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Recovery of quiet standing balance and lower limb motor impairment early poststroke : how are they related?

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1 **Recovery of quiet standing balance and lower limb motor**  
2 **impairment early poststroke – how are they related?**

3 **Running title:** Quiet standing balance recovery poststroke

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27

## 1 *Abstract*

2           *Background.* Recovery of quiet standing balance early poststroke has been poorly  
3 investigated using repeated measurements.

4           *Objective.* To investigate (1) the time course of steady-state balance in terms of  
5 postural stability and inter-limb symmetry, and (2) longitudinal associations with lower limb  
6 motor recovery in the first 3 months poststroke.

7           *Methods.* Forty-eight hemiparetic subjects (age:  $58.9 \pm 16.1$  years) were evaluated at  
8 weeks 3, 5, 8 and 12 poststroke. Motor impairments concerned the Fugl-Meyer assessment  
9 (FM-LE) and Motricity Index total score (MI-LE) or ankle item separately (MI-ankle).  
10 Postural stability during quiet two-legged stance was calculated as the net center-of-pressure  
11 area ( $COP_{Area}$ ) and direction-dependent velocities ( $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ ). Dynamic control  
12 asymmetry (DCA) and weight-bearing asymmetry (WBA) estimated inter-limb symmetries  
13 in balance control and loading. Linear mixed models determined (1) time-dependent change  
14 and (2) the *between-* and *within-*subject associations between motor impairments and postural  
15 stability or inter-limb symmetry.

16           *Results.* Time-dependent improvements were significant for FM-LE, MI-LE, MI-  
17 ankle,  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$ , and tended to plateau by week 8. In contrast, DCA  
18 and WBA did not exhibit change. *Between-*subject analyses yielded significant regression  
19 coefficients for FM-LE, MI-LE and MI-ankle scores with  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$   
20 up until week 8, and with WBA until week 12. *Within-*subject regression coefficients of  
21 motor recovery with change in  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ , DCA or WBA were generally  
22 non-significant.

1            *Conclusions.* Postural stability improved significantly in the first 8 weeks poststroke,  
2 independent of lower limb motor recovery at the most affected side *within* subjects. Our  
3 findings suggest that subjects preferred to compensate with the less affected side, making  
4 inter-limb asymmetries in balance control and weight-bearing invariant for change in the first  
5 3 months poststroke.

6    **Clinical Trial Registration:** Clinicaltrials.gov. unique identifier NCT03728036

7    **Keywords:** Stroke, Longitudinal study, Posturography, Standing balance, Recovery, Postural  
8 sway

## 1 *Introduction*

2           Regaining steady-state balance during quiet standing is mainly achieved within the  
3 first 3 months poststroke<sup>1,2</sup> and is a prerequisite for accomplishing independent gait and most  
4 activities of daily life.<sup>2-4</sup> Despite its clinical importance, a limited number of observational  
5 studies have investigated how lower limb motor recovery associates longitudinally with  
6 steady-state balance improvements within this time window.

7           A few longitudinal studies<sup>5-9</sup> have suggested that lower limb motor recovery follows a  
8 proportional and predictable time course in the first 3 to 6 months poststroke. This includes  
9 clinical improvements in synergistic independent motor control,<sup>5,7-9</sup> as measured with the  
10 Fugl-Meyer lower extremity motor score (FM-LE), and strength,<sup>6,7</sup> as measured for example  
11 with the Motricity Index (MI-LE). These findings corroborate observations of the upper  
12 limb<sup>5,7,10</sup> as significant improvements occur in most patients up until week 5<sup>5,6</sup> to 8<sup>7</sup>  
13 poststroke, and a small proportion (10 to 15%) fail to show any motor recovery.<sup>8</sup>

14           At the same time, steady-state balance control remains deficient after independent  
15 stance is regained, with stroke patients exhibiting greater postural sway of the net center-of-  
16 pressure (COP) than healthy controls and loading more body weight on the less affected  
17 leg.<sup>11-13</sup> More recent posturographic studies<sup>14-16</sup> examined the individual-limb COP  
18 trajectories to show that this weight-bearing asymmetry (WBA) is further characterized by an  
19 asymmetric exertion of stabilizing ankle torques. This so-called dynamic control asymmetry  
20 (DCA) reflects the most affected leg's contribution to balance control in the sagittal plane,  
21 relative to the less affected side.<sup>14,16</sup> It has been suggested that the DCA is associated with  
22 impairment severity,<sup>17</sup> although Roelofs and colleagues<sup>16</sup> have recently shown that even  
23 patients with (almost) complete FM-LE recovery may still exhibit significant balance control

1 asymmetries favoring the less affected leg. How this relationship develops *within* subjects  
2 over the first weeks after stroke is currently unclear.

3 To investigate the quality of movement regarding steady-state balance poststroke, the  
4 literature<sup>15,17</sup> recommends complementing conventional instability measures, such as the net  
5 COP sway area ( $COP_{Area}$ )<sup>12,13,17</sup> and velocities in frontal ( $COP_{Vel-ML}$ ) and sagittal planes  
6 ( $COP_{Vel-AP}$ ),<sup>14,16</sup> with metrics that reflect asymmetries, such as DCA and WBA. These  
7 metrics may yield different, yet complementary information about how an improved postural  
8 stability is achieved in patients with hemiparesis, by distinguishing “normalization” of inter-  
9 limb symmetry from persistent compensatory stabilization through the less affected leg, in  
10 reference to a control population of healthy adults. So far, very few attempts have been made  
11 to implement such metrics in stroke recovery studies<sup>11,18,19</sup> and an earlier study by De Haart  
12 and colleagues<sup>14,17</sup> investigated recovery using repeated measurements at arbitrary time-  
13 points, often beyond the period in which the recovery of muscle synergies and strength  
14 plateaus. According to this knowledge gap, the overall aim of the present observational study  
15 was to prospectively investigate the time course of quiet standing balance in terms of posture  
16 stabilization and recovery from inter-limb asymmetries early after stroke onset. Subsequently,  
17 we aimed to relate these fine-grained task performance changes to motor recovery at the level  
18 of the entire lower limb (i.e., FM-LE and MI-LE) and ankle separately (by using the  
19 dorsiflexion item of the Motricity Index [MI-ankle]), considering that steady-state balance is  
20 mainly controlled through ankle torques.<sup>20</sup> The following research questions were addressed:

- 21 **1.** What is the time course of muscle synergies (i.e., FM-LE) and strength (i.e., MI-LE  
22 and MI-ankle) in the most affected leg within the first 3 months poststroke?

- 1       **2.** What is the time course of postural stability (i.e.,  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$ )  
2           and inter-limb symmetry (i.e., DCA and WBA) during quiet stance within the first 3  
3           months poststroke?
- 4       **3.** How is the severity of motor impairments (i.e., FM-LE, MI-LE and MI-ankle)  
5           associated with postural instability (i.e.,  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$ ) and inter-  
6           limb asymmetry (i.e., DCA and WBA) during quiet stance *between* subjects within  
7           the first 3 months poststroke?
- 8       **4.** How are improvements in motor impairments (i.e., FM-LE, MI-LE and MI-ankle)  
9           associated with change in postural instability (i.e.,  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$ )  
10          and inter-limb asymmetry (i.e., DCA and WBA) during quiet stance *within* subjects  
11          over the first 3 months poststroke?

