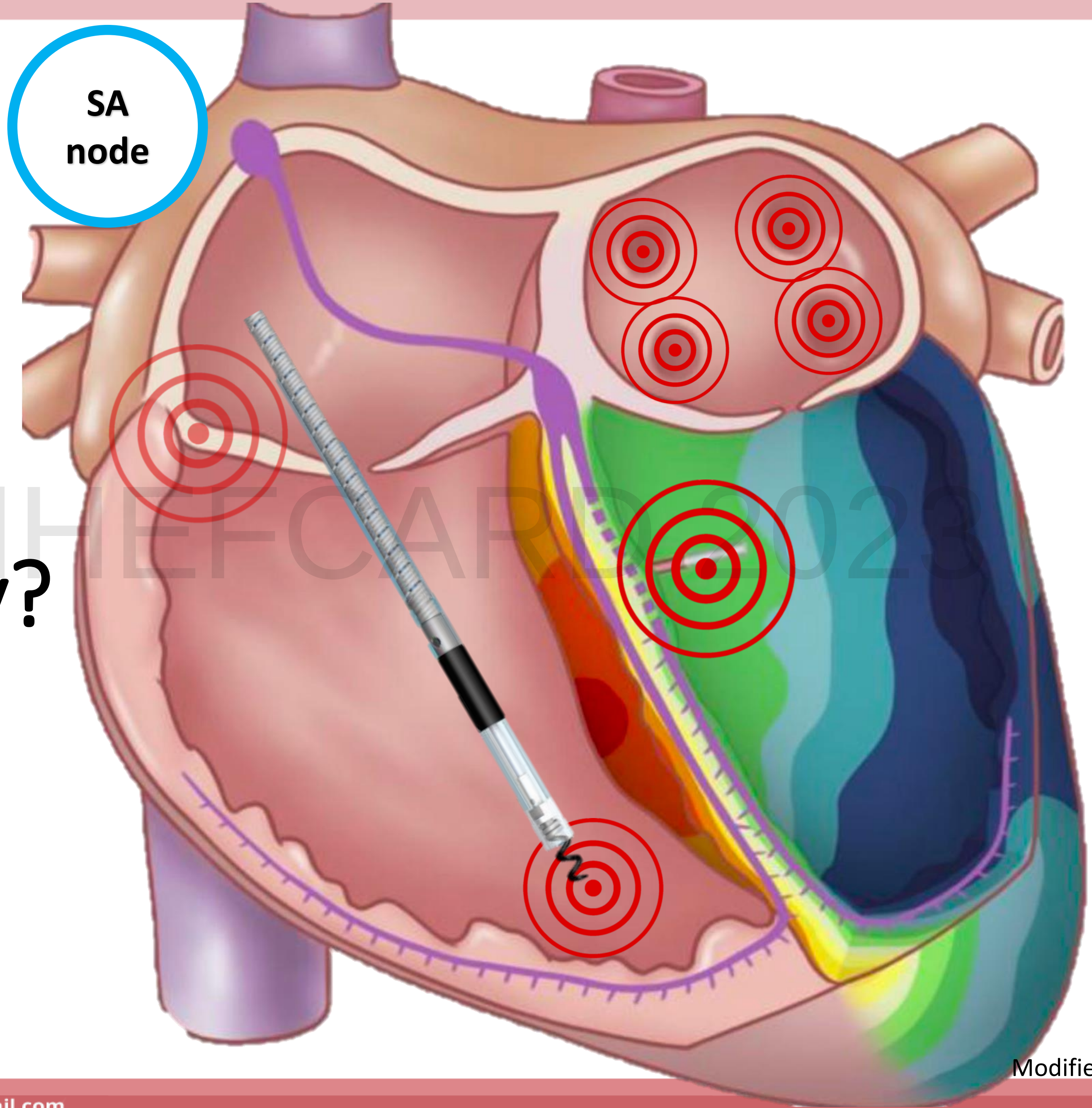
The 3rd Indonesia Symposium on Heart Failure and Cardiometabolic Disease 2023

How electrical dyssynchrony worsens Heart Failure

Anggia Chairuddin Lubis

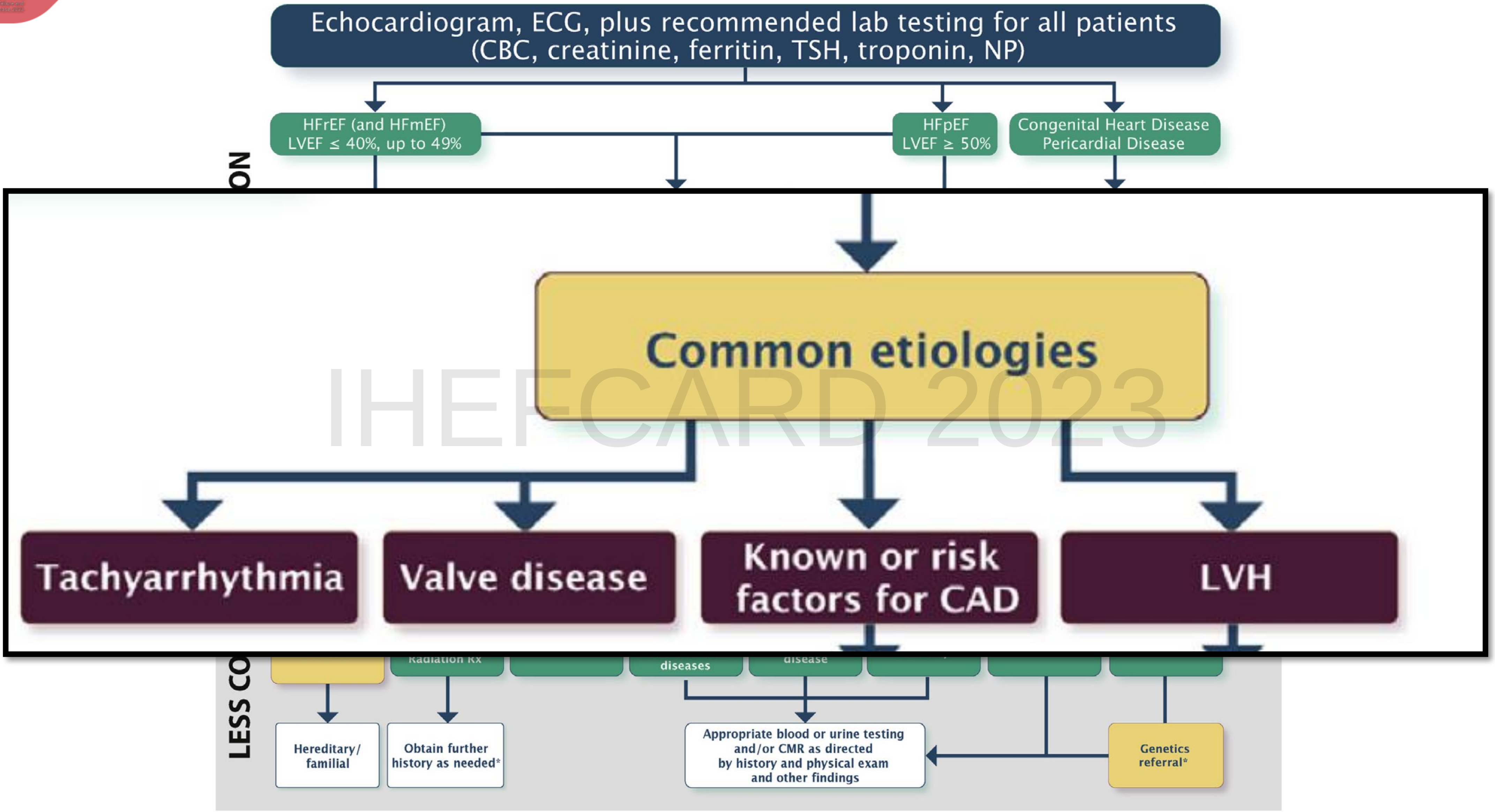
20 min


SA node



Dyssynchrony?

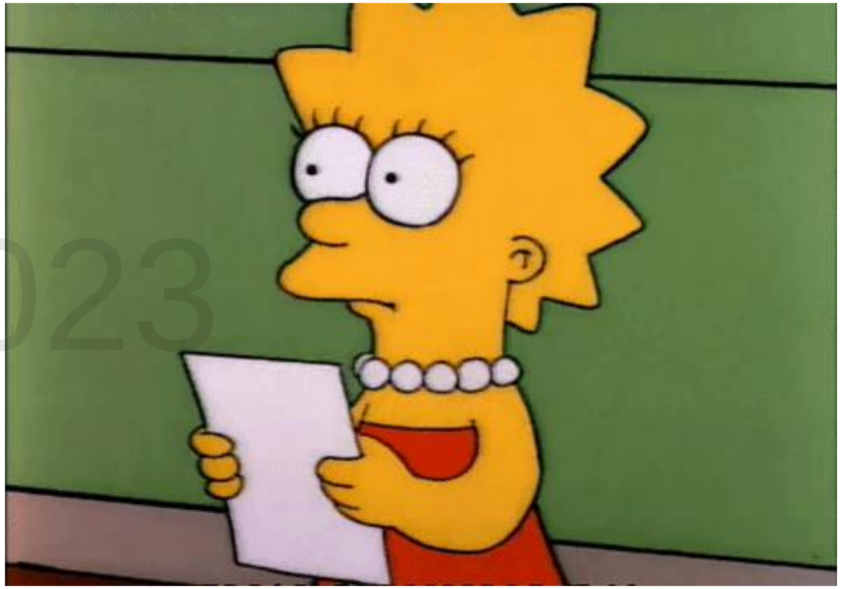
Modified from DOI 10.3389/fcvm.2022.843969



