The REHAB-HCM Project

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Disclosures

- None relevant

Funding

- CCS-BMS HCM Award
- CAPP

REHAB-HCM:

Cardiac REHABilitation to improve metabolic health in Hypertrophic CardioMyopathy

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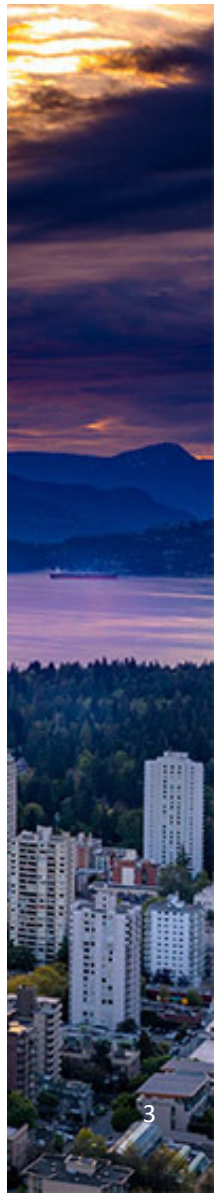
Canadian Cardiovascular Society

Bristol Myers Squibb

HiRO HCM

Members of the SPH HCM and VGH/SPH Cardiac Rehab Programs

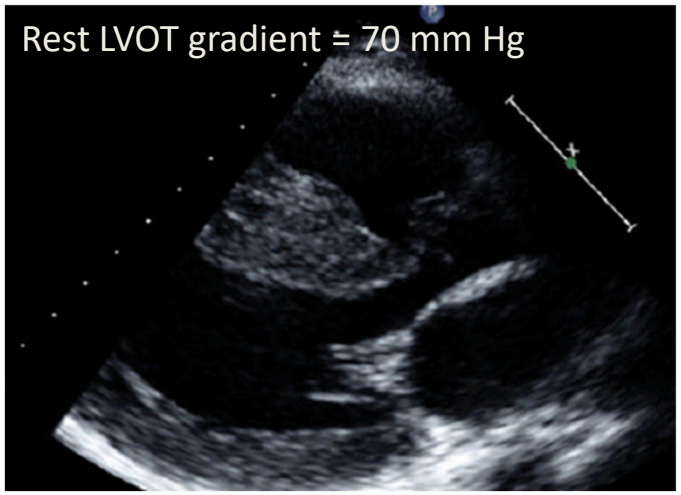


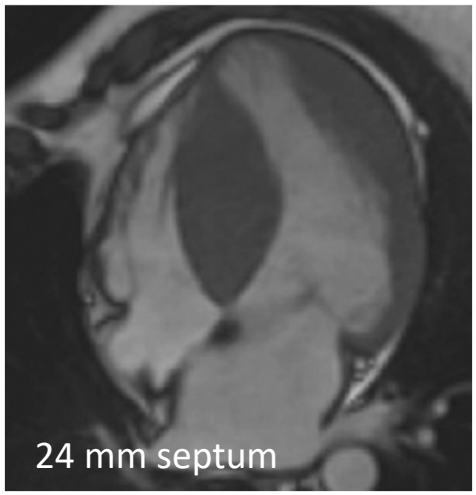
Case Presentation

- ID: 49 yo male
- PMHx: “mild” HTN, pre-diabetes, BMI 30, not on medications
- No family hx suggestive of HCM
- HPI:
  - Progressive dyspnea on exertion for 6 months
  - Hot day this summer – pre-syncopal for hours walking on seawall
  - Presents to ER for assessment
- Physical Exam: Grade 2/6 SEM RUSB
- ECG: NSR, NSTT changes
- Discharged after IV fluids & observation, outpatient echo

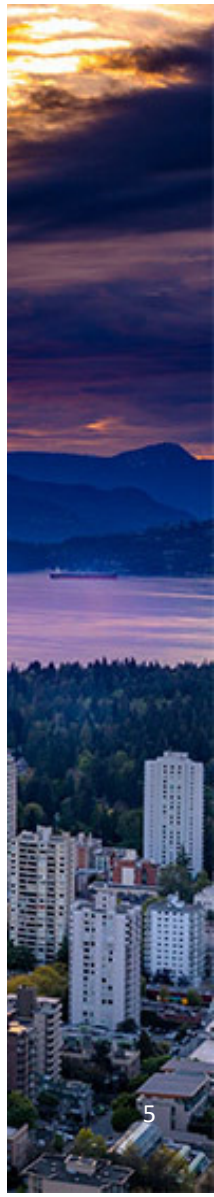
Case Presentation

- Cardiac Imaging:





