Conoscere e Curare il Cuore 2019

VENERDI' 1 MARZO

FIBRILLAZIONE ATRIALE NELLO SCOMPENSO CARDIACO. QUANDO RICORRERE ALL'ABLAZIONE.

Riccardo Cappato

Humanitas Clinical & Research Center
Dipartimento di Scienze Biomediche Humanitas University, Rozzano - MI

Disclosure Statement of Financial Interest

- Consultant to: Boston Scientific; Medtronic; St. Jude; Biosense Webster; ELA Sorin; Boehringer Ingelheim; Bayer HealthCare; Abbott; Pfizer
- Speaker's Bureau: Boston Scientific; Medtronic; St. Jude; Biosense Webster; BARD; Sanofi; Boehringer Ingelheim; Bayer HealthCare; Abbott
- Investigator: Medtronic; Biosense Webster; Sanofi; Cameron Health, BARD; Bayer HealthCare; Abbott; Pfizer
- Grants: Boston Scientific; Medtronic; St. Jude; Biosense Webster; BARD; ELA Sorin
- Equity and Intellectual Property Rights: Cameron Health, Atacor Inc.

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AF in Pts with CHF: When to Perform Catheter Ablation?

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Preamble

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AF in Pts with CHF: When to Perform Catheter Ablation?

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- CHF and AF are not a specific disease

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- Rather, they represent the common final evolution of several clinical and electrical conditions

AF in Pts with CHF: When to Perform Catheter Ablation?

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- CHF and AF are not a specific disease
- Rather, they represent the common final evolution of several clinical and electrical conditions
- As a consequence, histopathological and electrophysiological substrates may differ considerably among patients

AF in Pts with CHF: When to Perform Catheter Ablation?

Heart failure: definition

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Heart failure: definition

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not by a reduced ejection fraction!

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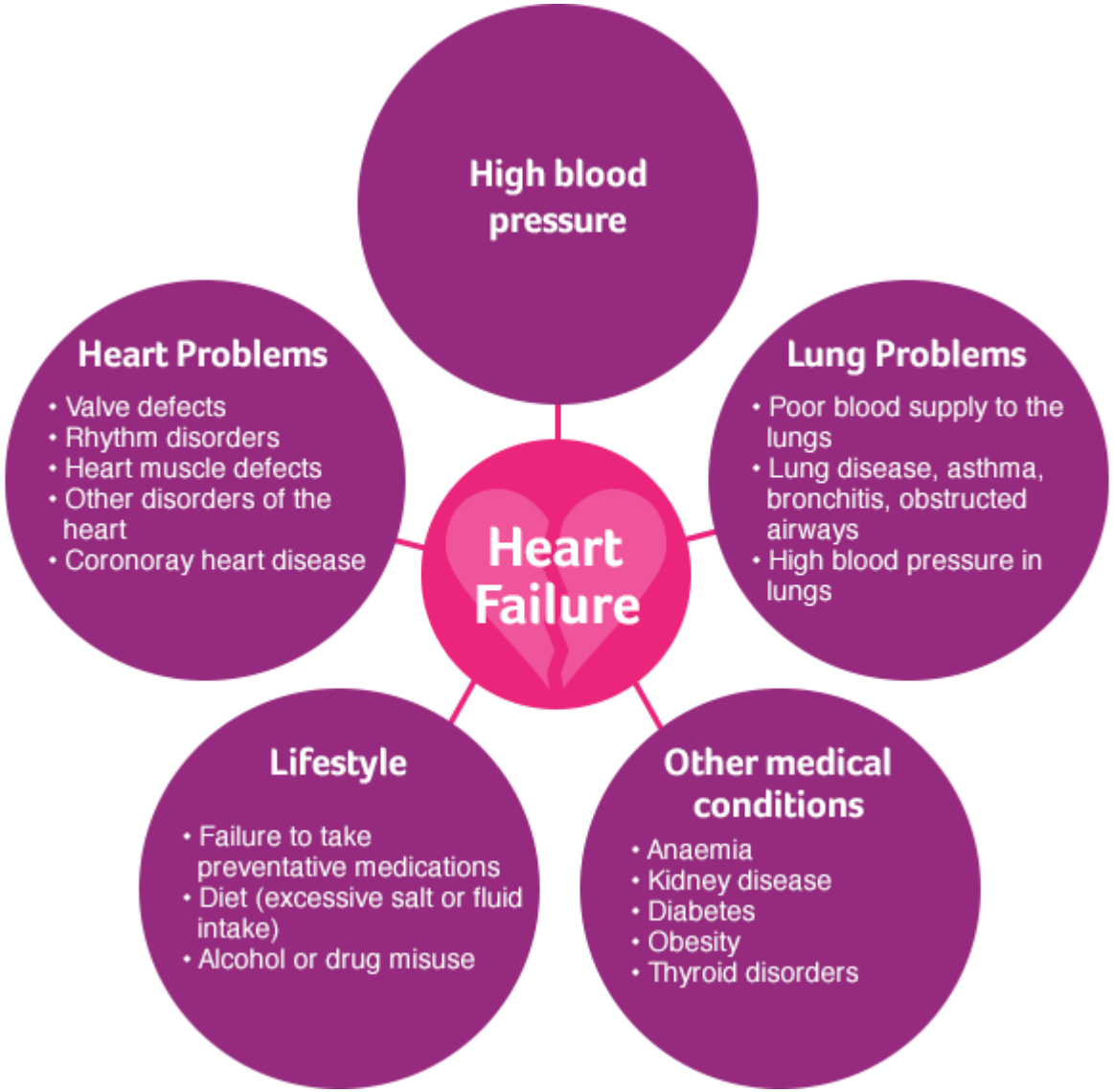
AF in Pts with CHF: When to Perform Catheter Ablation?



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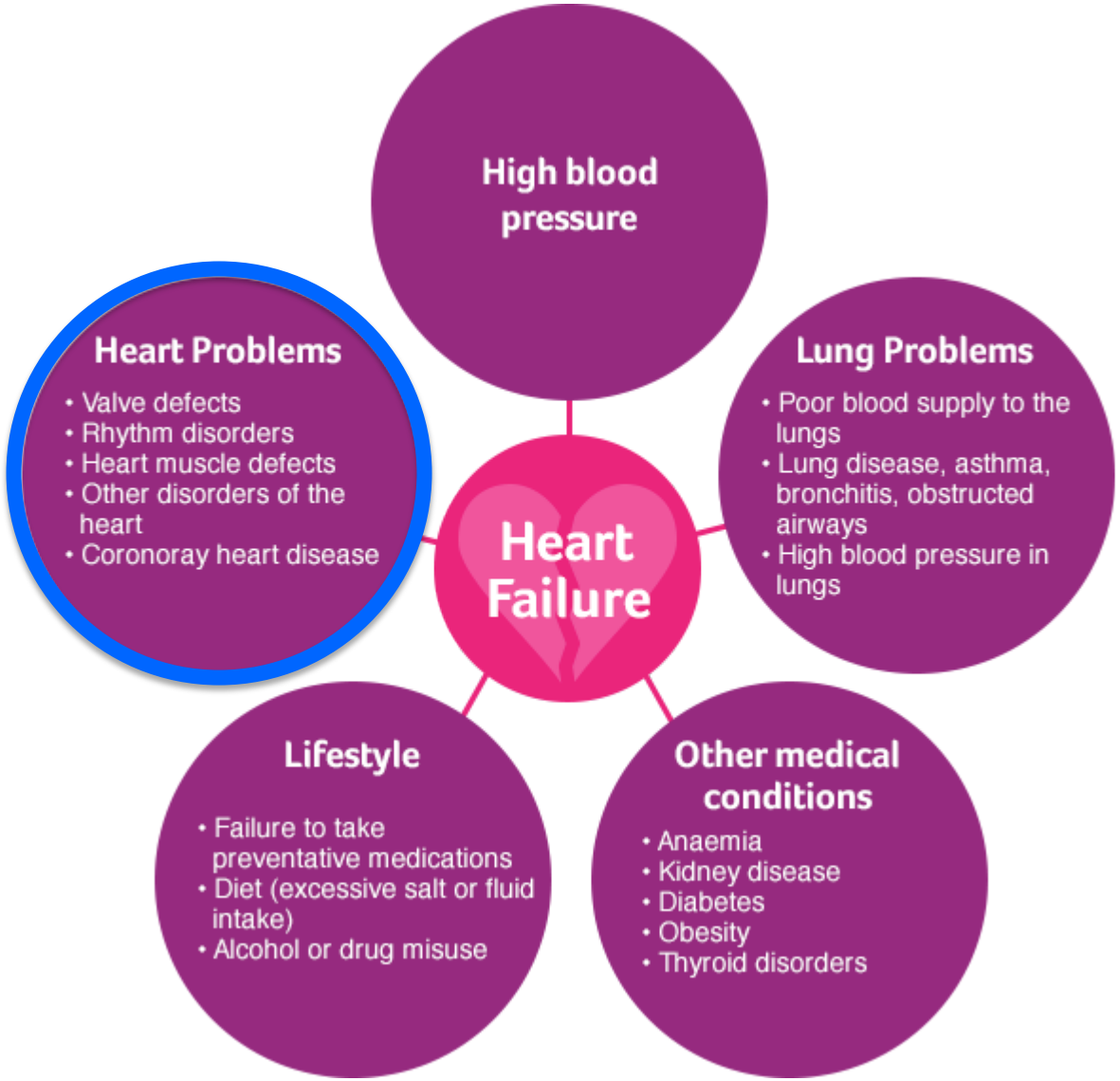

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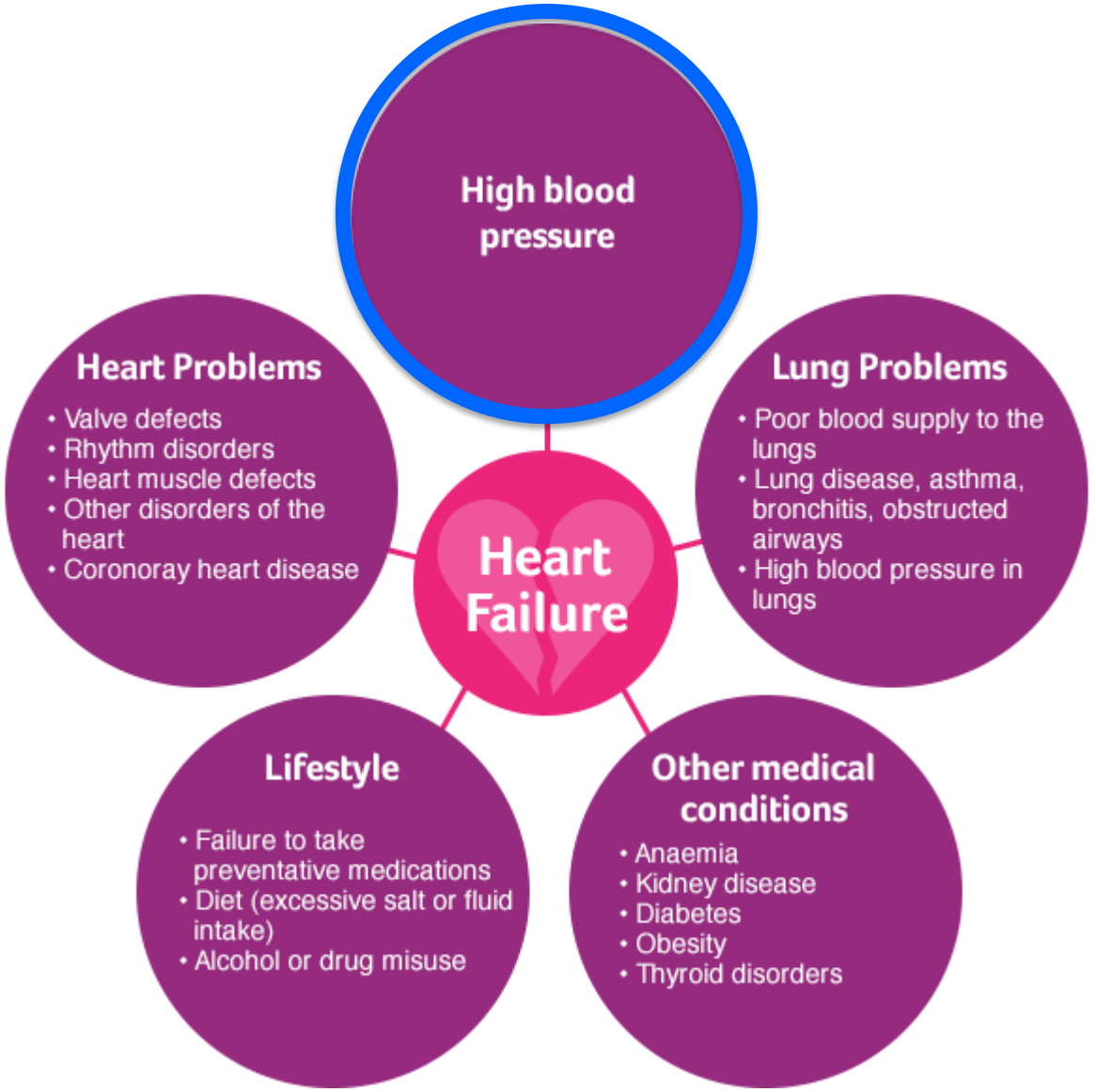

