SYSTEMATIC REVIEW

REVISED Comparing upper limb motor recovery in subacute ischaemic stroke and intracerebral haemorrhage: A Systematic Review.

[version 2; peer review: 1 approved, 2 approved with reservations]

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Abstract

Background

The pathophysiology and medical management between ischaemic stroke and intracerebral haemorrhage differ as do their functional independence and mortality outcomes. This paper aims to establish whether their respective upper limb motor impairment and recovery differ. This information could inform discussions with patients about their recovery prognosis as well as identify appropriate rehabilitation settings.

Methods

A PROSPERO registered systematic search of three databases (MEDLINE, CINAHL, Embase) identified studies that measured upper limb motor function (Fugl-Meyer assessment scale for upper extremity) in participants with first stroke (ischaemic stroke or intracerebral haemorrhage) within 31 days post-stroke and at least one follow-up assessment. Risk of bias was assessed using the Critical Appraisal Skills Programme.

Results

Open Peer Review

Approval Status ✓ ? ?

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version 2 (revision) 06 May 2025	✓ view		? view
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Any reports and responses or comments on the article can be found at the end of the article.

The search identified 1108 studies of which three met inclusion criteria, with a total of 258 participants (200 ischaemic stroke, 58 intracerebral haemorrhage). All studies had low to moderate risk of bias. At baseline, participants with intracerebral haemorrhage had greater upper limb motor impairment on the Fugl-Meyer assessment scale, but at six months post-stroke, the stroke subtypes reached similar upper limb motor function. Improvements were greatest early after stroke.

Conclusions

Despite greater severity at baseline, intracerebral haemorrhage survivors appeared to reach the same level of arm function at six months post stroke. However, these findings need to be interpreted with caution due to limited studies and small number of participants included in this review and warrant further research.

PROSPERO registration

CRD42020159110 (19/02/2020).

Plain Language Summary

Is arm recovery different between a stroke caused by a clot or a bleed? Clinicians make decisions of care pathways and medical treatment for patients early after stroke by what they expect their recovery will be. Most people have a stroke caused by a clot and a lot of research has been done about their recovery. But we don't know if recovery is the same in people who had a stroke caused by a bleed, rather than a clot. The purpose of this study is to see if previous studies can show if arm recovery is the same between these stroke types. We investigated arm recovery because it is the most common difficulty after stroke. We performed a literature search to find studies that measured arm recovery using the Fugl-Meyer upper limb assessment in both stroke types, from before 31 days after stroke and performed at least one follow-up assessment. We identified 3 studies with a total of 258 participants (200 individuals who had a stroke cause by a clot and 58 a stroke caused by a bleed). At the first assessment individuals with a stroke caused by a bleed had more arm weakness but at six month the arm weakness was very similar between the stroke types. Athough individuals with a stroke caused by a clot have more arm weakness early after stroke, they appear to recovery more. However, further studies need to investigate differences in recovery of arm function between these stroke types because our investigation only included a small number of studies.

Keywords

Ischaemic stroke, Intracerebral haemorrhage, motor recovery, upper limb

This article is included in the Neurology gateway.

This article is included in the Stroke Association gateway.

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REVISED **Amendments from Version 1**

We have added the motor recovery domain of the upper limb, and the time point after stroke.

The authors have stated the aim of the study more clearly in the introduction.

We have added a paragraph on upper limb recovery and changed the wording to aim at the end of the paragraph.

We have clarified the statement regarding healthcare negativity in ICH survivors to: The knowledge will shape goal setting and discharge planning. Furthermore, this information could assist clinical decision-making with regards to life saving interventions early after stroke and rehabilitation pathways at later time points

We have included references for the CASP checklists.

We clarified the description of the analysis of attrition.

We rewrote the sentence describing data synthesis and analysis.

We expanded on the use of the Pearson's chi-square test as a measure to investigate categorical distribution and incorporated the specific tests in the sentence structure rather than having them referred to in brackets.

We clarified the sentence that described the inclusion of ten three studies in the analysis

We have clarified in the text that the degree of the risk of bias has been reported for the respective studies as indicated by the references. We have added the description of ROB.

We believe that we have outlined the key ROB factors in the paragraph and reference the relevant papers where this was the case. However, for further clarity we have restructured some sentences and added further detail.

We removed this statement – "All used the FMA-UE to measure upper limb motor function."

We included signposting to the data in Supplementary material Table 6.

We have further clarified how this study could inform the choice of life saving intervention.

We addressed grammatical error in the text.

Any further responses from the reviewers can be found at the end of the article

Introduction

Stroke places a significant burden on society and is the third-leading cause of death and disability globally[1,2]. Despite Intracerebral Haemorrhage (ICH) being globally far less common than ischaemic stroke (27.9% vs 62.4%), it accounts for a greater proportion of the global burden[2]. The burden of stroke can be attributed to many factors, with the most common impairment after stroke being upper limb motor weakness[3,4], from which recovery is poor[5,6]. Arm weakness impacts on stroke survivors' independence, quality of life and ability to maintain previous life roles[7,8]. Despite significant recent advances in stroke care, over 20% *of* stroke survivors do not recover functional use of their arm[3]. The impact of poor arm recovery is considerable with an estimated 100,000 strokes occurring in the UK every year, and 1.2 million stroke survivors alive at any time[9]. However, longitudinal epidemiological studies of stroke recovery are very rare[10] and the natural history of recovery after stroke not well understood, especially in ICH. Arm recovery is influenced by patient demographics, stroke severity and acute care[11,12]. However, it is currently unclear whether upper limb impairment and recovery differs between ICH and ischaemic stroke because stroke recovery tends to be reported without differentiating between stroke types.

The pathophysiology of ischaemic stroke and intracerebral haemorrhage is fundamentally different. Ischaemic stroke is caused by an occlusion in a cerebral blood vessel[13] with the ischaemia-related cascade causing alterations in the function of glial cells and neurons[14]. In contrast, ICH is caused by the rupture of a blood vessel with resultant blood in brain tissue. Therefore, in addition to ischaemia, the pathophysiology of ICH involves the mass effect of the haematoma on cerebral tissue[15,16], and the interaction between components of the haematoma and the brain[17]. In light of these pathophysiological differences, it is likely that upper limb motor recovery differs with regards to the extent as well as timeline for these stroke subtypes.

