb spasticity is warranted. More detailed knowledge about the affected cortical regions related to upper limb spasticity will provide a rationale for development of treatment modalities to target these neurophysiological areas.

Whilst this review was conducted and reported in accordance with the PRISMA recommendations [42], it is not without limitations. Grey literature was not searched for this review which could have further strengthened the methodology. As four studies were reported as low quality, the results should be viewed with caution. The study population had a larger proportion of males than females which could have led to some gender bias. In particular, the papers poorly reported about the selection of the sample, length of follow-up and any adjustments in analysis. Due to the included papers reported prediction using inconsistent type of analyses, the narrative analysis presents the values as odds ratios, regression or coefficient data and even p values. Papers reported calculated prediction using different methods of analysis and therefore, The MAS is the most popular test to measure spasticity at the neurological hospital however, the outcome measure has limited reliability and poor validity [43]. The tool does not distinguish between neural and non-neural factors of spasticity. Therefore, the selection of MAS as the primary outcome measure by the majority of studies

has fundamental limitations. Modified Tardieu Scale which measures resistance to movement at different velocities, seems more appropriate in evaluating spasticity [43]. Future research should therefore reconsider the use of this outcome measure in this population.

Conclusions

Upper limb spasticity is common post-stroke. This review identified age as a significant predictor. Motor, somatosensory deficits and haemorrhagic stroke were also identified as predictors for upper limb spasticity within the first month post-stroke. Narrative analysis showed that severity of motor impairments, limitations in activities of daily living and low quality of life were also predictors of upper limb spasticity in the first six months post-stroke. Future research should further explore the biomechanical and neurophysiological predictors of upper limb spasticity. By identifying such predictors this will then allow physiotherapists to select patients with stroke who are at high risk and choose treatment accordingly.

Ethical Approval

Not needed

Conflicts of Interest

None

Systematic review registration number: PROSPERO (ID: CRD42016027642).

Contribution of the paper:

- Motor impairments, sensory deficits, haemorrhagic stroke and stroke were identified as a significant predictors of upper limb spasticity

- Future work should explore the biomechanical and neurophysiological factors contributing to spasticity

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Figure Captions

Figure 1: PRISMA Flow Diagram showing process of the selection of studies
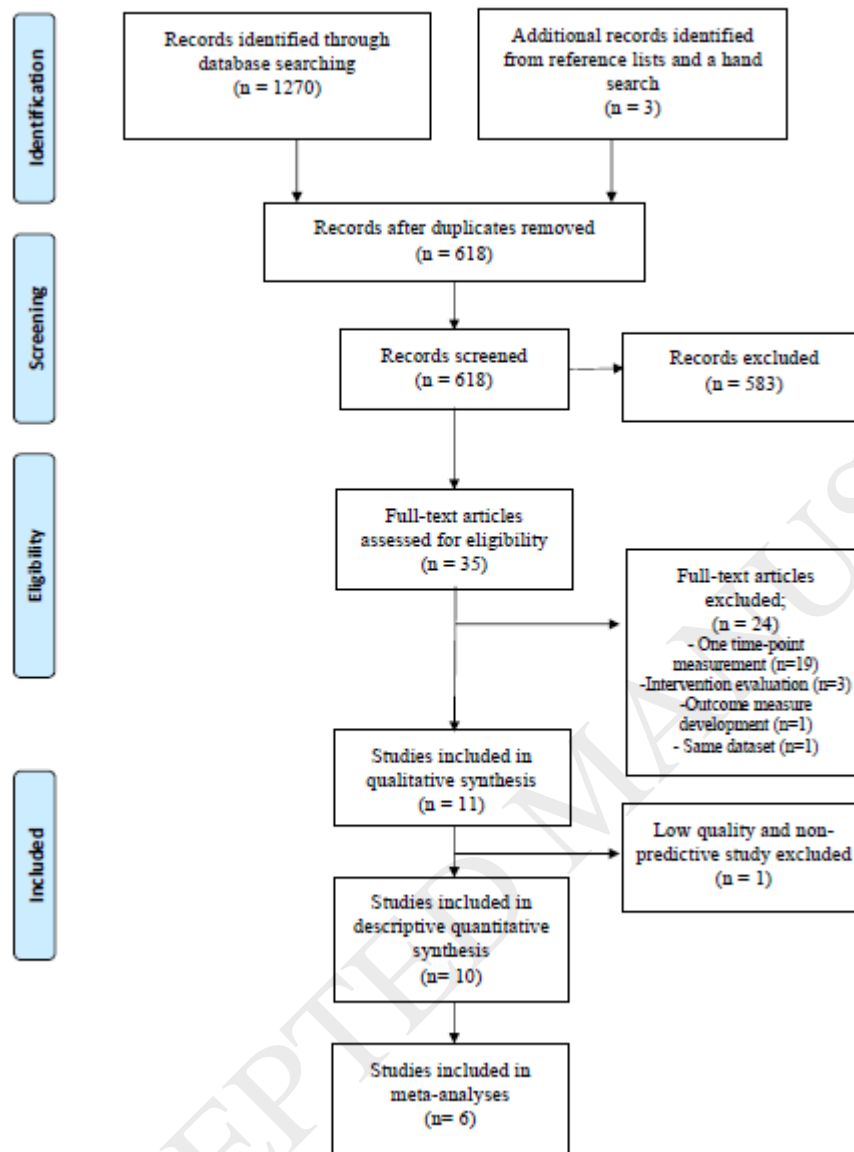

