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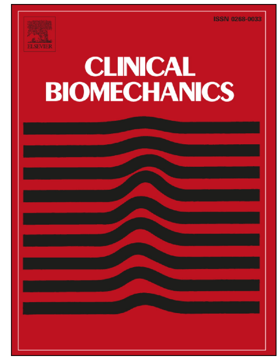

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A New Methodology based on Functional Principal Component Analysis to study Postural Stability Post-stroke.

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Abstract

Background: A major goal in stroke rehabilitation is the establishment of more effective physical therapy techniques to recover postural stability. Functional Principal Component Analysis provides greater insight into recovery trends. However, when missing values exist, obtaining functional data presents some difficulties. The purpose of this study was to reveal an alternative technique for obtaining the Functional Principal Components without requiring the conversion to functional data beforehand and to investigate this methodology to determine the effect of specific physical therapy techniques in balance recovery trends in elderly subjects with hemiplegia post-stroke.

Methods: A randomized controlled pilot trial was developed. Thirty inpatients post-stroke were included. Control and target groups were treated with the same conventional physical therapy protocol based on functional criteria, but specific techniques were added to the target group depending on the subjects' functional level. Postural stability during standing was quantified by posturography. The assessments were performed once a month from the moment the participants were able to stand up to six months post-stroke.

Findings: The target group showed a significant improvement in postural control recovery trend six months after stroke that was not present in the control group. Some of the assessed parameters revealed significant differences between treatment groups (P<0.05).

Interpretation: The proposed methodology allows Functional Principal Component Analysis to be performed when data is scarce. Moreover, it allowed the dynamics of recovery of two different treatment groups to be determined, showing that the techniques added in the target group increased postural stability compared to the base protocol.

Keywords: *Functional Principal Component Analysis, stroke, postural stability, posturography, Romberg*

Clinical trial registration number: NCT02250040

1. Introduction

Postural control and balance are essential prerequisites for the realization of any voluntary movement[1]. Therefore, postural control disabilities, caused by motor-sensory impairment after stroke, produce balance deficits that have an important impact on independence, social participation, and quality of life[1,2]. As more than 80% of subjects after first stroke have balance disability in the sub-acute phase[3], the establishment of more effective physical therapy (PT) techniques to recover postural stability is a major goal in stroke rehabilitation[4].

When studying the functional recovery process post-stroke, particular attention must be paid to the considerable inter-subject variability[5]. Concerning this, conventional statistical analysis has some limitations and Functional Data Analysis (FDA) provides greater insight into subtle differences[6]. Functional Principal Component Analysis (FPCA) is one of the most commonly employed tools from FDA in biomedical data analysis[7,8,9] and it is very suitable for the analysis of the recovery dynamics in subjects post-stroke[5].

FPCA allows the description of a time dependent function as a linear combination of a small set of curves called Functional Principal Components (FPCs)[10]. This procedure allows any function to be represented as a linear combination of a set of curves statistically extracted from the sample according to equation (1), where $\mathrm{\mu(t)}$ is the mean curve, $\xi_i(t)$ the Functional Principal Components (FPCs), $\epsilon(t)$ the error and c_i the scores of each FPC.

$$y(t)=\mathrm{\mu(t)} + \sum_{i=1}^{N} c_i \cdot \xi_i(t) + \epsilon(t) \qquad (1)$$

Nevertheless, when performing longitudinal studies involving subjects it is frequent to have missing values. In that sense, subjects lost to follow up, late recruitments and those with difficulties in attending some of the measurement sessions are some of the problems that researchers usually face. When missing values exist, obtaining functional data implies extrapolation. For this reason, data from these participants are commonly not taken into consideration to extract the FPCs. In order to avoid this problem, in this study, an alternative methodology extracting the FPCs directly from the sampled data is presented.

Therefore, the aim of this study was to present an alternative technique for obtaining the FPCs from the whole set of data without requiring the conversion to functional data beforehand and to explore the proposed methodology to identify the effect of specific PT techniques in balance recovery trends in elderly subjects with hemiplegia post-stroke.

2. Methods

2.1. Participants

All subjects who had suffered a stroke and been admitted to (*blinded*) were consecutively screened for eligibility from January 2013 to July 2014. Inclusion criteria were: (1) a single stroke episode with residual hemiplegia or hemiparesis; (2) 55 years or older; (3) candidate to begin a rehabilitation program; (4) capacity to walk before suffering the stroke; (5) ability to understand and follow simple verbal instructions; and (6) hemodynamically stable within the first week post-stroke. Exclusion criteria included pathologies or disorders hampering the development of the study (e.g., blindness, prosthetics, severe cognitive impairment, etc.). A convenience sample of 30 stroke survivors was recruited.

2.2. Study design

A prospective, randomized, controlled, double-blind trial was carried out. The study was conducted according to the Declaration of Helsinki for human experiments[11]. Approval was obtained from the Hospital's Ethical Committee. All participants were informed about all aspects of the trial. Written informed consent was signed by each subject.

A computer generated random-number table was used for allocation. The doctor who determined if a subject was eligible for inclusion in the trial was unaware as to which group the subject would be allocated when this decision was being made.

Assessors were unaware as to which group the subjects had been assigned. Moreover, participants were also unaware of the treatment group to which they belonged. All were treated by the same physiotherapist and the base protocol was the same in both treatment groups.