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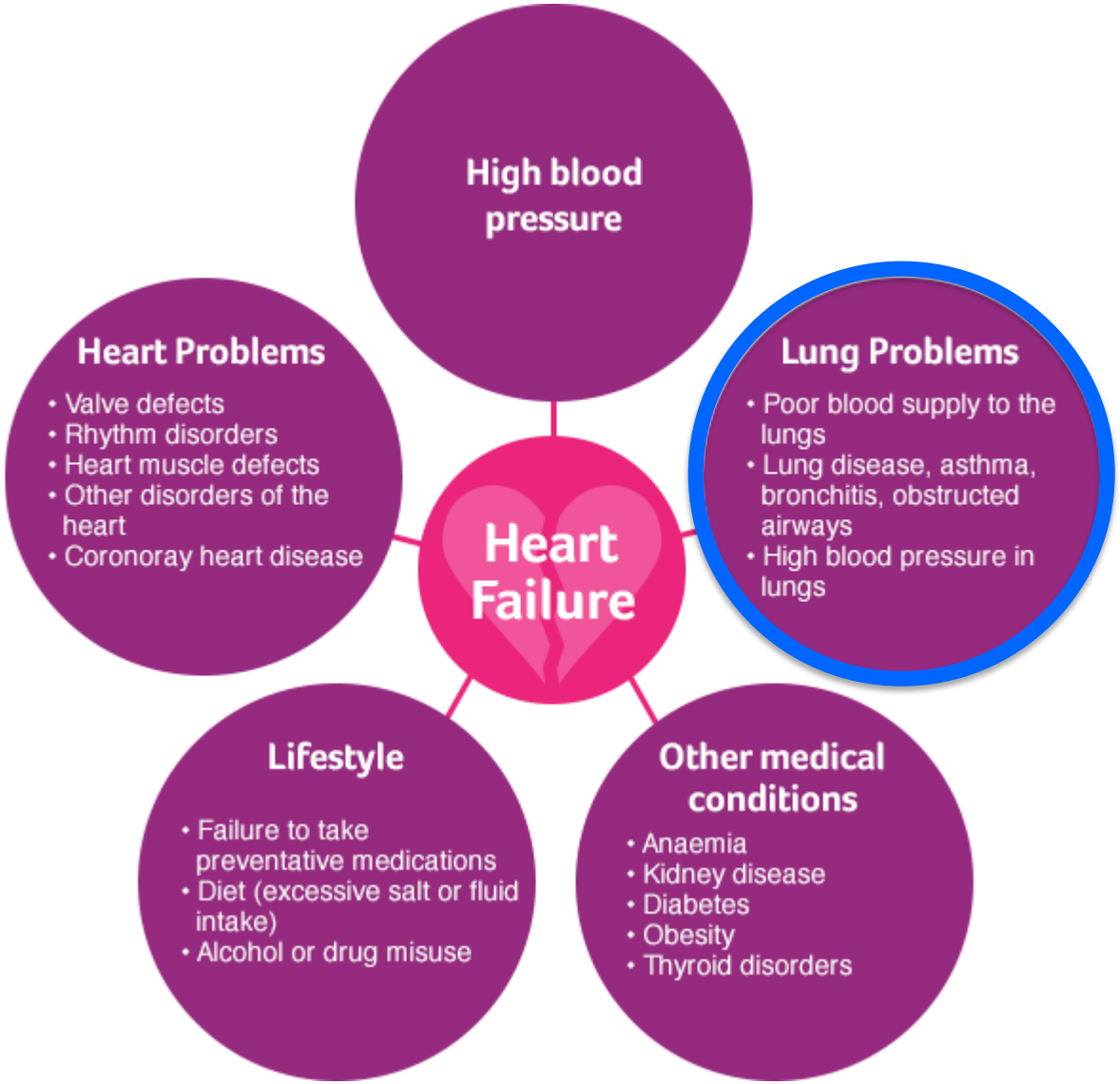

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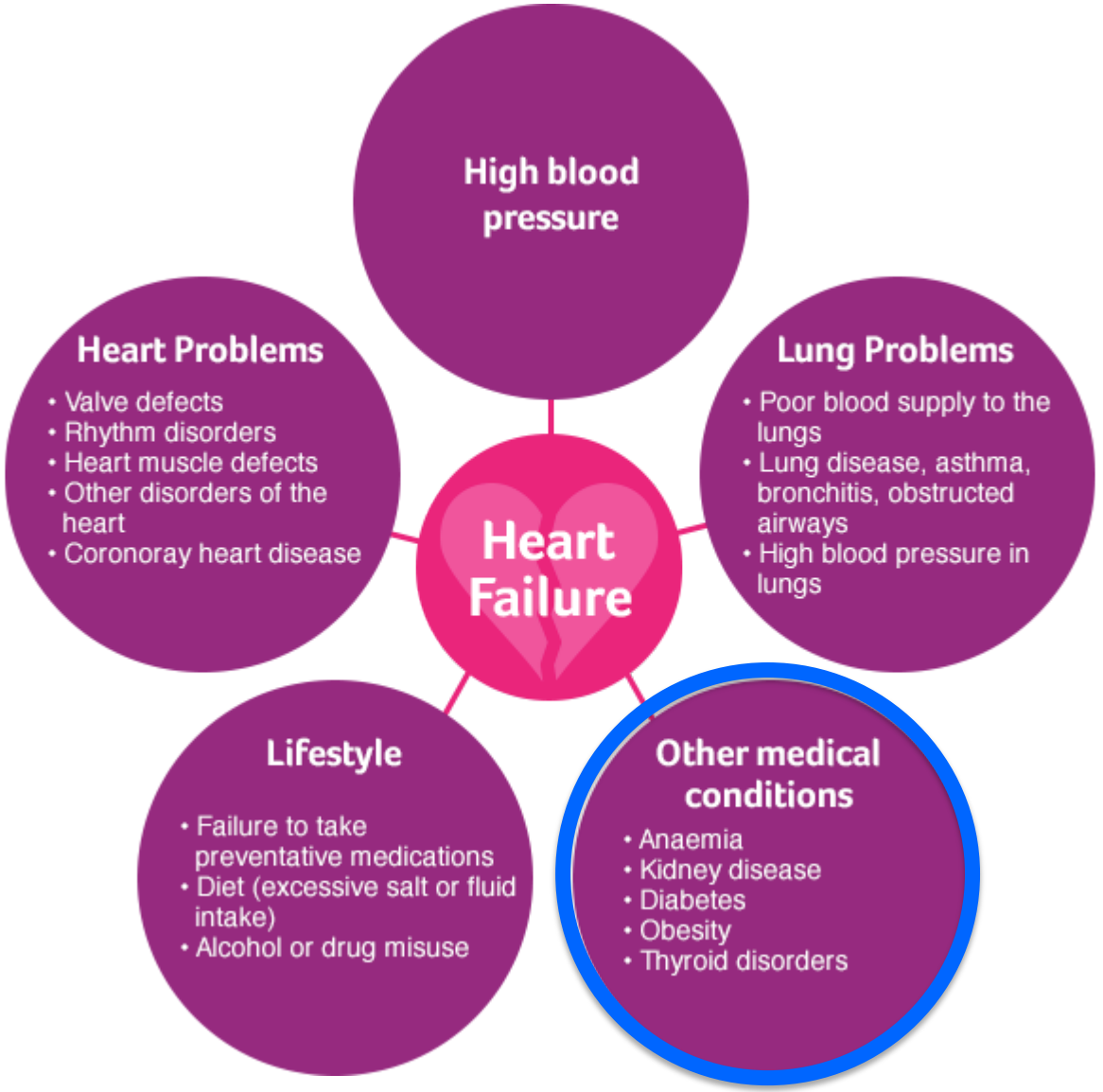

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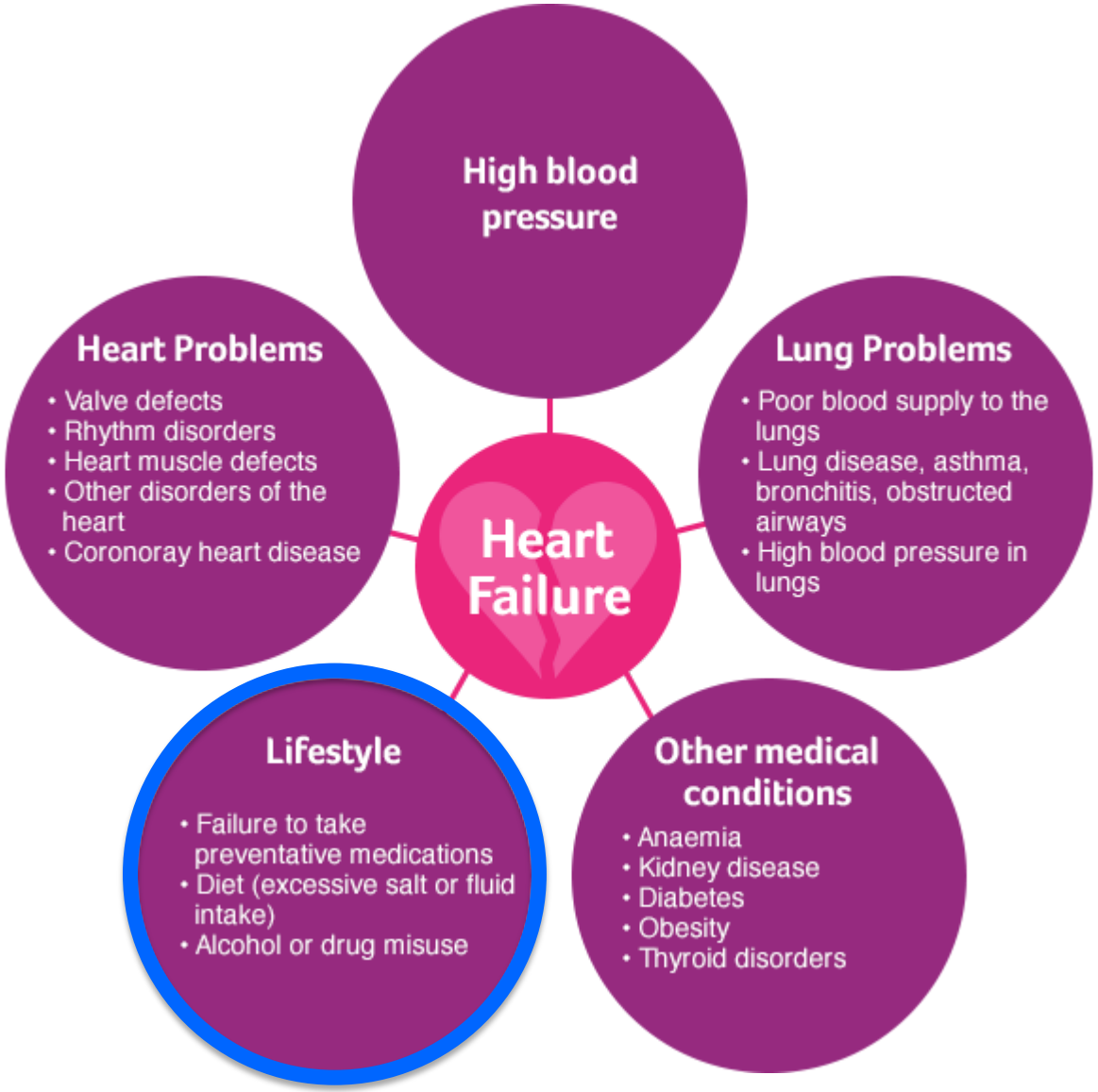
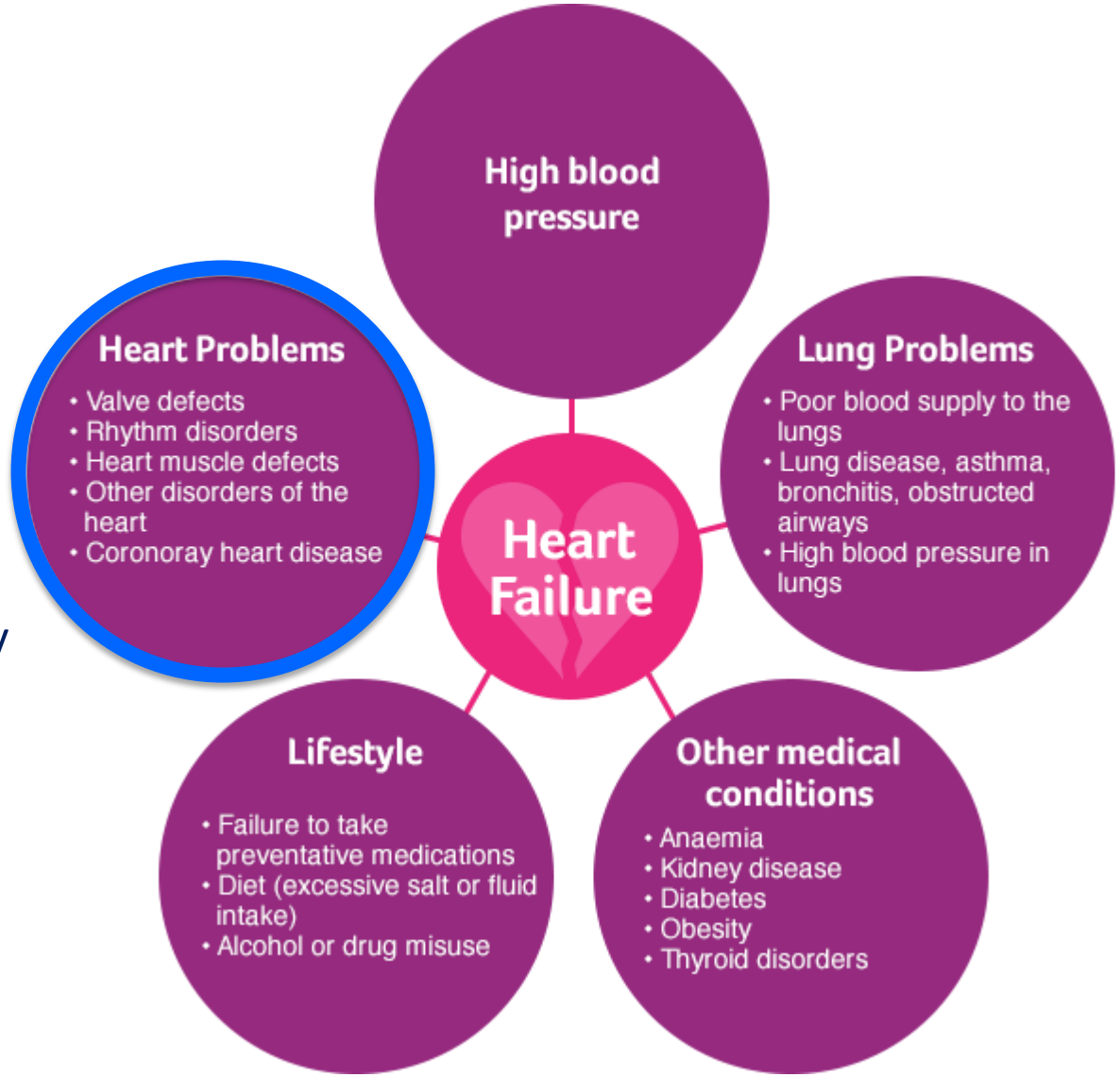


