AF in ACHD; Incidence, Mechanism, and Antiarrhythmic Drugs

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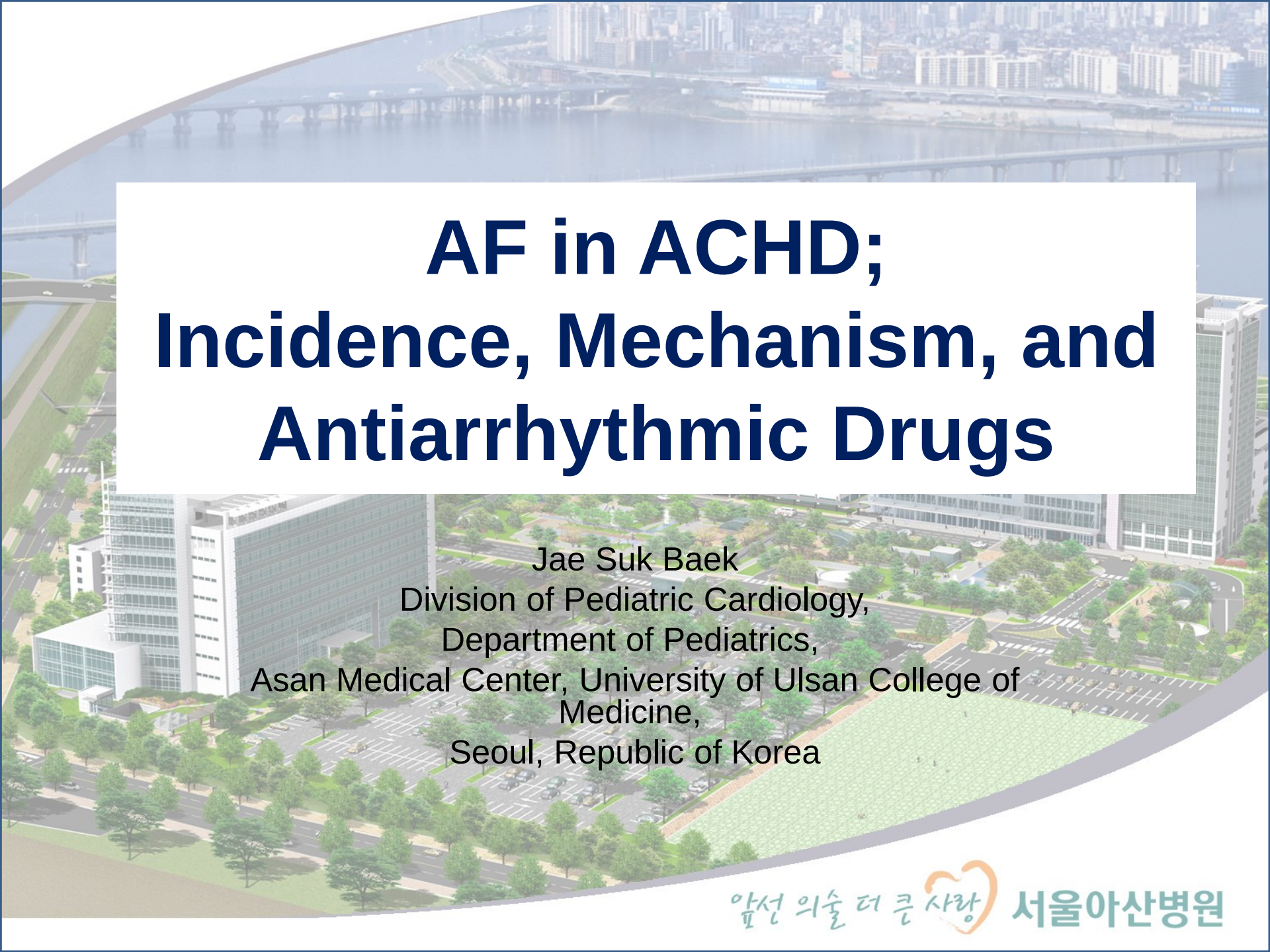
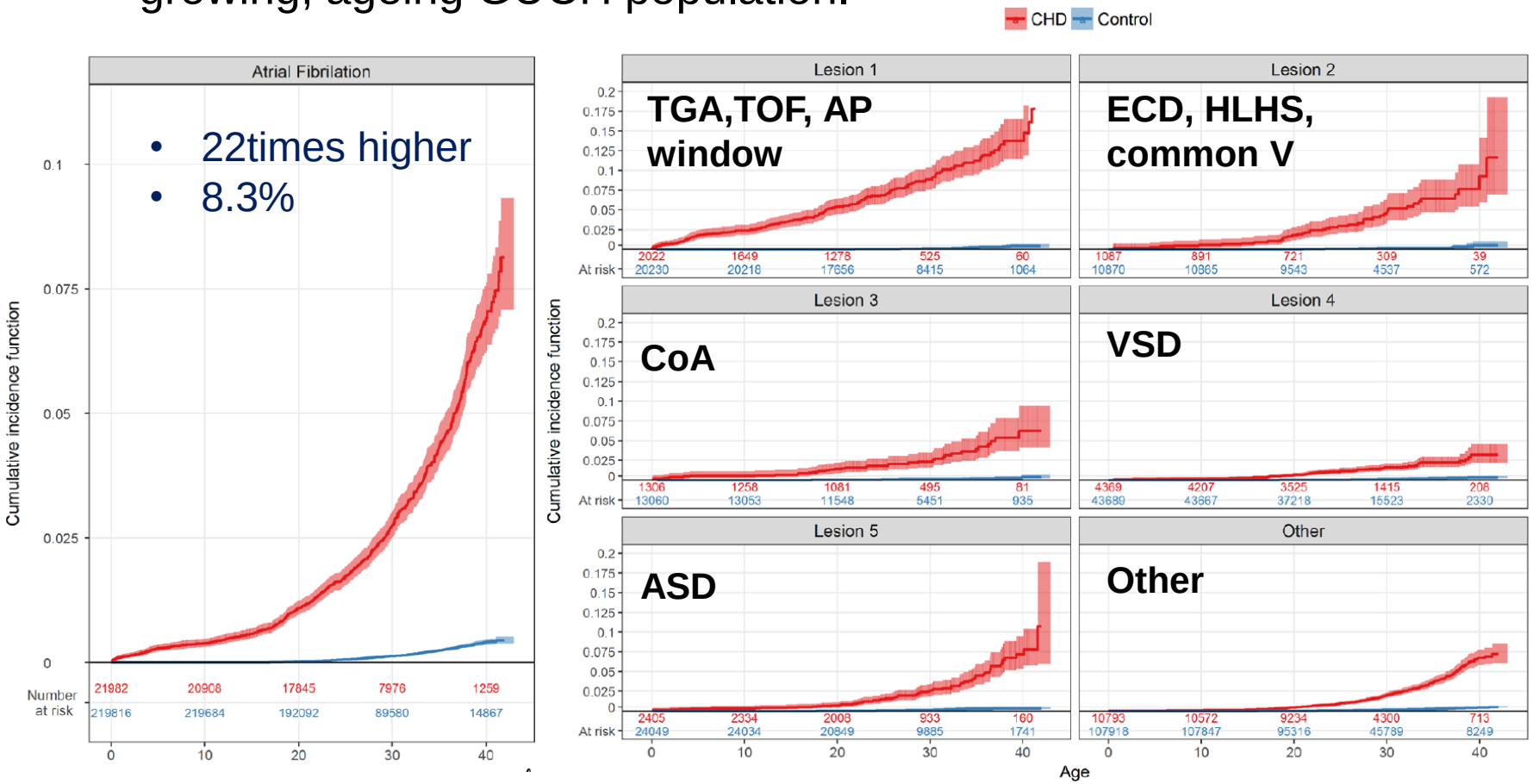


