RESEARCH PAPER

"Adaptive Precision Exercise To Optimize Cardiac Performance And Physical Function In Older Adults: Study Protocol Of A Smart Trial"

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ABSTRACT

Background: Older adults often exhibit heterogeneous responses to exercise-based interventions targeting cardiovascular health and physical function. Conventional fixed exercise prescriptions may not adequately address this variability. Sequential Multiple Assignment Randomized Trial (SMART) designs provide a framework for developing adaptive, response-guided interventions.

Objective: To evaluate the feasibility and preliminary effects of an adaptive precision exercise intervention, developed using a SMART approach, on resting blood pressure, functional capacity, and knee-related physical function in older adults.

Methods: This pilot SMART trial enrolled 30 older adults (60–75 years) who completed a 12-week supervised exercise program. All participants received a standardized combined aerobic and resistance exercise intervention during Stage 1 (Weeks 0–6). At Week 6, participants were classified as responders or non-responders based on predefined changes in systolic blood pressure, functional capacity (6-Minute Walk Test), or knee function (WOMAC Index). Responders continued the initial program with progression, while non-responders were re-randomized to either aerobic intensification or strength–neuromuscular-focused exercise during Stage 2 (Weeks 7–12). Outcomes were assessed at baseline, Week 6, and Week 12.

Results: Overall, significant improvements were observed from baseline to Week 12. Resting systolic blood pressure decreased from 146.2 ± 9.8 mmHg to 134.5 ± 8.6 mmHg (mean change −11.7 mmHg, $p < 0.001$), and diastolic blood pressure decreased from 89.6 ± 6.4 mmHg to 82.1 ± 5.7 mmHg (mean change −7.5 mmHg, $p < 0.001$). Functional capacity improved, with a mean increase of 56.5 m in the 6-Minute Walk Test ($p < 0.001$), and total WOMAC scores decreased by 18.9 points ($p < 0.001$). At the Week-6 decision point, 18 participants (60%) were classified as responders and demonstrated significantly greater improvements than non-responders ($p < 0.001$). Among non-responders, aerobic intensification yielded greater improvements in blood pressure and functional capacity, while the strength-focused strategy resulted in superior knee function improvements.

Conclusion: This pilot SMART trial demonstrates the feasibility of implementing an adaptive precision exercise intervention in older adults and suggests that response-guided exercise adaptation may enhance cardiovascular and functional outcomes. The findings provide preliminary support for future fully powered SMART trials to optimize adaptive exercise strategies in geriatric rehabilitation..

Keywords: Adaptive exercise, SMART design, older adults, blood pressure, functional capacity, precision rehabilitation

How to cite this article: Verma A, Nallathambi M, B S, Saxena A, Babu J, Bisht H, Mou I, Sarkar R.., "Adaptive Precision Exercise To Optimize Cardiac Performance And Physical Function In Older Adults: Study Protocol Of A Smart Trial".Int J Drug Deliv Technol. 2026;16(2s): 861-869; DOI: 10.25258/ijddt.16. 861-869

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Population aging is associated with progressive deterioration in cardiovascular efficiency, skeletal muscle mass, and neuromuscular coordination, resulting in reduced exercise tolerance and functional independence in older adults[1]. Age-related structural and functional changes, including arterial stiffening, endothelial dysfunction, and impaired cardiac autonomic regulation, contribute to elevated blood pressure and reduced cardiac reserve[2]. These

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changes significantly increase the risk of cardiovascular morbidity, frailty and disability[3].

Exercise therapy is a well-established non-pharmacological strategy for improving cardiac performance and physical function in older adults[4]. Aerobic exercise enhances endothelial function, improves autonomic balance, and reduces resting blood pressure, thereby lowering cardiovascular risk[5]. Resistance training counteracts sarcopenia, improves muscle strength, and enhances mobility and balance, which are critical determinants of functional independence[6]. Evidence suggests that combined aerobic and resistance exercise programs produce superior improvements in cardiovascular health and physical function compared to single-modality interventions[7].