- Seen in general cardiology clinic:
  - Lab tests: HbA1c 7.2%, LDL 3.2, TG 3.2, BNP 450
  - Verapamil, exercise restriction: “nothing too intense”
  - Genetic testing & family screening recommended
- **What is contributing to this patient’s HCM phenotype?**



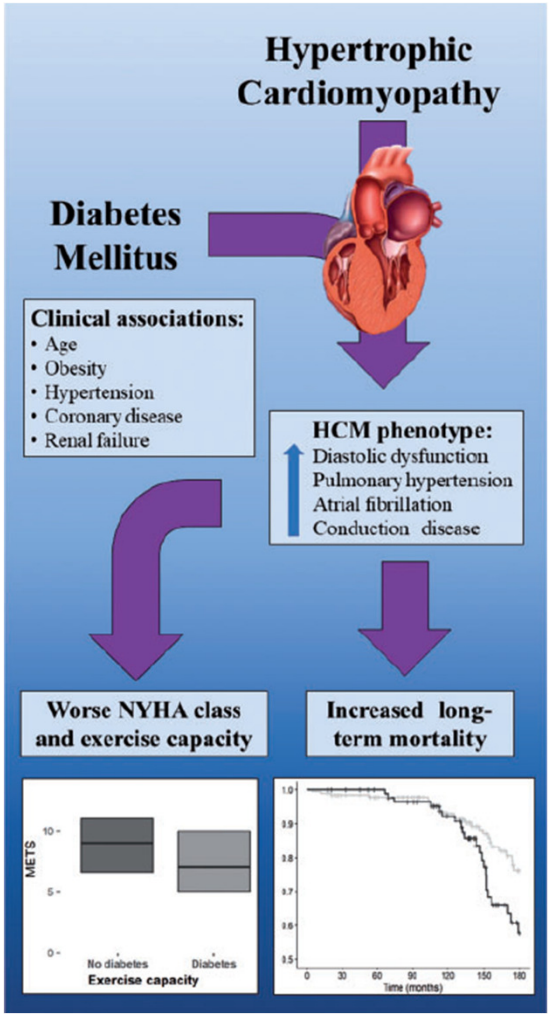
HCM as a Cardiometabolic Disease

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 1671–1677
doi:10.1093/eurheartj/ehy625

CLINICAL RESEARCH
Heart failure/cardiomyopathy

The impact of diabetes mellitus on the clinical phenotype of hypertrophic cardiomyopathy

- About 10% of patients have overt DM at the time of HCM diagnosis
- Worse symptoms
- Lower functional status
- Greater mortality