AF in Pts with CHF: When to Perform Catheter Ablation?

Tachycardiomyopathy



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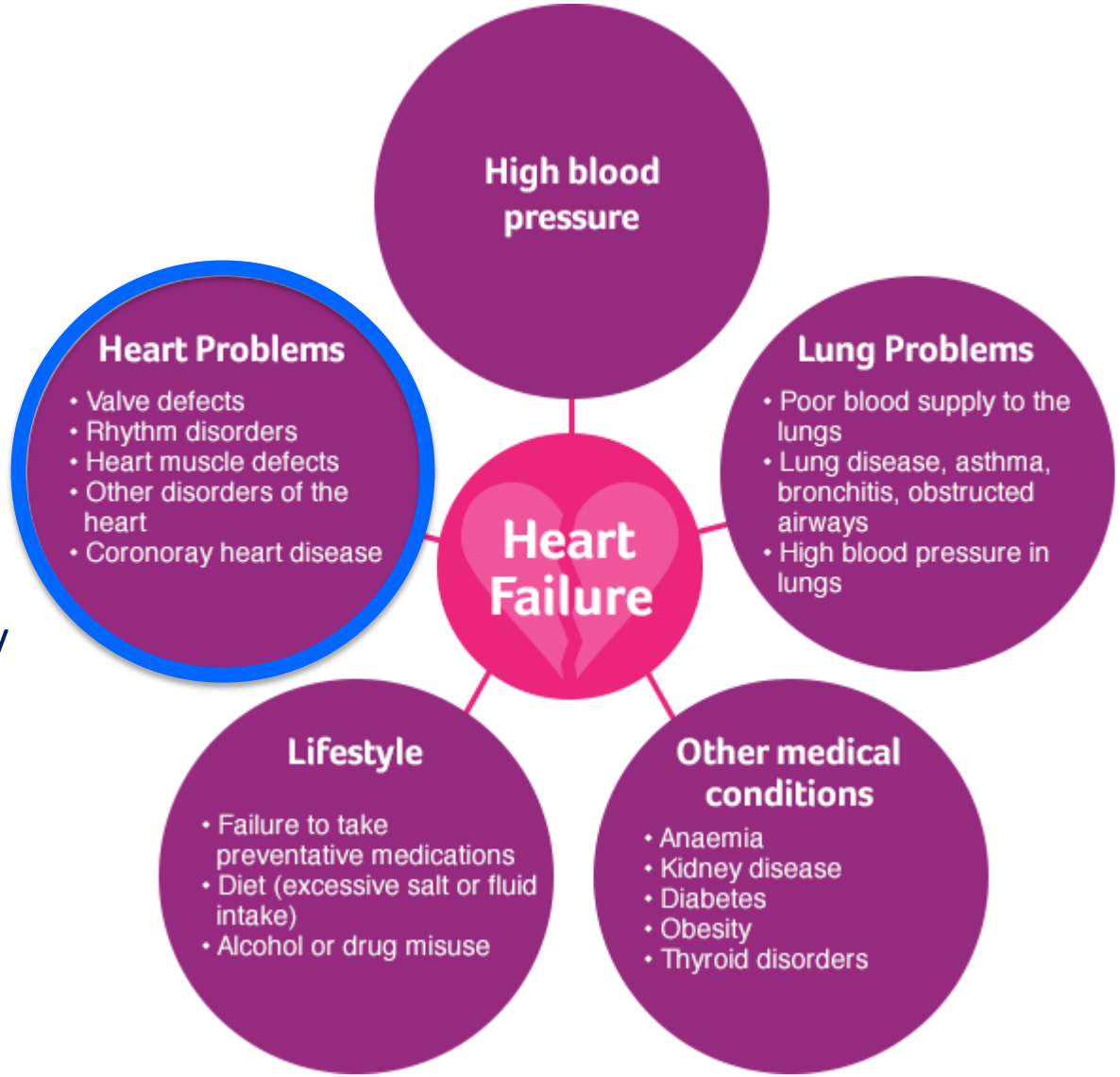
Tachycardiomyopathy

Atrial fibrillation



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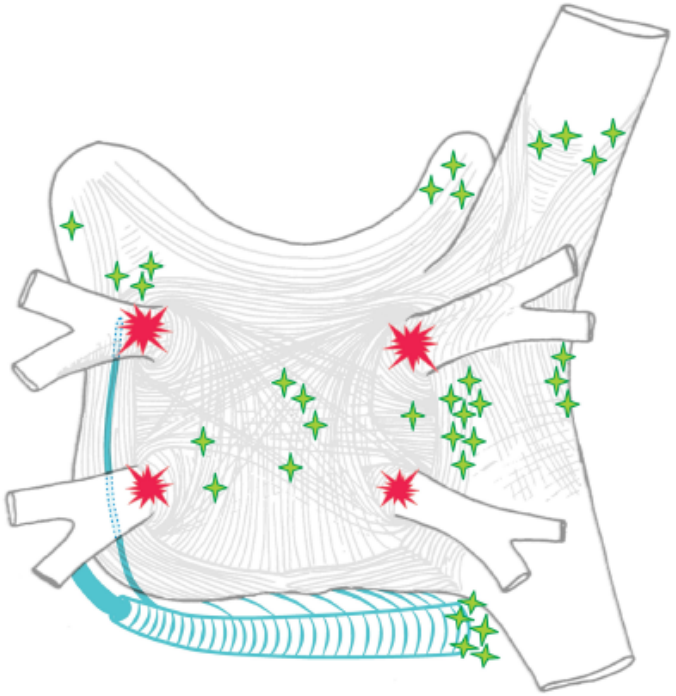
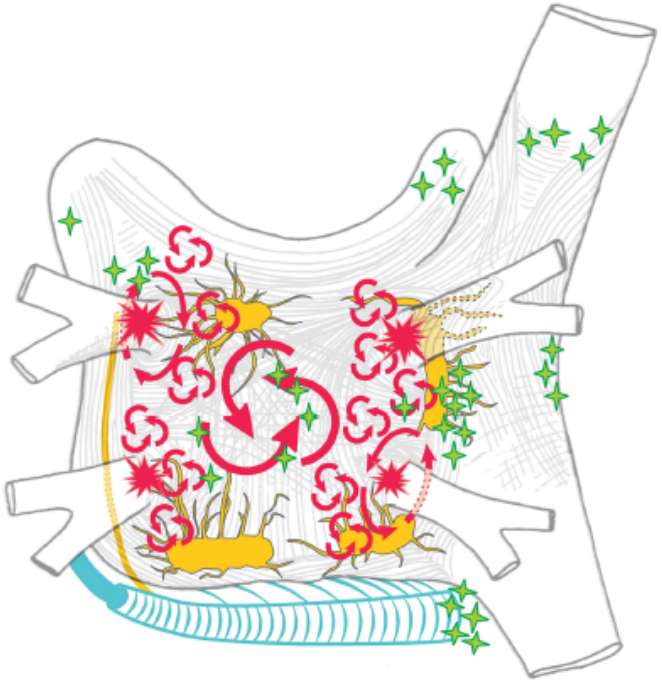
AF in Pts with CHF: When to Perform Catheter Ablation?

Mechanisms of atrial fibrillation





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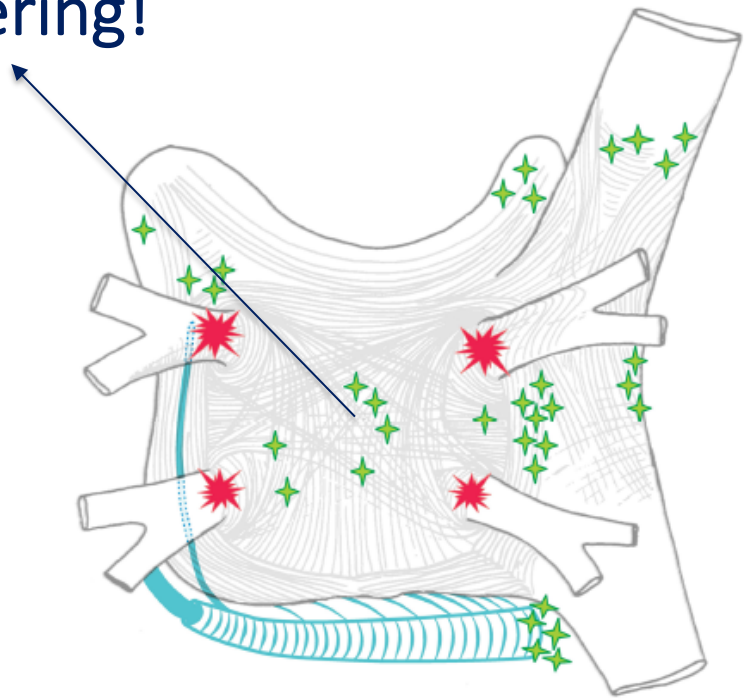
triggering!



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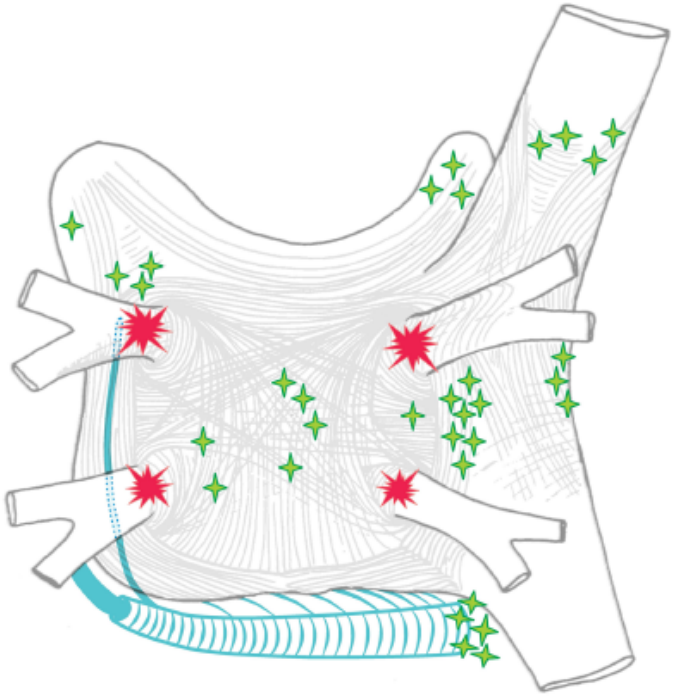

perpetuation??????

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Preamble

- Combining AF and CHF in a reproducible model for prescription of therapy delivery represents an oversimplification

Fibrillazione Atriale nello Scompenso Cardiaco: Quando Ricorrere alla Ablazione Transcatetere?

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Fibrillazione Atriale nello Scompenso Cardiaco: Quando Ricorrere alla Ablazione Transcatetere?

Quale Fibrillazione Atriale? Quale Scompenso Cardiaco?