2.3. Interventions

Both groups of participants underwent a conventional PT protocol based on clinical and functional criteria. As recommended by the literature, this base protocol consisted of techniques from various neurological PT approaches[12]. Techniques were adapted depending on the subjects' functional level. Hospital of Sagunto (HS) Functional Classifications were used to determine the functional level of each participant [13,14,15]. Moreover, specific techniques aiming to strengthen sensitivity, movement dissociation and balance, were added to the target group also depending on their functional level. These techniques are described elsewhere in detail[5].

2.4. Outcome measures

Postural stability during standing was quantified by posturography, which was performed on the force plate Dinascan/IBV using the NedSVE®/IBV system (Valencia, Spain)[16]. Participants were asked to seek the position of greatest stability whilst standing barefoot with their arms relaxed by their side and feet positioned so that the heels were touching and the toes were diverging at an angle of 30º. Postural stability was measured under various static conditions with increasing difficulty (sensory analysis): Romberg with: 1) open eyes (ROE); 2) closed eyes (RCE); 3) open eyes on a foam mattress (RFO); and 4) closed eyes on a foam mattress (RFC). Moreover, the limits of stability (LoS) test was conducted. In the LoS test, subjects were asked to maintain their previous position, and without altering their base of support, the participants had to move a cursor which reflected the position of their center of gravity towards eight targets located in their theoretical LoS at intervals of 45º. The subjects were given eight seconds to move their center of gravity to each target and had to remain there as long as possible. The distance at which each of them appeared depended on the age and height of the subject.

The assessments were performed once a month from the moment participants were able to stand up to six months post-stroke. They were made by two physiotherapists who were trained to perform the measurements and to handle the system. Each physiotherapist assessed the subjects independently of their treatment group and the same assessor tested the same participant each time. Intrinsic Motivation Inventory (IMI) was used to discard differences in the results of the biomechanical tests due to participant motivation[17].

2.5. Statistical analysis

All analyses were performed using the SPSS v.22 (licensed from author´s institution) and the free software R[18].

Differences in categorical data were analyzed by the Fisher exact or Wald´s chi-square tests as appropriate. Depending on the type of distribution (assessed by the Shapiro-

Wilk test), either the Student's t-test or the Mann Whitney U test was used to compare the baseline characteristics of the target and control groups.

FPCA was employed to determine the effect of the proposed PT intervention on the parameters of posturography. Some values were missing due to the absence of some participants at the assessment sessions. Therefore, as for a non-negligible sample of subjects, the approach of Ramsay and Silverman (2006)[10] can compromise the analysis due to the need to extrapolate or remove subjects with missing values, an alternative technique for obtaining the FPCs was developed.

Consequently, when the data coming from all participants were recorded, the FPCs were extracted according to the following procedure:

1) All the functional data were described as cubic splines with vertices at days 5, 55 and 208 (five days after the beginning of PT in the ward was the minimum number of days that participants needed to achieve the complete ROE and the last assessment in the cohort was at 208 days)

2) The mean curve, $\mu(t)$ in (1), was extracted with the whole set of measurements by least-squares fitting to the spline basis.

3) Each FPC was obtained by Sequential Least Squares Programming (SLSQP) using the python implementation of the original library of Kraft (1985)[19].

4) The minimization function by SLSQP was the variance of the residuals in order to obtain the functions that maximized the explained variance.

5) The restrictions to obtain the curves were the same as those described by Ramsay and Silverman (2006)[10]:

    a) Amplitude constraint: The maximum value of each of the FPCs must be equal to one:

$$\int_a^b \xi_i(t)^2 \cdot dt = 1 \tag{2}$$

b) Orthogonality: Each FPC must be orthogonal to the other FPCs:

$$\int_a^b \left[\xi_i(t) \cdot \xi_j(t)\right] \cdot dt = 0, \nabla i \neq j \tag{3}$$

After the extraction of the FPCs, the scores corresponding to each FPC for each subject were obtained. As numerical variables, these scores were treated with traditional statistical analysis. Afterward, ANOVA or the Mann Whitney U test, as appropriate, was used to analyze the differences per group (target or control) in every score. When significant differences were obtained, the marginal means (in the ANOVA) or the means (in the Mann Whitney U test) of the scores per group were retained. Finally, to interpret the results, the Marginal Mean Curves were reconstructed in those scores that showed statistically significant differences.

Significance was set at $P<.05$. Effect size was measured with the product-moment correlation coefficient[20]. The inter-rater reliability was tested using the intra-class correlation coefficient (ICC). ICC(1.1) was calculated[21].

3. Results

During the recruitment periods, a total of 63 people suffered a stroke and were screened. 30 met the study criteria and were randomized (target group, n=15; control group, n=15). Due to different reasons (flowchart, Fig. 1), only 20 participants (60% men), aged between 55 and 88 years (Mean 73.20, SD 8.77), completed the study. Thus, of the 30 included subjects, 10 were excluded from the analysis. Baseline data comparisons resulted in no significant between-group differences (Table 1).

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Please, insert **Fig. 1 and Table 1**

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For each studied variable, a large variance between different measurements was observed. Four FPCs explained more than 70% of the variance. Each subject's curve was fitted to the FPCs and a reasonable fitting was obtained even when extrapolation was required. The results of the variable center of pressure (CoP) velocity in ROE are shown in Fig. 2 as an example.

