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ORIGINAL RESEARCH

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Sex differences in independence in activities of daily living early in stroke rehabilitation

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Abstract

Background: Current stroke research suggests that there are differences between females and males regarding incidence, stroke risk factors, stroke severity, outcome, and mortality. The few studies that have investigated sex differences in rehabilitation 8–12 months poststroke found that males are more independent, compared to females.

Objectives: To investigate if there is a difference in the improvement of independence in activities of daily living (ADL) between females and males in the acute phase (first 2 weeks) of stroke rehabilitation in a Danish population.

Methods: A prospective cohort study enrolling patients admitted to the hospital's rehabilitation ward with a stroke diagnosis from January 1, 2016, to March 17, 2017. Baseline and follow-up data regarding the primary outcome, Barthel-100 index, were analyzed using an adjusted linear mixed model.

Results: The study included 206 patients (83 females). Females were older at admission and more males lived with a partner. No differences in stroke severity or any of the risk factors were found. There were no differences between female and male scores at baseline. In the adjusted linear mixed model, quantifying the difference between follow-up and baseline Barthel-100 score, females increased their Barthel-100 score by 20.8 points (95% confidence interval (CI) 15.4–26.3) and males with 29.0 points (95% CI 24.6–33.4).

Conclusion: In a homogeneous sample of stroke survivors undergoing specialized 24-h stroke rehabilitation for 11–14 days, females were more dependent in ADL than males.

KEYWORDS
activities of daily living, Barthel-100 index, rehabilitation, sex differences, stroke

1 | INTRODUCTION

In 2016, there were 13.7 million new stroke cases worldwide, 80.1 million stroke survivors, 5.5 million stroke-related deaths, and 116.4 million disability-adjusted life years (GBD 2016 Stroke Collaborators, 2019). Research suggests that there are differences between females and males regarding stroke incidence, risk factors, and stroke severity. The incidence of stroke is higher in males than females (Appelros et al., 2009; Arnao et al., 2016), and males suffering a stroke are more often previous smokers, have daily alcohol consumption, and have a history of myocardial infarction (Kapral et al., 2005; Lai et al., 2005). However females are older at the onset of stroke, have more severe strokes, are more often unmarried, are more frequently institutionalized, and more functionally dependent before stroke (Appelros et al., 2009; Di Carlo et al., 2003; Gargano & Reeves, 2007; Kapral et al., 2005; Phan et al., 2017). The literature suggests sex differences regarding mortality with studies having reported differing mortality rates in favor of both females and males (Appelros et al., 2009; Arnao et al., 2016; Phan et al., 2017).

Few studies have investigated sex differences in functional outcome of rehabilitation after stroke. Gargano and Reeves (2007) and Paolucci et al. (2006) found that more males than females scored higher on the Barthel-100 index indicating a higher level of independency in activities of daily living (ADL) after stroke. Adams et al. (2004) found that males suffering a stroke were more likely to become independent regarding work after discharge, compared to females. Chau et al. (2009) found that females had higher levels of participation restriction 12 months poststroke.

These sex differences in rehabilitation outcomes have, however, only been investigated in a late phase at approximately 8 weeks to 12 months poststroke (Adams et al., 2004; Chau et al., 2009; Gargano & Reeves, 2007; Paolucci et al., 2006). It is not known whether the differences are detectable early during rehabilitation. At Nordsjællands Hospital, the stroke rehabilitation begins within 48 h of admission and continues until the patients are discharged for further rehabilitation in the municipality. Both are free of charge. If sex differences are present from early on, it could imply that in-hospital stroke rehabilitation should be tailored differently for females and males to obtain equivalent improvements of independency.

The hypothesis of this study was that females were more dependent than males in ADL at the beginning of rehabilitation and that this difference is measurable with the Barhel-100 index after 2 weeks of stroke rehabilitation. Therefore, the aim of this study was to investigate if there was a difference in improvement of independency in ADL between females and males in the first 2 weeks of stroke rehabilitation in a Danish population with acute stroke.

2 | METHODS

2.1 | Setting and participants

This study was a prospective cohort study including all stroke patients transferred from the acute stroke ward to the stroke rehabilitation ward at Nordsjællands Hospital from January 1, 2016, to March 17, 2017. Patients with ischemic or hemorrhagic stroke with the following International Classification of Diseases (ICD-10) diagnoses were included: DI61, DI63, DI64, DI67 (except DI67.4), and DI68. The World Health Organization definition of stroke (Hatano, 1976) was used; however, patients with spontaneous subarachnoid hemorrhage were not included in this study, as these patients are primarily treated in neurosurgical departments during the acute phase and not in stroke departments in Denmark (Dansk selskab for apopleksi, 2013). Our Department of Neurology has a catchment area of approximately 310000 inhabitants. The stroke diagnoses were made by a neurologist based on clinical and radiological examinations. Computerized tomography scans and supplementary magnetic resonance imaging scans were performed to distinguish between hemorrhagic and ischemic strokes.

Patients admitted to the acute stroke ward were evaluated by a multidisciplinary team (physicians, physiotherapists, occupational therapists, speech therapists, nurses, and neuropsychologists) and were considered eligible for the stroke rehabilitation ward when their poststroke level of functioning was equivalent to the Modified Rankin Scale level 3–5 in combination with substantial discrepancies between physical and cognitive function before and after the onset of stroke. Patients who were institutionalized prior to the stroke or patients with a severe stroke, expected to lead to palliative care were not eligible for specialized rehabilitation.

Rehabilitation was initiated within the first 2 days of admission to the acute stroke ward. Approximately 23% of patients in the acute stroke ward are transferred to the rehabilitation ward yearly (unpublished results). Rehabilitation covers a wide array of different therapeutic approaches, including the Bobath and Affolter concept, Facial Oral Tract Therapy, strength training, balance training, and cardiovascular training. Patients received a combination of individual treatment sessions and group exercises. Individual treatment sessions with physiotherapists and occupational therapists (duration of 30 to 60 min) were offered four to seven times a week in accordance with the patient's needs and abilities. Patients who were able to participate in group sessions were offered those two to eight times a week, in addition to the individual sessions. Group exercises focused on either training of the affected upper extremity, sitting, or standing balance, strength and endurance, or activity-based training, such as preparing a meal and setting a dining table.