12           In line with recovery models of the paretic upper limb,<sup>10</sup> we hypothesized for the first  
13          question that significant time-dependent change in FM-LE, MI-LE and MI-ankle would occur  
14          within the first 8 weeks poststroke. For the second question, we hypothesized that steady-  
15          state balance would parallel motor recovery and follow the same pattern as previously  
16          described for upper limb motor performance.<sup>21,22</sup> Recovery of steady-state balance is here  
17          defined as posture stabilization reflected by decreases in  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$ .  
18          Concomitant reductions in asymmetries in DCA and WBA in the direction of norm values in  
19          age-matched healthy controls are seen as an indicator of an improved quality of movement.  
20          For the third question, we assumed that patients with lower FM-LE, MI-LE and MI-ankle  
21          scores would exhibit greater postural instability (i.e.,  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$ ) and  
22          asymmetries in DCA and WBA, with an increased involvement of the less affected leg.  
23          Lastly, we hypothesized concerning the fourth question that the *within*-subject associations  
24          between recovery of impairments and steady-state balance would be time-dependent. That is,  
25          rising FM-LE, MI-LE and MI-ankle scores would associate with reductions in postural

1 instability (i.e.,  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$ ) and asymmetries in DCA and WBA  
2 mainly within the first 8 weeks poststroke.

### 3 *Methods*

4         The present longitudinal study is part of the larger TARGET research project. TARGET  
5 is an acronym for Temporal Analyses and Robustness of hemiplegic Gait and standing  
6 balance Early poststroke, and was funded by the Research Foundation - Flanders (FWO,  
7 Flanders, Belgium; application no. 1S64819N). This project was approved by the Medical  
8 Ethics Committee of the University Hospital Antwerp (No. 18/25/305; Belgian trial  
9 registration no. B300201837010) and additional approval was obtained from the ethics  
10 committees of other hospitals involved. All procedures were conducted in accordance with  
11 the Declaration of Helsinki. The design of the study protocol has been reported elsewhere<sup>23</sup>  
12 and the protocol is also registered online (ClinicalTrials.gov identified: NCT03728036). The  
13 manuscript was written in conformity with the STROBE statement.<sup>24</sup>

### 14 *Participants*

15         Patients admitted to one of the three cooperating hospitals and two rehabilitation  
16 facilities (Antwerp region, Belgium) after an acute ischemic or hemorrhagic stroke were  
17 screened for participation between December 2018 and December 2021. Screening and  
18 recruitment were performed by the study coordinator (JS) together with the medical doctors  
19 and physiotherapists employed at the stroke units and rehabilitation facilities. All participants  
20 met the following inclusion criteria: (1) having experienced a first-ever hemispheric stroke  
21 confirmed by CT and/or MRI scan; (2) having been included within the first 3 weeks after  
22 stroke; (3) having reduced leg strength, defined as >0 points on item 6a/b of the NIHSS (i.e.,  
23 at least “drift within 5 seconds”) within 72 hours poststroke and an MI-LE score <91 (i.e., at  
24 least “movement against resistance but weaker” for one item) at inclusion; (4) age between



1 18 and 90 years; (5) premorbid independence in daily life activities (i.e., modified Rankin  
2 Scale score of 0-1); (6) no severe orthopedic condition of the lower limbs and trunk or  
3 another neurological illness present before stroke; (7) no severe cognitive or communicative  
4 deficit that may interfere with understanding instructions and study procedures; and (8)  
5 providing written informed consent. These criteria were chosen to recruit a cohort of initially  
6 hemiplegic patients with some residual motor impairment requiring inpatient rehabilitation  
7 care due to a primary stroke.

8           Additionally, we recruited age- and sex-matched adult subjects without reported  
9 history of neurological and/or orthopedic conditions to obtain healthy reference values of  
10 inter-limb symmetry while standing.

### 11 *Procedures*

12           In line with recommendations from the Stroke Recovery and Rehabilitation  
13 Roundtable (SRRR),<sup>25,26</sup> serial measurements were scheduled for each participant at weeks 3,  
14 5, 8 and 12 poststroke. At each time-point, clinical scales were complemented by  
15 posturographic measurements of steady-state balance. Two trained assessors (EE, JS) were  
16 available to administer clinical scales during face-to-face sessions, while the same observer  
17 conducted all serial measurements of individual participants. Posturography was performed  
18 by a single assessor (JS) who was trained in operating the measuring instruments. The same  
19 measurements were performed once in healthy controls for comparison.

### 20 *Clinical measurements*

21           During intake, subjects' sex, age, stroke type (i.e., ischemic or hemorrhagic) and most  
22 affected body side (i.e., left or right) were recorded. Serial follow-up measurements included,  
23 first, the "standing unsupported" item of the Berg Balance Scale (BBS-s) to determine if  
24 subjects were eligible for posturography. Second, impairments in synergistic depended motor

1 control and strength were evaluated at the most affected side using the FM-LE<sup>5</sup> and MI-LE,<sup>27</sup>  
2 respectively. Synergy was defined as a pathological pattern of muscle co-activation occurring  
3 with voluntary movement, referring to the clinical phenomenon of “abnormal muscle  
4 synergies”.<sup>28,29</sup> The FM-LE (0-34) is valid and highly reliable,<sup>30</sup> and we used a  
5 standardization method developed by See and colleagues.<sup>31</sup> The MI-LE (0-99) was  
6 administered by asking subjects to produce a maximum voluntary hip flexion, knee extension  
7 and ankle dorsiflexion against resistance. The MI-LE is valid and reliable.<sup>27</sup> We treated the  
8 MI-ankle as a separate outcome variable.

### 9 *Posturographic measurements*

10 The current study investigated steady-state balance defined by Shumway-Cook and  
11 Woollacott as “the ability to control the body’s center-of-mass (COM) relative to the base of  
12 support in fairly predictable conditions and non-changing environments”.<sup>32</sup> Accordingly,  
13 subjects were instructed to stand quietly on both legs for 40 seconds with their arms  
14 alongside their trunk and their eyes fixated on a non-moving visual target. The bare feet were  
15 positioned side-by-side in a standardized way (8.4 cm heel-to-heel distance and 9 degrees  
16 toe-out angle) and subjects were asked to stand still without further instructions regarding  
17 weight-bearing. Measurements started as soon as patients could stand (i.e., BBS-s >0) and, if  
18 tolerated, three trials were performed with seated resting breaks in between. The first 10  
19 seconds were removed from each trial.

20 We used either two laboratory-grade force plates (Type OR6-7 Biomechanics Force  
21 Platform, AMTI, MA, US) or a portable plantar pressure plate (0.5m Footscan pressure plate  
22 3D, RS Scan/Materialize, BE) to record ground reaction forces in- or outside the lab  
23 environment. The collected raw force data was converted to the net and individual-limb COP  
24 trajectories (appendix B, force data acquisition and COP calculations) which were low-pass

1 filtered with a 10 Hz second-order Butterworth filter. Comparability of the two instruments  
2 for measuring COP was assessed in advance in healthy controls during vision-deprived  
3 stance, yielding high consistency according to Pearson correlation coefficients, yet significant  
4 mean differences (appendix A, comparability analyses). To account for these systematic  
5 differences, serial *within*-subject measures were always performed with the same type of  
6 plate, while *between*-subject variations explained by the choice of measurement instrument  
7 were corrected by entering INSTRUMENT as an additional covariate in the final analyses  
8 (appendix A, correction method).

9         To align the individual-limb COP with the anatomical ankle position, the coordinate  
10 system was rotated. As subjects may have difficulties with maintaining the standardized  
11 position, the actual feet orientation was determined trial-by-trial with an optoelectronic  
12 device (Vicon Motion Systems Ltd, Oxford, UK) during force plate measurements, or by the  
13 plantar pressure distribution (Footscan, RS Scan/Materialize, BE). The AP axis was defined  
14 by a line drawn between the head of the second metatarsal bone and the heel, and the ML  
15 axis perpendicular to it.