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Please, insert **Fig. 2**
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It is noteworthy that the parameter that revealed statistically significant differences between groups in all tests was CoP velocity. Thus, statistically significant differences were found in CoP velocity scores 2 ($F(1)=4.650$, $P=0.047$; $r=0.48$) and 3 ($U=14.000$, $P=0.007$; $r=-0.61$) in ROE, score 3 ($F(1)=5.104$, $P=0.038$; $r=0.49$) in RCE, and score 2 ($F(1)=6.971$, $P=0.019$; $r=0.58$) in RFO.

Similarly, statistically significant differences between groups in the scores of anteroposterior (AP) and mediolateral (ML) displacements of the CoP were also repeated between tests, giving consistency to the results. Thus, scores 2 ($U=19.000$; $P=0.019$; $r=-0.52$) and 3 ($F(1)=6.203$; $P=0.024$; $r=0.53$) of AP displacement of the CoP in ROE showed statistically significant differences between groups. Moreover, scores 3 ($U=16.000$, $P=0.010$; $r=-0.58$) and 2 ($U=17.000$, $P=0.041$; $r=-0.48$) of ML displacement of the CoP in ROE and RFO, respectively, also presented statistically significant differences.

On the other hand, in general, four FPCs explained more than 80% of the variance in all parameters of LoS, except in the directional control of the front-right LoS in which the four CPFs explained 69.3% of the variance. Score 3 of the parameter of directional control in the right ($F(1)=5.119$; $P=0.039$; $r=0.50$) and left ($U=20.000$; $P=0.041$; r=-

0.47) LoS and in the average of LoS (F(1)=5.267; *P*=0.036;r=0.50) showed statistically significant differences between groups. Likewise, score 4 of the valuation index of the rear LoS also showed statistically significant differences between treatment groups (F(1)=9.662; *P*=0.007; r=0.63).

Marginal Mean Curves were reconstructed and allowed for the interpretation of the results of the FPCA in the sensory analysis (Fig. 3) and in LoS (Fig. 4). In summary, according to the proposed methodology, the target group showed a significant improvement in postural control recovery trend six months after stroke while the dynamic of the control group remained stable after two months.

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Please, insert **Fig. 3 and Fig. 4**

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Differences in the results of the biomechanical tests were not due to participant motivation because statistically significant differences were not found between groups in the IMI variable (*P*>.05).

Finally, the ICC results showed excellent reliability between the two raters in all the assessments tests (ROE: CoP velocity and CoP displacement in the AP axis, ICC=1.000; CoP displacement in the ML axis, ICC=0.973. RCE: CoP velocity, ICC=0.982; CoP displacement in the AP axis, ICC=1.000; CoP displacement in the ML axis, ICC=0.985. RFO: CoP velocity, ICC=0.947; CoP displacement in the AP axis, ICC=1.000; CoP displacement in the ML axis, ICC=0.986). Analogous results were obtained for the LoS test.

4. Discussion

This study aimed to present an alternative technique for obtaining FPCs from the set of data and to explore this methodology to determine the effect of specific PT techniques in balance recovery dynamics in elderly subjects with hemiplegia post-stroke. Our results showed that this methodology allows FPCA to be performed when the data is scarce or when there are missing values in part of the cohort at the beginning or the end of the assessment period. Additionally, it allowed us to determine the dynamics of recovery of two different treatment groups showing that the additional techniques increased standing postural stability compared to the base protocol. Therefore, the results obtained confirm the strengths of this new FPCA methodology to obtain useful information, especially when the main differences between groups are more related to the dynamics of the process than to the magnitude of the changes.

Although FPCA had been used previously in biomedical data analysis, evidence of its application in studies focused on recovery processes is scarce[5]. Moreover, as far as we know, this is the first study performing the calculation of FPCs by optimization using Sequential Least Squares Programming. The parameter used for optimization was the minimization of the residual variance after the adjustment, which is equivalent to obtaining the FPCs that best explain the variance of the sample (i.e., the final objective of FPCs analysis). Therefore, in this study, the FPCs were calculated without having to adjust the measurements of each participant to a function, assuming the hypothesis that the evolution of each of the analyzed variables behaves as a continuous function (i.e., the scores obtained in nearby periods of time, as on consecutive days, would be very similar). Thus, a new methodology is presented that addresses a frequent problem in biomedical research resulting from participants not attending measurement sessions during research studies.

On the other hand, there are few studies using posturography to study postural stability post-stroke[22,23,24,25]. Likewise, few studies have evaluated the LoS test[26,27,28,29,30] despite the fact that recovering the ability to transfer body weight is a key objective in rehabilitation post-stroke[31].

Therefore, the approach of this study could be relevant to understand the dynamics of recovery of Romberg and LoS tests in subjects with hemiplegia post-stroke during the subacute phase.

Thanks to the proposed methodology, significantly different recovery dynamics are observed between the two treatment groups in different parameters. Thus, the mean CoP velocity shows intergroup differences in all tests. It is remarkable that this parameter shows high validity and reliability in the clinical quantification of postural stability[32]. It is also considered the most sensitive parameter for detecting changes in balance due to aging or neurological disease[33]. Additionally, the mean recovery of this parameter showed by the sample of this study is greater (target group: 0.6cm/s; control group: 0.5cm/s) than that observed by other authors (0.13cm/s) during the subacute phase[34].

