



RECOVERY OF ARM FUNCTION DURING ACUTE TO CHRONIC STAGES OF STROKE QUANTIFIED BY KINEMATICS

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Objective: To quantify the longitudinal changes in upper limb kinematics within the first year after stroke and to identify the factors that are associated with these changes.

Methods: A total of 66 individuals with stroke from the Stroke Arm Longitudinal Study at the University of Gothenburg (SALGOT) cohort were included if they were able to perform the target-to-target task. Data from a virtual reality haptic target-to-target task at 6 time-points between 3 days and 12 months after stroke were analysed by linear mixed models, while controlling for the impact of cofactors (stroke severity, age, type and side of stroke, sex and presence of diabetes).

Results: Kinematic variables of movement time, mean velocity and number of velocity peaks improved over time and were positively associated with younger age, less severe stroke and ischaemic compared with haemorrhagic stroke. Most of the improvement occurred within 4 weeks after stroke, although movement time and number of velocity peaks also improved between 3 and 6 months after stroke.

Conclusion: Kinematic variables of movement time, mean velocity and number of velocity peaks were effective in quantifying the longitudinal changes in upper limb kinematics within the first year after stroke.

Key words: upper extremity; kinematics; outcome assessment; virtual reality; stroke recovery.

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Upper limb motor impairment occurs in approximately 50–80% of individuals in the acute stage of stroke (1–3) and continues in 40–50% in the chronic stage (2, 4). Approximately 65% of hospitalized individuals with initial motor deficits show some degree of motor recovery, while complete motor recovery occurs in less than 15% of individuals (5). Clinical recovery of upper limb motor function is most rapid during the first 4 weeks following stroke, and most recovery occurs during the first 3 months post-stroke (5, 6). Additional recovery has also been shown to occur after 3 months

LAY ABSTRACT

Recovery of arm function after stroke can be measured using virtual reality technology, which, in contrast to traditional clinical assessments, enables objective and highly precise measurement of different aspects of movement, such as speed and smoothness, termed kinematics. This study aimed to measure the recovery of arm movements between 3 days and 12 months after stroke using kinematic measures, and to identify factors that affect recovery. The results showed that movement time, mean velocity and smoothness improved with time after stroke. These data also suggest that younger stroke survivors, those with less severe stroke, and those with stroke caused by a clot, as opposed to a bleed, undergo greater improvements. Most of the improvement was seen early after stroke, within the first 4 weeks, but both movement time and smoothness also continued to improve between 3 and 6 months. The results show that kinematic analysis can effectively show the changes in arm movement within the first year after stroke.

following stroke, usually in combination with intensive rehabilitation (5–7).

The time course of functional recovery after stroke is dependent on several factors. There is a strong negative association of initial grade of stroke paresis and age with functional recovery after stroke (5, 8, 9). According to a retrospective observational study, individuals with haemorrhagic stroke had higher initial impairment compared with those with ischaemic stroke, as demonstrated by Fugl-Meyer Assessment of the Upper Extremity (FMA-UE) scores at admission (10). However, the haemorrhagic stroke group showed greater recovery in arm function and activity capacity, such that individuals in both groups had similar function at 3 months after stroke (11). It is not clear whether the same factors are reflected in the change in kinematic variables of arm function during the recovery of upper limb in individuals with stroke.

Kinematic measurements of movement performance are recommended as core measures to be included in every stroke recovery trial (12). Kinematic assessment of upper limbs after stroke is often performed using optoelectronic cameras (13–15), robotic techniques (16) and virtual reality (VR) (17, 18). VR coupled with haptic devices can provide sensitive assessment of the kinematic function of the upper limb after stroke (19, 20). Haptic-enabled VR can measure end-point

kinematics of common daily tasks, such as pointing, while allowing free arm movements in a 3D space (17). Despite VR systems being in use in stroke rehabilitation (21), there are sparse data from longitudinal studies, although some data on the responsiveness of upper limb kinematics are available from robotic studies (22–24). Haptic devices coupled with VR systems are suitable for use in the assessment and rehabilitation of post-stroke individuals, even in telemedicine settings (25).