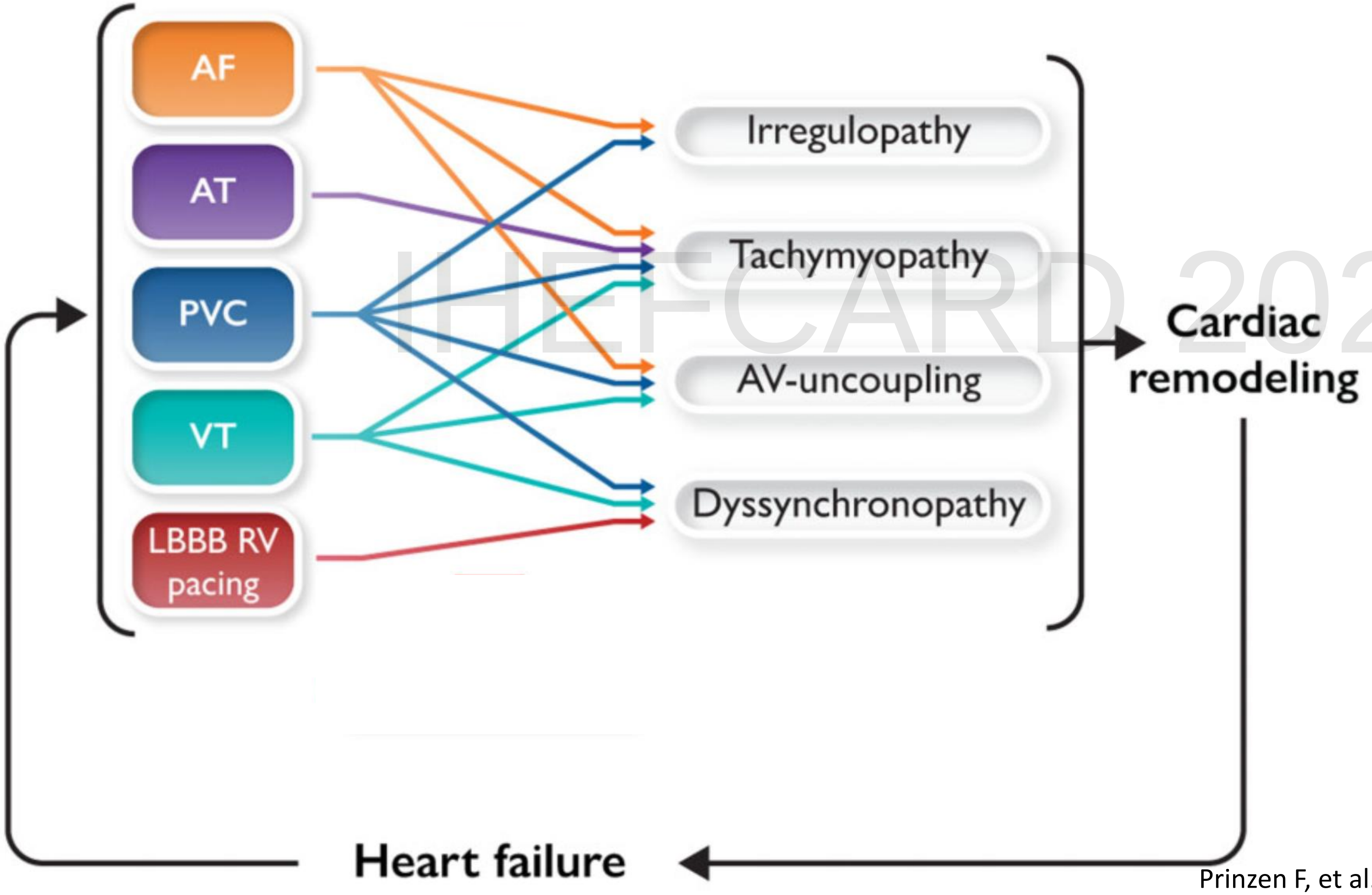
Ezekowitz, JA et al. Canadian Heart Failure Gudielines 2017

Table 1 Pathophysiological mechanisms of cardiomyopathies associated with arrhythmias or electrical disturbances

		Tachy-cardiomyopathy	PVC-mediated cardiomyopathy	AF-mediated cardiomyopathy	LBBB-mediated cardiomyopathy
Triggers	Rhythm	Fast but regular	Irregular	Irregular	Regular
	Post-extrasystolic potentiation	Absent	Present[a]	Variable	Absent
	AV coupling	Preserved[b]	Dissociated[c,d]	Non-existent	Preserved[e]
	LV dyssynchrony	Only present in VT	Intermittent[c,f]	None	Continuous
	Myocardial blood flow	Reduced[f]	??	Likely reduced	reduced (septum)
	Haemodynamic compromise	Present, low EF	(?) Likely present	(?) Likely present	Present, low EF
	Intrinsic autonomic nerve activity	(?) Unchanged	Significantly increased[f]	[g]	[g]
Cardiac intrinsic effects					
Tissue	Inflammation	Present[a]	Absent	[g]	[g]
	Fibrosis	Increased[a]	Mild[f]	[g]	Variable
	Oxidative, metabolic stress	Present	(?) Likely present	(?) Likely present	Present
Cellular	Ventricular electrical remodelling	Present	Present[f]	[g]	**Present**
	Ca^{2+} transient	Reduced[f]	Reduced[f]	[g]	Reduced[f]
	Action potential duration	Increased[f]	Prolonged[f] (heterogeneous)	[g]	Heterogeneous[f]
	β-adrenergic signalling	Decreased[f]	[g]	[g]	Decreased
Organ	Hypertrophy	Eccentric[a]	Eccentric[f]	[g]	Asymmetric, eccentric
	Ejection fraction	Reduced[a]	Reduced[a]	Reduced[d]	Reduced[a]
Extrinsic (non-cardiac) effects					
	Neurohumoral	+; BNP; Symp; RAAS	+; BNP; Symp; RAAS	+; BNP; Symp; RAAS	+; BNP; Symp; RAAS
Recovery	LV ejection fraction	Normalized[a]	Normalized[a]	Normalized[d]	Normalized[a]
	Dimensions	Partially dilated[a]	Normalized[a]	[g]	Normalized[d]
	Diastolic dysfunction	Persistent[d]	[g]	[g]	[g]
	Electrical remodelling	[g]	[g]	[g]	Partial reversal
	Hypertrophy	Reactive[a]	[g]	[g]	Partial reversal
	Fibrosis	Reactive/persistent[a]	(?) Persistent[f]	[g]	[g]

