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Predictors of upper limb recovery after stroke: a systematic review and meta-analysis

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Abstract

Objective: To systematically review and summarize the current available literature on prognostic variables relating to upper limb recovery following stroke. To identify which, if any variables predict upper limb recovery following stroke.

Data sources: We completed searches in MEDLINE, EMBASE, AMED, CINAHL and Cochrane CENTRAL databases. Searches were completed in November 2010.

Review methods: Studies were included if predictor variables were measured at baseline and linked to an outcome of upper limb recovery at a future time point. Exclusion criteria included predictor variables relating to response to treatment and outcome measurements of very specific upper limb impairments such as spasticity or pain. Two independent reviewers completed data extraction and assessed study quality.

Results: Fifty-eight studies met the inclusion criteria. Predictor variables which have been considered within these studies include; age, sex, lesion site, initial motor impairment, motor-evoked potentials and somatosensory-evoked potentials. Initial measures of upper limb impairment and function were found to be the most significant predictors of upper limb recovery; odds ratio 14.84 (95% confidence intervals (CI) 9.08–24.25) and 38.62 (95% CI 8.40–177.53), respectively.

Conclusions: Interpretation of these results is complicated by methodological factors including variations in study populations, upper limb motor outcome scales, timing of baseline and outcome assessments and predictors selected. The most important predictive factors for upper limb recovery following stroke appears to the initial severity of motor impairment or function.

Keywords

Arm, predictors, rehabilitation

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Introduction

Stroke is a major public health concern worldwide[1] and in the UK is the most prevalent cause of severe adult disability.[2] Consequently, stroke is a major source of health and social care expenditure[3] and has been identified as a priority area for the British National Health Service (NHS).[4,5] One of the most common deficits following stroke is upper limb motor impairment,[6] which can significantly impact on disability and health.[7,8] Variability in the nature and extent of upper limb recovery is well recognized.[9–11]

The different patterns of recovery of upper limb function mean that individual patients will have different rehabilitation needs.[12] Currently, we lack good practical examples of stratification and individualization of rehabilitation programmes for the upper limb.[12,13] Ideally, we would identify variables which reliably predict upper limb recovery. Such information would be useful to both clinicians and researchers[14] to optimize rehabilitation, to clarify outcomes and the effects of therapy, to improve the design and analysis of clinical trials, to identify appropriate interventions, and to accurately inform patients of likely outcomes.

Several studies have investigated a number of variables for their ability to predict upper limb recovery.[10,15–17] A systematic review[18] reported in 2009 that neurophysiological measures and initial sensorimotor abilities were the best predictors of voluntary arm movement after stroke. This review focused on categorizing the predictive variables and associated outcome measures in terms of the International Classification of Functioning, Disability and Health. In contrast, we wished to provide a more wide-ranging and comprehensive summary of reported predictive variables and their association with upper limb recovery. A further review of prediction of motor recovery[19] considered only the predictive value of motor impairment scores, neuroimaging and neurophysiological assessment. The aim of the current review was to systematically review and summarize the current, available literature regarding prognostic variables relating to upper limb recovery following stroke.

Methods

We carried out a systematic review of variables which may predict upper limb recovery following stroke.

We followed the MOOSE guidelines for Meta-Analyses and Systematic Reviews of Observational Studies to complete and report this review.[20]

A study was eligible for inclusion if it met the following criteria:

1. Full published article.
2. Observational study that investigated at least one variable (explanatory variable) measured at baseline and its relationship with a measure of upper limb recovery (response variable) measured at a future time point.
3. The study population included individuals with upper limb deficits following stroke.
4. Outcomes included upper limb function/functional movement or impairment.

A study was excluded if:

a. no extractable data were available for independent variables,
b. only outcomes relating to specific upper limb impairments (such as pain, contractures) were available,
c. it explored response to treatment in one or more subgroups of a clinical trial.

To identify relevant studies we searched: MEDLINE (1950–November 2010), EMBASE (1980–November 2010), AMED (1985–November 2010), CINAHL (1982–November 2010) and Cochrane CENTRAL. Reference lists of included studies were also searched to identify any additional studies.

Our search strategy was generated following consultation with a medical librarian, consideration of appropriate literature[21] and using search terms developed by the Cochrane Stroke

Group.[22] Keywords relating to stroke, upper limb and prediction were included. Titles were initially screened, following which two independent reviewers (FC and either PL or AP) screened relevant abstracts and appropriate full papers. Where disagreement existed, consensus was reached through discussion.

Data extraction

Using specifically developed forms two reviewers (FC and PL or AP) extracted the following information: study setting, participant details, inclusion and exclusion criteria, rehabilitation received, predictive variables, duration of follow-up, outcomes and data on associations between variables and outcomes of upper limb recovery.

The quality of each individual study was assessed using criteria previously proposed[23,24] for assessing the validity of studies dealing with prognosis. The methodological criteria included questions concerning the sample of patients, follow-up, outcome measurement, predictive variables, analysis, and treatment or other confounders.

Completion of the checklist was completed by two reviewers (FC and PL or AP) and any disagreements were resolved through discussion.

Data analysis

We expected to find variations in the explanatory variables studied and statistical methodologies applied and so our analysis combined several approaches.

Initially data were analysed using a simple vote-counting methodology. We identified the number of studies investigating a particular explanatory variable and recorded the number of these studies that reported a statistically significant ($P < 0.05$) association between that variable and a recognized measure of upper limb recovery.

The information gained from the vote-counting analysis was summarized using a classification of the strength of the evidence using four levels of evidence.[25,26]

- Strong: Consistent findings ($\geq$80%) in at least two high-quality cohorts
- Moderate: One high-quality cohort and consistent findings ($\geq$80%) in one or more low-quality cohorts
- Limited: Findings of one cohort or consistent findings in one or more low-quality cohorts
- Inconclusive: Inconsistent findings regardless of study quality.

Statistical pooling was performed using, where available, odds ratios (OR) of associations presented in the original papers. Where odds ratios were not presented but raw data were available we calculated an odds ratio and 95% confidence interval (CI) for the association between each variable and a measure of upper limb recovery. This involved ascribing cut-offs to both the explanatory variable and measure of upper limb recovery. Where possible the cut-offs used to calculate the odds ratios were selected to match those used in other studies (e.g. Medical Research Council (MRC) scale power 0–2 versus 3–5). We calculated odds ratios to show the group most likely to achieve a better upper limb outcome. This involved inverting some odds ratios presented in the original papers. We used the inverse variance approach to combine odds ratios in a random effects meta-analysis. All analyses were undertaken using the Cochrane software package RevMan 4.2.[27]

In the final form of analysis we took a consensus approach to categorizing the evidence based on the consistency of the evidence from the vote counting and the magnitudes of the odds ratios from the meta-analysis. Greater emphasis was given to larger studies.

