A 70-year-old woman with tachycardia-bradycardia syndrome

전남대학교병원 순환기내과
박형욱

Pacemaker ?

Yes !!!

하지만,,,

Reverse Remodeling of Sinus Node Function After Catheter Ablation of Atrial Fibrillation in Patients With Prolonged Sinus Pauses

Hocini M, et al. Circulation *2003; 108: 1172-1175*

Pacing-Induced Chronic Atrial Fibrillation Impairs Sinus Node Function in Dogs. Electrophysiologic remodeling

Elvan A, et al. Circulation *1996; 94: 2953-2960*

Pacing or ablation: which is better for paroxysmal atrial fibrillation-related tachycardia-bradycardia syndrome?

Chen YW, et al. PACE 2014;37:403-11

…..

Debate는 이미 끝났다? !!!

결론은 이미 정해져 있다?

이대로 물러설 수는 없다.
달려들어 물기라도
해야 한다.

Report of the Atrial fibrillation – '1187'

Rabbi Mosheh ben Maimon

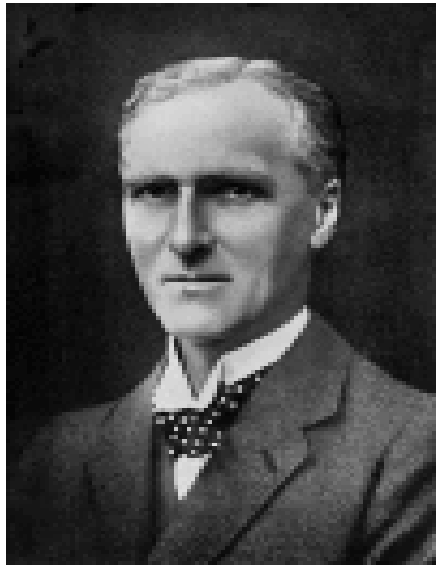
(1135년 3월 30일 ~ 1204년 12월 13일)은 유대인 철학자, 의사이다.

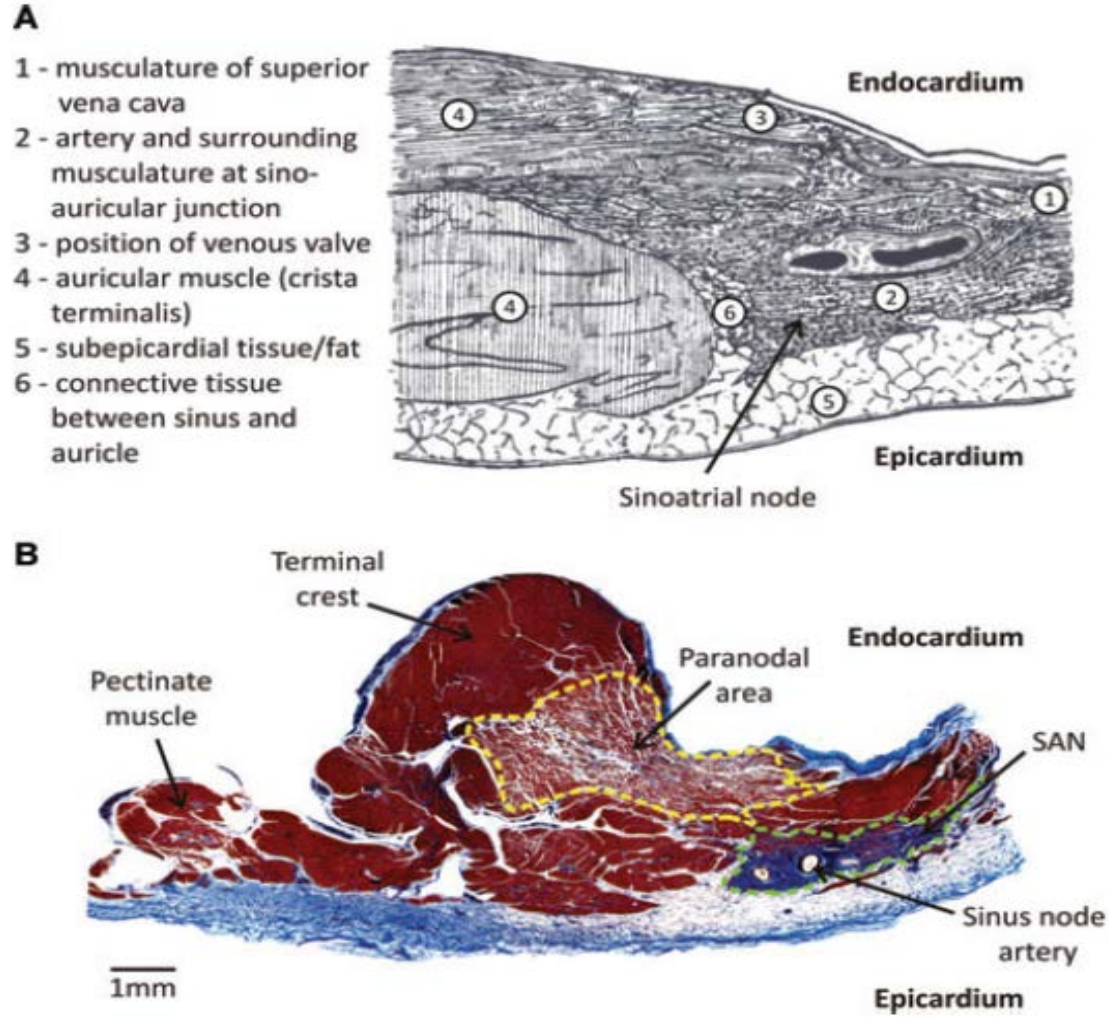
Evaluation of the peripheral pulse has fascinated physicians for centuries. In approximately 1187, Moses Maimonides presented aphorisms pertaining to the pulse. He described an irregular pulse that was regularly irregular and one that becomes completely irregular (1). He was at least partially correct when he mentioned, with regard to the origin of the regularity, "all types of pulses which are irregular in more than one beat are a direct result of an abnormal constitution of the heart which is also irregular or due to an affliction arising in the stomach or in one's strength". Before the electrocardiographic confirmation of atrial fibrillation, many observant physicians commented on grossly irregular pulses that, in at least some cases, were likely atrial fibrillation. William Stokes (2), in his classic

Textbook of cardiovascular medicine, 3rd ed. Eric Topol

Discovery of the Sinus Node

1907 by Sir Arthur Keith





Keith A, Flack M. J Anat Physiol 1907; 41:172–189

“The sick sinus syndrome in atrial disease”

Although little basic information exists regarding atrial disease, certain clinical states can be grouped into a syndrome resulting from a failing sinoatrial (SA) node.

One or more of the following symptoms appears: persistent, severe, and unexpected sinus bradycardia; cessation of sinus rhythm for short intervals with other rhythms supervening; long periods of sinus arrest without rescue rhythm, which produces cardiac arrest; untreated chronic atrial fibrillation with slow ventricular rate; no sinus rhythm after cardioversion; SA exit block.

Symptoms spring from hypoperfusion of vital organs.

Ferrer MI, JAMA. 1968 ;206:645-6.

Sick Sinus Syndrome

- Sinus bradycardia
- Sinoatrial exit block
- Sinus pause or arrest
- **Tachycardia-bradycardia**

…… and symptoms associated with hypoperfusion

SND and AF

Evidence that AF leads to SND, or vice versa

SND, AF

- Atrial fibrillation (AF) develops in up to 50% of patients with SND, and the development of AF may further exacerbate SND due to the high atrial rate.

- On the other hand, the bradycardia-related inhomogeneous refractoriness in SND enhances the AF vulnerability.