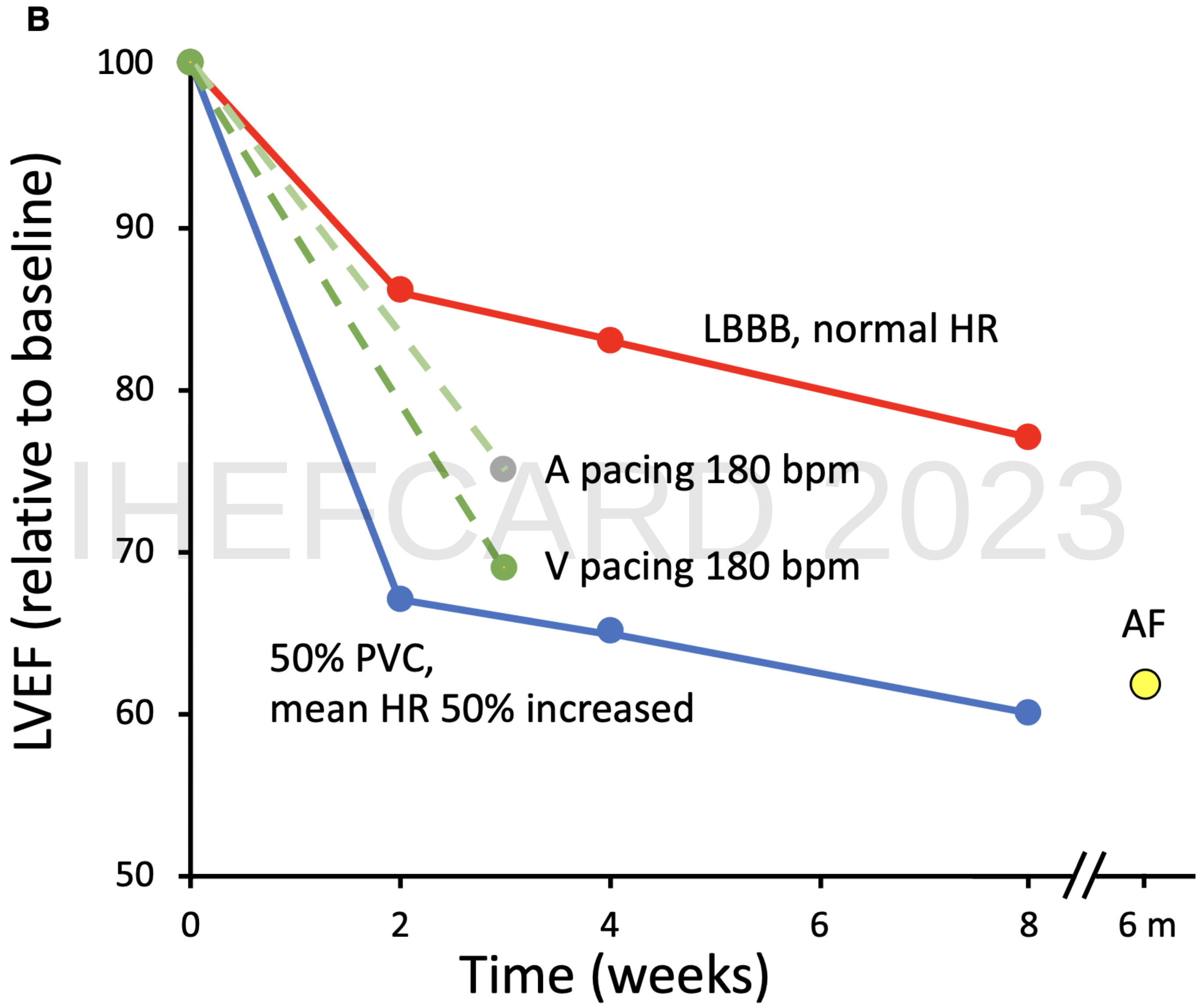


Dyssynchrony by mechanism



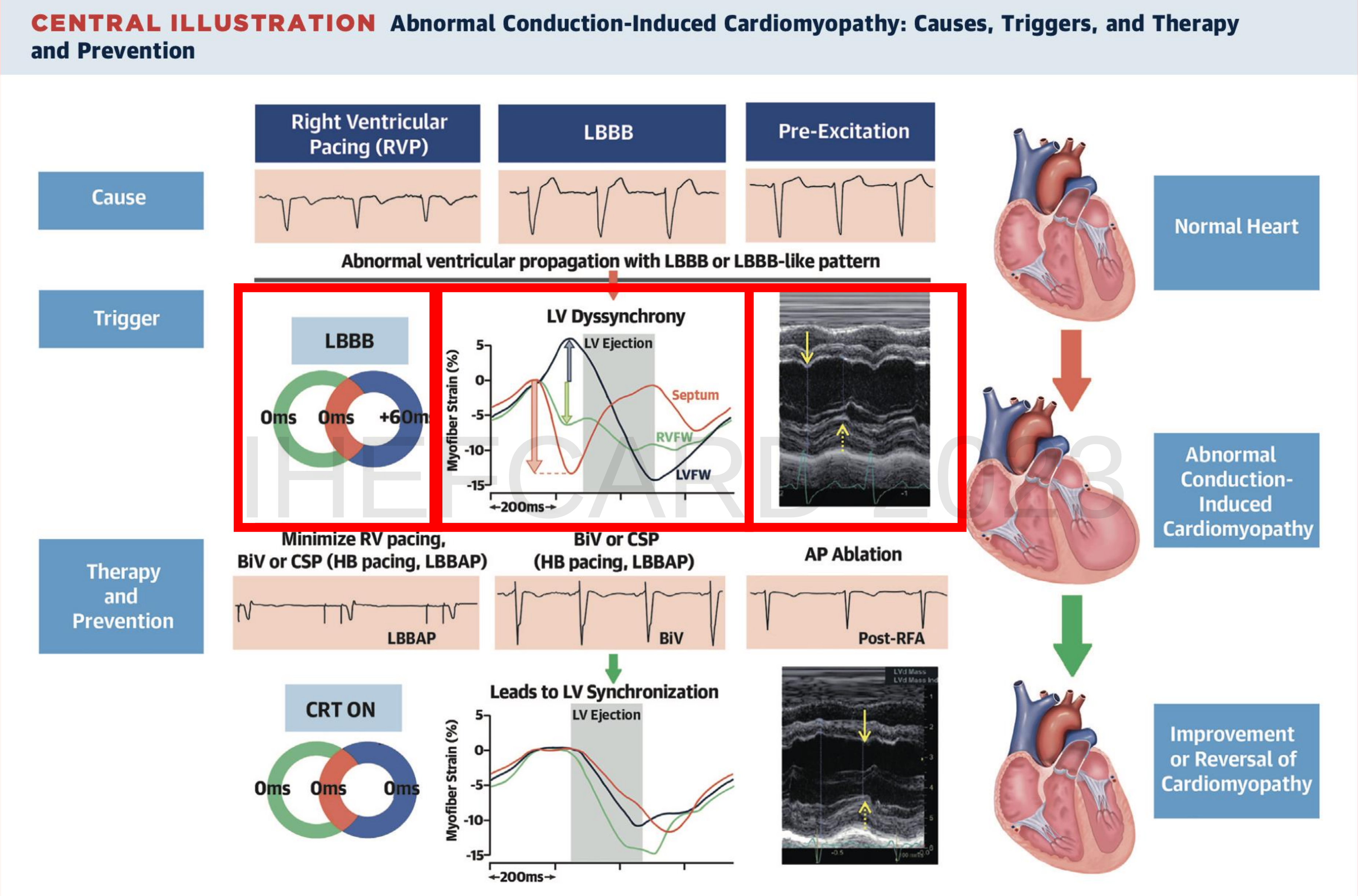
Multiple mechanisms observed in different arrhythmia!

Prinzen F, et al. European Heart Journal 2022;43:1917-1927



Prinzen F, et al. European Heart Journal 2022;43:1917-1927

Dys-synchronopathy



Huizar JF, et al. J Am Coll Cardiol. 2023;81(12):1192-1200.

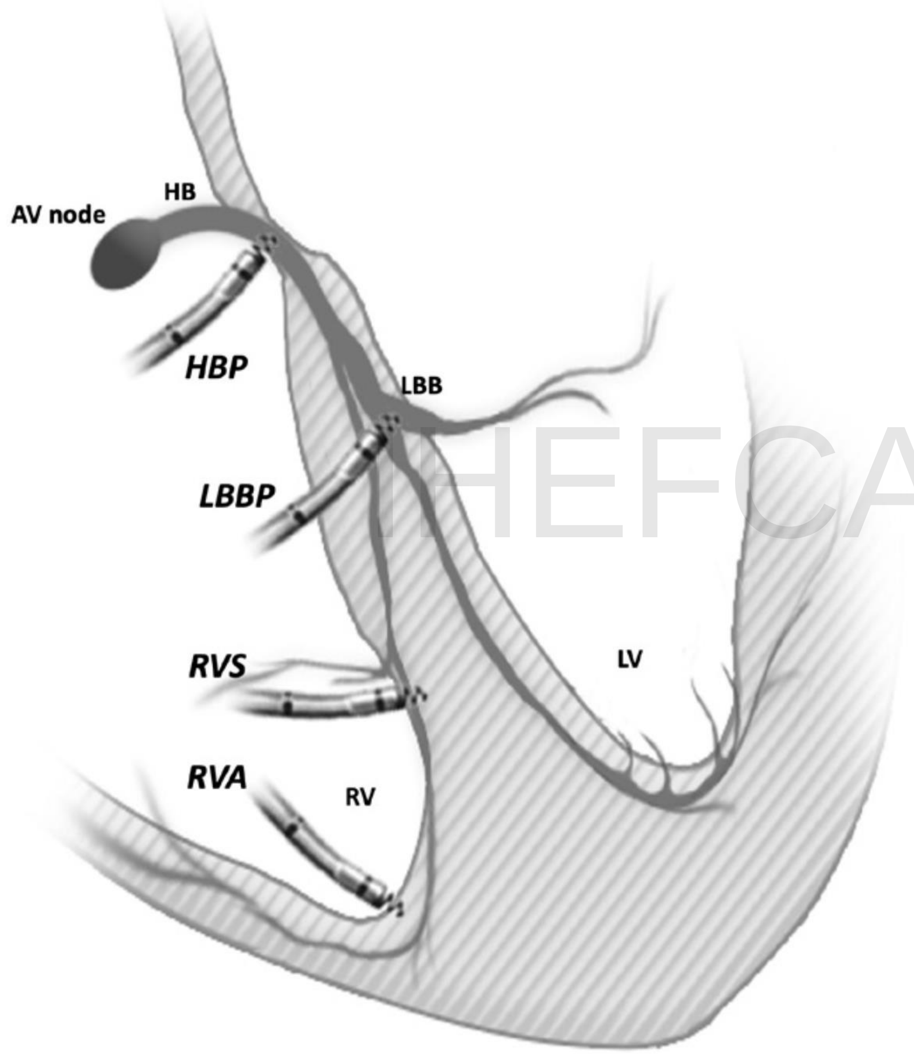
Huizar JF, et al. J Am Coll Cardiol. 2023;81(12):1192-1200.

TABLE 1 Summary of Conduction Abnormality-Induced CM

	RVP-CM	LBBB-CM	Pre-Excitation-CM
Incidence	Unknown	17%-38% after 4 y of LBBB diagnosis[5,29]	Unknown
Prevalence	12%-20% after 1-15 y[20-23]	2%-20% in patients with CM and LBBB referred for CRT (4-11 y)[30,31,42]	65% in patients with pre-excitation and LV dysfunction[37]
Risk factors/predictors	Time with high RVP (mo-y) RVP burden >40% (min 20%)[22,23,27] Older age[27] Intrinsic QRS duration[20] Paced QRS duration (>160 ms)[21,26,27] Prior LV systolic dysfunction[20] LV dyssynchrony[12,22] Global longitudinal strain[28] Male sex[3,20] Higher myocardial scar[27]	Time from LBBB diagnosis >4 y Older population	Right-sided and septal AP[36,37] Younger population (children)[35,37] Must rule out incessant or recurrent tachycardia
Treatment	CRT (LBBAP preferred over BiV or His pacing)	CRT (LBBAP preferred over BiV or His pacing)	Radiofrequency ablation[36,37] Antiarrhythmic (flecainide)[47]
Predictors of recovery	Shortening QRS duration,[a] QRS duration >150 ms, body mass index <30 kg/m^2, LA volume, female[39]	LV diastolic diameter and mild LV systolic dysfunction (>42%)[37,39] Shortening QRS duration,[a] QRS duration >150 ms, body mass index <30 kg/m^2, LA volume, female[39]	Age <6 y[37]
Outcomes	Improves LV function, NYHA functional class, and probably outcomes (no data)	Improves LVEF, NYHA functional class Decrease mortality and HF admissions	Improves LV function and dimensions[37]; unknown outcomes (no data)

[a]Data derived from overall super-responder cardiac resynchronization therapy (CRT) data likely representing right ventricular pacing (RVP)-cardiomyopathy (CM) and left bundle branch block (LBBB).
BiV = biventricular pacing; HB = His bundle; LBBAP = left bundle branch area pacing; LV = left ventricular; NYHA = New York Heart Association.

Huizar JF, et al. J Am Coll Cardiol. 2023;81(12):1192-1200.