Despite strong evidence supporting exercise therapy, conventional rehabilitation programs often rely on standardized exercise prescriptions, assuming uniform physiological responses among participants[8]. However, older adults demonstrate substantial inter-individual variability in exercise adaptation due to differences in comorbidities, medication use, baseline fitness, and recovery capacity[9]. Consequently, a significant proportion of individuals fail to achieve clinically meaningful improvements in blood pressure, endurance, or functional performance when exposed to uniform exercise protocols[10].

Precision exercise aims to individualize exercise prescription by adjusting intensity, volume, and modality based on patient-specific characteristics and early response indicators[11]. Adaptive exercise interventions allow timely modification of training parameters when predefined clinical targets are not met, thereby optimizing effectiveness while maintaining safety[12]. Such approaches are particularly relevant in older adults, where excessive training loads may provoke adverse cardiovascular responses, fatigue, or musculoskeletal injury[13].

SMART design in rehabilitation research

Sequential Multiple Assignment Randomized Trial (SMART) designs provide a robust methodological framework for developing and testing adaptive intervention strategies[14]. Unlike traditional randomized controlled trials, SMART designs permit re-randomization of non-responders to alternative intervention options, facilitating the identification of optimal dynamic treatment regimes[15]. These designs are increasingly advocated for complex rehabilitation and behavioral interventions that require flexibility and personalization[16].

Although adaptive and precision-based exercise strategies are gaining attention in chronic disease management, their application in geriatric cardiac and functional rehabilitation remains limited[17]. There is a clear need for evidence-based adaptive exercise protocols that simultaneously optimize cardiac performance and physical function in older adults. Therefore, this study aims to present the protocol of a SMART trial evaluating an adaptive precision exercise program designed to enhance cardiovascular performance and functional outcomes in older adults.

METHODOLOGY

Study Setting

Participants will be recruited from outpatient physiotherapy and community health centers. Recruitment will be conducted through physician referral and physiotherapy screening clinics.

Target Population

The target population comprises **older adults** with age-related cardiovascular risk and functional limitations who are suitable for structured exercise-based rehabilitation.

Inclusion Criteria

Age **60 to 75 years**

Resting systolic blood pressure between **130–160 mmHg**, with or without antihypertensive medication

Ability to ambulate independently with or without an assistive device

Presence of self-reported knee pain or functional limitation during daily activities

Medical clearance for participation in moderate-intensity exercise

Exclusion Criteria

Unstable cardiovascular disease (e.g., uncontrolled arrhythmia, recent myocardial infarction within 6 months)

Severe musculoskeletal disorders limiting exercise participation (e.g., advanced knee osteoarthritis requiring surgery)

