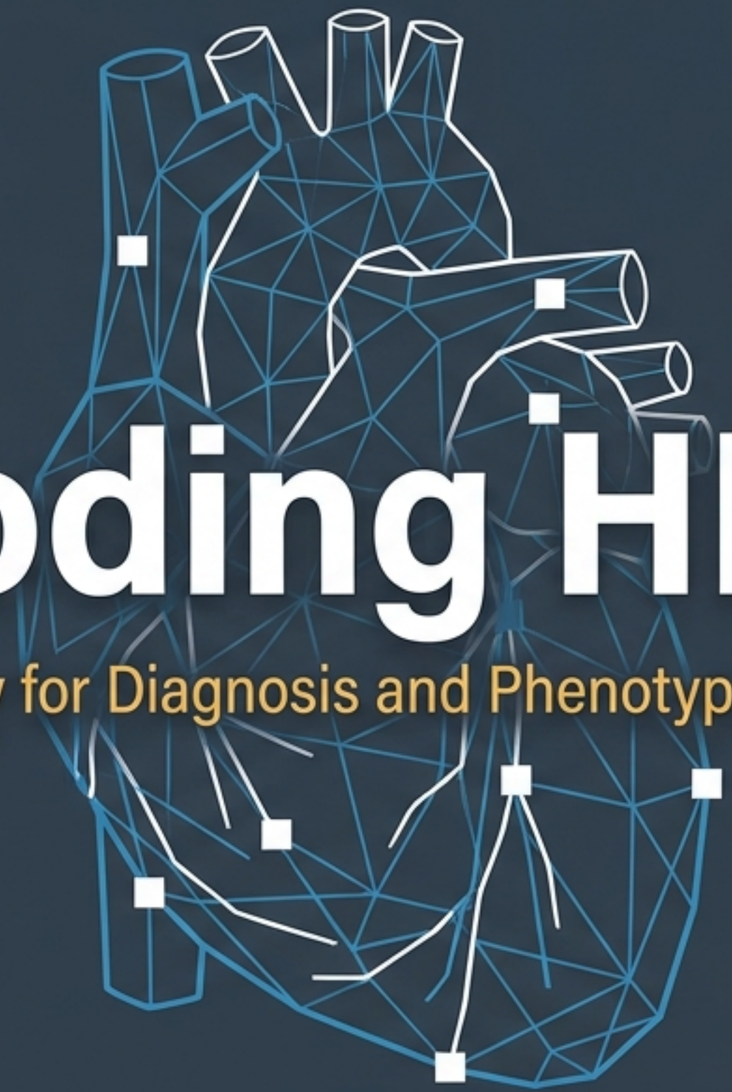


Decoding HFpEF

The Precision Pathway for Diagnosis and Phenotype-Driven Management

Clinical Reference Architecture | Based on 2026 Guidelines

480,000

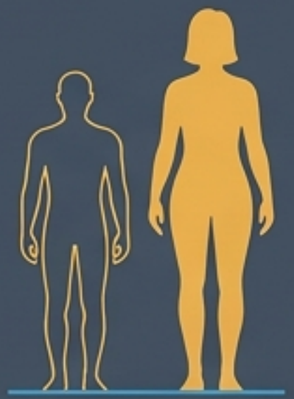
Prevalence & Trajectory

Australians living with Heart Failure.
HFpEF now accounts for ~50% of all cases and is rising with population ageing.

60%

The Sex Disparity

Female. HFpEF disproportionately affects women, contrasting sharply with HFrEF populations.

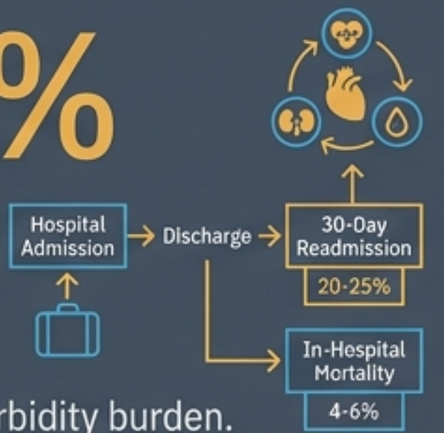


$3.7B

Health System Impact

Leading cause of preventable hospitalisation (age ≥65). Direct annual HF management cost in Australia is $3.7B.

20-25%



Clinical Severity

30-day readmission rate.
4-6% in-hospital mortality.
Driven heavily by severe comorbidity burden.