Results

Our search identified 5022 titles. Fifty-eight studies (with 67 associated publications)[9,10,12,14–17,28–87] met the inclusion criteria.

The main characteristics of the included studies, including the predictor variables investigated and outcome measures used are presented in Table 1.

Table 1. Characteristics of included studies

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
Alagona 2001[28] Delaux 2003[29]	25; 22 (follow-up). For one analysis $n = 16$: Inpatients	Age ($\leq$55/>55), sex (M/F), global disability (NIH; <11/$\geq$11), TMS variables (MEP; FDI muscle of the hand, present/absent), side of stroke (L/R), UL impairment (MRC score, 0–5; $\geq$2/<2)	BI motor (0–57; $\geq$20/<20) MRC FDI (0–5; $\geq$4/<4)	6 months post stroke (12 months for one analysis)
Al-Rawi 2009[30]	22: Acute inpatients	UL impairment (MRC scale), SSEP	MRC scale (0–5)	3 months post stroke
Au-Yeung 2009[31]	70; 57 (follow-up): Acute inpatients	UL impairment (Motricity Index), side of stroke, stroke location (lacunar or no obvious lesion, cortical, subcortical or combined subcortical and cortical lesions), overall disability (NIHSS), cognition and perceptual (neurobehavioural cognitive status examination), UL sensation (two-point discrimination)	ARAT (0–57; $\geq$35/<35)	6 months post stroke
Barreca 1999[32]	16: Consecutive admissions to tertiary rehabilitation care centre	UL functional movement (UEFT score), cognition and perception (Halstead Category test score), time post stroke, UL impairment (Chedoke McMaster stroke assessment arm and hand subscore)	Upper extremity function test (0–100)	Last week of rehabilitation (mean 77 days)
Beebe 2009[33]	33; 28 (follow-up): Inpatients	UL impairment (NIHSS motor arm score; $\leq$2/>2)	ARAT (0–57; $\geq$40/<40)	3 months post stroke
Binkofski 2001[34]	52; 15 (follow-up): Inpatients	UL functional movement (arm and hand function score, 0–32; $\leq$16/>16), lesion size, lesion localization (subcortical/cortical)	Multifactorial score for arm and hand function (0–32; inverted scale, $\leq$16/>16)	Up to 180 days after admission
Canning 2004[35]	22: Rehabilitation inpatients	Upper limb functional movement (MAS), UL impairment (strength; torques)	MAS (item 6 – upper arm function; 0–6)	27 weeks post stroke
Catano 1995[36]	40: Inpatients	TMS (MEP responses; FDI and ADM muscles; present/absent)	MRC (FDI and ADM muscle; 0–5)	90 days post-stroke
Catano 1997[37]	49: Inpatients	TMS (EMG silence – silent period following MEP; SPD stable vs. SPD reduced by increasing facilitation)	MRC (FDI muscle) (0–5; $\geq$4/<4)	90 days after stroke onset
Cho 2007[38]	55: Inpatients	DTT (integrity of corticospinal tract)	Modified Brunnstrom classification	6 months after stroke onset

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
Cruz-Martinez 1999[39]	20; 15 (initial UL deficits): Unclear	TMS variables (MEPs; thenar muscles, present/absent), age ($\leq$55/>55), sex, size of lesion (1–3 cm/>3 cm), side of lesion (L/R), UL impairment (CNS distal arm score; 1.0/<1.0)	CNS (distal arm score; 0–1.5; $\geq$1.0/<1.0)	6 months post stroke
Dachy 2003[40]	56; 48 (follow-up): Rehabilitation inpatients	TMS variables; (MEPs; abductor digiti minimi muscles, present/absent), side of lesion	Motricity index (UL; 0–100)	Late stage of rehabilitation (mean 76 $\pm$ 17 days post stroke)
De Souza 1980[41]	14: Outpatient stroke unit	UL impairment (arm, trunk and hand movement; >50%/<50%)	Assessment of arm, trunk and hand movement (>80%/<80%)	32 weeks post stroke
De Weerdt 1987[42]	111; 58 (follow-up): Inpatients	Age, sex, pre-stroke ability, pre-stroke mental status, duration for stroke to develop, handedness, global impairment, speech disorders, side of lesion (side of hemiplegia), number of previous strokes, visual disorders (visual field loss), seventh cranial nerve, pain in arm (spontaneous arm pain), shoulder complications, UL impairments (F-M), UL functional movement (ARAT), sensation (light touch), cognition and perception (post-stroke mental status)	ARAT (0–57)	6 months post stroke
Escudero 1998[43]	50: Inpatients	UL impairment (MRC abductor pollicis brevis), global disability (BI), TMS variables (MEPs; abductor pollicis brevis present/absent)	MRC score (abductor pollicis brevis muscle; 0–5)	6 months post stroke
Feys 2000[44] Feys 2000[45] Feys 2000[14]	100; 96 (follow-up) (some analysis on $n = 48$): Inpatients	Global disability (BI), TMS variables (MEPs; abductor pollicis brevis, present/absent), SSEPs; median nerves at the wrist present/absent, infarction location, age, sex, UL impairment (F-M UL section), side of hemiparesis, UL sensation (tactile), visual disorders (hemianopia; not occurring/occurring)	F-M (UL section; 0–66)	6 months post stroke

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
		cognition and perceptual (MMSE); no deficit ≥ 24/deficit < 24), speech disorders (not occurring/occurring), mood (Hospital Anxiety and Depression Scale; no deficit > 10/deficit ≤ 10), shoulder complications (shoulder pain; absent/present)		
Gowland 1982[46]	229; 223 (follow-up): Consecutive admissions to rehabilitation centre	Age ($\leq 55/> 55$), UL sensation (normal sensation/sensory involvement), perception (without deficit/deficit), global impairment (hemiparesis/hemiplegia), time since stroke (onset < 12 weeks/> 12 weeks), side of stroke (side of hemiplegia R/L)	Brunnstrom stages of arm motor recovery (1–6; $\geq 2/< 2$ stages of improvement)	Discharge from rehabilitation centre
Hatakenaka 2007[47]	34: Inpatient rehabilitation unit	Sex, UL impairment (F-M UL section), distribution of upper extremity paresis (proximal or distal), TMS variables (MEPs; biceps brachii potentials presence/absence), size of lesion	Functional category of upper extremity (A–D; A–B/D)	End of inpatient rehabilitation (mean 108 ± 17 days)
Heald 1993[48]	118; 76 (follow-up): Inpatients	TMS variables (central motor conduction time; normal, delayed or absent)	NHPT (rate of positioning of pegs per second)	12 months post stroke
Hendricks 1994[49] Hendricks 1997[50]	29; 20 (follow-up but $n = 29$ used for analysis): Inpatient neurology department	MEPs (abductor digiti quinti muscle, present/absent), SEPs (median nerve stimulation; present/absent)	Motor recovery (voluntary motor action) (presence/absence of motor recovery)	1–4 years post stroke (mean 2.4 years)
Hendricks 2003[51]	43; 40 (follow-up): Consecutive admissions to inpatient neurology department	TMS variables (MEPs; biceps brachii muscle, present/absent)	F-M (arm score; 0–30; arm motor recovery yes/no)	26 weeks post-stroe
Higgins 2005[52]	56; 55 (follow-up): Consecutive admissions from acute inpatients	Age, sex, UL functional movement (FAT), UL impairment (strength; Jamar), general motor impairment (Stroke Rehabilitation Assessment of Movement), lower limb impairment (gait speed; 5-minute walk test), number of comorbid conditions, type of stroke, side of lesion	Box and block test (number of blocks in 1 minute)	5 weeks post stroke