Figure 2: Forest plot displaying the odds ratio analysis for upper limb motor impairments and spasticity
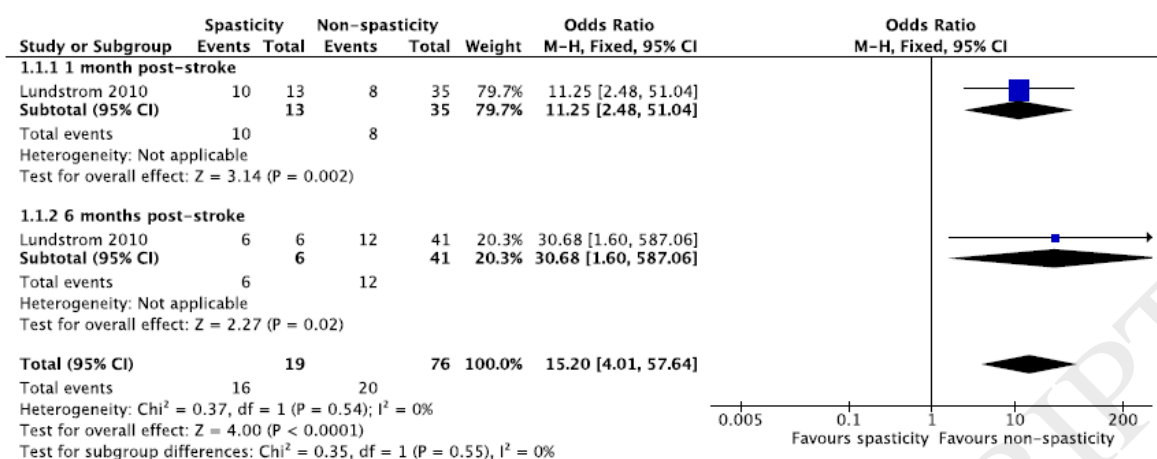
Figure 3: Forest plot displaying the odds ratio analysis for upper limb somatosensory impairments and spasticity
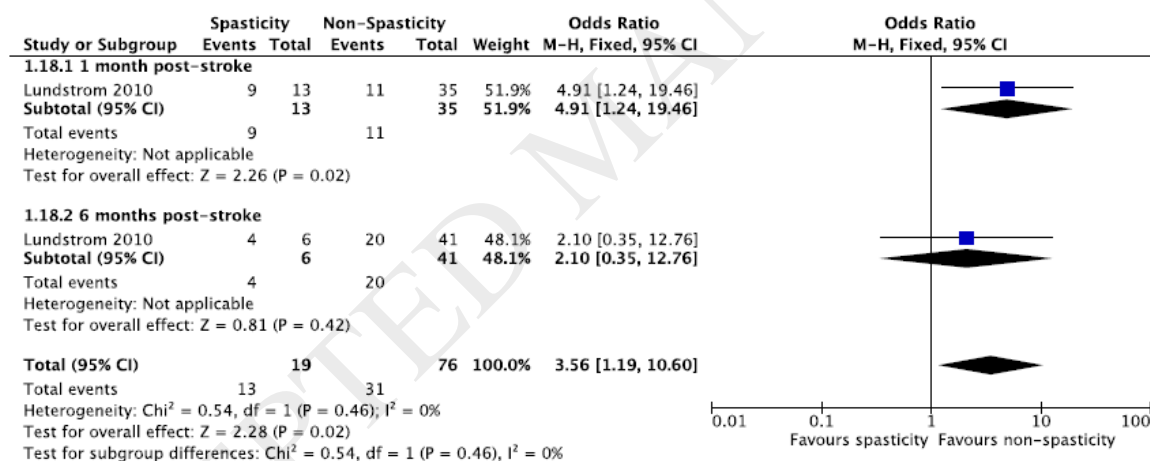
Figure 4: Forest plot displaying the odds ratio analysis for haemorrhagic stroke and upper limb spasticity

