



KNIGHT
CARDIOVASCULAR
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nHCM and HFpEF Overlap: An Opportunity or a Trap?

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oHCM vs. nHCM

oHCM

nHCM

LVOT gradient

No unifying “measured” variable

NTproBNP

Troponin

E/e’

Functional outcome

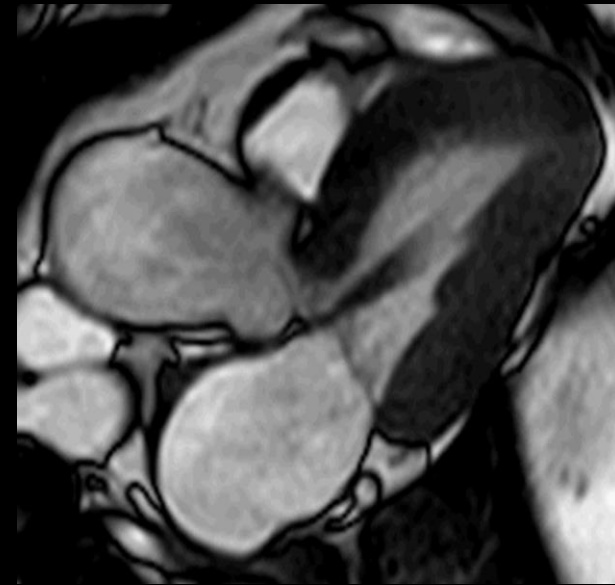
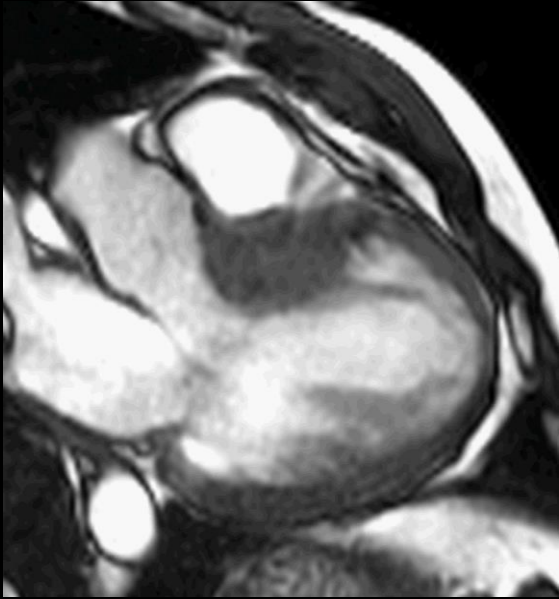
Functional outcome

