ELSEVIER

Physiotherapy 107 (2020) 216–223

Physiotherapy

Recovery of upper limb function is greatest early after stroke but does continue to improve during the chronic phase: a two-year, observational study☆

Karen N. Borschmann[a,b,c,d,*], Kathryn S. Hayward[b,c,e]

[a] School of Allied Health, La Trobe University, Bundoora, Australia
[b] AVERT Early Rehabilitation Research Group, Stroke Theme, The Florey Institute of Neuroscience and Mental Health, Heidelberg, Australia
[c] NHMRC Centre of Research Excellence Stroke Rehabilitation and Brain Repair, Australia
[d] St Vincent's Hospital, Melbourne, Australia
[e] Department of Physiotherapy, Melbourne School of Health Sciences, University of Melbourne, Parkville, Australia

Abstract

Objectives Investigate upper limb (UL) capacity and performance from <14-days to 24-months post stroke.
Design Longitudinal study of participants with acute stroke, assessed ≤14-days, 6-weeks, 3-, 6-, 12-, 18-, and 24-months post stroke.
Setting Two acute stroke units.
Main outcome measures Examination of UL capacity using Chedoke McMaster Stroke Assessment (combined arm and hand scores, 0–14), performance using Motor Activity Log (amount of movement and quality of movement, scored 0–5), and grip strength (kg) using Jamar dynamometer. Random effects regression models were performed to explore the change in outcomes at each time point. Routine clinical imaging was used to describe stroke location as cortical, subcortical or mixed.
Results Thirty-four participants were enrolled: median age 67.7 years (IQR 60.7–76.2), NIHSS 11.5 (IQR 8.5–16), female n = 10 (36%). The monthly rate of change for all measures was consistently greatest in the 6-weeks post baseline. On average, significant improvements were observed to 12-months in amount of use (median improvement 1.81, 95% CI 1.35 to 2.27) and strength (median improvement 8.29, 95% CI 5.90 to 10.67); while motor capacity (median improvement 4.70, 95% CI 3.8 to 5.6) and quality of movement (median improvement 1.83, 95% CI 1.37 to 2.3) improved to 18-months post stroke. Some individuals were still demonstrating gains at 24-months post stroke within each stroke location group.
Conclusion This study highlights that the greatest rate of improvement of UL capacity and performance occurs early post stroke. At the group level, improvements were evident at 12- to 18-months post stroke, but at the individual level improvements were observed at 24-months.

Clinical trial registration ACTRN12612000123842.

Keywords: Stroke; Upper limb; Recovery; Arm use; Motor control

Abbreviations: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MAL, Motor Activity Log; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; UL, upper limb.
☆ Conference presentations: This paper was presented at World Stroke Congress, Montreal 17–20 October 2018.
* Corresponding author at: The Florey Institute of Neuroscience and Mental Health, 245 Burgundy Street, Heidelberg, 3084, Australia.
E-mail address: Karen.borschmann@florey.edu.au (K.N. Borschmann).
URLs: @kate_hayward (K.N. Borschmann), @karenborschmann (K.S. Hayward).

https://doi.org/10.1016/j.physio.2019.10.001

Introduction

Up to 70% of individuals experience difficulties using their upper limb (UL, arm and hand) to perform meaningful activities after stroke [1]. There is an assumption that when a stroke survivor demonstrates a change in activity, it is underpinned by an improvement in their capacity (i.e. what a person can do in the clinical environment) and performance (i.e. does a person actually use their UL in real world environments outside of the clinic) [2]. However, UL recovery post stroke is unlikely to be this simplistic [3]. Understanding how capacity and performance change over years post stroke might help to identify which patients to target and when during their recovery.

Previous research has noted distinct recovery profiles during inpatient [4,5] and outpatient [6] rehabilitation. Firstly, survivors may demonstrate improvements in both capacity and performance after stroke. Secondly, survivors may demonstrate an improvement in capacity but not performance. Lastly, survivors may demonstrate little or no change in both capacity and performance. An improvement in performance but not capacity has not been documented in the literature. Combined, these profiles support our rationale that UL capacity and performance are interrelated, yet are different constructs that must be measured separately.

Stroke recovery is a long-term goal. It is important to complete observational studies that track recovery to establish whether there is a discrepancy between capacity and performance in the long-term. To date, longitudinal tracking of recovery has largely lacked investigation of natural recovery from an acute time point post stroke (first 7- to 14-days), long-term follow up of patients beyond 3- to 6-months post stroke, and characterisation of stroke variables such as lesion type and location that may modify or interact with observed recovery profiles [7].

In this exploratory study our objectives were to determine (1) whether UL capacity and performance improve over the first 24-months after stroke; and (2) if there is a window of greatest improvement in UL capacity and performance. This information is important to develop an understanding of the longterm timecourse of recovery after stroke to support evidence-based clinical practice guidelines to inform upper limb rehabilitation services.