Likewise, the largest statistically significant decrease in the CoP displacement in the AP axis in the ROE of the target group is of special relevance since some authors relate the increase of this parameter with falls in the elderly[35].

Regarding the LoS test, the directional control parameter is that shows differences between groups in more variables. The subjects of the intervention group managed to move their CoP with a more precise trajectory mainly in the frontal plane. This is of great interest as static and dynamic imbalance in this plane is a specific postural consequence of stroke and may be closely related to the difficulty in transferring weight during walking[36,37,38]. This result agrees with those obtained by Tung et al. (2010)[27] who observed significant intragroup improvement of the directional control parameter in the experimental group when training the task of getting up and sitting, although these authors did not find differences between groups. The employment of more sensitive assessment methods such as a force plate rather than tests and clinical scales could have helped in the observation of these differences between the groups[16,39]. Moreover, FPCA, which deals with participants' patterns of recovery and not with specific values at determined temporal assessments, provided us with a useful approach to establish differences between both PT protocols[5].

Since other authors revealed improvements in all LoS parameters except directional control after balance training with visual feedback[28], the directional control parameter may be more related to the improvement in the strength and sensorimotor control of the paretic lower limb than to the specific training of balance, especially if it is not carried out considering the context and the task[40].

Some limitations were identified in this study, such as the small sample size. Since this was a pilot study, a convenience sample of 30 participants could prevent us from generalizing the results. Besides, the inclusion and exclusion criteria were incompatible with quite frequent comorbidities in the elderly. Moreover, subjects discharged to nursing homes were lost to follow up and were not taken into account in the statistical analysis. Therefore, the generalizability of the results of this study with regard to the whole elderly population is difficult because the participants represent a population group of elderly people with mild or moderate sequelae post-stroke and with family support. Finally, it is noted that people post-stroke show a reduction in the performance of one or both tasks when performing motor and cognitive tasks simultaneously[30]. However, although subjects with severe cognitive impairment were excluded, the cognitive impairment of participants was not evaluated. It is likely that the randomized study design had homogenized this variable in both groups, though this particular aspect has not been controlled.

Future research should include elderly post-stroke subjects with more severe physical disabilities and it is also recommended including a third group of subjects that combines the extra treatment techniques added to the target group with double cognitive task training.

5. Conclusions

The suggested methodology allows FPCA to be performed when the data is scarce. Therefore, it could be a feasible solution for the analysis of the differences in the dynamics of a recovery process when there are missing values in part of the cohort at the beginning or the end of the assessment period. Consequently, thanks to the proposed methodology, significantly better dynamics of recovery were found in several parameters of the postural stability during standing and the LoS test in our target group.

Conflicts of interest: none.

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Figure legends

Fig. 1. CONSORT diagram presenting subject flow from recruitment to data analysis.

Fig. 2. The results of the alternative technique presented in this paper for obtaining Functional Principal Components (FPCs). Thus, the results of the variable center of pressure (CoP) velocity in Romberg with open eyes are shown as an example. a) In this plot, CoP mean velocity for all subjects and all measurements is indicated by points and the mean curve estimated by least squares fitting is presented by the solid line. There is a slight decrease in this parameter as sessions progress. This reduction in CoP velocity over time was expected as smaller CoP velocity indicates better postural control. b) In the graphic, a good fitting of the curve along the whole set of days can be observed for a subject of the control group who attended all the measurements sessions. c) A good fitting of the curve over time can also be observed for a subject of the target group who attended all the assessments. d) In this graphic, the adjustment of the curve for a subject of the control group who missed the first evaluation sessions can be seen. Although extrapolation of the data is always an intricate issue, it can be observed that in this case, the fitting of the scores to the data produces reasonable extrapolation curves.

Fig. 3. Curves reconstructed from marginal means of the scores with statistically significant differences between groups in the sensory analysis. a), b) and c) The Marginal Mean Curves indicate that the target group had a greater statistically significant reduction of center of pressure (CoP) velocity in Romberg with open eyes (ROE), Romberg with closed eyes (RCE) and Romberg with open eyes on a foam mattress (RFO) than the control group, which persisted over time. d) and e) In these graphics it can be seen that the target group presented a greater statistically significant curtailment of CoP displacement in anteroposterior and mediolateral axes in ROE than the control group, which persisted over time (up to six months post-stroke). f)

Regarding the statistically significant differences between groups in score 2 of mediolateral displacement of the CoP in RFO, the control group appeared to reduce the ML displacement more markedly during the first month post-stroke; however, between the second and third months both groups showed a similar evolution of this parameter which remained constant over time. ROE, Romberg with open eyes; RCE, Romberg with closed eyes; RFO, Romberg with open eyes on a foam mattress; RFC, Romberg with closed eyes on a foam mattress; CoP, center of pressure.