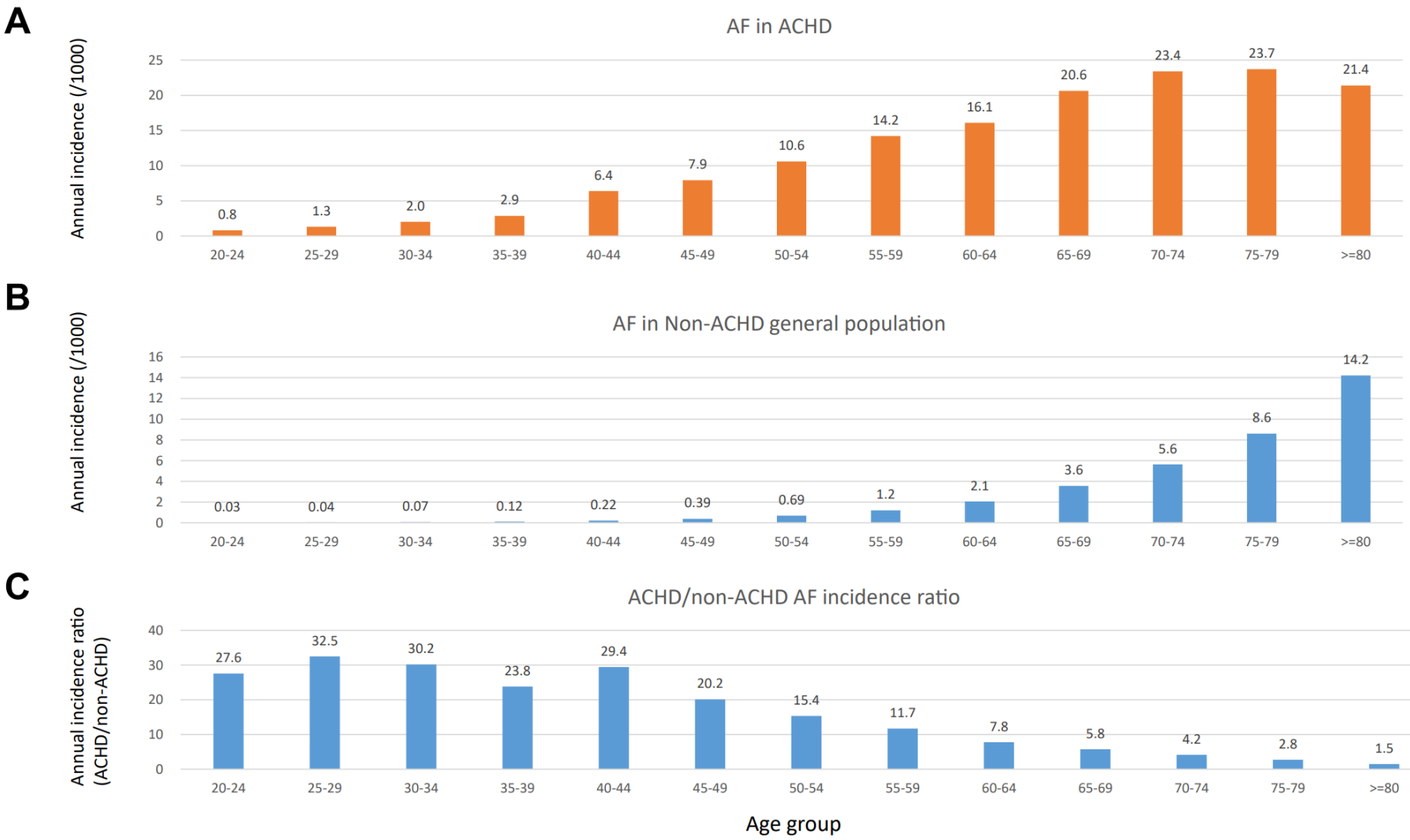
Prevalence

- AFib is becoming increasingly important in the management of the growing, ageing GUCH population.