Methods

Study design

A multicentre, 24-month observational study of post stroke recovery was completed [12]. Here we report the UL recovery sub-study. Participants were recruited within 2-weeks of stroke onset from public acute stroke units in Melbourne (Australia). Assessments were completed by an experienced physiotherapist (KB) at baseline (<14-days post stroke), 6-weeks, and 3-, 6-, 12-, 18- and 24-months post stroke. Recruitment was undertaken between May 2010 and May 2014.

Ethical approval was received from Austin Health [H2008/03428] and Northern Health [P4/13] ethics committees, and participants or their substitute decision maker provided informed written consent. The study was registered with the Australia New Zealand Clinical Trials registry: ACTRN12612000123842, and is reported here according to STROBE guidelines [13].

Study participants

Eligible participants had a diagnosis of first ever stroke, were medically stable, unable to walk independently, and able to follow simple verbal commands. Exclusion criteria were other neurological conditions, diabetes, significant musculoskeletal condition (e.g. amputation) and use of bone active medications (e.g. bisphosphonates).

Measurements

The following outcome measures were assessed at each timepoint, except NIHSS which was only recorded at baseline to describe stroke severity.

Stroke characteristics

Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS [14]). Participants were classified as mild (NIHSS < 8), moderate (8–16), or severe (NIHSS > 16) [15]. The modified Rankin score (mRS, 0 = no stroke symptoms, 6 = dead) was used to assess disability [16]. NIHSS and mRS were performed by certified examiners. Stroke classification was recorded using the Oxfordshire Classification [17]. A qualified neurologist documented lesion location and hemisphere from clinical chart reports and review of scans (CT/MRI). The lesion for each participant was defined as cortical, subcortical or mixed (cortical and subcortical) [18]. Adverse medical events were recorded at each time point including death (and cause), UL injuries, and any research related event that required nursing or medical attention.

Motor capacity

The combined score from two subscales (arm and hand) of the Chedoke McMaster Stroke Assessment was used to evaluate motor capacity of the paretic UL [19]. Each subscale was given a rating out of seven, corresponding to Brunnstrom's stages of motor recovery: 1 = flaccid paralysis; 7 = "normal" variety of rapid, age appropriate complex movement patterns are possible. Consistent with our approach, arm and hand subscales have been combined in previous research to give a full score out of 14 [20]. This scale has demonstrated high inter-rater reliability for assessment of people with acute stroke [19] (ICCs = 0.93–0.98), and has excellent concurrent validity with the Fugl-Meyer Upper Limb assessment [19] (r = 0.95, $P < 0.001$).

Motor performance

Upper limb motor performance was assessed using the Motor Activity Log (MAL) [21], a self-report interview that contained 30 items of common UL activities, for example drinking from a glass, brushing teeth. For each relevant item, participants rated the *amount of use* of their paretic UL compared to pre stroke (0 = does not use weaker arm, 5 = uses weaker arm as often as before the stroke) and *quality of movement* (0 = weaker arm not used at all, 5 = ability to use weaker arm is as good as pre stroke). Amount of use and quality of movement ratings were tallied separately then divided by the total number of items rated, to give a score out of 5. The MAL has high test-retest reliability [22], with adequate inter-rater reliability and internal consistency [23,24]. Construct validity is fair to moderate with measures of arm impairment and activity in subacute stroke [25], and high in people with chronic stroke (r = 0.91 and 0.97) [26].

Grip strength

Grip strength (kg) was measured using a Jamar hydraulic hand dynamometer (Sammons Preston Rolyan, IL, USA). The average score of three trials was recorded. This device has good to excellent test-retest reliability in stroke populations [28].

Statistical analysis

Random effects regression models with time points as inputs and individual patients as random effects were used to explore the change since baseline in motor capacity, motor performance, and grip strength at each time point. Given that assessment time-points were not equally spaced from baseline, for each time-point the average monthly rate of change from baseline was calculated by dividing the regression model outputs for each time-point by the total number of months since baseline. All available data were included in analyses as these models allow for missing-at-random data. Data from participants who died were not included as these cannot be assumed to be missing-at-random. Analyses were performed using STATA v13 IC statistical software (StataCorp LP, College Station, Texas, USA). A significance level of $P \leq 0.05$ was set for all statistical tests and no correction for multiplicity was undertaken due to the exploratory nature of analyses. The sample size was calculated for the published study [12], so this sub-study was not powered to detect UL improvements across measures.

Table 1
Demographics and stroke characteristics.