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
Jang 2010[53]	53: Consecutive admissions from acute inpatietns	TMS variable (MEP; abductor pollics brevis, present/absent), DTT imaging (CST integrity, present/absent)	Motricity Index (0–100; $>62/<62$)	6 months post stroke
Jorgensen 1999[54] Nakayama 1994[9]	826; 619 (follow-up): Consecutive admissions from inpatient stroke unit	Upper limb impairment (Scandinavian Stroke Scale subscores for arm and hand; mild or moderate/severe)	BI (subscores for feeding and grooming; full or partial function/no function)	6 months post stroke
Katrak 1990[17]	29: Inpatient rehabilitation centre	UL impairment (hand movement scale, 1–6; $>2/\leq 2$ and shoulder shrug; present/absent)	MAS; hand movement section (1–6)	Discharge from hospital (average 125 days post stoke)
Katrak 1998[55]	57; 46 (follow-up): Inpatient rehabilitation unit	Age, sex, UL impairment (hand movement scale, 1–6; 1/2 or 3), UL sensation (incorporating light touch, sensory inattention and proprioception), side of stroke (side of hemiparesis)	Hand function test (1–4) – 'good' hand function – able to complete one of the tasks.	3 months post stroke
Keren 1993[56] Keren 1995[57]	19: Rehabilitation hospital	SEPs (median nerve, present/absent)	Rancho Los Amigos (17 UL activities)	Follow-up (30–40 days after discharge)
Kwakkel 2003[10]	102; 100 (follow-up): 7 hospital sites	Age ($<70/\geq 70$), sex, UL impairment (Motricity Index arm, 0–100; $\geq 11/<11$), urinary incontinence (BI subsection; absent/present), type of stroke (OCSP), side of stroke (L/R), time since stroke, cognition and perception (MMSE; no deficit/deficit), consciousness during initial 24 hours (Glasgow Coma Scale), sitting balance (Trunk Control Test; no deficit/deficit), global disability (BI), UL sensation (thumb-finding test), visual deficits (hemianopia; no/yes), social support (present/absent), lower limb impairment (F-M leg; $\geq 25/<25$)	ARAT (0–57; $>10/\leq 9$)	6 months
La Joie 1982[58]	68: Inpatient rehabilitation hospital	SSEPs evoked potentials (median nerve; present; absent), UL function at admission (present/absent)	UL functional return (self-care activity, functional return; no functional return)	Discharge (mean 84; 44–205 days)

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
Lin 2009[59]	57: Unclear population	Age, sex, side of stroke, time since stroke, global disability (NIHSS), UL impairment (F-M distal section)	Motor Activity Log (QOM scale; 0–5)	End of intervention period (3 weeks long). Mean of 12 months post stroke on entry to study
Loewen 1990[60]	57; 50 (follow-up): Emergency department	Age, sitting balance (Modified MAS component), sit to stand (Modified MAS component), UL functional movement (Modified MAS; combined arm score), bowel function (BI component), urinary incontinence/bladder function (BI component)	Modified MAS (combined arm score; sum of scores on upper arm function, hand movements and advanced hand movement sections)	Discharge
Loubinoux 2003[61]	9: Neurology department	Global disability (NIHSS, $<11/\geq 11$)), UL impairment (Motricity Index UL section, 0–100; $\geq 11/<11$), UL functional movement (NHPT; able to complete/unable to complete), global impairment (Motricity Index; $\geq 66/<66$)	Motricity Index (UL section, 0–100; $\geq 66/<66$)	28 days after first assessment
Meldrum 2004[12] Meldrum 2000[62]	114; 108 (follow-up): Hospital inpatients	Age ($<65/65–74/\geq 75$), type of stroke (OCSP), UL sensation (normal/impaired/absent or unable to assess), UL impairment (Rivermead arm score), global disability (Orpington Prognostic score)	Rivermead Arm Score (0–15; 5–15/0–4/death)	6 months
Nagao 1992[63]	13: Unclear population	Age($\leq 55/>55$), sex, side of stroke (L/R), TMS variables (MEP; thenar muscles, present/absent), UL impairment (Manual Motor Test, 0–5; $>2/\leq 2$), time since stroke (day 0/$\geq$ day 1)	Manual Motor Test (0–5; ≥ 2 (fair and good/ <2 (poor)	3 months after initial assessment
Nascimbeni 2006[16]	19: Hospital inpatients	TMS (MEP; first dorsal interosseous muscle, present/absent) UL impairment (Motricity Index, upper limb subscale; $\geq 11/<11$), global disability (NIHSS, $<11/\geq 11$)	MRC scale (hand, 0–5; $\geq 2/<2$)	4 months post stroke
Nijland 2010[64]	188; 156 (follow-up): Acute inpatients	Age ($<70/\geq 70$), sex, side of stroke (L/R), type of stroke (OCSP classification), time since stroke, recombinant tissue plasminogen (no/yes), comorbidity, visual deficits (hemianopia no/yes),	ARAT (0–57; ≥ 10 regained some dexterity/ ≤ 9 no dexterity regained)	6 months post stroke