PIONEER HCM: 25 screened, 21 enrolled

MAVERICK: 150 screened, 59 enrolled

EXPLORER HCM: 429 screened, 251 enrolled

The Many Imaging Phenotypes of nHCM with preserved LVEF



Complex Phenotypes and Comorbidities

Aging
Depression
Anxiety
OSA

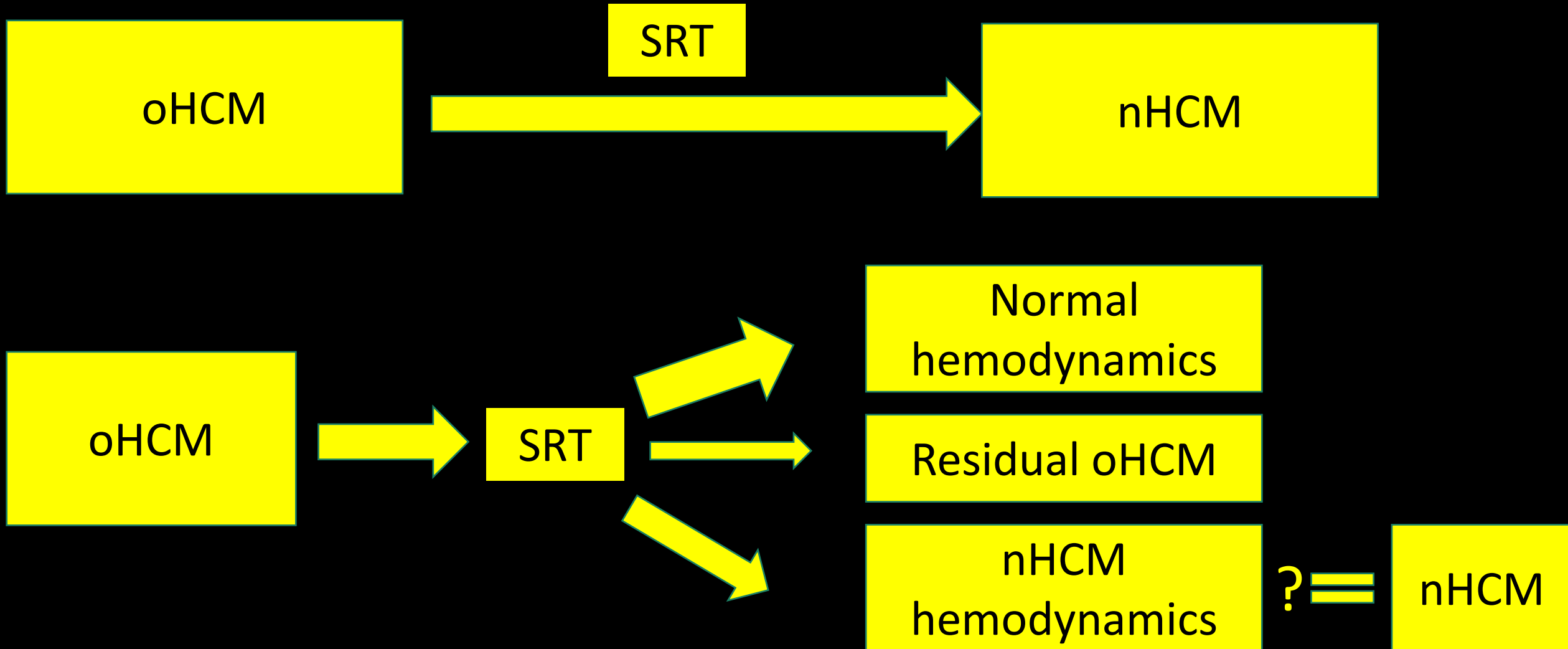
Diabetes
CKD
Liver disease



Genotype
Hypertension
Fibrosis
CAD
AF
VT/VF/SCD
Conduction disease
Devices
PH
RV dysfunction

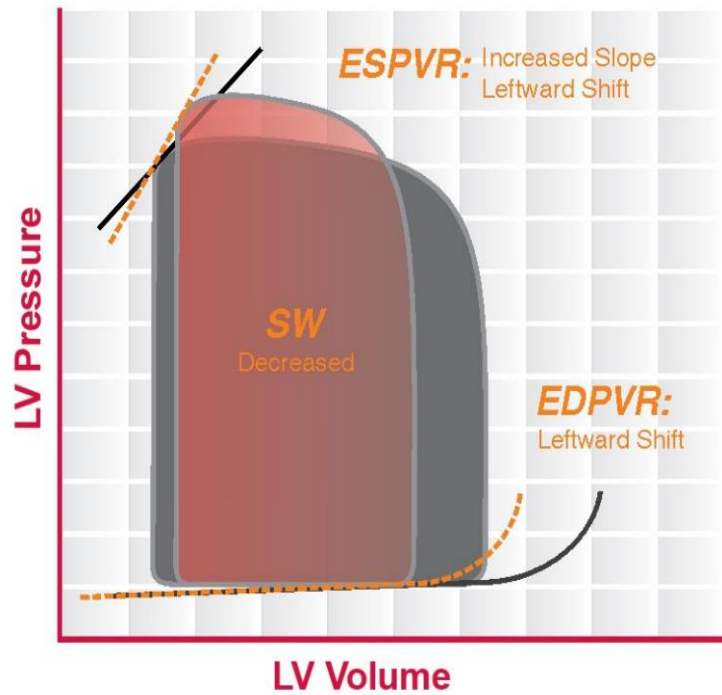
Sedentary lifestyle
Orthopedic conditions
Metabolic syndrome
Obesity