#### 16         *Performance measures of steady-state balance*

17         To quantify postural stability, we first calculated the  $COP_{Area}$  by fitting an ellipse in  
18  $mm^2$  that encloses about 85% of the entire signal, using principal component analysis.<sup>33</sup> This  
19 metric served as a general stability index by estimating the total amount of postural sway.  
20 Second, the root mean square of the AP- and ML-COP velocities ( $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ ; in  
21 mm/s) served as estimates of the global balance control efficacy in specific sway  
22 directions.<sup>14,16</sup>

23         Quality of movement was operationally defined by comparing stroke subjects' task  
24 performance directly with that of healthy controls.<sup>34</sup> That means, the better they were able to

1 achieve postural stability with equal contributions by both limbs, the higher their movement  
2 quality.<sup>23</sup> To estimate how the stabilizing mechanism of ankle torques in each leg contributed  
3 to balance control, we calculated the DCA in percentage as a symmetry index of the  
4 individual-limb  $COP_{Vel-AP}$ .<sup>14,16</sup> It is restricted to the sagittal plane, since ankle torques are less  
5 relevant to frontal plane balance.<sup>20</sup> A score of 0% estimates symmetry. Positive and negative  
6 values reflect greater contribution of the less and most affected leg, respectively. WBA was  
7 calculated by dividing the average  $F_z$  below the most affected leg by the total  $F_z$  (i.e., body-  
8 weight), to establish a subject's preferred stance. A value of 50% was subtracted from WBA,  
9 such that 0% means symmetry comparable to DCA. Posturographic outcomes were averaged  
10 over three (or at least two) successive trials per session to maximize reliability.<sup>35</sup>

### 11 *Statistical analyses*

12 To investigate time courses (questions 1 and 2), we first plotted individual time-series  
13 of the outcome variables FM-LE, MI-LE, MI-ankle,  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ , DCA  
14 and WBA, to observe trends in recovery. Next, for each outcome variable, a multivariable  
15 linear mixed model was applied, treating the main fixed effect, that of TIME (week 3, week  
16 5, week 8, week 12), as a categorical predictor variable reflecting progress of time after  
17 stroke onset. AGE (years), SEX (female, male), AFFECTED SIDE (left, right) and  
18 INSTRUMENT (force plates, pressure plate) were included as covariates. A random intercept  
19 per subject was added to account for dependency between repeated measurements. Post-hoc  
20 analyses involved Tukey's HSD multiple comparison method, yielding regression  
21 coefficients ( $\beta$ ) for time-dependent change over the entire period (i.e., weeks 3-12) and across  
22 each epoch (i.e., weeks 3-5, weeks 5-8, weeks 8-12). DCA and WBA values were  
23 statistically compared between stroke and healthy subjects at each time-point using the non-  
24 parametric Steel's test for multiple pair-wise comparisons, with the healthy values treated as  
25 control. The significance level was set at  $<.05$ .

1 Question 3 was addressed using linear mixed models, with  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  
2  $COP_{Vel-AP}$ , DCA or WBA as the dependent variable, and either FM-LE or MI-LE as the  
3 independent variable. TIME, AGE, SEX, AFFECTED SIDE and INSTRUMENT were added  
4 as covariates with a subject-specific intercept. Sub-analyses included four separate models at  
5 weeks 3, 5, 8 and 12. For question 4, the *within*-subject associations were calculated using the  
6 same model architecture but using change scores (i.e.,  $\Delta$ ) with sub-analyses across the three  
7 different epochs. For questions 3 and 4, the final regression coefficient ( $\beta$ ) predicts change in  
8  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ , DCA or WBA for a one-unit increase in either FM-LE or MI-  
9 LE. Multiple testing was accounted for by using Bonferroni-corrected probability values (i.e.,  
10  $P < .05/n$ ).

11 All models were fitted using JMP Pro (version 16). Histograms and Q-Q plots of  
12 residuals were inspected to check model assumptions.

## 13 *Results*

14 Figure 1 shows a flow chart of the recruitment of subjects and serial measurements.  
15 Approximately 250 first-ever stroke survivors were screened during the recruitment period,  
16 of which 66 patients were enrolled for this cohort study. Forty-eight of these subjects  
17 participated in at least 2 posturographic measurements and were subsequently included in the  
18 analyses. Table 1 shows their main baseline characteristics at 3 weeks poststroke. As shown,  
19 the included subjects had a mean (SD) age of 58.9 (16.1 years, 19 were female, 36 had  
20 suffered an ischemic stroke and 25 had left-sided impairments. Ten healthy control subjects  
21 were additionally included with a similar mean age of 46.9 (14.1) years and sex ratio (40%  
22 female).

23 As summarized in Figure 1, four measurements were missed at week 3. Out of the 44  
24 subjects that could be tested, 37 were able to stand independently and participated in the

1 posturographic measurement. At week 5, two measurements were missing and three subjects  
2 had too poor balance to perform the posturographic task. At week 8 and 12, five and twelve  
3 measurements were missed, respectively. The main reason was unavailability after hospital  
4 discharge. As a result, 24 participants could be tested at all four occasions. Fifteen and 9  
5 subjects participated in three and two serial measurements, respectively. The mean time after  
6 stroke onset (SD, range) and the number of participants whose data was available at each  
7 time-point were as follows: 24.88 (1.79, 22-28) days and N=37 for week 3; 38.61 (2.10, 35-  
8 42) days and N=43 for week 5; 59.17 (2.16, 55-63) days and N=43 for week 8; 88.18 (3.66,  
9 84-103) days and N=36 for week 12.

10

11 &lt;INSERT FIGURE 1 ABOUT HERE&gt;

12

13 &lt;INSERT TABLE 1 ABOUT HERE&gt;

14

15 *1. Effects of time on recovery of lower limb muscle synergies and strength*

16 Figure 2A depicts individual and mean time-dependent change in FM-LE, MI-LE and  
17 MI-ankle. TIME was a significant factor ( $P<.001$ ) affecting recovery of FM-LE ( $\beta=3.84$ ,  
18  $95\%CI[2.58;5.11]$ ,  $P<.001$ ), MI-LE ( $\beta=12.37$ ,  $95\%CI[7.77;16.97]$ ,  $P<.001$ ) and MI-ankle  
19 ( $\beta=4.99$ ,  $95\%CI[2.92;7.05]$ ,  $P<.001$ ) from week 3 to 12. As further shown in Table 2,  
20 significant time-dependent change was found between weeks 3 and 5 for FM-LE ( $\beta=1.66$ ,  
21  $95\%CI[0.50;2.82]$ ,  $P=.002$ ), MI-LE ( $\beta=5.63$ ,  $95\%CI[1.43;9.84]$ ,  $P=.004$ ) and MI-ankle  
22 ( $\beta=2.83$ ,  $95\%CI[0.92;4.71]$ ,  $P<.001$ ). A significant increase was also seen for FM-LE between  
23 weeks 5 and 8 ( $\beta=1.49$ ,  $95\%CI[0.36;2.61]$ ,  $P=.004$ ), whereas a non-significant change was

1 found in MI-LE and MI-ankle scores ( $P>.05$ , Table 2). TIME was not a significant factor  
 2 from week 8 onwards.

3

4 <INSERT FIGURES 2A-C ABOUT HERE>

5

## 6 *2. Effects of time on recovery of steady-state balance during quiet stance*

7 Figures 2B-C show individual and mean time-dependent change in postural stability  
 8 and symmetry metrics, respectively. As shown in Table 2, TIME was a significant factor for  
 9 improvements from week 3 to 12 in COP<sub>Area</sub> ( $\beta=-175.0$ , 95%CI[-263.0;-87.0], $P<.001$ ),  
 10 COP<sub>Vel-ML</sub> ( $\beta=-4.71$ , 95%CI[-6.73;-2.69], $P<.001$ ) and COP<sub>Vel-AP</sub> ( $\beta=-3.14$ , 95%CI[-5.09;-  
 11 1.18], $P<.001$ ), after correction for INSTRUMENT as the only significant covariate for  
 12 change in COP<sub>Area</sub> ( $\beta=134.3$ , 95%CI[77.4;191.3], $P<.001$ ), COP<sub>Vel-ML</sub> ( $\beta=4.86$ ,  
 13 95%CI[2.90;6.83], $P<.001$ ) and COP<sub>Vel-AP</sub> ( $\beta=6.28$ , 95%CI[4.40;8.16], $P<.001$ ). Further sub-  
 14 analyses yielded significant reductions in COP<sub>Area</sub> between weeks 5 and 8 ( $\beta=-79.8$ , 95%CI[-  
 15 158.4;-1.2], $P=.045$ ) and in COP<sub>Vel-ML</sub> between weeks 3 and 5 ( $\beta=-1.90$ , 95%CI[-3.75;-  
 16 0.06], $P=.041$ ).