Pacing Induced Cardiomyopathy

LVEF <50%

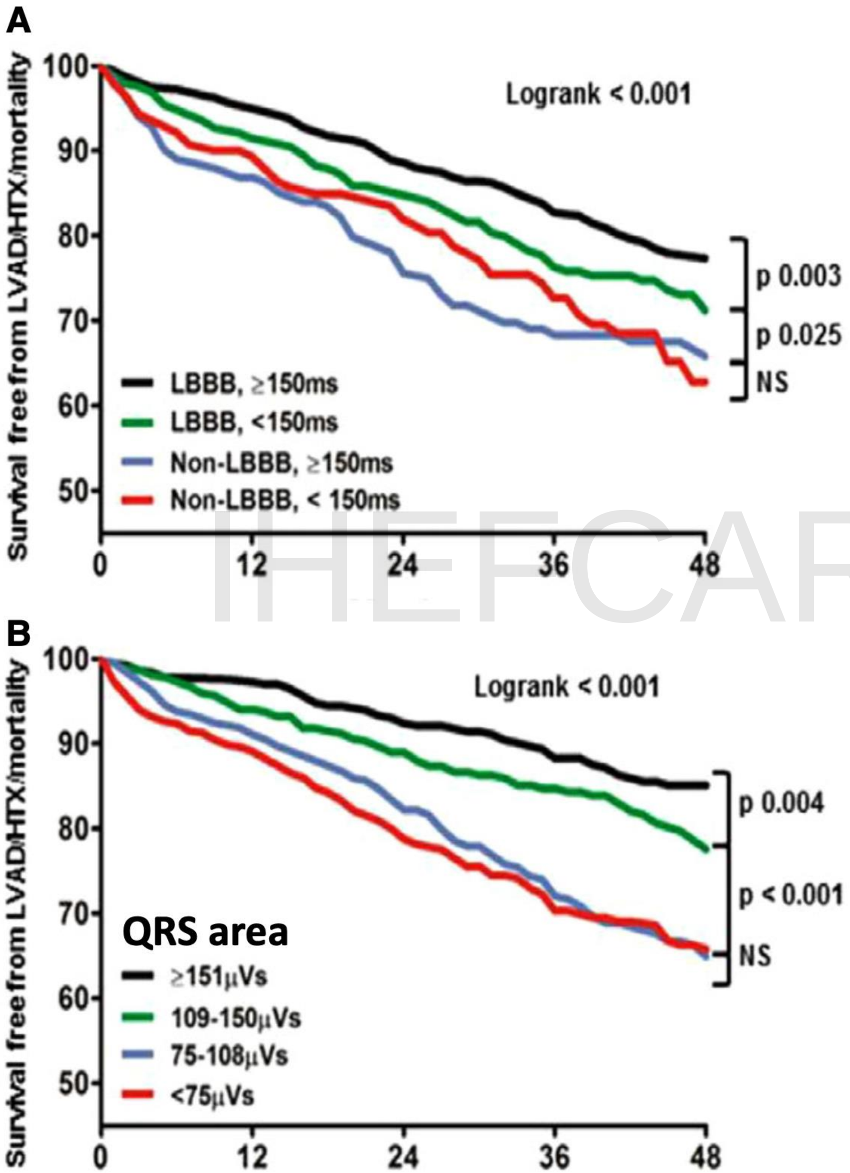
ΔEF >10%

HF hospitalisation

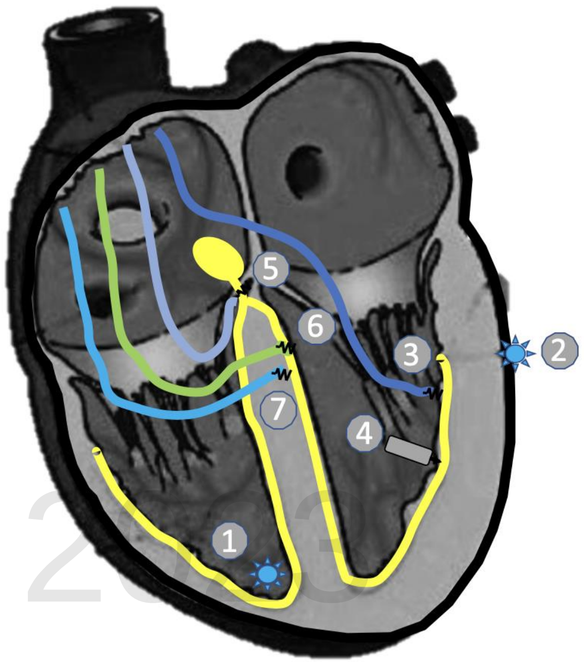
New onset AF

Ponnusamy SS, *et al*. *Heart* 2023;**0**:1–9

CRT: patient selection



CRT: pacing sites



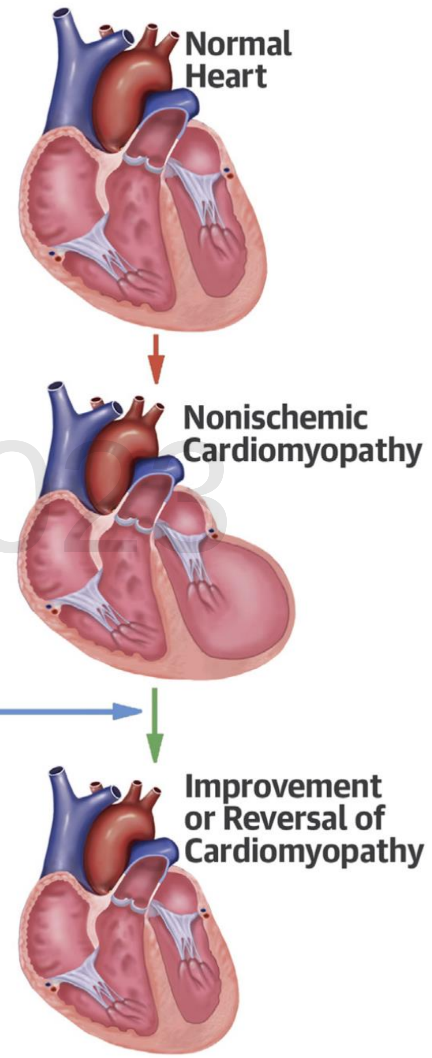
1+2 conventional epicardial CRT
1+3 endocardial CRT
1+4 wireless endocardial CRT
5 His bundle pacing
6 LBB pacing
7 LV septal pacing

Prinzen F, et al. European Heart Journal 2022;43:1917-1927

Tachy-myopathy
Irregulopathy
AV un-coupling

CENTRAL ILLUSTRATION **Arrhythmia-Induced Cardiomyopathies: Possible Triggers, Mediators, Effect, and Recovery**

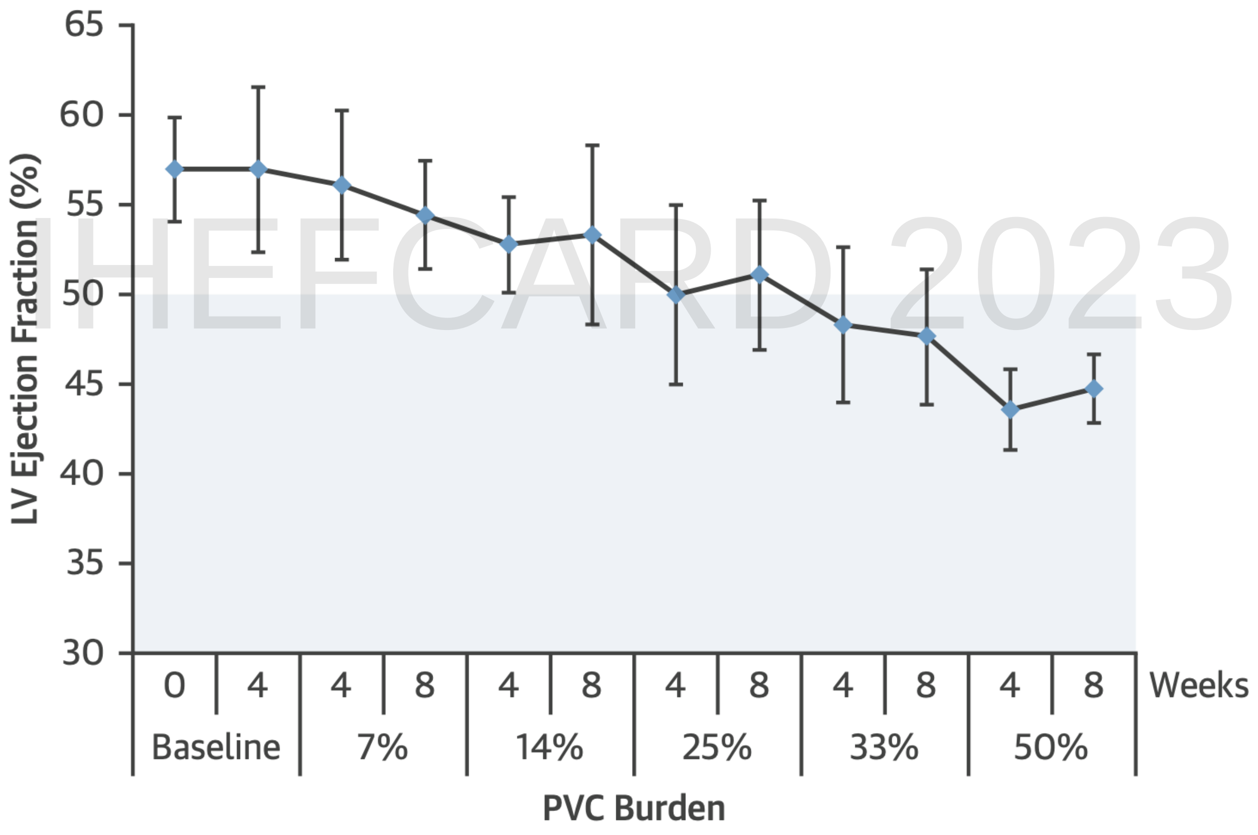
	Tachycardia	Frequent PVCs	Atrial Fibrillation
Triggers	Increased HR	• LV dyssynchrony • AV dissociation • HR irregularity • Intermittent tachycardia • Sympathetic dysregulation • Post-extrasystolic potentation	• HR irregularity • Sympathetic dysregulation • Loss of atrial contraction
Mediators	• Ca^{2+} overload • Ca^{2+} mishandling	• Ca^{2+} overload • Ca^{2+} mishandling ???	• Ca^{2+} mishandling ???
Effect	• Fibrosis • Myocyte and electrical remodeling • Contractile dysfunction • Neurohormonal activation	• Myocyte and electricial remodeling • Contractile dysfunction ? Fibrosis	• Contractile dysfunction ???
Arrhythmia Suppression	Ablation	Antiarrhythmic drugs	
Recovery	• Normalized LVEF • Ventricular dilatation • Diastolic dysfunction • Reactive hypertrophy • Persistent fibrosis	• Normalized LVEF and dimensions	• Normalized LVEF ???