Study or Subgroup	Spasticity Events	Total	Non-Spasticity Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
1.17.1 1 month post-stroke							
Lundstrom 2010	5	13	3	35	28.2%	6.67 [1.31, 33.94]	
Mirbagheri 2011	7	9	8	12	43.0%	1.75 [0.24, 12.64]	
Subtotal (95% CI)		22		47	71.2%	3.70 [1.05, 12.98]	
Total events	12		11				

Heterogeneity: Chi^2 = 1.05, df = 1 (P = 0.30); I^2 = 5%
Test for overall effect: Z = 2.04 (P = 0.04)

Study or Subgroup	Spasticity Events	Total	Non-Spasticity Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	
1.17.2 6 months post-stroke							
Lundstrom 2010	2	6	6	41	28.8%	2.92 [0.43, 19.61]	
Subtotal (95% CI)		6		41	28.8%	2.92 [0.43, 19.61]	
Total events	2		6				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)

Total (95% CI)		28		88	100.0%	3.47 [1.22, 9.89]	
Total events	14		17				

Heterogeneity: Chi^2 = 1.11, df = 2 (P = 0.57); I^2 = 0%
Test for overall effect: Z = 2.33 (P = 0.02)
Test for subgroup differences: Chi^2 = 0.04, df = 1 (P = 0.84), I^2 = 0%