Rehabilitation is thought of as a 24-h concept where all health professionals support the patients in achieving their rehabilitation goals. The multidisciplinary team attempts to integrate rehabilitative approaches into all everyday activities, including both bodily, activity, and participatory aspects, with the common aim of supporting and enhancing the patient's self-care capability and independence.

2.1.1 | Data collection

The following demographic variables were registered in electronic medical records by the admitting physician and supplemented by therapists: sex, date of birth, type of residence, marital status (living with a partner or living alone), alcohol consumption above or under the official Danish guidelines (maximum 7/14 units of alcohol weekly for females/males, respectively), smoking (current, former, or never) and history of diabetes, atrial fibrillation, acute myocardial infarction, hypertension, stroke, transient ischemic attack, the dates for admission and discharge, and discharge residence. The admitting physician assessed stroke severity using Scandinavian Stroke Scale (SSS) on which a high score indicates few neurological symptoms and thereby a less severe stroke (Scandinavian Stroke Study Group, 1985). Primary and secondary outcomes were assessed within 48 h of admission by a physiotherapist and occupational therapists (baseline tests) and again at 11–14 days after the baseline tests.

All assessments and treatments of the patients in this study were common practice, and therefore there was no need for approval from a Danish ethics committee. All data were retrospectively retrieved from the electronic medical records. This procedure was approved by the Danish Health Authority (journal number: 3-3013-2065/1) and the Danish Data Protection Agency (journal number: 2012-58-0004).

2.1.2 | Primary outcome

The primary outcome was independency in ADL after stroke measured by the Barthel-100 index. Barthel-100 index is a measurement of a patient's ability to perform 10 everyday activities (personal hygiene, bathing, feeding, toileting, stair climbing, dressing, bladder and bowel control, ambulation, and transfer). The score ranges from 0 to 100 where a high score indicates independency (Shah et al., 1989). Barthel-100 index is reliable and valid in stroke populations (Duffy et al., 2013; Quinn et al., 2011).

2.1.3 | Secondary outcomes

The *Assessment of Motor and Process Skills* is an international, cross-cultural, and standardized assessment of ADL that evaluates a patient's performance on two known daily activities (e.g., cooking, cleaning, bathing; Fisher & Jones, 2010). The two known activities are selected in collaboration with the patient. Reliability has been found to be excellent and validity to be moderate to excellent in stroke populations (Poulin et al., 2013).

The *Berg Balance Scale (BBS)* measures a patient's ability to maintain balance during 14 tasks. A high score means that the patient's overall balance is good (Berg et al., 1989). BBS has presented good to excellent reliability and validity in stroke populations (Blum & Korner-Bitensky, 2008).

The *Functional Oral Intake Scale* is an ordinal scale ranging from 1 to 7, which illustrates the patient's ability to swallow. A score of 7 indicates a normal oral diet and 1 indicates no oral intake. The scale has not yet been fully validated, but the initial evaluation shows it is a reliable and valid scale (Crary et al., 2005).

The *Motor Assessment Scale (MAS)* was developed for patients with stroke and consists of eight items giving a score ranging from 0 to 6, where 6 indicates good quality of movement (Carr et al., 1985). MAS has been found reliable and valid in a population of acute stroke patients (Carr et al., 1985; Malouin et al., 1994; Poole & Whitney, 1988).

The *10 meters walk test (10MWT)* was developed to monitor improvement in patients suffering a stroke. In this study, the fast-speed version of the test was used (Watson, 2002). Both versions of the test have been found reliable in a population of stroke survivors (Kollen et al., 2006).

2.2 | Statistical analysis

Sex differences in baseline characteristics and primary (Barthel-100) and secondary outcomes measured at baseline and follow-up were examined using the two-sample *t*-test or the Wilcoxon signed-rank test when appropriate for quantitative outcomes and the Chi-square or Fisher's exact test for categorical outcomes. Bonferroni adjustment of the *p*-values for the secondary outcome variables was made to account for multiple testing at baseline and follow-up. To account for repeated measures, the association between sex and the Barthel-100 index over time (baseline and follow-up) was investigated using a linear mixed model. The model included a random intercept for each patient. The fixed part included an interaction between sex and test occasion. Analyses were performed unadjusted and adjusted for potential confounders: age, stroke severity, type of residence, marital status, atrial fibrillation, diabetes, peripheral arterial disease, and acute myocardial infarction.

All data were analyzed with the statistical software SAS version 9.4 and statistical significance was set at 5%.

3 | RESULTS

A total of 206 patients (83 females) were transferred to the hospital's rehabilitation ward during the study period (Figure 1). Females were older than males (mean age 74.2 vs. 70.4, $p = .006$) at admission. No differences in severity of stroke were found (median SSS 43 vs. 40 for males and females, $p = .42$; Table 1). There were no differences in the distribution of ischemic or hemorrhagic strokes between the sexes. All patients resided in their own homes, except for five women of whom two were admitted from a temporary stay at another rehabilitation facility, and three lived in senior or protected housing. Place of residence was therefore not considered a confounder in this study. More males lived with a partner ($p = .003$). No differences were found in consumption of alcohol, history of smoking, diabetes, acute myocardial infarction, atrial fibrillation, peripheral arterial disease, hypertension, previous stroke, or transient ischemic attack (Table 1). The total length of stay and discharge residence were not statistically significantly different amongst the sexes (Table 1). The proportion of missing values were equally distributed among females and males (results not shown).