Neurological disorders affecting mobility or balance

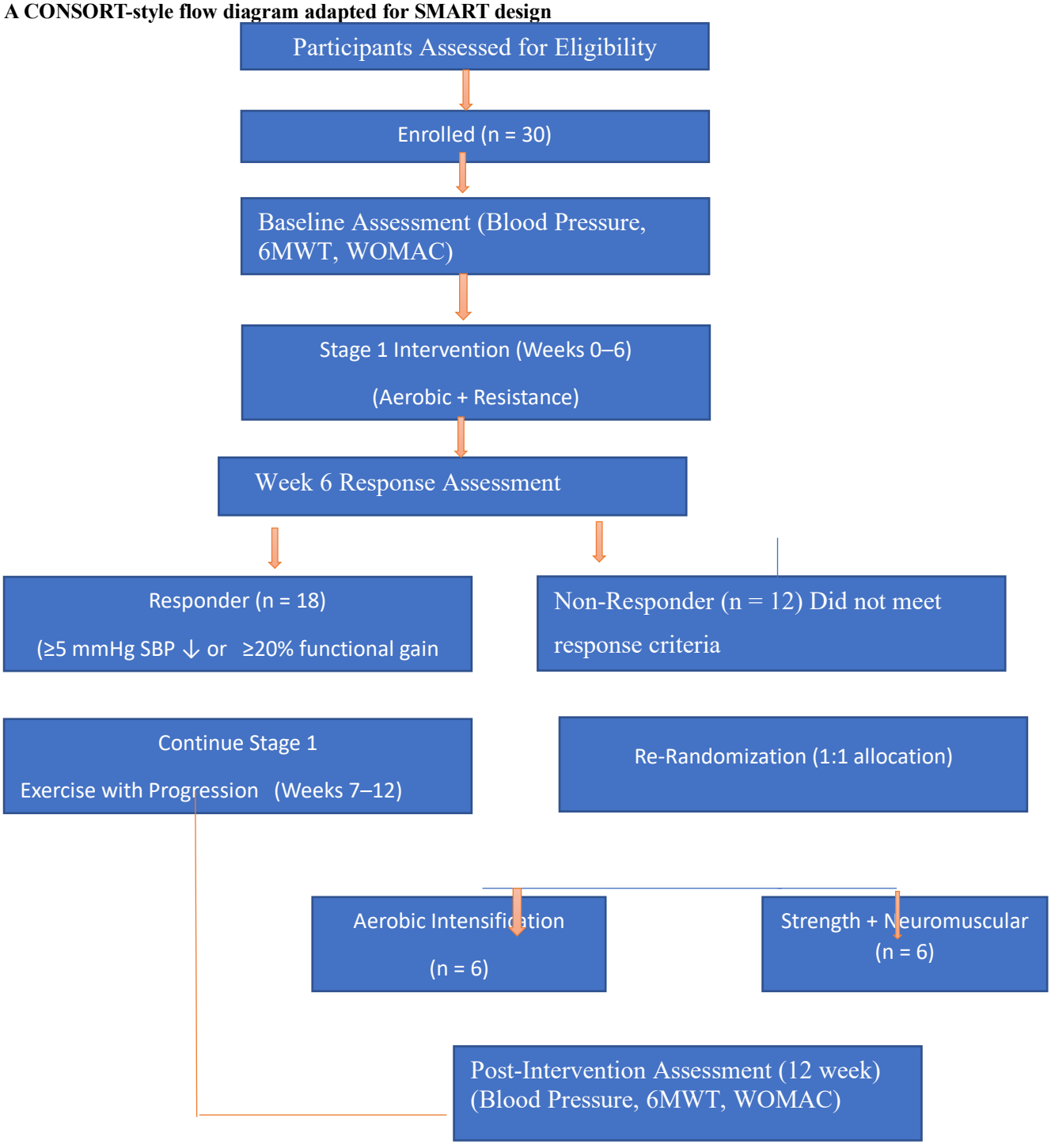
Cognitive impairment preventing understanding of instructions or informed consent

Participation in structured exercise programs within the previous 3 months

Sample Size Considerations

A total sample size of **30 participants** is selected for this pilot SMART trial.

A CONSORT-style flow diagram adapted for SMART design



INTERVENTION PROTOCOL
The intervention consists of a **two-stage adaptive precision exercise program** delivered over **12 weeks,** designed using a **Sequential Multiple Assignment Randomized Trial (SMART)** framework. The program includes two intervention stages separated by a predefined decision point at 6 weeks, allowing modification of exercise strategies based on early treatment response.

STAGE 1 INTERVENTION (WEEKS 0–6): INITIAL EXERCISE STRATEGY

Aerobic Training
Participants will perform aerobic exercise using stationary cycling.
Intensity: 40–60% heart rate reserve (HRR)
Duration: 20–30 minutes per session
Frequency: 5 sessions per week
Heart rate and perceived exertion will be monitored to ensure adherence to prescribed intensity.

Resistance training

Resistance training will target major lower-limb muscle groups particularly the quadriceps, hamstrings and hip stabilizers.
Intensity: 60–70% of one-repetition maximum (1RM)
Volume: 2–3 sets of 10 repetitions
Frequency: 3 sessions per week

RESPONSE ASSESSMENT AT 6 WEEKS

At the end of week 6, participants will be classified as **responders or non-responders** based on predefined clinical criteria:
≥5 mmHg reduction in resting systolic blood pressure
≥20% improvement in functional capacity or pain-related outcomes
Early response assessment is critical in adaptive interventions to guide treatment modification and maximize therapeutic benefit.

STAGE 2 INTERVENTION (WEEKS 7–12): ADAPTIVE STRATEGIES

Responders: Continued Standard Exercise with Progression
Non-Responders: Non-responders will undergo **r**

e-randomization to one of two adaptive strategies:

Adaptive Strategy A: Aerobic Intensification
Aerobic intensity progressed to 60–70% HRR
Duration increased to 30–40 minutes
Introduction of interval-based aerobic exercise

Adaptive Strategy B: Strength and Neuromuscular training
Resistance training intensity increased to 70–80% 1RM
Addition of balance and task-oriented functional exercises
Aerobic exercise maintained at moderate intensity

Safety Monitoring
Heart rate, blood pressure and perceived exertion will be monitored throughout all sessions.

