

## CLINICAL VIGNETTE

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# A Novel Hybrid Cardiac and Vascular Rehabilitation Program Versus Standard Care in Patients with Combined Coronary and Peripheral Arterial Disease

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### **Introduction**

Cardiac rehabilitation (CR) has been applied widely to patients with coronary artery disease (CAD) and congestive heart failure (CHF) with excellent results. Enrolling patients in CR reduces mortality and myocardial infarction by 20-30% in patients who undergo percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).<sup>1</sup> In addition, heart failure patients with an ejection fraction < 35% participating in CR programs have experienced improved quality life, reduced hospitalizations and decreased mortality.<sup>2</sup>

Exercise based rehabilitation also offers benefit to patient with symptomatic peripheral arterial disease (PAD). Supervised exercise therapy (SET) has been shown to increase walking times and reduces need for repeat endovascular interventions.

Patients with both CAD and PAD are an especially high risk patient cohort, with mortality increased 60-70% over patients with CAD alone.<sup>3</sup> To date, there has not been a comprehensive exercise-based rehabilitation program targeting patients with concomitant PAD and CAD. This review will describe the background data and protocol for a novel hybrid cardiac and vascular supervised exercise therapy program (HSET) aimed at improving both coronary and peripheral arterial outcomes in this challenging group of patients.

### **Evidence for Cardiac Rehabilitation**

Mounting evidence supports use of CR in patients that have undergone coronary revascularization (PCI or CABG). Medicare patients who attended CR after revascularization experienced a 47% reduced all-cause mortality and a 31% reduction in myocardial infarction (AMI).<sup>4</sup> A Cochrane review of 63 trials involving 14,486 patients, showed a 27% reduction in all-cause mortality in patients who underwent CR versus usual care post coronary revascularization.<sup>5</sup> Exercise tolerance in patients with chronic stable angina also improves with CR, with a meta-analysis of 14 trials statistically reporting significant improvement in exercise capacity.<sup>6</sup> Post-CABG patients were also 70% less likely to be hospitalized if they enrolled in 36 sessions of CR.<sup>7</sup>

Cardiac rehabilitation also confers significant benefit to patients with CHF. The first trial examining CR in CHF was the HF-ACTION trial, which was statistically equivocal due to poor

adherence in the exercise arm.<sup>8</sup> In contrast, the ExTraMATCH study showed exercise training significantly reduced mortality (hazard ratio [HR] 0.65) in patients with chronic CHF, while also meeting statistical significance with the secondary end points of death or re-hospitalization (HR 0.72).<sup>9</sup>

### **Evidence of Supervised Walking Therapy in Symptomatic PAD**

Management of symptomatic peripheral arterial disease (PAD) includes medical therapy and secondary prevention of cardiovascular events, endovascular and surgical revascularization for intermittent claudication (IC), and home-based or SET programs. The goal of SET is to relieve symptoms, improve cardiovascular risk factors, avoid amputations, and preserve walking and functional status.<sup>10</sup> Programs that incorporate walking at least three times per week (30 to 60 minutes per session) for at least 36 sessions are recommended as first line therapy with a Class I, a level of recommendation from both American College of Cardiology and Society for Vascular Surgery.<sup>11,12</sup>

There are several randomized controlled trials supporting the use of SET in management IC. The CLEVER trial compared supervised exercise with stenting in patients with aortoiliac disease who were receiving medical therapy. Supervised exercise resulted in significantly greater mean peak walking time at 6 months (5.8 vs. 3.7 minute).<sup>13</sup> The ERASE trial further sought to assess if SET in combination with endovascular revascularization was superior to SET alone. The primary endpoint was total walking distance (TWD) at 12 months with endpoints measured at 1, 6 and 12 months. Secondary endpoints included quality of life measures. TWD improved significantly in both groups though patients in the combination therapy group had statistically greater improvement in TWD. Quality of life (QOL) scores were also significantly improved in the combination therapy arm, and despite 32 percent of the combination patients experiencing hemodynamically significant restenosis, only four underwent repeat revascularization.<sup>14</sup> In May of 2017, the preponderance of data supporting SET prompted the Centers for Medicare & Medicaid Services (CMS) to cover SET for beneficiaries with intermittent claudication.