0.01 0.1 1 10 100
Favours spasticity Favours non-spasticity

Table 1: Summary of selected papers

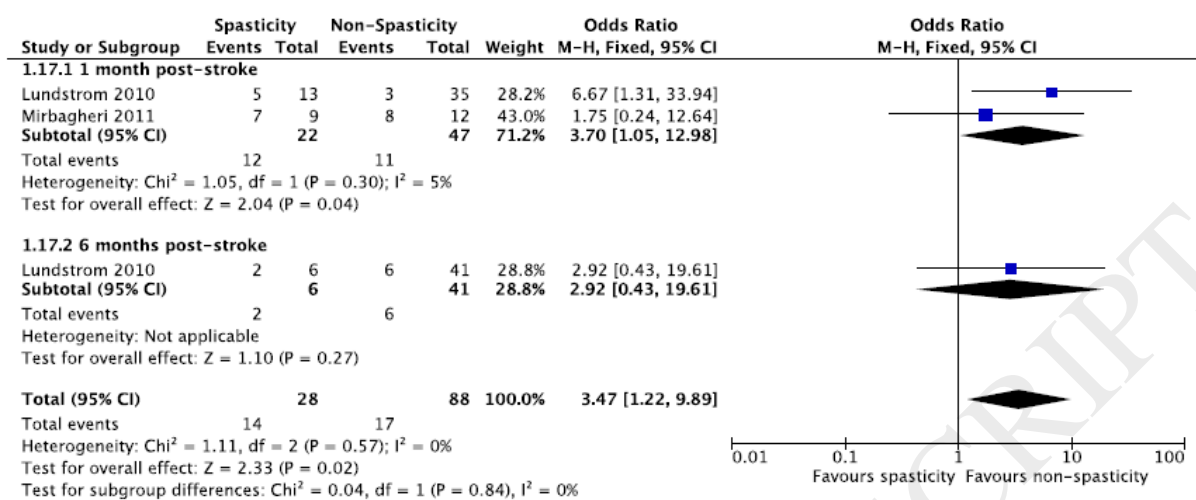| Selected Paper	Aim of paper	Sample Size included in the study (N)	Participant Characteristics	Time-point for baseline assessments	Time-points for follow-up spasticity assessment post-stroke	Variables collected at baseline
Opheim et al. 2015	To identify predictor variables and the optimal time for early prediction of any spasticity and sever severe spasticity in the upper limb 1 year post-stroke	117	Mean (SD) age: 67.2 (12.0) years Gender: 60M, 40F Type of stroke: 82I; 18H Median (range) NIHSS arm: 2 (1-4)	At admission to stroke unit and at 3 days	-3 and 10 days -4 weeks -12 months	Clinical: At admission: -Age - Gender - Smoking - Side of paresis - Stroke location At 3 days: - Upper limb motor impairments - Upper limb sensation
Picelli et al. 2014a	To determine the association between stroke lesion location and severe upper limb post-stroke spasticity using brain voxel-based lesion symptom mapping procedures	39	Mean (SD) age: 72.7 (7.19) years Gender: 24M, 15F Type of stroke: 39I Mean (SD) ESS: 74.4 (20.5)	<7 days	-3-6 months	Neurophysiological: Lesion Tracing using MRI*
Picelli et al. 2014b	To investigate the prognostic value of topical distribution of initial paresis of the upper limb for predicting clinically relevant spasticity in patients with ischemic stroke	72	Mean (SD) age: 70.6 (10.4) years Gender: 48M, 24F Type of stroke: 72I	<7 days	- 6 months	Clinical: Motor items of ESS*
Kong et al. 2012	To conduct a prospective study to document the temporal development and evolution of upper limb spasticity and	163	Mean (SD) age: 63.8 (10.7) years Gender: 111M, 52F Type of stroke: 163I	Admission to rehabilitation	- 6 months - 12 months	Clinical: - Age - Gender - Stroke location

	establish clinical correlates and predictors of upper limb spasticity in a cohort of stroke patients admitted to an inpatient rehabilitation unit		Mean (SD)UEMI: 35.8(30.8)			- Severity of stroke - Sensation - Upper extremity motor strength
Mirabegheri et al. 2011	To quantify the changes in neural and muscular properties associated with spasticity in the upper extremity of stroke survivors at different time-intervals over 1-year post-stroke	21	Mean (SD) age: 64 (12) years Gender: 11M, 10F Type of stroke: 6I; 15H Mean (SD) FMA at 1 month: 25 (23)	1 month	- 2 months - 3 months - 6 months - 12 months	Clinical: - Upper limb motor impairments Bio-mechanical/ Neurophysiological: -Servo position-controlled motor to drive elbow position to measure stiffness. EMGs recorded from biceps, brachioradialis and triceps
Lundstorm et al. 2010	To explore the occurrence of and risk factors for spasticity until first 6 months after stroke	49	Median (min-max) age: 74 (35-84) years Gender: 28M; 21F Type of stroke: 41I; 8H	2-10days	- 1 month - 6 months	Clinical: - Age - Gender - Stroke type (Ischemic/Hemorrhagic) - Stroke severity - Disability - Sensory distribution of pain
Urban et al. 2010	To investigate the prevalence of spasticity after motor stroke and to identify clinical predictors of subsequent spasticity	301	Mean (SD) age: 68(13) years Gender: 131M; 80F Type of stroke: 301I Mean (SD) NIHSS score: 6.6 (4.6)	<5 days	- 6 months	Clinical: - Age - Gender - Stroke severity

Wissel et al. 2010	To follow a cohort of patients from immediate days after stroke to assess frequency and development of spasticity and identifies risk-factors for development of post-stroke spasticity	94	Mean age: 69 years Gender: 38% Female Type of stroke: 86%I; 14%H	<12 days	- 6 weeks - 16 weeks	Clinical: - Age - Gender - Type of stroke (Ischemic/Hemorrhagic) - Lesion site - Lesion side
Ada et al. 2006	To determine the relative contribution of weakness to the secondary impairment contracture of spasticity	27	Mean (SD) age: 63(11) years Gender: 20M; 7F	2 weeks	• 4 weeks • 6 weeks • 9 weeks • 17 weeks • 26 weeks • 39 weeks • 52 weeks	Bio-mechanical/ Neurophysiological: -Potentiometer and EMG* amplifier to measure strength and contracture at elbow
Sommerfeld et al. 2004	To describe the extent spasticity occurs and is associated with disabilities initially and 3 months after stroke	95	Mean (SD) age: 78(9.5) years Gender: 35M; 60F	Mean 5.4 days	- 3 months	Clinical: - Upper limb Motor impairments