Fig. 4. Curves reconstructed from marginal means of the scores with statistically significant differences between groups in the limits of stability (LoS) test. a) Regarding the right LoS, the graphic shows that although a greater variability was observed in the target group, its recovery pattern showed better linearity of the center of pressure (CoP) trajectory in the final assessment period compared to the recovery pattern of the control group. b) The Marginal Mean Curves indicate that despite both treatment groups presenting some variability in the recovery pattern of the left LoS, the improvement in the linearity of the trajectory to the left was extended in time in the target group more than in the control group. c) In this graphic, the recovery dynamic of the target group displays a greater improvement in the linearity of the CoP trajectory in the average of LoS in the subacute phase post-stroke. Meanwhile, the control group reached its maximum improvement at 105 days post-stroke. d) The target group presented a better recovery dynamic of the rear LoS. In fact, although the valuation index of the rear LoS improved in both treatment groups during the subacute phase post-stroke, the Marginal Mean Curves showed a significant improvement in the target group compared to the control group.

Table 1. Baseline comparisons of anthropometrics, stroke characteristics and functional status at hemodynamic stability.

	Total (n=20)			Target group (n=10)			Control group (n=10)			*P*-value
Anthropometrics Data										
Sex (man), n (%)		12 (60)			6 (60)			6 (60)		1.000[a]
	P25	P50	P75	P25	P50	P75	P25	P50	P75	
Age (y)	67	75	80	64	75	79	68	77	81	0.401[b]
BMI (Kg/m^2)	26.9	28.8	29.9	27.5	29.2	30.1	25.1	28.3	29.6	0.556[b]
Stroke characteristics										
Ischemic, n (%)		17 (85)			10 (100)			7(70)		0.210[a]
PS right, n (%)		10 (50)			5 (50)			5 (50)		1.000[a]
Inpatient time (days)	P25	P50	P75	P25	P50	P75	P25	P50	P75	0.963[b]
	40	47	62	40	47	63	40	46	64	
Basal functional status (hemodynamic stability)										
	P25	P50	P75	P25	P50	P75	P25	P50	P75	
BI		n=18			n=9			n=9		0.170[c]
	5	5	25	5	15	25	3	5	15	
BBS	3	3	5	3	3	3	3	4	7	0.301[c]
CNS		n=14			n=7			n=7		0.844[c]
	6	8	8	6	8	8	7	8	9	
TCT		n=19			n=9			n=10		0.260[b]
	36	49	61	43	49	61	24	43	61	
FACHS	0	1	1	0	1	1	0	0	1	0.185[d]
FAC	0	0	0	0	0	0	0	0	0	1.000[d]
MMT_TA		n=18			n=10			n=8		0.098[d]
	1	2	4	1	2	4	0	1	3	
MMT_QDC		n=18			n=10			n=8		0.924[d]
	3	3	4	3	3	4	2	4	4	
MMT_IS		n=18			n=10			n=8		1.000[d]
	2	3	4	2	3	4	2	4	4	
Physical therapy sessions										
	P25	P50	P75	P25	P50	P75	P25	P50	P75	
Inpatient period	30	35	46	30	34	46	30	35	46	0.878[b]
Outpatient period	0	41	53	14	46	53	0	25	55	0.466[c]
Total	42	84	92	45	85	94	37	65	91	0.449[c]

Between-group comparisons were analyzed by using: [a] Fisher exact test. [b] Student's t test. [c] Mann Whitney U test. [d] Wald´s $\chi 2$ test. Significance was set at p<.05. BMI, Body mass index; PS, paretic side; BI, Barthel Index; BBS, Berg Balance Scale; CNS, Canadian Neurological Scale; TCT, Trunk Control Test; FACHS, Functional Ambulation Classification of the Hospital of Sagunto; FAC, Functional Ambulation Classification of Massachusetts General Hospital; MMT_TA, MMT_QDC y MMT_IS, Manual Muscle Test of the muscles tibialis anterior, quadriceps and iliopsoas, respectively.

Highlights

- Postural Stability recovery trends in elderly subjects with hemiplegia post-stroke
- Analysis of the recovery trends of posturography when missing values exist
- Performing Functional Principal Component Analysis when the data is scarce
- Optimization using Sequential Least Squares Programming