17 No significant time-dependent change was found for DCA and WBA. Comparison  
 18 with mean symmetry values in healthy subjects (DCA: 16.3%, SD=31.8; WBA: -1.1%,  
 19 SD=3.5) showed significant differences in WBA at week 3 (difference=7.7%, standard error  
 20 [SE]=3.0, $P=.001$ ), week 5 (difference=7.2%, SE=2.9, $P=.005$ ), week 8 (difference=7.5%,  
 21 SE=2.9, $P=.009$ ) and week 12 (difference=8.3%, SE=3.0, $P=.008$ ). Differences in DCA were  
 22 statistically significant at week 8 (difference=42.5%, SE=20.8, $P=.029$ ) and week 12

1 (difference=51.2%, SE=21.2,  $P=.012$ ). Figures 3A-B depict sway profiles measured at each  
2 time-point in a single subject.

3

4 <INSERT TABLE 2 ABOUT HERE>

5

6 <INSERT FIGURES 3A-B ABOUT HERE>

7

### 8 *3. Between-subject associations of lower limb impairment severity with steady-state balance*

9 Table 3 shows the *between*-subjects analyses applied cross-sectionally at weeks 3, 5, 8 and 12  
10 for either FM-LE, MI-LE or MI-ankle with  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ , DCA or WBA.  
11 Scatterplots of these associations with their linear regression lines are provided in the  
12 supplement (Supplementary figure 3, appendix C). The main effects of FM-LE, MI-LE or  
13 MI-ankle were significant for  $COP_{Area}$ ,  $COP_{Vel-ML}$ , and  $COP_{Vel-AP}$ , as well as for WBA  
14 ( $P<.001$ ). Additional significant covariates were INSTRUMENT ( $P<.001$ ) for the  
15 associations with  $COP_{Area}$ ,  $COP_{Vel-ML}$  and  $COP_{Vel-AP}$  as the dependent variables; TIME  
16 ( $P<.05$ ) for  $COP_{Area}$  and  $COP_{Vel-ML}$ ; and AFFECTED SIDE ( $P<.05$ ) for  $COP_{Area}$  (Table 3).  
17 *Between*-subject analyses with DCA yielded non-significant results.

18 Sub-analyses concerning FM-LE, MI-LE and MI-ankle scores yielded significant  
19 regression coefficients up until week 8 for  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$  and WBA ( $P<.01$ ,  
20 see Table 3 for more detail). At week 12, FM-LE remained a significant predictor of  $COP_{Vel-}$   
21  $ML$  ( $\beta=-0.49$ , 95%CI[-0.77;-0.22],  $P<.001$ ) and WBA ( $\beta=-0.64$ , 95%CI:-1.09;-0.21,  $P=.005$ ).



1 Additionally, a single significant coefficient was identified for MI-LE scores at week 12  
2 concerning WBA ( $\beta=-0.20$ , 95%CI[-0.34;-0.06], $P=.008$ ).

3

4 &lt;INSERT TABLE 3 ABOUT HERE&gt;

5

6 *4. Within-subject associations of lower limb motor recovery with change in steady-state*  
7 *balance*

8 Regression coefficients between  $\Delta$ FM-LE,  $\Delta$ MI-LE or  $\Delta$ MI-ankle on the one hand,  
9 and  $\Delta$ COP<sub>Area</sub>,  $\Delta$ COP<sub>Vel-ML</sub>,  $\Delta$ COP<sub>Vel-AP</sub>,  $\Delta$ DCA or  $\Delta$ WBA on the other were estimated for  
10 weeks 3–5, weeks 5–8 and weeks 8–12, using 36, 38 and 35 individual change scores,  
11 respectively. Scatterplots with their linear regression lines are provided in the supplement  
12 (Supplementary figure 4, appendix C). As shown in Table 4, the main effects of  $\Delta$ FM-LE,  
13  $\Delta$ MI-LE and  $\Delta$ MI-ankle were not significant for any dependent variable. Sub-analyses across  
14 the three epochs yielded a single significant regression coefficient for  $\Delta$ MI-LE with  $\Delta$ COP<sub>Vel-</sub>  
15 <sub>ML</sub> between weeks 8 and 12 ( $\beta=-0.12$ , 95%CI[-0.21;-0.04], $P=.007$ ).

16

17 &lt;INSERT TABLE 4 ABOUT HERE&gt;

18

19 *Discussion*

20 The present prospective cohort study involving 48 subjects investigated the time  
21 course of steady-state balance during quiet stance in relation to lower limb motor recovery

1 within the first 3 months poststroke. Controlling a high-positioned COM above a small base  
2 of support while standing is an easily standardized, yet skilled motor task requiring  
3 continuous postural corrections by the lower limbs. Unlike other prospective recovery studies  
4 in this field,<sup>11,14,17-19</sup> we were interested in how clinically assessed impairments in muscle  
5 synergies (i.e., FM-LE) and strength (i.e., MI-LE and MI-ankle) of the most affected leg are  
6 associated with postural stability (i.e.,  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ ) and asymmetric limb  
7 contributions to balance (i.e., DCA, WBA) during quiet two-legged stance. We therefore  
8 performed serial measurements in the same subjects and at fixed times poststroke.<sup>25,26</sup> Our  
9 main findings are summarized below.

- 10     ▪ A restricted time window of recovery concerning motor impairments and postural  
11       stability that occurs within the first 8 weeks poststroke. (Table 2)
- 12     ▪ Stroke subjects differ significantly from healthy controls with respect to inter-limb  
13       asymmetry in DCA and WBA.
- 14     ▪ Lack of recovery from asymmetries in DCA and WBA in the first 3 months  
15       poststroke, despite significant motor improvements in the most affected leg. (Table 2)
- 16     ▪ Significant *between*-subject associations between motor impairment severity and  
17       postural instability (i.e.,  $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ ) as well as a preferred  
18       asymmetric stance (i.e., WBA) within the first 3 months poststroke. (Table 3)
- 19     ▪ Lack of significant *between*-subject associations of motor impairment severity with  
20       DCA. (Table 3)
- 21     ▪ An overall lack of significant *within*-subject associations between improved muscle  
22       synergies and strength of the lower limb and change in postural stability and  
23       symmetry. (Table 4)

1 In agreement with our first hypothesis, the contribution of the progress of time as a  
2 reflection of spontaneous neurobiological recovery<sup>7</sup> was most pronounced for FM-LE, MI-  
3 LE and MI-ankle between weeks 3 and 5 poststroke. Approximately half of the total observed  
4 change occurred within this relatively short epoch (FM-LE: 43.2%, MI-LE: 45.5%, MI-ankle:  
5 56.7%; Table 2). Recovery rapidly leveled off thereafter, which is in agreement with previous  
6 studies.<sup>5-7</sup> In the literature, this restricted time window has also been described for the paretic  
7 upper limb<sup>5,10</sup> as well as for other neurological impairments including visuospatial  
8 inattention<sup>36</sup> and aphasia,<sup>37</sup> suggesting spontaneous neurological restitution within the first 5  
9 to 8 weeks poststroke.