Longitudinal studies of upper limb recovery after stroke using optoelectronic cameras have shown that movement time and smoothness improved up to 3 months after stroke (14, 15, 26). Kinematic movement deficits observed at 3 months post-stroke remained unchanged at 12 months in individuals with mild stroke impairment (13). Thus, the recovery of kinematics seems to follow a similar recovery pattern as observed in clinical assessments, although the evidence in kinematics remains sparse and varies between studies. In addition, longitudinal changes in the kinematics of the upper limb after stroke have not been studied using the pointing task in 3D virtual space.

The aims of this study were to quantify the longitudinal changes in upper limb kinematics between day 3 and month 12 after stroke, and to identify the factors that affect this change, using the target-to-target pointing task performed in VR.

METHODS

Study design and participants

Study participants were extracted from the Stroke Arm Longitudinal Study of University of Gothenburg (SALGOT) cohort, which consisted of 122 unselected adults living in the Gothenburg urban area, having impaired upper limb function following first-ever stroke and admitted within 3 days of stroke onset (27). World Health Organization (WHO) collaborative criteria were used to determine if the individual had stroke (28). Exclusion criteria for SALGOT were: upper limb condition prior to stroke that has an impact on functional use of the arm; severe multi-impairment or diminished physical condition before the stroke that will affect arm function; life expectancy less than 12 months due to other illness or severity of stroke injury; and not Swedish speaking prior to the stroke incident. The SALGOT trial was registered with register number NCT01115348 at clinicaltrials.gov, on 4 May 2010. Ethical approval was obtained from Regional Ethical Review Board, Gothenburg, Sweden (number 225-08, 511-01). The inclusion process of the study is shown in Fig. 1.

Individuals from the SALGOT cohort who were able to perform the target-to-target pointing task (FMA-UE score 31–66) at any of the assessment points were included in the current study. Assessments were performed by 2 trained physiotherapists at 3 days, 10 days, 4 weeks, 3 months, 6 months and 12 months after stroke. Day 3 after stroke was considered as acute stage of stroke, day 10, week 4 and month 3 as early subacute stage, month 6 as late subacute stage, and month 12 as chronic stage of stroke (29). From

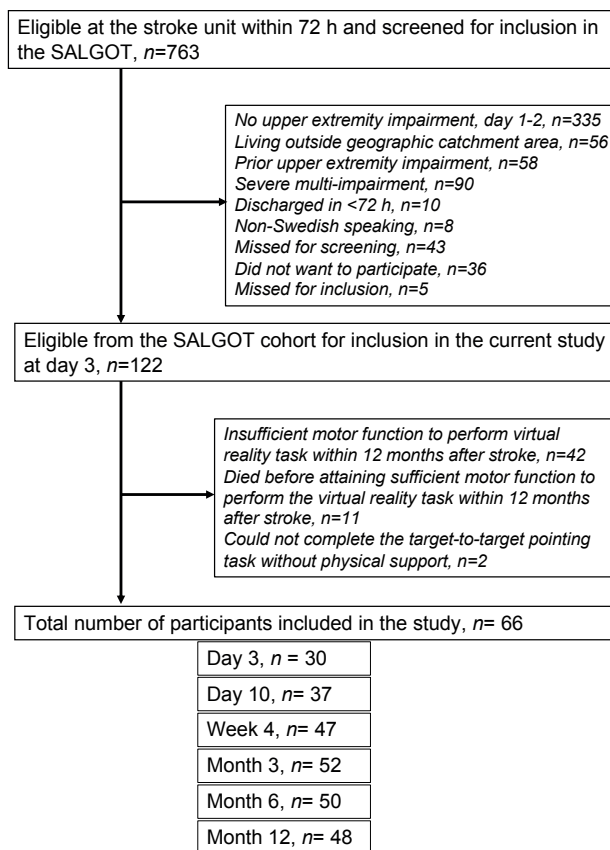


Fig. 1. Flowchart of study inclusion process. SALGOT: Stroke Arm Longitudinal Study at the University of Gothenburg.

the whole cohort of 66 participants, 30 (45%) performed the target-to-target task for first time at 3 days after stroke and 64% and 82% performed the task for the first time within 10 days and 4 weeks after stroke, respectively (Fig. 1 and Table S1¹). All participants received multi-professional team-based rehabilitation according to Swedish National Guidelines, and no specific intervention was provided to participants as part of the study (30). The VR system used in the current study was not part of the standard assessment or intervention during the study period. No specific power analysis was performed prior to this study, but all available data from the SALGOT cohort were screened for inclusion. Power analysis for the SALGOT has been reported previously (27).