Post-SRT nHCM

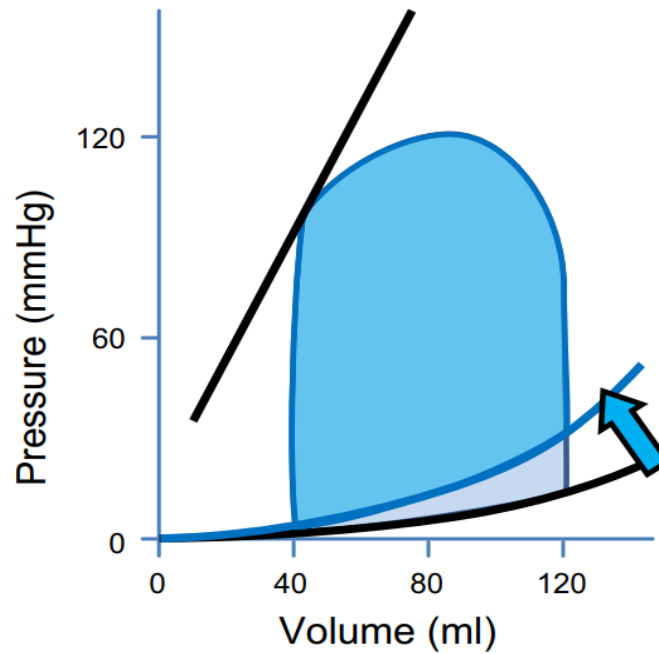


Are Hemodynamics Homogenous?