The Demographic Gap

2.7x Age-Adjusted Prevalence. Aboriginal and Torres Strait Islander peoples experience onset 10-15 years earlier, driven by compounded risks (obesity, T2DM, Rheumatic Heart Disease).

Remote Access Barriers

38% of Indigenous populations live in remote areas. Limited access to advanced diagnostics (Echo, RHC, Cardiac MRI) necessitates telehealth, point-of-care NP testing, and portable echocardiography.

Culturally Safe Care Models

Delivery must respect cultural obligations and integrate with ACCHOs (e.g., Central Australian Aboriginal Congress) using Closing the Gap PBS (CTG-PBS) for critical medications.

The LVEF Classification Matrix

HFrEF (Reduced)	HFmrEF (Mildly Reduced)	HFpEF (Preserved)	HFimpEF (Improved)
≤40% in Clinical Ochre	41-49% in Clinical Ochre	≥50%	Previously ≤40%, now >40%
Established evidence base for neurohormonal therapy.	Intermediate phenotype; growing evidence base.	Heterogeneous syndrome; SGLT2i and GLP-1 RA now evidence-based.	Treated HFrEF with recovered LVEF; must continue GDMT.

The Diagnostic Funnel (HFA-PEFF)

1

Step 1: Pre-Test Assessment

Filter by symptoms, risk factors, and basic biomarkers (NT-proBNP >125 pg/mL or BNP >35 pg/mL).

2

Step 2: Echo & NP Scoring

Apply the HFA-PEFF score (0-6 points). Integrates structural, functional, and peptide data. (Score ≥5 = Diagnostic).

3

Step 3: Functional Testing

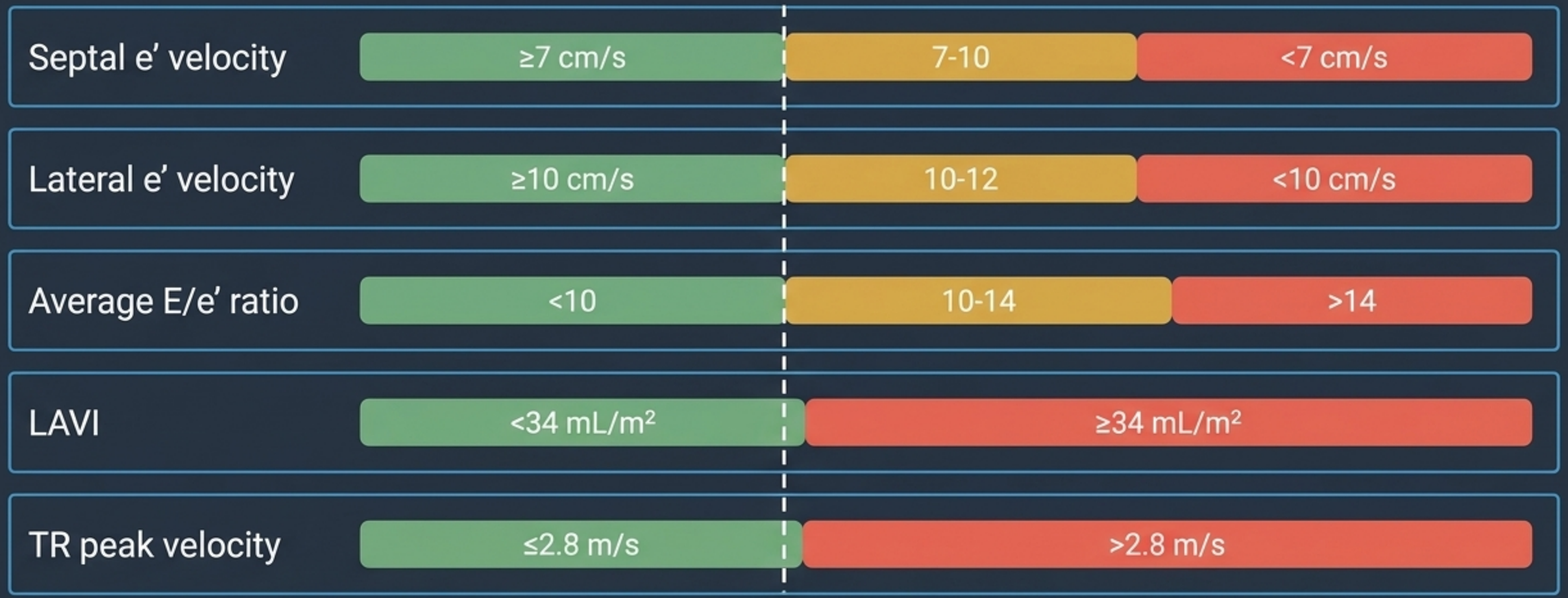
For intermediate scores (2-4). Stress echocardiography or invasive haemodynamics to unmask occult disease.