Wasserstrum et al, EHJ 2019

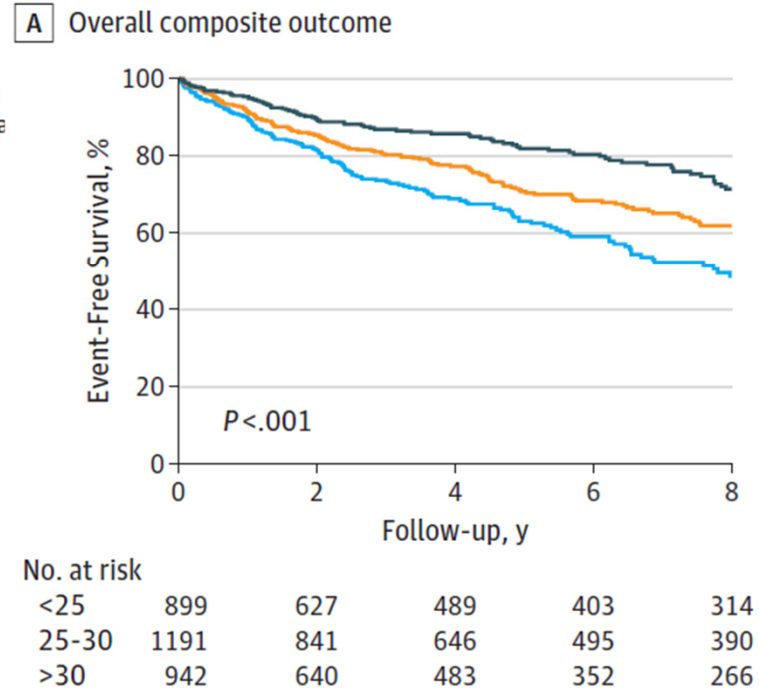
HCM as a Cardiometabolic Disease

JAMA Cardiology | Original Investigation

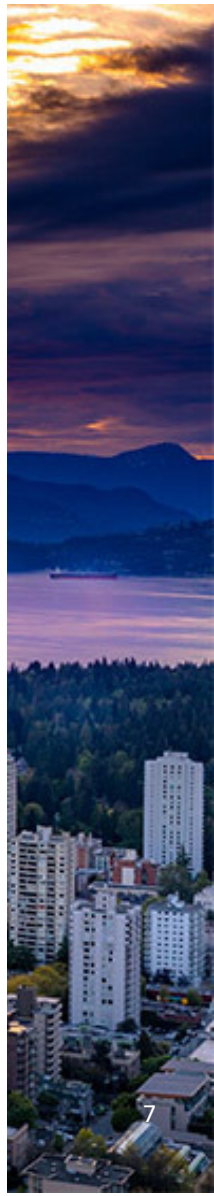
Association of Obesity With Adverse Long-term Outcomes in Hypertrophic Cardiomyopathy

Carlo Fumagalli, MD; Niccolò Maurizi, MD; Sharlene M. Day, MD; Euan A. Ashley, MRCP, DPhil; Michelle Michels, MD, PhD; Steven D. Colan, MD; Daniel Jacoby, MD; Niccolò Marchionni, MD; Justin Vincent-Tompkins, MS; Carolyn Y. Ho, MD; Iacopo Olivotto, MD; for the SHARE Investiga

- One-third of HCM patients have obesity
- Worse LVOT obstruction
- More symptoms
- More adverse major events