OUTCOME MEASURES
Resting systolic and diastolic blood pressure (mmHg)
Functional capacity (6-Minute Walk Test)
Knee function (WOMAC Index)

STATISCAL ANALYSIS
Statistical analyses were performed to evaluate preliminary effects of the adaptive precision exercise intervention and to explore response-guided adaptive pathways within the SMART framework. All **30 participants** who initiated Stage 1 intervention were included in the analysis under an **intention-to-treat approach.**
Responders: n = 18
Non-responders: n = 12

Table: 1 Baseline characteristics

Variables	**mean ± SD**
Age	66.8 ± 4.9 years
Resting SBP	146.2 ± 9.8 mmHg
Resting DBP	89.6 ± 6.4 mmHg
6MWT distance	382.4 ± 52.6 m
WOMAC total score	55.2 ± 9.1

Table: 2 Pre and Post-Intervention Comparison of Resting Blood Pressure

Outcome	Baseline	Week 12	Mean Change	t value	p value
SBP (mmHg)	146.2 ± 9.8	134.5 ± 8.6	11.7	7.42	<0.001
DBP (mmHg)	89.6 ± 6.4	82.1 ± 5.7	7.5	6.18	<0.001

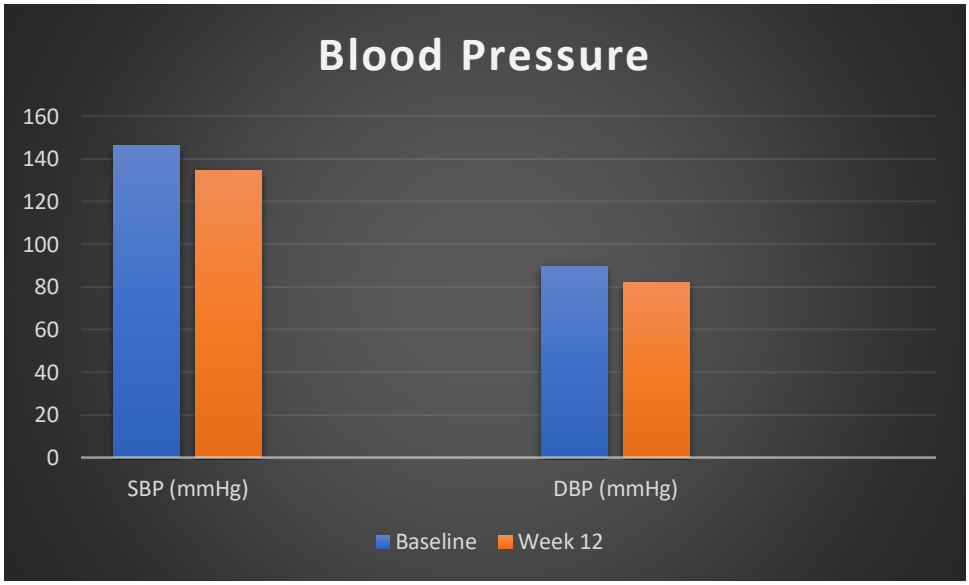


Table: 3 Pre and Post-Intervention Comparison of Functional Capacity (6MWT)

Outcome	Baseline	Week 12	Mean Change	t value	p value
6MWT (m)	382.4 ± 52.6	438.9 ± 55.1	56.5	6.94	<0.001