Follow-up tests were planned at 11–14 days after the baseline tests, but in reality, this varied with a median of 13 days, where six males and four females were tested ≤ 10 days after admission, and 10 males and three females were tested ≥ 15 days after baseline tests. A total of 89% of the patients were tested within the planned interval. There were no differences between female and male scores at baseline or follow-up when considering the Bonferroni adjustment (Table 2). The mean difference in the Barthel-100 index was borderline significant (mean score females vs. males 55.5 vs. 66.9, $p = .06$). Not all males and females

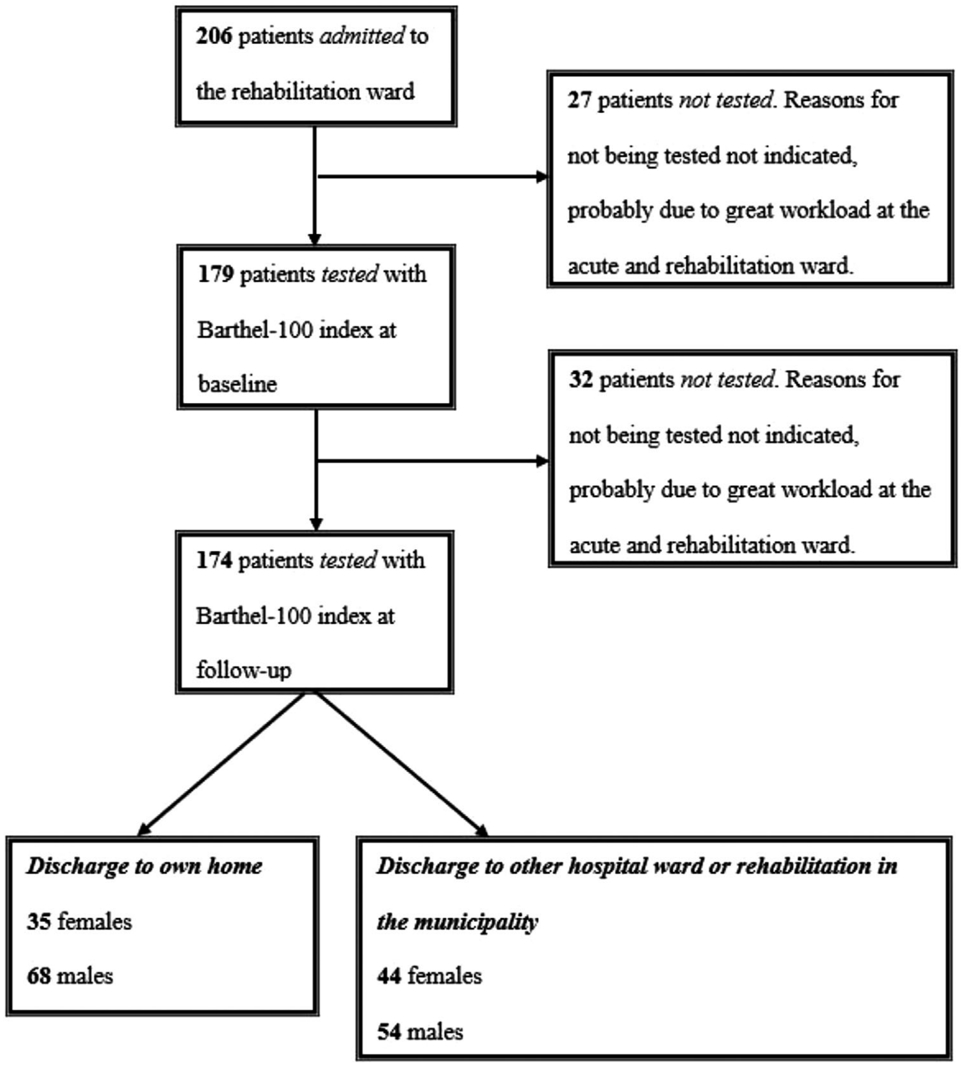

FIGURE 1 Flowchart showing the number of patients tested with Barthel-100 index, through the patients' trajectory at the rehabilitation ward

were assessed at follow-up, but the proportions of missing values were equally distributed among the sexes, apart from the 10MWT, where more males than females had been tested. The most common reason for the 10MWT to not have been done was that the patient was unable to walk, indicating greater difficulties in walking ability in females, compared to males.

An interaction between sex and test occasion (baseline and follow-up; $p = .02$ in the adjusted mixed model) on the Barthel-100 score was found. Figure 2 shows the estimated mean Barthel-100 scores for each sex at each test occasion. In the adjusted model (Table 3), females increased the Barthel-100 score by 20.8 points (95% confidence interval (CI) 15.4–26.3) from baseline to follow-up, whereas males increased with 29.0 points (95% CI 24.6–33.4). The Barthel-100 score decreased 0.5 points (95% CI 0.2– 0.9) per year of age. Barthel increased with 1.3 per one-point SSS (95% CI 1.0–1.5). Living alone versus with a partner did not seem to relate to differences in the Barthel-100 index (1.5 points, 95% CI −5.6–8.7). Previous history of diabetes, peripheral arterial disease, atrial fibrillation, and acute myocardial infarction was not associated with the Barthel-100 in the adjusted model.

4 | DISCUSSION

This study investigated differences in improvement in ADL between females and males in the first 2 weeks of stroke rehabilitation. This study shows that females increased their Barthel-100 scores less than males. There were no differences in demographic data at baseline, except that females were older and more often lived alone.

Our findings are supported by other studies (Adams et al., 2004; Chau et al., 2009; Gargano & Reeves, 2007; Paolucci et al., 2006; Scrutinio et al., 2017). Paolucci et al. (2006) did a case-control study in an Italian population of 440 patients (50% females), matched on age, stroke severity, and time from stroke onset to admission. Gargano and Reeves (2007) compared sex differences 3 months post-discharge with data collected by telephone interviews with 270 patients from a US stroke

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TABLE 1 Baseline characteristics and discharge data of females and males included in this study