Equipment and procedure

The equipment comprised a semi-immersive VR workbench, 3D shuttered glasses and a haptic device. When observed through the shuttered glasses, the mirror on the VR workbench showed 3D objects in virtual space. This illusion of seeing 3D objects was made possible due to the synchronization of image sequences between the shuttered glasses and the infrared transmitter on the VR workbench. Kinematic data were captured using a PHANTOM® Omni™ (SensAble Technologies, USA) haptic stylus. The haptic stylus could be moved freely in the virtual workspace, whose dimensions were 160 × 120 × 120 mm. The

¹<http://www.medicaljournals.se/jrm/content/?doi=10.2340/16501977-2813>

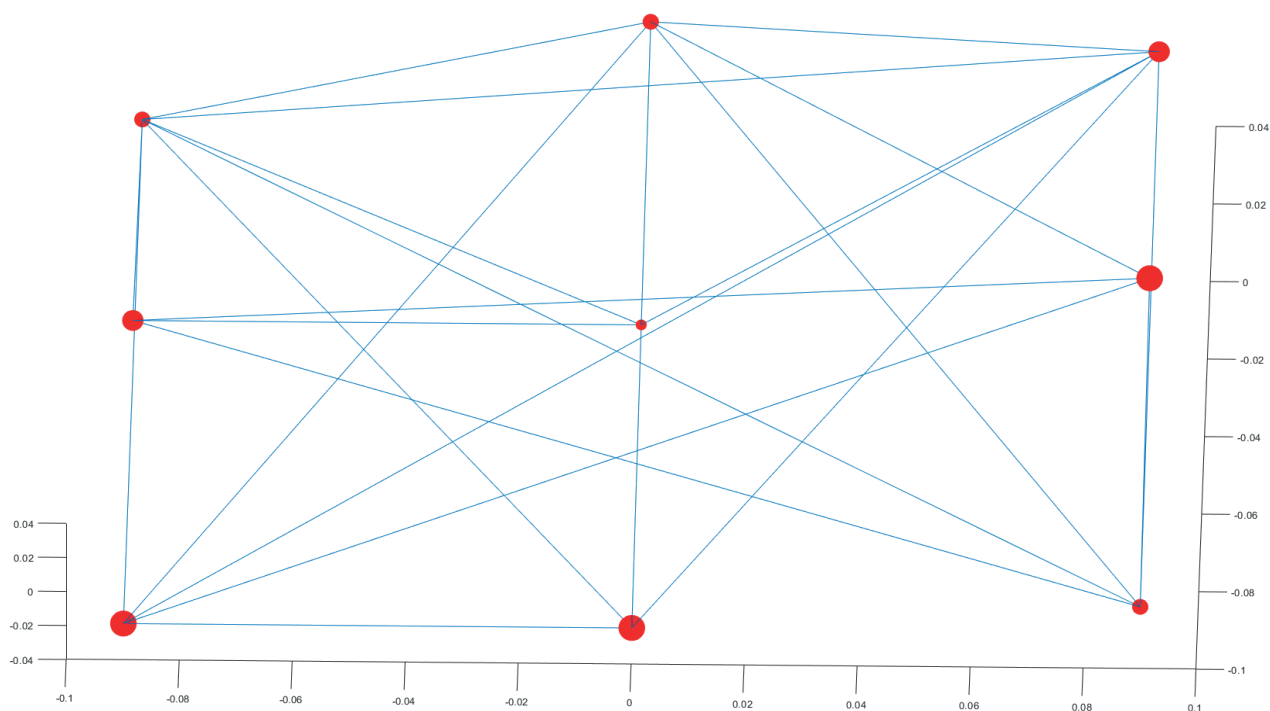


Fig. 2. Position of the 32 partly overlapping targets in 3D space. A larger circle indicates that the target is displayed closer and a smaller size that it is displayed further away from the viewer in the 3D space. The targets are displayed one at the time in a pre-programmed order. The task comprises 31 movement segments with varying distance and direction. Distances scaled in m.

stylus provided touch sensation when it came close to a virtual object and provided force feedback when the virtual object was pointed at. The participant wore 3D shuttered glasses and sat on a height-adjustable chair in front of the VR workbench. The participant sat close enough to the workbench to have a good view of the 3D space displayed on the computer screen. The maximum distance between the table edge and the far end of the possible position of the haptic pointer was 30 cm.