4

Step 4: Aetiology & Phenotyping

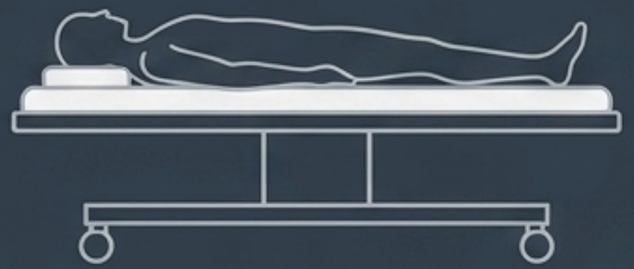
Precision targeting. Cardiac MRI, PYP scans, genetic testing to isolate specific pathophysiological drivers.

The Echo Grey Zone Slider



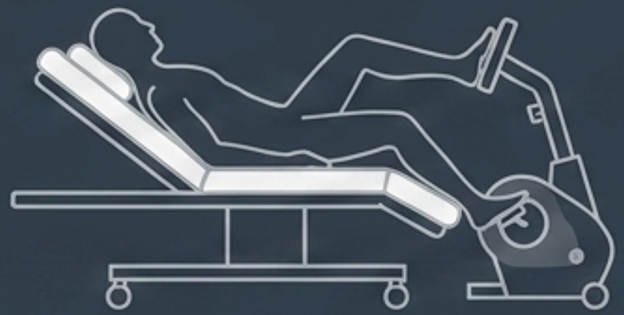
Clinical Pitfall: No single parameter is sufficient. Diastolic assessment must be integrated with clinical context. E/e’ loses sensitivity in obesity and AF. LAVI must integrate with MBS item 55114.

Unmasking Occult HFpEF: Invasive Haemodynamics



Resting PCWP ≥15 mmHg

Diagnostic of elevated left-sided filling pressures at baseline.



Exercise PCWP ≥25 mmHg

Diagnostic of ‘exertional’ or occult HFpEF when resting haemodynamics are deceptively normal.

MBS Integration: Right heart catheterisation (MBS 38218).
Exercise RHC available at select tertiary centres (e.g., Royal Melbourne, RPAH, Alfred).

The HFpEF Treatment Paradigm Shift

The Therapeutic Desert (Pre-2021)

Symptom management only. Repeated negative outcome trials for ACEi, ARBs, and beta-blockers in broad HFpEF populations.

The SGLT2i Breakthrough

EMPEROR-Preserved (Empagliflozin) and DELIVER (Dapagliflozin) demonstrate significant reduction in CV death and HF hospitalisation across the LVEF spectrum.