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
		cognition and perception (visual inattention no/yes), urinary incontinence (BI no/yes), sensory loss (no/yes), UL impairment (Motricity Index shoulder abduction 0/ ≥ 9), LL impairment (Motricity Index $< 25/ \geq 5$), sitting balance ($<25/25$)		
Olsen 2007[65]	66: Consecutive admissions to rehabilitation unit	UL impairment (MRC scale 0–5; $> 2/ \leq 2$), global disability (BI $\geq 60/ < 60$)	BI (UL sections; prepare tray and feed self and dress upper body; 0–11, $\geq 9/ < 9$)	Discharge
Paci 2007[66]	121; 107 (follow-up): Rehabilitation department	Age, sex, side of stroke, length of stay, time since onset of stroke, UL impairment (motricity subscore of F-M upper extremity), UL sensation (F-M upper extremity sensory score), shoulder complications (shoulder pain; absence/presence)	F-M (upper extremity score)	Follow-up (30–40 days after discharge)
Park 2008[67]	222; 166 (follow-up) but data imputed for all $n = 222$: Assumed outpatients	UL motor impairment (FM), age, sex, side of stroke, global disability (Functional level), sensation (FMA light touch), UL functional measures (Wolf Motor Function Test (WMFT) functional ability scale), time after stroke, type of stroke, cognition and perception (impaired visual perception)	Motor Assessment Log (QOM) scale (0–5; $\geq 3/ < 3$)	12 months post treatment
Parker 1986[68]	266; 152 (follow-up): Stroke register of all acute stroke patients	UL impairment (Motricity Index, 0–100; ≥ 33 (mild or moderate)/ < 33 (severe))	FAT (0–5; $\geq 4/ < 4$)	3 months
Pennisi 1999[69]	15: Inpatient hospital setting	Age($\leq 55/ > 55$), sex, infarction location (subcortical or cortico-subcortical), lesion size, side of stroke, global disability (NIHSS, $< 11/ \geq 11$)	Scale derived from MRC (0–5; $\geq 2/ < 2$)	Day 365
Pizzi 2009[70]	52; 38 (follow-up) Consecutive admissions to a neurorehabilitation department	TMS (MEP; EDC present/absent), UL impairment (MRC scale EDC $\geq 2/ < 2$)	FAT (0–5; $\geq 2/ < 2$)	12 months

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
Prabhakaran 2008[71]	41: Inpatient stroke service	Age, sex, UL impairment (F-M upper extremity), lesion location, lesion volume, time to reassessment.	F-M upper extremity change score (0–66)	Approx. 3 months post infarct
Putman 2007[72]	532; 419 (follow-up): Consecutive admissions to 4 stroke rehabilitation units across Europe	Socioeconomic status (educational level, equivalent income)	Rivermead Motor Assessment (arm section 0–15; 11–15/6–10/0–5)	Discharge
Rapisarda 1996[73]	26: Neurological unit	TMS (MEP; hand muscles, present/absent), global disability (NIH, $<11/\geq 11$)	Scale derived from MRC scale (hand; 0–5; $\geq 2/<2$)	Day 14
Renner 2009[74]	16: Rehabilitation unit	UL impairment	ARAT (0–57)	6 weeks post enrolment
Roy 1995[75]	76: Consecutive admissions to acute hospital inpatient setting	Shoulder complications (shoulder pain; absence/presence), cognition, UL sensation (touch sensation) and urinary incontinence (absent/present)	FAT (0–5)	12 weeks
Shelton 2001[15] Shelton 2001[76]	171: Consecutive admissions to rehabilitation unit	Age, sex, UL impairment (F-M; UL motor section), cognition (MMSE), type/class of stroke (hemiparetic motor deficits, hemiparetic motor plus hemisensory deficit or hemianopic visual deficits, motor plus hemisensory plus hemianopic visual deficits or other combinations of deficits), lower limb impairment (F-M; lower limb motor section), global impairment (F-M), lesion location (cortical/subcortical/mixed), handedness (right/left/ambidextrous), side of stroke, time since stroke (interval from stroke to admission; <2 weeks/2–4 weeks/>4 weeks), global disability (Functional Independence Measure (FIM))	F-M (UL 0–58)	Discharge (mean 38 ± 17 days)
Smania 2007[77]	47; 37 (follow-up): Consecutive admissions to neurology department	UL impairment (hand movement scale, 1–6; $>3/\leq 3$)	NHPT (time to pick up and insert pegs)	180 days after stroke

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
Stinear 2007[78]	21; 17 (follow-up): 3 hospital and one rehabilitation facility	Age ($\leq$55/ > 55), sex, side of stroke (hemisphere affected (L/R)), time since stroke < 29 months/ > 29 months), hand grip asymmetry (force transducer), TMS variables (MEPs; extensor carpi radialis, present/absent), global disability (NIHHS, $\leq$ 4/ > 4), UL impairment (F-M UL movement section, 0–32; $\geq$ 11/ < 11), infarction location (motor cortex damage), sensory loss (cutenous sensation; no sensation loss/sensation loss)	F-M (UL movement section; 0–32; $\geq$2/ < 2 points of improvement)	30 days
Sunderland 1989[79]	38; 31 (follow-up): Inpatient hospital	UL impairment (Motricity Index, 0–100; > 18/ < 18), UL functional movement (FAT; > 0/0)	FAT (0–5; >0/0)	6 months
Trompetto 2000[80]	21; 14 (follow-up): Consecutive admissions to acute admission setting	TMS variables (MEPs; thenar muscles, present/ absent), age (<70/ $\geq$ 70), sex, side of stroke (L/R), global disability (Scandinavian stroke scale 0–58; > 29/ $\leq$ 29), UL impairment (Scandinavian stroke scale hand motor score, 0–6; 0/ $\geq$ 1)	Scandinavian Stroke Scale (subscore for hand motor function; 0–6; $\geq$4/ < 4)	6 months
Turton 1996[81]	21: Stroke unit inpatients	Age (55/>55), sex (M/F), side of stroke (L/R), UL impairment (Motricity Index UL section >11/11), TMS (MEPs response/no response)	NHPT (only available for TMS variable) Motricity Index (UL section 0-100; > 66/ < 66)	6 weeks (NHPT outcome only); 6 months
Tzvetanov 2004[82] Tzvetanov 2005[83]	102; 94 (follow-up): Stroke unit	SSEPs (median nerve, normal/absent/amplitude ratio < 0.5 but > 0), age, UL impairment (MRC score), sex, side of stroke.	MRC scale (0–5)	6 months
Van Kuijk 2009[84]	39; 35 (follow-up) Department of neurology	UL impairment (F-M; presence/absence of any motor recovery of the upper extremity), TMS (MEPs; present/absent), lower limb impairment (F-M lower limb section; presence/absence of motor recovery)	F-M hand section (0–14; >3/ $\leq$ 3)	6 months

(continued)