10 Confirming our second hypothesis, the present study shows that progress of time is also  
11 an independent factor contributing to improved postural stability. Significant reductions in  
12  $COP_{Vel-ML}$  and  $COP_{Area}$  were most prominent within the first 8 weeks poststroke, responsible  
13 for about 75% of the total observed change (Table 2). Although  $COP_{Vel-AP}$  was not  
14 statistically significant within a specific epoch, it displayed a similar pattern of change in the  
15 first 12 weeks poststroke (Figure 2B). As such, steady-state balance became increasingly  
16 efficient, as reflected by a general COP sway reduction, in approximately the same time  
17 window as that seen for lower limb motor recovery.

18 A shared period of significant recovery has also been found in kinematic studies  
19 investigating the quality of upper limb motor performance relative to the Fugl-Meyer arm  
20 motor score.<sup>21,22</sup> In contrast, the present study showed that DCA and WBA were, on average,  
21 invariant for change over time (Figure 2C). The persistent asymmetry of approximately 45 to  
22 60% greater contribution of the less affected limb in terms of DCA approaches values  
23 reported in chronic patients.<sup>16</sup> Moreover, an unchanged asymmetric weight-bearing (about  
24 40% of body-weight on the most affected leg) despite significant COP sway reductions over

1 time, agrees with other longitudinal studies starting their measurements within the first 3  
2 months poststroke.<sup>14,18,19,38</sup> Obviously, subjects preferred to keep and control their balance  
3 predominantly with their less affected side to achieve posture stabilization while standing.  
4 Figures 3A-B illustrate persistent asymmetries in a typically behaving subject.

5 In agreement with our third hypothesis, relatively strong *between*-subject associations  
6 were found, such that a preferred asymmetric stance appears strongly dependent on the lower  
7 limb impairment severity. It was previously shown in healthy subjects that a gradually loaded  
8 leg is increasingly involved in balance control.<sup>15,39,40</sup> Thus, persistent loading of the less  
9 affected leg may indicate an attempt to actually increase the contribution of this leg's  
10 stabilizing ankle torques while standing. Our subsequent finding of a significant time-  
11 dependent association of impairment severity with postural instability up until week 8  
12 poststroke (Table 3), furthers point towards an optimization of this compensatory strategy  
13 after independent stance is regained. Interestingly, impairment severity was not significantly  
14 associated with the DCA when comparing *between* subjects. This dissociation was already  
15 shown in the chronic phase poststroke<sup>16</sup> and may involve significant reliance on  
16 compensatory stabilization with the less affected leg even in mildly affected subjects  
17 (Supplementary figure 3, appendix C).

18 As shown in Table 4, a dissociation between impairment scales and DCA was also found  
19 within subjects over time. A mismatch between motor improvements of the paretic leg on the  
20 one hand, and persistent inter-limb asymmetries on the other is a novel finding, as earlier  
21 longitudinal studies<sup>14,18,19,38</sup> lacked measurements of change within the window of  
22 spontaneous neurobiological recovery. This finding may further explain our subsequent  
23 finding that FM-LE, MI-LE and MI-ankle recovery neither explained *within*-subject postural  
24 stability improvements (fourth hypothesis), despite a shared recovery time window at the

1 group level. Seemingly, recovery of the most affected leg did not significantly contribute to  
2 an improved steady-state balance from 3 weeks poststroke onwards, complementing our  
3 finding of persistent asymmetries favoring the less affected side. Our results corroborate  
4 findings from electromyography (EMG) studies by Garland and colleagues.<sup>19,38,41</sup> showing  
5 that balance reactions with the most affected leg in anticipation of rapid arm movements  
6 hardly normalize in the first 3 months poststroke,<sup>19,38,41</sup> even after a mild stroke.<sup>19</sup> Instead,  
7 significant anticipatory change was consistently observed on the less affected side.<sup>19,38,41</sup> The  
8 same studies<sup>19,38</sup> found an asymmetric control during quiet stance, similar to the present  
9 findings, suggesting that this compensatory postural strategy generalizes across tasks.

10 It should be noted, however, that the present recovery study does not give an answer to  
11 *why* patients preferred compensatory strategies despite significant motor improvements at the  
12 most affected side. Obviously, steady-state balance while standing is a multifactorial skill.  
13 Besides motor impairments, postural deficits have also been linked to stroke-related  
14 somatosensory<sup>42</sup> and vestibular<sup>43</sup> impairments, a resultant greater visual dependency<sup>44</sup> and  
15 misperception of verticality,<sup>45</sup> as well as reduced balance confidence to prevent falls.<sup>46</sup> To  
16 disentangle the relative importance of other impairments, cognition and mood, we should  
17 have measured these factors as well in a longitudinal way. Alternatively, one may assume  
18 that observed *intra*-limb improvements in FM-LE and MI-LE (Table 2) were too small and  
19 incomplete for introducing restitution of *inter*-limb symmetry. Instead, relying on their less  
20 affected side may have been perceived as more efficient by patients. Similar to our findings,  
21 Roelofs and colleagues also showed that even those with (near) complete FM-LE recovery  
22 may show a significant dynamic control asymmetry, suggesting that DCA is a more  
23 responsive marker of remaining motor deficits than traditional clinical scales.

1 In summary, our findings suggest that stroke subjects recover their quiet standing balance  
2 mainly in the first 8 weeks poststroke by optimizing, rather than “normalizing” compensatory  
3 strategies involving the less affected limb. The independency of steady-state balance  
4 improvements and motor recovery of the most affected limb further suggests that only  
5 instrumented performance measures reflecting inter-limb asymmetry, such as DCA, are  
6 suitable to address the quality of movement in order to improve our understanding of balance  
7 recovery mechanisms poststroke.

### 8 *Limitations*

9 Several limitations of the present study should be considered. First, our sample size is  
10 limited and larger epidemiological studies incorporating serial instrumented performance  
11 measures are needed to generalize our findings. Second, since we started our assessments at 3  
12 weeks poststroke, we may have missed some early changes in motor performance. Despite  
13 this, the study was successful in collecting data serially *within* subjects by applying a postural  
14 task with relatively low functional demands. A third limitation is that our results are restricted  
15 to quiet two-legged standing, which obviously allows compensation strategies. This may  
16 have prevent us from measuring the extend of “true” neurological recovery in the most  
17 affected leg for controlling balance. Third, as emphasized, our analyses are restricted to  
18 motor impairments in terms of FM-LE and MI-LE. Consequently, we did not investigate  
19 recovery in other potentially relevant impairments, such as muscle tone,<sup>47</sup> sensation<sup>44</sup> or  
20 visuospatial perception.<sup>48</sup> Additionally, the FM-LE and MI-LE assess distal motor control  
21 through movement range and strength in ankle dorsiflexion, whereas quiet standing balance  
22 is mainly controlled by plantarflexor activity that resists forwards toppling due to gravity.<sup>49</sup>  
23 This “narrow” emphasis of clinical scales on foot elevation alone, may have prevented us  
24 from finding significant associations. Fourth, we used two measuring instruments to allow  
25 data acquisition in various settings. Since we used the same instrument *within* subjects and

1 added the covariate INSTRUMENT systematically to our final analyses, we believe that the  
2 use of two different platform types did not affect our conclusions. Nevertheless, more  
3 research is needed for the development and validation of portable instruments to enable even  
4 larger longitudinal studies with longer follow-ups beyond hospitalization. Lastly, we did not  
5 monitor treatment content and are unable to decide whether our findings were influenced by,  
6 for example, therapy dose or focus.