NNT ~31

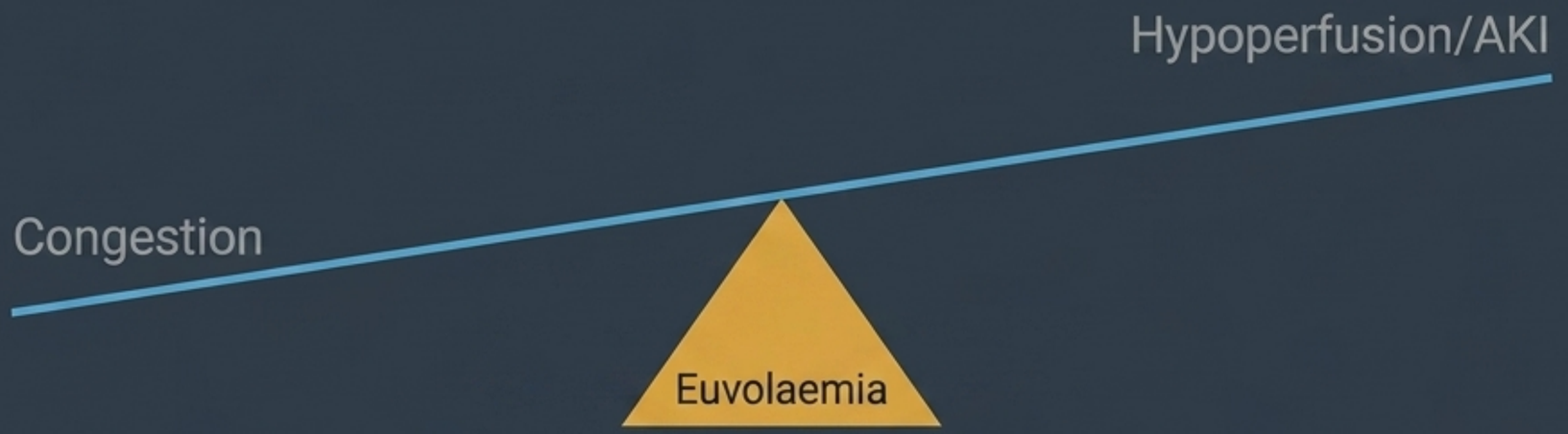
over 2 years

Universal Anchors: SGLT2 Inhibitors

Empagliflozin (Jardiance®)	Dapagliflozin (Forxiga®)
Dose: 10 mg PO daily.	**Dose:** 10 mg PO daily.
Renal Baseline: Initiate if eGFR ≥20 mL/min/1.73 m². Can continue below threshold.	**Renal Baseline:** Initiate if eGFR ≥20 mL/min/1.73 m².
Key Trial: EMPEROR-Preserved (HR 0.79).	**Key Trial:** DELIVER (HR 0.82).
PBS: General Benefit (T2DM) / Authority Required (HF without DM).	**PBS:** General Benefit (T2DM) / Authority Required (HF without DM).

WARNING: Anticipate an initial eGFR dip of 3-5 mL/min—this is a haemodynamic effect, not acute injury. Monitor for genital mycotic infections (~5%).