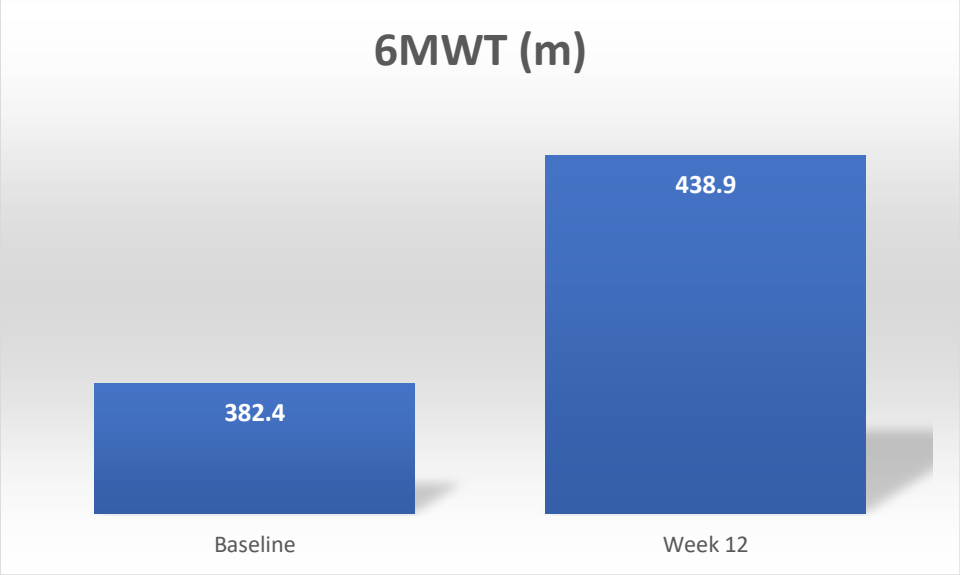


Table: 4 Pre and Post-Intervention Comparison of Knee Function (WOMAC)

Domain	**Baseline**	**Week 12**	**Mean Change**	**p value**
Pain	11.6 ± 2.9	6.8 ± 2.4	4.8	<0.001
Stiffness	5.4 ± 1.6	3.1 ± 1.2	2.3	<0.001
Physical Function	38.2 ± 7.5	26.4 ± 6.8	11.8	<0.001
Total WOMAC	**55.2 ± 9.1**	**36.3 ± 8.4**	**18.9**	**<0.001**

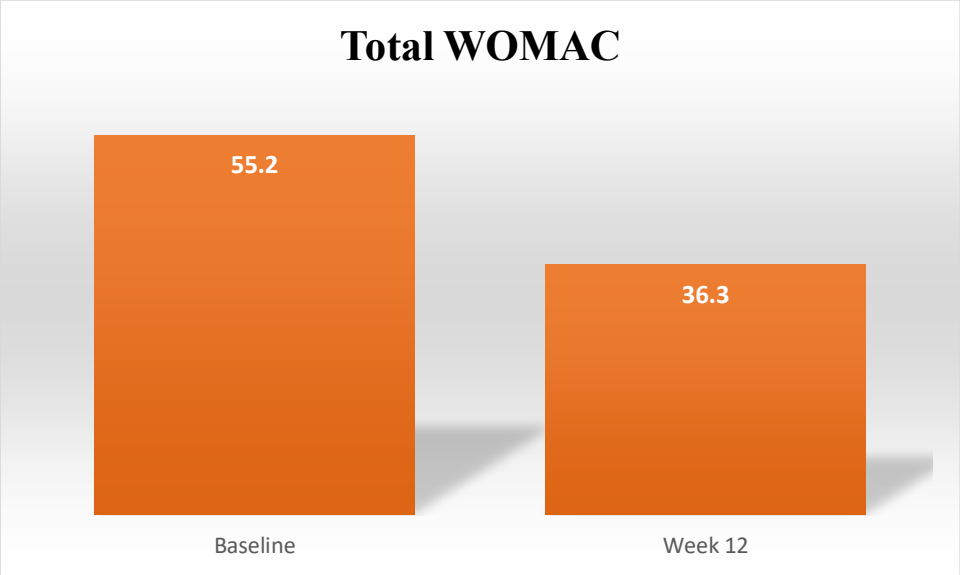


Table: 5 SMART-Based Responder vs Non-Responder Outcomes at Mid-Intervention (Week 6)

Outcome	**Responders (n=18)**	**Non-Responders (n=12)**	**p value**
SBP (mmHg)	8.9 ± 3.4	2.1 ± 2.8	<0.001
6MWT (m)	38.6 ± 14.2	11.4 ± 12.7	<0.001
WOMAC Total	14.1 ± 5.3	5.2 ± 4.8	<0.001