The task for the participant was to reach and point at round disc-shaped targets ($\sim 3.0^\circ$ viewing angle, 3.8-cm diameter) in the virtual space using the haptic stylus as rapidly and as accurately as possible (17). Participants were asked to hold the stylus using a pen grip, and whenever a pen grip was not possible, they were allowed to use whole hand cylinder grip for the task. There were 32 targets in total, and the task started when the first target was pointed at by the participant. The position of the targets appeared to be random for the participant, but they were actually pseudo-randomized by the software for uniformity. When the participant pointed at a target, it disappeared and a new target appeared in a different location in the virtual space. The task ended when the participant had made all 32 targets disappear. The shortest distance between any 2 targets was 76 mm and the longest distance was 180 mm. Fig. 2 shows the position of targets in 3D space.

Kinematic variables

The end-point kinematic data from the haptic device were captured and extracted using custom-made software Curictus™ (Curictus AB, Gothenburg, Sweden) and MATLAB® (Mathworks, USA). The entity between the appearance of a target and its disappearance was called a movement segment, and the target-to-target pointing task comprised 31 movement segments.

Each kinematic variable was calculated as the mean of all 31 movement segments in the entire task. The delay between hitting a target and appearance of a new target was 0.3 s. All kinematic variables were reported inclusive of this delay.

Four kinematic variables were selected for analysis: movement time, mean velocity, peak velocity, and number of velocity peaks (17). The chosen variables have shown to be effective in discriminating arm function between individuals with mild-to-moderate stroke and healthy controls (17). The concurrent validity of the kinematic variables of movement time, mean velocity and number of velocity peaks were previously established against the FMA-UE and the Action Research Arm Test, a measure of activity capacity (18). These variables have been shown to be valid and are frequently used in kinematic assessment following stroke (31).

Movement time was the mean of the times taken to complete each movement segment included in the task. Mean velocity was defined as the mean of the velocity reported over all movement segments. Peak velocity was the mean of the maximum absolute velocity recorded during each movement segment. The smoothness of movement was measured using number of velocity peaks. Velocity peak was defined as the period between a local minima and maxima, whenever the difference between them exceeded 20 mm/s. In addition, the time between 2 adjacent peaks had to be at least 150 ms (32). A lower velocity peak value indicates a smoother movement.

Clinical assessment

National Institute of Health Stroke Scale (NIHSS) scoring was performed at the time of hospital admission to determine the severity of stroke impairment, where higher NIHSS scores

Table I. Demographics and clinical characteristics of the study population

Demographic data, clinical characteristics and assessments at admission	Mean (SD), <i>n</i> (%) or median (range, IQR) (<i>n</i> = 66)
Age, mean (SD)	65.7 (13.4)
Female, <i>n</i> (%)	27 (41)
Ischaemic/haemorrhagic stroke, <i>n</i> (%)	81/19
Right-hand dominant, <i>n</i> (%)	63 (95)
Right hemiparesis, <i>n</i> (%)	29 (44)
NIHSS total score, mean (SD)	6.24 (5.1)
Diabetic status, <i>n</i> (%)	7 (10)
Score <9 in BNI pre-screening, <i>n</i> (%)	5 (7)
FMA-UE score	58(31–66, 54–62)
Decreased sensation (≤11 points, FMA), <i>n</i> (%)	6 (10)
Impaired passive joint motion (≤23 points, FMA), <i>n</i> (%)	10 (15)
Pain during passive movements (≤23 points, FMA), <i>n</i> (%)	5 (8)
Spasticity of the elbow or wrist joint (≥1 point, MAS), <i>n</i> (%)	1 (1)