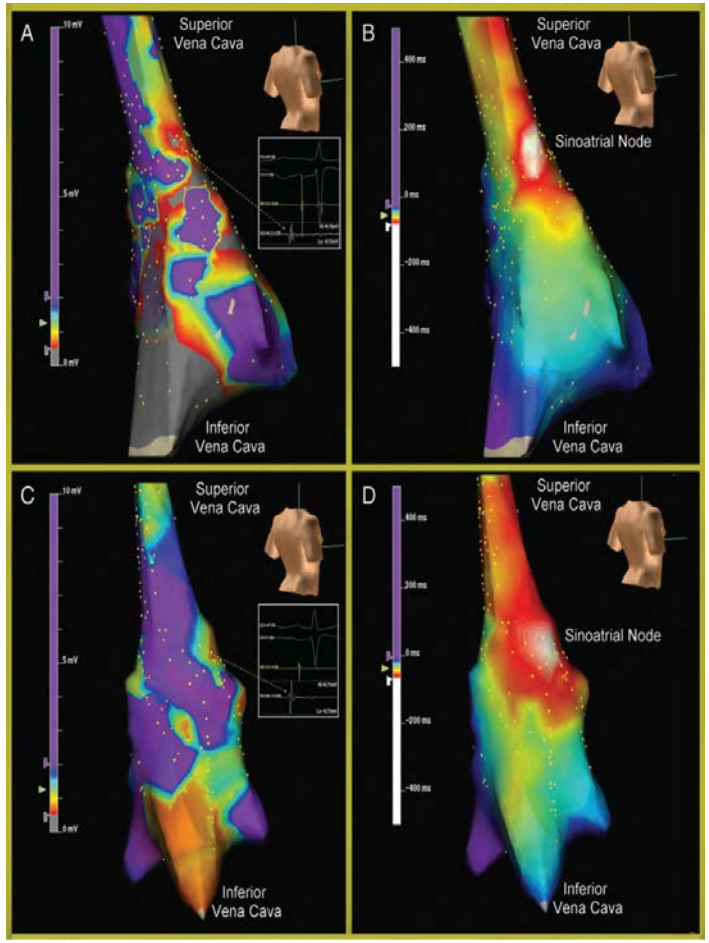
Chang HU, et al. Europace 2012;15: 205-11

SND and AF

- Both diseases are **associated with atrial structural remodeling.**

- Even before the development of atrial arrhythmias, patients with other conditions associated with atrial remodeling and atrial stretch may demonstrate significant sinus node dysfunction.

Sinus node dysfunction in atrial fibrillation patients: the evidence of regional atrial substrate remodeling

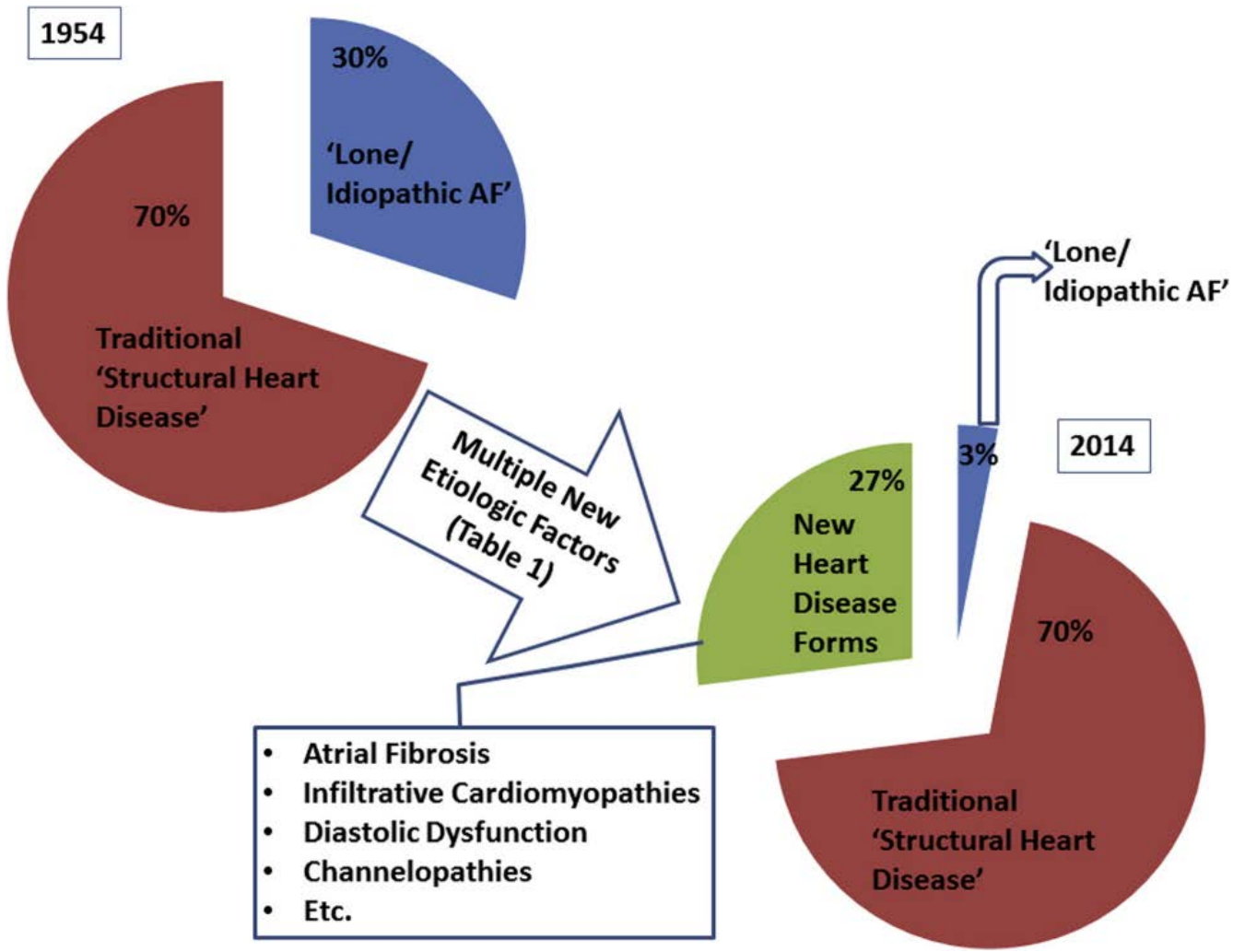


Advanced regional atrial substrate change near the SN area was associated with a prolonged SNRT, a longer RA activation time, a lower voltage of the sinoatrial node area, and a slower conduction velocity along the crista terminalis.

This study indicates the important role of the atrial substrate near the SN area in the maintenance of sinus nodal function in AF patients

Chang HU, et al. Europace 2012;15: 205-11

From: Lone Atrial Fibrillation: Does it Exist?



J Am Coll Cardiol. 2014;63(17):1715-1723.