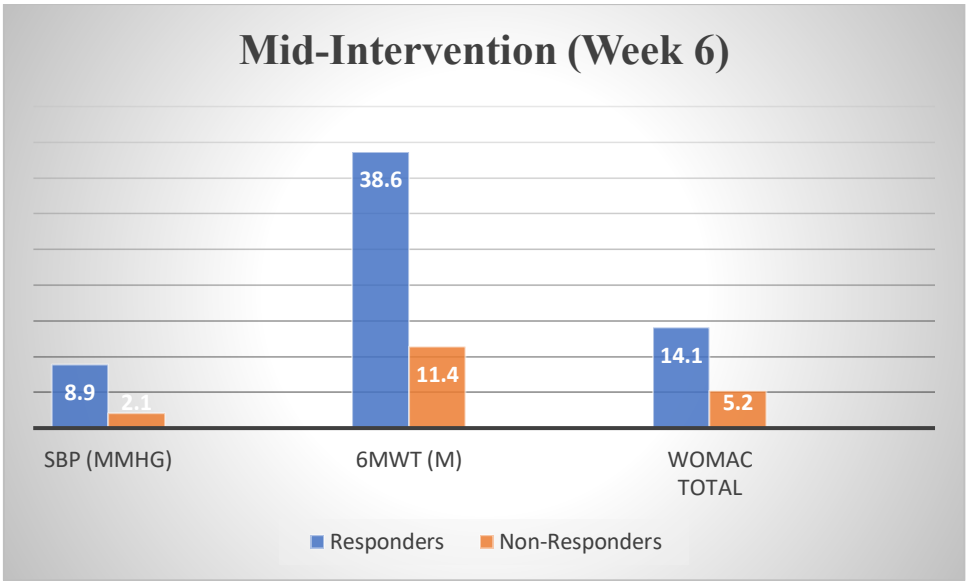
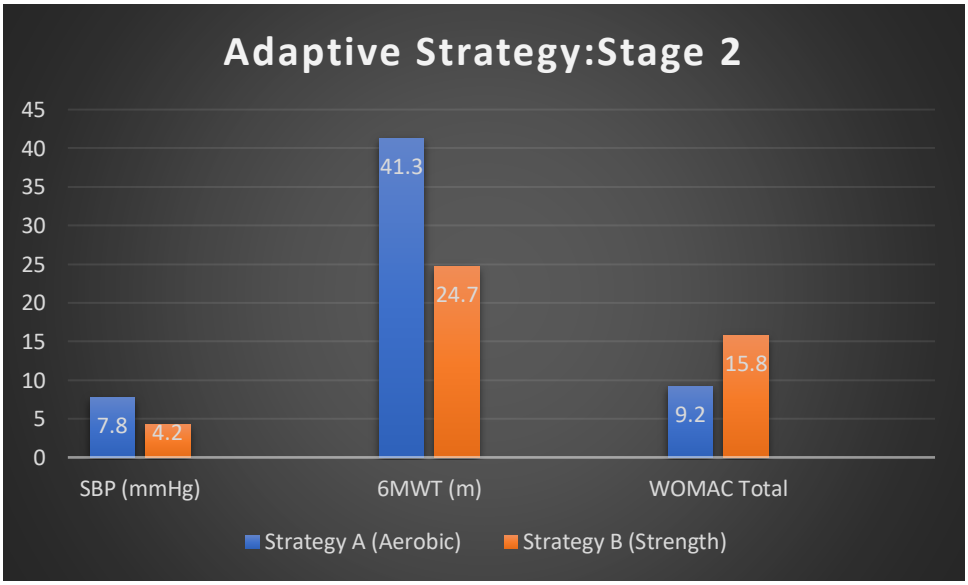


Table: 6 Comparison of Adaptive Strategy Outcomes among Non-Responders during Stage 2 of the SMART Trial

Outcome	Strategy A (Aerobic) n=6	Strategy B (Strength) n=6	p value
SBP (mmHg)	7.8 ± 3.1	4.2 ± 2.9	0.04
6MWT (m)	41.3 ± 15.6	24.7 ± 13.9	0.04
WOMAC Total	9.2 ± 4.1	15.8 ± 5.0	0.01



RESULT:

A total of 30 older adults completed the 12-week adaptive precision exercise intervention. Overall, significant improvements were observed in cardiovascular and functional outcomes. Resting systolic blood pressure decreased from 146.2 ± 9.8 mmHg at baseline to 134.5 ± 8.6 mmHg at Week 12 (mean change −11.7 mmHg, $p < 0.001$), while diastolic blood pressure reduced from 89.6 ± 6.4 mmHg to 82.1 ± 5.7 mmHg (mean change −7.5 mmHg, $p < 0.001$). Functional capacity, assessed by the 6-Minute Walk Test, improved significantly with an increase of 56.5 ± 21.4 m ($p < 0.001$) and knee-related outcomes showed marked improvement, with total WOMAC scores

decreasing from 55.2 ± 9.1 to 36.3 ± 8.4 ($p < 0.001$). At the Week-6 decision point, 18 participants (60%) were classified as responders and demonstrated significantly greater reductions in systolic blood pressure, greater gains in walking distance, and larger improvements in WOMAC scores compared to non-responders ($p < 0.001$ for all). Among non-responders who underwent re-randomization, aerobic intensification resulted in greater improvements in systolic blood pressure and functional capacity, whereas the strength-neuromuscular strategy produced superior improvements in knee-related pain and physical function, indicating differential benefits of adaptive strategies within the SMART framework.

DISCUSSION:

This pilot SMART trial explored the feasibility and preliminary effects of an adaptive precision exercise intervention on cardiovascular and functional outcomes in older adults. The intervention demonstrated clinically meaningful reductions in resting systolic and diastolic blood pressure, along with improvements in functional capacity and knee-related pain and physical function. These findings suggest that response-guided adaptation of exercise strategies may enhance outcomes compared to a uniform exercise prescription[32].

The observed reduction in resting blood pressure following the adaptive exercise program is consistent with previous evidence demonstrating the antihypertensive effects of structured aerobic and combined exercise in older adults.[33,34] Moderate-intensity aerobic exercise improves endothelial function, arterial compliance, and autonomic balance, which collectively contribute to blood pressure reduction[34]. The magnitude of blood pressure change observed in this study is clinically relevant, as even modest reductions in systolic blood pressure are associated with meaningful reductions in cardiovascular risk[35].

Improvements in 6-minute walk distance indicate enhanced submaximal functional endurance, reflecting improved cardiovascular efficiency and mobility[36]. Concurrent reductions in WOMAC pain, stiffness, and physical function scores suggest that the intervention was effective in addressing knee-related functional limitations. Resistance and functional strengthening exercises have been shown to reduce pain and improve physical function in older adults with knee symptoms, supporting the plausibility of the observed improvements[37,38].

A key contribution of this study is the application of a SMART framework to exercise-based rehabilitation in older adults. The responder versus non-responder analysis highlights substantial heterogeneity in early treatment response, reinforcing the limitations of standardized exercise prescriptions[39]. By re-randomizing non-responders to alternative adaptive strategies, the SMART design enabled exploration of multiple dynamic treatment regimes, providing insights into how interventions may be optimized over time[40].

Subgroup analyses suggest that aerobic intensification may be more effective for individuals with inadequate cardiovascular response, whereas strength and neuromuscular emphasis may yield greater improvements in knee-related outcomes. These findings align with the principle of precision exercise medicine, which emphasizes matching exercise modality and dose to individual physiological and functional needs[41]. Although exploratory, these results support the concept that different adaptive strategies may be required to address distinct outcome domains.

From a clinical perspective, the findings underscore the potential benefits of incorporating early response assessment into exercise prescription for older adults. Adaptive exercise strategies may improve efficiency, reduce unnecessary training burden, and enhance patient-centered care. From a research standpoint, this pilot study provides preliminary effect estimates and feasibility data that can inform the design of a fully powered SMART trial aimed at testing optimized adaptive exercise interventions[12].

CONCLUSION:

In summary, this pilot SMART-based study demonstrates the feasibility of implementing an adaptive precision exercise intervention targeting both cardiac performance and physical function in older adults. The findings support the potential value of response-guided exercise adaptation and provide a strong rationale for future optimization-focused trials in geriatric rehabilitation.

CONFLICT OF INTEREST:

None

FUNDING:

None

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