SD: standard deviation; IQR: interquartile range; MAS: Modified Ashworth Scale; FMA: Fugl-Meyer Assessment; FMA-UE: Fugl-Meyer Assessment of the Upper Extremity; NIHSS: National Institute of Health Stroke Scale.

indicated more severe impairment (33). FMA-UE was used to assess the sensorimotor function of the upper limb (34). A maximum score of 66 in FMA-UE indicates best test performance. The non-motor domains of FMA-UE (sensation, passive joint motion and pain) were also assessed. The Modified Ashworth Scale (MAS) was used to determine the presence of spasticity of elbow and wrist joints (35). The background characteristics of the participants are summarized in Table I.

Statistical analyses

Statistical analyses were performed using IBM SPSS® software, version 24 (IBM, USA). Distributions of included variables were evaluated by visual inspection of histograms. Natural log transformation (ln) was performed for all dependent variables, so that they were approximately normally distributed. Outliers >3 standard deviations (SD) present in all dependent variables were included in model building. The significance level for variables in the models was set at $p < 0.05$.

Linear mixed model analysis was performed to assess the longitudinal changes over time for each kinematic variable. In the initial models, fixed effect of time, random effect of time and intercepts were included. Fixed effect of time captures the constant change over time that is common to all individuals. Random effect of time captures the inter-subject variation in change across the 6 time-points and the inter-subject variation of the intercept, which cannot be explained by fixed effects. An adjusted model was then built by adding the cofactors of stroke severity, age, type of stroke, side of stroke paresis, sex and presence of diabetes, one at a time. The interaction effect

of the significant cofactors with time was also tested. The log likelihood ratio test was used to determine the significance of each new model with the added variable in comparison with the base model. Estimates of residuals were checked for each model, and the residual plots for final models were checked for linearity, constant variance and normal distribution by means of residual analysis and predicted probability plots.

When a fixed effect of time was found, Wilcoxon’s signed-rank test was used to find those time-points between which differences exist. The strength of difference between groups was determined by effect size (ES) estimates, using point bi-serial correlation (36). Cohen’s guidelines were followed while interpreting the effect sizes, where 0.1, 0.3, and 0.5 indicate small, medium, and large effect sizes, respectively (36). Since multiple comparisons were performed (3 kinematic variables and 5 comparisons over time), Bonferroni correction with a significance level of 0.003 was applied.

RESULTS

Of all eligible 763 individuals at the stroke unit within 3 days post-stroke, 122 were included in the SALGOT cohort and 66 of those were included in the current study. The size of the cohort varied at different time-points, partly due to missing data and partly due to insufficient motor function at early time-points (Table S1¹). The flowchart of the inclusion process is shown in Fig. 1.

There was a significant fixed effect of time ($p < 0.0001$) on kinematic variables of movement time, mean velocity and number of velocity peaks between day 3 and month 12 after stroke. There was no random effect of time and no interaction between the effect of time and co-factors in any of the kinematic models. In the 3 significant kinematic models, younger age, less severe stroke, and ischaemic stroke (compared with haemorrhagic stroke) positively associated with the effect of time. For mean velocity, additional factors, namely, female sex, being non-diabetic and having right-sided paresis also positively associated with the effect of time. No effect of time was found for the dependent variable of peak velocity. The predicted probability plots of residuals were close to normal distribution and a scatter plot of residuals against predicted values showed a random pattern around zero. The estimates and p -values of all effects included in significant models are shown in Table II.

Table II. Results of linear mixed model analysis. Variables with significant effect ($p < 0.05$) on stroke recovery in the final models are displayed

Dependent variable	Log movement time		Log mean velocity		Log number of velocity peaks	
	Estimate	<i>p</i> -value	Estimate	<i>p</i> -value	Estimate	<i>p</i> -value
Intercept	0.257	0.016	-1.338	<0.0001	0.962	<0.0001
Time since stroke, weeks	-0.005	<0.0001	0.004	<0.0001	-0.003	0.001
NIHSS score at onset	0.015	0.001	-0.023	<0.0001	0.011	0.005
Age	0.008	<0.0001	-0.007	<0.0001	0.006	<0.0001
Type of stroke (1 = ischaemic, 0 = haemorrhagic)	-0.238	<0.0001	0.251	<0.0001	-0.173	<0.0001
Side of stroke paresis (1 = right, 2 = left)	-	-	0.080	0.024	-	-
Sex	-	-	-0.274	<0.0001	-	-
Presence of diabetes	-	-	-0.358	<0.0001	-	-