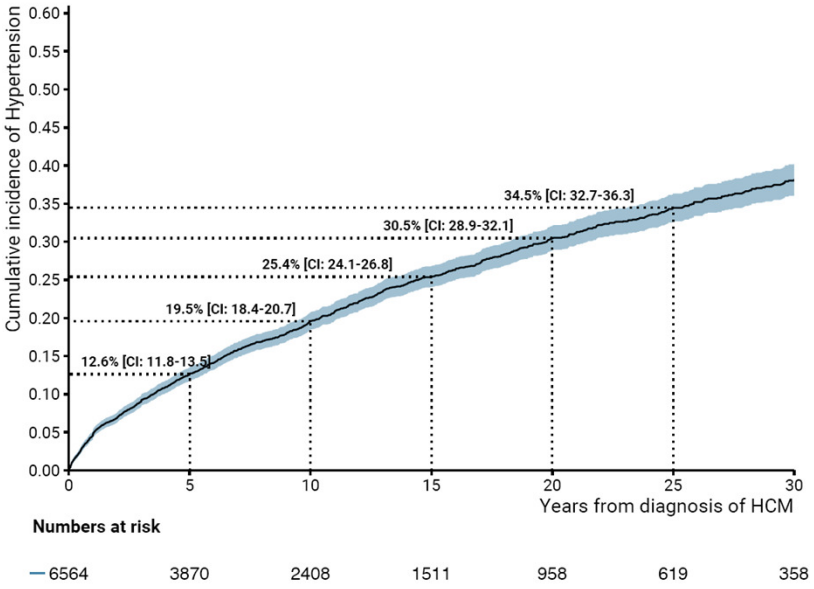


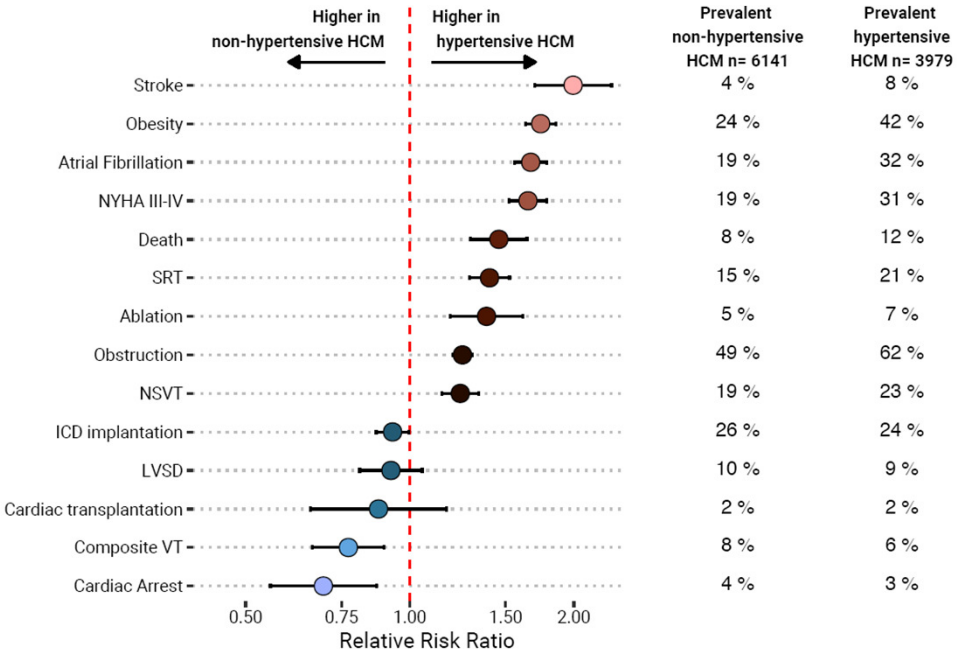
Fumagalli et al, JAMA Card 2019



HCM as a Cardiometabolic Disease

- HTN is common at HCM diagnosis **AND** during follow-up
- Associated with greater risk of severe adverse outcomes





Roston…Ho. Unpublished data.

Exercise is SAFE in Patients with HCM

- High quality data have **reversed** the long-standing misconception that vigorous physical activity is dangerous in HCM

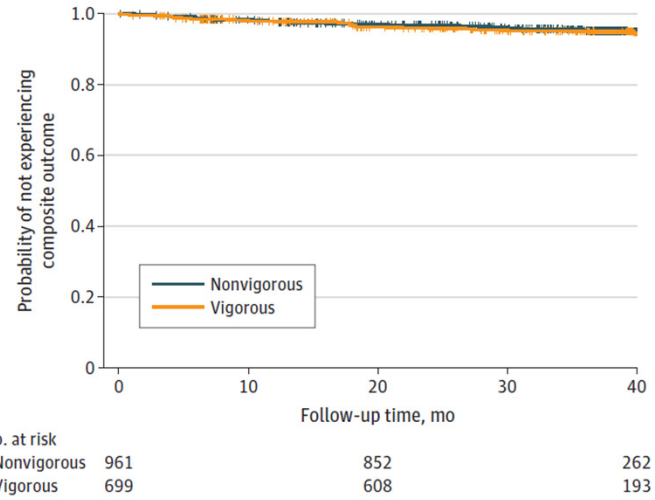
LIVE-HCM Study

JAMA Cardiology | Original Investigation

Vigorous Exercise in Patients With Hypertrophic Cardiomyopathy

Rachel Lampert, MD; Michael J. Ackerman, MD, PhD; Bradley S. Marino, MD; Matthew Burg, PhD; Barbara Ainsworth, PhD, MPH; Lisa Salberg; Maria Teresa Tome Esteban, MD, PhD; Carolyn Y. Ho, MD; Roselle Abraham, MD; Seshadri Balaji, MBBS, PhD; Cheryl Barth, BS; Charles I. Berul, MD; Martijn Bos, MD; David Cannom, MD; Lubna Choudhury, MD; Maryann Concannon, MSW; Robert Cooper, MD; Richard J. Czosek, MD; Anne M. Dubin, MD; James Dziura, PhD; Benjamin Eidem, MD; Michael S. Emery, MD; N. A. Mark Estes, MD; Susan P. Etheridge, MD; Jeffrey B. Geske, MD; Belinda Gray, MBBS, PhD; Kevin Hall, MD; Kimberly G. Harmon, MD; Cynthia A. James, PhD; Ashwin K. Lal, MD; Ian H. Law, MD; Fangyong Li, MS; Mark S. Link, MD; William J. McKenna, MD; Silvana Molossi, MD, PhD; Brian Olshansky, MD; Steven R. Ommen, MD; Elizabeth V. Saarel, MD; Sara Saberi, MD, MS; Laura Simone, MS; Gordon Tomaselli, MD; James S. Ware, MD; Douglas P. Zipes, MD; Sharlene M. Day, MD; for the LIVE Consortium