An understanding of recovery differences in upper limb motor function between ICH and ischaemic stroke will inform discussions about recovery prognosis between clinicians and patients. The knowledge will shape goal setting and discharge planning. Furthermore, this information could assist clinical decision-making with regards to life saving interventions early after stroke and rehabilitation pathways at later time points. Currently, negativity of ICH outcome prevails, and clinicians do not instigate lifesaving interventions including admission to intensive care and neurosurgical evacuation of the haematoma when patients with ICH present with severe impairments at baseline[18]. We here aim to establish whether there is evidence of differences in upper limb motor recovery between ischaemic stroke and ICH by performing a systematic review of the literature.

Methods

This review was reported according to PRISMA guidelines (Supplementary Table 1[19]) and was registered prospectively with PROSPERO (CRD42020159110) on 19th February 2020.

Patient and Public Involvement

There was no Patient and Public Involvement in the delivery of this systematic review.

Eligibility criteria

We included observational, randomised and non-randomised controlled trials (RCT) conducted in adults with stroke. Studies were included if they recruited at least 15 participants each with ischaemic stroke and ICH. Smaller studies would increase the risk of a type-2 error. Studies needed to measure upper limb motor function using the Fugl-Meyer Assessment Upper Extremity Subscale (FMA-UE) within 31 days of stroke onset (baseline) in addition to follow-up measures. Data had to be reported separately for stroke subtypes. Studies were excluded if (i) participants with previous stroke could not be excluded from the dataset, (ii) stroke subtype was not reported and (iii) raw data was not provided to address the above requirements. For RCTs, data from the treatment arm were excluded if there was a significant statistical difference between groups.

Search strategy and study selection
A systematic search was conducted in Medline, Embase and CINAHL on the 17th of December 2020. Search strings were based on concepts of 'stroke', 'early,' 'motor recovery', and 'upper limb'. Searches were limited to studies published in English from 2000 to 2020, coinciding with the start of stroke units[20] (Supplementary Table 2[21]). The titles, abstracts and full texts were consecutively screened independently by two reviewers (LG and UH). Disagreement regarding inclusion was resolved through discussion. In addition, the references from key included publications were hand-searched for completeness of inclusion. Raw data were requested from authors in cases of 1) inclusion of participants with previous stroke, 2) some participants with baseline data after 31 days post-stroke or 3) if outcomes were not reported separately for ischaemic stroke and ICH patients.

Data extraction
Data were extracted (LG) to Microsoft Excel and checked thoroughly (UH). When datasets (containing individual patient data) were obtained, participants with previous stroke and participants without baseline data before 31 days post-stroke were excluded. The data sought was upper limb motor function measured using the Fugl-Meyer Assessment Scale for the Upper Extremity (FMA-UE) at timepoints up to one year post-stroke. Baseline timepoints were at less than seven days and 3–4 weeks after stroke. Follow-up timepoints at which data were collected were at ten days, three weeks and one, three, six and twelve months after stroke.

Risk of bias assessment
Study quality was assessed by two reviewers using the randomised control trial (RCT) and cohort studies Critical Appraisal Skills Programme (CASP) checklists respectively. We tabulated attrition observed in the three studies (Supplementary Table 3). In addition to documenting the missing numbers at each time point for the two stroke types, we compared their baseline impairment. To established whether attrition caused a risk of bias through missingness of more severely affected individuals. To do this we calculated the mean FMA-UE score for the missing participants at baseline and subtracted the mean FMA-UE baseline score for the stroke type in the study. Thereby a negative score would indicate that more severe individuals were missing for followed-up for the respective stroke type and highlight bias.

Data synthesis and analysis
Descriptive statistics, using SPSS version 27, were used to calculate data separately for ischaemic stroke and ICH. Statistical tests to establish differences in baseline characteristics and outcomes between stroke types used independent samples t-test for normally distributed data, Mann Whitney U-test for non-normal data and Pearson's chi-square test to investigate categorical distribution. Mean outcome measure scores at the respective time point for each stroke subtype and in each study were plotted on a chart. Trajectories of upper limb motor recovery of the two groups were compared.

As one study excluded the reflex measurement component from the FMA-UE[22], the outcome measure was converted to a percentage of the respective maximum score (66 or 60) and are represented as this throughout.

Results
Study identification
The search yielded 1108 studies after removal of duplicates (Figure 1, PRISMA Flow Chart). After title and abstract screen, 413 full texts were screened, of which, 393 were excluded. Of the remaining 20 studies, one study reported outcome measures separately for stroke type and 19 reported that they included both IS and ICH survivors but did not report separate outcomes. Eligibility of these studies was dependent on the provision of separate outcomes for ischaemic stroke and ICH or raw data. Data from seven from the above 19 studies were obtained, but five studies were excluded because they did not satisfy all eligibility criteria, resulting in the inclusion of three studies in the review.

Data for ischaemic stroke and ICH baseline characteristics and outcome measure scores were collated (Table 1 and Supplementary Table 4).

Risk of bias
The risk of bias (Supplementary Table 4 and 5[23,24]) in the reported studies was moderate to low[25] and moderate[22,26] for the respective studies. This was largely due to the fact that important established confounding factors had not been identified or accounted for 22,26. Furthermore, baseline measures of impairments were not matched and the study groups did not receive the same level of care[25]. Attrition bias was observed (Supplementary Table 3[27]) but this was no greater in the ICH group than the IS group. Instead, there were more IS patients that were lost to follow-up and the patients lost to follow-up were more severely affected than the mean sample in IS than ICH. Therefore, the difference between the groups that we observed was not over-estimated, if anything attrition could have led to the improvements in the ischaemic stroke group being over-estimated.