### 7 *Future directions*

8 An unaddressed key question arising from the current study is: “*Why* do clinical  
9 improvements in muscle synergies and strength of the most affected leg hardly generalize to  
10 an improved quality of steady-state balance?” Addressing this question requires future studies  
11 with serial measurements of sensory and cognitive perception deficits as well as patients’  
12 mood (e.g., by using standardized questionnaires of balance confidence<sup>50</sup>). In addition, future  
13 studies with serial EMG measurements are needed to show if the actual changes in intra-limb  
14 coordination of the paretic leg make a beneficial contribution to posture stabilization or,  
15 alternatively, should be seen as “noise” that needs to be suppressed while standing.  
16 Unravelling a potential mismatch between the preferred postural strategy and subjects’  
17 capacity to normalize their quality of movement by an increased balance contribution from  
18 the most affected leg is important to address another unsolved question: “Are therapies  
19 aiming to restore symmetry, such as the Bobath approach<sup>51</sup> or visual feedback training,<sup>52</sup>  
20 counterproductive if we aim at posture stabilization and avoiding falls?” Building an  
21 evidence base for effective rehabilitation strategies is important, as falls remain a major  
22 health care problem at all stages of the disease.<sup>53</sup>

23 To drive the field forward, it is important to reach agreement on a shared language  
24 and the metrics applied to assess qualitative aspects of movement. The SRRR mobility task

1 force – a group of experts in the field of balance and gait research – currently gathers  
2 intending to build consensus on how future trials should address recovery. This will include  
3 standardized recommendations on taxonomy, timing and choice of assessments as well as the  
4 metrics used to measure the quality of quiet standing balance and mobility performance  
5 within the first 6 months poststroke.

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13 **Data availability:** The datasets supporting the results of this article are available from the  
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## 1 *Tables*

<b>Demographics and stroke information (N=48)</b>	
Study subjects	48
Age, years*	58.9 ± 16.1
Sex, female/male	19/29
Body weight, kg*	74.3 ± 13.2
Affected body side, left/right	25/23
Stroke type, ischemic/hemorrhagic	36/12
Measuring instrument, force plates/pressure plate	19/29
Time poststroke, days*	24.9 ± 1.8
<b>Clinical characteristics (N=44)</b>	
FM-LE score (0-34)*	21.9 ± 7.4
MI-LE score (0-99)*	61.2 ± 23.7
MI-ankle score (0-33)*	18.6 ± 8.8
BBS-s score (0-4)*	2.8 ± 1.5
<b>Posturographic characteristics (N=37)</b>	
COP <sub>Area</sub> (mm <sup>2</sup> )*	302.7 ± 359.8
COP <sub>Vel-ML</sub> (mm/s)*	10.0 ± 9.5
COP <sub>Vel-AP</sub> (mm/s)*	11.7 ± 9.3
DCA (%)*	44.1 ± 65.8
WBA (%)*	6.6 ± 9.9

2

### 3 **Title:**

4 Table 1: Subject characteristics at baseline (i.e., 3 weeks poststroke)

### 5 **Legend:**

6 Abbreviations: FM-LE, Fugl-Meyer lower extremity motor score; MI-LE, Motricity Index  
 7 lower extremity score; BBS-s, standing unsupported item of the Berg Balance Scale; COP,  
 8 center-of-pressure; COP<sub>Area</sub>, area of the net COP; COP<sub>Vel-ML</sub>, rms velocity of the net COP in  
 9 the frontal plane; COP<sub>Vel-AP</sub>, rms velocity of the total COP in the sagittal plane; DCA,  
 10 dynamic control asymmetry; WBA, weight-bearing asymmetry.

11 Values are means ± SD if marked (\*), otherwise counts are shown. Demographics and stroke  
 12 information was collected from all included subjects (N=48) at enrollment. Clinical

1 characteristics were obtained in 44 subjects that could be tested at week 3, of which 37 could  
2 stand independently to perform the standardized balance task. Their posturographic baseline  
3 characteristics are also shown (N=37).

4

		Week 3 - 12	Week 3 - 5	Week 5 - 8	Week 8 - 12
$\Delta$ FM-LE (0-34)	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	<b>3.85 (0.46)</b> <b>2.58; 5.12</b> <b>&lt;.001</b> <b>100%</b>	<b>1.66 (0.44)</b> <b>0.50; 2.82</b> <b>.002</b> <b>43.2%</b>	<b>1.49 (0.43)</b> <b>0.36; 2.61</b> <b>.004</b> <b>38.8%</b>	0.70 (0.45) -0.47; 1.86 .408 18.2%
$\Delta$ MI-LE (0-99)	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	<b>12.38 (1.76)</b> <b>7.78; 16.99</b> <b>&lt;.001</b> <b>100%</b>	<b>5.65 (1.61)</b> <b>1.44; 9.85</b> <b>.004</b> <b>45.5%</b>	3.77 (1.57) -0.32; 7.86 .083 30.5%	2.97 (1.63) -1.27; 7.22 .266 24.0%
$\Delta$ MI-ankle (0-33)	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	<b>4.99 (0.79)</b> <b>2.92; 7.05</b> <b>&lt;.001</b> <b>100%</b>	<b>2.83 (0.72)</b> <b>0.92; 4.71</b> <b>&lt;.001</b> <b>56.7%</b>	1.07 (0.70) -0.77; 2.9 .428 21.4%	1.09 (0.73) -0.81; 3.00 .445 21.9%
$\Delta$ COP <sub>Area</sub> * (mm <sup>2</sup> )	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	<b>-175.0 (33.7)</b> <b>-263.0; -87.0</b> <b>&lt;.001</b> <b>100%</b>	-64.6 (31.1) -145.6; 16.4 .166 36.9%	<b>-79.8 (30.1)</b> <b>-158.4; -1.2</b> <b>.045</b> <b>45.4%</b>	-30.6 (31.3) -112.3; 51.2 .763 17.7%
$\Delta$ COP <sub>Vel-ML</sub> * (mm/s)	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	<b>-4.71 (0.77)</b> <b>-6.73; -2.69</b> <b>&lt;.001</b> <b>100%</b>	<b>-1.90 (0.71)</b> <b>-3.75; -0.06</b> <b>.041</b> <b>40.4%</b>	-1.47 (0.71) -3.26; 0.33 .149 31.1%	-1.34 (0.71) -3.20; 0.52 .244 28.5%
$\Delta$ COP <sub>Vel-AP</sub> * (mm/s)	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	<b>-3.14 (0.75)</b> <b>-5.09; -1.18</b> <b>&lt;.001</b> <b>100%</b>	-1.12 (0.69) -2.91; 0.68 .370 35.4%	-1.31 (0.67) -3.05; 0.43 .210 42%	-0.71 (0.69) -2.52; 1.10 .730 22.9%
$\Delta$ DCA* (%)	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	7.07 (6.23) -9.18; 23.33 .623 n/a	5.98 (5.70) -8.90; 20.86 .721 n/a	1.57 (5.54) -12.88; 16.03 .992 n/a	-0.48 (5.76) -15.50; 14.54 .999 n/a
$\Delta$ WBA* (%)	$\beta$ (SE) 95% CI <i>P</i> -value % of total change	-2.51 (1.13) -5.45; 0.43 .122 n/a	-1.98 (1.03) -4.67; 0.72 .227 n/a	-0.22 (1.00) -2.84; 2.39 .996 n/a	-0.31 (1.04) -3.03; 2.41 .991 n/a

1

2 **Title:**

3 Table 2: Effects of time on recovery of muscle synergies and strength, and metrics reflecting  
4 steady-state balance during quiet stance within the first 12 weeks poststroke.

5 **Legend:**

6 Abbreviations:  $\Delta$ , change scores; FM-LE, Fugl-Meyer lower extremity motor score; MI-LE,  
7 Motricity Index lower extremity score; MI-ankle, Motricity Index ankle item; COP, center-  
8 of-pressure; COP<sub>Area</sub>, area of the net COP; COP<sub>Vel-ML</sub>, rms velocity of the net COP in the  
9 frontal plane; COP<sub>Vel-AP</sub>, rms velocity of the net COP in the sagittal plane; DCA, dynamic

1 control asymmetry; WBA, weight-bearing asymmetry; n/a, not applicable as the effect of  
2 TIME was not significant.