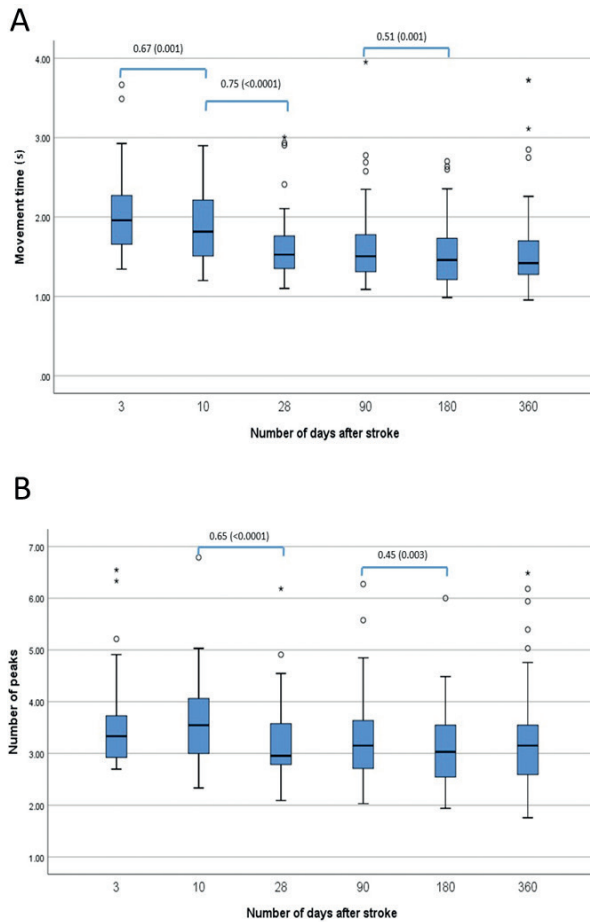


Fig. 3. Boxplots (median±interquartile range (IQR)) showing changes in: (A) movement time; and (B) number of velocity peaks of individuals with stroke over time. Values greater than 4 and 7 units for movement time and number of velocity peaks, respectively, were removed from the graphical representation in order to show the boxplots in adequate size. Effect size and *p*-value are shown in case of significant differences between adjacent time-points.

The longitudinal changes in all kinematic variables are shown in Fig. 3 and Fig. 4 and Table III. Movement time and mean velocity showed improvements between days 3 and 10 (ES 0.67 and 0.53, $p=0.001$), and between day 10 and week 4 (ES 0.75 and 0.56, $p<0.001$). Num-