Characteristics of the studies and participants
The studies comprised a RCT and two cohort studies, which were all conducted in Scandinavian countries (Table 1). The sample sizes were small comprising 61, 80 and 117 stroke survivors[22,25,26] with smaller percentages of ICH than ischaemic stroke participants (20, 24 and 28% respectively). Although there were more male participants overall, the gender distribution did not differ between stroke subtypes. In general, the groups were well matched except in one study where stroke severity was significantly greater[25] and in another study where age was significantly lower[26] in the ICH group. Baseline measurement was performed either within the first week[25,26] or at three to four weeks post-stroke[22].

Upper limb motor function
Upper limb motor function at baseline, measured by the normalised FMA-UE score, was lower in all studies for ICH

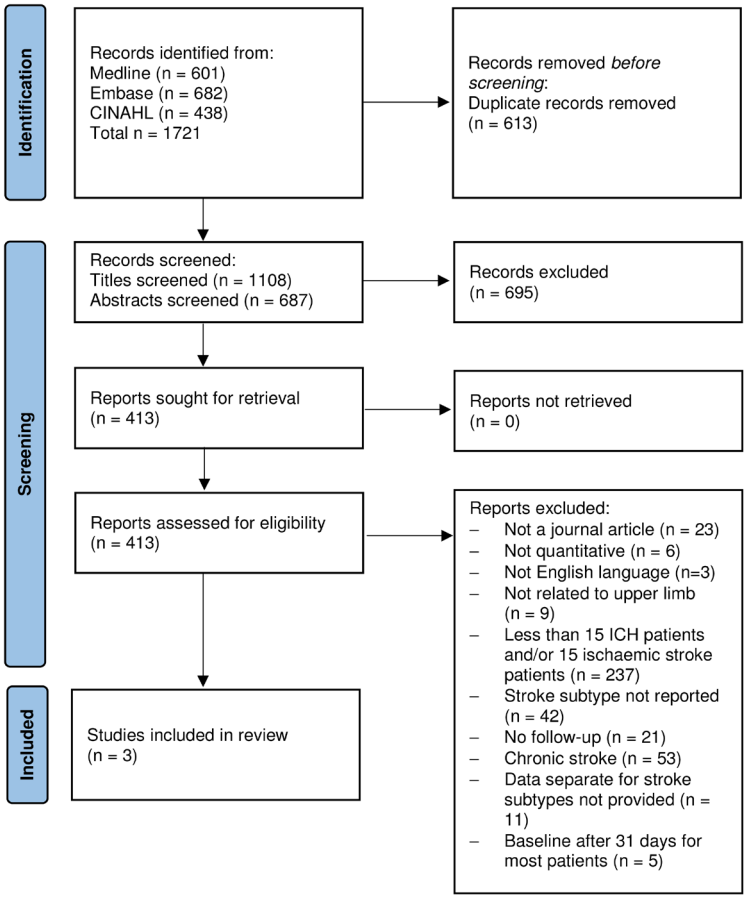

Figure 1. PRISMA flow diagram.

survivors (Figure 2, Supplementary Table 6[28]) by between 4–10 points on the FMA-UE (Table 1). In effect the mean scores for ICH were lower than any mean IS scores (Figure 2). Over time, the FMA-UE score increased in all studies for both stroke types. At 6-month follow-up the difference between the groups had substantially reduced and was between less than 1 to 4 points of the FMA-UE (Supplementary Table 7[29]).

Discussion

This systematic review identified three studies with data that allowed an exploration of differences in upper limb motor recovery using the FMA-UE between ICH and ischaemic stroke in the subacute phase after stroke. The studies had low to moderate risk of bias and included 258 participants with stroke (ischaemic stroke n=200, ICH n=58). We found that recovery was greater in ICH than ischaemic stroke. This related to individuals with ICH having more severe motor impairment at baseline but at 6-month follow-up, motor impairment was more similar to ischaemic stroke patients. The limited number of studies, low number of included participants and variability in the datasets/papers make firm conclusions impossible. However, these findings echo clinicians' perceptions of worse baseline motor impairment of ICH survivors with subsequent greater recovery and warrant further exploration.

Our data confirm that most recovery occurs early after stroke[30] both in ischaemic stroke and ICH. From evidence in animal models, these early improvements are largely attributed to spontaneous recovery mediated by altered brain activity on a molecular and cellular basis in response to injury[30–32]. Underlying processes for the recovery are thought to include the salvation of brain cells within the penumbra[33] and unmasking of latent synaptic pathways[34]. However, these findings are largely based on ischaemic stroke models. We observed greater baseline motor impairment in ICH survivors in our dataset, which can probably be attributed to the additional pathological processes in ICH[15,16]. Specifically, these processes include mass effect from the space occupying haematoma as well as the detrimental interaction between blood and brain parenchyma early after insult[16]. However, over the first two weeks, the mass effect reduces, and the haematoma resolves within 3 months[17,35]. We found that at six months post-stroke, the stroke subtypes had

Table 1. Included study details and baseline characteristics of participants.

