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Overground robotic exoskeleton vs conventional therapy in inpatient stroke rehabilitation: results from a pragmatic, multicentre implementation programme

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Abstract

Background Despite the reported efficacy of overground robotic exoskeleton (ORE) for rehabilitation of mobility post-stroke, its effectiveness in real-world practice is still debated. We analysed prospectively collected data from Improving Mobility Via Exoskeleton (IMOVE), a multicentre clinical implementation programme of ORE enrolling participants with various neurological conditions and were given options to choose between 12 sessions of ORE or conventional therapy (control).

Methods This is analysis of participants under IMOVE who fulfilled the following criteria (i) primary diagnosis was stroke (ischemic, hemorrhagic; first or recurrent), (ii) onset of stroke was within 9 months and (iii) the intervention was during inpatient stay. They should also fulfill the general IMOVE inclusion and exclusion criteria which were resembling general clinical and manufacturing criteria of ORE. Outcome measures included Functional Ambulatory Category (FAC), Rivermead Mobility Index (RMI), Functional Independence Measure (FIM) and Clinical Outcome Variable Scale (COVS), measured immediately before and after the 12 sessions of therapy, and mean distance walked per session.

Results Of 149 participants (105 OREs and 44 controls), both groups improved significantly in motor outcomes with no significant between-group differences. Participants with baseline FAC 1 had significantly greater improvement in motor sub-score of FIM (FIM-motor) compared to controls (mean difference 8.4, 95% CI 0.65–16.07, $\eta_p^2 = 0.136$, $p = 0.034$). The mean distance walked per session for ORE group was almost three times that of control for those with baseline FAC 0 (121.5 [SD 31.1]m vs 35.0 [SD 41.0]m, 95% CI 62.2–110.9, $d = 2.54$ $p < 0.001$) and FAC 1 (145.8 [SD 31.6]m vs 52.2 [SD 42.5]m, 95% CI 61.8–125.2, $d = 2.71$, $p < 0.001$). The difference was not observed for FAC 2 to 3 (162.9 [SD 29.2]m vs 134.2 [SD 87.5]m, 95% CI −22.2 to 79.7, $d = 0.41$, $p = 0.252$).

Conclusion In a pragmatic setting, use of ORE for gait training enabled patients with lower ambulatory capacity to walk longer distances during therapy sessions. Patients who required continuous assistance during ambulation (FAC 1) had significantly better gains in FIM-motor compared to conventional therapy, suggesting possible benefit of ORE for this group.

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Trial Registration The trial was registered with clinicaltrials.gov (NCT05659121) on April 14, 2022.
Keywords Stroke, Exoskeleton, Robotic, Gait, Rehabilitation

Background

Studies from across Europe, America and Asia have found that at least 60% of patients have difficulty in ambulation after a stroke [1–3]. Retraining the ability to walk is a priority in post-stroke rehabilitation. Intensity, task-specificity and amount of walking practice is crucial in the rehabilitation of ambulatory function [4] and different types of robotic gait training devices have been developed to augment the intensity and dosage of gait-related training, including exoskeletons and end-effectors [5]. Overground robotic exoskeletons (ORE) have gained popularity in recent years, with advantages of allowing greater interaction with the environment, full weight-bearing, more appropriate sensorimotor integration, more degrees of freedom of movement, greater variability in gait parameters and mobility tasks that can be trained, compared to platform-tethered, body weight-supported robotic devices[6].

Despite multiple studies examining the efficacy of robotic gait training, the role of ORE in real world post-stroke rehabilitation is unclear. A Cochrane review including all electromechanical gait training devices concluded that robotic gait training in combination with physiotherapy increased the odds of independent walking after stroke, with greater benefit in the early phase of stroke [7]. While some studies suggest the benefits of various OREs to improve walking capacity and speed [6], others have reported mixed results[8–12]. Meta-analyses comparing ORE use with conventional therapy post-stroke, which included a heterogenous collection of single- and multi-joint devices, found greater improvement in walking speed, balance, longer-term mobility, with equivocal benefits reported for endurance [13, 14]. However, as data were mostly derived from randomised clinical trials (RCTs), patient selection criteria are typically more stringent, the intensity of therapy, including duration and step count per session and total number of sessions, are typically higher than usual clinical practice, and parameter settings of the device and control interventions are also more strictly controlled. RCTs therefore might provide an inadequate estimate of the actual effectiveness of robotic device in real-world clinical settings [15]. Patients who are typically excluded in RCTs, such as those with recurrent stroke or co-morbidities, may not have the same response rates and magnitude as those reported in RCTs [16].