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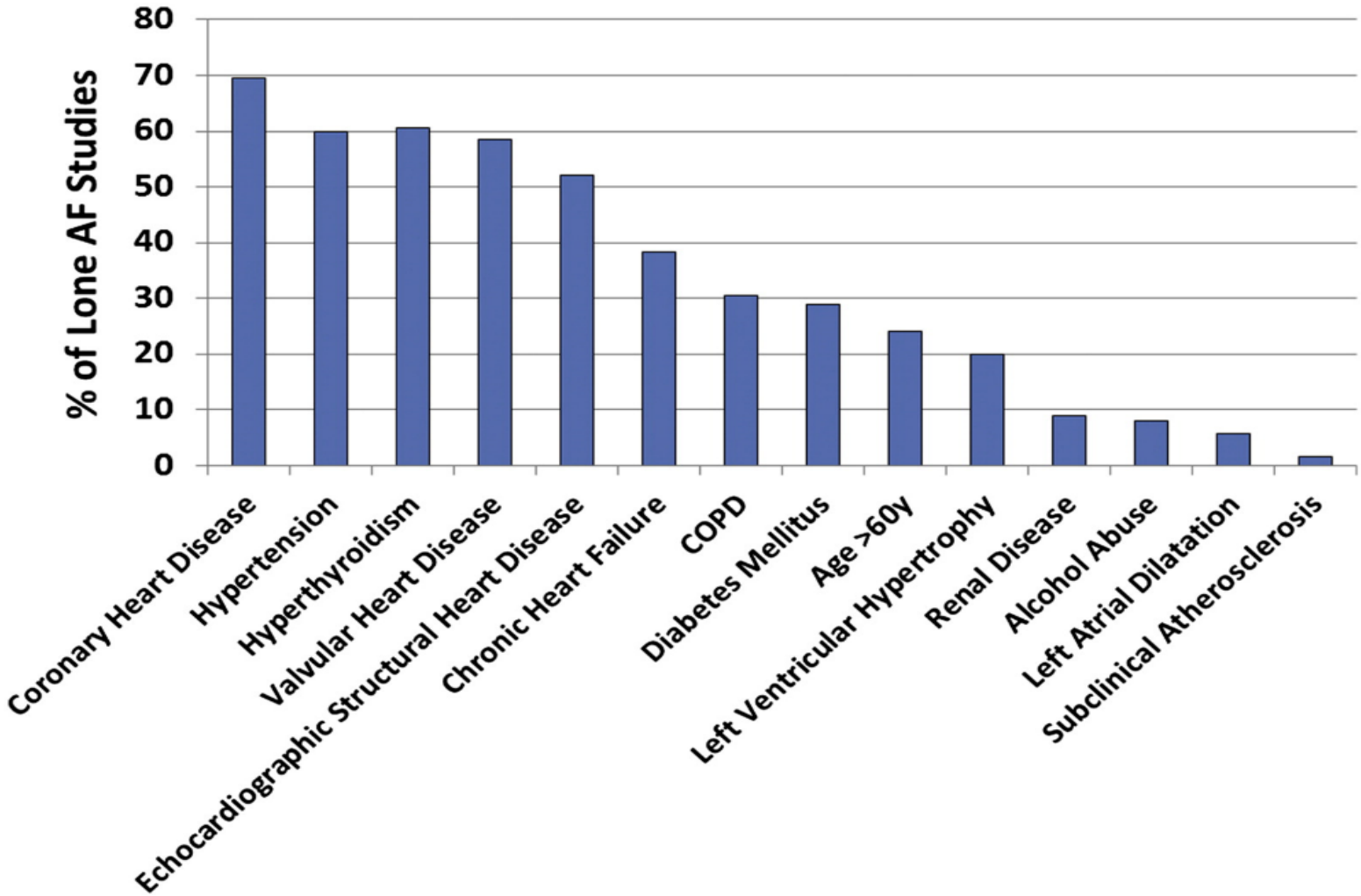
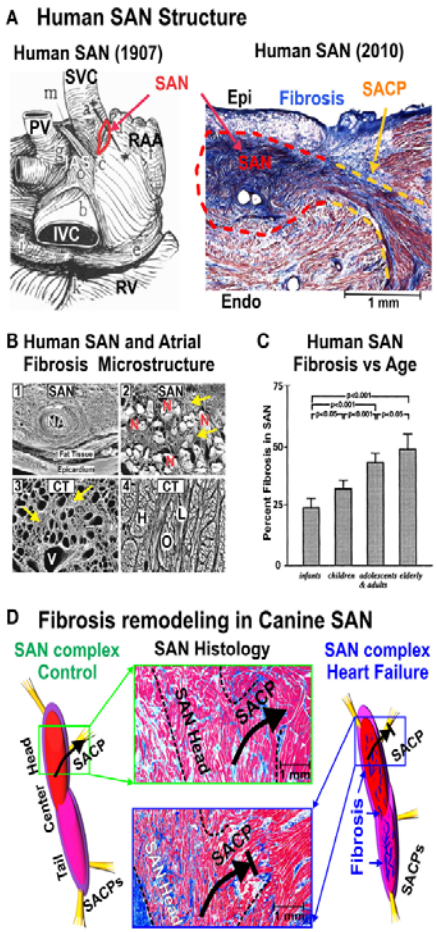
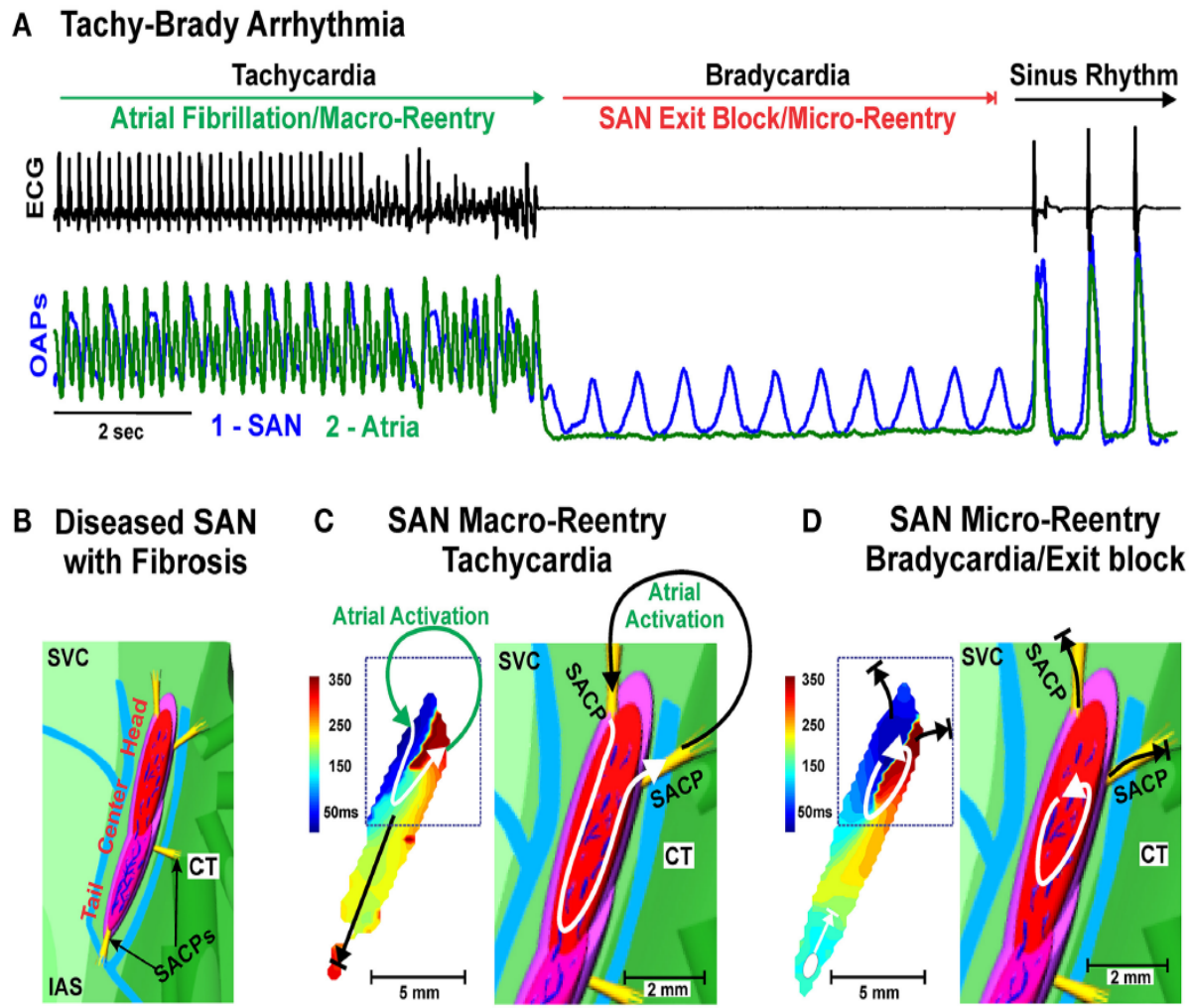