		Ghaziani *et al.*, 2018[25]		Persson *et al.*, 2016[26]		Plantin *et al.*, 2019[22]	
Study type		RCT		Cohort		Cohort	
Country		Denmark		Sweden		Sweden	
n		80		117		61	
Baseline post stroke		<7 days		3 days		3–4 weeks	
Subtype		**IS**	**ICH**	**IS**	**ICH**	**IS**	**ICH**
n (%)		61 (76%)	19 (24%)	98 (84%)	19 (28%)	41 (67%)	20 (33%)
Gender	**Male** **Female**	33 (54%) 28 (46%)	7 (37%) 12 (63%)	56 (57%) 42 (43%)	9 (47%) 10 (53%)	27 (66%) 14 (34%)	14 (70%) 6 (30%)
		$x^2_{(80)}$=1.73; p=0.189		$x^2_{(117)}$=0.616; p=0.433		$x^2_{(61)}$=0.106; p=0.746	
Age, years mean (SD)		72 (11)	70 (15)	71 (13)	63(10)	54 (2[&])	50 (2[&])
		$t_{(23.87)}$=0.441; p=0.663		$t_{(115)}$=2.495; p=0.014*		$t_{(37)}$=1.128; p=0.266	
Stroke severity mean (SD)		45 (9)	37 (11)	8 (6)	10 (6)	8 (1[&])	8 (1[&])
		SSS $U_{(80)}$= 805.5; p=0.011*		NIHSS $U_{(115)}$=675; p=0.073		NIHSS $t_{(37)}$=0.01; p=0.999	
FMA-UE baseline mean SD		37(19)/66	27(21)/66	30(25)/66	20(22)/66	26(4[&])/60	22(6[&])/60
FMA-UE baseline normalised (%)		56(28.9)%	41(31.3)%	45(38.1)%	30(32.6)%	43(6.7[&])%	37(10[&])%
Stroke location	**RH** **LH** **Bilateral** **Cerebellum** **Brainstem**	28 (46%) 33 (54%)	8 (42%) 11 (58%)	49 (50) 44 (45%) 4 (4%) 1 (1%)	11 (58%) 7 (37%) 1 (5%)	27 (66%) 14 (34%)	10 (50%) 10 (50%)

Key: *RCT: randomised controlled trial, FMA-UE: Fugl-Meyer Assessment for upper extremity, IS: ischaemic stroke, ICH: intracerebral haemorrhage, n: number of participants, SD: standard deviation, SSS: Scandinavian Stroke Scale (higher score means lower stroke severity), NIHSS: National Institutes of Health Stroke Scale (higher score means higher stroke severity), RH: right hemisphere, LH: left hemisphere, * statistical significance p<0.05,* [&] measures likely to represent the standard error of the mean (rather than SD).

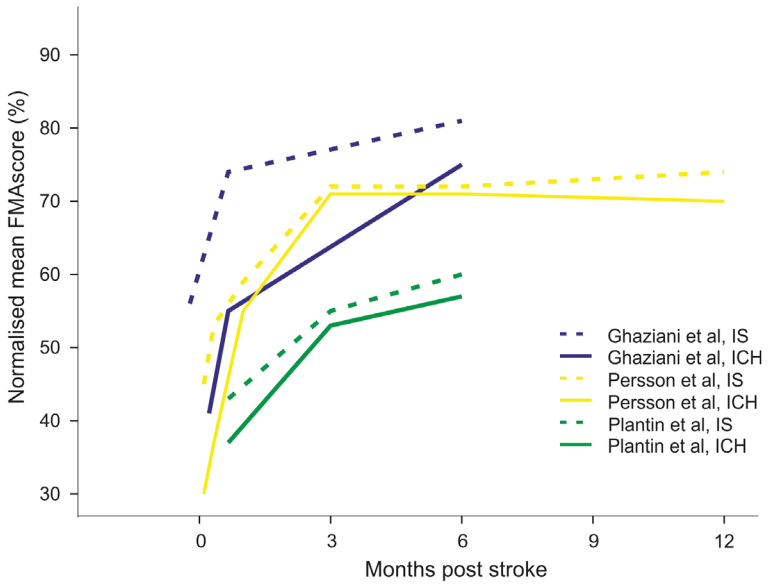

Figure 2. Comparison of longitudinal changes of the normalised FMA-UE score between ICH and IS survivors. Blue: Ghaziani *et al.* 2018, yellow: Persson *et al.* 2016, green: Plantin *et al.* 2019, continuous line: ICH, dotted line: ischaemic stroke.

similar levels of upper limb motor function. After the subacute period, both ICH and ischaemic stroke survivors are essentially left with the damage caused by hypoperfusion of brain tissue[34].

At baseline, there were differences between ICH and ischaemic stroke survivors FMA-UE score. In all studies ICH survivors' mean FMA-UE score categorised them as having severe impairment (<28)[36], whereas this was only the case in one study for ischaemic stroke survivors[22]. The difference in arm impairment severity between ICH and IS survivors was in excess of the minimal clinically important difference in two studies[37].

The question of interest is however, the amount and pattern of recovery, and therefore the extent and nature of change[38]. A commonly used model to understand the relationship between baseline severity and recovery is the proportional recovery rule[39]. It proposes that recovery scales with severity and that 70% of stroke survivors will regain 70% of their lost motor function. Thereby, individuals with more impairment are postulated to have greater numerical improvement on the FMA-UE. However, this is not the case for the most severely affected stroke survivors, who tend to fall into the 30% of survivors who do not follow the proportional rule and do not recovery arm function. Recovery of ICH survivors in this small dataset appears not to comply with the rule. The rule is violated in two way. Firstly it appears as though individuals with ICH appear to recover more than those with ischaemic stroke since they started from lower levels of upper limb motor function. In addition, individuals with severe impairment do recover. Whether the recovery in the ICH group exceeds the 70% of lost function, as proposed in the Proportional Recovery Rule[39], is not clear in our small sample. Future work should establish whether recovery differs between ICH and ischaemic stroke in a cohort matched for baseline severity.

In this systematic review, we compared recovery of impairment, measured by the upper extremity component of the Fugl-Meyer Assessment. The FMA-UE was designed to measure stages of arm recovery, from severe paralysis to motor control without the use of stereotypical synergy patterns[40,41]. Recovery of other impairments and limitations of activity could therefore differ. However, in previous work recovery has been found to be remarkably similar regardless of whether it is measured by the FMA-UE, the Motricity Index (strength)[42,43] or the ARAT[44] which measures limitations in activity.

These findings do need to be interpreted with caution as the review has some limitations. Spontaneous recovery is the greatest early after stroke[32] but the included studies measured baseline FMA-UE, at up to three[26], seven[25] and 31 days[22] post stroke. It is therefore highly likely that some recovery had already occurred in the participants in that specific study[22]. Rather than changing the findings this could have diminished the magnitude of the differences in baseline measures and the change we observed between the stroke types. In addition, the impact of high attrition needs to be considered when interpreting the findings. In these studies missing data often constituted a missed follow-up appointment, rather than dropping out of the study. Attrition bias is evident in ischaemic stroke survivors in our database (Supplementary table 3), as missed data was observed in individuals with predominantly poor upper limb motor function at baseline. This resulted in artificially high mean improvement in the ischaemic stroke subgroup. In our dataset, this does not appear to apply to the group with ICH, since very few patients did not attend for follow-up assessments and those who did not, were not consistently more severely impaired.