The aim of this study was to evaluate the effectiveness of ORE in real-world clinical settings by analysing prospectively collected data from a cohort with pragmatic selection criteria and treatment protocol. The "Improving Mobility Via Exoskeleton" (IMOVE) programme, a philanthropy-funded multicentre ORE clinical programme in Singapore which sought to implement the use of EksoGT® ORE at various rehabilitation settings (inpatient and outpatient tertiary, community hospital settings and community day rehabilitation centres) from the acute to chronic phases of rehabilitation. IMOVE patient recruitment, treatment group allocation, treatment dosage, progression and duration of intervention reflected real-world practices, so as to inform clinical practices related to ORE application.

Methods

The IMOVE programme

IMOVE was implemented at 7 sites across 6 organizations in Singapore, targeting individuals requiring gait rehabilitation from acute to chronic stages of recovery, due primarily to neurological diseases. The inclusion and exclusion criteria for IMOVE programme were designed to reflect usual clinical practice and included ORE manufacturer's recommendations [17, 18]. The inclusion criteria included: age 21–90 years old; requiring rehabilitation of mobility due to neurological injuries; Functional Ambulatory Category (FAC) 0–3 [19]; able to follow instructions and tolerate at least 10 minutes of supported standing. Exclusion criteria included severe osteoporosis, uncontrolled medical conditions, expected survival <1 year, wounds at points of contact with the exoskeleton, fixed contractures, unstable fractures or severe pain.

Participants were screened for eligibility for IMOVE by therapists at the various centres. Those who agreed to join the programme provided informed consent. Participants were given the option of participation in ORE or control group. Those in ORE group received 12 sessions of physiotherapy with use of ORE. Those who refused ORE were assigned as control group and received 12 sessions of conventional physiotherapy.

The EksoGT® (EksoBionics, Richmond, CA, USA) was used in gait training for the ORE group. This device may be set to provide fixed or variable assistance based on individual perceived effort, as determined by weight shift targets, torque at the joints and a reference trajectory [20]. Each ORE session lasted one hour and included EksoGT® training and other functional task training such as squats and weight shifts. Step initiation and targets were tailored according to individual

abilities. All participants began their ORE sessions in fixed trajectory mode, with assistance given to both lower limbs. Physiotherapists conducting the ORE sessions were given autonomy in progressing the sessions based on their clinical judgement. However, general principles guided the therapists in their progression. For example, during initial sessions, the assistance for swing phase would be set to adaptive assistance as much as patient needs, before progressing to a set limit of assistance, with settings adjusted according to feedback output from the EksoGT. As participants improved in the volitional control of their limbs, therapists would consider changing from fixed trajectory for both limbs to unilateral fixed trajectory of the paretic limb for stance and swing, while allowing free movement of the unaffected limb for stepping. Amount of assistance given to the paretic limb was adjusted in each session to provide appropriate challenge, number of steps and intensity of training. Each ORE session targeted a moderate level of exertion, measured by the Borg Rating of Perceived Exertion.

Participants in the control group received 12 sessions of conventional physiotherapy for an hour each session, which included strength and flexibility exercises, trunk control and balance training, pre-gait tasks such as weight shifting and stepping practice in standing, and therapist-assisted gait training with or without body weight-support systems, as deemed appropriate by therapists.

Outcome measures of the IMOVE programme were chosen to reflect various aspects of mobility. They included Functional Ambulatory Category (FAC), a 6-point gross measurement of walking ability ranging from 0 (unable to walk) to 5 (independent walking everywhere including stairs) [19]; Rivermead Mobility Index (RMI), a self-reported measure of mobility (gait, balance and transfer) with 14 out of the 15 item rated by the participant and the remaining item rated by observation [21]; Clinical Outcome Variables Scale (COVS), a measure of functional mobility through 10 mobility tasks rated from 13 to 91 which takes into account use of walking aids and environmental barriers [22]; Functional independence Measure (FIM) [23], an 18-item measure of basic daily functional abilities and burden of care rated on a 7-point scale with score from 18 to 126; and the distance walked during each session, which was measured by the number of laps completed along a marked walkway during each session. The mean distance walked was averaged over the 12 sessions. For the ORE group, the number of steps taken during each training session was extracted from the device. All functional measures were performed immediately before and after the 12 intervention sessions for both groups. The assessments were performed by therapists who were not blinded to the group allocation.