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Fibrillazione Atriale nello Scompenso Cardiaco: Quando Ricorrere alla Ablazione Transcatetere?

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Quale Tecnica di Ablazione?

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AF in Pts with CHF: When to Perform Catheter Ablation?

Rationale for AF Ablation in CHF

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Rationale for AF Ablation in CHF

- AF has proven as an independent predictor of outcome in patients with CHF

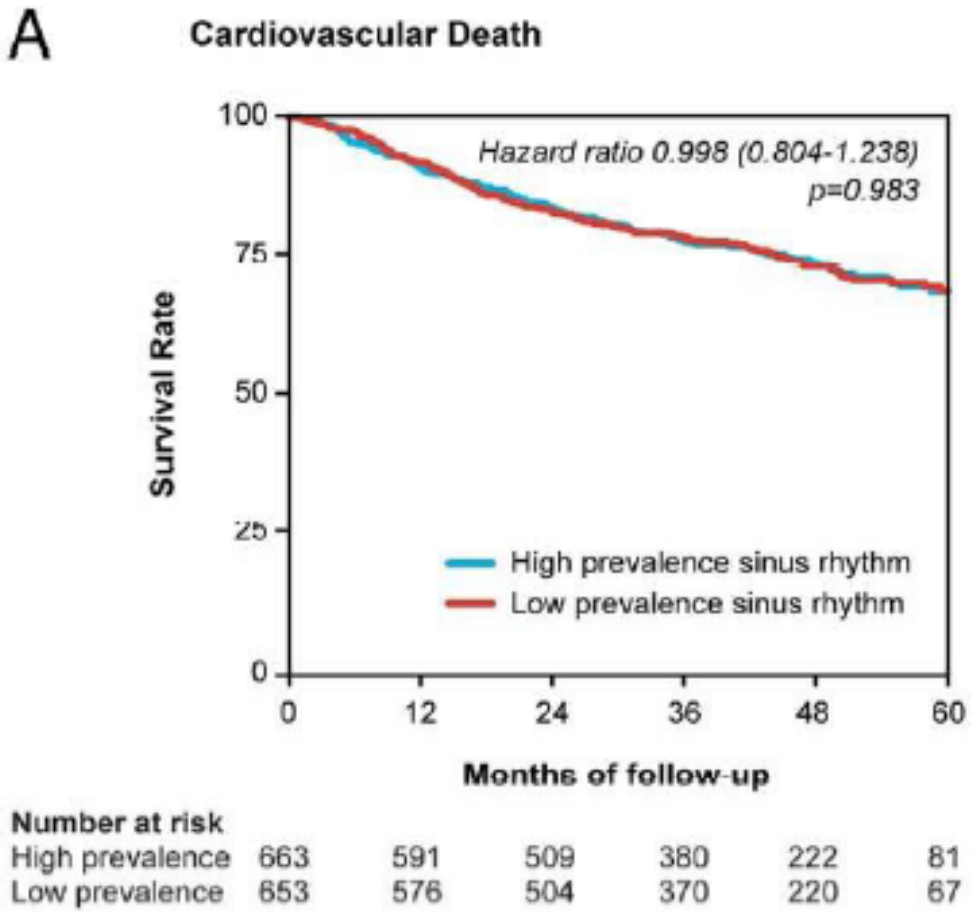
AF in Pts with CHF: When to Perform Catheter Ablation?

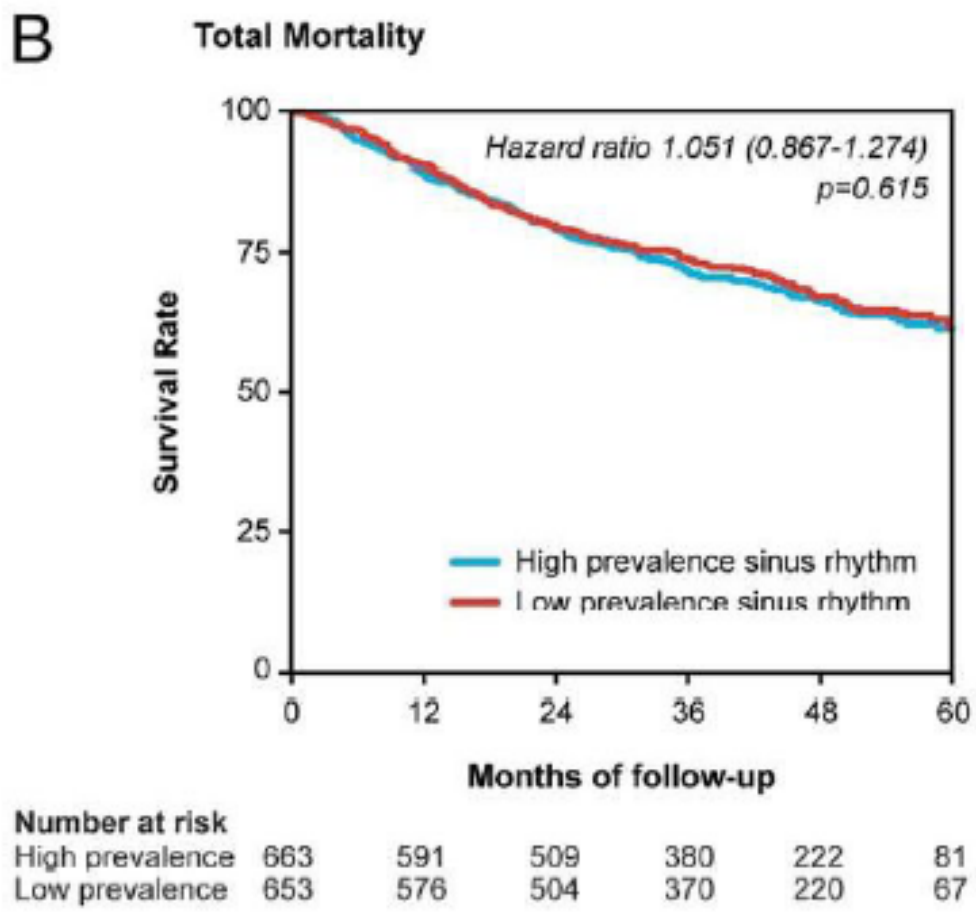
Rationale for AF Ablation in CHF

- AF has proven as an independent predictor of outcome in patients with CHF
- Strategies aimed at restoring and maintaining sinus rhythm over time may contribute to prolong patient survival

AF in Pts with CHF: When to Perform Catheter Ablation?

AF-CHF: secondary endpoints





Talajic M, et al, 2010

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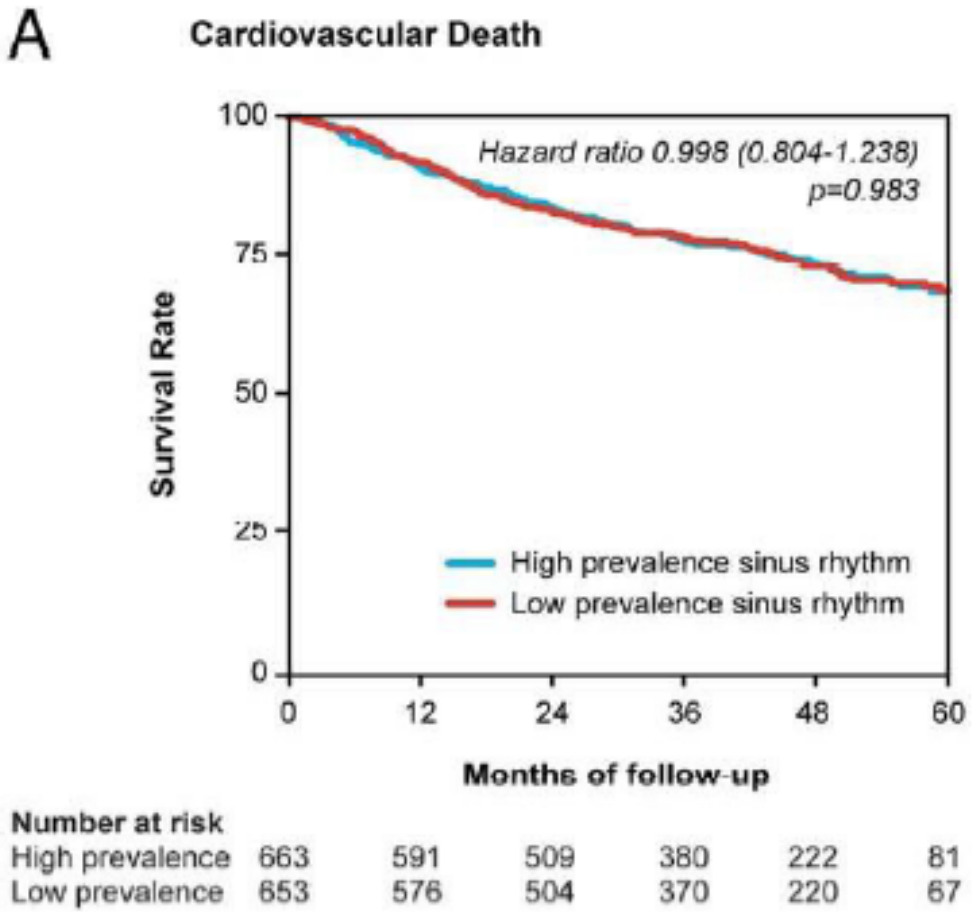

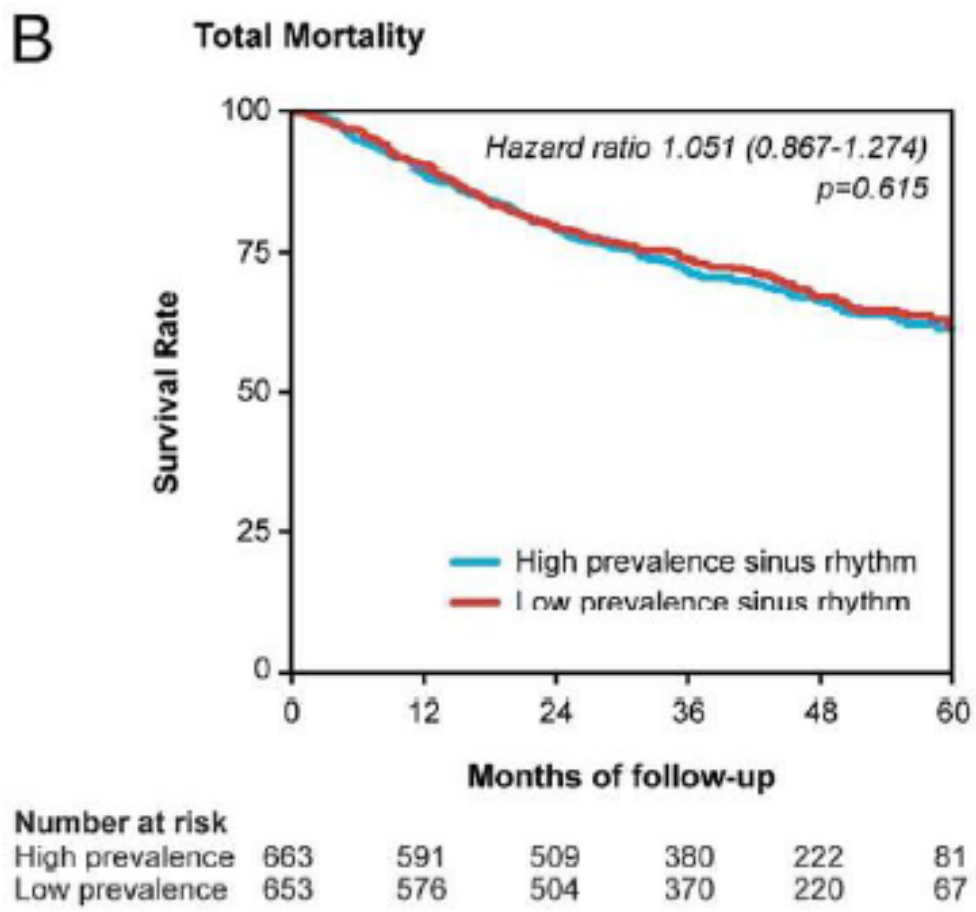

Negative inotropism by AAAs!