Table 1. Continued

Author, year	No of participants: Study population	Explanatory/predictive variables	Outcome measure of upper limb recovery	Follow-up
Wagner 2007[85]	9: Hospital inpatients receiving rehabilitation	UL impairments (composite active range of motion), shoulder complications (shoulder pain), sensation (composite light touch)	Accuracy of reaching	Mean 108.7 ± 16.5 days
Yagura 2003[86]	947: Inpatients from general and rehabilitation wards	Time since stroke, upper limb functional movement (category B–D)	Upper extremity functional category (A–D, reaching independence (category A)	Discharge (mean 101.18 ± 27.3 days)
Yoshioka 2008[87]	17: Unclear	DTT imaging data (FA ratio, (($>0.75/\leq 0.75$), age ($\leq 55/>55$), gender, stroke location, stroke volume ($<15/>15$ ml), UL impairment (MMT $>2/\leq 2$), lower limb impairment ($>2/\leq 2$)	Manual motor test (0–5; $\geq 3/<3$)	3 months

NIH, National Institute for Health; BI, Barthel Index; TMS, transcranial magnetic stimulation; MEP, motor-evoked potential; FDI, first dorsal interosseous; UL, upper limb; MRC, Medical Research Council; SSEP, somatosensory-evoked potentials; NIHSS, National Institute for Health Stroke Scale; UEFT, Upper Extremity Function Test; MAS, Motor Assessment Scale; DTT, diffusion tensor tractography; CNS, Canadian Neurological Scale; F-M, Fugl-Meyer Scale; ARAT, Action Research Arm Test; APB, abductor pollicis brevis; MMSE, Mini Mental State Examination; FAT, Frenchay Arm Test; OCSP, Oxford Community Stroke Project classification of stroke; NHPT, Nine Hole Peg Test; LL, lower limb; QOM, quality of movement.

The type of study design was often not reported. We categorized all studies as some form of cohort study, with the exception of eight studies.[30,35,37,38,66,74,75,87] Six studies were reported as cohorts embedded within randomized controlled trials.[10,14,52,67,79,85]

The sample size reported within the included studies ranged from nine[61] to 1197.[54] Twenty-nine studies [16,17,28,30,32,33,35–37,39,41,47,50,51,57,61,63,69,71,73,74,77–81,84,85,87] included 50 participants or less and only 15 studies[10,12,14,42,46,48,54,64,66–68,72,76,83,86] had an initial sample size of 100 or more participants. Of the 31 studies that reported loss to follow-up,[10,12,14,28,31,33,34,40,42,43,46,48,50–52,54,55,60,64–68,70,72,77–80,83,84] the percentage of participants lost varied between 2%[10] and 48%.[42] The mean (or median) time since stroke ranged from within 24 hours[34,52,54,69,73,77] (or admission to acute hospital) to 29 months.[78]

Thirty-six studies[10,14,16,17,28,31,33–39,41,43,46,50,51,53,55,59,61,64,65,67,69–73,78–81,84,85] explicitly reported some form of upper limb impairment at onset as an inclusion criterion; however, the definitions of such ranged considerably. Fifty-two studies (as above and[30,32,40,48,52,54,58,62,63,68,74,75,77,83,86,87]) provided details on initial upper limb impairment in terms of a mean score on a clinical measure or by using general descriptions. Six studies[42,47,57,60,66,76] did not report any details on initial upper limb impairment.

A wide range of predictor variables was reported (Table 1) so we grouped together variables of similar constructs (for example measures of cognition and perception). This process identified 41 groups of variables, of which 25 (Table 2) were reported by more than one study. Variables that were reported by only one study were not included in any further analysis due to the limited information available.

As it was impossible to anticipate the full range of predictor variables studied the process of categorizing the predictor variables into the above groups was undertaken by consensus, after data extraction but prior to data analysis. Only one predictor variable per categorized group was chosen for each included study. This was achieved through consensus.

The studies also used a wide range of outcome measures (see Table 1), follow-up periods and statistical analyses. Twenty-four different outcome measures were reported and considered in our analysis. If a measure of upper limb function or functional movement (for example, Action Research Arm Test[88]) was available this was included in the analysis, otherwise measures of upper limb impairment were used (for example, Fugl-Meyer Scale[89]). Twenty-nine studies[10,17,28,31–35,42,47,48,52,54,55,57–60,64,65,67,68,70,74,75,77,79,81,86] reported an upper limb function or functional movement outcome. If both final outcome scores and change scores were presented, outcome scores were used in preference.

Where more than one follow-up measurement was available we took the default position of using data closest to the six-month outcome measurement for use in the analysis.

From the data presented in 26 studies[16,17,28,33,34,37,39,41,46,51,53,54,58,61,63,65,67,68–70,73,78–81,84,87] we were able to calculate crude odds ratios with 95% confidence intervals. Six studies[10,31,47,50,55,64] reported odds ratios which we used in the analysis.

The methodological characteristics of the studies were often poorly reported; where reported, the methodological quality was very variable. We elected not to exclude studies based on quality but took this into account in the interpretation of results.

Table 2 provides an overview of the 25 categorized variables that were described in at least two studies plus the evidence for their association with better upper limb recovery. The variables are presented in groups of comparable variables. These groups were agreed by consensus between two reviewers and reflected the nature of the variables (e.g. demographic variables). Statistical analysis for variables for which data were available is presented in Figure 1.

Table 2. Overview of the evidence for 25 categorized variables that were described in at least two studies