Characteristic	$n = 28$
Sex, female, *n* (%)	10 (36)
Age, median (IQR)	68 (61 to 76)
Lived with others, *n* (%)	21 (75)
Education, *n* (%)	
Incomplete secondary or less	7 (25)
Complete secondary	3 (11)
Apprenticeship/diploma	10 (36)
University degree/post grad	7 (25)
Missing	1 (4)
Employment, *n* (%)	
Full time employment	10 (36)
Part time employment/student	4 (14)
Retired/home duties	14 (50)
Past medical history present *n* (%)	
Hypertension	12 (43)
High cholesterol	8 (29)
Ischaemic heart disease	3 (11)
Atrial fibrillation	6 (21)
Musculoskeletal	12 (43)
Stroke severity, NIHSS, median (IQR)	11.5 (8.5 to 16)
Mild 0 to 7, *n* (%)	4 (14)
Moderate 8 to 15, *n* (%)	18 (64)
Severe ≥16, *n* (%)	6 (21)
Upper Limb NIHSS subscore, 0 to 4, median (IQR)	4 (2 to 4)
Stroke classification, *n* (%)	
TAC	15 (54)
PACI	8 (29)
LACI	3 (11)
Haemorrhage	2 (7)
mRS, median (IQR)	5 (4 to 5)
Dominant UL affected, *n* (%)	11 (39)

NIHSS = National Institutes of Health Stroke Scale; TACI = total partial anterior circulation infarct to PACI = partial anterior circulation infarct to LACI = lacunar circulation infarct. mRS = modified Rankin Score.

Results

Participant demographics, retention and adverse events

Thirty-four participants were recruited (median age 69.5 years (IQR 62.4–76.6), NIHSS 11 (IQR 9–16), female $n = 12$, 35%) (Table 1). Within 24-months of stroke, six participants died, resulting in 28 participants for analysis, Fig. 1. The sample had moderate to severe UL impairment at stroke onset (NIHSS UL item on hospital admission was median 4 out of 4 points (IQR 2–4)). Baseline assessment was completed on average at 7.5-days post stroke.

At 24-months, four people were unwell (hospitalised for fracture, severe depression, multiple co-comorbidities, heart failure) and declined physical assessment but did provide health information via telephone. Four others did not get to complete a 24-month assessment: three people were less than 24-months post stroke at the end of the study period, and one participant was uncontactable after moving interstate. There were no adverse events related to the study. Six participants reported that they received injuries to their UL as the result of falling over: soft tissue injuries $n = 6$, fractured radius $n = 2$;

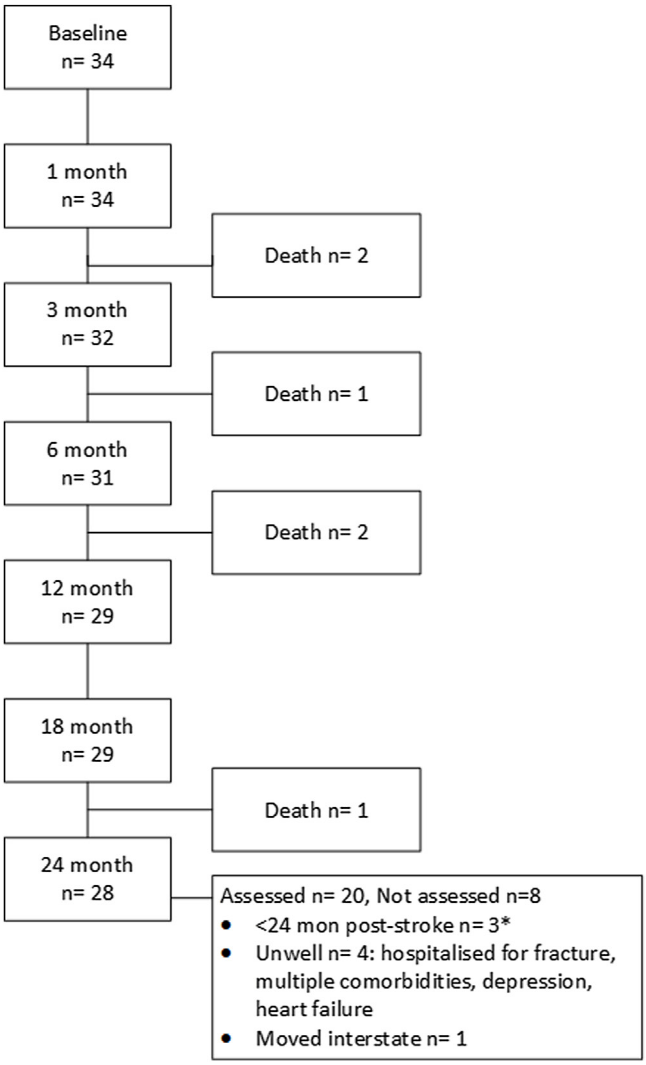

Fig. 1. Retention of participants through study from baseline to 24-months post stroke. *As this sub-study was run during the main study [12], 3 participants were <2 years post stroke (<12-mon $n = 2$, <18-mon $n = 1$) at close of main study and were not assessed at 24-months.

and one participant reported receiving a cortisone injection for shoulder pain.

Upper limb recovery

Motor capacity

The combined arm and hand Chedoke McMaster Stroke Assessment demonstrated low scores on the stroke affected UL at baseline that improved over time but remained impaired at 24-months ($P = 0.001$, Table 2). Within the first month after baseline (∼6-weeks post stroke), the mean combined arm and hand capacity score increased on average by 1.82 (95% CI 0.98, 2.66, $P < 0.001$), Fig. 2. This was the highest change per month observed across 24-months. On average, improvements were observed to 18-months (4.70, 95% CI 3.78, 5.61). As displayed in Fig. 3, some individuals (across all three lesion classifications – cortical, sub-cortical and mixed) continued to demonstrate improvements to 24-months post stroke.