Variables	Females (n = 83)	Males (n = 123)	p-value
Age at admission, total n (%)	83 (100)	123 (100)	.006[a]
– Mean ± SD	74.2 ± 8.7	70.4 ± 10.8	
Scandinavian Stroke Scale (SSS) at admission, total n (%)	77 (93)	113 (92)	.42[b]
– Median (interquartile range (IQR))	40 (26–48)	43 (28–50)	
Type of stroke, total n (%)	83 (100)	123 (100)	.67[c]
– Ischemic, n (%)	67 (81)	103 (84)	
– Haemorrhagic, n (%)	14 (17)	19 (15)	
– Both, n (%)	2 (2)	1 (1)	
Residence, total n (%)	82 (99)	119 (97)	.01[c]
– Own home, n (%)	77 (94)	119 (100)	
– Other, n (%)	5 (6)	0 (0)	
Living with partner, total n (%)	75 (90)	113 (92)	.003[d]
– Yes, n (%)	31 (41)	72 (64)	
– No, n (%)	44 (59)	41 (36)	
Alcohol above the guidelines, total n (%)	69 (83)	105 (85)	.64[d]
– Yes, n (%)	10 (14)	18 (17)	
– No, n (%)	59 (86)	87 (83)	
Smoking, total n (%)	66 (80)	100 (81)	.19[d]
– Current, n (%)	17 (26)	27 (27)	
– Former, n (%)	16 (24)	36 (36)	
– Never, n (%)	33 (50)	37 (37)	
History of diabetes, total n (%)	76 (92)	111 (90)	.87[d]
– Yes, n (%)	13 (17)	18 (16)	
– No, n (%)	63 (83)	93 (84)	
History of acute myocardial infarction, total n (%)	76 (92)	112 (91)	.06[c]
– Yes, n (%)	2 (3)	17 (15)	
– No, n (%)	74 (97)	95 (85)	
History of atrial fibrillation, total n (%)	77 (93)	111 (90)	.88[d]
– Yes, n (%)	23 (30)	32 (29)	
– No, n (%)	54 (70)	79 (71)	
History of hypertension, total n (%)	77 (93)	110 (89)	.76[d]
– Yes, n (%)	50 (65)	69 (63)	
– No, n (%)	27 (35)	41 (37)	
History of peripheral arterial disease, total n (%)	75 (90)	112 (91)	.052[c]
– Yes, n (%)	1 (1)	25 (22)	
– No, n (%)	74 (99)	87 (78)	
Previous stroke, total n (%)	76 (92)	112 (91)	.18[d]
– Yes, n (%)	11 (14)	5 (4)	
– No, n (%)	65 (86)	107 (96)	
Previous transient ischemic attack, total n (%)	75 (90)	112 (91)	1.00[c]
– Yes, n (%)	3 (4)	5 (4)	
– No, n (%)	72 (96)	107 (96)	
Total length of stay in days, total n (%)	83 (100)	123 (100)	.19[b]
– Mean ± SD	36.0 ± 15.3	33.3 ± 13.1	
Discharge residence, total n (%)	80 (96)	123 (100)	.34[c]
– Own home, n (%)	35 (44)	68 (55)	
– Rehabilitation in the municipality, n (%)	41 (51)	52 (42)	
– Other hospital ward, n (%)	3 (4)	2 (2)	
– Other, n (%)	1 (1)	1 (1)	

Note: Mean ± SD is only showed for normally distributed data.
[a]Wilcoxon signed-rank test.
[b]Two sample *t*-test.
[c]Fisher's exact test.
[d]Chi-square test.

registry. Both studies found that females had lower Barthel scores, compared to males (Gargano & Reeves, 2007; Paolucci et al., 2006). Adams et al. (2004) conducted a retrospective study on 127 American patients and found that males had higher odds of independency at discharge versus needing any kind of assistance. Chau et al. (2009) found that females have higher odds of being restricted in participation 12 months poststroke in a sample of 118 Chinese stroke survivors (38% females, total sample mean age 71.7 ± 10.2 years). On the other hand, Bassi et al. (2010) and Norlander et al. (2016) did not find any differences in females and males after stroke rehabilitation in the Italian (n = 126) and Swedish (n = 145) population, respectively. These conflicting results could be due to differences in study design. In our study, stroke rehabilitation began within 48 h of admission, and in Bassi et al. (2010), it began within 30 days of onset of stroke. The difference in onset of stroke rehabilitation may influence the degree of functional gain. Norlander et al. (2016) investigated differences between sexes, 10 years poststroke on the Barthel-100 index or the modified Frenchay Activities Index. They did not find differences in the overall

TABLE 2 Primary and secondary outcomes at baseline and follow-up

Variables	Baseline Females (*n* = 83)	Baseline Males (*n* = 123)	*p*-value-[a]	Follow-up Females (*n* = 83)	Follow-up Males (*n* = 123)	*p*-value[a]
Primary outcome						
Barthel-100, total *n* (%)	73 (88)	106 (86)		66 (80)	108 (88)	
– Mean	31.3	34.5	.38	55.5	66.9	.06
– Median (IQR)	21 (4–51)	30 (7–58)		60 (22–91)	74 (42–97)	
Secondary outcomes						
Assessment of Motor Skills, total *n* (%)	46 (55)	76 (62)		51 (61)	88 (72)	
– Mean	0.05	−0.08	.51	0.5	0.8	.02
– Median (IQR)	0.5 (−1.0– 0.8)	0.2 (−0.7–0.7)		0.5 (0.1–0.9)	0.9 (0.3–1.2)	
Assessment of Process Skills, total *n* (%)	46 (55)	76 (62)		51 (61)	88 (72)	
– Mean	−0.06	0.01	.71	0.2	0.4	.15
– Median (IQR)	0 (−0.2–0.3)	0.05 (−0.3– 0.4)		0.2 (−0.4–1.0)	0.4 (−0.05–1.0)	
Berg Balance Scale, total *n* (%)	46 (55)	71 (58)		60 (72)	96 (78)	
– Mean	12.4	13.2	.54	23.0	30.8	.02
– Median (IQR)	4 (1–15)	5 (2–20)		19 (3–41)	38 (7–50)	
Functional Oral Intake Scale, total *n* (%)	82 (99)	121 (98)		77 (93)	116 (94)	
– Mean	5.2	5.7	.09	5.7	6.0	.06
– Median (IQR)	5 (5–7)	7 (5–7)		7 (5–7)	7 (6–7)	
Motor Assessment Scale (MAS) part 1, total *n* (%)	37 (45)	56 (46)		53 (64)	85 (69)	
– Mean	2.4	3.5	.02	3.8	4.5	.09
– Median (IQR)	2 (0–5)	4 (2–6)		5 (1–6)	6 (3–6)	
MAS part 2, total *n* (%)	35 (42)	56 (46)		53 (64)	85 (69)	
– Mean	4.1	4.8	.03	4.5	5.4	.006
– Median (IQR)	5 (2–6)	6 (3.5–6)		6 (2–6)	6 (6–6)	
MAS part 3, total *n* (%)	36 (43)	55 (45)		55 (66)	85 (69)	
– Mean	2.9	3.0	.54	3.8	4.0	.51
– Median (IQR)	2 (1–4)	3 (2–4)		4 (3–6)	4 (3–5)	
MAS part 4, total *n* (%)	35 (42)	56 (46)		55 (66)	85 (69)	
– Mean	1.9	2.6	.25	2.5	3.2	.06
– Median (IQR)	1 (1–2)	2 (1–5)		2 (1–5)	2 (2–6)	
MAS part 5, total *n* (%)	34 (41)	56 (46)		55 (66)	85 (69)	
– Mean	1.2	1.3	.35	2.1	3.0	.04
– Median (IQR)	0 (0–2)	1 (0–2)		1 (0–4)	3 (0–5)	
MAS part 6, total *n* (%)	36 (43)	55 (45)		55 (66)	85 (69)	
– Mean	2.1	3.2	.07	3.5	4.1	.13
– Median (IQR)	1 (0–4.5)	4 (1–5)		5 (1–6)	5 (2–6)	
MAS part 7, total *n* (%)	35 (42)	54 (44)		55 (66)	84 (68)	
– Mean	1.6	2.6	.052	3.3	4.0	.12
– Median (IQR)	0 (0–4)	2 (0–5)		4 (0–6)	5 (1–6)	
10 meters walk test, total *n* (%)	11 (13)	18 (15)		26 (31)	60 (49)	
– Mean	11.8	12.6	.95	14.8	9.8	.10
– Median (IQR)	10.5 (8.7–14.6)	10.4 (7.9–17.4)		10.8 (7.4–20.7)	9.0 (6.9–11.4)	

