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Study Protocol Sequenced Hybrid Electromechanically Assisted and Conventional Gait Training for Concurrent Optimization of Weight Management, Blood Pressure Regulation, and Functional Mobility in Chronic Stroke Survivors: A Multicenter Randomized Controlled Trial

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Ethical Approval: Obtained from institutional review boards of all participating centers
Registration: https://doi.org/10.6084/m9.figshare.30983740 Data
OSF Reg https://osf.io/bf3jd/overview
Preprint https://osf.io/preprints/mediarxiv/hm8ze_v1

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1. **Background & Rationale** Stroke is a leading cause of long-term disability and death worldwide, with chronic survivors often experiencing gait disturbances (affecting up to 80%), reduced physical activity, and cardiometabolic comorbidities like obesity and hypertension. These increase risks of recurrent events and diminish quality of life. Electromechanically assisted gait training (EAGT) provides high-intensity, repetitive practice, while conventional gait training (CGT) enhances real-world functional transfer. Evidence gaps exist in the optimal sequencing of these approaches for concurrent improvements in weight management, blood pressure (BP), and mobility, particularly in high-risk chronic stroke populations. This multicenter RCT addresses these gaps by evaluating a sequenced hybrid protocol.
2. **Objectives & Hypotheses Primary Objective**: Evaluate the efficacy of sequenced hybrid EAGT followed by CGT compared to EAGT-only or CGT-only in promoting concurrent improvements in body weight, BP, and gait parameters in chronic stroke survivors with overweight/obesity and hypertension. Secondary Objectives: Assess retention of gains at 3-month follow-up; explore mechanistic insights into cardiometabolic loading; identify prognostic factors.

Hypotheses: Hybrid sequencing leads to greater weight loss (≥3 kg) and systolic BP reduction (≥10 mmHg) without compromising gait improvements. Obese participants (BMI ≥30 kg/m²) show stronger cardiometabolic responses. Gains are retained better in the hybrid group at follow up.

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3. **Study Design** Prospective, assessor-blinded, three-arm parallel-group RCT Allocation: 1:1:1 Duration: 12 weeks intervention + 3-month follow-up (total 6 months) Setting: Five rehabilitation centers in Pakistan (e.g., Swat Psychiatric Care & Rehabilitation Center,

   Al-Makki Rehabilitation Center, Hashoo Foundation Rehabilitation Center, Model Addiction Treatment & Rehabilitation Centre - Swat, and one additional site).

4. **Participants Inclusion**: Age 45–78; ischemic/hemorrhagic stroke ≥6 months prior; Functional Ambulation Category (FAC) ≥3; BMI ≥25 kg/m²; systolic BP ≥130 mmHg (stable antihypertensives allowed); able to provide informed consent. Exclusion: Unstable cardiovascular conditions; severe cognitive impairment (MMSE <20); other neurological disorders affecting gait; musculoskeletal issues limiting training; recent intensive exercise programs; life expectancy <12 months. Recruitment: Outpatient clinics, stroke registries, referrals, community outreach. Target sample: 144 (48 per group) Sample size justification: Detect 3 kg weight change (SD 4 kg) and 10 mmHg systolic BP change (SD 12 mmHg), 80% power, α=0.05, 15% attrition, accounting for multicenter clustering (ICC 0.01).
5. **Randomization & Blinding Sequence**: Computer-generated permuted blocks (sizes 3,6,9), stratified by FAC (3 vs. ≥4) and BMI (25–29.9 vs. ≥30 kg/m²) Concealment: Secure web-based central system (backup: sequentially numbered, opaque envelopes) Implementation: Site coordinators enroll; independent platform assigns Blinding: Assessors and statisticians blinded; participants/therapists unblinded (intervention nature); groups coded in database.
6. **Interventions All groups**: 30 sessions over 12 weeks (3–5/week, 45–60 min), heart rate monitored (60–80% reserve). No additional exercise or diet interventions.

Group A (Hybrid: EAGT → CGT): Weeks 1–6: EAGT (exoskeleton/end-effector devices; 30–50% body-weight support, speed 1.5–2 km/h, ≥800–1200 steps/session). Weeks 7–12: CGT (overground walking, obstacles, stairs, dual-tasks).

Group B (EAGT-only): Full 12 weeks EAGT, progressing parameters for intensity.

Group C (CGT-only): Full 12 weeks CGT, progressing complexity and demands.

7. **Outcome Measures Primary**: Change in body weight; systolic/diastolic BP. Secondary: 10-Meter Walk Test (speed); 6-Minute Walk Test (endurance); Berg Balance Scale; Barthel Index. Timepoints: Baseline, 6 weeks, 12 weeks, 3-month follow-up.
8. **Data Collection & Management Standardized forms**; secure, anonymized electronic

storage; adherence logs (attendance, steps, heart rate, adverse events).

9. **Statistical Analysis Intention-to-treat**; linear mixed-effects models (SPSS v28/R v4.3.2); fixed effects: group, time, interaction; random effects: participant/center;

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multiple imputation for missing data; subgroup analyses (BMI, post-stroke duration); Bonferroni adjustments; effect sizes (η^2p, Cohen's d).

10. Ethical Considerations Written informed consent; data confidentiality; minimized risks (fatigue monitoring); independent data monitoring committee for safety; adherence to Helsinki Declaration and GCP.
11. Timeline Recruitment: January 2022 – June 2024,Follow-up: Until June 2025
12. Protocol Deviations Any deviations will be reported and documented.

Sincerely,
Assistant Registrar

IMRAN KHAN

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