Talajic M, et al, 2010

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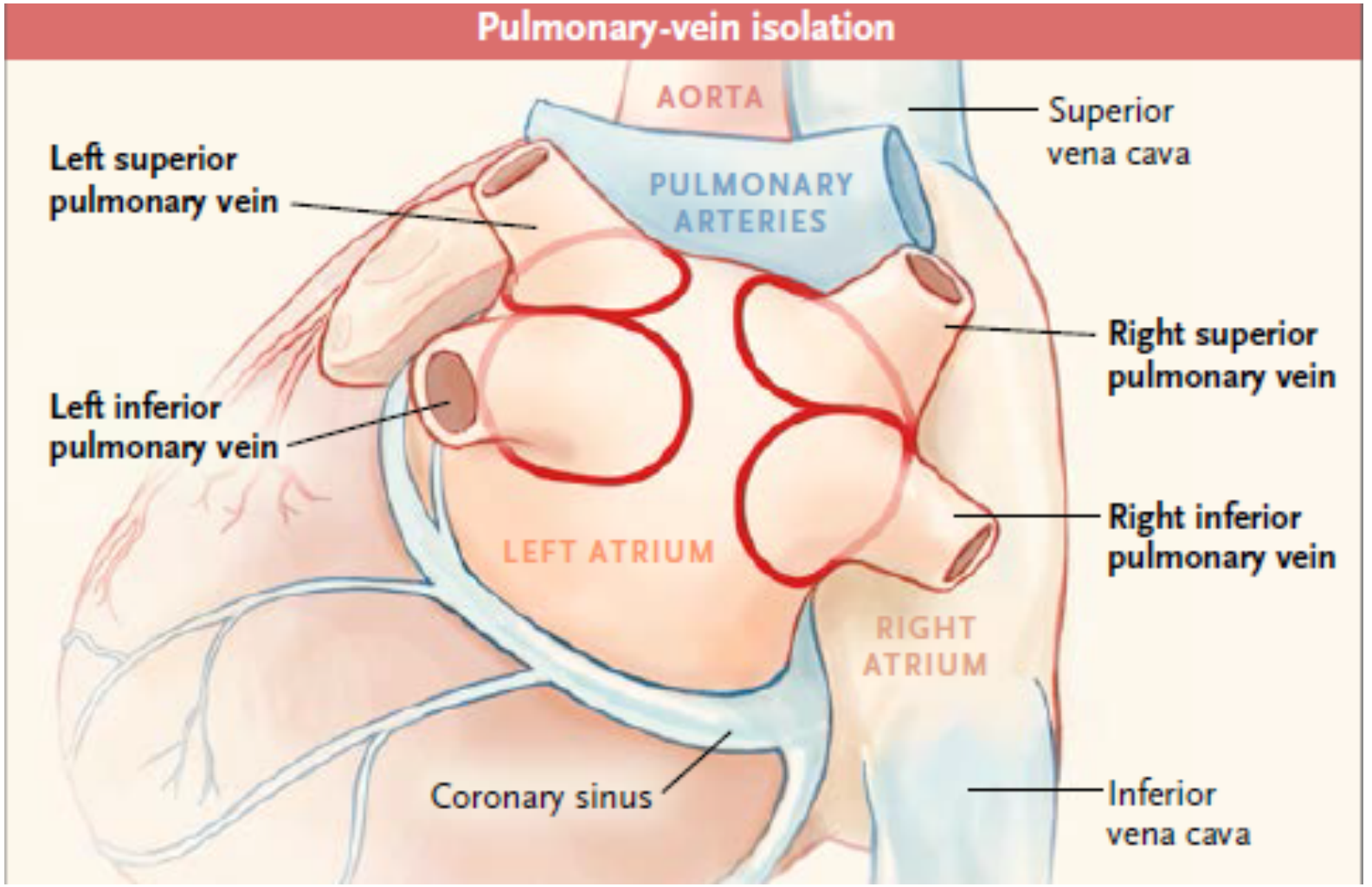
AF in Pts with CHF: When to Perform Catheter Ablation?

Ablation technique



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Study (year)	Patients (n)	Mean EF	Mean LA size	Freedom from AF*	Ref.
Chen *et al.* (2004)	94	36	4.7	73	[33]
Hsu *et al.* (2004)	58	35	5	69	[34]
Tondo *et al.* (2006)	40	33	4.8	62	[35]
Gentlesk *et al.* (2007)	53	43	NA	90‡	[36]
Khan *et al.* (2008)	41	27	4.9	71	[40]

*Freedom from AF without the use of antiarrhythmic drugs.
‡No atrial fibrillation with or without antiarrhythmic medication or greater than 90% reduction in AF burden.
AF: Atrial fibrillation; EF: Ejection fraction; LA: Left atrium; NA: Not applicable.

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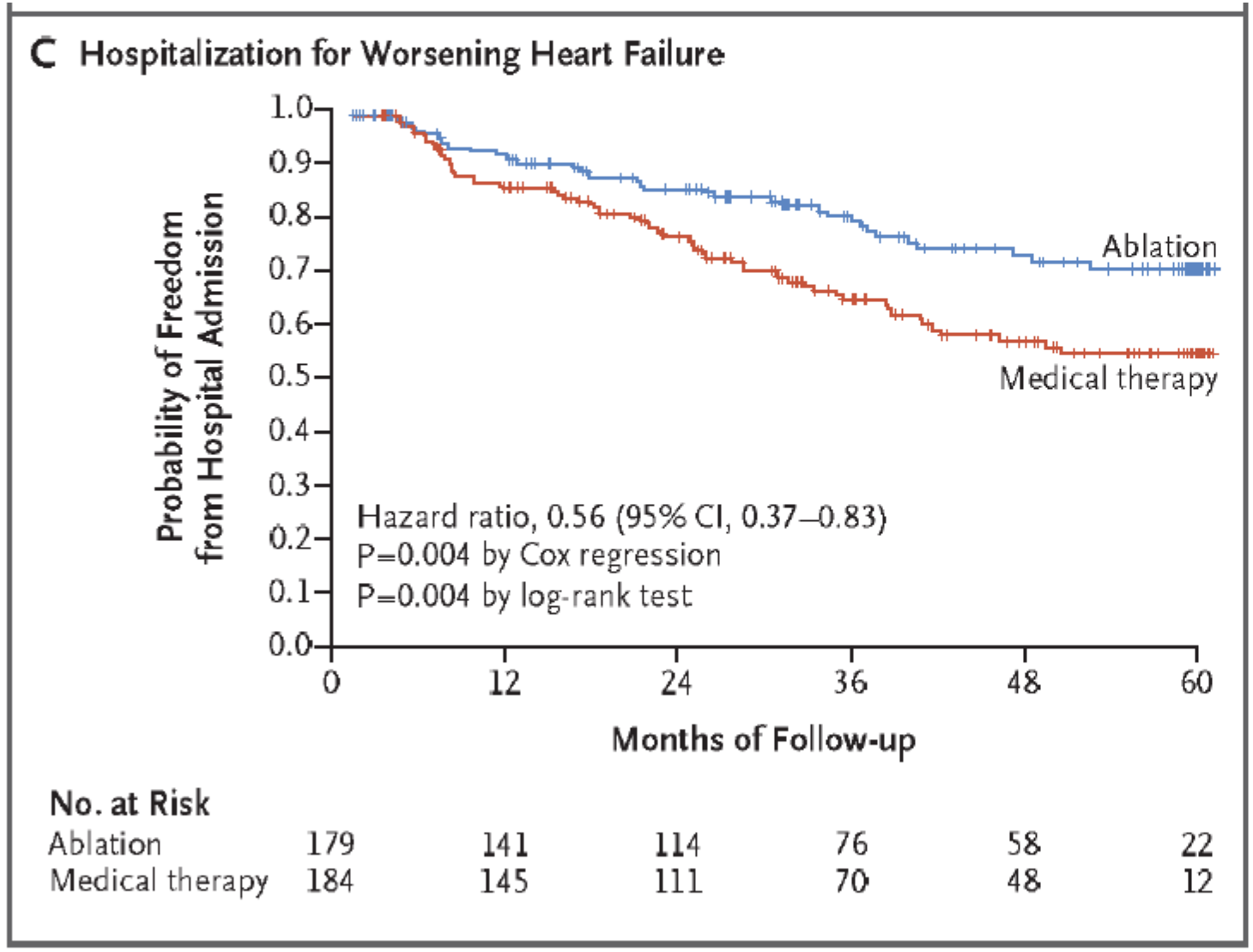
CASTLE-AF



Marrouche et al, 2018

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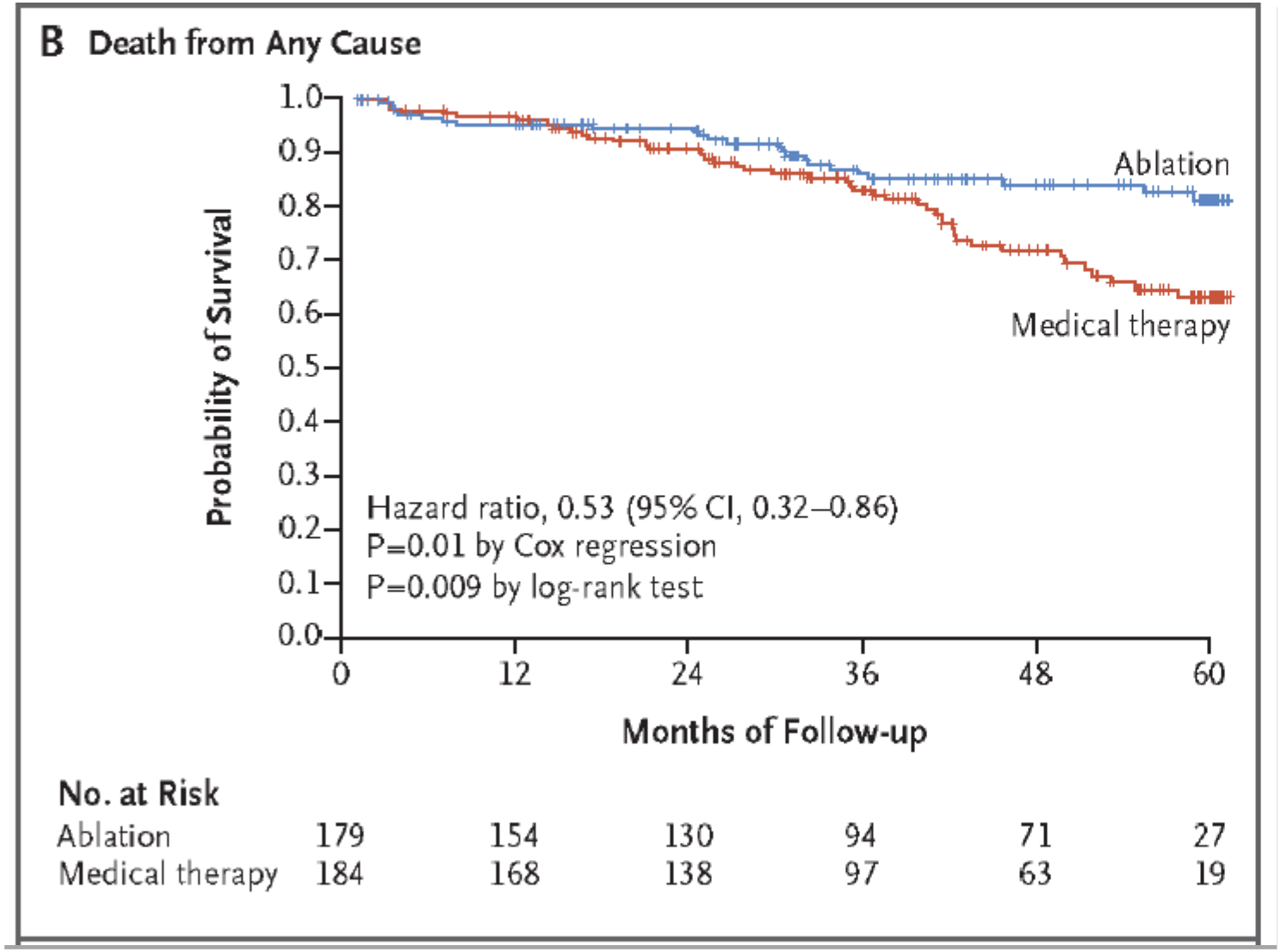

Marrouche et al, 2018

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AF in Pts with CHF: When to Perform Catheter Ablation?

CASTLE-AF

Characteristic	Treatment Type	
	Ablation (N=179)	Medical Therapy (N=184)
Age — yr		
Median	64	64
Range	56–71	56–73.5
Male sex — no. (%)	156 (87)	155 (84)
Body-mass index†		
Median	29.0	29.1
Range	25.9–32.2	25.9–32.3
New York Heart Association class — no./total no. (%)		
I	20/174 (11)	19/179 (11)
II	101/174 (58)	109/179 (61)
III	50/174 (29)	49/179 (27)
IV	3/174 (2)	2/179 (1)

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AF in Pts with CHF: When to Perform Catheter Ablation?

CASTLE-AF

Characteristic	Treatment Type	
	Ablation (N=179)	Medical Therapy (N=184)
Cause of heart failure — no. (%)‡		
Ischemic	72 (40)	96 (52)
Nonischemic	107 (60)	88 (48)
Type of atrial fibrillation — no. (%)		
Paroxysmal	54 (30)	64 (35)
Persistent	125 (70)	120 (65)
Long-standing persistent (duration >1 year)	51 (28)	55 (30)
Left atrial diameter		
Total no. of patients evaluated	162	172
Median — mm	48.0	49.5
Interquartile range — mm	45.0–54.0	5.0–55.0
Left ventricular ejection fraction		
Total no. of patients evaluated	164	172
Median — %	32.5	31.5
Interquartile range — %	25.0–38.0	27.0–37.0

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Marrouche et al, 2018

AF in Pts with CHF: When to Perform Catheter Ablation?