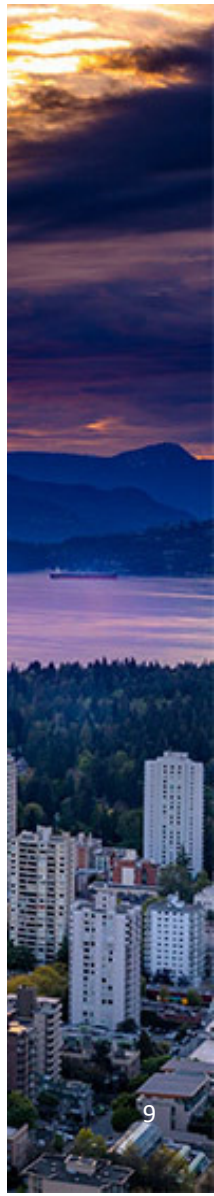
Figure 1. Kaplan-Meier Survival Curve for Freedom From Composite End Point (Death, Cardiac Arrest, Appropriate Implantable Cardioverter Defibrillator Shock, or Arrhythmic Syncope) by Exercise Group



No. at risk			
Nonvigorous	961	852	262
Vigorous	699	608	193

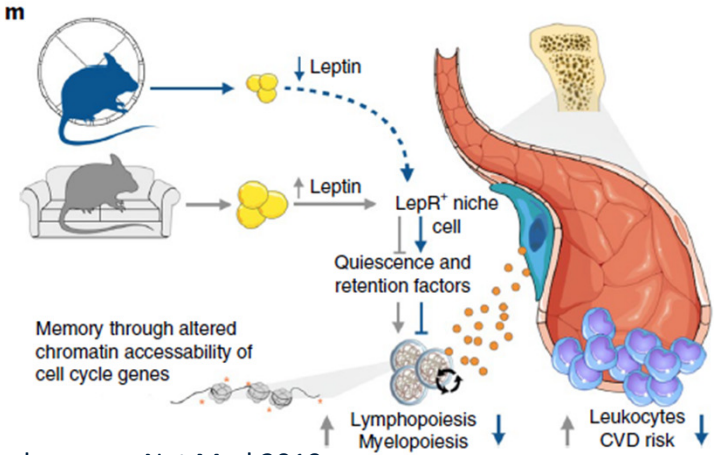
Vigorous and nonvigorous groups did not differ in freedom from composite end point.