## Proposal for a Novel Hybrid Cardiac and Vascular Rehabilitation Program in Patients with Indications for Both

Patients with indications for CR and who have IC represent a particularly high-risk cohort as they are functionally limited, require frequent hospitalization, and have a high mortality. We propose a novel combined cardiac and vascular rehabilitation program (HSET) that combines cardiac assessment and monitoring as is normally performed in CR, however differs from standard CR in that the focus also includes improving claudication symptoms. TWT and TWD, as well as quality of life scores are incorporated into the HSET program. We hypothesize that by combining CR with SET in a comprehensive program, the HSET protocol will maintain the benefits of CR including decreasing mortality and reducing hospitalization, while increasing walking times and reducing the need for endovascular or surgical therapies. Figure 1 graphically represents the proposed trial design. Patients are enrolled in the study either through the cardiac pathway in which they are initially found to have an indication for CR, or through the vascular pathway in which they are found to have symptomatic IC or are post intervention. Table 1 outlines inclusion and exclusion criteria for the study. Patients undergo initial evaluation outlining goals of the program, introduction to the HSET team and protocols, overview of safety precautions, and schedule of classes. Complete chart review will identify potential exclusion criteria. The initial patient interview will involve risk factor assessment and suggestions for modifications including smoking cessation. An initial treadmill test will establish the patient's baseline claudication time. The claudication pain scale, in addition to the Borg Rating of Perceived Exertion scale, will be used to design the initial exercise prescription. Outcomes for the trial include all-cause mortality, cardiovascular mortality, total walking time and distance, QOL inventories including the Duke activity status, Dartmouth and Ferrance and Powers QOL scores, Walking Impairment questionnaire, need for coronary or peripheral intervention, and repeat hospitalization. We believe the HSET program will both decrease cardiovascular mortality, improve QOL, reduce hospitalizations, while reducing the need for repeat peripheral interventions.

### Case Study

The first patient enrolled in the HSET program was a 68-year-old with a history significant for tobacco use, hypertension, hyperlipidemia, diabetes mellitus type 2, who underwent CABG x 2 in addition to aortic valve replacement and mitral valve repair. He had iliac stents placed in 2009 and continued to complain of Rutherford category 3 intermittent claudication symptoms. Figure 2 shows that the patient had significant improvement in total walking time and distance after 36 sessions of the program. Figure 3 shows significant improvement in all QOL scores showing increase in physical fitness, social activity and overall health, as well as increase in walking distance and speed with a decrease in weakness and pain.

## Conclusion

The benefits of CR are well established, including reduction in mortality, improvement in QOL, and reduction in hospitalization. Vascular rehabilitation similarly improves functional status, walking distance, and reduces the need for repeat interventions in patients with intermittent claudication. Patients presenting with the combination of both coronary artery and peripheral arterial disease represent the highest risk cohort of patients. In patients presenting with indications for both cardiac and vascular rehabilitation, we hypothesize that a hybrid rehabilitation program combining both cardiac and vascular rehabilitation will improve both cardiac and vascular outcomes.

Figure 1: Study design for novel hybrid supervised exercise therapy protocol (HSET).