Analysis of IMOVE inpatient stroke cohort

We analysed the participants of the IMOVE programme who had (i) a diagnosis of stroke (ischemic or haemorrhagic, of any locations, first or recurrent), (ii) onset of stroke was within 9 months of recruitment, and (iii) received the intervention during the inpatient rehabilitation stay.

Statistical analysis

Statistical analysis was performed using SPSS version 25. For comparison of baseline data and the mean distance walked between the two groups, Welch's *t*-test was used for unequal group sizes. Mann-Whitney *U* test was used to analyse FAC, while Chi square test was used for other categorical data.

To account for bias due to non-random group allocation, we used regression to adjust for baseline differences in the outcome measures as well as stratification of participants based on their baseline FAC value to minimize the bias arising from non-randomised design [24]. For continuous variables, generalised linear model was used with baseline data of the outcome concerned set as a covariate and the group (ORE vs control) was included as fixed factor. For categorical outcomes, binary logistic regression was used with baseline data and group as covariates.

Data was presented as mean (standard deviation, SD) except for FAC, which was presented as median (interquartile range, IQR). For missing data, a complete case analysis approach was taken such that only records with pre- and post-intervention data were used for analysis. All analyses were done based on an alpha level of 0.05.

Ethics approval, study registration and funding

Both the IMOVE programme and the current analysis were approved by the local ethics board (National Healthcare Group Domain-Specific Review Board of Singapore, reference number DSRB 2018/00368 and DSRB 2019/01141) and registered at clinicaltrials.gov (NCT05659121). The IMOVE programme was funded by Temasek Foundation Cares, Trailblazer Foundation, and Community Silver Trust, Singapore.

Results

Between February 2019 to April 2023, there were 296 participants received rehabilitation following strokes under IMOVE programme. Of these, 149 stroke participants in the IMOVE programme fulfilled the criteria of our current study—105 from the ORE group, and 44 from controls (Fig. 1). The ORE group had a lower baseline FAC