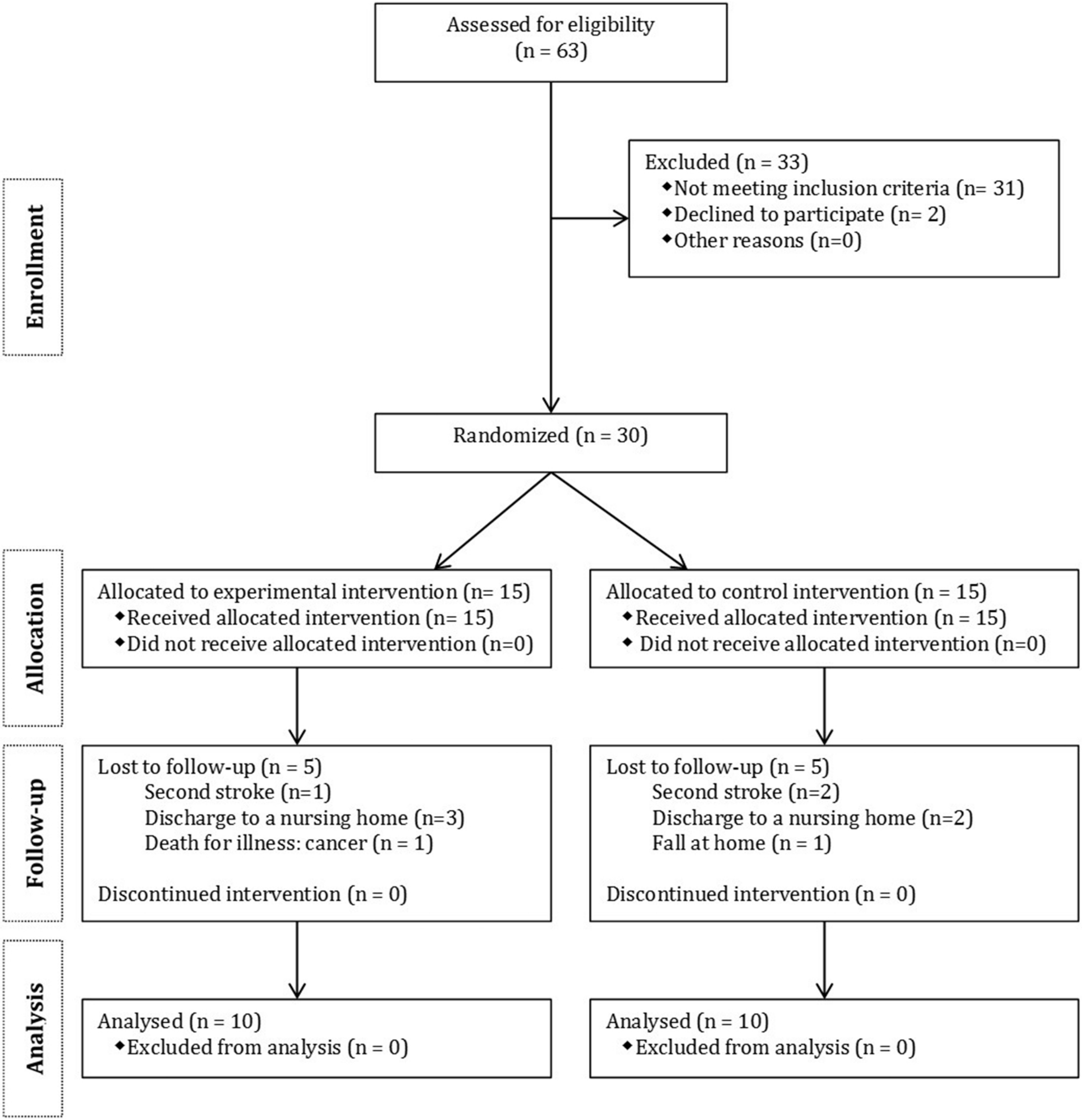
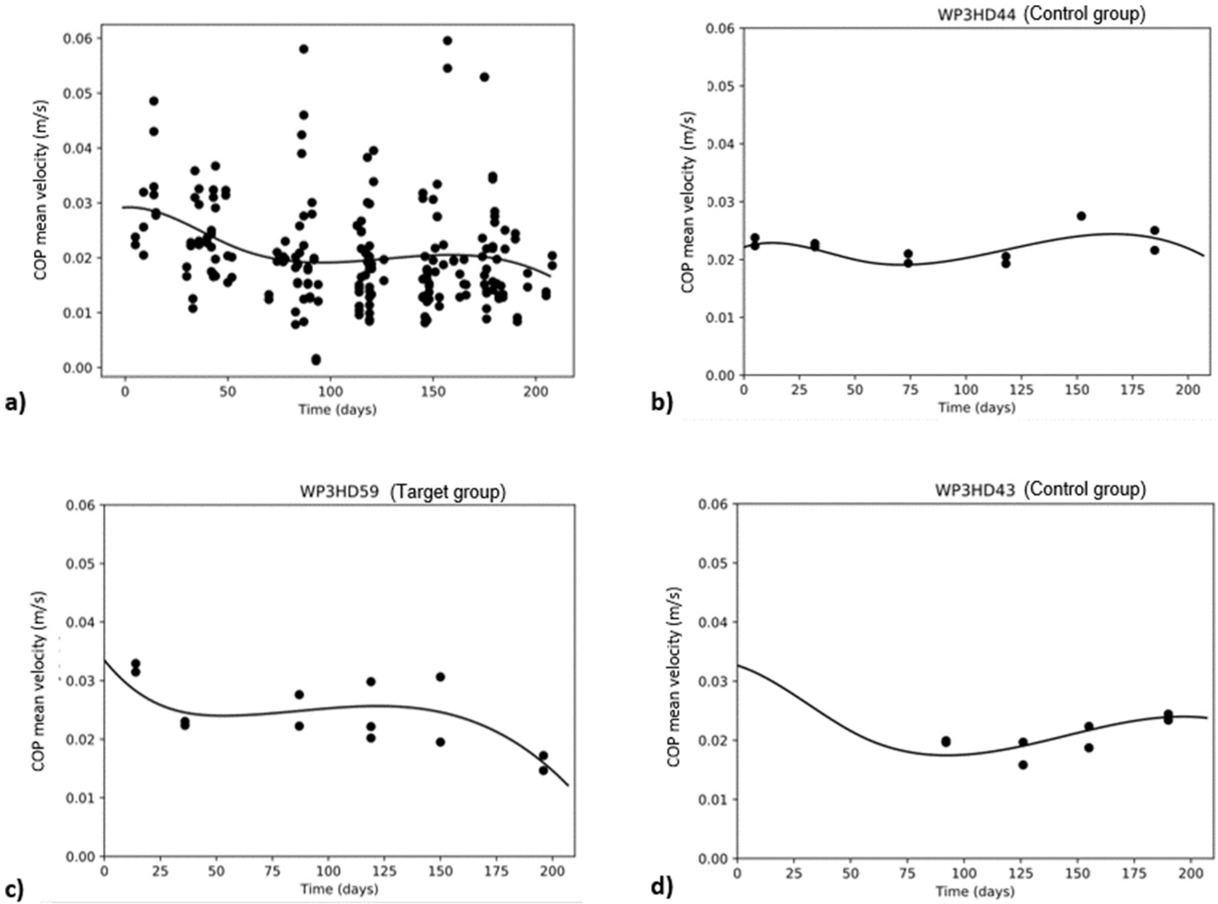