Considering that this review analysed data of only 58 participants with ICH, and found a high attrition bias in the IS group, further research is required to answer the research question with more confidence. A number of factors influence recovery after stroke including age, acute care and stroke severity which are difficult to control for in small studies. Conclusive evidence of recovery differences between stroke types would be important because in addition to informing patient and carer conversations about prognosis they are vital to inform appropriate care decisions. ICH survivors are far more likely to be placed on a palliative care pathway than ischaemic stroke survivors, irrespective of their baseline severity or other prognostic factors[18]. Thereby they miss out on lifesaving early interventions including intensive care, neurosurgical interventions and specialist rehabilitationto optimise recovery. Evidence of the recovery potential of ICH survivors should be integrated into prognostic models that inform early medical decision making.

Conclusion

In the limited studies that compare arm impairment and recovery in ischaemic stroke and ICH, baseline arm impairment was more severe in ICH. Despite this, the ICH survivors recovered arm movement to a similar level at six months after stroke. This indicates that there are differences in the recovery between these stroke types.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Zenodo: Table 2: Search Strategies. https://doi.org/10.5281/zenodo.10079312[21].

Zenodo: Table 3: Attrition for IS and ICH patients in the three studies and comparison of FM baseline mean between missing participants and sample mean. https://doi.org/10.5281/zenodo.10059673[27].

Zenodo: Table 4: Quality appraisal results using the Critical Appraisal Skills Programme RCT checklist. https://doi.org/10.5281/zenodo.10059677[23].

Zenodo: Table 5: Quality appraisal results using the Critical Appraisal Skills Programme Cohort Studies checklist. https://doi.org/10.5281/zenodo.10059684[24].

Zenodo: Table 6: Normalised FMA-UE scores at different timepoints, according to study and stroke subtype. https://doi.org/10.5281/zenodo.10059689[28].

Zenodo: Table 7: FMA-UE scores at different timepoints, according to study and stroke subtype. https://doi.org/10.5281/zenodo.10059695[29].

Reporting guidelines

Zenodo: PRISMA checklist for 'Comparing motor recovery in ischaemic stroke and intracerebral haemorrhage: A systematic review'. https://doi.org/10.5281/zenodo.10059192[19].

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Open Peer Review

Current Peer Review Status: ✔ ? ?

Version 2

Reviewer Report 02 June 2025

https://doi.org/10.21956/healthopenres.14923.r29432

?

Salman Ikramuddin
University Texas Health Sciences Houston, Houston, TX, USA

The authors set out to address an important and under appreciated area in the literature. Namely, a description of recovery trajectories comparing IS and ICH. While the concept is strong it is notable that only 3 studies directed provided the data they needed resulting in a small N compared to the existing data (just 58 with ICH). Of the 3 studies, there is some important heterogeneity including one with median age in the 50s, and another with much higher stroke severity. These issues make it difficult for the authors to answer the question they seek to address. If done well, this would be a well cited manuscript and inform recovery trials in the future. Current strengths of the manuscript include the concept, and a particularly strong discussion that puts the findings into context.

Major Comments
1. It is not entirely clear what search terms were used, it would be reasonable to include in exact terms what booleans were used with the full date ranges (including month, day, year) for each search tool (medline, etc) in the main text of the manuscript.

2. The number of excluded studies is very high, it may be worthwhile to reach out to the first authors of excluded studies to inquire if the data separated out by stroke subtype is available.

Minor Comments
1. Introduction paragraph 1: the rate of hemorrhagic stroke reported here seems higher than those typically cited, I did not clearly see it laid out in citation#2 where this number comes from. I would revisit this.

2. Discussion paragraph 4: typo, "The rule is violated in two way**s**."

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Partly

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke Recovery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 07 May 2025

https://doi.org/10.21956/healthopenres.14923.r29399

Margit Alt Murphy
[1] Sahlgrenska University Hospital, Gothenburg, Sweden
[2] Clinical Neuroscience, University of Gothenburg, Gothenburg, Västra Götaland County, Sweden

I dont have any more questions.

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Partly

Are sufficient details of the methods and analysis provided to allow replication by others?
Partly

Is the statistical analysis and its interpretation appropriate?
Partly

Are the conclusions drawn adequately supported by the results presented in the review?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Upper limb motor rehabilitation in stroke

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 03 January 2024

https://doi.org/10.21956/healthopenres.14537.r27658

?

Pradeepa Nayak
Manchester Metropolitan University, Manchester, England, UK

The manuscript addresses a significant gap in the literature and is well written. This systematic review follows PRISMA guidelines and summarises the literature on motor recovery in ischemic stroke and intracerebral haemorrhage. There is logical reporting throughout the manuscript which makes it easy to read. To enhance clarity, some components of the manuscript could be further expanded.

Title reads as: Comparing motor recovery in ischaemic stroke and intracerebral haemorrhage: A Systematic Review. In the title, authors might want to be specific and consider the addition of 'upper limb' motor recovery and stage of stroke recovery of the chosen population (acute and subacute), as well as the chosen outcome measure (FMA UE), as the review focused only on upper extremity motor recovery and is very specific to the outcome measure used i.e. FMA (other outcome measures of motor recovery were not included) and focused on acute and subacute stroke (excluded adults with chronic stroke).

Abstract: It might be good to add aim/objective of the review under the 'background' than stating the implications of the research. This line can be replaced with the aim of the review - "This information could inform discussions with patients about their recovery prognosis as well as identify appropriate rehabilitation settings."