Motor performance

Amount of use and quality of movement of the paretic UL were less at baseline compared to self-reported pre stroke status (both $P < 0.001$). Within the first month after baseline (∼6-weeks post stroke), amount of use increased on average by 0.75 (95% CI 0.30, 1.19, $P = 0.001$), and quality of movement increased by 0.67 (95% CI 0.24, 1.10, $P = 0.002$). For both measures, this was the highest rate of change observed per month across 24-months. Continued improvements were observed in amount of use, on average to 12-months (1.81, 95% CI 1.35 to 2.27) and in quality of movement, on average to 18-months (1.83, 95% CI 1.37 to 2.3). As shown in Fig. 3, there are individuals within all lesion classifications who continued to improve up to 24 months post stroke.

Grip strength

Grip strength of the paretic UL was median 0 kg (IQR 0–6.5) at baseline, and 24.67 kg (IQR 16–32.5) in the non-paretic UL (between limb difference 24.67 kg, $P < 0.001$). At 24-months, the between-limb difference reduced to 14.6 kg (SD 11.2), $P < 0.001$. Within the first month after baseline (∼6-weeks post stroke), grip strength of the paretic UL increased on average by 2.76 kg (95% CI 0.50 to 5.03, $P = 0.017$). This was the highest rate of change per month observed across 24-months. Continued improvements were observed on average to 12-months (8.29, 95% CI 5.90 to 10.67) and per Fig. 3, there are individuals within all lesion classifications who continued to improve up to 24 months post stroke.

Discussion

This unique sample of stroke survivors with moderate to severe UL impairment demonstrated varying trajectories and extents of improvement over the first 24-months post stroke. Our findings demonstrated that greatest rate of recovery occurred in the first month post baseline. It is considered that this window is the period of heightened neural plasticity [8,29], highlighting a critical period for intensive behavioural interventions to be tested. These findings are consistent with previous research which also demonstrated that the greatest rate of improvement in motor impairment (Fugl Meyer [30]) and motor control8 occurred during the first month post stroke. Despite these findings, less than 11% of all recovery trials (UL and lower limb) have enrolled participants on average less than 30-days post stroke onset [31]. Together, this supports the assertion that there is a mismatch between our understanding of the biology of recovery and clinical trial design.

Despite demonstration of a period of early and steep improvement, grip strength (capacity) and amount of use (performance) continued to improve on average to 12-

Table 2
Upper limb capacity, strength and performance change at each epoch of assessment over the first 24-months post stroke, median (IQR).

Chedoke McMaster	<14 days $n = 27$	~6-weeks $n = 27$	3 months $n = 24$	6 months $n = 26$	12 months $n = 23$	18 months $n = 20$	24 months $n = 20$
Arm, 0 to 7	2 (1 to 2)	2 (2 to 5)	3 (2 to 5.5)	4 (2 to 6)	5 (2 to 6)	4 (2 to 7)	4.5 (2 to 6.5)
Hand, 0 to 7	1 (1 to 3)	2 (1 to 5)	3 (2 to 5)	3.5 (2 to 6)	4 (2 to 7)	4 (2 to 7)	4 (2 to 6)
Combined, 0 to 14	3 (2 to 5)	4 (3 to10)	6 (4 to 10.5)	7.5 (4 to 12)	11 (4 to 13)	9 (4 to 13)	9 (4 to 12)
Grip strength	$n = 28$	$n = 27$	$n = 25$	$n = 26$	$n = 23$	$n = 21$	$n = 20$
Paretic, kg	0.0 (0.0 to 4.8)	2.0 (0.0 to 11.3)	2.0 (0.0 to 13.3)	6.3 (1.3 to 17.7)	12.7 (2.3 to 24.0)	11.7 (3.3 to 19.0)	9.8 (1.7 to 20.7)
Non-paretic, kg	24.7 (17.7 to 35.7)	28.2 (18.7 to 33.7)	27.3 (20.7 to 32.7)	27.0 (18.7 to 35.0)	28.3 (18.0 to 35.7)	27.0 (19.0 to 34.8)	26.3 (19 to 34.8)
Motor Activity Log	$n = 27$	$n = 27$	$n = 25$	$n = 27$	$n = 24$	$n = 21$	$n = 20$
Amount of use, 0 to 5	0.0 (0.0 to 0.0)	0.14 (0.0 to 2.1)	0.57 (0.0 to 3.7)	1.3 (0.0 to 4.4)	2.4 (0.0 to 4.6)	2.6 (0.0 to 3.9)	2.5 (0.1 to 3.9)
Quality, 0 to 5	0.0 (0.0 to 0.0)	0.2 (0.02 to 1.9)	0.3 (0.0 to 3.7)	0.6 (0.0 to 3.6)	2.2 (0.0 to 4.2)	2.5 (0.0 to 4.1)	2.6 (0.1 to 4.0)