Enrollment
Assessed for eligibility (n = 63)
Excluded (n = 33)
Not meeting inclusion criteria (n= 31)
Declined to participate (n= 2)
Other reasons (n=0)
Randomized (n = 30)
Allocation
Allocated to experimental intervention (n= 15)
Received allocated intervention (n= 15)
Did not receive allocated intervention (n=0)
Allocated to control intervention (n = 15)
Received allocated intervention (n = 15)
Did not receive allocated intervention (n=0)
Follow-up
Lost to follow-up (n = 5)
Second stroke (n=1)
Discharge to a nursing home (n=3)
Death for illness: cancer (n = 1)
Discontinued intervention (n = 0)
Lost to follow-up (n = 5)
Second stroke (n=2)
Discharge to a nursing home (n=2)
Fall at home (n = 1)
Discontinued intervention (n = 0)
Analysis
Analysed (n = 10)
Excluded from analysis (n = 0)
Analysed (n = 10)
Excluded from analysis (n = 0)

Figure 1



a)
COP mean velocity (m/s)
Time (days)
b)
WP3HD44 (Control group)
COP mean velocity (m/s)
Time (days)
c)
WP3HD59 (Target group)
COP mean velocity (m/s)
Time (days)
d)
WP3HD43 (Control group)
COP mean velocity (m/s)
Time (days)