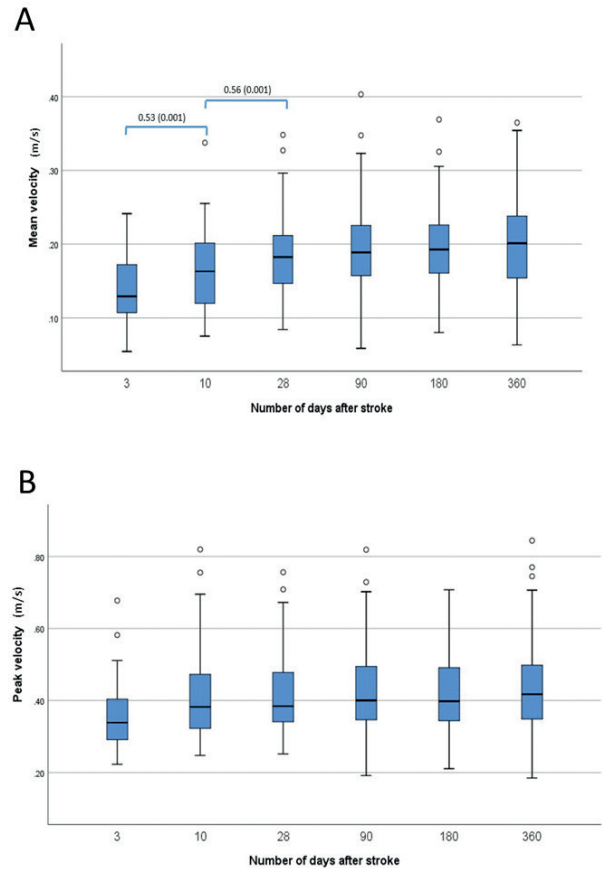


Fig. 4. Boxplots (median±interquartile range (IQR)) showing changes in: (A) mean velocity and (B) peak velocity of individuals with stroke over time. Effect size and *p*-value are shown in case of significant differences between adjacent time-points.

ber of velocity peaks showed improvement between day 10 and week 4 (ES 0.65, $p<0.0001$). Movement time (ES 0.51, $p=0.001$) and number of velocity peaks (ES 0.45, $p=0.003$) also showed improvements between 3 and 6 months. While the kinematic measures of movement time and mean velocity improved continuously over the time-points measured, the best performance on number of movements was reached at week 4.

Table III. Median and interquartile range of kinematic variables at all time-points

Kinematic variables,	Day 3 (<i>n</i> =30)	Day 10 (<i>n</i> =37)	Week 4 (<i>n</i> =47)	Month 3 (<i>n</i> =52)	Month 6 (<i>n</i> =50)	Month 12 (<i>n</i> =48)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Movement time, s	1.98 (1.6–2.5)	1.83 (1.5–2.2)	1.53 (1.3–1.7)	1.52 (1.3–1.8)	1.47 (1.2–1.7)	1.42 (1.2–1.7)
Mean velocity, mm/s	129.21 (106.9–174.1)	16.07 (118.5–201.6)	182.52 (144.9–212.4)	188.71 (155.0–227.1)	192.67 (156.9–226.5)	201.14 (151.2–238.0)
Number of velocity peaks	3.36 (2.9–4.5)	3.59 (3.0–4.2)	2.97 (2.7–3.6)	3.15 (2.7–3.7)	3.03 (2.5–3.5)	3.15 (2.5–3.5)
		<i>p</i> -value	<i>p</i> -value	<i>p</i> -value	<i>p</i> -value	<i>p</i> -value
		0.001	<0.0001	0.006	0.001	0.66
		0.001	0.001	0.006	0.04	0.16
		0.03	<0.0001	0.40	0.003	0.60

$p<0.003$ is indicative of significant difference, in contrast to the previous time-point, confirmed with Wilcoxon's signed-rank test.

DISCUSSION

Kinematic variables of movement time, mean velocity and number of velocity peaks improved over time and were positively associated with younger age, less severe stroke and ischaemic compared with haemorrhagic stroke. In addition to these factors, recovery of mean velocity was positively associated by female sex, being non-diabetic and having right-sided paresis. This study also showed that most of the improvement in upper limb kinematics occurred during the acute and early subacute stage, within 4 weeks of stroke. Two variables, movement time and number of velocity peaks, also showed improvement in the late subacute stage, between 3 and 6 months post-stroke. The detected improvement in the late subacute stage, as seen in the current study, suggests that movement time and number of velocity peaks can be used to capture improvements in the late subacute stage of stroke, where many traditional clinical scales reach a ceiling effect.

As shown in previous studies, the movement time, mean velocity and number of velocity discriminate between mild and moderate stroke impairment, as well as healthy controls (17) and correlate both with upper limb impairment assessed by FMA-UE and with activity capacity assessed by Action Research Arm Test (18). The results from the current study extend the evidence by showing that these kinematic variables are also effective for capturing change over time and can therefore be used in measuring the recovery of arm function in individuals with stroke. The target-to-target VR task is also easy to use in clinical settings (37).