Note: Bonferroni adjustment (0.05/12) = $p < .004$ for baseline and follow-up, respectively.
[a]Wilcoxon signed-rank test.

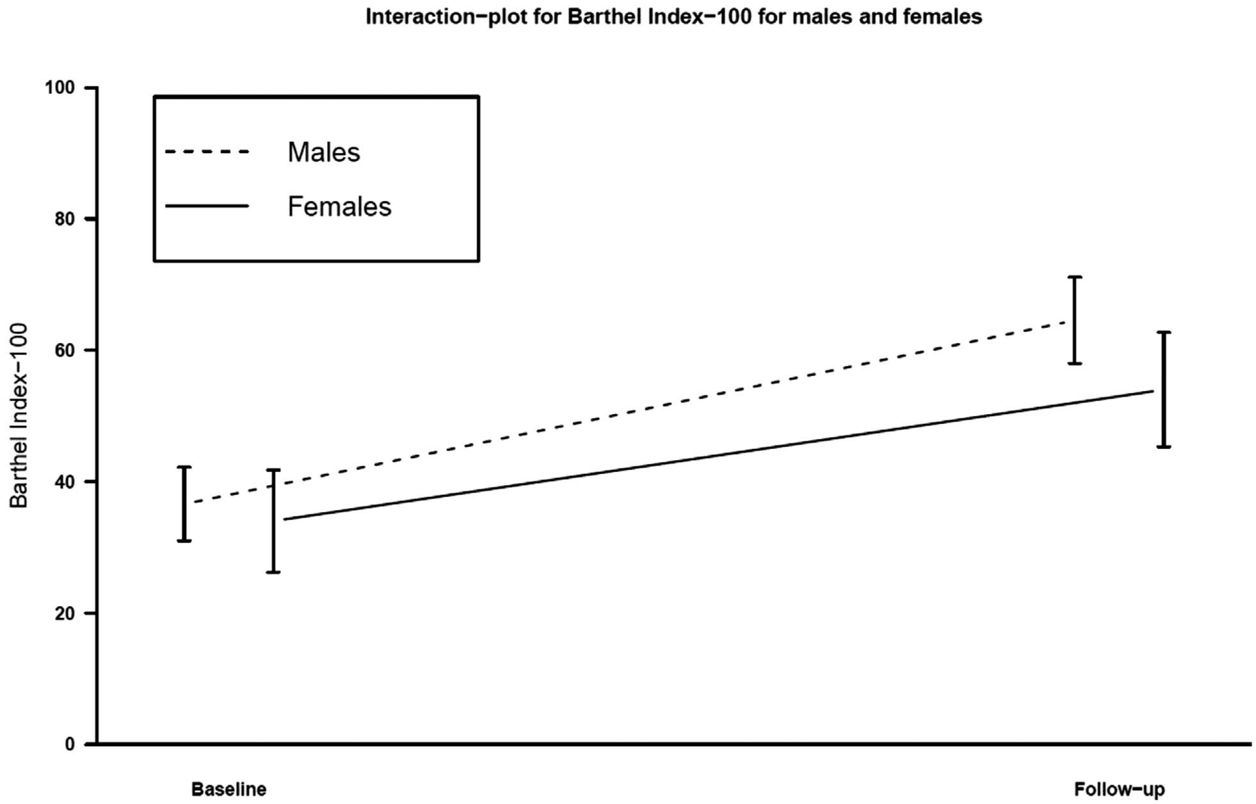

FIGURE 2 Demonstrating how mean Barthel-100 index scores depend on time for each sex (estimates and confidence interval obtained from the unadjusted linear regression model)

activity level, but they did find a difference in forms of activities males and females participated in. Norlander et al. (2016) did not mention if or how the patients were rehabilitated, which makes the comparison between their and our study difficult. The patients in Norlander et al. (2016) were younger at the onset of stroke (mean age at follow-up 78 and 75 years for females and males, respectively) than the patients in our study. The oldest patients and those with more severe strokes could have died before follow-up, so only those with the highest level of independency were left at follow-up.