3 Values shown are estimated regression coefficients ( $\beta$ ), standard error (SE), 95% confidence  
4 interval (95% CI), probability estimates (*P*-value) and the percentage of total observed  
5 change (% of total change).  $\beta$ -values show time-dependent change corrected for covariates  
6 AGE, SEX and SIDE in metrics reflecting lower limb muscle synergies (FM-LE), strength  
7 (MI-LE), postural stability ( $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ ) and inter-limb symmetry (DCA,  
8 WBA). If marked with \*, values include an additional correction for INSTRUMENT. A  
9 statistically significant (i.e.,  $P < .05$ ) coefficient is highlighted in **bold**.

		FM-LE (0-34)					MI-LE (0-99)					MI-ankle (0-33)				
		Main	W3	W5	W8	W12	Main	W3	W5	W8	W12	Main	W3	W5	W8	W12
COP <sub>Area</sub> (mm <sup>2</sup> )	$\beta$	<b>-16.13<sup>ab</sup></b>	<b>-23.30<sup>a</sup></b>	<b>-4.99<sup>a</sup></b>	<b>-14.52<sup>a</sup></b>	-7.32 <sup>a</sup>	<b>-4.99<sup>abc</sup></b>	<b>-9.00<sup>a</sup></b>	<b>-5.93<sup>a</sup></b>	<b>-5.04<sup>a</sup></b>	-1.74 <sup>a</sup>	<b>-11.04<sup>ab</sup></b>	<b>-20.98<sup>a</sup></b>	<b>-16.59<sup>a</sup></b>	<b>-12.78<sup>ac</sup></b>	-3.05 <sup>a</sup>
	(SE)	(3.25)	(8.15)	(0.97)	(2.88)	(3.29)	(0.97)	(2.26)	(1.59)	(0.85)	(1.08)	(2.46)	(6.68)	(3.80)	(2.14)	(2.78)
	95%CI	<b>-22.60; -9.66</b>	<b>-39.91; -6.69</b>	<b>-6.92; -3.06</b>	<b>-20.36; -8.69</b>	-14.03; -0.61	<b>-6.92; -3.06</b>	<b>-13.62; -4.38</b>	<b>-9.17; -2.71</b>	<b>-6.76; -3.33</b>	-3.95; 0.47	<b>-15.93; -6.14</b>	<b>-34.57; -7.35</b>	<b>-24.30; -8.90</b>	<b>-17.11; -8.45</b>	-8.72; 2.63
	<i>P</i>	<b>&lt;.001</b>	<b>.008</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.034	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.119	<b>&lt;.001</b>	<b>.004</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.282
COP <sub>Vel-ML</sub> (mm/s)	$\beta$	<b>-0.60<sup>a</sup></b>	<b>-0.97<sup>a</sup></b>	<b>-0.14<sup>a</sup></b>	<b>-0.55<sup>a</sup></b>	<b>-0.49<sup>a</sup></b>	<b>-0.14<sup>ab</sup></b>	<b>-0.27<sup>a</sup></b>	<b>-0.19<sup>a</sup></b>	<b>-0.18<sup>a</sup></b>	-0.10 <sup>a</sup> (0.05)	<b>-0.24<sup>ab</sup></b>	<b>-0.69<sup>ac</sup></b>	<b>-0.48<sup>a</sup></b>	<b>-0.45<sup>a</sup></b>	-0.17 <sup>a</sup>
	(SE)	(0.09)	(0.14)	(0.03)	(0.13)	(0.13)	(0.03)	(0.05)	(0.05)	(0.04)		(0.07)	(0.14)	(0.12)	(0.10)	(0.12)
	95%CI	<b>-0.78; -0.42</b>	<b>-1.25; -0.68</b>	<b>-0.20; -0.08</b>	<b>-0.79; -0.26</b>	<b>-0.77; -0.22</b>	<b>-0.20; -0.08</b>	<b>-0.37; -0.18</b>	<b>-0.29; -0.09</b>	<b>-0.26; -0.10</b>	-0.20; -0.01	<b>-0.38; -0.09</b>	<b>-0.98; -0.41</b>	<b>-0.74; -0.22</b>	<b>-0.65; -0.24</b>	-0.43; 0.08
	<i>P</i>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.047	<b>.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.170
COP <sub>Vel-AP</sub> (mm/s)	$\beta$	<b>-0.51<sup>a</sup></b>	<b>-0.69<sup>a</sup></b>	<b>-0.12<sup>a</sup></b>	<b>-0.49<sup>a</sup></b>	<b>-0.40<sup>a</sup></b>	<b>-0.12<sup>a</sup></b>	<b>-0.18<sup>a</sup></b>	<b>-0.18<sup>a</sup></b>	<b>-0.16<sup>a</sup></b>	-0.06 <sup>a</sup> (0.06)	<b>-0.29<sup>a</sup></b>	<b>-0.52<sup>a</sup></b>	<b>-0.50<sup>a</sup></b>	<b>-0.41<sup>a</sup></b>	-0.13 <sup>a</sup>
	(SE)	(0.09)	(0.13)	(0.03)	(0.12)	(0.18)	(0.03)	(0.04)	(0.05)	(0.04)		(0.07)	(0.11)	(0.12)	(0.10)	(0.16)
	95%CI	<b>-0.69; -0.33</b>	<b>-0.94; -0.43</b>	<b>-0.18; -0.07</b>	<b>-0.74; -0.24</b>	<b>-0.77; -0.03</b>	<b>-0.18; -0.07</b>	<b>-0.27; -0.09</b>	<b>-0.28; -0.08</b>	<b>-0.23; -0.08</b>	-0.19; 0.06	<b>-0.43; -0.16</b>	<b>-0.75; -0.29</b>	<b>-0.74; -0.25</b>	<b>-0.60; -0.21</b>	-0.44; 0.19
	<i>P</i>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.035	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.301	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.422
DCA (%)	$\beta$	-0.06	<b>-3.27<sup>d</sup></b>	-0.31	-2.28	-2.30	-0.31	<b>-1.08<sup>d</sup></b>	-0.65	-1.00	-0.76	-1.01	<b>-3.05<sup>d</sup></b>	-1.30	<b>-2.88</b>	-2.68
	(SE)	(0.89)	(1.73)	(0.26)	(1.40)	(1.43)	(0.26)	(0.52)	(0.45)	(0.43)	(0.45)	(0.62)	(1.43)	(1.41)	<b>(1.06)</b>	(1.09)
	95%CI	-1.83; 1.72	<b>-6.79; 0.26</b>	-0.83; 0.20	-5.11; 0.54	-5.22; 0.63	-0.83; 0.20	<b>-2.14; -0.01</b>	-1.56; 0.27	-1.86; -0.13	-1.68; 0.16	-2.23; 0.21	-5.96; -0.13	-3.61; 1.02	<b>-5.02; -0.74</b>	-4.89; -0.46
	<i>P</i>	.949	.068	.234	.110	.119	.234	.048	.161	.025	.103	.105	.041	.264	<b>.009</b>	.020
WBA (%)	$\beta$	<b>-0.75</b>	<b>-1.19</b>	<b>-0.23</b>	<b>-0.62</b>	<b>-0.64</b>	<b>-0.23</b>	<b>-0.36</b>	<b>-0.26</b>	<b>-0.17</b>	<b>-0.20</b>	<b>-0.37</b>	<b>-0.90</b>	<b>-0.63</b>	-0.34	-0.32
	(SE)	(0.12)	(0.20)	(0.04)	(0.15)	(0.22)	(0.04)	(0.06)	(0.05)	(0.05)	(0.07)	(0.10)	(0.19)	(0.13)	(0.14)	(0.19)
	95%CI	<b>-0.98; -0.51</b>	<b>-1.60; -0.78</b>	<b>-0.30; 0.15</b>	<b>-0.93; -0.31</b>	<b>-1.09; -0.21</b>	<b>-0.30; -0.15</b>	<b>-0.49; -0.24</b>	<b>-0.37; -0.16</b>	<b>-0.27; -0.06</b>	<b>-0.34; -0.06</b>	<b>-0.56; -0.17</b>	<b>-1.28; -0.51</b>	<b>-0.90; -0.36</b>	-0.61; -0.06	-0.70; -0.07
	<i>P</i>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>.005</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>.002</b>	<b>.008</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	.018	.103

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2 **Title:**

3 Table 3: *Between*-subject associations of lower limb motor impairment severity with steady-state balance during quiet stance at week 3, 5, 8 and  
 4 12 poststroke.

