

## Introduction

- Coronary heart disease (CHD) is a leading cause of death and disability in the United States. Thus, practices that can reduce CHD morbidity/mortality have significant clinical value.
- Cardiorespiratory fitness (CRF), as measured by  $VO_{2Peak}$  is a strong and proven clinical indicator of long-term cardiovascular health.
- Cardiac Rehabilitation (CR) is an exercise program that improves CRF and prevents adverse cardiovascular events in patients referred for CHD or heart failure with reduced ejection fraction (HFrEF).
- CR normally follows Moderate Continuous Training (MCT; 60-70% MPRH), which has been shown to substantially improve CRF and long-term cardiovascular outcomes in 50% of patients with HFpEF. The other 50% of patients show no discernable improvement.
- Currently, there is no approach to determine which patients will/will not respond effectively to CR.

## HFpEF

- Heart failure with preserved ejection fraction (HFpEF) is a common phenotype of heart failure that is caused by prolonged left ventricular afterload (seen in chronic hypertension, obesity, and aging).
- HFpEF consequences are severe with 5-year morbidity, mortality, and rehospitalization rates exceeding 70%.
- The clinical criteria for diagnosing HFpEF lacked uniformity until recently. Previously, a LVEDP  $\geq 15$  was required for diagnosis, a measurement that could only be collected through invasive testing. Increased pressures can now be determined non-invasively
- There is a substantial number of patients with undiagnosed HFpEF due to the complexity in determining the diagnosis and lack of provider assessment.
- Currently, patients with HFpEF are not referred to CR. Smaller studies have shown CR employing MCT improves  $VO_{2Peak}$  in many HFpEF patients, but the long-term impact of CR on HFpEF patients is unknown.
- Similar to HFrEF, there is no approach to determine which patients will/will not respond effectively to CR.
- The risk factors for developing HFpEF are very similar to those for coronary heart disease. Thus, many patients who are enrolled in CR with CHD may have undiagnosed HFpEF.
- The proportion of patients in the Veteran population that have CHD concurrent with HFpEF has not been determined.
- Also, the long-term impact of CR on patients with HFpEF + CHD is poorly defined.

## Objectives

- Define the clinical characteristics of the Columbia VA CR patient population including evidence for HFpEF
- Determine how the miRNA profile changes in response to CR.
- Generate a diagnostic tool that can help determine which patients would be responsive to cardiac rehabilitation treatment.

## Methods

- Determine the impact of exercise (HIIT or MCT) in improving  $VO_{2Peak}$  in 40 Veterans referred to CR at the Columbia VA. CR training will be 3 times a week for 12 weeks.
- Before and after the CR, measure the miRNA profiles of participants, conduct exercise testing to measure  $VO_2$  max, Echocardiogram (Echo) screening, and administer Quality of Life of Questionnaires.
- Determine the participants who have HFpEF through Echo testing measurement of the following variables:
  - PCWP  $\geq 15$  mmHg at rest or  $\geq 25$  mmHg during exercise
  - LVEDP  $> 15$
  - LVEF  $\geq 50\%$  and end-diastolic volume index  $\leq 97$  ml/m<sup>2</sup>
  - $> 50\%$  of the following (at least 3 components must be assessed):
    - Average E/e'  $> 14$
    - Septal e' velocity  $< 7$  cm/s or Lateral e' velocity  $< 10$  cm/s
    - TR velocity  $> 2.8$  m/s
    - LA volume index  $> 34$  ml/m<sup>2</sup>
- In addition to physical parameters, patients must be symptomatic to have a HFpEF diagnosis.
- If symptoms are not present, categorized as Preclinical Diastolic Dysfunction (PDD).
- For patients that already have a HFpEF diagnosis, follow the same procedure as a confirmatory measure.
- All the same characteristics are assessed again after CR to examine any changes.

## Results

**Table 1.** Example of Source Document

Subject ID \_\_\_\_\_ Protocol # \_\_\_\_\_ 2

### Function and Quality of Life:

Parameter:	Pre-Value:	Post-Value:
Peak VO2		
Maximum Workload		
Maximum Exercise Time		
Ventilatory anaerobic threshold		
Workload at Ventilatory AT		
Resting HR		
Maximum HR		
Resting BP		
Maximum BP		
Heart Rate Reserve (HRR)		
O2 Pulse (VO2/HR)		
Ventilatory Reserve		
Respiration Rate		
Respiratory Exchange Ratio		
6-minute walk test (meters)		
SF-36 Physical Functioning Score		
MLFH Physical Score		
MLFH Emotional Score		
MLFH Total Score		

## Results

- Information from the various forms of testing will be compiled in a source document.
- Based off of the Questionnaires and Echo values, it will be determined which individuals who are participating in the pilot study have HFpEF.
- Determine the proportion of the Veterans population that has HFpEF + CHD.
- Examine the demographics/background of the individuals with HFpEF + CHD.
- The implications of this diagnosis and beneficial treatment options will be further understood upon analysis of the miRNA profiles, exercise testing, and follow-up Echos after the completion of cardiac rehabilitation.

## Future Directions

- The infrastructure for the various types of testing is established and in place.
- Two prospective patients are currently being assessed for participation in the study
- Upon successful completion of the pilot study, we will expand the study size and scope.

## References

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