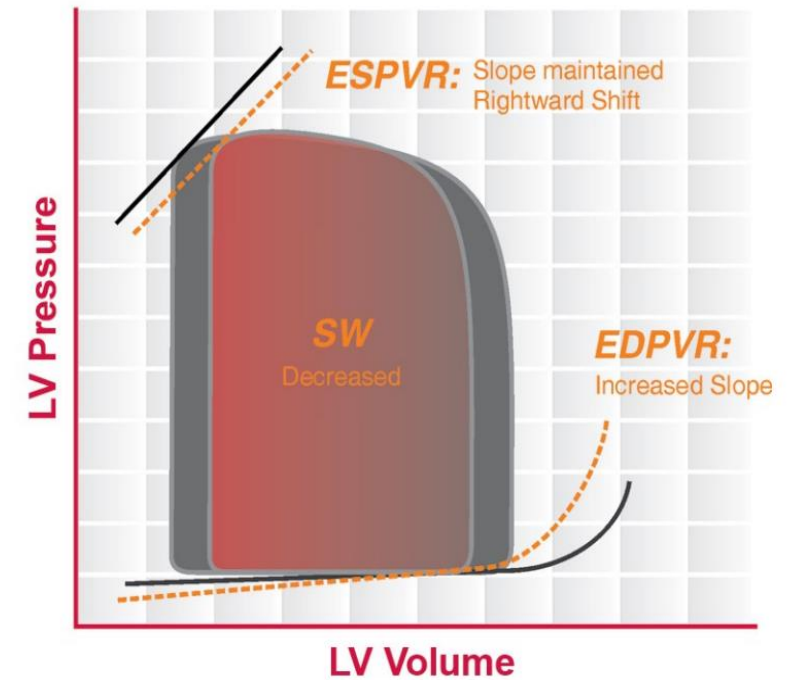
Hypertrophic



Diastolic dysfunction

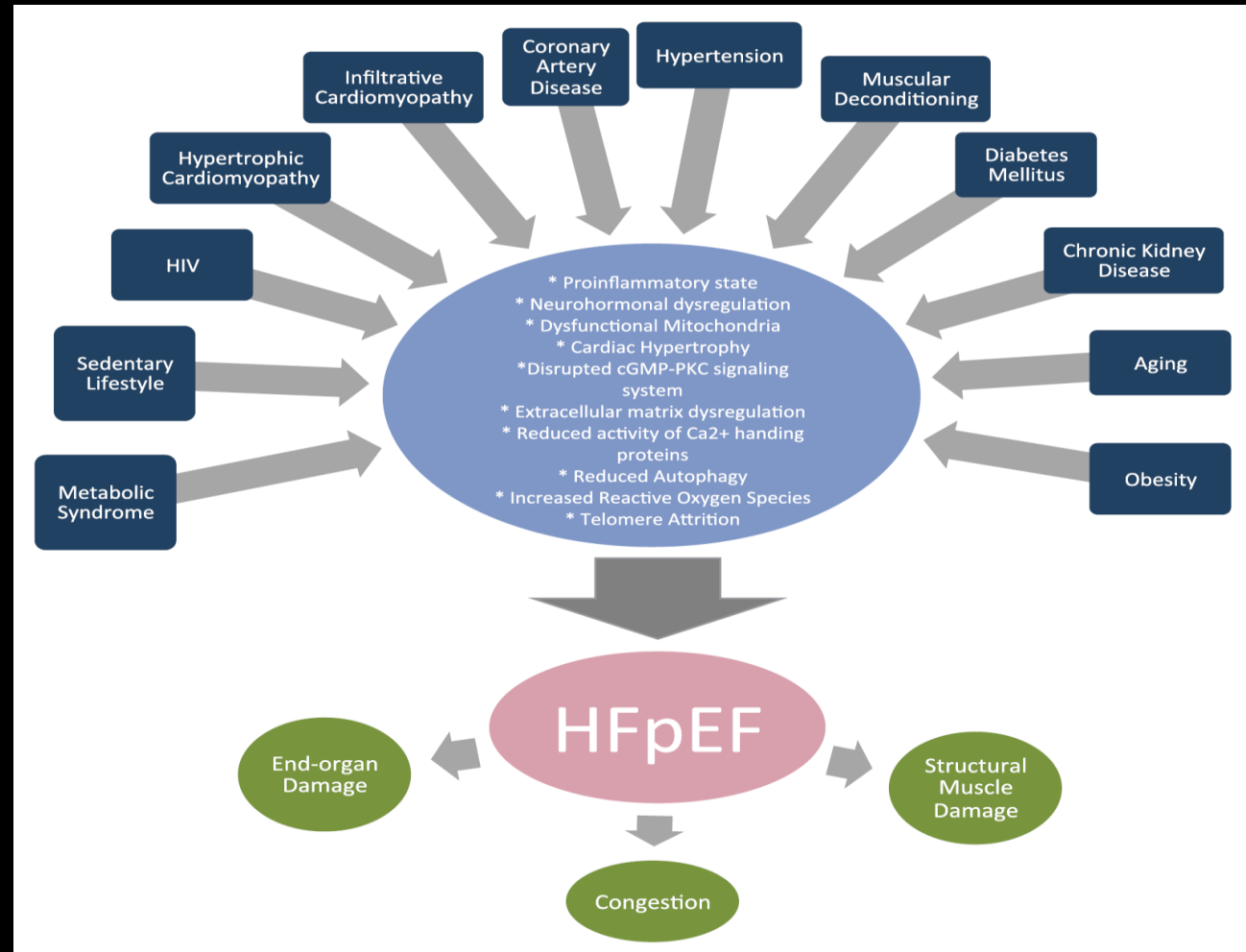


Restrictive



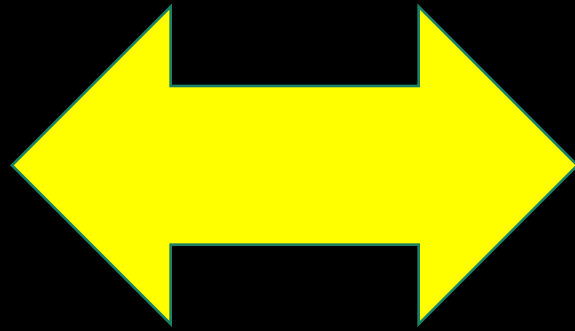
HFpEF: Failures Driving Knowledge

- Barking up the wrong tree
 - Neurohormonal blockade
- Imitating HFrEF trials
- A mixed bag
 - Phenotypes and comorbidities



What's Past is Prologue

HFpEF



nHCM

nHCM = HFpEF + hypercontractility + LVH ?

Clinical Trials Endpoints

- NYHA class
- PROs (KCCQ, HCMSQ-SoB)
- NtproBNP, troponin
- Exercise time / 6MWT
- Peak VO₂, VE/VCO₂
- Imaging endpoints
- Hierarchal/ordinal composite outcome
- Heart failure admissions, transplant, death

Complexity of nHCM → Complex Endpoint?

Four Main Domains*

Symptoms

PROs

Functional
endpoint

Biomarkers

*Imaging variables as secondary domains

Acknowledgement

Patients living with HCM and HF

OHSU HCM clinical and research teams