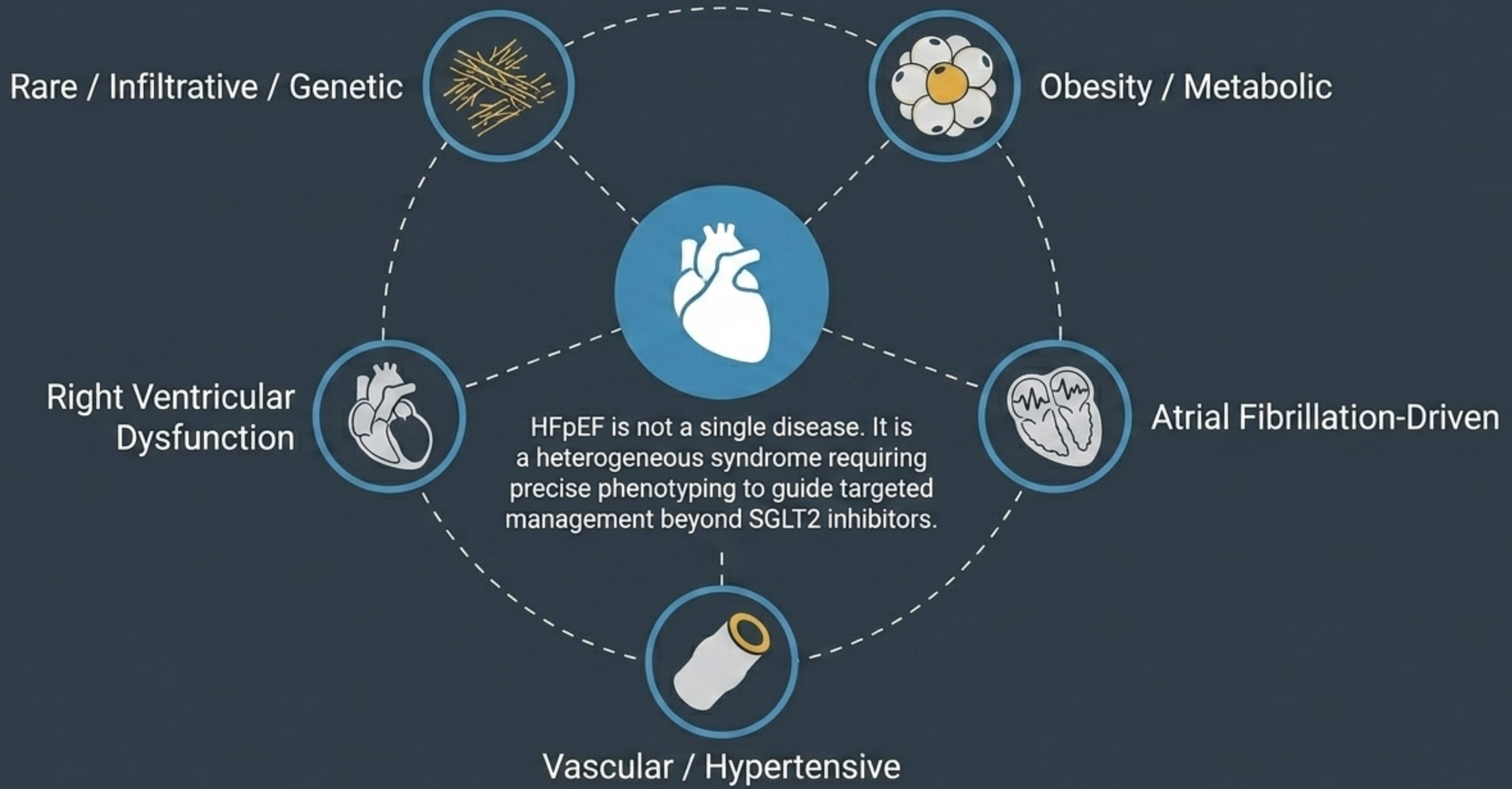
The Symptom Engine: Diuretics



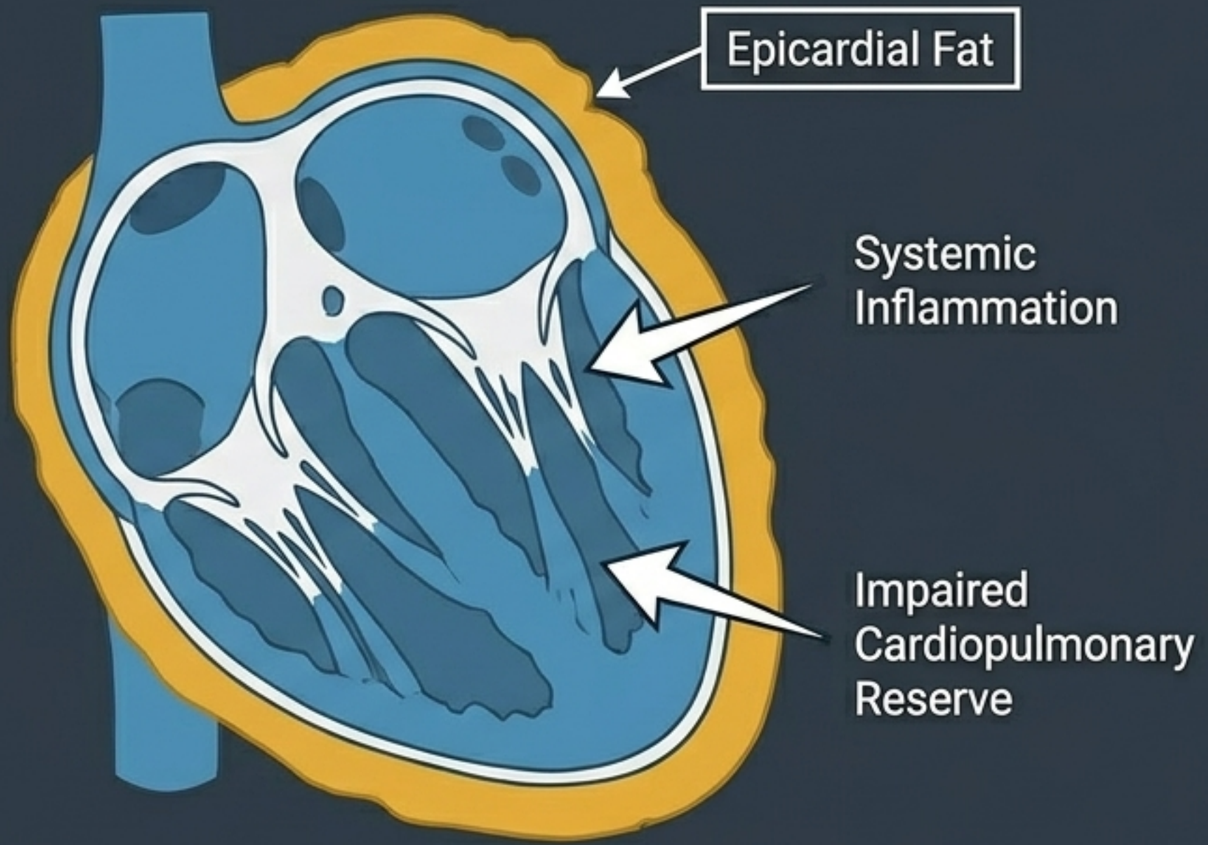
Loop diuretics provide no mortality benefit but are essential for symptom control. Target the lowest effective dose.