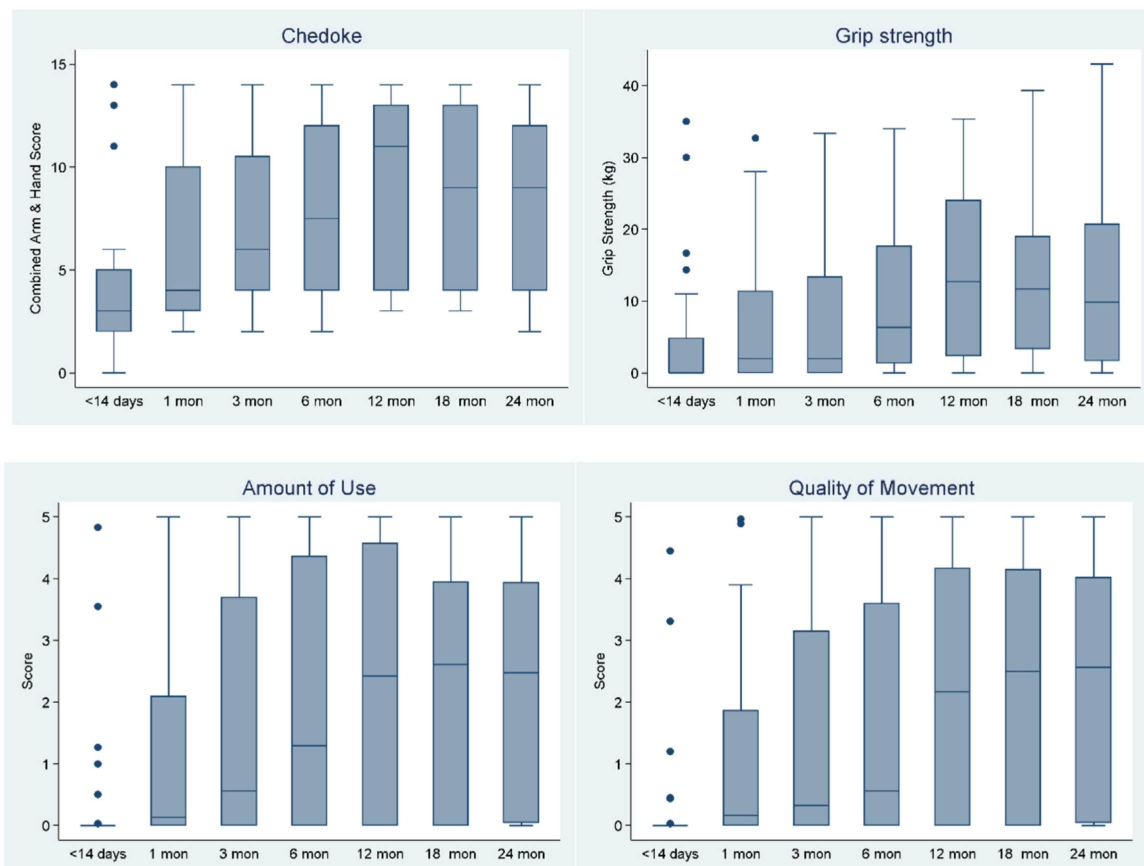

Fig. 2. Upper limb motor capacity (Chedoke), performance (quality of movement & amount of use), and grip strength over 24-months post stroke ($n = 28$). *Note:* Chedoke score reported is combined score of arm and hand (0–14). Amount of use and Quality of Movement scored using Motor Activity Log (MAL, 0–5). Assessment time points are post stroke.

months, while Chedoke (capacity) and quality of movement (performance) continued to improve on average to 18-months post stroke. It is unlikely that the failure to demonstrate continued, significant average improvements represents a ceiling effect of the outcome measures used, as very few participants achieved the highest possible score (Chedoke $n = 3$ MAL $n = 1$, grip strength paretic arm = non-paretic arm $n = 2$). Further, some individuals continued to improve to 24-