Variable	No. of studies (participants)	Significant association reported No. of studies (participants)	Strength of evidence analysis[27]	Statistical analysis No. of studies (participants) Odds ratio (95% CI)	Considered judgement
Demographic factors					
Age (younger vs. older)	23[10,28,39,42,44,46,52,55,59,60,62,63,64,66,67,69,71,76,78,80,81,83,87] ($n = 1695$)	2[12,59] ($n = 165$)	Strong evidence of no association	11[10,28,39,46,63,64,69,78,80,81,87] ($n = 590$) 1.54 (1.06–2.25)	Inconclusive evidence. Suggestion that younger people are more likely to have better UL recovery
Sex (male vs. female)	21[10,14,28,39,42,47,52,55,59,63,64,66,67,69,71,76,78,80,81,83,87] ($n = 1371$)	0	Strong evidence of no association	11[10,28,39,47,63,64,69,78,80,81,87] ($n = 424$) 1.61 (1.11–2.33)	Inconclusive evidence. Suggestion that males are more likely to have better UL recovery
Time since stroke (less vs. more time)	11[10,32,46,59,63,64,66,67,76,78,86] ($n = 2006$)	5[10,59,67,78,86] ($n = 1326$)	Inconclusive evidence	5[10,46,63,64,78] ($n = 486$) 1.13 (0.90–1.40)	Inconclusive evidence. Suggestion of no association between time since stroke and UL recovery
Severity of stroke – global factors					
Global disability (less vs. more disability)	16[10,12,14,16,28,31,43,59,61,65,67,69,73,76,78,80] ($n = 919$)	9[10,12,14,31,43,59,65,67,69] ($n = 771$)	Inconclusive evidence	9[10,16,28,61,65,69,73,78,80] ($n = (288)$ 3.64 (1.63–8.10)	Moderate evidence that less disability is associated with better UL recovery
Type/class of stroke (less vs. more severe)	7[10,12,43,52,64,67,76] ($n = 862$)	4[10,12,64,76] ($n = 535$)	Inconclusive evidence	2[10,64] ($n = 256$) 3.54 (0.46–27.34)	Inconclusive evidence
Global impairment (less vs. more impairment)	5[42,46,52,61,76] ($n = 493$)	3[42,52,76] ($n = 284$)	Inconclusive evidence	2[46,61] ($n = 209$) 2.19 (0.35–13.90)	Inconclusive evidence
Lesion size/volume (smaller vs. larger)	5[34,39,47,69,87] ($n = 132$)	0	Limited evidence of no association	3[39,47,87] ($n = 65$) 1.32 (0.74–2.38)	Limited evidence of no association
Urinary incontinence (absent vs. present)	4[10,60,64,75] ($n = 382$)	2[10,64] ($n = 256$)	Inconclusive evidence	2[10,64] ($n = 256$) 4.12 (1.82–9.32)	Inconclusive evidence
Severity of stroke – focal factors					
UL baseline impairment measures (less vs. more impairment)	39[10,12,14,16,17,29,30–33,35,39,41–43,47,52,54,55,59,61,63–68,70,74,76–82,84,85,87] ($n = 2715$)	25[10,12,14,17,30,31,32,42,47,54,59,61,63–68,70,76,79,81,82,84,85] ($n = 2349$)	Strong evidence of association	20[10,16,29,33,39,41,54,55,61,63,64,65,68,70,78–80,81,84,87] ($n = 1425$) 14.84 (9.08–24.25)	Strong evidence that less impairment is associated with better UL recovery

(continued)

Table 2. Continued

Variable	No. of studies (participants)	Significant association reported No. of studies (participants)	Strength of evidence analysis[27]	Statistical analysis No. of studies (participants) Odds ratio (95% CI)	Considered judgement
UL baseline functional measures (more vs. less function)	10[34,35,42,52,58,60,61,67,79,86] ($n = 1512$)	9[34,35,42,52,58,60,67,79,86] ($n = 1503$)	Strong evidence of association	4[34,58,61,79] ($n = 158$) 38.62 (8.40–177.53)	Strong evidence that more upper limb function is associated with better UL recovery
Lower limb impairment (less vs. more impairment)	6[10,52,64,76,84,87] ($n = 534$)	5[10,52,64,76,84] ($n = 517$)	Moderate evidence of association	4[10,64,84,87] ($n = 308$) 11.83 (6.53–21.42)	Moderate evidence that less leg impairment is associated with better UL recovery
Cofactors					
Side of stroke (left vs. right)	21[10,14,28,31,39,40,42,46,52,55,59,63,64,66,67,69,76,78,80–82] ($n = 1506$)	2[10,64] ($n = 256$)	Strong evidence of no association	11[10,28,31,39,46,63,64,69,78,80,81] ($n = 624$) 1.47 (1.07–2.01)	Inconclusive evidence. Suggestion that left hemisphere stroke may be associated with better UL recovery
UL sensation (no deficit vs. deficit)	11[10,14,31,42,46,55,62,66,75,78,85] ($n = 859$)	6[10,31,42,47,62,66] ($n = 584$)	Inconclusive evidence	3[10,46,78] ($n = 271$) 1.92 (1.41–2.61)	Inconclusive evidence. Suggestion that absence of sensory deficit is associated with better recovery.
Cognition and perception (no deficit vs. deficit)	10[10,14,31,32,42,46,64,67,75,76] ($n = 1101$)	4[32,42,64,76] ($n = 401$)	Inconclusive evidence	4[10,31,46,64] ($n = 462$) 1.86 (0.91–3.78)	Inconclusive evidence
Stroke location	8[14,31,34,69,71,76,78,87] ($n = 398$)	3[31,34,76] ($n = 280$)	Inconclusive evidence	NA	Inconclusive evidence. Unable to combine data
Shoulder complications (absent vs. present)	5[14,42,66,76,85] ($n = 376$)	2[42,75] ($n = 134$)	Inconclusive evidence	NA	Inconclusive evidence
Visual disorders (absent vs. present)	4[10,14,42,64] ($n = 410$)	3[10,42,64] ($n = 314$)	Moderate evidence of association	2[10,64] ($n = 256$) 5.22 (2.40–11.36)	Moderate evidence that absence of visual disorder is associated with better UL recovery

(continued)

Table 2. Continued

Variable	No. of studies (participants)	Significant association reported No. of studies (participants)	Strength of evi dence analysis[27]	Statistical analysis No. of studies (participants) Odds ratio (95% CI)	Considered judgement
Sitting balance (no deficit vs. deficit)	3[10,60,64] ($n = 306$)	1[64] ($n = 156$)	Inconclusive evidence	2[10,64] ($n = 256$) 4.75 (0.28–80.53)	Inconclusive evidence. Suggestion of no association between sitting balance and UL recovery
Speech disorders (absent vs. present)	2[14,42] ($n = 154$)	1[42] ($n = 58$)	Inconclusive evidence	NA	Inconclusive evidence
Handedness (right vs. left vs. ambidextrous)	2[42,76] ($n = 229$)	0	Limited evidence of no association	NA	Limited evidence of no association
Sensation (no deficit vs. deficit)	2[64,67] ($n = 378$)	1[64] ($n = 156$)	Inconclusive evidence	1[64] ($n = 156$) 9.15 (3.36–24.89)	Inconclusive evidence
No. of comorbid conditions (less vs. more)	2[52,64] ($n = 211$)	0	Limited evidence of no association	1[64] ($n = 156$) 1.96 (0.96–3.98)	Limited evidence of no association
Neurophysiological factors					
Motor-evoked potentials (present vs. absent)	20[14,16,28,36,37,39,40,43,47–50,53,63,70,73,78,80,81,84] ($n = 687$)	15[14,16,28,36,40,43,48–50,53,63,70,73,80,84] ($n = 551$)	Strong evidence of association	15[16,28,37,39,47,49,50,53,63,70,73,78,80,81,84] ($n = 425$) 11.76 (5.19–26.65)	Strong evidence that present MEPs are associated with better UL recovery
Somatosensory-evoked potentials (present vs. absent)	6[30,45,50,56,58,82] ($n = 280$)	6[30,45,50,56,58,82] ($n = 280$)	Strong evidence of association	2[50,58] ($n = 97$) 13.73 (2.73–69.10)	Strong evidence that present SSEPs are associated with better UL recovery
Diffusion tensor tractography (DTT) (preserved corticospinal tract or not)	3[38,53,87] ($n = 125$)	3[38,53,87] ($n = 125$)	Limited evidence of association	2[53,87] ($n = 70$) 35.46 (8.97–140.10)	Limited evidence that preserved corticospinal tract determined by DTT associated with better UL recovery

UL, upper limb; MEP, motor-evoked potential; SSEP, somatosensory-evoked potentials; DTT, diffusion tensor tractography.