Circulation. 2018;137:928–937

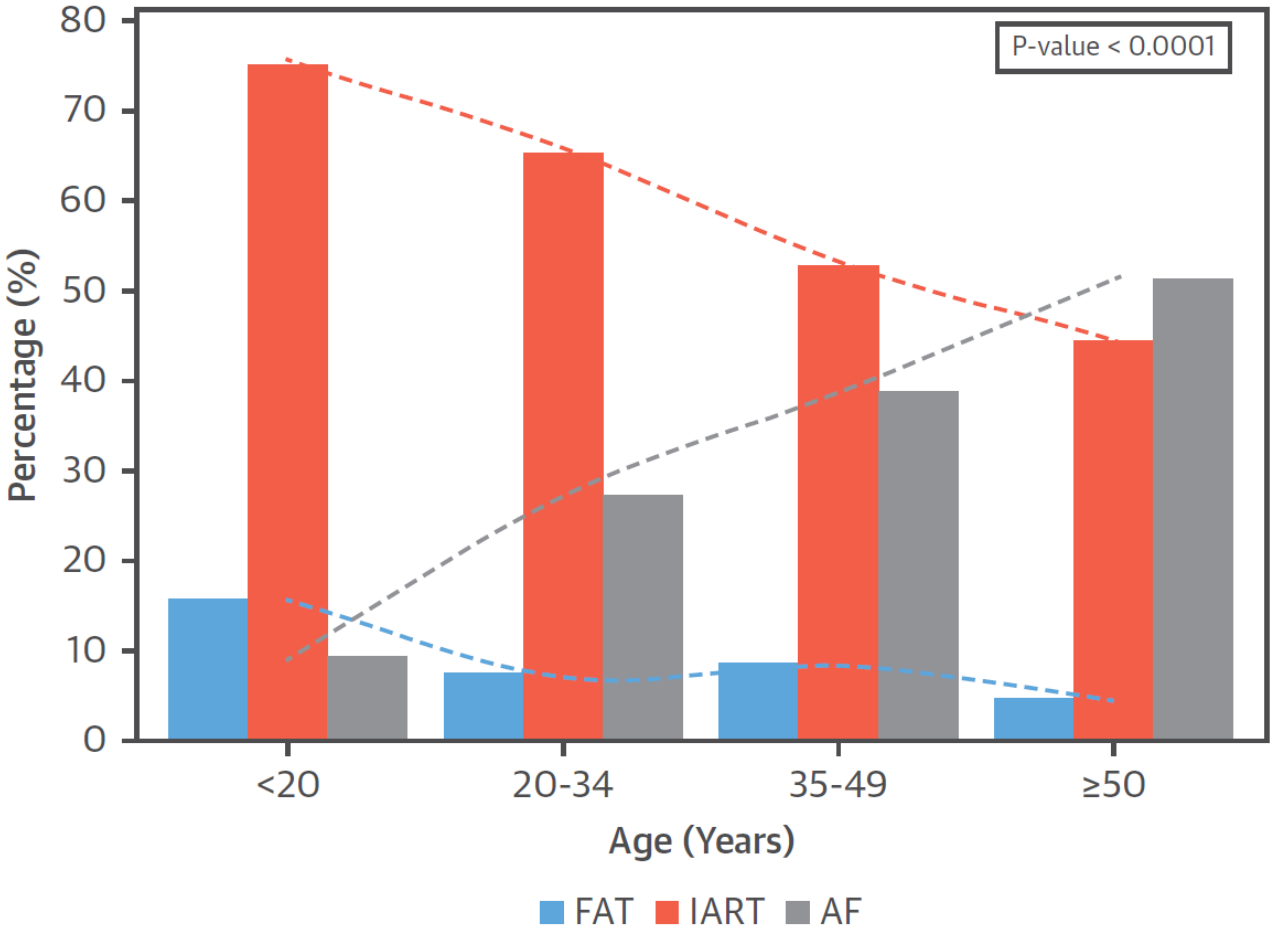
Annual incidence of AF



Heart Rhythm 2023;-:1–7

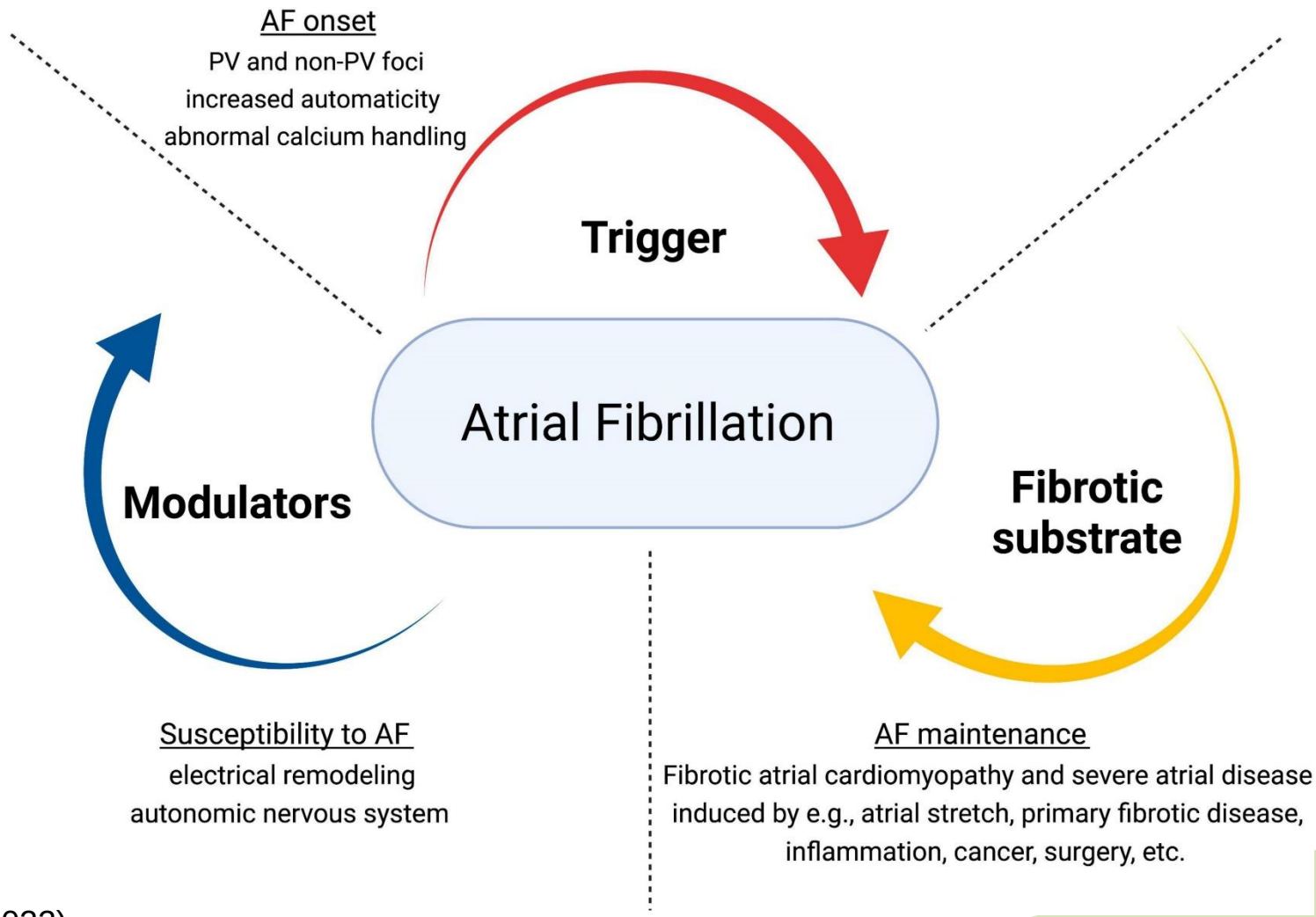
Atrial arrhythmia according to Age

Multicenter study, 482 pts



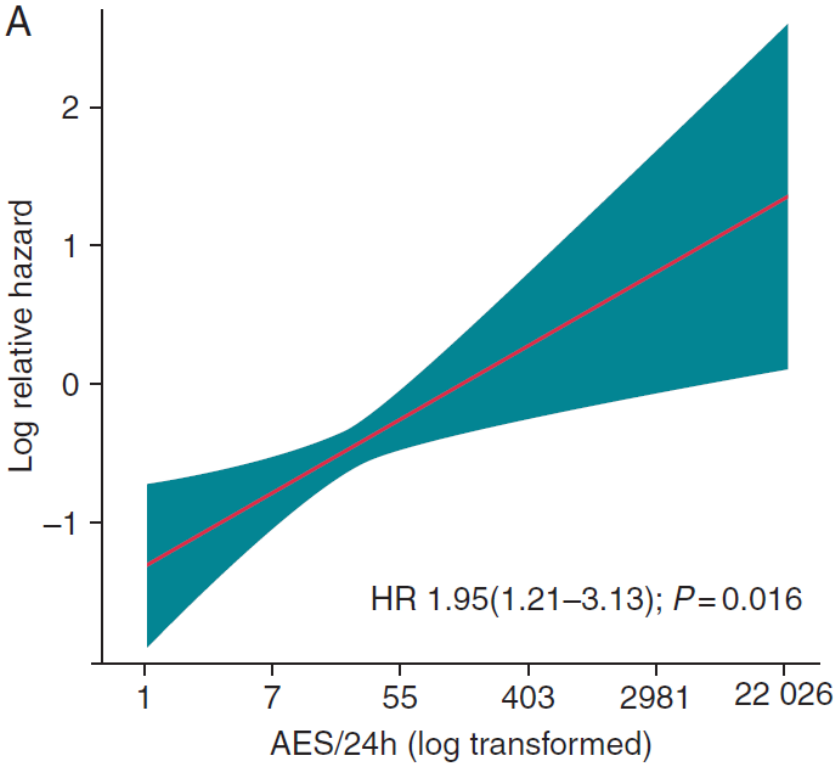
J Am Coll Cardiol 2017;70:857–65