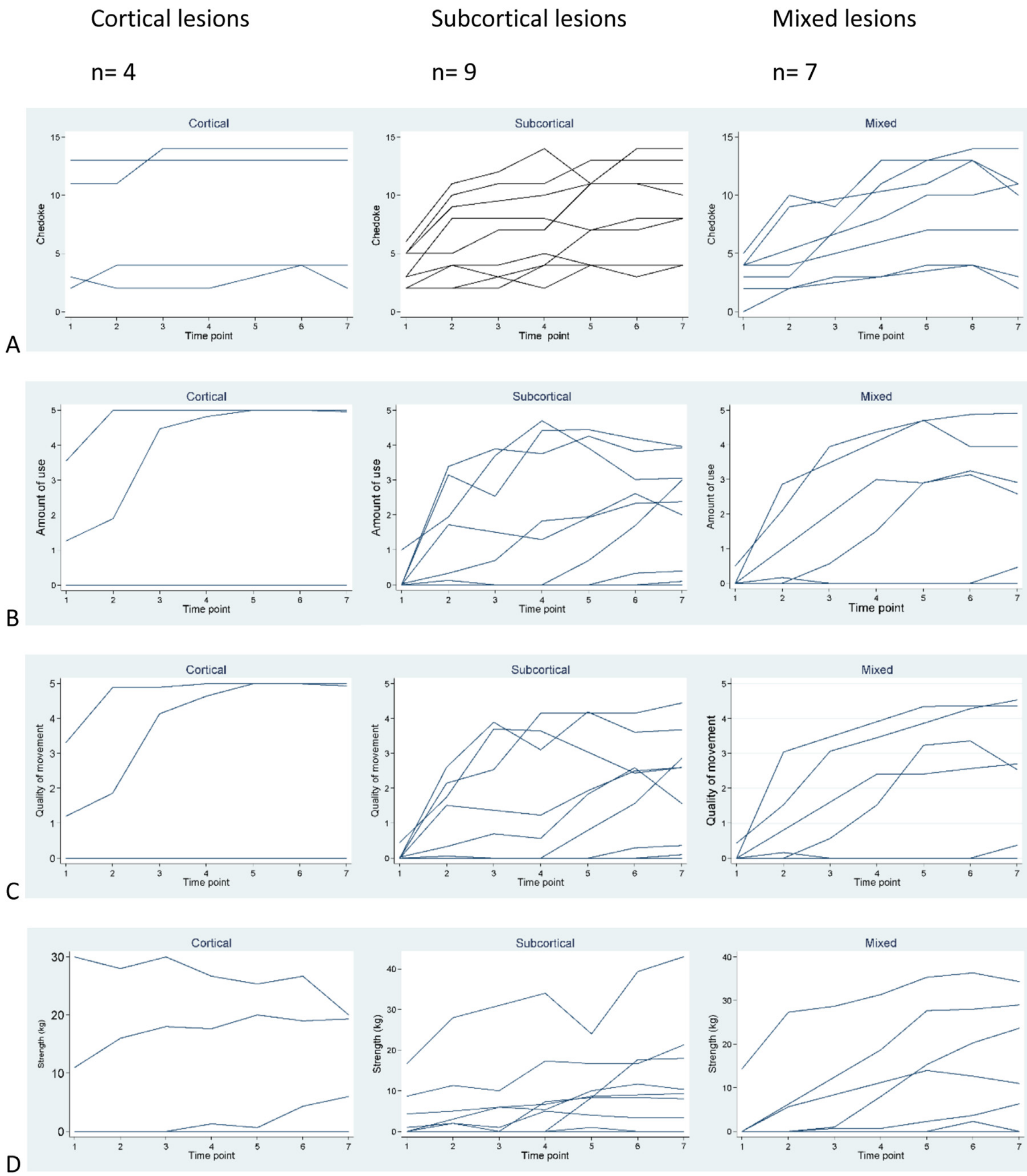

Fig. 3. Individuals' upper limb recovery trajectories grouped by brain lesion classification, demonstrating that trajectories are variable across lesion classification. All participants for whom all data are available across 24 months are included in this figure ($n = 20$). Participants' recovery trajectories are grouped by their classification of stroke lesion location (cortical $n = 4$, subcortical $n = 9$, mixed cortical and subcortical $n = 7$).
Panel A demonstrates Chedoke combined hand and arm scores (0–14).
Panel B demonstrates amount of use measured on Motor Activity Log (MAL, 0–5).
Panel C demonstrates quality of movement measured on Motor Activity Log (MAL, 0–5).
Panel D demonstrates grip strength (kg), measured by hand-held dynamometry.
Time points post stroke: 1 = <14 days, 2 = 1 month, 3 = 3 months, 4 = 6 months, 5 = 12 months, 6 = 18 months, 7 = 24 months.

months post stroke across all measures. This suggests that changes post stroke are not 'all or nothing', as the potential for improvement years post stroke is possible. Other studies have demonstrated this after high dose behavioural interventions [31,32]. However, from the measures that were used in this study and past studies [31,32], we remain unable to differentiate if later improvements are underpinned by true recovery (behavioural restitution [29]) or compensation [29]. Future studies need to include movement kinematics [32] to attempt to dissociate these constructs.

Past work has suggested that brain biomarkers may help advance our understanding of recovery phenotypes [33]. We only had available routine clinical scans (often CT, few MRI). This meant we could describe lesion location (as defined by a neurologist: cortical, subcortical, mixed). Unfortunately, this approach to analyse routine scans was not helpful to identify meaningful subgroups as we saw sustained upward trajectory of recovery in all lesion location subgroups. This finding suggests there is a need for longitudinal studies that include measures that are potentially more sensitive to change than clinical measures and lesion location. This could include biomarkers such as the impact of stroke on primary motor pathways (corticospinal tract) using transcranial magnetic stimulation to index motor evoked potential status (present or absent) [33], as well as more nuanced interpretations of lesion location (e.g. internal capsule impacted yes/no [35]) that account for primary motor pathway impact. There is an ongoing study focused on people with severe paresis that is focused on identifying brain biomarkers of recovery [36]. Together, advancements in biomarkers may improve prediction of recovery, patient selection, and individualised intervention.