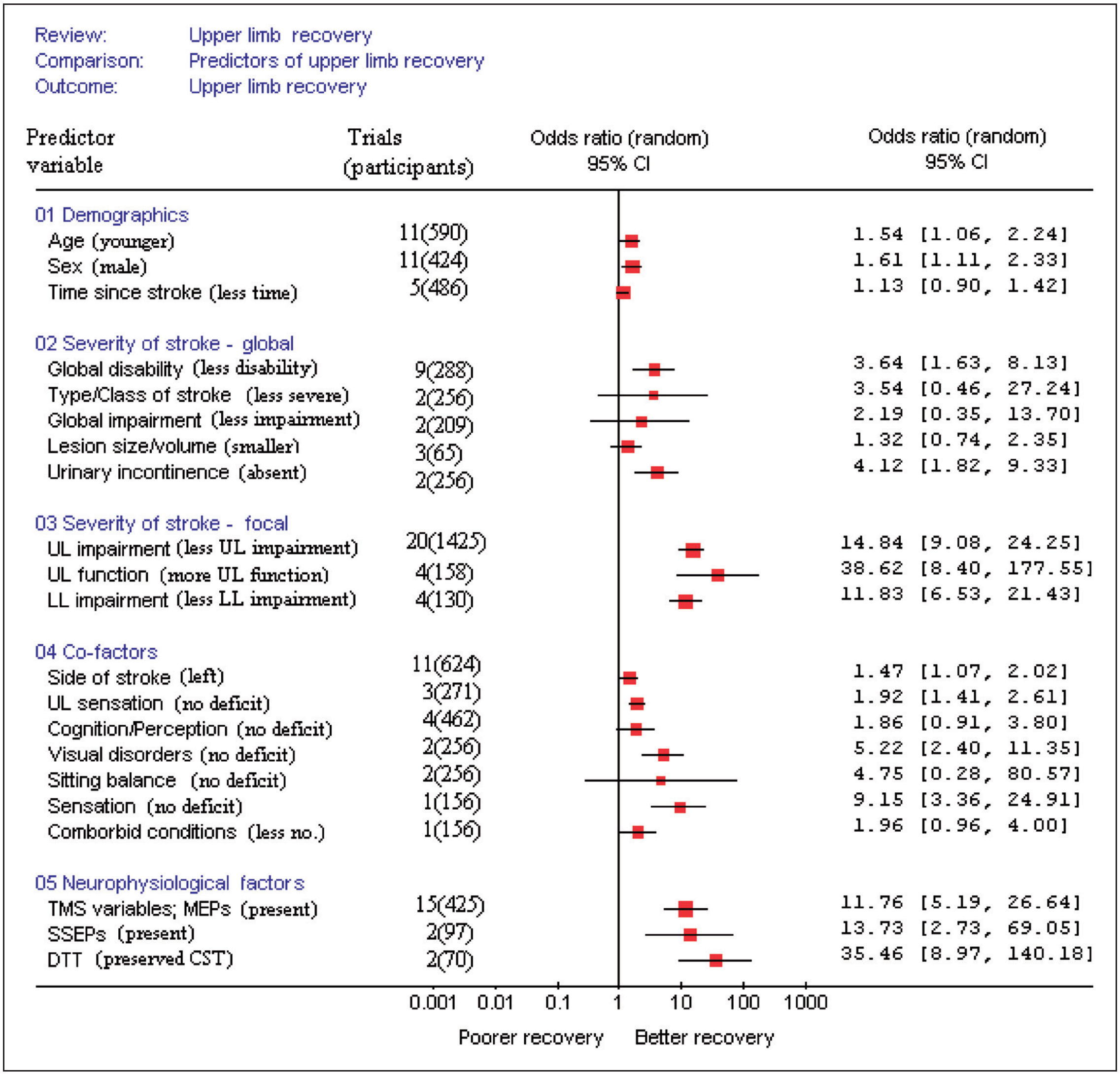

Figure 1. The association (odds ratio ≥95% confidence interval) of baseline variables with upper limb recovery. The figure shows the category of variable tested, the number of studies (participants) studied, the odds ratio (95% confidence interval) for a univariate association between the predictor and a 'good' upper limb outcome. Odds ratios are presented to show the group most likely to make a good outcome (as indicated in brackets). UL, upper limb; LL, lower limb; TMS, transcranial magnetic stimulation; MEP, motor-evoked potential; SSEP, somatosensory-evoked potentials; DTT, diffusion tensor tractography.

Demographic factors

Analyses for the variables of age and sex were inconclusive due to inconsistencies between data analyses. Vote-counting analysis did not identify any association with either of these variables and upper limb recovery, however a statistically significant result was found in both cases (OR 1.54 (95% CI 1.06–2.25) and OR 1.61 (95% CI (1.11–2.33) respectively). These statistical analyses suggest younger people and males respectively are more likely to have better upper limb recovery. Inconclusive evidence was found for time since stroke.

Severity of stroke – global factors

We identified inconclusive evidence in the vote-counting analysis for the variable of global disability. However, a statistically significant result was found in the statistical analysis of nine studies ($n = 288$), suggesting that those with less disability are more likely to have better upper limb recovery. We found inconclusive evidence for global motor impairment, urinary incontinence and type/class of stroke and limited evidence of no association for lesion size/volume.

Severity of stroke – focal factors

The most commonly investigated variable was a baseline measure of upper limb impairment. The overall qualitative conclusion was that there was strong evidence that a lesser degree of impairment is associated with better upper limb recovery. Although this was due to only 25 of the 39 studies reporting a significant association, this did encompass 87% of the included participants. Strong evidence of association was found for baseline upper limb functional measures and moderate evidence for baseline lower limb impairment.