Pathophysiology



FCVM(2022)

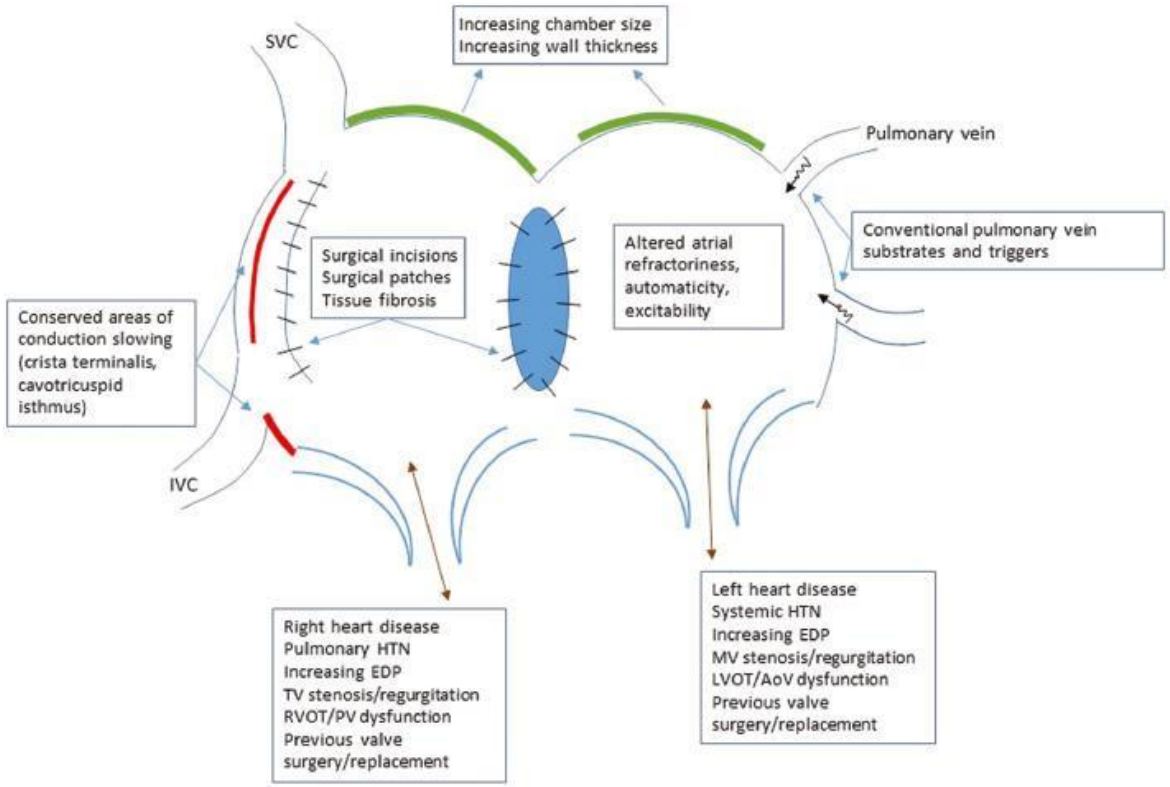
Pathophysiology - Role of triggers



- Origin of ectopic foci
  - Pul vein triggers vs non-pul vein triggers
  - RA, LSVC, RSVC
- Chronic atrial pressure and/or volume overload favour triggered activity→ premature beats or FAT

Europace (2018) 20, 25–32

Pathophysiology



- Structural remodelling through atrial fibrosis
  - Surgical scar
  - Atrial enlargement <- residual septal defects, valvular disease
  - Ventricular dysfunction or acquired conditions
  - Promote conduction delay and alter ion channel function
  - Chronic cyanosis