J Am Coll Cardiol. 2014;63(17):1715-1723

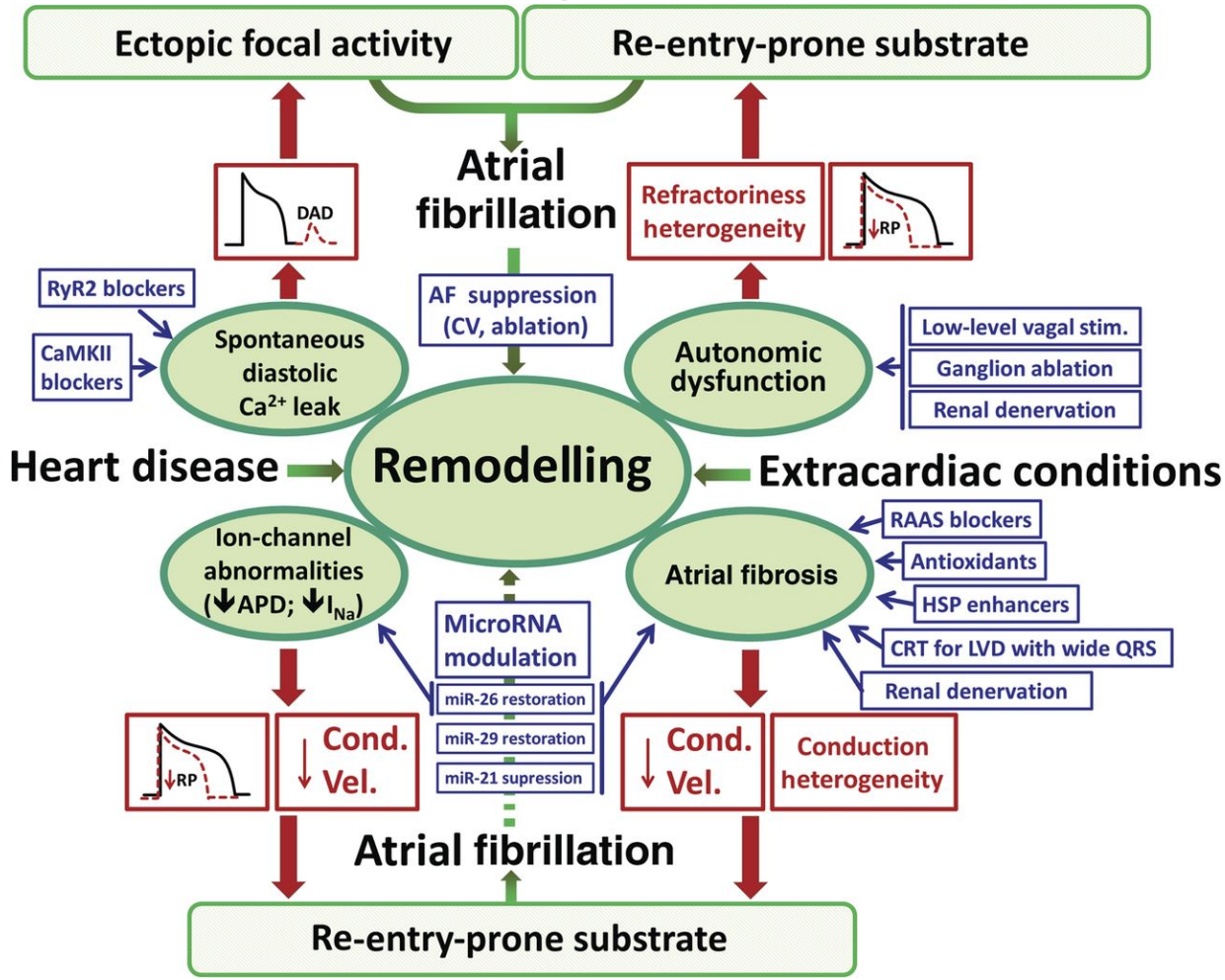
Fibrosis: a structural modulator of sinoatrial node physiology and dysfunction





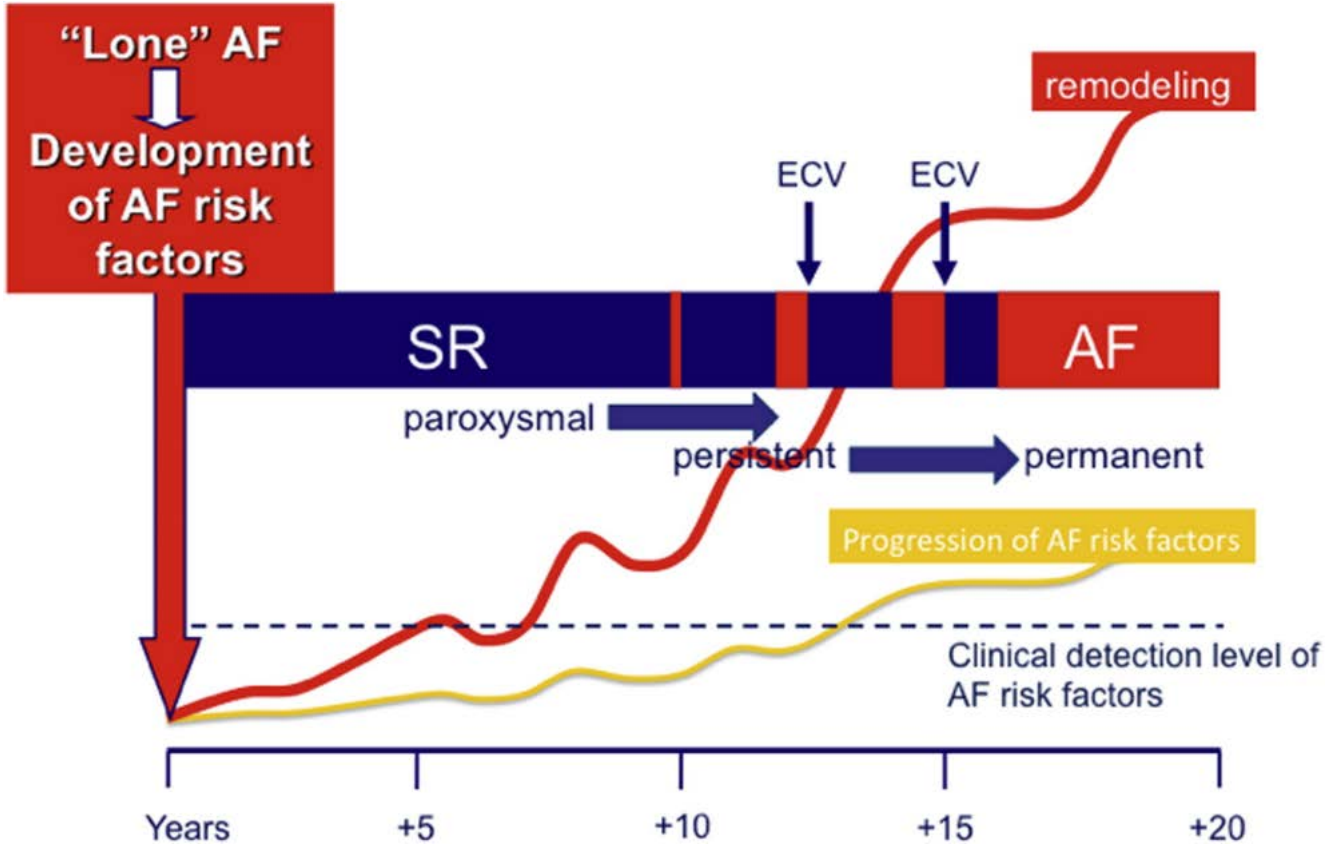
Csepe TA, et al. Front Physiol 2015 Feb 12;6:37. doi: 10.3389/fphys.2015.00037.