Introduction: Introduction looks brief. It would be good to give some background information/ literature available on the upper limb recovery in people with ischaemic and intracerebral haemorrhagic stroke under introduction. It is good to state the aim of the review in the last part of the introduction.
It's unclear how the following statement relates with the current study, as the current study examines the motor recovery post stroke. Authors might want to link the statement with the present study with the use of evidence - "Currently, negativity of ICH outcome prevails, and clinicians do not instigate lifesaving interventions including admission to intensive care and neurosurgical evacuation of the haematoma when patients with ICH present with severe impairments at baseline."

Methods
Risk of bias assessment: References needed for the checklists – “Study quality was assessed by two reviewers using the RCT and and cohort studies Critical Appraisal Skills Programme (CASP) checklists respectively.”
The following section is unclear and needs further explanation – “We calculated the mean FMA-UE score for the missing participants at baseline and subtracted the mean FMA-UE baseline score for the stroke type in the study. Thereby a negative score indicates that more severe individuals were not followed-up and vice versa.”

Data synthesis and analysis: Need to rephrase the sentence for clarity – “Descriptive statistics (SPSS version 27) were used to calculate data separately for ischaemic stroke and ICH, and statistical tests (Independent Samples T-Test for normally distributed data, Mann Whitney U-Test for non-normal data and Person’s Chi-square test for distribution) were conducted for differences in baseline characteristics and outcomes between the two groups (ischemic stroke and ICH).” Contents within the bracket needs to be presented in a running sentence format. Unclear if authors mean Pearson’s Chi-square test was used for checking the normal distribution? It might be good to use Shapiro wilk or Kolmogorov-Smirnov test to test the normality.

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Authors can consider the use of intention to treat analysis to make appropriate adjustments to the data of patients with attrition and making scientific judgement - “Rather, there were more IS patients that were lost to follow-up and the patients lost to follow-up were more severely affected than the mean sample in IS than ICH. Therefore, the difference between the groups that we observed was not over-estimated, if anything attrition could have led to the improvements in the ischaemic stroke group being over-estimated.”

Characteristics of the studies: This statement can be removed as the FMA UE was the inclusion criteria – “All used the FMA-UE to measure upper limb motor function.”
Table 1.: It would be good to add follow up scores of FMA UE (mean, SD) and follow up sample size in Table 1 along with the duration of follow up in each study. In addition, providing mean differences observed in each group over the time would add value. Figure 2. Should be presented before the discussion section to maintain the logical flow of the content.

Discussion: It’s unclear how current study informs the choice of life saving early interventions. It would be beneficial to explain further before making the following conclusions “Conclusive evidence of recovery differences between stroke types would be important because in addition to informing patient and carer conversations about prognosis they are vital to inform appropriate care decisions. These include lifesaving early interventions of intensive care, neurosurgical

interventions and specialist rehabilitation to optimise recovery."
In the discussion, authors state there were significant drop outs in the ischemic stroke group and that resulted in amplifying the mean improvements in the ischemic group stroke. It would be good to consider the use of intention to treat analysis to make the adjustments and draw scientific conclusions on the data.

Grammatical errors seen in the following sentences: "..the 30% of survivors who do not follow the proportional rule and do not recovery arm function."; "Individuals with ICH appear to recover more than those with ischaemic stroke since they started from lower levels of upper limb motor function and individuals with severe impairment do recover"; "A number of factors influence recovery after stroke including ages, acute care and stroke severity which are difficult to control....."

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Partly

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke rehabilitation, physical activity, behaviour change, mhealth

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 06 Feb 2025

Ulrike Hammerbeck

Dear Reviewer Thank you for taking the time to review this paper. Please see itemised responses to your remarks.

The manuscript addresses a significant gap in the literature and is well written. This systematic review follows PRISMA guidelines and summarises the literature on motor recovery in ischemic stroke and intracerebral haemorrhage. There is logical reporting throughout the manuscript which makes it easy to read. To enhance clarity, some components of the manuscript could be further expanded.

Title reads as: Comparing motor recovery in ischemic stroke and

intracerebral haemorrhage: A Systematic Review. In the title, authors might want to be specific and consider the addition of 'upper limb' motor recovery and stage of stroke recovery of the chosen population (acute and subacute), as well as the chosen outcome measure (FMA UE), as the review focused only on upper extremity motor recovery and is very specific to the outcome measure used i.e. FMA (other outcome measures of motor recovery were not included) and focused on acute and subacute stroke (excluded adults with chronic stroke).

Author response: *We have added the motor recovery domain of the upper limb and the time point after stroke. We have termed it subacute stroke as acute is often seen as the first 2 weeks after stroke which this paper does not investigate. The authors believe that the Fugl-Meyer is a widely accepted measure of upper limb impairment and believe that it is very clear from the abstract and manuscript that this was used and therefore have not included it in the title. Comparing upper limb motor recovery in subacute ischemic stroke and intracerebral hemorrhage: A Systematic Review*

Abstract: It might be good to add aim/objective of the review under the 'background' than stating the implications of the research. This line can be replaced with the aim of the review - "This information could inform discussions with patients about their recovery prognosis as well as identify appropriate rehabilitation settings."

Author response: *The authors feel that the previous sentence can be turned into a statement from a current question and thereby fulfil the purpose of stating the aim without changes to the word count. We have rephrased to: This paper aims to establish whether their respective upper limb motor impairment and recovery differ.*

Introduction: Introduction looks brief. It would be good to give some background information/ literature available on the upper limb recovery in people with ischaemic and intracerebral haemorrhagic stroke under introduction. It is good to state the aim of the review in the last part of the introduction.