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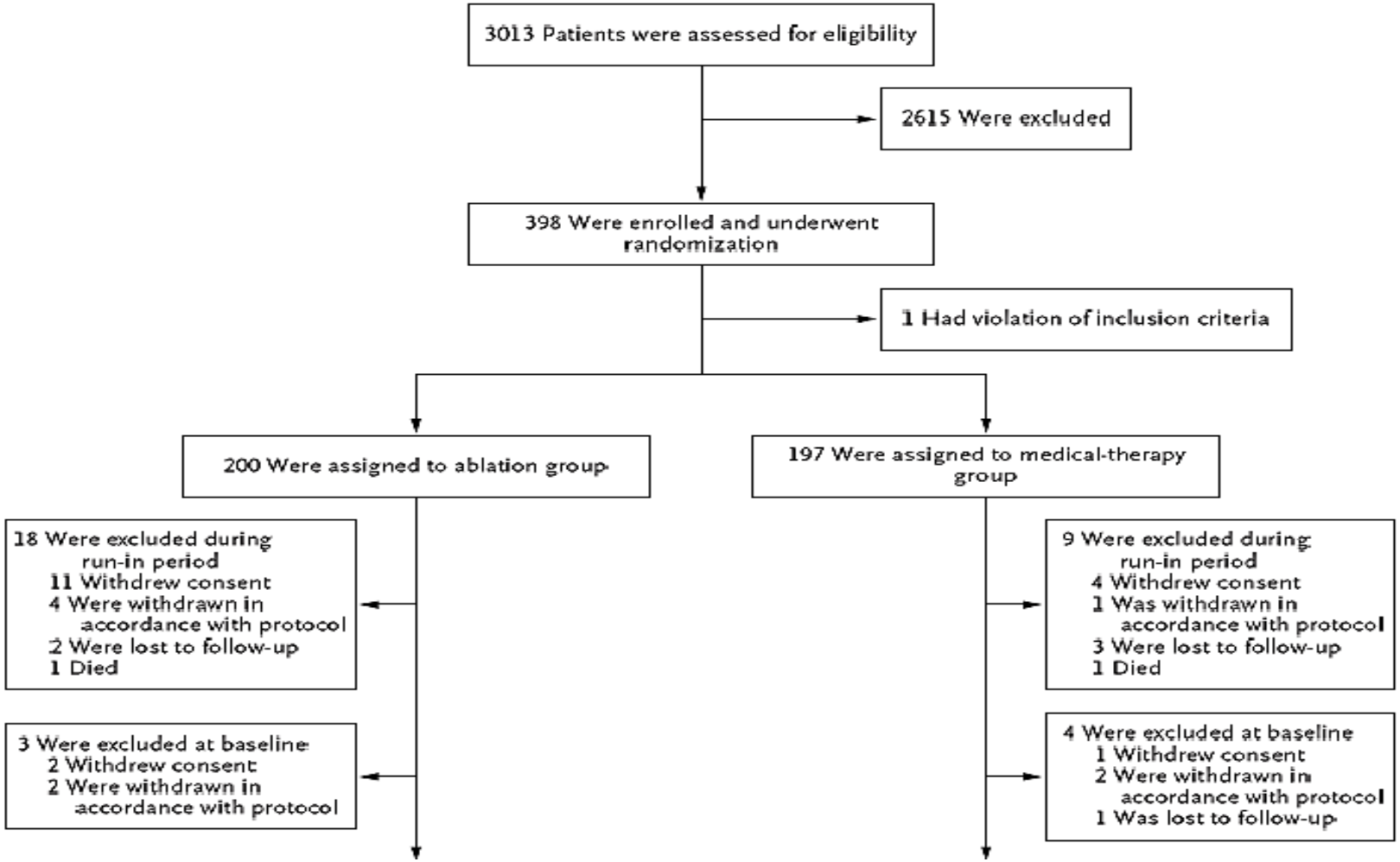

Marrouche et al, 2018

AF in Pts with CHF: When to Perform Catheter Ablation?

CASTLE-AF

Table 2. Primary and Secondary Clinical End Points.*

End Point	Ablation (N = 179)	Medical Therapy (N = 184)	Hazard Ratio (95% CI)	P Value	
				Cox Regression	Log-Rank Test
	number (percent)				
Primary†	51 (28.5)	82 (44.6)	0.62 (0.43–0.87)	0.007	0.006
Secondary					
Death from any cause	24 (13.4)	46 (25.0)	0.53 (0.32–0.86)	0.01	0.009
Heart-failure hospitalization	37 (20.7)	66 (35.9)	0.56 (0.37–0.83)	0.004	0.004
Cardiovascular death	20 (11.2)	41 (22.3)	0.49 (0.29–0.84)	0.009	0.008
Cardiovascular hospitalization	64 (35.8)	89 (48.4)	0.72 (0.52–0.99)	0.04	0.04
Hospitalization for any cause	114 (63.7)	122 (66.3)	0.99 (0.77–1.28)	0.96	0.96
Cerebrovascular accident	5 (2.8)	11 (6.0)	0.46 (0.16–1.33)	0.15	0.14

Marrouche et al, 2018

AF in Pts with CHF: When to Perform Catheter Ablation?

CASTLE-AF

Table S1. Characteristics of the Primary Analysis Patient Population at Enrollment

Characteristic	Treatment of Atrial Fibrillation	
	Ablation group (179 patients)	Pharmacological group (184 patients)
†Left ventricular ejection fraction – %	29.0 (25.0-32.0)	30.0 (25.0-32.0)
Medication	n=179	n=183
ACE-inhibitor or ARB – no. (%)	168 (94%)	166 (91%)
Beta-blocker – no. (%)	164 (92%)	174 (95%)
Diuretics including spironolactone – no. (%)	170 (95%, vs. 93%*)	168 (92%, vs. 93%*)
Digitalis – no. (%)	36 (20%, vs. 18%*)‡	56 (31%)‡
Antiarrhythmic drug (class Ia, Ic, or III) – no. (%)	51 (29%, vs. 32%*)	51 (28%, vs. 31%*)
Amiodarone – no. (%)	50 (28%, vs. 31%*)	46 (25%), n=182, (vs. 26%*)

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Rationale for AF Ablation in CHF

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Cardiac Index

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Rationale for AF Ablation in CHF

$$\text{Cardiac Index} = \frac{\text{Cardiac Output}}{\text{Body Surface Area}}$$

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$$\text{Cardiac Index} = \frac{\text{Cardiac Output}}{\text{Body Surface Area}} = \frac{\text{Systolic Volume x Heart Rate}}{\text{Body Surface Area}}$$

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$$\text{Cardiac Index} = \frac{\text{Cardiac Output}}{\text{Body Surface Area}} = \frac{\text{Systolic Volume x Heart Rate}}{\text{Body Surface Area}} = 2.6 - 4.2 \text{ L/min}$$

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CASTLE-AF

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With a recurrence rate of 50% in the study group at 60 months FU

Marrouche et al, 2018

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With 63% of patients in the study group presenting with stable sinus rhythm between 48 and 60 months FU

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Marrouche et al, 2018

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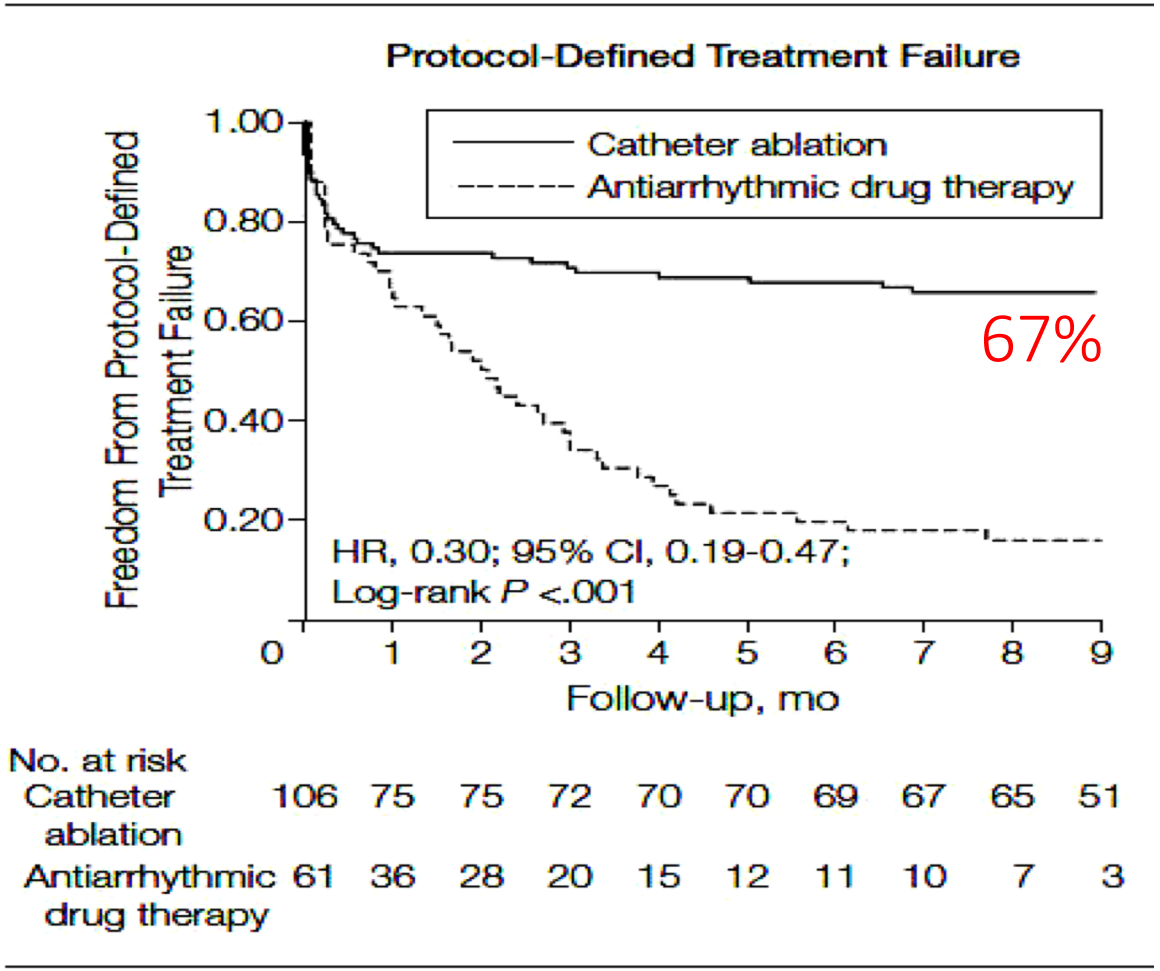
Efficacy



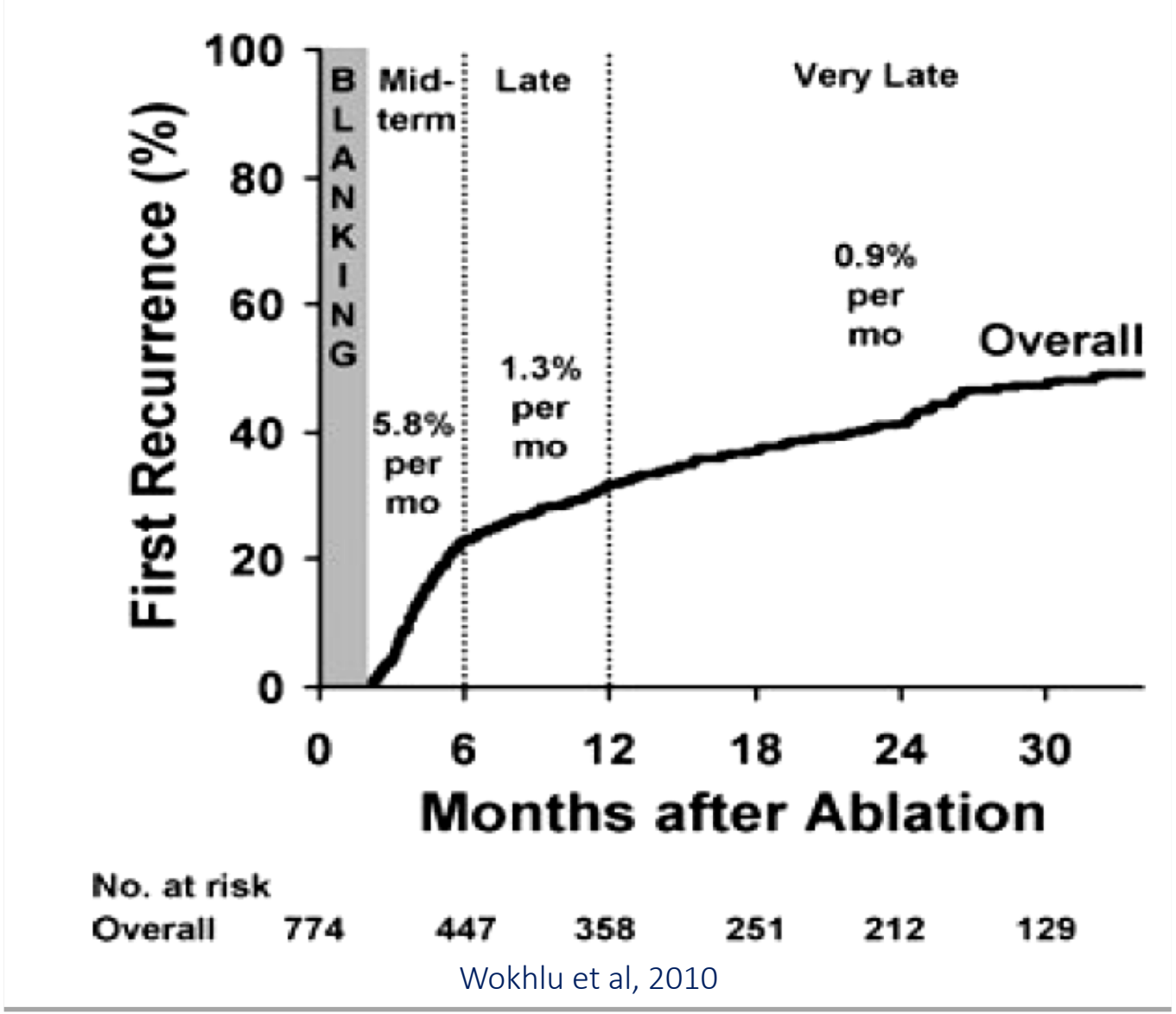
Wilber et al, 2010

Methodological adv.