Antiarrhythmic Drugs

- Recommendations for antiarrhythmic drug use (normal structure)

NO structural HD	CAD	HF	Severe ventricular hypertrophy(HCMP)
First line			
Flecainide Propafenone Dronedarone Sotalol	Sotalol Amiodarone Dronedarone Dofetilide	Amiodarone Dofetilide	Amiodarone
Second line			
Amiodarone Dofetilide			Disopyramide
	Avoid flecainide, propafenone	Avoid flecainide, propafenone, dronedarone	Avoid flecainide, propafenone

Circulation. 2012;125:381–389

Antiarrhythmic Drugs

- Rhythm control is generally preferred to rate control in patients with moderate or complex forms of CHD.
- **Choice** of pharmacologic therapies should take into consideration **various factors**
  - Ventricular function
  - Conduction disturbances, such as sinus node dysfunction, impaired AV nodal conduction
  - Pregnancy plans
  - Comorbidities such as kidney or hepatic failure that may affect pharmacokinetics
  - Concomitant therapies with potential significant interactions.

Class Ic drugs

- Not recommended in patients
  - Coronary artery disease
  - Moderate to severely impaired systolic function of a systemic or sub-pulmonary ventricle
- Reserved for simple or moderate CHD without any risks

Class III drugs

- More effective than any other class in preventing atrial arrhythmia recurrences.
- Adverse events are common
- AE lead to discontinuation of therapy
- Mostly described with amiodarone
- High risk subgroups
  - Fontan circulation
  - Women
  - Cyanotic conditions
  - BMI< 21kg/m2

Amiodarone in ACHD

Side effect	Frequency	Percentage	Amiodarone discontinued?
Any side effect	32	56	
SE causing discontinuation	24	42	
Thyroid dysfunction[a]	24	42	
AIT	17	30	17/17
AIH	8	14	1/8
Skin[b]	4	7	4/4
Significant photosensitivity	3	5	
Blue-gray discoloration	1	2	
Rash	1	2	
Significant bradycardia[a]	3	5	0/3
ILD	1	2	1/1
Peripheral neuropathy	1	2	1/1
Keratopathy with visual symptoms	1	2	0/1
Alopecia	1	2	0/1
Severe nausea	1	2	0/1

- Significant A/E = 56%
- Thyroid dysfunction – M/C
  - Thyrotoxicosis 30% , hypothyroidism 14%

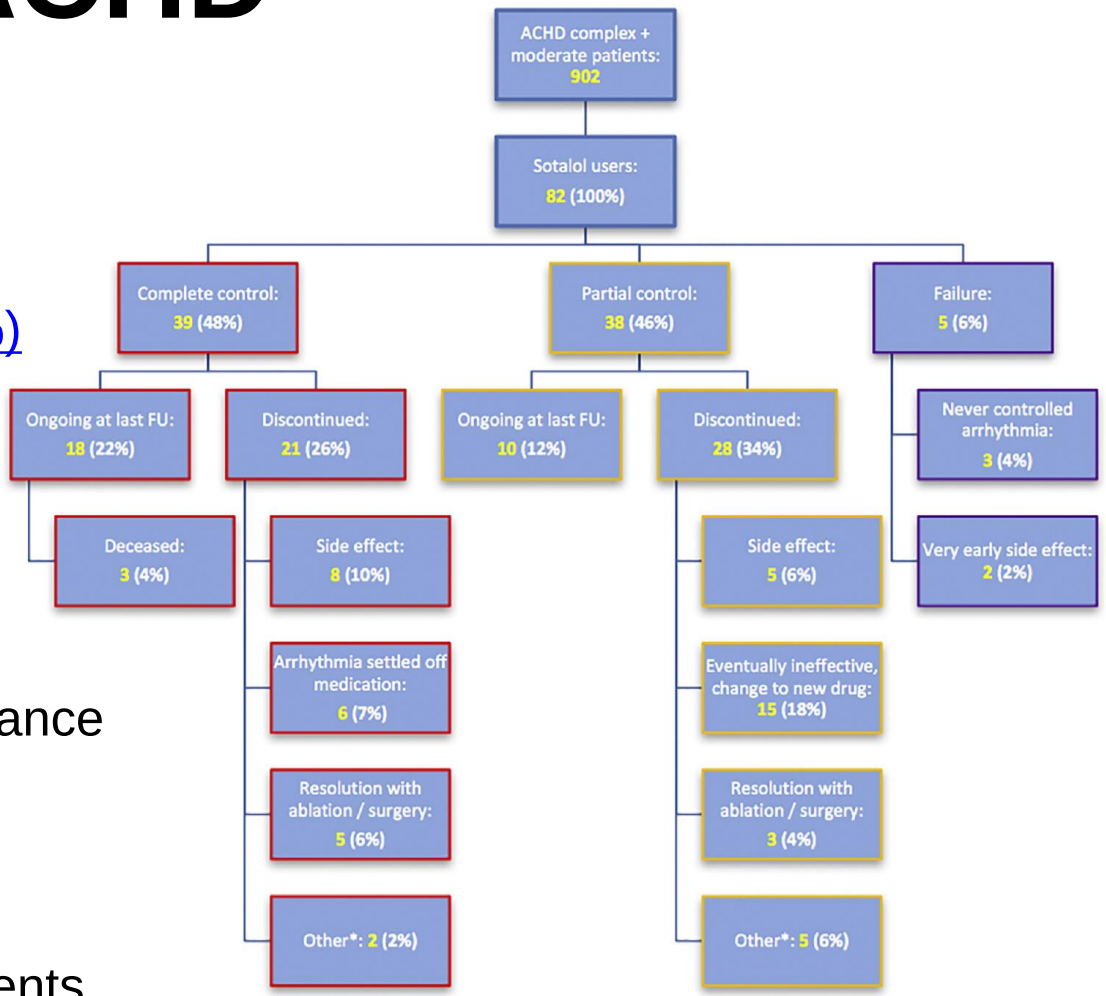
Congenital Heart Disease. 2018;13:944–951.