* BI=Barthel Index; BL= Birgitta Lindmark Motor Assessment; EMG=Electromyography; ESS= European Stroke Scale; F= Female; FMA=Fugl Meyer Assessment; H= Haemorrhagic; I= Ischaemic; M=Male; MAS=Modified Ashworth Scale; MBI=Modified Barthel Index; MRI=Magnetic Resonance Imaging; MoAS=Motor Assessment Scale; MRS=Modified Rankin Scale; NIHSS=National Institutes of Health Stroke Scale; UEMI=Upper Extremity Motricity Index

Table 2: Odds ratios and statistical heterogeneity for dichotomous predictors

Predictor Variable	Post-Stroke Assessment Interval	Participants (N Studies)	OR (95% CI)	I2/Chi2
Age	Cumulative	96	0.01 (0.00, 69.86)	94% / P<0.0001
Gender (male)	Cumulative	227 (4)	1.73 (0.96, 3.12)	24% / P=0.26
	1	108 (3)	1.99 (0.86, 4.47)	24% / P=0.26
	6	119 (2)	1.47 (0.62, 3.49)	24% / P=0.26
Gender (female)	Cumulative	227 (4)	0.73 (0.40, 1.32)	0% / P=0.87
	1	108 (3)	0.77 (0.34, 1.76)	0% / P=0.87
	6	119 (2)	0.68 (0.29, 1.61)	0% / P=0.87
Smoking	6	72 (1)	1.74 (0.68, 4.45)	Not estimatable
Handedness (Right)	6	72 (1)	1.67 (0.41, 6.80)	Not estimatable
Handedness (Left)	6	72 (1)	0.60 (0.15, 2.45)	Not estimatable
Upper limb motor impairments	Cumulative	95 (1)	15.20 (4.01, 57.64)*	0% / P=0.54
	1	48	11.25 (2.48, 51.04)*	0% / P=0.55
	6	47	30.68 (1.60, 587.06)*	0% / P=0.55
Upper limb somatosensory impairments	Cumulative	95 (1)	3.56 (1.19, 10.60)*	0% / P=0.46
	1	48 (1)	4.91 (1.24, 19.46)*	0% / P=0.46
	6	47 (1)	2.10 (0.35, 12.76)	0% / P=0.46
Side of Stroke (Left)	Cumulative	132 (3)	0.84 (0.42, 1.67)	0% / P=0.49
	1	60 (2)	1.24 (0.44, 3.52)	0% / P=0.49
	6	72 (1)	0.60 (0.23, 1.55)	0% / P=0.49
Side of Stroke (Right)	Cumulative	132 (3)	1.20 (0.60, 2.40)	0% / P=0.49
	1	60 (2)	0.80 (0.28, 2.27)	0% / P=0.49
	6	72 (1)	1.67 (0.65, 4.30)	0% / P=0.49
Location of stroke (Subcortical)	1	39 (1)	0.35 (0.08, 1.57)	Not estimatable
Location of stroke (Cortical)	1	39 (1)	1.25 (0.24, 6.57)	Not estimatable
Location of stroke (Mixed)	1	39 (1)	2.10 (0.56, 7.81)	Not estimatable
Type of Stroke (Ischaemic)	Cumulative	116 (2)	0.29 (0.10, 0.82)	0% / P=0.57
	1	69 (2)	0.27 (0.08, 0.95)	0% / P=0.57
	6	47 (1)	0.34 (0.05, 2.31)	0% / P=0.57
Type of Stroke (Haemorrhagic)	Cumulative	116 (2)	3.47 (1.22, 9.89)*	0% / P=0.57
	1	69 (2)	3.70 (1.05, 12.98)*	0% / P=0.57
	6	47 (1)	2.92 (0.43, 19.61)	0% / P=0.57

*=significant