Basic mechanisms underlying AF-related remodelling and therapy



Stanley Nattel et al. Eur Heart J 2014;eurheartj.ehu028

From: Lone Atrial Fibrillation: Does it Exist?

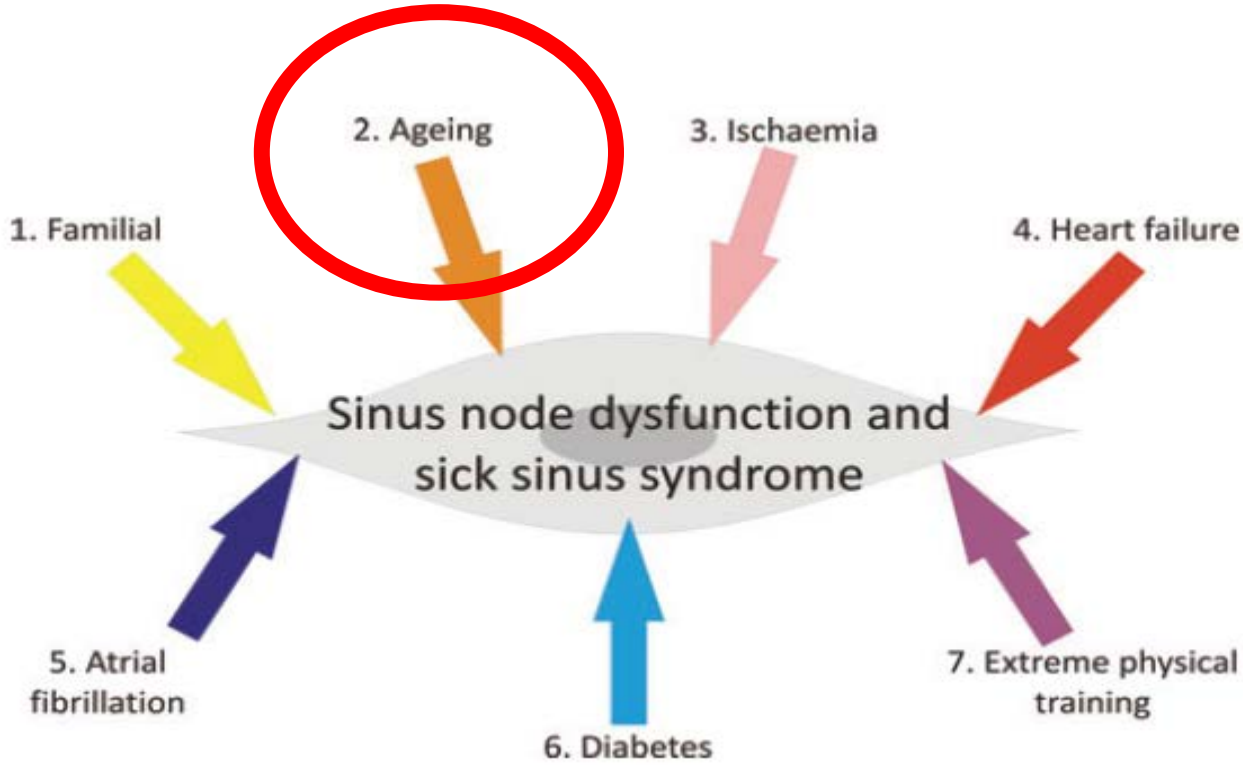


J Am Coll Cardiol. 2014;63(17):1715-1723.

SND and AF and Age

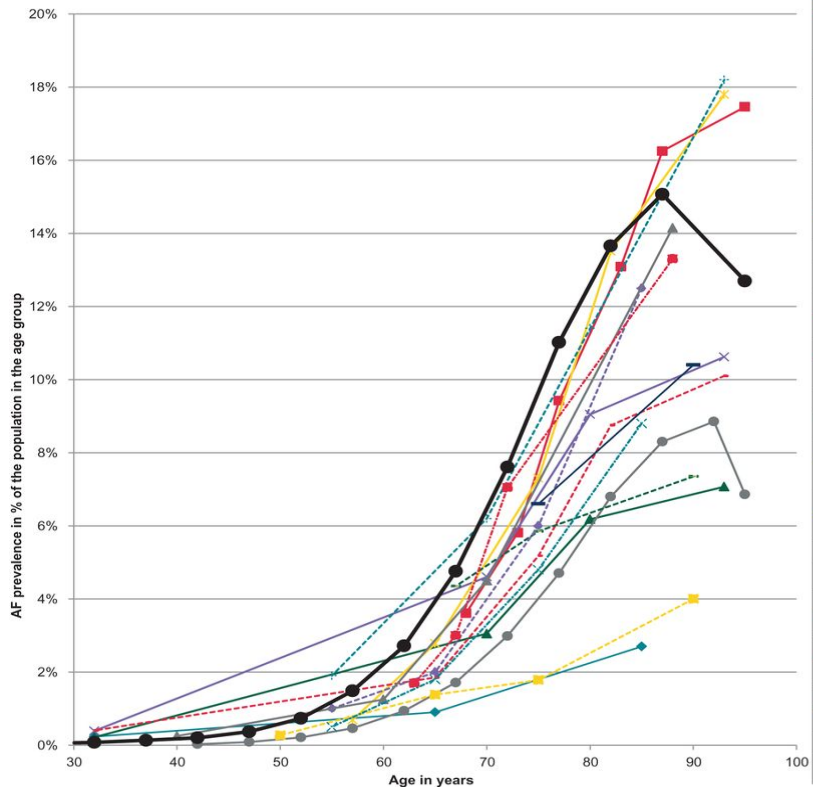
Both disease are more common in aged people’s heart

Multifactorial etiology of SAN dysfunction, Whereby multiple diverse pathologies can lead to the same disease phenotype