Recovery of kinematic variables was positively influenced by lower stroke severity, lower age and ischaemic stroke compared with haemorrhagic stroke. These factors are known to affect clinical recovery, and the current study also establishes their role in recovery of kinematic measures (5, 8, 11). Improvements in mean velocity were also influenced positively by right-sided stroke paresis, female sex and being non-diabetic. A past study showed that individuals with affected dominant arm show better hand strength, less muscle tone and less pain than those with affected non-dominant arm at the chronic stage of stroke (38). In addition, healthy adults are known to demonstrate higher velocity of movement in their dominant hand (39). Given that 95% of individuals in the current study were right-hand dominant, being stroke-affected on the right side (i.e. the dominant side) might have motivated them to use the affected arm to train on daily life tasks, especially those tasks requiring fast movements. Possible reasons for individuals with diabetes to show lower mean velocity could be decreased sensation, muscle weakness, limited joint mobility, or a combination of these factors, and further research surrounding this phenomenon is warranted in order to reach solid conclusions.

All kinematic variables, except peak velocity, showed improvement over time, with most of the improvement occurring between acute and early subacute stages of stroke. This recovery pattern is similar to the pattern measured using clinical scales (5). In addition, the current study showed improvement in movement time and number of velocity peaks between months 3 and 6 after stroke, which is beyond the period that is commonly assigned for natural clinical recovery (5, 6). In contrast to this result, an optoelectronic camera-based kinematic reaching study showed no improvement in movement duration and smoothness between week 8 and month 6 after stroke (26). One possible reason for this difference in results could be that the fast movements and increased precision requirements of the task in the present study made the subtle aspects of functional deficits more prominent, compared with movements in normal pace and with no requirement on precision. Since recovery of fast and precise movements occurs even beyond 3 months post-stroke, continued stroke rehabilitation after first 3 months post-stroke might be beneficial as there is still potential for functional improvement.

Similar to the results of the current study, movement time and smoothness during a drinking task improved over the first 3 months after stroke (15). Individuals with high motor function (FMA-UE ≥ 60) showed no change in movement time and smoothness during a drinking task between 3 and 12 months after stroke (13). Thus, it is possible that improvements in movement time and number of velocity peaks seen beyond 3 months post-stroke in the current study are mostly due to the contribution from low functioning individuals of the cohort. High inter-individual variability in recovery of reaching movements after stroke was also observed in a robotic study, in which some individuals reached full motor recovery as early as 6 weeks post-stroke, while others did not reach full recovery even after 26 weeks (24). This finding is consistent with that of the current study, where longitudinal change was recorded between day 3 and month 6.

The strength of this study is the relatively large and well-defined cohort recruited at as early as 3 days and followed up until 1 year after stroke. The study included individuals with FMA-UE score between 31 and 66, so the results could be generalized to individuals with mild-to-moderate arm impairment. As individuals with stroke use similar strategies for reaching in reality and virtual reality, it is possible that the findings from this study are also applicable in real-world settings (40).

This study has some limitations. Since the participants performed the pointing tasks many times throughout the course of the study, there could be a learning effect, but it is probably negligible because the

assessments were spread over as long as one year. The presence of several outliers may have influenced the results, but they were retained during the analyses because the study results did not differ significantly when the outliers were removed from the analysis, and the characteristics of the outliers were not different from the rest of the group. The variables extracted from the pointing task quantify the end-point (hand) movement in 3D space and therefore automatically also include compensatory movement patterns, for example, of the trunk. This needs to be considered when interpreting the results. The study design allowed the participants to join the study at later time-points if they were not able to perform the pointing task during the earlier assessments. Of the total 66 participants included in the study, approximately 82% entered the study within the first 4 weeks after stroke and the number of participants at each time-point ranged from 30 to 52. Missing data are often a problem in longitudinal studies and should be considered when interpreting the results. In the current study, statistical analyses that are able to adjust for missing data have been used and the proportion of participants who joined late due to poor arm function was 10% or less at each test occasion.

CONCLUSION

Kinematic variables of movement time, mean velocity and number of velocity peaks were found to be effective in quantifying the recovery of the upper limb during the first year after stroke. The rate of recovery was dependent on factors such as age, stroke severity and type of stroke. While most of the recovery occurred within the first 4 weeks post-stroke, kinematic measures of movement time and number of velocity peaks also showed improvements between 3 and 6 months post-stroke. These late improvements in upper limb movement performance can be of particular interest in patients with high motor function when the traditional clinical scales might have reached the ceiling effect. The observed improvements in kinematics beyond the first 3 months after stroke also suggest that continued upper limb rehabilitation beyond 3 months after stroke is warranted.

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