Huizar, J.F. et al. J Am Coll Cardiol. 2019;73(18):2328-44.

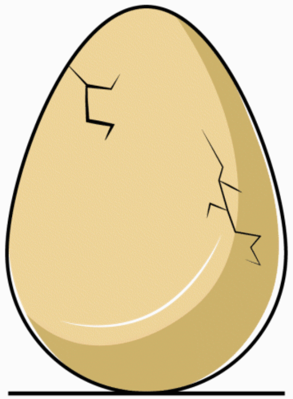
LVEF progression significantly affected by PVC burden

FIGURE 3 **Linear Decrease of LV Ejection Fraction With Sequential Increase in PVC Burden in an Experimental Model**



Huizar, J.F. et al. J Am Coll Cardiol. 2019;73(18):2328–44.

	CM resulting in PVCs	PVCs causing CM
Patient characteristics	Older with known heart disease	Healthy otherwise
Comorbidities	CAD, myocarditis, RV dysplasia[a]	No prior cardiac hx
Echocardiogram	Segmental hypokinesis, LVEF <25%	Global hypokinesis, LVEF 35 ± 10%[b]
Cardiac MRI (late gadolinium enhancement)	Significant scar	Absence or minimal scar burden (≤9 g)
PVC frequency	<5000/24 h (<5%)	≥10 000/24 h (≥10%)
PVC pattern	Multifocal	Monomorphic
QRS morphology	Non-specific	RVOT/LVOT/ epicardial
Response to PVC suppression	No change in LV function	Improvement of LV function



Prinzen F, et al. European Heart Journal 2022;43:1917-1927

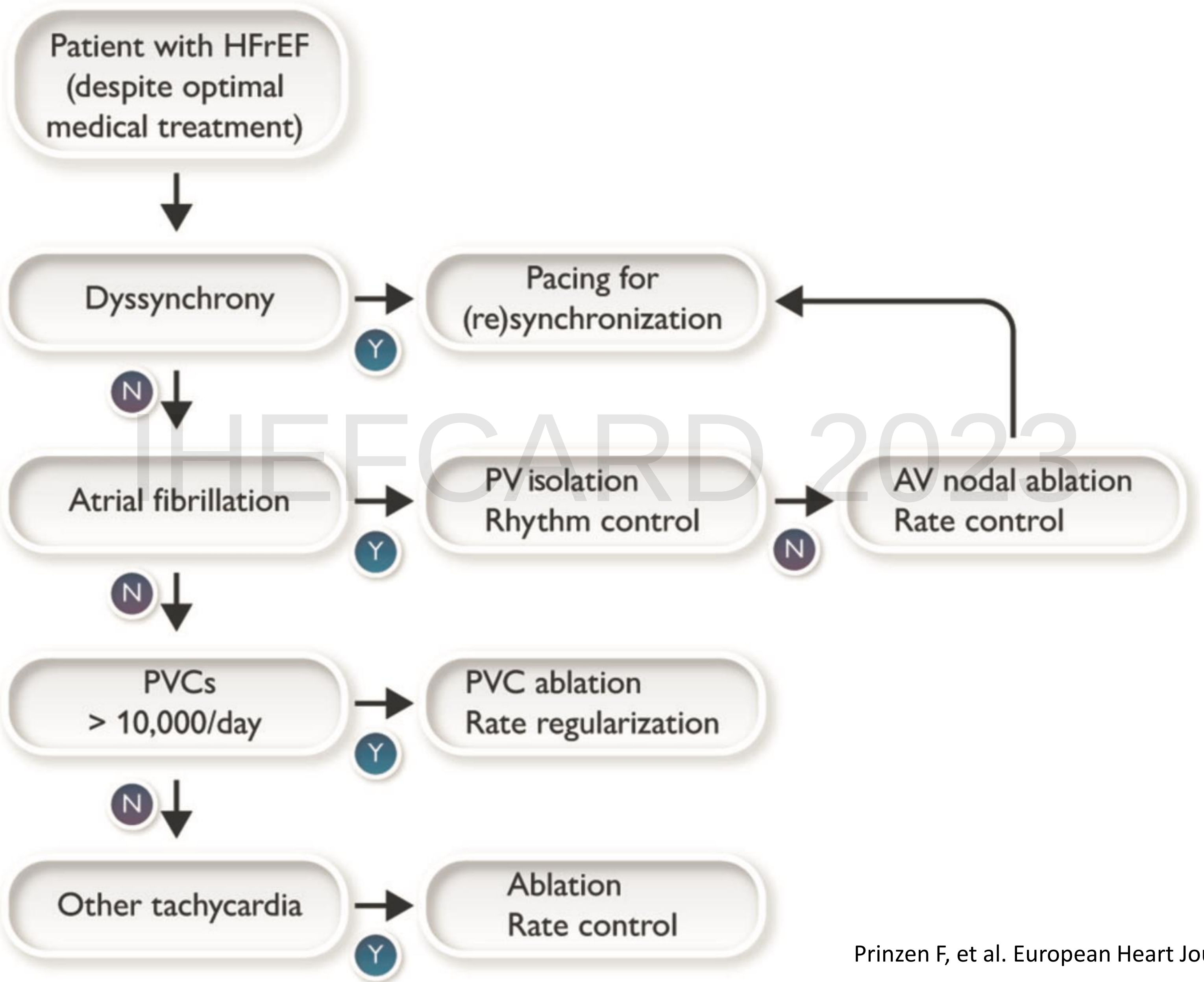
Management Strategies

Know your enemy..

TABLE 2 Reversible and Irreversible Causes of Cardiomyopathy

Reversible	Irreversible
Transient ischemia/post-cardiac arrest	Extensive/multiple myocardial infarctions
Subacute valvular heart disease	Hypertrophic cardiomyopathy
Uncontrolled hypertension	Cardiac sarcoidosis
LBBB – cardiomyopathy	End-stage valvular heart disease
Pacing-induced cardiomyopathy	Infectious (e.g., Chagas disease)
Drug or alcohol abuse	
Endocrine (severe hypothyroidism)	
PVC-induced cardiomyopathy	
Stress-induced cardiomyopathy	
Peripartum cardiomyopathy	
Inflammatory/infectious (e.g., myocarditis, sepsis)	

Huizar, J.F. et al. J Am Coll Cardiol. 2019;73(18):2328-44.