There are many reasons for sex differences, both biological and psychological. It is well established that testosterone affects a person's ability to build muscle mass and that elderly immobilized patients suffer from atrophy. This makes it harder for females to retrieve lost muscle mass during the rehabilitation phase. In a recent review, Carcel et al. (2020) described different sex-specific risk factors for stroke, which was related to female biology, among others. For instance, stillbirths were associated with the risk of any type of stroke later in life, and gestational hypertension increased the risk of hemorrhagic stroke over five times. Contrarily, breastfeeding for more than 2 years lowered the risk of stroke later in life. While for males, erectile dysfunction increased their risk of stroke. This indicates that sex hormones play a role in sex differences in stroke incidence, and it is plausible, that sex hormones could impact the brain's plasticity and thereby also affect the course of the rehabilitation. Stroke symptoms also present differently in the sexes, where incontinence, dysphagia, and loss of consciousness have a higher occurrence in females, compared to males (Carcel et al., 2020). These three factors would impact the result of the Barthel-100 index, with a lower score for females, which could be attributing to the lower results for females in this study. There were no differences in the sexes regarding outcomes after thrombolysis or thrombectomy (Carcel et al., 2020). These biological differences are important to be aware of but are not something we can necessarily influence.

Another reason for the observed difference between females and males in our study could be differences in coping strategies in males and females. It was observed in French patients with mild to moderate chronic obstructive pulmonary disease, undertaking a 4-week rehabilitation program, that females more frequently used emotion-focused strategies, and males more often used problem-focused strategies (Ninot et al., 2006). These findings are supported by a cross-sectional questionnaire study from 2004, investigating stress and coping in a sample of 2816 (56% females) Spanish people (Matud, 2004). Problem-focused coping may be more effective when coping with stroke. It is plausible, that if patients actively seek movement and engage in exercise by themselves, then they are aiding their recovery. If males are more prone to a problem-focused coping, this could be one reason for them achieving a higher level of independence after stroke rehabilitation. Taking different coping mechanisms into consideration during a rehabilitation course, one could perhaps secure more patient involvement and thereby aiding the patients into ownership of the training offered. This also applies to goal setting. A German study from

TABLE 3 Unadjusted and adjusted linear mixed models quantifying the difference between follow-up and baseline Barthel-100 index for each sex. The unadjusted and adjusted models have different amounts of missing Barthel-100 measurements[a]

	Unadjusted analysis[a,b]		Adjusted analysis[c]	
	Estimate (95% CI)	*p*-value	Estimate (95% CI)	*p*-value
Intercept	36.3 (30.5–42.1)	< .001*	23.8 (−3.0–50.7)	.08
Sex[d]				
– Female (ref. males)	−3.9 (−13.0–5.3)	.40	0.05 (−8.3–8.4)	.99
Difference between baseline and follow-up				
– Females	21.0 (15.9–26.1)	< .001*	20.8 (15.4–26.3)	< .001*
– Males	29.0 (24.9–33.1)	< .001*	29.0 (24.6–33.4)	< .001*
Age			−0.5 (−0.9– −0.2)	.005*
SSS			1.3 (1.0–1.5)	< .001*
Marital status				
– Living alone (ref. living with partner)			1.5 (−5.6–8.7)	.68
History of diabetes				
– Yes (ref. no)			4.1 (−5.6–13.7)	.41
History of peripheral arterial disease				
– Yes (ref. no)			−5.9 (−22.4–10.6)	.48
History of atrial fibrillation				
– Yes (ref. no)			6.0 (−2.2–14.1)	.15
Acute myocardial infarction				
Yes (ref. no)			1.7 (−10.5–14.0)	.78

Abbreviations: Ref. = reference group in analysis, CI = confidence interval, visit 1 = baseline test and visit 2 = follow-up test after 11–14 days.
[a]When the unadjusted analysis was based on the same number of measurements, similar estimates were found (results not shown).
[b]59 missing measurements of baseline or follow-up Barthel-100 index.
[c]96 missing measurements of baseline or follow-up Barthel-100 index.
[d]The main effect of sex corresponds to the estimated difference at baseline.
*Statistically significant $p < .05$.

2011 (Grande & Romppel, 2011) investigated sex differences in recovery goals for patients with acute myocardial infarction. Females more often preferred rehabilitation goals aiming at maintaining and regaining independency in household duties and ADL. Males on the other hand were more motivated for improved endurance and reduced stress at their work. Differences in goal settings give rise to reflection upon the different exercise options that the rehabilitation facility offers. In our study, a broad array of group and individual exercise options were available. However, most group trainings were focusing on strength, endurance, and balance training and not ADL, which could lead to females being less motivated to participate.

4.1 | Strengths and limitations

Although the data were retrospectively collected from the patients' electronic medical records, the data were prospectively generated, which decreased the risk of information bias. The use of validated and standardized measurements, which were applied by trained physiotherapists and occupational therapists, also decreases the risk of information bias. However, the Danish translation of the Barthel-100 index has not yet been validated. Another factor in poststroke outcomes could be the patients' comorbidities pre-stroke. Seeing as males were younger than females at the onset of stroke, it is also likely that males were more independent because they, in general, had fewer diagnosed comorbidities. According to a recent review (Carcel et al., 2020), there are differences in pre-stroke comorbidities in females and males, but we did not find this in our study, probably due to fewer participants. The mixed model was adjusted for age and the most common comorbidities in stroke patients.

A limitation of this study was the amount of missing data. The most common reason for missing data for the primary and secondary outcomes was that the patient could not manage the tests due to not being able to comply with test instructions. There were no differences between females and males regarding the amount of missing data, except the 10MWT. The analysis of the primary outcome by a linear mixed model is valid when the missing mechanism can be assumed missing at random (Schafer, 1997), namely, that conditional on all available information incorporated in the model (covariates and outcomes) missingness does not depend on the value of the missing observation. This may be a strong assumption. Another limitation is the lack of knowledge about the patients' pre-stroke physical activity level. Krarup et al. (2008) found that a high level of pre-stroke physical activity, measured with Physical Activity Scale for the Elderly Questionnaire in a Danish population with ischemic stroke aged 40 or above and with the ability to walk unassisted, was associated with a less severe stroke, measured with SSS. Pre-stroke physical activity should be incorporated in future studies. Furthermore, the reproducibility and generalizability are affected by the unprecise inclusion criteria for the rehabilitation ward and the small sample size. Last, we do not have any data regarding the exact amount of training for females and males, respectively, because each intervention is tailored for the patient's needs and resources as inpatients. It is possible, that males were more outreaching in relation to self-training and thereby obtaining more overall training than females. We also do not know how many contacts the patients had with the nurses, and it is also possible that females were more outreaching for help from the staff and thereby not as active in everyday activities as they could have been. These two factors could also affect the result of this study and needs to be considered in future studies.