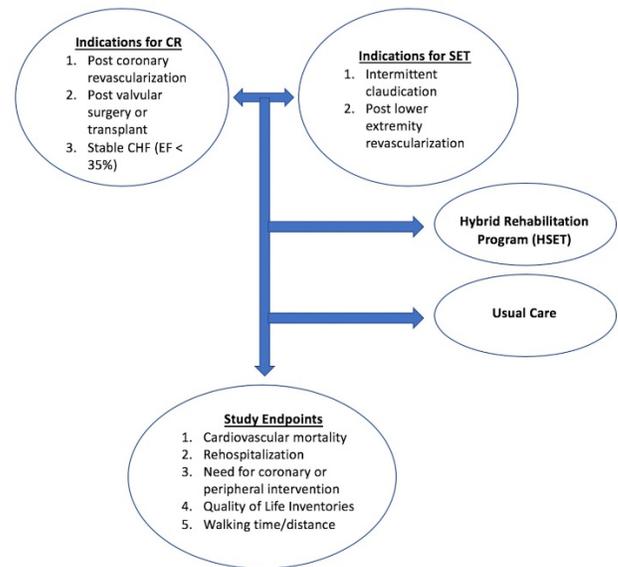


Figure 2: Total walking time in minutes (A) and total walking distance in miles (B) on the first session of the HSET program and after 36 sessions.

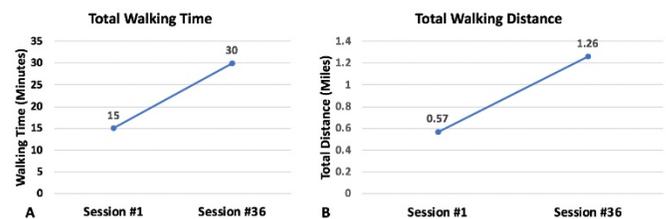
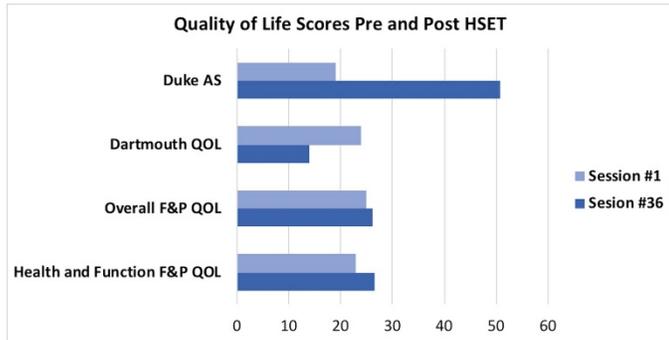


Figure 3: Quality of life and walking impairment questionnaire results after 36 sessions of the HSET program.



Duke AS = Duke Activity Status; F&P = Ferrans and Powers Overall QOL and Health and Function QOL scores

Table 1: Inclusion and exclusion criteria for the HSET

Inclusion Criteria	Exclusion criteria
<p><u>Acute Coronary Syndrome within last 12 months:</u></p> <ol style="list-style-type: none"> <li>1. Myocardial infarction</li> <li>2. CABG</li> <li>3. PCI</li> <li>4. Stable Angina</li> <li>5. Valvular replacement or repair</li> <li>6. Stable heart failure with EF &lt; 35% and NYHA class II-IV symptoms on optimal medical therapy for at least 6 weeks</li> </ol> <p><u>Peripheral Arterial Disease:</u></p> <ol style="list-style-type: none"> <li>1. Diagnosed by ankle-brachial index (ABI), duplex ultrasound, computed tomographic angiography (CTA), magnetic resonance imaging (MRA), or conventional angiography.</li> <li>2. Post exercise ABIs, measured immediately after exercise can also be used.</li> <li>3. Patients must have intermittent claudication</li> </ol>	<p><u>Cardiac Contraindications:</u></p> <ol style="list-style-type: none"> <li>1. Acute infection</li> <li>2. Acute pericarditis</li> <li>3. Active or suspected myocarditis</li> <li>4. Third degree A-V block without pacing</li> <li>5. Recent history of pulmonary embolism</li> <li>6. Recent significant changes in resting ECG</li> <li>7. Severe, untreated aortic or mitral stenosis</li> <li>8. Suspected or known dissecting aneurysm</li> <li>9. Decompensated CHF, unstable angina, or arrhythmias</li> <li>10. Uncontrolled diabetes mellitus</li> </ol> <p><u>Peripheral Arterial Contraindications:</u></p> <ol style="list-style-type: none"> <li>1. Critical or acute limb ischemia</li> <li>2. Presence of wounds on the lower extremities</li> </ol>

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