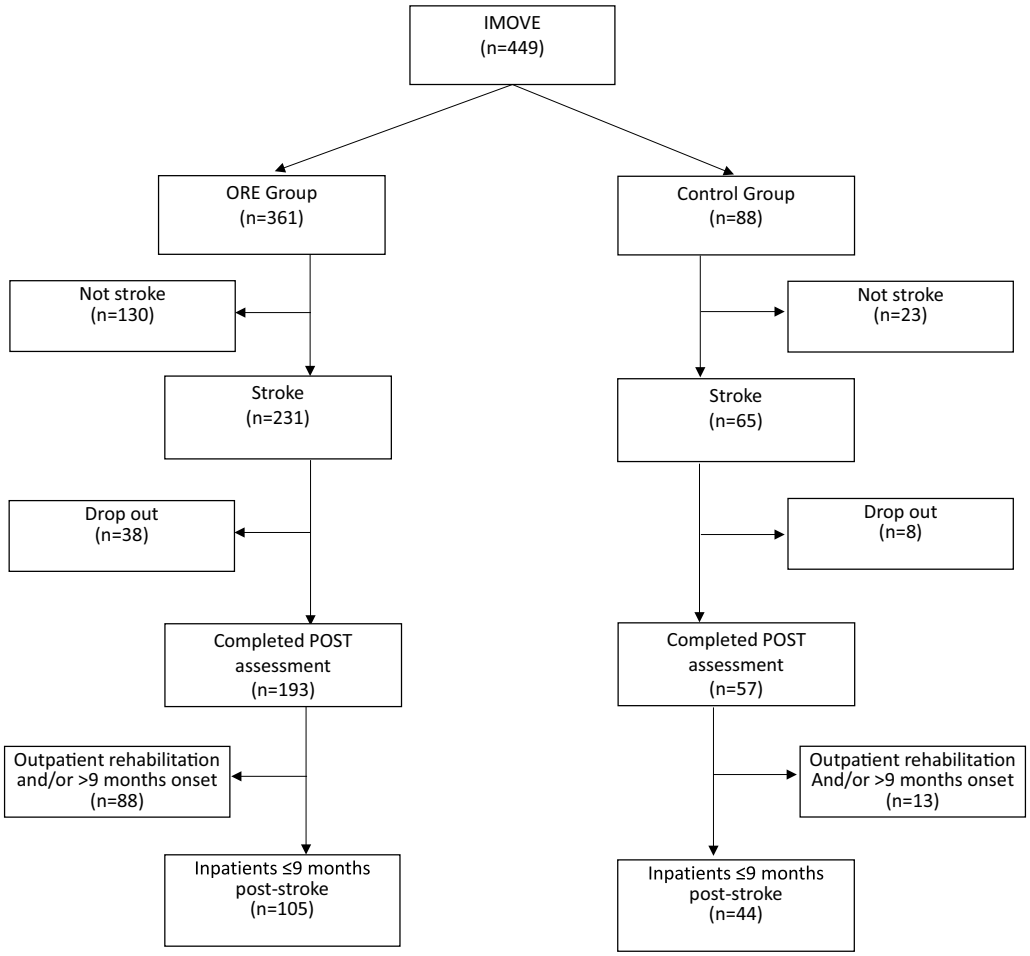

Fig. 1 CONSORT flow diagram

(0.0 [IQR 1.0]) than the control group (1.0 [IQR 2.0]) ($p = 0.013$). Mean time to recruitment was within 1 month of stroke onset in both groups. Other demographic data were not significantly different at baseline (Table 1). Both groups improved significantly in all 4 measures ($p < 0.001$). The ORE group had significantly greater improvement in the cognitive subscore of FIM (FIM-cog) (mean difference 1.0, 95% confidence interval [CI] 0.02–2.01, $p = 0.046$), but was below the minimal clinically important difference (MCID) threshold of 3 [25] and the effect size was small (η_p^2=0.037). Between-group differences were not significant for other outcomes (Table 2b).

When stratified by baseline FAC, those who were FAC 1 at baseline and received ORE, had significantly better improvements in FIM motor sub-score (FIM-motor) (18.7 [SD 9.8]) than controls (10.7 [SD 7.4]) (mean difference 8.4, 95% CI 0.65–16.07, $\eta_p^2 = 0.136$, $p = 0.034$), and only the mean improvement in the ORE surpassed the MCID threshold of 17 [25]. FIM-cog improved significantly in the ORE group from 28.9(SD 6.5) to 31.0(SD 5.3) ($p = 0.006$) but not for controls (29.3[SD 7.4) to 29.4 [SD 7.4], $p = 0.347$). Between-group difference was not significant (mean difference 1.9, 95% CI −0.21 to 4.04, $\eta_p^2 = 0.099$, $p = 0.075$). There was a trend towards better performance in the rest of the mobility outcomes scores (FAC, RMI and COVS) in the ORE group compared to controls in the FAC 1 sub-group, although these did not reach statistical significance. For those with baseline FAC 0 or 2 to 3, all outcome measures improved post-intervention in both groups with no significant differences found between groups (Table 2).

Overall, the mean distance walked by the stroke cohort (FAC 0–3) during therapy with the ORE was almost twice that of the control group. The difference was significant and more marked in the FAC 0 and 1 subgroups (121.5 [SD 31.1]m vs 35.0 [SD 41.0]m, 95% CI 62.2–110.9, $d = 2.54$, $p < 0.001$ for FAC 0; and 145.8 [SD 31.6]m vs 52.2 [SD 42.5]m, 95% CI 61.8 to 125.2, $d = 2.71$, $p < 0.001$ for FAC 1); but not significant for the FAC 2 to 3 subgroup (162.9 [SD 29.2]m vs 134.2 [SD 87.5]m, 95% CI −22.2

Table 1 Baseline data

		ORE	Control	*p* value
Gender n (%)	M	77 (73.3%)	30 (68.2%)	0.524
	F	28 (26.7%)	14 (31.8%)	
Side of weakness n (%)	Left	54 (51.9%)	27 (61.4%)	0.509
	Right	45 (43.3%)	16 (36.4%)	
	Bilateral	5 (4.8%)	1 (2.3%)	
Time since onset (days) Mean(SD)		26.5 (15.4)	28.8 (30.2)	0.629
Age (years) Mean(SD)		58.5 (10.5)	59.7 (11.7)	0.563
Baseline FAC n (%)	0	53 (50.5%)	16 (36.4%)	0.017*
	1	36 (34.3%)	11 (25.0%)	
	2	15 (14.3%)	15 (34.1%)	
	3	1 (1.0%)	2 (4.5%)	
FIM-motor Mean(SD)		42.8 (9.4)	46.1 (12)	0.137
FIM-cog Mean(SD)		25.7 (7.2)	27.2 (7.6)	0.307
RMI Mean(SD)		3.9 (2.9)	4.1 (3.0)	0.735
COVS Mean(SD)		41.6 (12)	45.6 (14.8)	0.140