Author response: *We have added a paragraph on upper limb recovery and changed the wording to aim at the end of the paragraph. Arm weakness impacts on stroke survivors' independence, quality of life and ability to maintain previous life roles 7,8. Despite significant recent advances in stroke care, over 20% of stroke survivors do not recover functional use of their arm 3. The impact of poor arm recovery is considerable with an estimated 100,000 strokes occurring in the UK every year, and 1.2 million stroke survivors alive at any time 9. However, longitudinal epidemiological studies of stroke recovery are very rare 10 and the natural history of recovery after stroke not well understood, especially in ICH. Arm recovery is influenced by patient demographics, stroke severity and acute care 11,12. However, it is currently unclear whether upper limb impairment and recovery differs between ICH and ischaemic stroke.. We here aim to establish whether there is evidence of differences in upper limb motor recovery between ischaemic stroke and ICH by performing a systematic review of the literature.*

It's unclear how the following statement relates with the current study, as the current study examines the motor recovery post stroke. Authors might want to link the statement with

the present study with the use of evidence - “Currently, negativity of ICH outcome prevails, and clinicians do not instigate lifesaving interventions including admission to intensive care and neurosurgical evacuation of the haematoma when patients with ICH present with severe impairments at baseline.”

Author response: *We have clarified this statement. The knowledge will shape goal setting and discharge planning. Furthermore, this information could assist clinical decision-making with regards to life saving interventions early after stroke and rehabilitation pathways at later time points*

Methods

Risk of bias assessment: References needed for the checklists – “Study quality was assessed by two reviewers using the RCT and and cohort studies Critical Appraisal Skills Programme (CASP) checklists respectively.”

Author response: *Included*

The following section is unclear and needs further explanation – “We calculated the mean FMA-UE score for the missing participants at baseline and subtracted the mean FMA-UE baseline score for the stroke type in the study. Thereby a negative score indicates that more severe individuals were not followed-up and vice versa.”

Author response: *This section now reads: To established whether attrition caused a risk of bias through missingness of more severely affected individuals. To do this we calculated the mean FMA-UE score for the missing participants at baseline and subtracted the mean FMA-UE baseline score for the stroke type in the study. Thereby a negative score indicates that more severe individuals were missing for followed-up for the respective stroke type.*

Data synthesis and analysis: Need to rephrase the sentence for clarity – “Descriptive statistics (SPSS version 27) were used to calculate data separately for ischaemic stroke and ICH, and statistical tests (Independent Samples T-Test for normally distributed data, Mann Whitney U-Test for non-normal data and Person’s Chi-square test for distribution) were conducted for differences in baseline characteristics and outcomes between the two groups (ischemic stroke and ICH).” Contents within the bracket needs to be presented in a running sentence format. *Done* Unclear if authors mean Pearson’s Chi-square test was used for checking the normal distribution? It might be good to use Shapiro wilk or Kolmogorov-Smirnov test to test the normality.

Author response: *The use of the Pearson’s chi-square test as a measure to investigate categorical distribution has been expanded upon. The section now reads: Descriptive statistics, using SPSS version 27, were used to calculate data separately for ischaemic stroke and ICH. Statistical tests to establish differences in baseline characteristics and outcomes between stroke types used independent samples t-test for normally distributed data, Mann Whitney U-test for non-normal data and Pearson’s chi-square test to investigate categorical distribution.*

Results: In the below statement authors state five out of seven studies were excluded giving an impression of two studies were retained. Could be re written for the clarity - “Data from seven from the above 19 studies were obtained, but five studies were excluded because they did not satisfy all eligibility criteria, resulting in the inclusion of three studies in the review.”

Author response: *Done*

Risk of bias: It would be good to define what is considered as moderate to low and what is considered as low in this statement – “The risk of bias (Supplementary Table 4 and 5) in the reported studies was moderate to low and moderate.” It would be good to provide some information on the domains assessed for ROB and the findings for each study in main text.

Author response: *We have clarified in the text that the degree of the risk of bias has been reported for the respective studies as indicated by the references. We have added the description of ROB. We believe that we have outlined the key ROB factors in the paragraph and reference the relevant papers where this was the case. However, for further clarity we have restructured some sentences and added further detail.*

Authors can consider the use of intention to treat analysis to make appropriate adjustments to the data of patients with attrition and making scientific judgement - “Rather, there were more IS patients that were lost to follow-up and the patients lost to follow-up were more severely affected than the mean sample in IS than ICH. Therefore, the difference between the groups that we observed was not over-estimated, if anything attrition could have led to the improvements in the ischaemic stroke group being over-estimated.”

Author response: *We report on studies that investigated outcome after either ICH or ischemic stroke. It appears as though the studies did indeed use an intention to treat analysis for their respective analyses. However, the two health conditions are quite different, and ICH has far worse health outcomes. Therefore, there is a danger of Risk of Bias, and overestimation of effect, introduced by attrition in this population with an intention to treat analysis. We however established that attrition did not introduce a risk of bias and thereby an overestimation of effect.*

Characteristics of the studies: This statement can be removed as the FMA UE was the inclusion criteria – “All used the FMA-UE to measure upper limb motor function.” *Removed.*
Table 1.: It would be good to add follow up scores of FMA UE (mean, SD) and follow up sample size in Table 1 along with the duration of follow up in each study. In addition, providing mean differences observed in each group over the time would add value.

Author response: *We have already included this information in the supplementary Table 6. We have included signposting to this data in the text and believe that due to the complexity of timepoints it is better to present in its entirety here. We have changed the order of the supplementary tables accordingly.*

Figure 2. Should be presented before the discussion section to maintain the logical flow of the content.

Author response: *Formatting is done by the journal and we don't have any concerns regarding this.*

Discussion: It's unclear how current study informs the choice of life saving early interventions. It would be beneficial to explain further before making the following conclusions "Conclusive evidence of recovery differences between stroke types would be important because in addition to informing patient and carer conversations about prognosis they are vital to inform appropriate care decisions. These include lifesaving early interventions of intensive care, neurosurgical interventions and specialist rehabilitation to optimise recovery."

Author response: *This has been clarified and now reads: ICH survivors are far more likely to be placed on a palliative care pathway than ischaemic stroke survivors, irrespective of their baseline severity or other prognostic factors 12. Thereby they miss out on lifesaving early interventions including intensive care, neurosurgical interventions and specialist rehabilitation to optimise recovery. Evidence of the recovery potential of ICH survivors should be integrated into prognostic models that inform early medical decision making.*

In the discussion, authors state there were significant drop outs in the ischemic stroke group and that resulted in amplifying the mean improvements in the ischemic group stroke. It would be good to consider the use of intention to treat analysis to make the adjustments and draw scientific conclusions on the data.