Sotalol in ACHD

- Complete control

: 48%

- AE
  - Fatigue/lethargy(13,16%)
  - Significant bradycardia(11,13%)
  - Bronchospasm/dyspnea
  - Nausea/vomiting
  - Erectile dysfunction
  - Headache/visual disturbance
  - Dizziness/hypotension
  - Loss of taste
  - Severe depression
- It should not be used in patients with significant ventricular systolic dysfunction.



International Journal of Cardiology 274 (2019) 74–79

Dofetilide

Study	Design	n	Age	Type of CHD	Type of AT	Drug	Dosage	CV Achieved	Adverse Events[§]
Wells et al. 2009[54]	Retrospective	20	30 (19–53) years	Simple 5% Moderate 15% Complex 80%	AF 35% IART 65%	Dofetilide	125 µg twice daily* 125 µg three times a day* 250 µg twice daily* 500 µg twice daily*	85%[†]	10%TdP 55% QTc prolongation
Banchs et al. 2014[52]	Retrospective	13	40 ± 11 years	Simple 15% Moderate 31% Complex 54%	AF 15% AFL 31% Focal AT 54%	Dofetilide	250 µg twice daily* 500 µg twice daily*	70%	10% TdP
El-Assaad et al. 2016[53]	Retrospective	64	42 ± 14 years	Simple 14% Moderate 31% Complex 52% Unclassified 3%	AF 55% IART 45%	Dofetilide	125 µg twice daily* 250 µg twice daily* 500 µg twice daily*	68%	1.5%TdP 1.5% VT 1.5% QTc prolongation 1.5% SND