Monfredi O, et al. PACE 2010;33:1392-1406

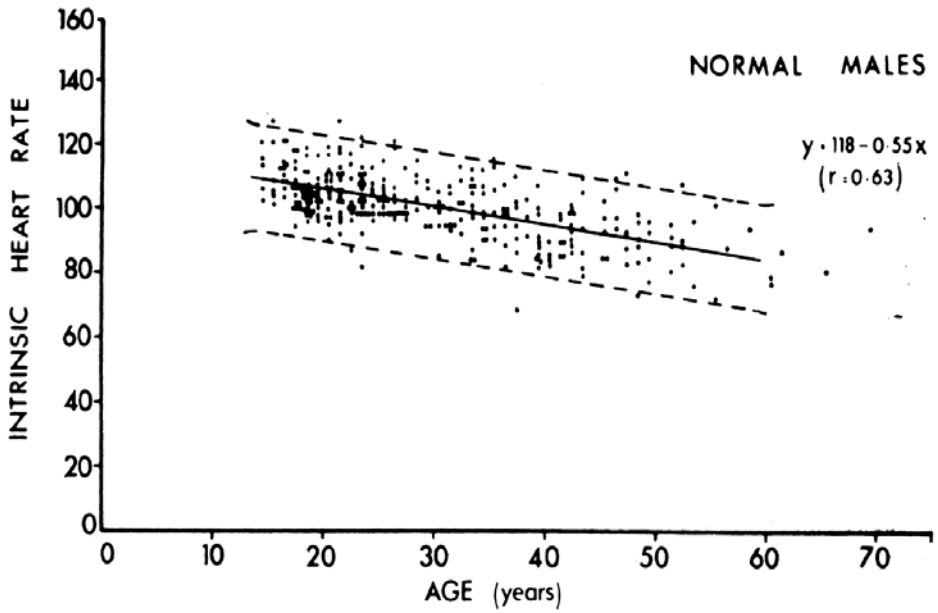
A depiction of the AF prevalence distribution found by each studies published to date

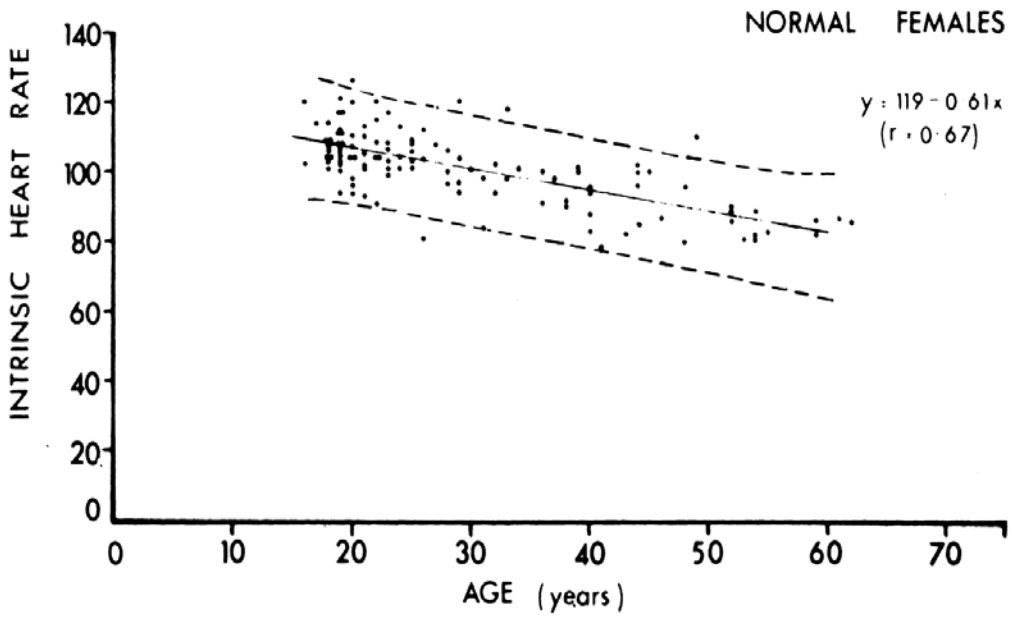


Authors	Data source	Country	Study period
Ohsawa et al., 2005 [5]	Population-based survey	Japan	1980-2000
Piccini et al., 2012 [8]	5% sample of Medicare beneficaries ≥ 65 years	United States	1991-2007
Murphy et al., 2007 [9]	Data from primary care practices	Scotland	April 2001-March 2002
Majeed et al., 2001 [10]	Patients registered in 211 general practices	UK	1994-1998
Heeringa et al., 2006 [13]	Community-based cohort study	Nether-lands	1990-1993
Rietbrock et al., 2008 [14]	General Practice Research Database	UK	1993-2005
Miyasaka et al., 2006 [15]	Community-based cohort study	United States	1980-2000
Go et al., 2001 [16]	Cross-sectional study of adults enrolled in a large HMO	United States	July 1 1996-December 31 1997
Furberg et al., 1994 [17]	Random sample of Medicare recipients	United States	Not known
Naccarelli et al., 2009 [18]	Market scan/ Medicare databases	United States	July 1 2004-December 31, 2005
Jeong, 2005 [19]	Community-based cross-sectional study	Korea	April 2000-December 2000
Phillips et al., 1990 [20]	Community-based cohort study	United States	n.a.
Wolf et al., 1991 [21]	Population-based survey	United States	1948-1990
Lake et al., 1989 [22]	Population-based survey	Australia	1966-83
Bonhorst et al., 2010 [23]	Cross-sectional study of the Portugese population	Portugal	n.a.
Wilke et al., 2012	Claims data of two mandatory insurance funds	Germany	2006 - 2008

Thomas Wilke et al. Europace 2013;15:486-493

Intrinsic heart rate





Jose AD, et al. Cardiovasc Res 1970;4:160–167

Resting Heart Rate and Incident Atrial Fibrillation in the Elderly

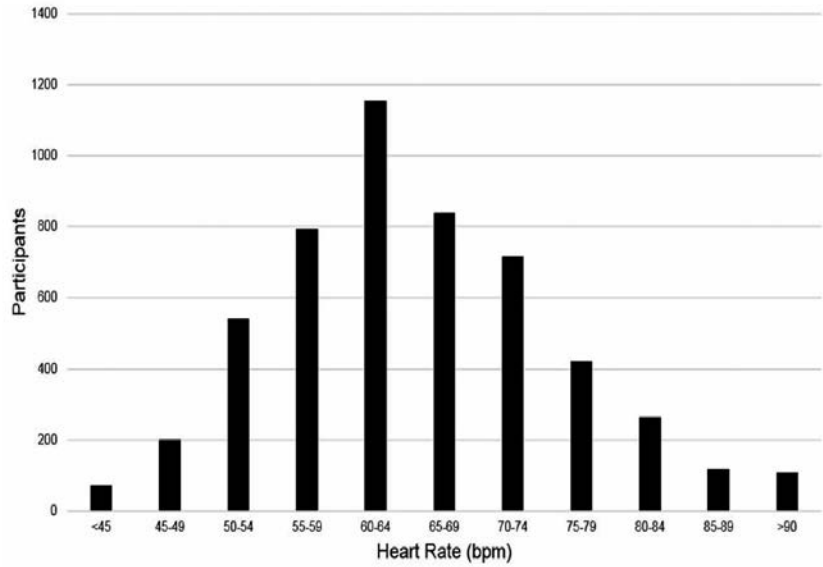


Figure 1. *Distribution of heart rate among study participants.*

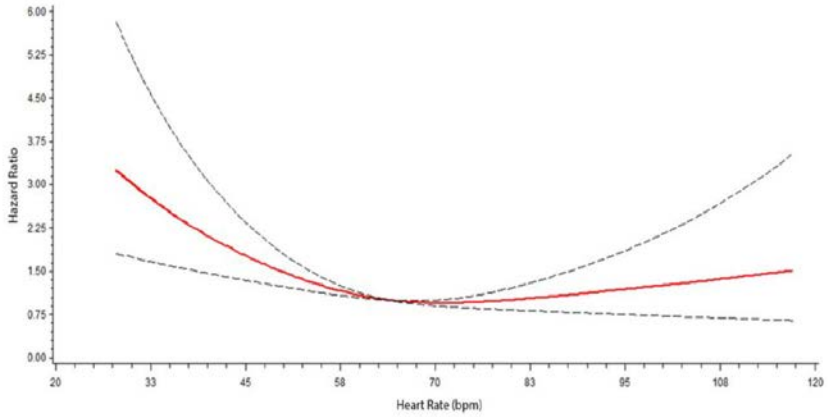


Figure 2. *Risk of AF by heart rate.**
**Each hazard ratio was computed with the median heart rate value of 64 beats/min as the reference. Dotted lines represent the 95% confidence interval. AF = atrial fibrillation.*

*Each hazard ratio was computed with the median heart rate value of 64 beats/min as the reference.