Furosemide (Lasix®)	Bumetanide (Burinex®)	Metolazone
20-80 mg PO daily/BD. Highly variable oral bioavailability (~50%). Higher doses (up to 250-500mg) required in eGFR <30.	0.5-2 mg PO. More predictable bioavailability (~80%).	2.5-5 mg PO. Used for 3-5 days as sequential nephron blockade in diuretic resistance. High risk of electrolyte depletion.

The Phenotype Constellation



Phenotype 1: Obesity & Metabolic Profile



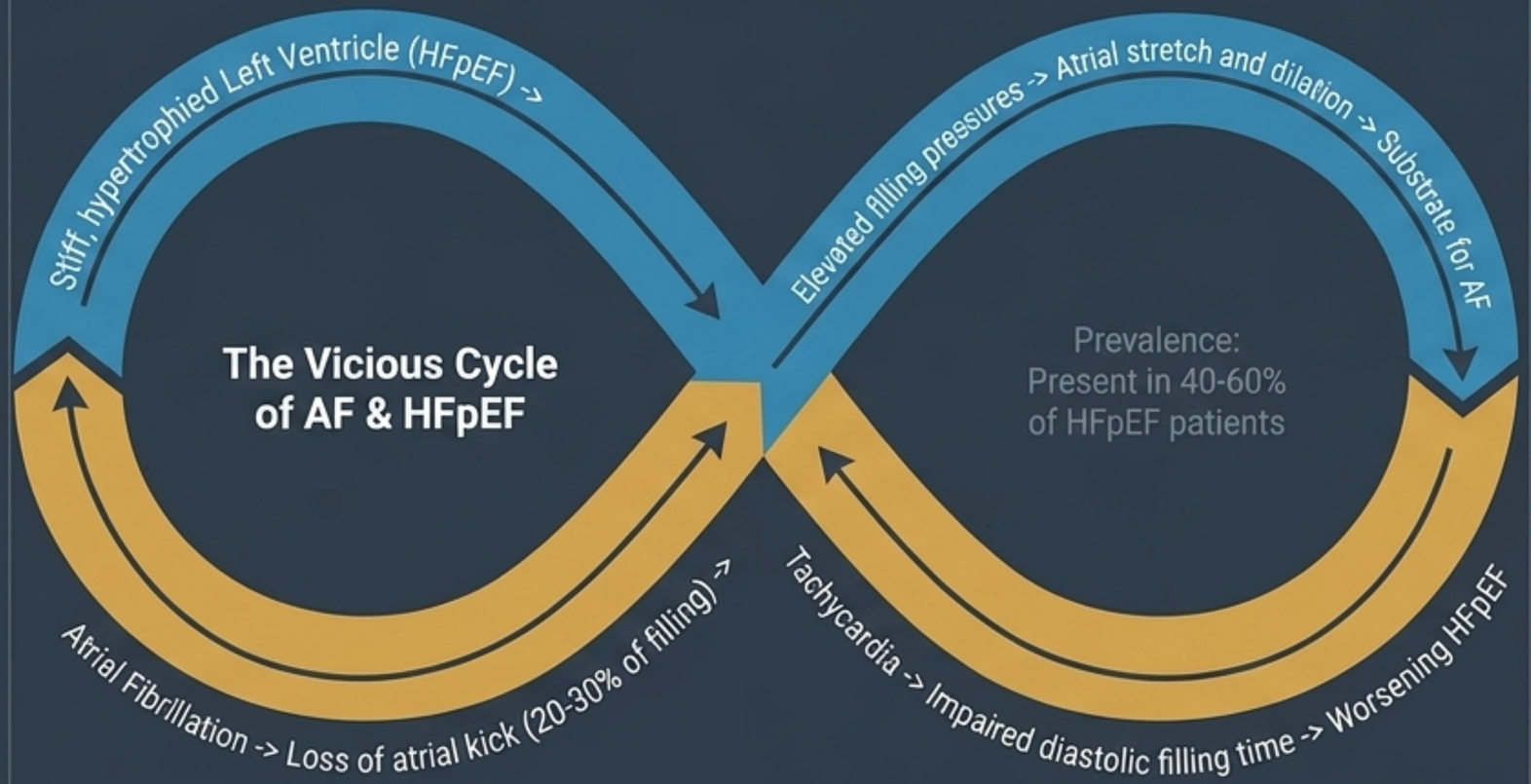
The STEP-HFpEF Breakthrough	
Intervention:	Semaglutide 2.4 mg SC weekly (Wegovy®).
Outcomes:	Mean weight loss **−13.3%**. Significant improvement in KCCQ score (**+7.8 points**) and 6MWD (**+20.3 m**).
CRP:	**−38.5%** relative reduction (targeting the inflammatory driver).