Cofactors (related to stroke impairment)

In terms of side of stroke only two of 21 studies reported an association; however, statistical analysis suggests that left hemisphere stroke is significantly associated with better upper limb recovery. The evidence was inconclusive for cognition and perception, stroke location, shoulder complications, sitting balance, speech disorders and sensation. Evidence was also inconclusive for an association between upper limb sensory deficits and upper limb recovery. Limited evidence of no association was found for both handedness and the number of comorbid conditions.

Neurophysiological factors

We found consistent results between studies indicating strong evidence for the association between the presence of evoked potentials (both motor and somatosensory) and better upper limb recovery. Limited evidence was found for an association between preserved corticospinal tract (determined by diffusion tensor tractography) and better upper limb recovery.

Discussion

We have identified and summarized the results of 58 studies that have reported on the predictive value of a number of variables for upper limb recovery following stroke. A wide range of variables and outcome measures have been considered within the literature. However, despite a number of variables being investigated, only baseline upper limb functional and impairment measures and neurophysiological factors (motor-evoked potentials and somatosensory-evoked potentials) were consistently identified as being strongly associated with upper limb recovery following stroke.

We also found moderate evidence that less disability and lower limb impairment were associated with better upper limb recovery. No predictive value was found for lesion size. Despite having different objectives and using different methods of data analysis, our findings are largely consistent with the other previous reviews in this area.[18,19]

The main limitation of our review relates to the heterogeneity of the studies. This includes the varying definitions of initial upper limb problems, differing predictive variables and measurements, outcome measures, length of follow-up and data presentation. Ascribing arbitrary cut-offs to variables, including continuous measures, which were not consistent across the studies further adds to the potential heterogeneity.

Another weakness of our review was that prior to data extraction, we did not stipulate how we would categorize predictor variables, or what cut-offs we would use for dichotomizing variables and outcomes of interest. However, where possible we wanted to include as many relevant studies as possible within the statistical analysis.

Publication bias is also a concern with this type of review. Studies with significant results are more likely to be published, have more than one associated publication and also are more likely to be identified through the searching process.[90]

We addressed this through a rigorous searching process. It is reassuring that our search identified a very similar group of studies to the other recent reviews of this area.[18,19]

The quality assessment criteria we used were based on sound theoretical considerations. However, consensus between the reviewers was difficult to obtain as a number of subjective decisions had to be made due to frequent poor reporting of methodological aspects. For this reason the methodological quality of the studies was not used to exclude studies. However, it should be recognized that conclusions with moderate evidence of association could potentially be overturned by more methodologically robust studies.

Upper limb recovery is a broad concept and differences in how this is defined are apparent. For this review we took the default position of determining upper limb recovery in terms of either functional recovery of the upper limb or recovery of impairment, where measures of functional recovery were not available. If we had only included functional measures as an outcome, this may have led to some differences in the conclusions. However, the direction of effect is likely to be unchanged. In general, upper limb impairments have been found to be associated with functional ability of the upper limb.[91]

We were mainly interested in answering the question 'Is there any evidence of effect between individual variables and upper limb recovery?' and we believe our approach to data analysis is suitable for answering this question. Our data analysis included vote counting, which is recognized as having limitations.[92] However, this allowed the inclusion of the greatest number of studies and we supplemented it with quantitative analyses. Statistical analysis of predictive studies is also recognized as raising significant challenges.[21] However, we felt that the statistical analysis of the studies added another dimension and reduced the subjectivity in interpreting the evidence. There was a good level of consistency between the conclusions of the statistical and other analytical approaches.

Within this review we have based our findings on information from univariate analyses. We recognize that these univariate results are not adjusted for potential confounders. However, this review was intended to identify which predictor variables were available and their individual ability to predict of upper limb recovery. The way we elected to group individual predictor variables and the outcome measures that we chose to include in the analysis may have influenced our results. However, there is no suggestion that our main conclusions would have changed had we chosen alternative groupings or outcomes.

The main strength of our review is that we have used a rigorous systematic review methodology and included a large number of studies. Furthermore, we have used a rigorous, explicit and prospective approach to identify, appraise, combine and synthesize a lot of complex data into a clear and concise format. The included studies showed a reasonable consistency of results, which adds to the confidence in the conclusions of the review.

Implications for practice

Although clinical practice is becoming more evidence based it is not routine practice to use prognostic tests and indicators to prescribe therapeutic programmes. Upper limb level of impairment and function at baseline and intact motor-evoked potentials or somatosensory potentials appear to be the most powerful predictors of upper limb recovery. Evoked potentials are usually only collected in the context of clinical research trials and therefore clinical measures will be far more useful to clinicians.

Implications for research

For stratification in clinical trials researchers should consider using those measures which have been found to be strongly associated with recovery (for example, baseline Fugl-Meyer, Action Research Arm Test).

This review has highlighted the need for improved quality of reporting of predictive studies in this area. In addition, large high-quality cohort studies would be useful to validate the strength of evidence of this systematic review. Further studies could also investigate multivariate models and their usefulness for predicting upper limb recovery. For further studies to be relevant to clinical practice and research we suggest that it would be useful to establish an international consensus on a core set of relevant predictive variables and standardized outcome criteria for upper limb recovery.

Conclusions

This systematic review found strong evidence that initial measures of upper limb function and impairment and neurophysiolgical measures can predict upper limb recovery. We also identified a number of variables for which moderate evidence was available. A number of limitations with the available evidence are discussed.

Clinical messages

- Initial measures of upper limb function and impairment and neurophysiological measures can predict upper limb recovery.
- Heterogeneity and poor quality of studies makes interpretation of evidence difficult.

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Appendix 1– Search strategy

1. exp cohort studies/
2. incidence.sh.
3. exp mortality/
4. follow-up studies.sh.
5. prognos$.tw.
6. predict$.tw.
7. course$.tw.
8. predictor$.tw.
9. exp models, statistical/
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. cerebrovascular disorders/or exp basal ganglia cerebrovascular disease/or exp brain ischemia/ or exp carotid artery diseases/or cerebrovascular accident/or exp brain infarction/or exp cerebrovascular trauma/or exp hypoxia- ischemia, brain/or exp intracranial arterial diseases/or intracranial arteriovenous malformations/or exp 'Intracranial Embolism and Thrombosis'/ or exp intracranial hemorrhages/or vasospasm, intracranial/or vertebral artery dissection/.
12. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
13. hemiplegia/or exp paresis/
14. (hemipleg$ or hemipar$ or paresis or paretic).tw.
15. 11 or 12 or 13 or 14
16. exp Upper Extremity/
17. (upper adj3 (limb$ or extremity)).tw.
18. (arm or shoulder or elbow or forearm or hand or wrist or finger or fingers).tw.
19. 16 or 17 or 18
20. 10 and 15 and 19