Dotted lines represent the 95% confidence interval. AF = atrial fibrillation.

O'Neal WT, et al. PACE. 2015;38:591-7

Resting Heart Rate and Incident Atrial Fibrillation in the Elderly

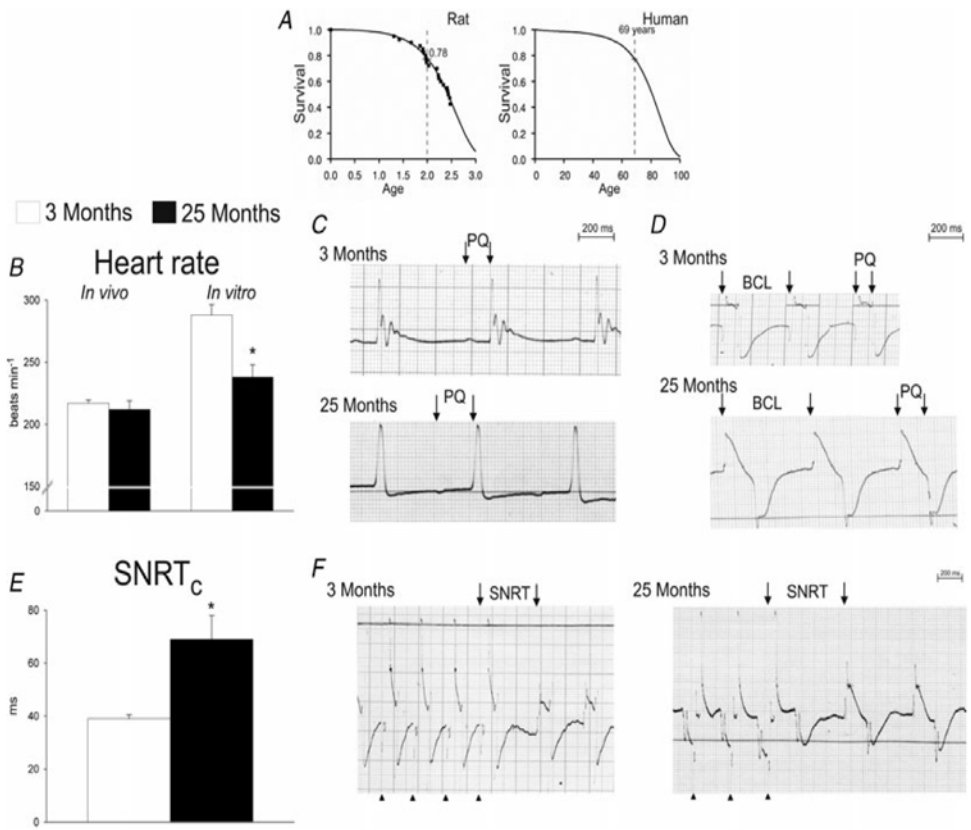
Risk of AF by Baseline Heart Rate (N = 5,226)

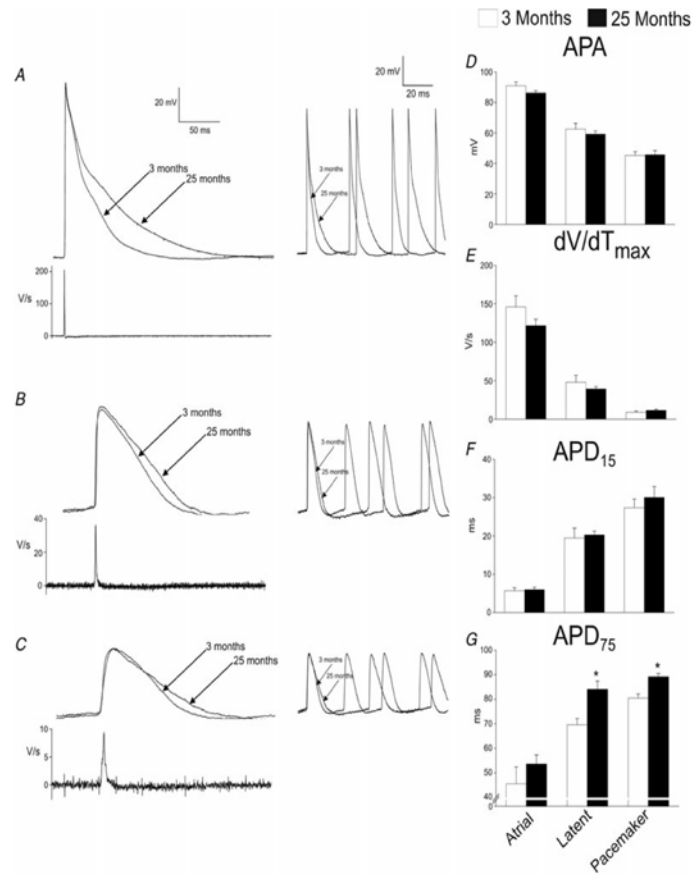
	Events/No. at Risk	Incidence Rate per 1,000 Person-Years (95% CI)	Model 1* HR (95% CI)	P Value	Model 2† HR (95% CI)	P Value
60< Heart rate beats/min ≤90	289/3,270	7.4 (6.6, 8.3)	1.0	–	1.0	–
Heart rate >90 beats/min	7/92	8.4 (4.0, 17.6)	1.1 (0.53, 2.4)	0.77	1.1 (0.52, 2.3)	0.81
Heart rate ≤60 beats/min	236/1,864	9.8 (8.6, 11.1)	1.3 (1.1, 1.6)	0.0025	1.3 (1.1, 1.5)	0.0050
Heart rate per 5 beats/min decrease‡	532/5,226	8.3 (7.6, 9.0)	1.06 (1.02, 1.1)	0.0060	1.06 (1.01, 1.1)	0.011

*Adjusted for age, sex, race, education, and income.
†Adjusted for Model 1 covariates covariates plus baseline CVD, smoking, systolic blood pressure, diabetes, body mass index, total cholesterol, HDL cholesterol, aspirin, statins, antihypertensive and antiarrhythmic medications, and log(hs-CRP).
‡Incidence rate is for all AF cases.
AF = atrial fibrillation; CI = confidence interval; CVD = cardiovascular disease; HDL = high-density lipoprotein; HR = hazard ratio; hs-CRP = high-sensitivity C-reactive protein.