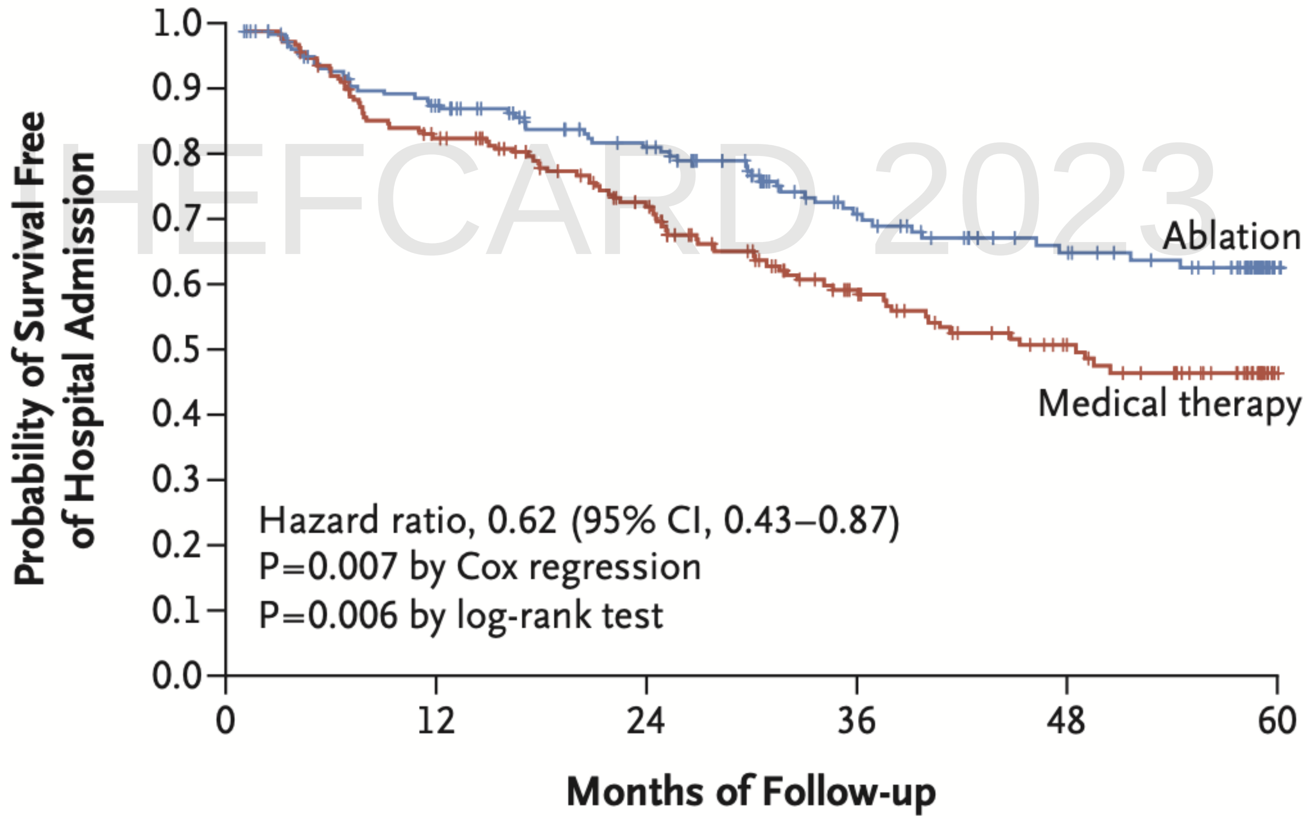


Prinzen F, et al. European Heart Journal 2022;43:1917-1927

Catheter Ablation for Atrial Fibrillation with Heart Failure

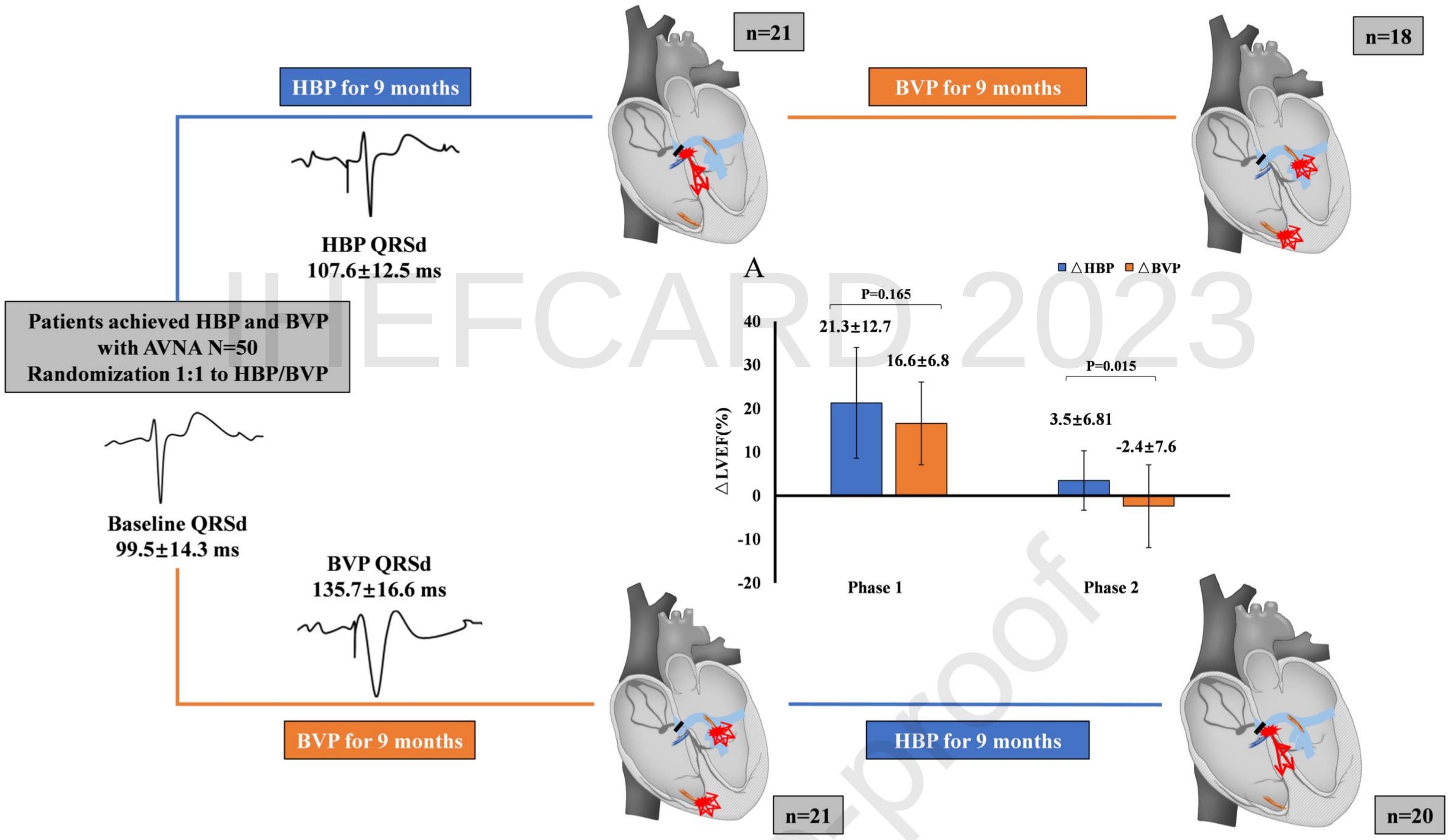
Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

Death or Hospitalization for Worsening Heart Failure



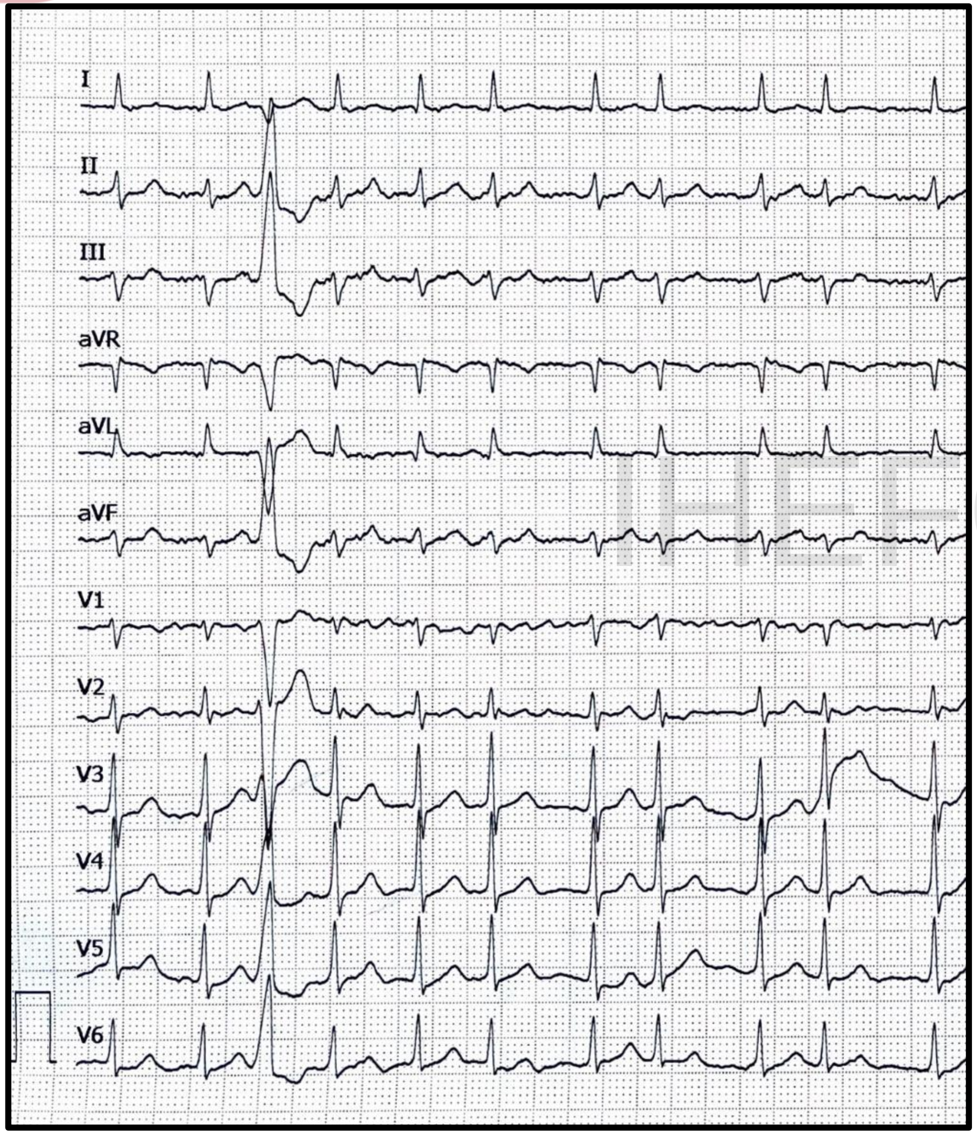
Marrouche NF, et al. NEJM 2018

His Bundle Pacing vs Biventricular Pacing Following Atrioventricular Node Ablation in Patients with Atrial Fibrillation and Reduced Ejection Fraction: A Multicenter, Randomized, Crossover Study. The ALTERNATIVE-AF trial.