- Multi-center
- Prospective
- Randomized
- Reproducible ablation design (PV isolation)
- Paroxysmal AF
- Outcome judged by external referee committee

AF in Pts with CHF: When to Perform Catheter Ablation?

Long-term outcome



Wokhlu et al, 2010

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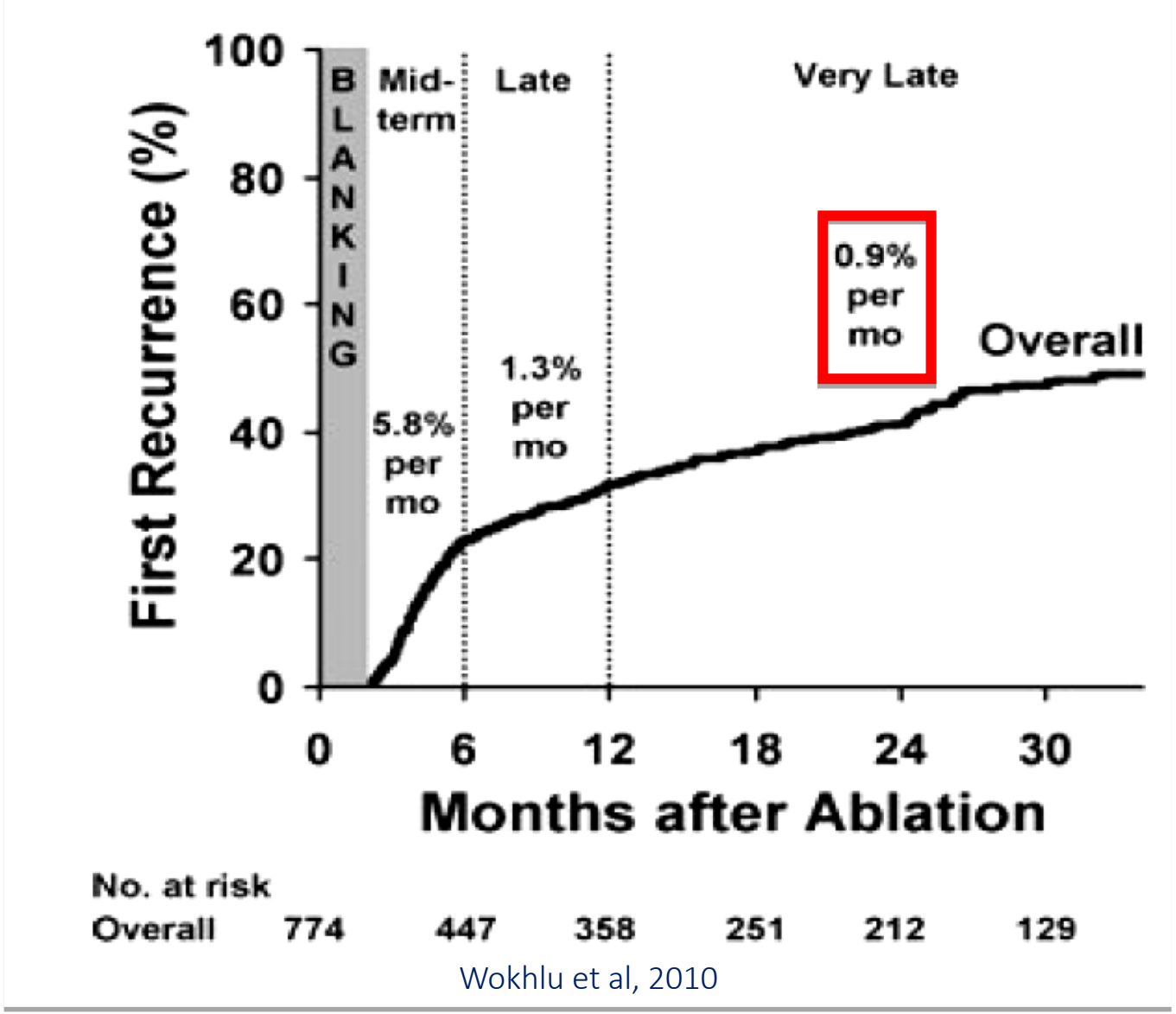

Wokhlu et al, 2010

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AF in Pts with CHF: When to Perform Catheter Ablation?

Efficacy model for ablation in CASTLE-AF

- Success rates at catheter ablation of persistent and long-standing persistent AF
  - 67% in 1/3 of pts
  - 38% in 1/3 of pts
  - 27% in 1/3 of pts

  44% mean success rate in the aggregate population! during 9 months FU!!!
- Role of follow-up in favoring AF recurrences after catheter ablation
- Role of sinus rhythm in determining clinical outcome

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AF in Pts with CHF: When to Perform Catheter Ablation?

Trends in complications of AF ablation

	Overall	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	*P* Value
Any procedural complications	6.29	5.33	5.53	6.01	7.17	6.32	5.10	6.17	6.66	5.93	6.49	7.48	0.108
In hospitalization death	0.42	0.44	0.55	0.63	0.30	0.61	0.15	0.45	0.53	0.27	0.52	0.47	0.492
Vascular complications	1.53	0.89	0.66	1.16	1.12	0.95	1.31	0.60	0.97	1.02	0.97	1.33	0.500
Postop hemorrhage	3.38	1.78	2.54	2.53	2.39	3.38	2.77	3.13	3.52	3.75	3.46	4.90	<0.001
Postop hemorrhage requiring transfusion	0.58	0.30	0.22	0.32	0.30	0.61	0.34	0.45	0.87	0.65	0.44	1.03	0.020
Vascular complications including	1.01	0.30	0.11	0.21	0.22	0.26	0.34	0.05	0.10	0.03	0.04	0.04	0.060
Cardiac complications	2.54	1.63	1.66	1.37	2.69	2.42	1.90	1.69	2.90	2.90	3.06	3.53	<0.001
Iatrogenic cardiac complications	1.18	1.33	0.88	0.63	1.19	1.13	0.83	0.90	1.54	1.33	0.93	1.76	0.050
Pericardial complications	1.52	0.74	0.44	0.63	1.49	0.87	1.31	1.00	1.83	1.84	2.14	2.24	<0.001
Myocardial infarction	0.37	0.30	0.55	0.32	0.60	0.69	0.29	0.30	0.34	0.37	0.32	0.26	0.650
Requiring open heart surgery	0.28	0.44	0.22	0.11	0.07	0.09	0.24	0.30	0.24	0.24	0.36	0.47	0.460
Respiratory complications	1.3	1.48	1.66	1.27	1.79	1.21	1.12	1.59	1.79	1.16	1.09	0.77	0.109
Pneumothorax	0.39	0.59	0.66	0.63	0.82	0.52	0.44	0.50	0.29	0.31	0.24	0.04	0.020
Postop respiratory failure	0.77	0.74	0.88	0.53	0.75	0.61	0.49	0.90	1.16	0.68	0.85	0.73	0.575
Other iatrogenic respiratory complications	0.18	0.15	0.33	0.11	0.30	0.09	0.24	0.20	0.43	0.20	0.00	0.00	0.030
Neurological complications (postop stroke/TIA)	1.02	0.89	1.11	1.79	1.57	1.13	0.68	1.39	0.53	0.78	0.93	1.20	0.013
Postop infectious complications	0.38	0.15	0.11	0.21	0.45	0.43	0.29	0.50	0.72	0.24	0.40	0.43	0.235

AF indicates atrial fibrillation; Postop, postoperative; and TIA, transient ischemic attack.

Deshmukh et al, 2010

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AF in Pts with CHF: When to Perform Catheter Ablation?

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In paroxysmal AF!!

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AF in Pts with CHF: When to Perform Catheter Ablation?

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AF in Pts with CHF: When to Perform Catheter Ablation?

Conclusions

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AF in Pts with CHF: When to Perform Catheter Ablation?

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- Studies in the literature provide elusive methodology and unrealistic data to be extrapolated to a general population
- Too much enthusiasm may lead to an excess procedural risk exposure
- Selected patients (at best those with tachymyopathy) may be considered for AF ablation

AF in Pts with CHF: When to Perform Catheter Ablation?

What to do?

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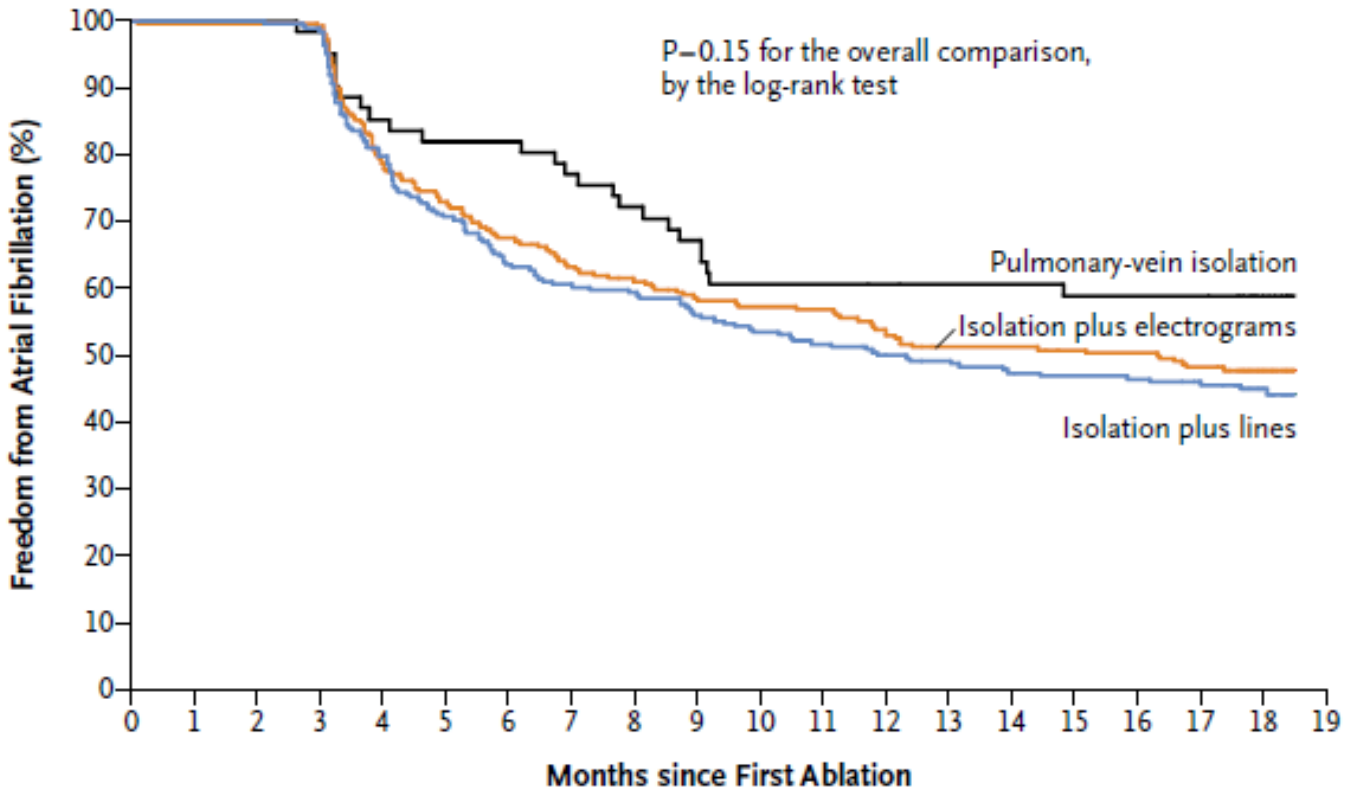
CASTLE-AF



No. at Risk						
Pulmonary-vein isolation	61	60	50	41	36	23
Isolation plus electrograms	244	242	161	137	124	72
Isolation plus lines	244	240	152	133	115	57

Verma et al, 2015

AF in Pts with CHF: When to Perform Catheter Ablation?

Rationale for AF Ablation in CHF

CI =

AF in Pts with CHF: When to Perform Catheter Ablation?