Lampert at al, JAMA Card 2023

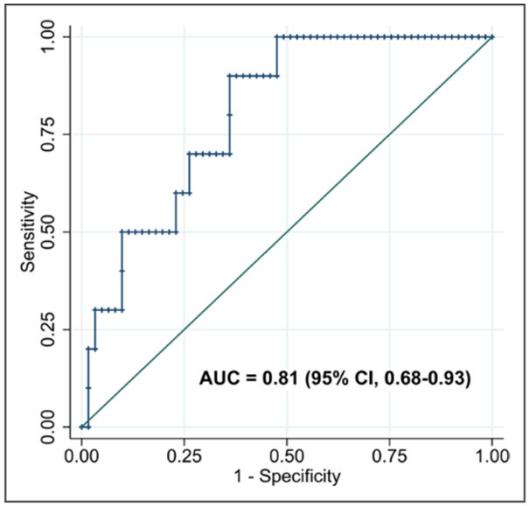


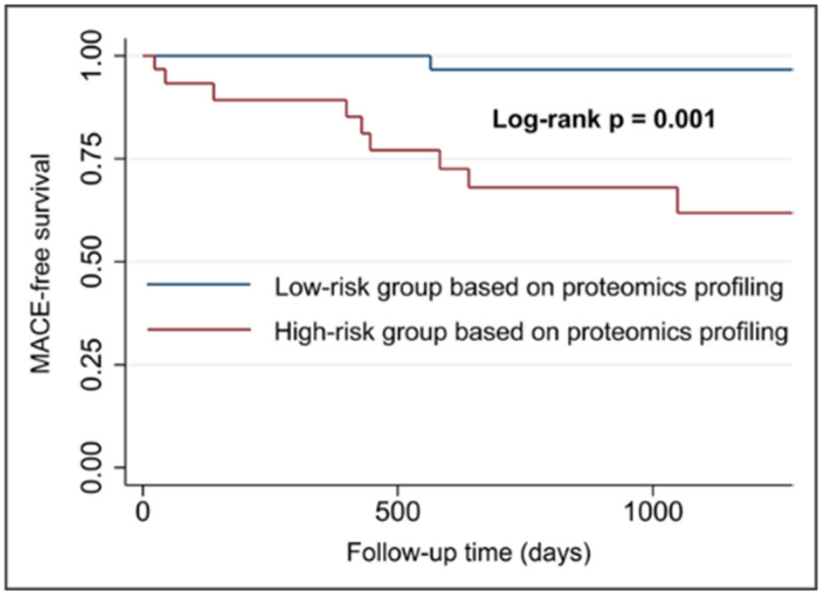
HCM, Inflammation, and Exercise

- Upregulation of inflammatory pathways are associated with increased risk of major adverse cardiac events in HCM, associated with worse diastology
- Exercise has been shown to downregulate these inflammatory pathways in other cardiometabolic diseases



Frodermann, Nat Med 2019





Shimada, Circ GPM 2022

Cardiac REHABilitation to Improve Metabolic Health in Hypertrophic CardiomMopathy (REHAB-HCM)

Based on the premise that HCM is a complex genetic and acquired cardiometabolic disorder, we believe that physical activity has untapped benefits in individuals with HCM and metabolic syndrome

Design: Prospective observational pilot study
Population: Adults 18-80 years of age at SPH HCM Clinic with guideline-based diagnosis of HCM and of metabolic syndrome
Intervention: Cardiac Rehabilitation for 3-months (3 classes per week)

Month 0-3	Month 4-6	Month 7-12
Participant Screening & Recruitment Phase	Cardiac Rehabilitation Program Phase	Post-CR Program Physical Activity Monitoring Phase

Aim 1: Assessing for improvements in metabolic risk factors, cardiorespiratory fitness, psychological well-being, and physical activity levels and attitudes

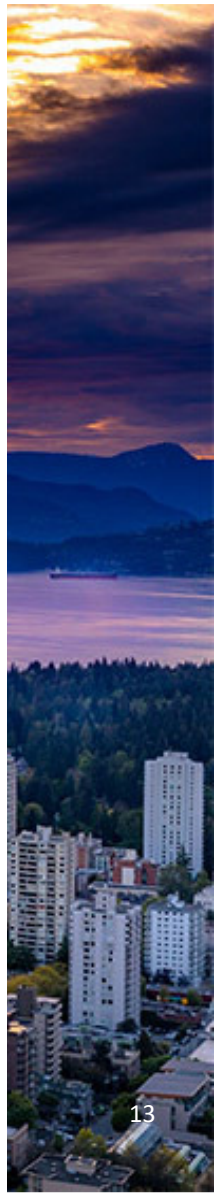
- Determine magnitude of effect of CR effect on key metabolic risk factors (Table)
- Compare these findings pre-CR, immediately post-CR, and after 6-months follow-up

Exploratory Outcomes of Interest	Descriptors
Lipids	LDL (c)
	HDL (c)
	Non-HDL (c)
	Triglycerides
Glycemic Control	Fasting glucose
	Hemoglobin A1c
Resting Hemodynamics	Systolic Blood Pressure
	Diastolic Blood Pressure
	Heart Rate
Body Measurements	Body Mass Index
	Waist Circumference
Cardiorespiratory Fitness	Peak Oxygen Consumption
	Peak Respiratory Exchange Ratio
	Exercise Duration
	Peak Heart Rate
	Heart Rate Reserve
IPAQ Questionnaire	Measure of health-related physical activity involvement
FAcTS-HF Questionnaire	Measure of kinesiophobia (fear of exercise/movement)
Minnesota Living with Heart Failure Questionnaire	Measure of quality of life with heart failure
Kansas City Cardiomyopathy Questionnaire	Measure of quality of life with cardiomyopathy