ORE Overground robotic exoskeleton, *FAC* Functional Ambulatory Category, *FIM* Functional Independence Measure, *FIM-motor* motor sub-score of FIM, *FIM-cog* cognitive sub-score of FIM, *RMI* Rivermead Mobility Index, *COVS* Clinical Outcome Variables Scale, *SD* Standard deviation

to 79.7, $d = 0.41$, $p = 0.252$) (Fig. 2). In the ORE group, the mean step-count per session increased with better baseline FAC, ranged from 412.2(SD 120.8) for FAC 0 to 516.5(SD 151.0) for FAC 2-3, with an average of 455.4(SD 140.7) overall (Fig. 2 and Supplementary Table S1).

Due to administrative reasons, there were missing data for most of the outcomes with the exception of FAC. Sensitivity analysis showed no between-group differences among those with and without missing data (Supplementary Table S2).

Discussion

To the best of our knowledge, this is the largest prospective, pragmatic study comparing mobility outcomes of participants with stroke between ORE and conventional therapy. In this cohort of participants with a pragmatic selection criteria, we found ORE significantly increased the distance walked during therapy for those severely impaired (FAC 0–1), but not for those more mildly affected (FAC 2–3). The motor outcomes were similar between those who received ORE and those who received conventional therapy only, with the exception of better FIM-motor gains for those who required continuous manual contact during ambulation at baseline (FAC 1), suggesting that those moderately impaired might respond more readily to ORE.

Previous controlled trials have reported the benefits of robotic gait training in those who are initially non-ambulatory, and in the initial months post-stroke [7]. Pragmatic studies better reflect the benefits of interventions in real-world practices, where patients are not rigorously selected, protocols are not strict nor conditions ideal, and where treatment teams may not be highly experienced [26]. All patients who were judged to benefit from ORE were recruited, and therapists made clinical decisions on goals, treatment dose, tasks and progression according to their usual practices in IMOVE. One clear difference to previous published trials was the dose of training delivered. As compared to the 800–1200 steps/ session typically reported in clinical trials that demonstrated superior mobility outcomes in non-ambulatory subacute stroke patients [27, 28], our ORE group achieved a mean of 455 steps/session. This dose is similar to that reported from retrospective analysis of an inpatient rehabilitation programme using the same ORE [17] and reflects what was practical within a typical hour-long session in an inpatient clinical setting, with multiple competing priorities in terms of functional goals and tasks to be trained. The relatively low dose and number of sessions may account for the lack of observed benefit in FAC, COVS and RMI in general. For the non-ambulatory group (baseline FAC=0), more sessions may be required and modest functional gains may not be reflected in the measures of mobility used. Number of repetitions is critical in locomotor interventions to promote motor learning and neuroplasticity, with a clear dose-response relationship [4, 29]. While studies of optimal dosage of ORE training are lacking, step-counts of >1000 were required in animal models to induce locomotor improvement after neural injury [30]. Most trials with robotic gait training that have reported positive outcomes with robotic gait training, had programmes over 800–1200 min, 5 days a week for 4 weeks [31]. Programmes lasting >4 weeks showed significantly better mobility outcomes with greater effect size [13, 14]. Appropriate dosing needs to take into consideration severity of motor as well as non-motor impairments. Those with greatest motor impairment are also more likely to have non-motor impairments and to make more protracted recovery with poorer outcomes [1]. The lack of observable between-group differences in the most severe and mildly impaired patients may also be related to the responsiveness of the scales and/ or a floor or ceiling effect [31–33].