Study limitations

Our assessment measures are inconsistent with those recommended by the Stroke Rehabilitation and Recovery Roundtable [32,33], as our study was completed prior to publication of these recommendations. Our analysed sample size was small ($n = 28$), however very few studies have tracked UL recovery beyond 12-months (e.g. Ref. [38]), therefore our study contributes important information about longer term recovery post stroke in the current stroke rehabilitation and recovery environment. In this study we did not include an objective measure of UL use e.g. accelerometers [39]. A recent study reported a discrepancy between self-report and objective accelerometer indexed measurement of use [40], which suggests that self-report measures are subject to recall bias. Future longitudinal work would benefit from including objective measures of real-world arm use, as well as sensitive measures of cognition, neglect and sensation which may interact with UL recovery. Finally, we do not have information about dose of UL therapy provided. Past observations [41] in similar populations of Australian stroke survivors suggest that the dose of therapy received would likely be too low to an important mediating variable in this study.

Conclusion

This study highlights that the greatest rate of improvement of UL capacity and performance occurred early after stroke (between 2 to 6-weeks post stroke), suggesting that this is the time window to target testing of behavioural interventions. However, capacity and performance measures improved on average to 12–18 months post stroke, with some individuals continuing to demonstrate improvements at 24 months. This data supports a long-term view of recovery that must be considered clinically and in research design. Crude stroke location classification did not enhance our understanding of subgroups, suggesting more targeted and specific brain biomarkers are required. Further exploration of the phenotypes of recovery are warranted across a 24-month window to advance our understanding of motor recovery post stroke.

Funding

This study was funded by the Australian Research Council (ARCFT09901086), Austin Health Medical Research Fund and La Trobe University Faculty Research Grant.

Ethical approval

Ethical approval was received from Austin Health [H2008/03428] and Northern Health [P4/13] Human Research Ethics Committees.

Conflict of interest

None.

Key messages

- This study takes a long-term view to upper limb recovery after stroke to identify critical periods of improvement in the first 2-years post stroke.
- The period of greatest improvement in all measures occurred in the first 6-weeks post stroke.
- At the group level, improvements were evident to 12- to 18-months post stroke, but at the individual level improvements were still being observed at 24-months; this pattern was observed across lesion classifications.

References

[1] Nakayama H, Jorgensen HS, Raaschou HO, Olsen TS. Recovery of upper extremity function in stroke patients: the Copenhagen Stroke Study. Arch Phys Med Rehabil 1994;75(4):394–8.
[2] Doman CA, Waddell KJ, Bailey RR, Moore JL, Lang CE. Changes in upper-extremity functional capacity and daily performance during outpatient occupational therapy for people with stroke. Am J Occup Ther 2016;70(3), 7003290040p7003290041-7003290040p7003290011.
[3] Bernhardt J, Borschmann K, Boyd L, Carmichael TC, Corbett D, Cramer SC, *et al.* Moving rehabilitation research forward: developing consensus statements for rehabilitation and recovery research. Neurorehabil Neural Repair 2017;31(8):694–8.
[4] Rand D, Eng JJ. Disparity between functional recovery and daily use of the upper and lower extremities during subacute stroke rehabilitation. Neurorehabil Neural Repair 2012;26(1):76–84.