Table 1: Variables of interest

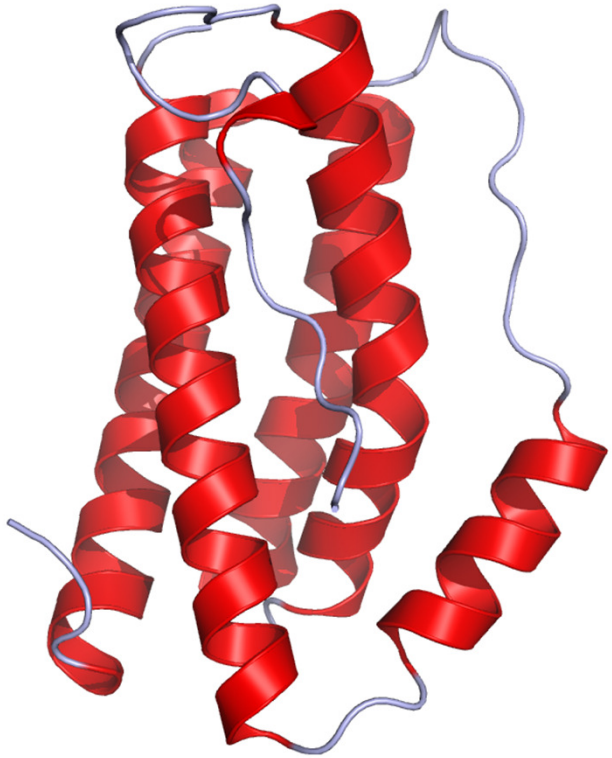
Aim 2: Assessing for sustained improvements in physical activity patterns, attitudes, and tolerance

- Wearable accelerometer
- Adherence to CR program sessions & completion
- IPAQ long form
- Questionnaire on quality of life and kinesiophobia (fear of exercising)



Aim 3: Assessing for changes in established cellular markers of systemic inflammation