In our study, we observed greater gains in FIM-motor gains without observed difference in FAC improvement in the FAC 1 subgroup. Others have reported similar FIM-motor gains with tethered robotic exoskeleton

Table 2 Comparison of outcome measure between two groups

(a) FAC

		n	Pre-intervention (T1)[a]	Post-intervention (T2)[a]	Number (%) with FAC improvement ≥1	*p* value
All FAC	ORE	105	0.0 (1.0)	2.0 (3.0)	89 (94.8%)	0.917[b]
	Control	44	1.0 (1.0)	3.0 (2.0)	36 (83.7%)	
Baseline FAC =0	ORE	53	0.0 (0.0)	1.0 (1.0)	43 (81.1%)	0.293
	Control	16	0.0 (0.0)	1.5 (3.0)	11 (68.8%)	
Baseline FAC=1	ORE	36	1.0 (0.0)	3.0 (2.0)	34 (94.4%)	0.675
	Control	11	1.0 (0.0)	2.0 (1.0)	10 (90.9%)	
Baseline FAC = 2 to 3	ORE	16	2.0 (0.0)	4.0 (2.0)	12 (75.0%)	0.144
	Control	17	2.0 (0.0)	4.0 (1.0)	15 (93.8%)	

(b) COVS, RMI and FIM

							T1 vs T2	ORE vs Control		
			n	Pre-intervention (T1)[c]	Post-intervention (T2)[c]	T2–T1[c]	*p* value	Mean difference (95% CI)	η_p^2	*p* value
All FAC	COVS	ORE	97	41.6 (12.0)	57.4 (14.7)	15.8 (10.0)	<0.001*	−0.2 (−4.02 to 3.56)	0.000	0.905
		Control	37	45.6 (14.8)	61.2 (15.2)	15.5 (9.8)	<0.001*			
	FIM-motor	ORE	70	42.8 (9.4)	57.7 (13.6)	14.9 (9.4)	<0.001*	0.8 (−2.95 to 4.63)	0.002	0.662
		Control	40	46.1 (12.0)	60.2 (15.0)	14.1 (9.7)	<0.001*			
	FIM-cog	ORE	70	25.7 (7.2)	28.4 (5.8)	2.8 (3.5)	<0.001*	1.0 (0.02 to 2.01)	0.037	0.046*
		Control	40	27.2 (7.6)	28.6 (6.5)	1.4 (2.2)	<0.001*			
	RMI	ORE	85	3.9 (2.9)	7.6 (3.9)	3.7 (3.4)	<0.001*	0.3 (−0.98 to 1.54)	0.002	0.660
		Control	39	4.1 (3.0)	7.4 (3.9)	3.4 (3.3)	<0.001*			
Baseline FAC= 0	COVS	ORE	50	33.4 (8.1)	49 (12.3)	15.6 (11.4)	<0.001*	−2.1 (−8.51 to 4.37))	0.007	0.523
		Control	16	35.3 (12.0)	52.4 (15.1)	17.2 (11.0)	<0.001*			
	FIM-motor	ORE	35	37.3 (7.7)	49.7 (9.4)	12.5 (7.9)	<0.001*	−0.7 (−6.06 to 4.72)	0.001	0.803
		Control	15	35.1 (11.4)	48.9 (13.2)	13.7 (11.1)	<0.001*			
	FIM-cog	ORE	35	22.6 (6.8)	26.2 (5.5)	3.7 (3.7)	<0.001*	0.8 (−0.95 to 2.53)	0.018	0.365
		Control	15	22.3 (7.8)	25.3 (6.4)	2.9 (2.8)	0.001*			
	RMI	ORE	40	2.8 (2.6)	5.8 (3.3)	3.0 (3.4)	<0.001*	0.4 (−1.46 to 2.3)	0.004	0.653
		Control	15	3.4 (2.7)	5.7 (3.5)	2.3 (2.9)	0.009*			
Baseline FAC= 1	COVS	ORE	33	48.6 (8.1)	65.8 (11.2)	17.1 (9.3)	<0.001*	4.1 (−2.04 to 10.26)	0.043	0.184
		Control	11	48.1 (9.2)	61.2 (11.3)	13.1 (6.6)	<0.001*			
	FIM-motor	ORE	25	45.8 (7.0)	64.6 (12.4)	18.7 (9.8)	<0.001*	8.4 (0.65−16.07)	0.136	0.034*
		Control	9	50.0 (8.1)	60.7 (11.3)	10.7 (7.4)	0.003*			
	FIM-cog	ORE	25	28.9 (6.5)	31.0 (5.3)	2.1 (3.5)	0.006*	1.9 (−0.21 to 4.04)	0.099	0.075
		Control	9	29.3 (7.4)	29.4 (7.4)	0.1 (0.3)	0.347			
	RMI	ORE	31	4.6 (2.7)	9.2 (3.3)	4.6 (3.1)	<0.001*	1.9 (−0.32 to 4.06)	0.071	0.093
		Control	11	3.1 (1.9)	6.4 (3.3)	3.3 (3.0)	0.005*			
Baseline FAC= 2 to 3	COVS	ORE	14	54.1 (9.9)	67.9 (11.6)	13.8 (4.9)	<0.001*	−3.6 (−10.21, 2.96)	0.059	0.265
		Control	10	59.5 (11.3)	75.1 (7.3)	15.6 (11.1)	0.002*			
	FIM-motor	ORE	10	54.4 (5.8)	68.5 (13.0)	14.1 (10.8)	0.003*	−2.3 (−10.82, 6.19)	0.014	0.579
		Control	16	54.2 (4.5)	70.6 (10.7)	16.4 (9.5)	<0.001*			
	FIM-cog	ORE	10	28.3 (5.5)	29.7 (5.5)	1.4 (1.8)	0.034*	0.6 (−0.52, 1.75)	0.052	0.273
		Control	16	30.5 (5.1)	31.2 (5.0)	0.7 (0.9)	0.015*			
	RMI	ORE	14	5.5 (3.4)	9.3 (4.3)	3.8 (3.8)	0.002*	−1.0 (−3.77, 1.78)	0.022	0.467
		Control	13	5.7 (3.5)	10.4 (3.4)	4.7 (3.8)	0.001*			