Profile: BMI ≥30, metabolic syndrome, insulin resistance. The most common phenotype (≥60% of HFpEF).

Clinical Note: Target ≥10% body weight reduction. Bariatric surgery is a valid consideration for BMI ≥40.

Phenotype 2: The AF-Driven Loop

The Vicious Cycle of AF & HFpEF



Targeted Strategy

Rate Control

Default first strategy.
Target rest HR <80 bpm.
(Bisoprolol, Digoxin, Diltiazem).

Rhythm Control

Catheter ablation is increasingly favored (CASTLE-HFpEF emerging data) for symptomatic patients.

Anticoagulation

DOACs preferred over warfarin (calculate CHA2DS2-VASc).

Left-Sided Vascular Overload

Phenotype 3: Vascular / Hypertensive

Driver

Long-standing hypertension, arterial stiffness, concentric LVH.

Target

Aggressive BP control **<130/80 mmHg**.

Therapies

ACEi/ARBs or **CCBs** first line. Consider **ARNI** (Sacubitril/Valsartan) especially in women or LVEF close to 50% (PARAGON-HF data). **Spironolactone** (TOPCAT Americas data) for persistent congestion.

Right-Sided RV Uncoupling

Phenotype 4: RV Dysfunction

Driver

RV-pulmonary arterial uncoupling, elevated pulmonary vascular resistance.

Implication

Associated with significantly **worse prognosis**. Monitor via serial echo.

Targets

Targets include **stringent diuresis** and **assessing for PAH**.

Phenotype 5: The ‘Must Not Miss’ Infiltrative Profile

The Profile

Cardiac ATTR Amyloidosis. Elderly Australians, especially men >75 years with aortic stenosis or bilateral carpal tunnel syndrome.

The Diagnostic Key

Technetium-99m Pyrophosphate (PYP) Scintigraphy. Sensitivity/specificity >95% (with concurrent immunofixation to exclude AL amyloid). Available at major tertiary centres (Royal Melbourne, RPAH).

Disease-Specific Therapy

Tafamidis (Vyndaqel®). TTR stabilizer. ATTR-ACT trial showed 30% reduction in all-cause mortality. PBS-listed (Authority Required).