- Initial response : 68~85%

European Cardiology Review 2021;16:e06

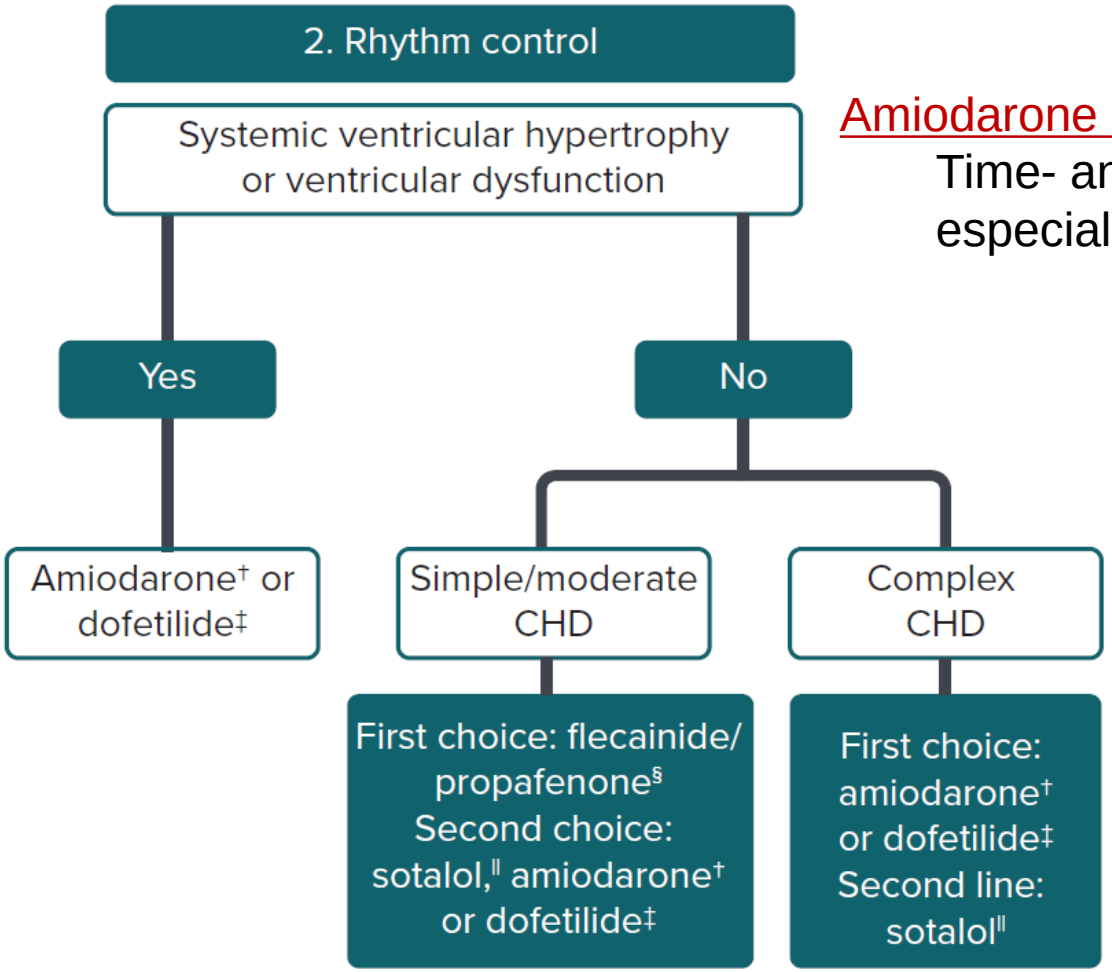
Dofetilide

- In ACHD
  - PACES/HRS 2014, IIa
    - First-line alternative to amiodarone or a second-line therapy for patients with severe forms of CHD or systemic ventricular dysfunction
  - ESC 2018
    - Alternative to amiodarone or first line therapy in patients with normal systemic ventricular function/ second line therapy in those with systemic ventricular dysfunction.
- CIx
  - Creatinine clearance <20 ml/min, hypokalemia, QTc >440 ms
- Cardiac monitoring for 72 hours after initiation

Dronedarone

- Extrapolating data from the general population
- **Not recommended**
  - Moderate or complex CHD
  - HF or at least moderate ventricular dysfunction
- Because of the concerns of augmented mortality, worsening of heart failure and stroke.

Maintenance of sinus rhythm



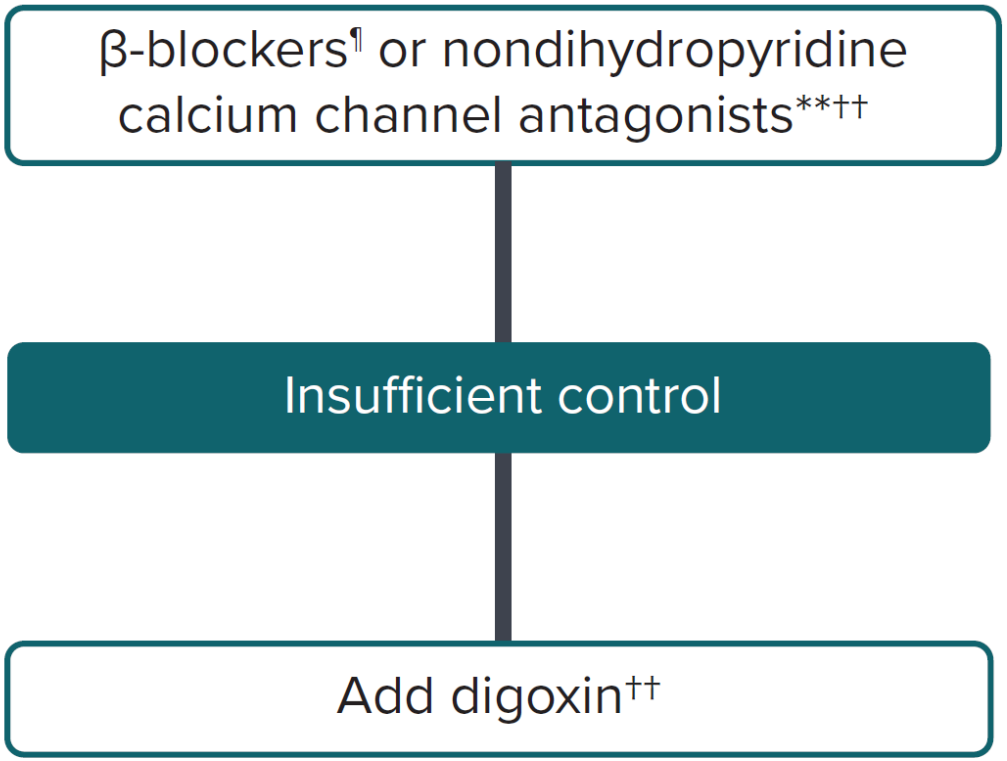
Amiodarone : most effective agents

Time- and dose-dependent side effect especially in young population

European Cardiology Review 2021;16:e06

Rate control

- Whenever rhythm control strategy is abandoned, rate control is essential to avoid secondary development of tachycardiomyopathy or worsening heart failure.



European Cardiology Review 2021;16:e06

Summary

- AFb is the **most common** presenting arrhythmia in patients with ACHD **over the age of 50 years**.
- Much remains to be learned about the impact of CHD and associated abnormalities on the pathophysiology and determinants of AFb.
- It seems to be likely than non–pulmonary vein triggers, be they focal or reentrant, play a relatively more important role in the CHD population.
- Class I agents may be considered as the first-line therapy for the simple/moderate forms of CHD without significant ventricular hypertrophy or dysfunction or myocardial scarring.
- Otherwise, amiodarone or dofetilide can be used.

Thank you for your attention