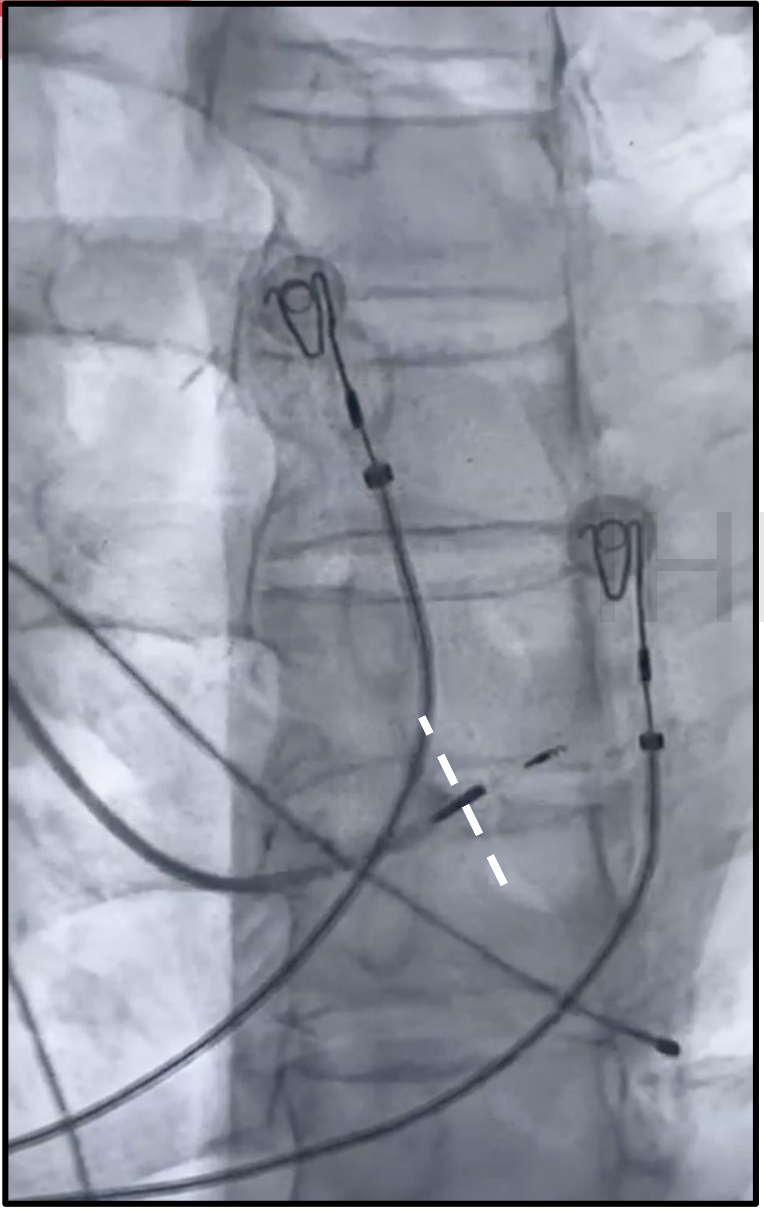
Huang W, et al. Heart Rhythm 2022

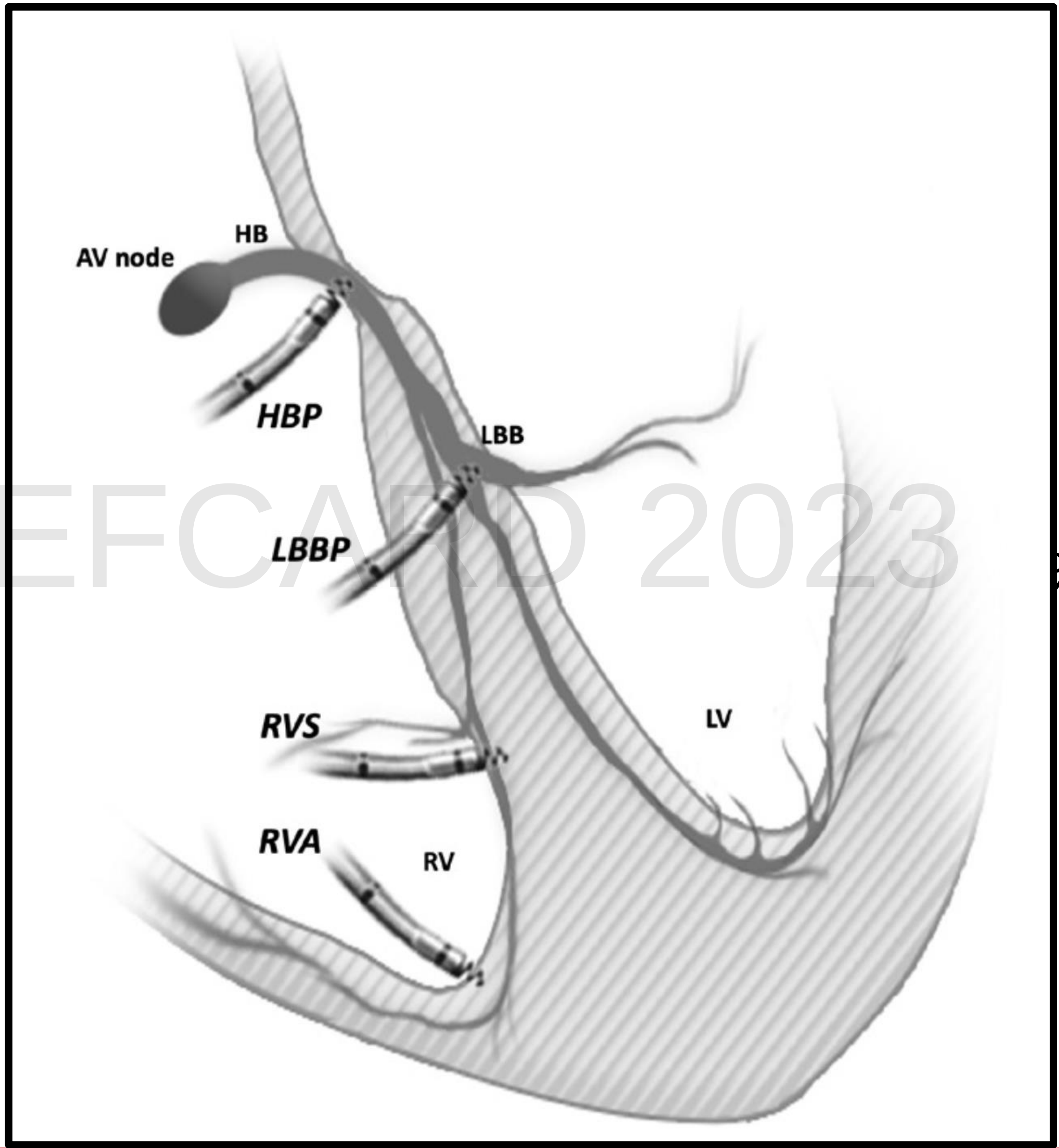
Case



Male, 71yo
HFrEF
LVEF 35%
Persistent AF, rate poorly controlled w/ BB and digoxin
Intolerant to ACEi / ARB

NT-pro-BNP 8305





→ I
% → 50%

Conclusion

Irregulopathy

Tachymyopathy

AV-uncoupling

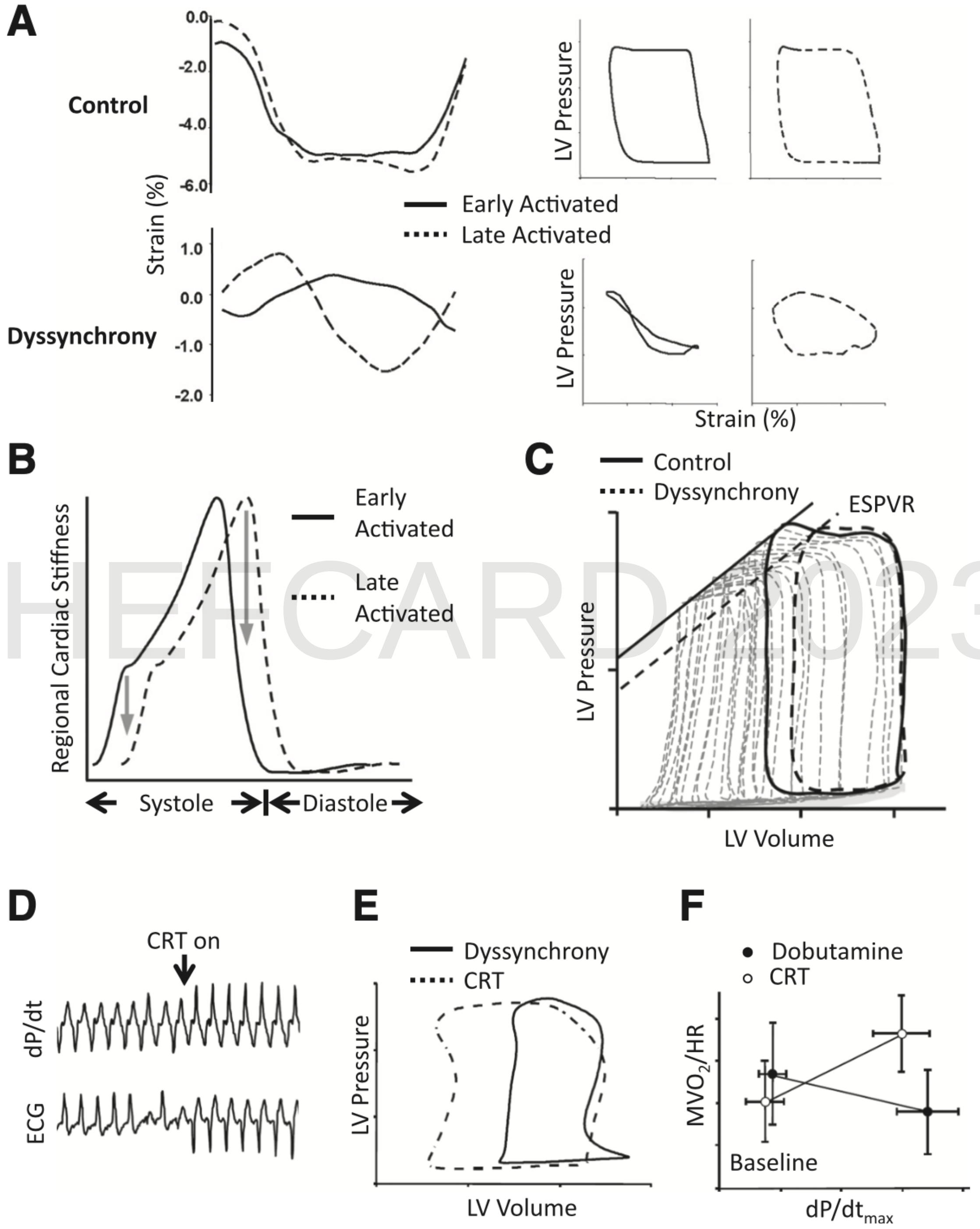
Dyssynchronopathy

- Prevent
- Detect: AF, RV pacing, PVC/VT, AT
- Know your enemy: reversible?
- Management:
    - Pharmacological
    - Catheter ablation
    - Device re-synchronization