5 **Legend:**



1 Abbreviations: FM-LE, Fugl-Meyer lower extremity motor score; MI-LE, Motricity Index lower extremity score; MI-ankle, Motricity Index  
2 ankle item; COP, center-of-pressure;  $COP_{Area}$ , area of the net COP;  $COP_{Vel-ML}$ , rms velocity of the net COP in the frontal plane;  $COP_{Vel-AP}$ , rms  
3 velocity of the net COP in the sagittal plane; DCA, dynamic control asymmetry; WBA, weight-bearing asymmetry; W, week poststroke.

4 Values shown are estimated regression coefficients ( $\beta$ ), standard error (SE), 95% confidence interval (95% CI), and probability estimates ( $P$ ).  $\beta$ -  
5 values predict change in postural stability ( $COP_{Area}$ ,  $COP_{Vel-ML}$ ,  $COP_{Vel-AP}$ ) and symmetry (DCA, WBA) from a one-point difference on the FM-  
6 LE, MI-LE or MI-ankle. Models were corrected for significant covariates with <sup>a</sup>, INSTRUMENT; <sup>b</sup>, TIME; <sup>c</sup>, SIDE; and <sup>d</sup>, SEX. A Bonferroni  
7 correction was applied for declaring significance (i.e.,  $P < .05/5$ ) as indicated in **bold**.

		$\Delta$ FM-LE (0-34)				$\Delta$ MI-LE (0-99)				$\Delta$ MI-ankle (0-33)			
		Main	W3-5	W5-8	W8-12	Main	W3-5	W5-8	W8-12	Main	W3-5	W5-8	W8-12
$\Delta$ COP <sub>Area</sub> (mm <sup>2</sup> )	$\beta$ (SE)	-1.85 (5.59)	-12.52 (11.62)	4.34 (12.38)	-9.73 (8.27)	-0.33 (1.28)	-7.83 (3.47)	3.01 (2.62)	-4.47 (1.80)	-2.24 (2.10)	-8.54 (3.49)	-3.71 (6.57)	-5.58 (4.34)
	95%CI	-12.97; 9.26	-36.29; 11.24	-20.67; 29.34	-26.65; 7.18	-2.88; 2.22	-14.92; -0.73	-2.33; 8.36	-8.14; -0.78	-6.44; 1.95	-15.69; -1.38	-17.10; 9.68	-14.47; 3.30
	<i>P</i>	.741	.290	.726	.249	.799	.032	.259	.019	.289	.021	.577	.209
$\Delta$ COP <sub>Vel-ML</sub> (mm/s)	$\beta$ (SE)	-0.23 (0.13)	-0.55 (0.23)	-0.16 (0.25)	-0.04 (0.21)	<0.01 (0.03)	-0.09 <sup>a</sup> (0.08)	0.08 (0.05)	<b>-0.12 (0.04)</b>	-0.04 (0.05)	-0.11 (0.08)	0.12 (0.13)	-0.24 (0.10)
	95%CI	-0.49; 0.03	-1.02; -0.07	-0.68; 0.35	-0.46; 0.39	-0.06; 0.06	-0.25; 0.07	-0.03; 0.18	<b>-0.21; -0.04</b>	-0.14; 0.05	-0.27; 0.05	-0.16; 0.39	-0.45; -0.04
	<i>P</i>	.084	.026	.517	.864	.927	.281	.164	<b>.007</b>	.364	.165	.389	.020
$\Delta$ COP <sub>Vel-AP</sub> (mm/s)	$\beta$ (SE)	-0.11(0.16)	-0.37 (0.22)	0.12 (0.28)	-0.15 (0.33)	-0.01(0.04)	-0.02 (0.07)	0.04 (0.06)	-0.15 (0.07)	-0.04 (0.06)	-0.05 (0.07)	-0.10 (0.15)	-0.34 (0.16)
	95%CI	-0.42; 0.21	-0.82; 0.09	-0.45; 0.69	-0.82; 0.52	-0.08; 0.06	-0.17; 0.13	-0.09; 0.16	-0.29; -0.01	-0.16; 0.07	-0.19; 0.09	-0.41; 0.21	-0.67; -0.01
	<i>P</i>	.500	.109	.678	.659	.786	.780	.563	.049	.429	.487	.509	.047
$\Delta$ DCA (%)	$\beta$ (SE)	2.38 (1.37)	3.52 (2.32)	2.98 (2.04)	-1.30 (2.63)	-0.01 (0.34)	0.05 (0.77)	0.06 (0.46)	-0.57 (0.61)	0.05(0.51)	0.45 (0.66)	-0.30 (1.13)	-2.17 (1.33)
	95%CI	-0.34; 5.09	-1.24; 8.27	-1.17; 7.14	-6.68; 4.08	-0.70; 0.67	-1.52; 1.62	-0.87; 1.00	-1.81; 0.68	-0.95; 1.06	-0.89; 1.79	-2.60; 2.00	-4.90; 0.55
	<i>P</i>	.085	.141	.154	.626	.967	.946	.890	.359	.917	.498	.792	.114
$\Delta$ WBA (%)	$\beta$ (SE)	0.39 <sup>a</sup> (0.24)	0.55 (0.51)	0.46 (0.42)	-0.72 (0.40)	0.14 <sup>a</sup> (0.06)	-0.04 (0.17)	0.20 (0.09)	0.09 (0.10)	0.14 <sup>a</sup> (0.07)	0.04 (0.14)	0.19 (0.23)	0.07 (0.22)
	95%CI	-0.08; 0.86	-0.50; 1.59	-0.39; 1.31	-1.55; 0.10	0.02; 0.26	-0.38; 0.29	-0.02; 0.37	-0.11; 0.29	-0.01; 0.29	-0.25; 0.33	-0.27; 0.65	-0.38; 0.53
	<i>P</i>	.102	.292	.279	.082	.026	.794	.030	.345	.061	.775	.415	.741

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2 **Title:**

3 Table 4: *Within*-subject associations of lower limb motor recovery and change in steady-state balance during quiet stance within the first 12  
4 weeks poststroke.

5 **Legend:**

6 Abbreviations:  $\Delta$ , change scores; FM-LE, Fugl-Meyer lower extremity motor score; MI-LE, Motricity Index lower extremity score; MI-ankle,

7 Motricity Index ankle item; COP, center-of-pressure; COP<sub>Area</sub>, area of the net COP; COP<sub>Vel-ML</sub>, rms velocity of the net COP in the frontal plane;

- 1 COP<sub>Vel-AP</sub>, rms velocity of the net COP in the sagittal plane; DCA, dynamic control asymmetry; WBA, weight-bearing asymmetry; W, week  
2 poststroke.
- 3 Values shown are estimated regression coefficients ( $\beta$ ), standard error (SE), 95% confidence interval (95% CI), and probability estimates ( $P$ ).  $\beta$ -  
4 values predict  $\Delta\text{COP}_{\text{Area}}$ ,  $\Delta\text{COP}_{\text{Vel-ML}}$ ,  $\Delta\text{COP}_{\text{Vel-AP}}$ ,  $\Delta\text{WBA}$  and  $\Delta\text{DCA}$  from a one-point increase on the FM-LE, MI-LE or MI-ankle. Models  
5 were corrected for significant covariates with <sup>a</sup>, INSTRUMENT. A Bonferroni correction was applied for declaring significance (i.e.,  $P < .05/4$ )  
6 as indicated in **bold**.