Author response: *The scientific data are drawn from the analysis using intention to treat but the ROB assessment showed that there was not an overestimation of the effect of ICH.*

Grammatical errors seen in the following sentences: "..the 30% of survivors who do not follow the proportional rule and do not recovery arm function."; "Individuals with ICH appear to recover more than those with ischaemic stroke since they started from lower levels of upper limb motor function and individuals with severe impairment do recover"; "A number of factors influence recovery after stroke including ages, acute care and stroke severity which are difficult to control....."

Author response: *Addressed all these in the text.*

Competing Interests: No competing interests were disclosed.

Author Response 13 Feb 2025

Ulrike Hammerbeck

Dear Reviewer Thank you for taking the time to review this paper. Please see itemised responses to your remarks.

Comments: The manuscript addresses a significant gap in the literature and is well written.

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Author response: *Done*

Comments: Risk of bias: It would be good to define what is considered as moderate to low and what is considered as low in this statement – “The risk of bias (Supplementary Table 4 and 5) in the reported studies was moderate to low and moderate.” It would be good to provide some information on the domains assessed for ROB and the findings for each study in main text.

Author response: *We have clarified in the text that the degree of the risk of bias has been reported for the respective studies as indicated by the references. We have added the description of ROB. We believe that we have outlined the key ROB factors in the paragraph and reference the relevant papers where this was the case. However, for further clarity we have restructured some sentences and added further detail.*

Comments: Authors can consider the use of intention to treat analysis to make appropriate adjustments to the data of patients with attrition and making scientific judgement - “Rather, there were more IS patients that were lost to follow-up and the patients lost to follow-up were more severely affected than the mean sample in IS than ICH. Therefore, the difference between the groups that we observed was not over-estimated, if anything attrition could have led to the improvements in the ischaemic stroke group being over-estimated.”

Author response: *We report on studies that investigated outcome after either ICH or ischemic stroke. It appears as though the studies did indeed use an intention to treat analysis for their respective analyses. However, the two health conditions are quite different, and ICH has far worse health outcomes. Therefore, there is a danger of Risk of Bias, and overestimation of effect, introduced by attrition in this population with an intention to treat analysis. We however established that attrition did not introduce a risk of bias and thereby an overestimation of effect.*

Comments: Characteristics of the studies: This statement can be removed as the FMA UE was the inclusion criteria – “All used the FMA-UE to measure upper limb motor function.” *Removed.* Table 1.: It would be good to add follow up scores of FMA UE (mean, SD) and follow up sample size in Table 1 along with the duration of follow up in each study. In addition, providing mean differences observed in each group over the time would add value.

Author response: *We have already included this information in the supplementary Table 6. We have included signposting to this data in the text and believe that due to the complexity of timepoints it is better to present in its entirety here. We have changed the order of the supplementary tables accordingly.*

Comments: Figure 2. Should be presented before the discussion section to maintain the logical flow of the content.

Author response: *Formatting is done by the journal and we don't have any concerns regarding this.*

Comments: Discussion: It's unclear how current study informs the choice of life saving early interventions. It would be beneficial to explain further before making the following conclusions "Conclusive evidence of recovery differences between stroke types would be important because in addition to informing patient and carer conversations about prognosis they are vital to inform appropriate care decisions. These include lifesaving early interventions of intensive care, neurosurgical interventions and specialist rehabilitation to optimise recovery."

Author response: *This has been clarified and now reads: ICH survivors are far more likely to be placed on a palliative care pathway than ischaemic stroke survivors, irrespective of their baseline severity or other prognostic factors 12. Thereby they miss out on lifesaving early interventions including intensive care, neurosurgical interventions and specialist rehabilitation to optimise recovery. Evidence of the recovery potential of ICH survivors should be integrated into prognostic models that inform early medical decision making.*

Comments: In the discussion, authors state there were significant drop outs in the ischemic stroke group and that resulted in amplifying the mean improvements in the ischemic group stroke. It would be good to consider the use of intention to treat analysis to make the adjustments and draw scientific conclusions on the data.

Author response: *The scientific data are drawn from the analysis using intention to treat but the ROB assessment showed that there was not an overestimation of the effect of ICH.*

Comments: Grammatical errors seen in the following sentences: "..the 30% of survivors who do not follow the proportional rule and do not recovery arm function."; "Individuals with ICH appear to recover more than those with ischaemic stroke since they started from lower levels of upper limb motor function and individuals with severe impairment do recover"; "A number of factors influence recovery after stroke including ages, acute care and stroke severity which are difficult to control....."

Author response: *Addressed all these in the text.*

Competing Interests: No competing interests were disclosed.

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The manuscript is well written and targets an important and timely issue. Taken the current changes in stroke care and rehabilitation, the understanding of motor recovery pattern in haemorrhagic strokes is important, and needed. The results of this study can guide stroke rehabilitation and improve adaptive selection of interventions. All parts of the manuscript are carefully and methodically reported, which makes the reading easy. The results are clearly stated, limitations pointed out and conclusions relevant and well inside the study research question.

Taken that only 3 studies could be included, and all were from similar regional context, makes the results less applicable for a wider geographical spread. But, this is acknowledged by the authors, but maybe could be pointed out even more clearly.

The authors have probably made a thorough search of the topic, and it seems that the evidence is limited. The limited number of studies is also a result of quite specific inclusion criteria used. So maybe some more discussion on that, and if there are other studies that could have been included if other outcome measures would have been allowed (ARAT, NIHS arm). It would also be nice to add some information on research base and evidence regarding motor recovery in general and not only upper limb. In summary, the manuscript could be indexed as it is, but it would be even more interesting if the discussion could include a somewhat wider perspective beyond the upper limb and Fugl-Meyer outcome.

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Upper limb motor rehabilitation in stroke

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.