Prinzen F, et al. European Heart Journal 2022;43:1917-1927


TERIMA KASIH
Emirates
FLY BETTER

Waktu	Symposium 4A	Peran
Sabtu, 24 Juni 2023 14.20-14.40	Topic 1 : How electrical dissynchrony worsens heart failure conditions	**Pembicara : Anggia Chairuddin Lubis, MD**



Kirk and Kass. *Circ Res*. 2013;113:765-776

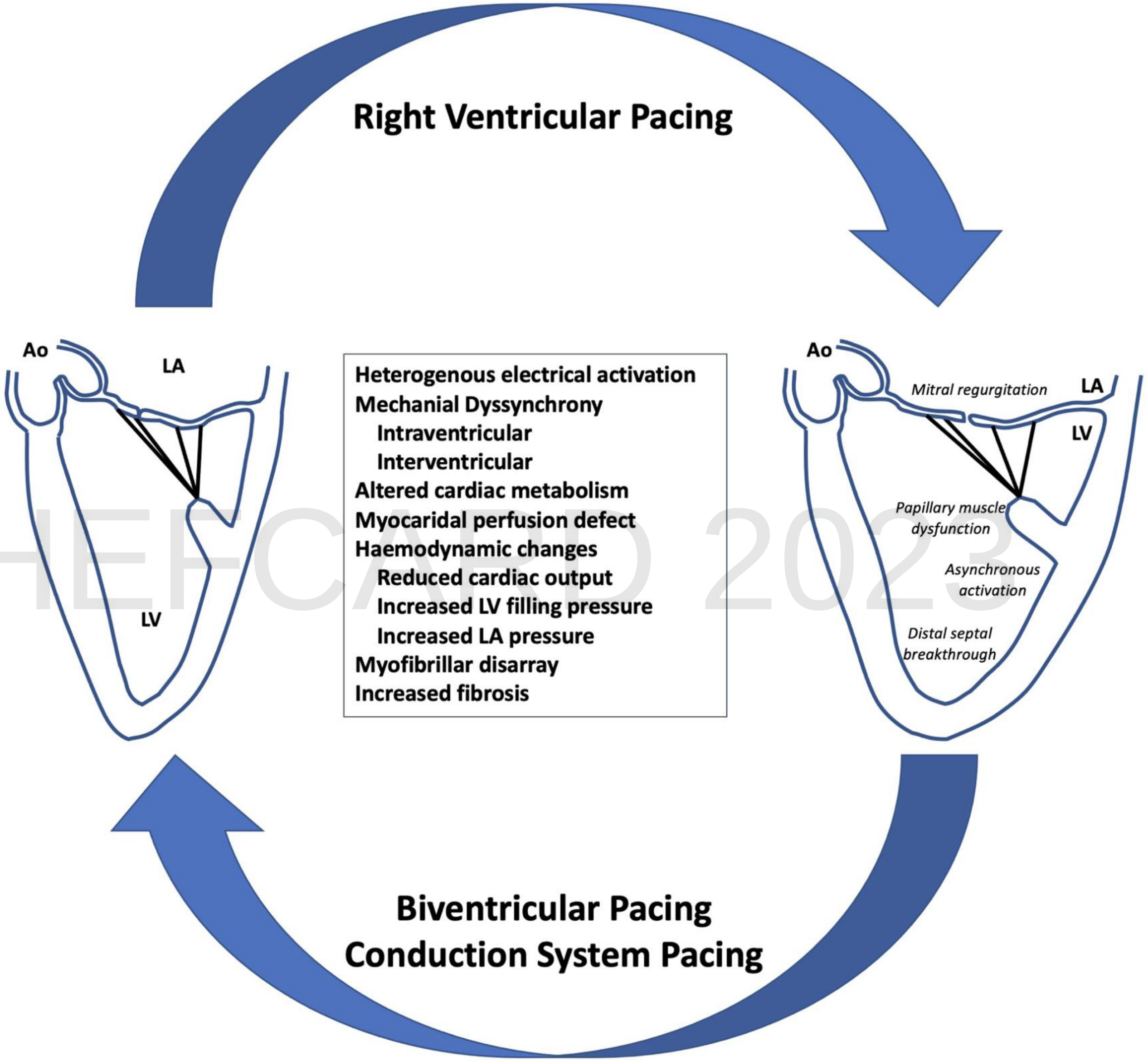


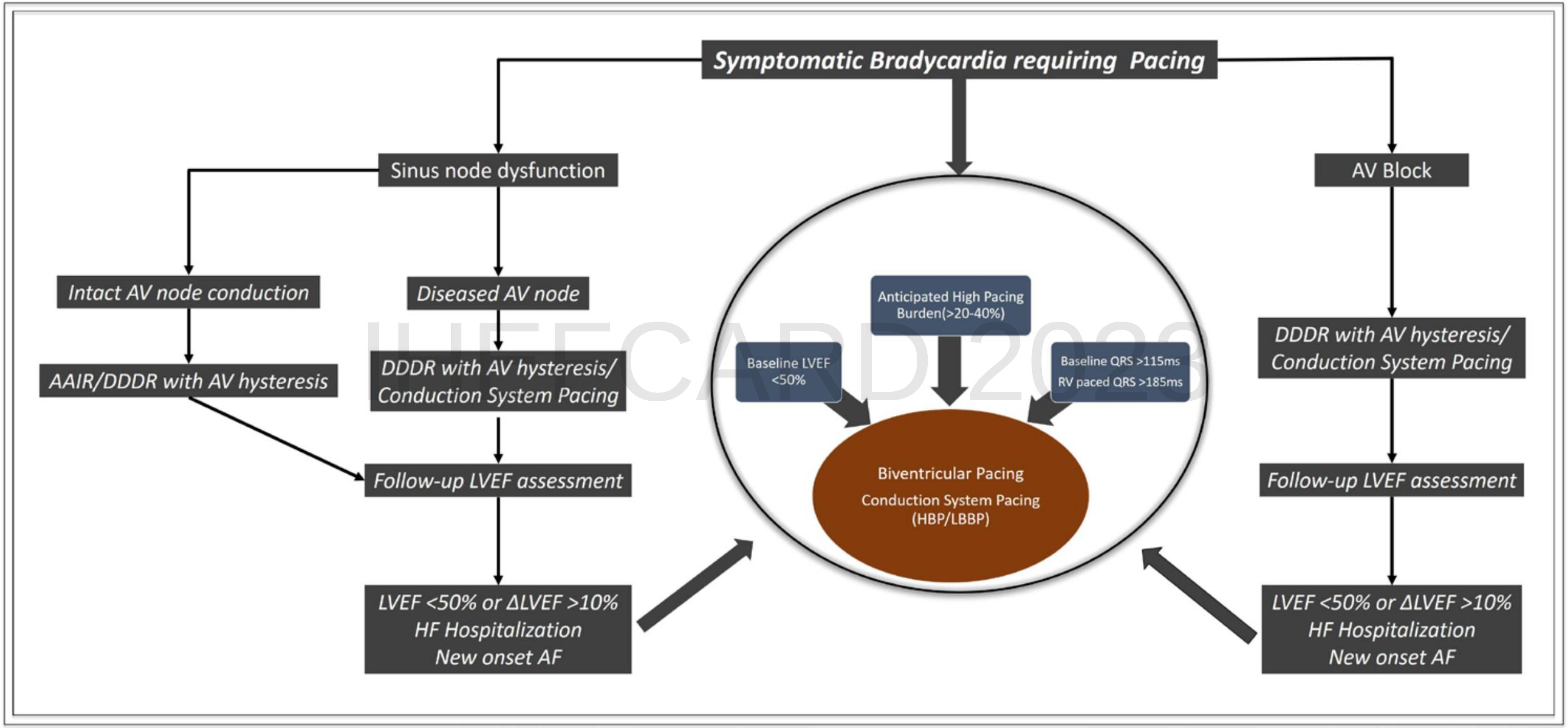
Figure 2 Pathogenesis of pacing induced cardiomyopathy. AO, aorta; LA, left atrium; LV, left ventricle.

Ponnusamy SS, *et al. Heart* 2023;**0**:1–9

Key messages

- ⇒ Pacing induced cardiomyopathy (PIC) is the terminology coined to describe the chronic RV pacing related left ventricular (LV) dysfunction, the incidence of which increases with the duration of RV pacing.
- ⇒ Most acceptable definition for PIC would be an LV ejection fraction (LVEF) of <50%, absolute decline of LVEF by ≥10% and/or new-onset heart failure (HF) symptoms after pacemaker implantation.
- ⇒ It will be clinically relevant to expand the definition of PIC beyond LV ejection fraction and to include HF hospitalisation due to systolic or diastolic dysfunction and new-onset atrial fibrillation (AF).
- ⇒ Male sex, advanced age, high RV pacing burden, coronary artery disease, pre-existing AF, baseline prolonged QRS duration, baseline low LVEF and prolonged paced QRS duration are the risk factors for the development of PIC.
- ⇒ Periodic assessment of patients with RV pacing is essential as nearly a fifth of them can develop PIC. A comprehensive device clinic programme may help in early diagnosis and better management of patients with PIC.
- ⇒ Cardiac resynchronisation therapy using biventricular pacing is the most commonly used approach for the management of PIC.
- ⇒ Conduction system pacing is a promising alternative both for prevention and treatment of PIC as it provides physiological activation of the ventricles and avoids dyssynchrony.

Ponnusamy SS, *et al*. *Heart* 2023;**0**:1–9



Ponnusamy SS, *et al*. *Heart* 2023;**0**:1–9