[a] Data expressed as Median (Interquartile range)

[b] Adjusted for baseline differences

Table 2 (continued)

[c] Data expressed as mean (standard deviation)

ORE Overground robotic exoskeleton, *FAC* Functional Ambulatory Category, *FIM* Functional Independence Measure; *FIM-motor* motor sub-score of FIM; *FIM-cog* cognitive sub-score of FIM; *RMI* Rivermead Mobility Index, *COVS* Clinical Outcome Variables Scale, *CI* Confidence Interval

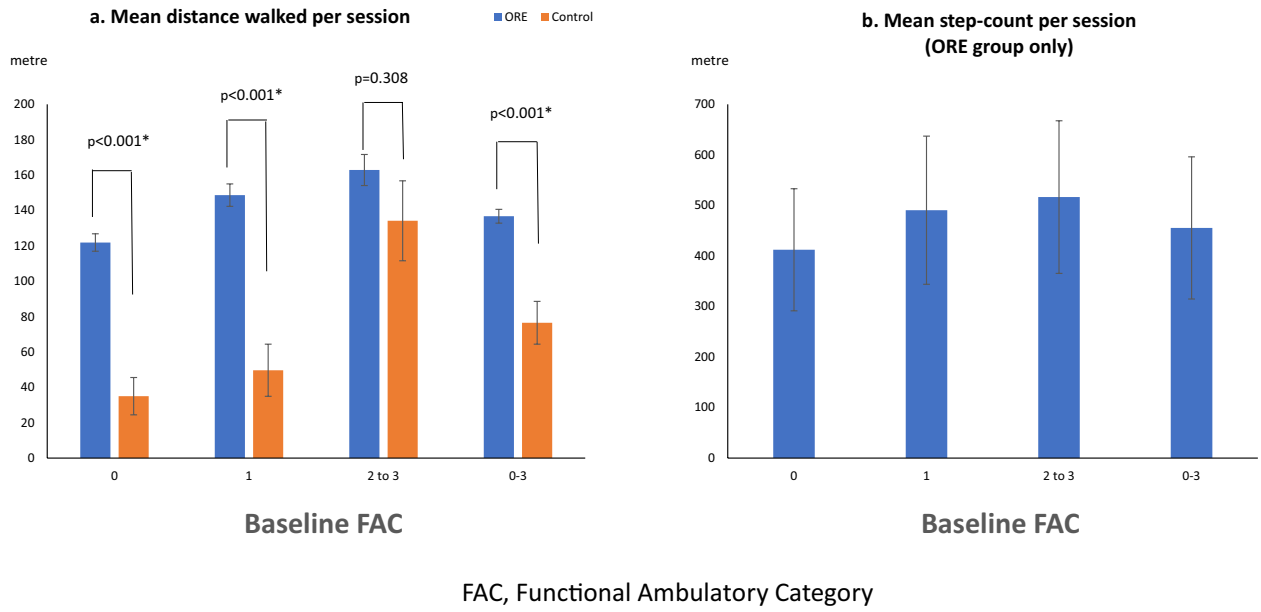

Fig. 2 Mean distance walked and step-count per session

training despite no difference in FAC gains in non-ambulatory inpatient stroke patients [34]. Apart from the difference in responsiveness of these measures, this dichotomy could reflect the benefits of ORE for improving balance and trunk control, which may not be reflected in FAC improvement, but which correlates well with FIM-motor gains in early stroke rehabilitation [35–37]. Other non-ambulatory benefits of ORE such as muscle mass and composition [38], aerobic capacity [39], muscle activation and brain connectivity [12] may also contribute to better activity tolerance, muscle activation, and better engagement in therapeutic activities, resulting in greater FIM-motor gains. These benefits have not been consistently reported and more studies are needed to determine the non-ambulatory benefits of ORE training. However, the small sample size and missing data in the subgroup analysis may also lead to spurious observed benefit.

We found no benefit of ORE for those FAC 2 and 3 at baseline. ORE imposes constraints on movement and may restrict the range of mobility tasks trained [6]. This, and the lack of difference in distance walked during therapy, are likely to contribute to the lack of benefit. Similar findings have been reported by others for those ambulatory at baseline [8, 40, 41].

Greater FIM-cog improvement was observed with ORE in the overall inpatient stroke group. Aerobic exercise has positive effects on cognitive domains such as attention and memory [42]. The higher number of repetitions in the ORE group may contribute to this, although this benefit needs to be confirmed in larger controlled trials.

The main limitation of the study is that results were derived from a pragmatic clinical programme. There is selection bias due to the non-randomised allocation, patients who were more impaired and younger were more likely to choose ORE [17]. We used regression and stratification based on baseline FAC to reduce for the selection bias [24] as baseline FAC was the most obvious unbalanced factor between ORE and control group. However, the subgroups are relatively small. In addition, other confounding factors such as history of stroke, cognitive impairment, comorbidities, spasticity, sensory impairment and ataxia, body weight and height were not controlled for in the regression. The assessments were also not blinded which could lead to bias. Due to the pragmatic design, we gave general guidance to the centres with regards to patient selection and ORE training progression and allowed therapists to use their own clinical judgment to decide on the modes and progression of the training. The lack of a standardized training