5 | IMPLICATIONS

The results of this study give reason to consider how stroke rehabilitation in the acute phase can be tailored individually for females and males, to obtain equivalent improvements of independency. Rehabilitation facilities need to be equipped to accommodate the different types of relevant interventions in relation to ADL-specific training. Further research in a larger and more heterogeneous sample is needed to generalize to a general stroke population and not only patients undergoing in-hospital rehabilitation. It will also be essential to investigate the long-term outcome for ADL and particularly its impact on participation. Qualitative studies regarding females' and males' expectations of rehabilitation, goal setting, and motivation for participation in exercise could enlighten whether the current stroke rehabilitation program embraces both female and male needs. Further research into the biological and psychological differences in the sexes with relation to stroke rehabilitation could also shed light on the complexity of this area and thereby ensure training environments and exercise options that appeal to both females and males.

6 | CONCLUSION

This study finds in a homogeneous sample of stroke survivors undergoing specialized 24-h stroke rehabilitation that females are less independent in ADL 11–14 days poststroke than males, when adjusting for age and comorbidities, among others. The reasons for sex differences are multifactorial and could be due to different biological and psychological factors. There is a need for future research into the mechanism in stroke rehabilitation and how we ensure that the therapeutic interventions target the needs of both sexes.

AUTHOR CONTRIBUTIONS

T. Christensen, L. Buus, and J. Stokholm conceived the database, sought the necessary approval, and collected the data. M. M. Liljehult, M. Euler-Chelpin, and S. Rosthøj conceived this study's design and analyzed the data including drafting the statistical model. M. M. Liljehult wrote the initial draft of the manuscript, and all authors revised and approved the final draft of the manuscript.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1002/brb3.2223.

DATA AVAILABILITY STATEMENT

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

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REFERENCES

Adams, R. A., Sherer, M., Struchen, M. A., & Nick, T. G. (2004). Post-acute brain injury rehabilitation for patients with stroke. *Brain Injury*, *18*(8), 811–823. https://doi.org/10.1080/02699050410001671810

Appelros, P., Stegmayr, B., & Terént, A. (2009). Sex differences in stroke epidemiology: A systematic review. *Stroke, A Journal of Cerebral Circulation*, *40*(4), 1082–1090. https://doi.org/10.1161/STROKEAHA.108.540781

Arnao, V., Acciarresi, M., Cittadini, E., & Caso, V. (2016). Stroke incidence, prevalence and mortality in women worldwide. *International Journal of Stroke*, *11*(3), 287–301. https://doi.org/10.1177/1747493016632245

Bassi, A., Colivicchi, F., Santini, M., & Caltagirone, C. (2010). Gender-specific predictors of functional outcome after stroke rehabilitation: Potential role of the autonomic nervous system. *European Neurology*, *63*(5), 279–284. https://doi.org/10.1159/000287583

Berg, K. (1989). Measuring balance in the elderly: Preliminary development of an instrument. *Physiotherapy Canada*, *41*(6), 304–311. https://doi.org/10.3138/ptc.41.6.304

Blum, L., & Korner-Bitensky, N. (2008). Usefulness of the Berg Balance Scale in stroke rehabilitation: A systematic review. *Physical Therapy*, *88*(5), 559–566. https://doi.org/10.2522/ptj.20070205

Carcel, C., Woodward, M., Wang, X., Bushnell, C., & Sandset, E. C. (2020). Sex matters in stroke: A review of recent evidence on the differences between women and men. *Frontiers in Neuroendocrinology*, *59*, 100870. https://doi.org/10.1016/j.yfrne.2020.100870

Carr, J. H., Shepherd, R. B., Nordholm, L., & Lynne, D. (1985). Investigation of a new motor assessment scale for stroke patients. *Physical Therapy*, *65*(2), 175–180. https://doi.org/10.1093/ptj/65.2.175

Chau, J. P.c, Thompson, D. R., Twinn, S., Chang, A. M., & Woo, J. (2009). Determinants of participation restriction among community dwelling stroke survivors: A path analysis. *BMC Neurology*, *9*, 49. https://doi.org/10.1186/1471-2377-9-49

Crary, M. A., Mann, G. D. C., & Groher, M. E. (2005). Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. *Archives of Physical Medicine and Rehabilitation*, *86*(8), 1516–1520. https://doi.org/10.1016/j.apmr.2004.11.049

Dansk selskab for apopleksi (2013). *Referenceprogram for behandling af patienter med apopleksi og TCI*. http://www.dsfa.dk/wp-content/uploads/REFERENCEPROGRAMFINAL20131.pdf

Di Carlo, A., Lamassa, M., Baldereschi, M., Pracucci, G., Basile, A. M., Wolfe, C. D. A., Giroud, M., Rudd, A., Ghetti, A., & Inzitari, D. (2003). Sex differences in the clinical presentation, resource use, and 3-month outcome of acute stroke in Europe: Data from a multicenter multinational hospital-based registry. *Stroke, A Journal of Cerebral Circulation*, *34*(5), 1114–1119. https://doi.org/10.1161/01.STR.0000068410.07397.D7

Duffy, L., Gajree, S., Langhorne, P., Stott, D. J., & Quinn, T. J. (2013). Reliability (inter-rater agreement) of the Barthel Index for assessment of stroke survivors systematic review and meta-analysis. *Stroke, A Journal of Cerebral Circulation*, *44*(2), 462–468. https://doi.org/10.1161/STROKEAHA.112.678615

Fisher, A., & Jones, K. (2010). *Assessment of motor and process skills: Development, standardization and administrative manual* (7th ed., Vol.1). Three Star Press.