Figure 2

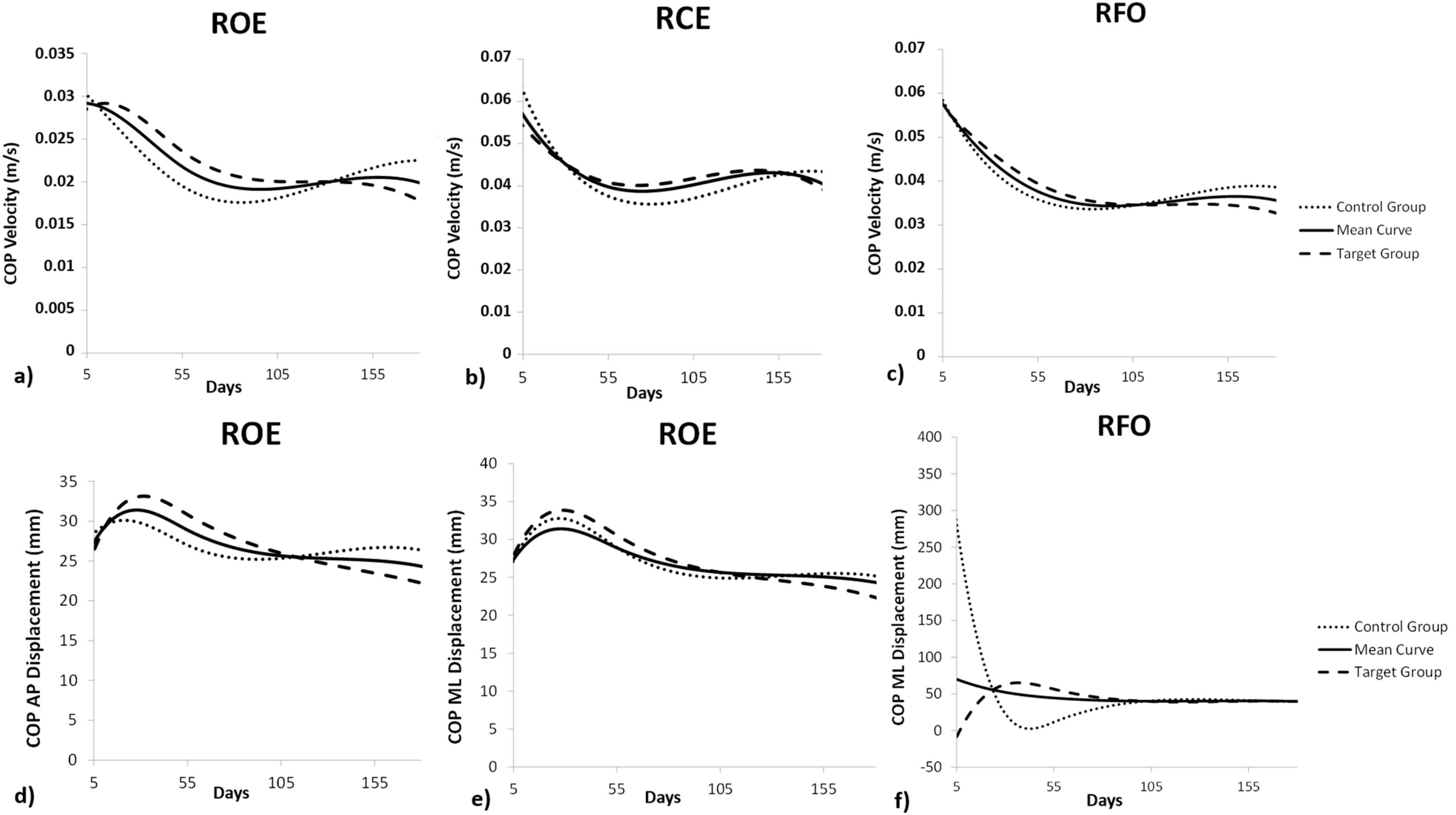

ROE
RCE
RFO
ROE
ROE
RFO
COP Velocity (m/s)
COP AP Displacement (mm)
COP ML Displacement (mm)
Days
5
55
105
155
a)
b)
c)
d)
e)
f)
Control Group
Mean Curve
Target Group

Figure 3

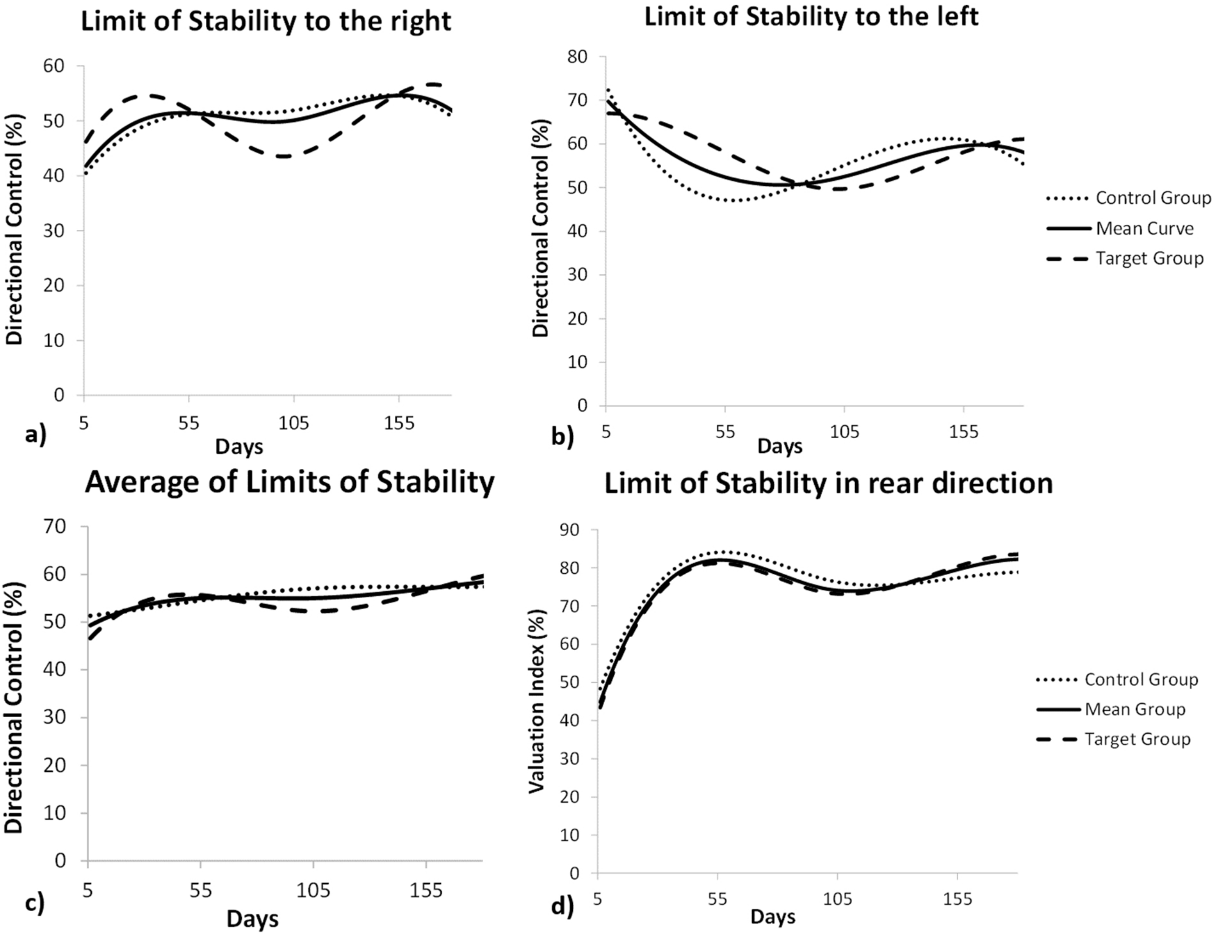

Limit of Stability to the right
Directional Control (%)
60
50
40
30
20
10
0
5
55
105
155
a)
Days
Limit of Stability to the left
Directional Control (%)
80
70
60
50
40
30
20
10
0
5
55
105
155
b)
Days
Control Group
Mean Curve
Target Group
Average of Limits of Stability
Directional Control (%)
70
60
50
40
30
20
10
0
5
55
105
155
c)
Days
Limit of Stability in rear direction
Valuation Index (%)
90
80
70
60
50
40
30
20
10
0
5
55
105
155
d)
Days
Control Group
Mean Group
Target Group

Figure 4