Rationale for AF Ablation in CHF

$$CI = \frac{CO}{BSA}$$

AF in Pts with CHF: When to Perform Catheter Ablation?

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$$CI = \frac{CO}{BSA} = \frac{SV \times HR}{BSA}$$

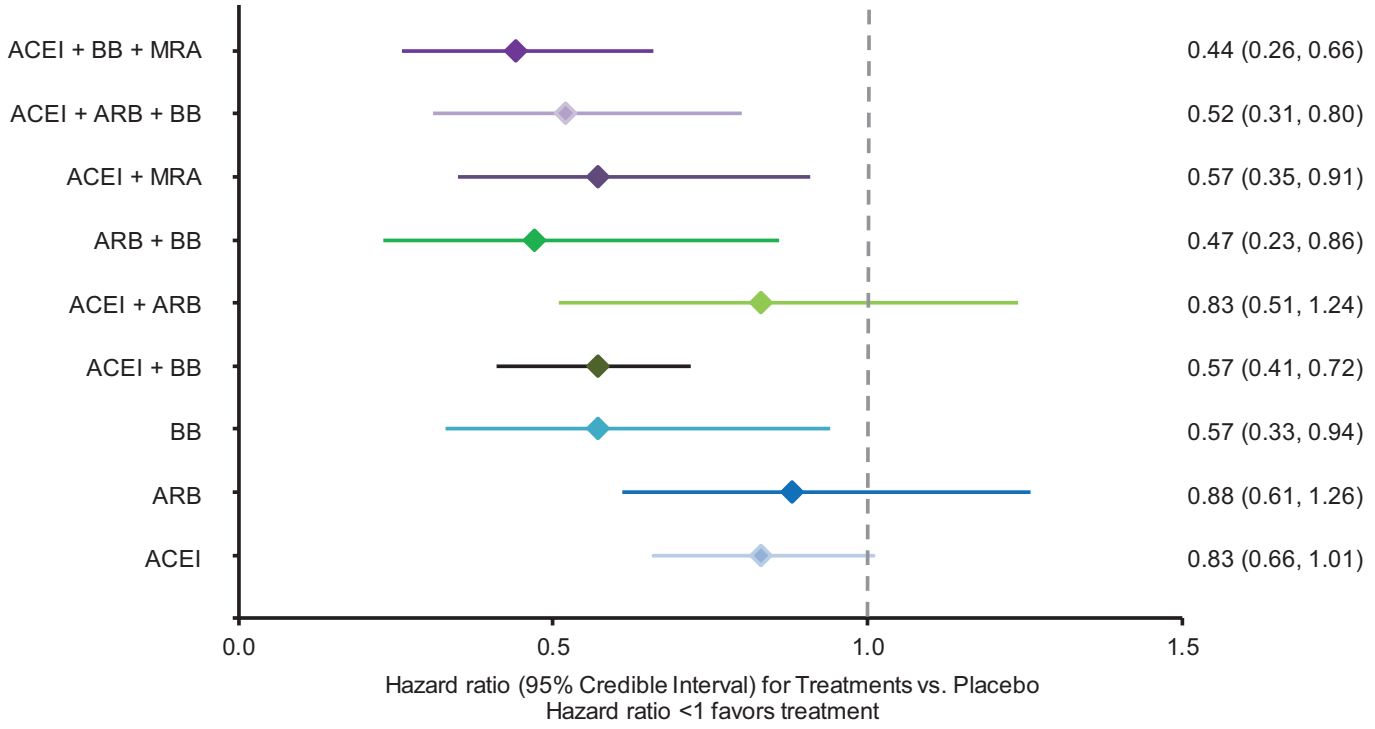
AF in Pts with CHF: When to Perform Catheter Ablation?

Rationale for AF Ablation in CHF

$$CI = \frac{CO}{BSA} = \frac{SV \times HR}{BSA} = 2.6 - 4.2 \text{ L/min}$$

Thirty Years of Evidence on the Efficacy of Drug Treatments for Chronic Heart Failure With Reduced Ejection Fraction

A Network Meta-Analysis



Circul HF 2017; 10 (1): e003529

AF in Pts with CHF: When to Perform Catheter Ablation?

Table 1. Etiology Of Atrial Fibrillation.

Cardiac	Non-cardiac
• Ischemic heart disease	• Pulmonary embolism
• Valvular disease	• Idiopathic
• Hypertension	• Medication noncompliance
• Congestive heart failure	• Thyroid disease
• Sick sinus syndrome	• Holiday heart syndrome
• Pericarditis	• Medication use
• Infiltrative heart disease	• Electrocution
• Cardiomyopathy	• Other pulmonary disease
• Cardiac surgery	• Chest trauma
• Myocarditis	• Hypokalemia
• Congenital heart disease	• Hypomagnesemia
	• Hypothermia

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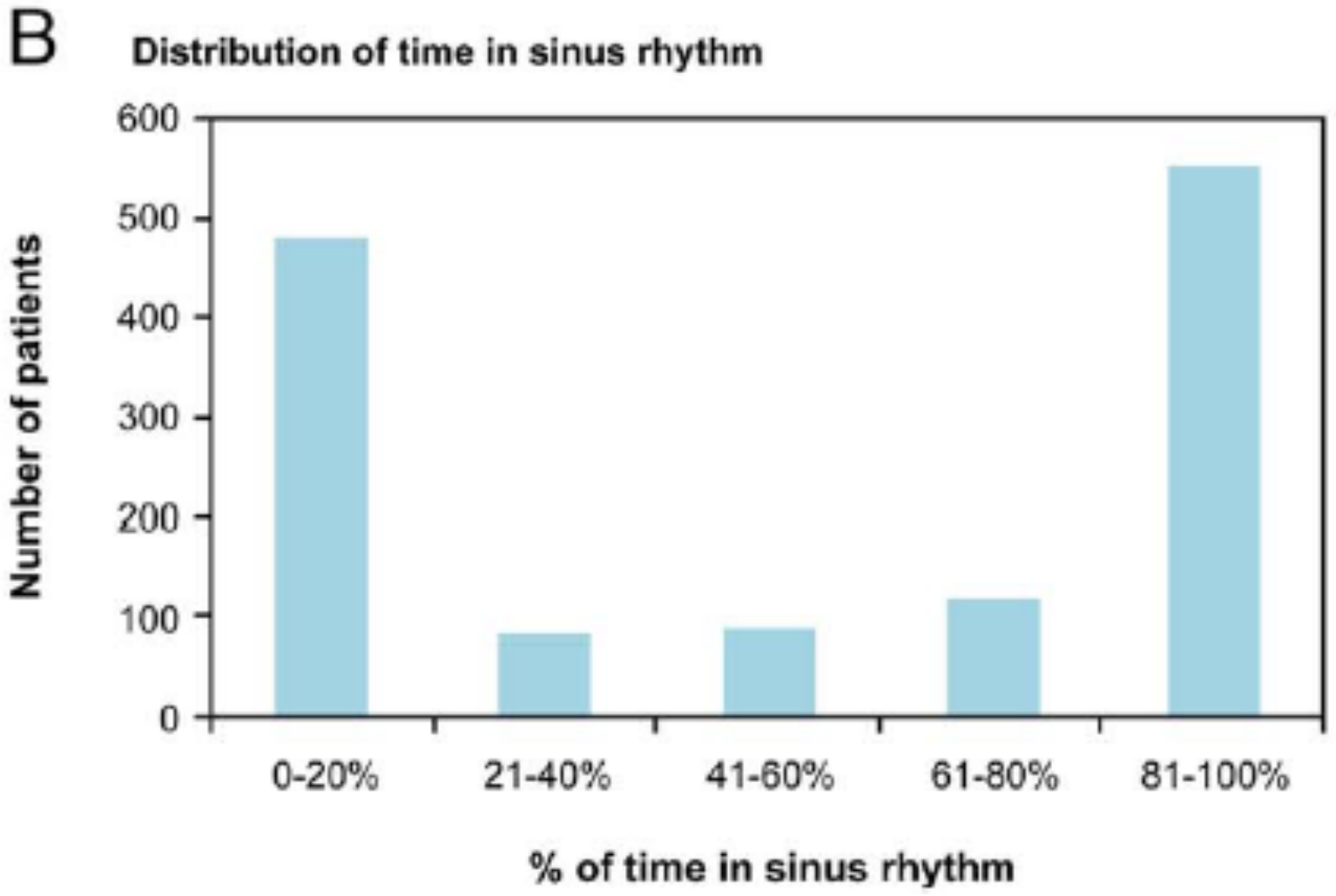
AF in Pts with CHF: When to Perform Catheter Ablation?

Heart failure: definition

- Clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary cracklers and peripheral oedema) caused by and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress

AF in Pts with CHF: When to Perform Catheter Ablation?

AF-CHF: secondary endpoints



Talajic M, et al, 2010

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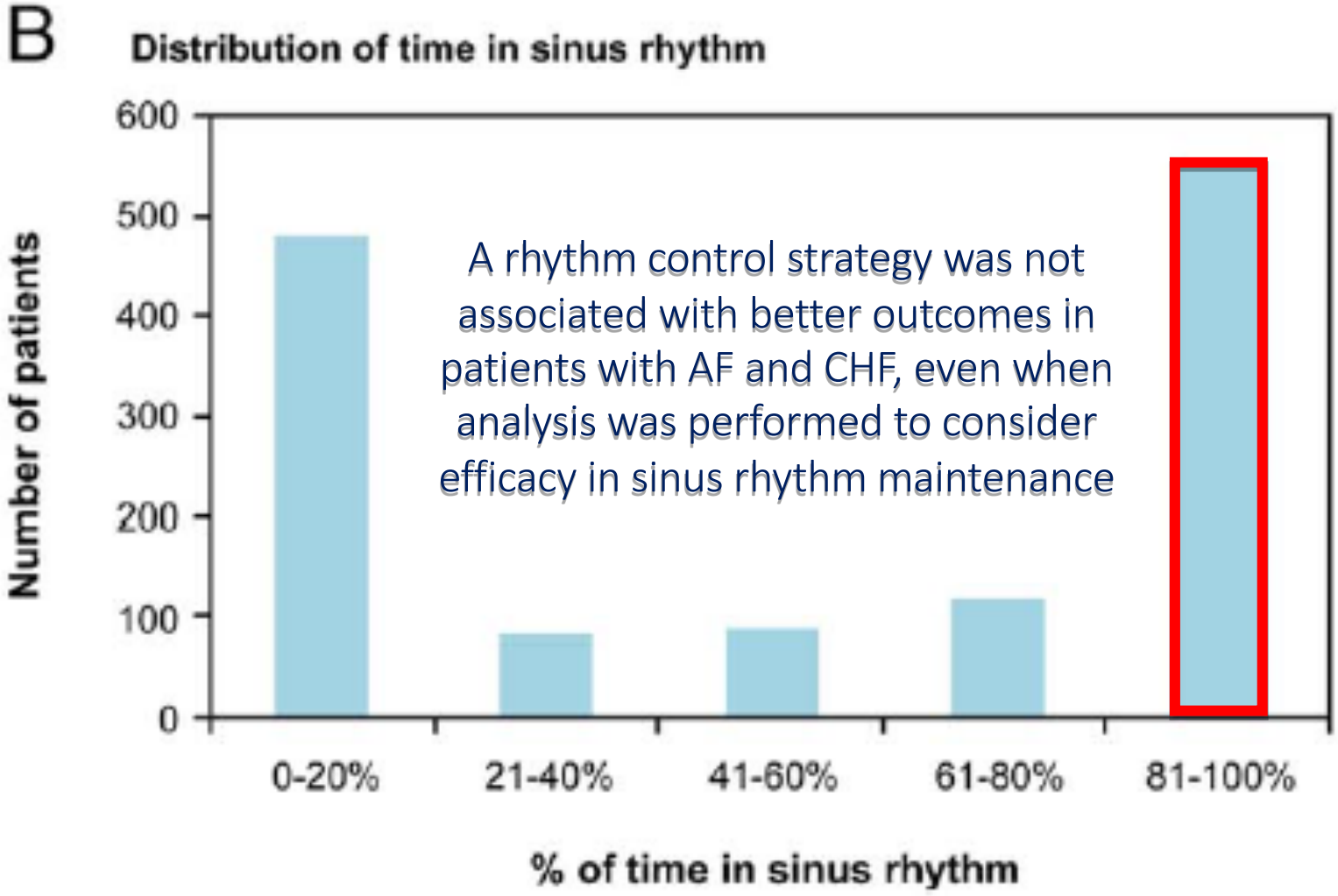

A rhythm control strategy was not associated with better outcomes in patients with AF and CHF, even when analysis was performed to consider efficacy in sinus rhythm maintenance

Talajic M, et al, 2010

AF in Pts with CHF: When to Perform Catheter Ablation?

Ablation technique

Study (year)	Patients (n)	Mean EF	Mean LA size	Freedom from AF*	Ref.
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*Freedom from AF without the use of antiarrhythmic drugs.
‡No atrial fibrillation with or without antiarrhythmic medication or greater than 90% reduction in AF burden.
AF: Atrial fibrillation; EF: Ejection fraction; LA: Left atrium; NA: Not applicable.

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