Gargano, J. W., & Reeves, M. J., (2007). Sex differences in stroke recovery and stroke-specific quality of life: Results from a statewide stroke registry. *Stroke, A Journal of Cerebral Circulation*, *38*(9), 2541–2548. https://doi.org/10.1161/STROKEAHA.107.485482

GBD 2016 Stroke Collaborators. (2019). Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurology*, *18*(5), 439–458. https://doi.org/10.1016/S1474-4422(19)30034-1

Grande, G., & Romppel, M. (2011). Gender differences in recovery goals in patients after acute myocardial infarction. *Journal of Cardiopulmonary Rehabilitation and Prevention*, *31*(3), 164–172. https://doi.org/10.1097/HCR.0b013e31820333c8

Hatano, S. (1976). Experience from a multicentre stroke register: A preliminary report. *Bulletin of the World Health Organization*, *54*(5), 541–553.

Kapral, M. K., Fang, J., Hill, M. D., Silver, F., Richards, J., Jaigobin, C., & Cheung, A. M. (2005). Sex differences in stroke care and outcomes: results from the Registry of the Canadian Stroke Network. *Stroke, A Journal of Cerebral Circulation*, *36*(4), 809–814. https://doi.org/10.1161/01.STR.0000157662.09551.e5

Kollen, B., Kwakkel, G., & Lindeman, E. (2006). Hemiplegic gait after stroke: Is measurement of maximum speed required? *Archives of Physical Medicine and Rehabilitation*, *87*(3), 358–363. https://doi.org/10.1016/j.apmr.2005.11.007

Krarup, L.-H., Truelsen, T., Gluud, C., Andersen, G., Zeng, X., Korv, J., Oskedra, A., & Boysen, G. (2008). Prestroke physical activity is associated with severity and long-term outcome from first-ever stroke. *Neurology*, *71*(17), 1313–1318. https://doi.org/10.1212/01.wnl.0000327667.48013.9f

Lai, S. M., Duncan, P. W., Dew, P., & Keighley, J. (2005). Sex differences in stroke recovery. *Preventing Chronic Disease*, *2*(3), A13.

Malouin, F., Pichard, L., Bonneau, C., Durand, A., & Corriveau, D. (1994). Evaluating motor recovery early after stroke: Comparison of the Fugl-Meyer Assessment and the Motor Assessment Scale. *Archives of Physical Medicine and Rehabilitation*, *75*, 1206–1212. https://doi.org/10.1016/0003-9993(94)90006-X

Matud, M. P. (2004). Gender differences in stress and coping styles. *Personality and Individual Differences*, *37(7)*, 1401–1415. https://doi.org/10.1016/j.paid.2004.01.010

Ninot, G., Fortes, M., Poulain, M., Brun, A., Desplan, J., Préfaut, C., & Varray, A. (2006). Gender difference in coping strategies among patients enrolled in an inpatient rehabilitation program. *Heart & Lung*, *35*(2), 130–136. https://doi.org/10.1016/j.hrtlng.2005.09.004

Norlander, A., Jönsson, A. -. C., Ståhl, A., Lindgren, A., & Iwarsson, S. (2016). Activity among long-term stroke survivors. A study based on an ICF-oriented analysis of two established ADL and social activity instruments. *Disability and Rehabilitation*, *38*(20), 2028–2037. https://doi.org/10.3109/09638288.2015.1111437

Paolucci, S., Bragoni, M., Coiro, P., De Angelis, D., Fusco, F. R., Morelli, D., Venturiero, V., & Pratesi, L. (2006). Is sex a prognostic factor in stroke rehabilitation?: A matched comparison. *Stroke, A Journal of Cerebral Circulation*, *37*(12), 2989–2994. https://doi.org/10.1161/01.STR.0000248456.41647.3d

Phan, H. T., Blizzard, C. L., Reeves, M. J., Thrift, A. G., Cadilhac, D., Sturm, J., Heeley, E., Otahal, P., Konstantinos, V., Anderson, C., Parmar, P., Krishnamurthi, R., Barker-Collo, S., Feigin, V., Bejot, Y., Cabral, N. L., Carolei, A., Sacco, S., Chausson, N., … Gall, S. (2017). Sex differences in long-term mortality after stroke in the INSTRUCT (INternational STRoke oUtComes sTudy): A meta-analysis of individual participant data. *Circulation: Cardiovascular Quality and Outcomes*, *10*(2), e003436. https://doi.org/10.1161/CIRCOUTCOMES.116.003436

Poole, J. L., & Whitney, S. L. (1988). Motor assessment scale for stroke patients: Concurrent validity and interrater reliability. *Archives of Physical Medicine and Rehabilitation*, *69*(3 Pt 1), 195–197.

Poulin, V., Korner-Bitensky, N., & Dawson, D. R. (2013). Stroke-specific executive function assessment: A literature review of performance-based tools. *Australian Occupational Therapy Journal*, *60*(1), 3–19. https://doi.org/10.1111/1440-1630.12024

Quinn, T. J., Langhorne, P., & Stott, D. J. (2011). Barthel index for stroke trials: development, properties, and application. *Stroke, A Journal of Cerebral Circulation*, *42*(4), 1146–1151. https://doi.org/10.1161/STROKEAHA.110.598540

Scandinavian Stroke Study Group. (1985). Multicenter trial of hemodilution in ischemic stroke–background and study protocol. *Stroke, A Journal of Cerebral Circulation*, *16*(5), 885–890. https://doi.org/10.1161/01.STR.16.5.885

Schafer, J. L. (1997). *Analysis of incomplete multivariate data* (1st ed.). Chapmann & Hall/CRC Press.

Scrutinio, D., Lanzillo, B., Guida, P., Mastropasqua, F., Monitillo, V., Pusineri, M., Formica, R., Russo, G., Guarnaschelli, C., Ferretti, C., & Calabrese, G. (2017). Development and validation of a predictive model for functional outcome after stroke rehabilitation: The Maugeri Model. *Stroke, A Journal of Cerebral Circulation*, *48*(12), 3308–3315. https://doi.org/10.1161/STROKEAHA.117.018058

Shah, S., Vanclay, F., & Cooper, B. (1989). Improving the sensitivity of the Barthel Index for stroke rehabilitation. *Journal of Clinical Epidemiology*, *42*(8), 703–709. https://doi.org/10.1016/0895-4356(89)90065-6

Watson, M. J. (2002). Refining the ten-metre walking test for use with neurologically impaired people. *Physiotherapy*, *88*(7), 386-397. https://doi.org/10.1016/S0031-9406(05)61264-3

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