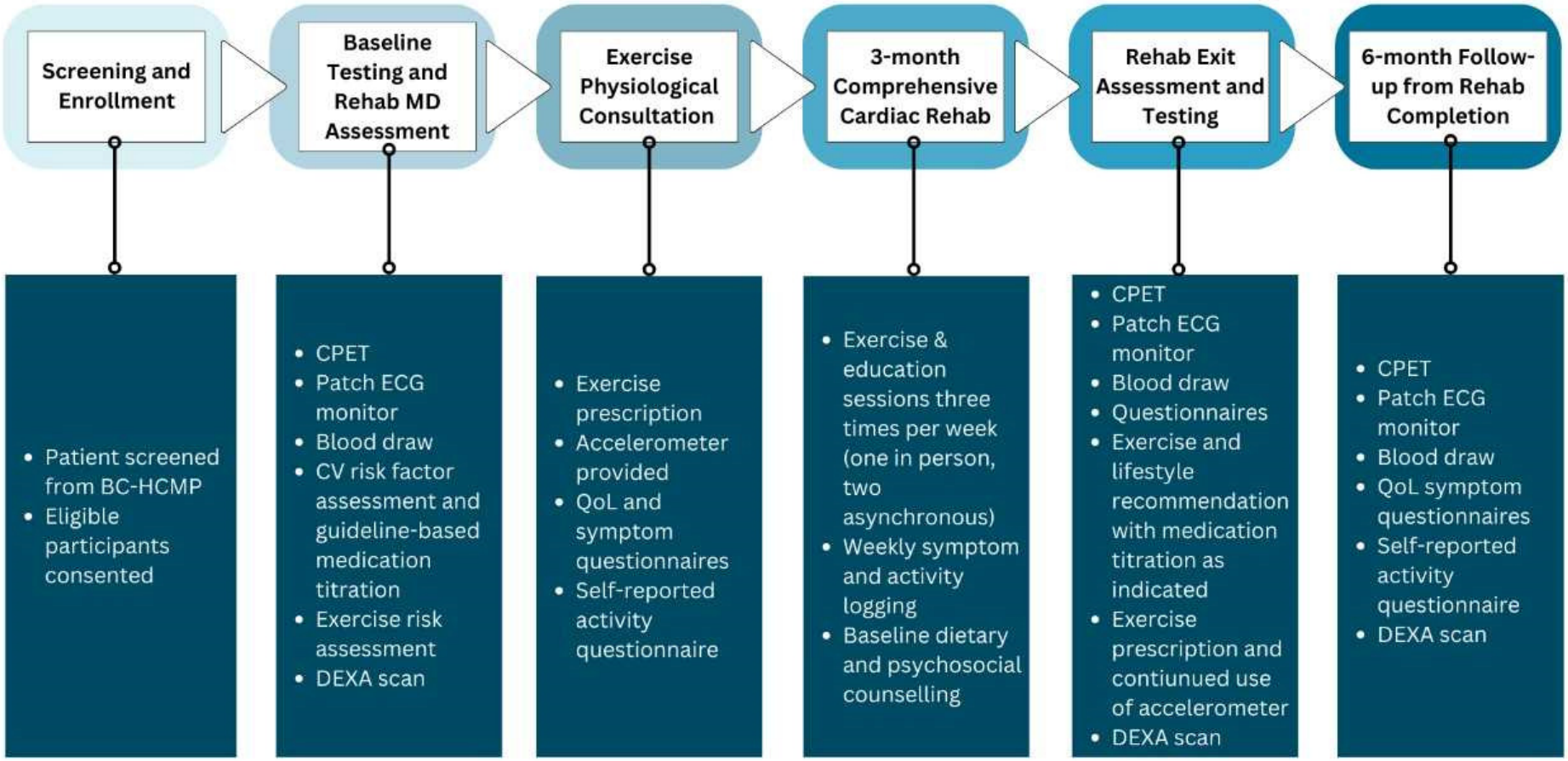
- Flow cytometric analysis of circulating immune cell populations
  - neutrophils, monocyte and T cell subsets
- Ex vivo assays of inflammatory cell function
  - monocyte cytokine production, phagocytosis
- Quantification of systemic inflammation
  - 13 human inflammatory cytokines/chemokines
- Comparison of markers pre-CR, post-CR, and after 6-months follow-up

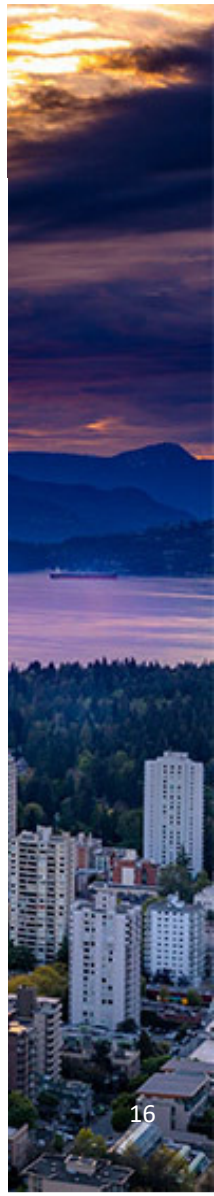


Special Considerations

- **Safety Adjudication**
  - Adverse events assessed by committee of HCM, CR, and EP cardiologist
  - Remove if exercise implicated in event
- **Feasibility**
  - Main barrier anticipated is CR class attendance
    - Hybrid option if recruitment slow
- **Equity & Diversity**
  - Females and non-white ethnicities under-represented in HCM literature
  - SPH HCM program ethnically diverse compared to existing publications
  - Recruitment patterns will be used to inform larger national study

Summary of Pilot Study





Conclusions & Future Directions

- A pilot study to understand the *feasibility & impact of exercise* on the common combination of both *HCM and metabolic syndrome*
- Early step towards understanding whether exercise could *reverse or delay phenotypic expression*
- Inform a large *national study of CR in HCM* leveraging our national network
- A ***collaborative*** effort between cardiogenetics and cardiac rehabilitation

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Members of the SPH HCM, VGH/SPH Cardiac Rehab Programs & HF/EP Programs
Jinelle Gelinas, PhD (study coordinator), Matthew Cheung, MD (IM resident)