protocol might lead to variability in ORE intervention and outcomes. There was missing data due to administrative reasons. Nevertheless, using complete case analysis may also contribute to bias. The uneven group size might affect statistical power [43]. Lastly, data was not available to assess longer term benefits of the programme. Despite the limitations inherent to a pragmatic study, this analysis provides important insights into patient selection for ORE training and dosage of training in real-world clinical practice.

Conclusions

In this analysis of a pragmatic clinical implementation programme of ORE for gait training, ORE was able to deliver significantly higher doses of training for non-ambulatory stroke patients. The gains in ambulatory function were similar between the two groups, although participants who were initially FAC 1 had better gains in motor function (FIM-motor) compared to controls. While those with moderate mobility limitation appear to benefit more readily from ORE training, consideration of other factors may be needed for those with severe mobility limitation, including dose of training. We found no benefit of ORE for those with milder mobility limitations in terms of dosage of training and functional gains. Our findings highlight the need for careful patient selection and consideration of training dosage to maximise the benefits of ORE. Future studies should focus on determining optimal dosage and duration of ORE intervention, according to severity of deficits and prognostic indicators.

Abbreviations

ORE	Overground robotic exoskeleton
FAC	Function Ambulatory Category
FIM	Functional Independecne Measure
FIM-motor	Motor subscore of FIM
FIM-cog	Cognitive subscore of FIM
COVS	Clinical Outcome Variable Scale
RMI	Rivermead Mobility Index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12984-024-01536-1.

Additional file 1.

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Author contributions

EC and RS designed and directed the study. NSBK, RS, ICA, JPPT, SMG, YCL, TYY and RLL were involved in subject recruitment and assessment. EC, PKT and TN were involved in data analysis and drafting of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the National Healthcare Group Domain-Specific Review Board of Singapore (2018/000368 and 2019/01141). All participants provided written informed consent to take part in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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