[5] Rand D, Eng JJ. Predicting daily use of the affected upper extremity 1 year after stroke. J Stroke Cerebrovasc Dis 2015;24(2):274–83.
[6] Doman CA, Waddell KJ, Bailey RR, Moore JL, Lang CE. Changes in upper-extremity functional capacity and daily performance during outpatient occupational therapy for people with stroke. Am J Occup Ther 2016;70(3):p1–11.
[7] Edwardson MA, Wang X, Liu B, Ding L, Lane CJ, Park C, *et al.* Stroke lesions in a large upper limb rehabilitation trial cohort rarely match lesions in common preclinical models. Neurorehabil Neural Repair 2017;31(6):509–20.
[8] Cortes JC, Goldsmith J, Harran MD, Xu J, Kim N, Schambra HM, *et al.* A short and distinct time window for recovery of arm motor control early after stroke revealed with a global measure of trajectory kinematics. Neurorehabil Neural Repair 2017;31(6):552–60.
[12] Borschmann K, Iuliano S, Ghasem-Zadeh A, Churilov L, Pang M, Bernhardt J. Upright activity and higher motor function may preserve bone mineral density within 6-months of stroke: a longitudinal study. Arch Osteoporos 2018;13(5).
[13] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet (London, England) 2007;370(9596):1453–7.
[14] Brott T, Adams H, Olinger C, Marler JR, Barsan WG, Biller J, *et al.* Measurements of acute cerebral infarction: a clinical examination scale. Stroke 1989;20:864–70.
[15] Briggs D, Felberg R, Malkoff M, Bratina P, Grotta J. Should mild or moderate strokes be admitted to an intensive care unit? Stroke 2001;32:871–6.
[16] de Haan R, Limburg M, Bossuyt P, van der Meulen J, Aaronson N. The clinical meaning of Rankin' handicap' grades after stroke. Stroke 1995;26:2027–30.
[17] Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. Lancet 1991;337(June):1521–6.
[18] Shelton FN, Reding MJ. Effect of lesion location on upper limb motor recovery after stroke. Stroke 2001;32(1):107–12.
[19] Gowland C, Stratford P, Ward M, Moreland J, Torresin W, Van Hullenaar S, *et al.* Measuring physical impairment and disability with the Chedoke-McMaster Stroke Assessment. Stroke 1993;24(1): 58–63.
[20] Barreca S, Gowland CK, Stratford P, Huijbregts M, Griffiths J, Torresin W, *et al.* Development of the Chedoke Arm and Hand Activity Inventory: theoretical constructs, item generation, and selection. Top Stroke Rehabil 2004;11(4):31–42.
[21] Taub E, Miller NE, Novack TA, Cook EW, Fleming WC, Nepomuceno CS, *et al.* Technique to improve chronic motor deficit after stroke. Arch Phys Med Rehabil 1993;74:347–54.
[22] Uswatte G, Taub E, Morris D, Vignolo M, McCulloch K. Reliability and validity of the upper-extremity Motor Activity Log-14 for measuring real-world arm use. Stroke 2005;36(11):2493–6.
[23] van der Lee J, Beckermann H, Knol D, de Vet H, Bouter L. Clinimetric properties of the Motor Activity Log for the assessment of arm use in hemiparetic patients. Stroke 2004;35:1410–4.
[24] Miltner W, Bauder H, Sommer M, Dettmers C, Taub E. Effects of constraint-induced movement therapy on patients with chronic motor deficits after stroke—a replication. Stroke 1999;30(3):586–92.
[25] Hammer A, Lindmark B. Responsiveness and validity of the Motor Activity Log in patients during the subacute phase after stroke. Disabil Rehabil 2010;32(14):1184–93.
[26] Park S, Wolf S, Blanton S, Winstein C, Nichols-Larsen D. The EXCITE trial: predicting a clinically meaningful motor activity log outcome. Neurorehabil Neural Repair 2008;22(25):486–93.
[28] Bohannon R. Measurement and nature of muscle strength in patients with stroke. Neurorehabil Neural Repair 1997;11(2):115–25.
[29] Bernhardt J, Hayward KS, Kwakkel G, Ward NS, Wolf SL, Borschmann K, *et al.* Agreed definitions and a shared vision for new standards in stroke recovery research: the Stroke Recovery and Rehabilitation Roundtable taskforce. Int J Stroke 2017;12:444–50.
[30] Duncan PW, Goldstein LB, Matchar D, Divine GW, Feussner J. Measurement of motor recovery after stroke. Outcome assessment and sample size requirements. Stroke 1992;23:1084–9.
[31] Stinear C, Ackerley S, Byblow W. Rehabilitation is initiated early after stroke, but most motor rehabilitation trials are not: a systematic review. Stroke 2013;44(7):2039–45.
[32] Kwakkel G, Lannin N, Borschmann K, English C, Ali M, Churilov L, *et al.* Standardised measurement of sensorimotor recovery in stroke trials: consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable (SRRR). Int J Stroke 2017;12:451–61.
[33] Boyd LA, Hayward KS, Ward NS, Stinear CM, Rosso C, Fisher RJ, *et al.* Biomarkers of stroke recovery: consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable (SRRR). Int J Stroke 2017;12:480–93.
[35] Shelton F, Reding MJ. Effect of lesion location on upper limb motor recovery after stroke. Stroke 2001;32:107–12.
[36] Hayward KS, Lohse KR, Bernhardt J, Lang CE, Boyd LA. Characterising Arm Recovery in People with Severe Stroke (CARPSS): protocol for a 12-month observational study of clinical, neuroimaging and neurophysiological biomarkers. BMJ Open 2018;8:e026435.
[38] Wade DT, Langton Hewer R, Wood VA, Skilbeck CE, Ismall HM. The hemiplegic arm after stroke: measurement and recovery. J Neurol Neurosurg Psychiatr 1983;46:521–4.
[39] Hayward KS, Eng JJ, Boyd LA, Lakhani B, Bernhardt J, Lang CE. The role of accelerometers in the measurement of real world arm use after stroke. Brain Impair 2016;17:16–33.
[40] Waddell KJ, Strube MJ, Bailey RR, Klaesner JW, Birkenmeier RL, Dromerick AW, *et al.* Does task-specific training improve upper limb performance in daily life poststroke? Neurorehabil Neural Repair 2017;31(3):290–300.
[41] Hayward KS, Brauer SG. Dose of arm activity training during acute and subacute rehabilitation post stroke: a systematic review of the literature. Clin Rehabil 2015;29(12):1234–43.