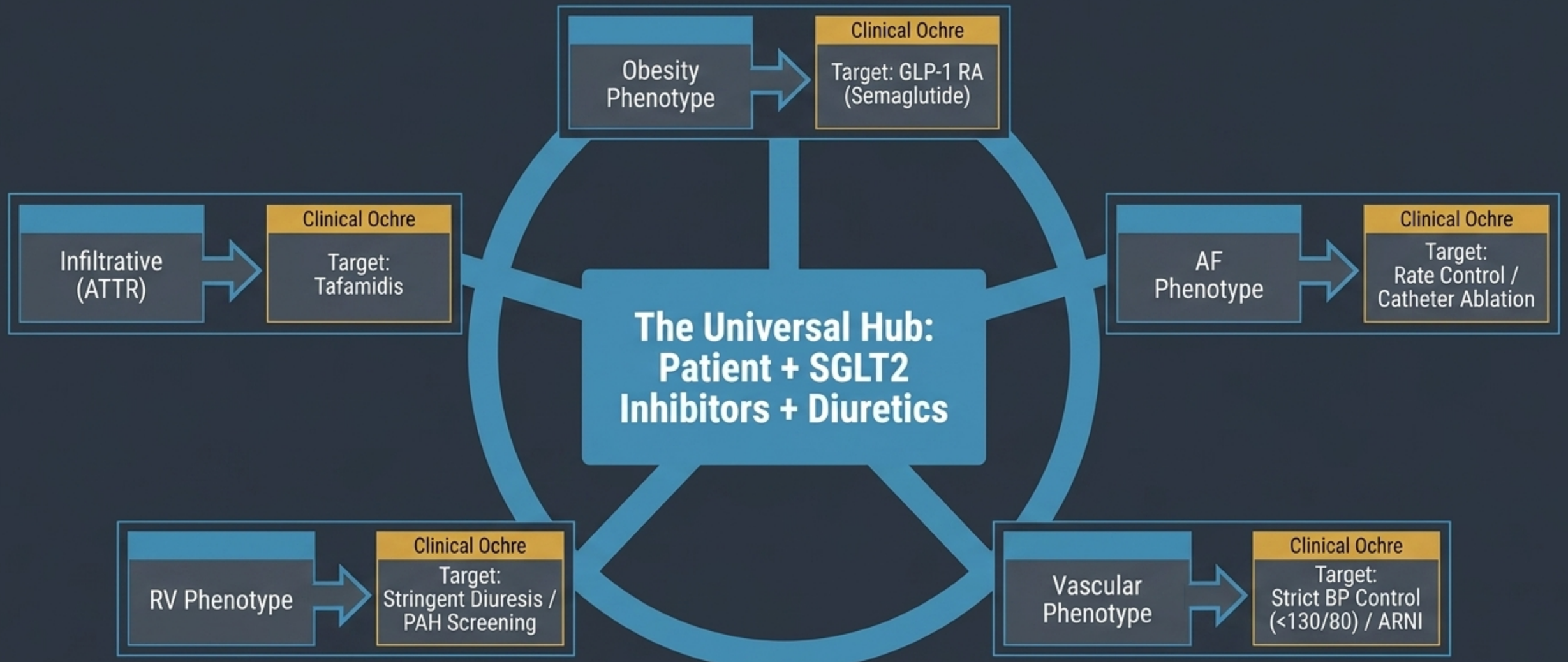
The Pharmacotherapy Command Center

Treatment Target	First-Line Agent	Duration	Clinical Caveats
Disease Mod	SGLT2i (Empa/Dapa)	Lifelong	Regardless of diabetes status.
Congestion	Furosemide 20-80mg	Titrated	Target lowest effective dose. Add metolazone if resistant.
Hypertension	ACEi/ARB or CCB	Ongoing	Target BP <130/80. Consider ARNI if LVEF ~50%.
Atrial Fibrillation	Beta-blocker/Diltiazem/Digoxin	Ongoing	Rate <80 bpm. Consider ablation.
Iron Deficiency	Ferric carboxymaltose IV	Single course	Replete if ferritin <100 (or 100-299 & TSAT <20%).
Obesity	Semaglutide 2.4mg	Ongoing	Weight loss 10-15%.

Special Populations Decision Grid

Pregnancy	[RED] SGLT2i and ACEi/ARBs absolutely contraindicated (teratogenic). Switch to methyldopa/labetalol. DOACs contraindicated.
Elderly ≥75	[AMBER] SGLT2i safe but monitor for falls/volume depletion. Start diuretics low (e.g., furosemide 20mg) to avoid pre-renal AKI. Target SBP 130-139.
Renal Impairment	[GREEN] SGLT2i initiated if eGFR ≥20. [AMBER] Loop diuretics require higher doses; Spironolactone avoid if eGFR <30 or K+ >5.0.
Hepatic Impairment	[AMBER] Avoid SGLT2i in Child-Pugh C. Monitor diuretics closely to prevent hypokalaemia-induced encephalopathy.

The Precision Treatment Web



Successful HFpEF management demands universal disease modification at the core, surrounded by aggressive, phenotype-specific comorbidity control.

Node 1

2-4 Weeks (Post-Initiation)

Check renal function (eGFR, K+) and BP after SGLT2i/diuretic start.

Assess volume status; ensure “sick-day rules” are understood.

Node 2

1-3 Months (Stability)

Review NYHA/KCCQ symptoms, weight, and HR.

Check UEC, BNP/NT-proBNP every 3 months.

Referral to Exercise-based Cardiac Rehabilitation (improves VO2 by 1.5-2.0 mL/kg/min).

Node 3

6-12 Months (Surveillance)

Repeat echocardiography (assess LV/LA/RV function).

Recheck Iron Studies; screen for silent AF (Holter).

Red Flags for Urgent Review Weight gain >2 kg in 3 days, new orthopnoea, escalating peripheral oedema.

The therapeutic desert is now a rapidly evolving frontier. Diagnosis requires rigorous filtering; treatment requires precision execution.

Novel Targets (Finerenone)

FINEARTS-HF (2024) met primary endpoints using non-steroidal MRAs, promising a safer potassium profile and HF event reduction.

Next-Gen Metabolic Agents

Dual GIP/GLP-1 RAs (Tirzepatide / SUMMIT trial) expected to push the boundaries of the obesity-HFpEF phenotype.

Advanced Phenotyping

Machine-learning phenogroups, multi-omics profiling, and advanced Cardiac MRI tissue characterization will redefine precision targeting.