O'Neal WT, et al. PACE. 2015;38:591-7

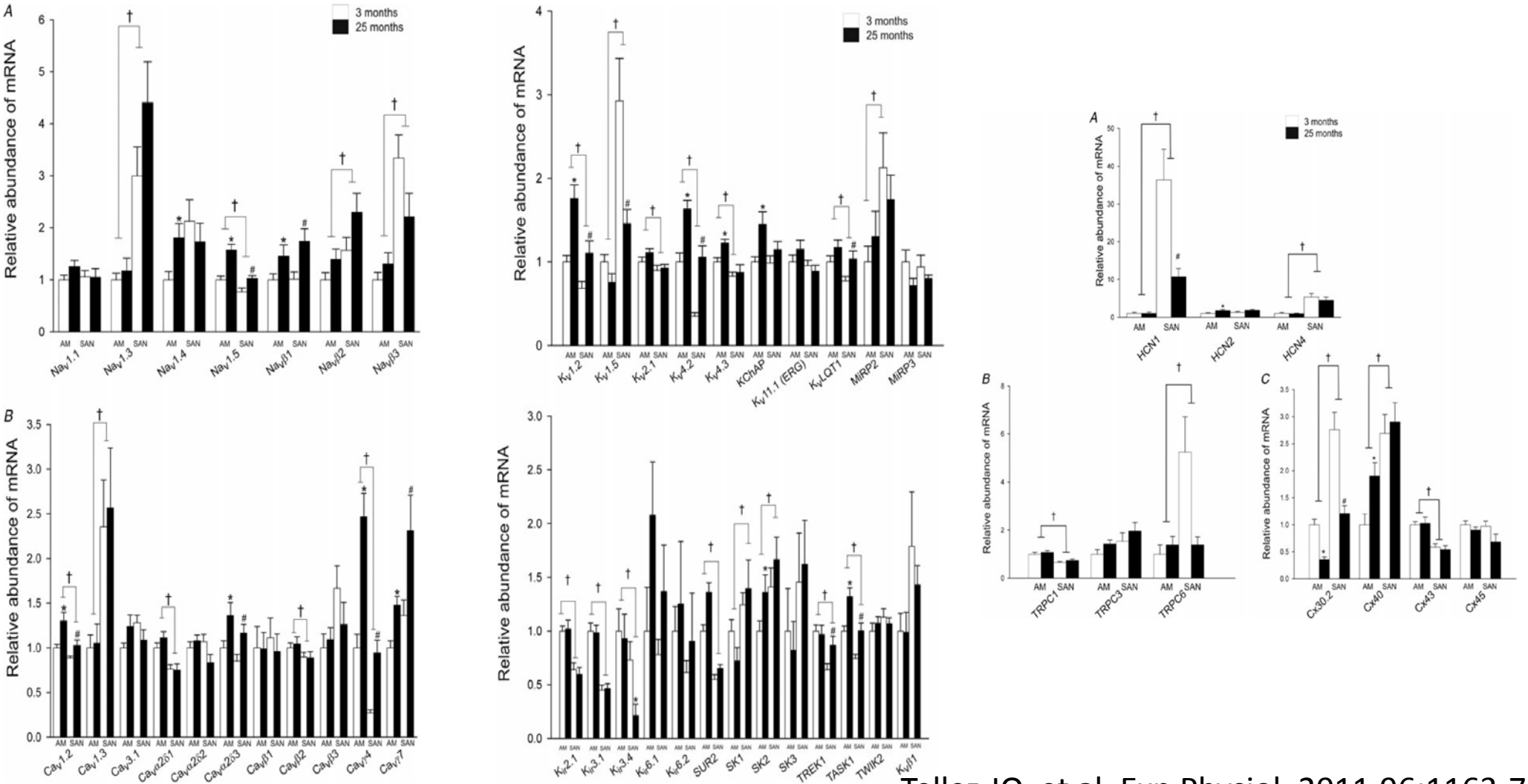
Ageing-dependent remodelling of ion channel and Ca2+ clock genes underlying sino-atrial node pacemaking





Tellez JO, et al. Exp Physiol. 2011;96:1163-78

Ageing-dependent remodelling of ion channel and Ca2+ clock genes underlying sino-atrial node pacemaking



Tellez JO, et al. Exp Physiol. 2011;96:1163-78

Ageing-dependent remodelling of ion channel and Ca2+ clock genes underlying sino-atrial node pacemaking

- This study has revealed that the expression profile of ion channel and Ca2+ clock genes in the SAN in the old animal differs greatly from that in the young.

- The changes in gene expression could be responsible for the decrease in the IHR (RYR2, HCN1 and TASK1), increase in SAN APD (Nav1.5, Navβ1, Cav1.2, Cavα2δ3 and Kv1.5), increase in SAN conduction time (Cx30.2) and decrease in parasympathetic regulation (Kir3.4) age.

Tellez JO, et al. Exp Physiol. 2011;96:1163-78

Ageing-dependent remodelling of ion channel and Ca2+ clock genes underlying sino-atrial node pacemaking

- These adaptations are on the background of significantly increased variability in the expression of most of the analysed transcripts in the old animals

- An understanding of the changes in gene expression underlying the decline in SAN pacemaker function with age could be important for the development of more effective treatments for pacemaker dysfunction.

Tellez JO, et al. Exp Physiol. 2011;96:1163-78

Sinus Node Dysfunction (SND) and Atrial Fibrillation (AF)

Two sides of the same coin

Sinus Node Dysfunction (SND) and Atrial Fibrillation (AF)

Reversibility should be considered more carefully

Electrophysiologic and Electroanatomic Changes in the Human Atrium Associated With Age (SVT)

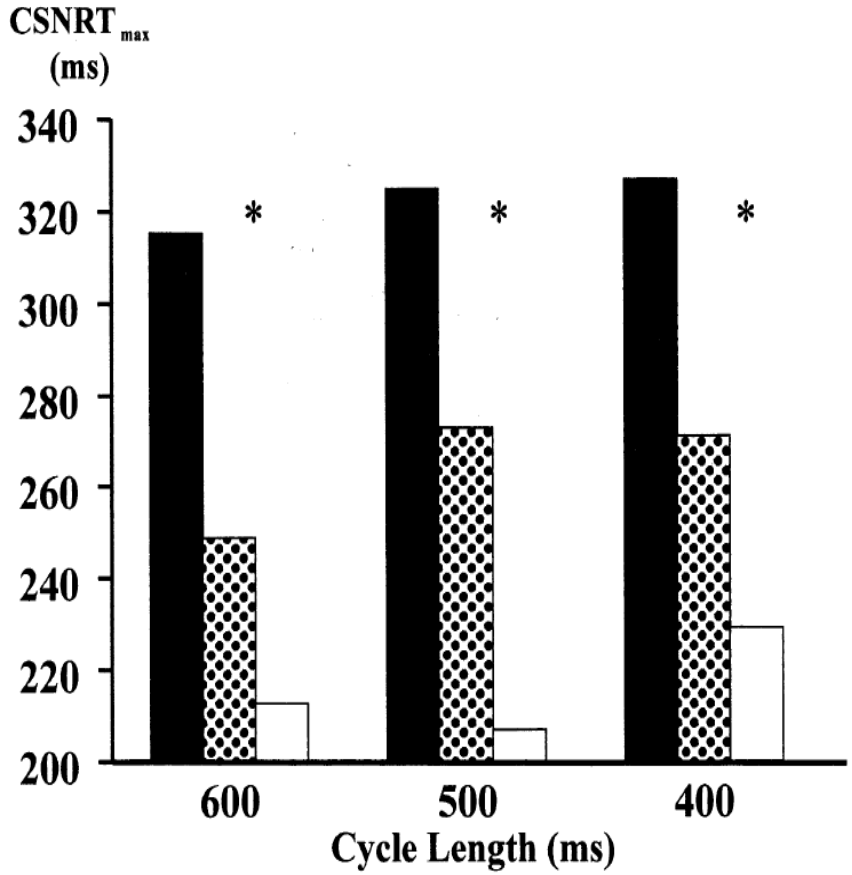
Table 1. Patient Characteristics

	Group A n = 13	Group B n = 13	Group C n = 15	p Value
Age (yrs)	66.4 ± 1.7	50 ± 2.1	24.7 ± 1.0	<0.0001
LA diameter (mm)	36 ± 0.9	35.3 ± 1.4	32 ± 1.7	NS
LVED diameter (mm)	46.9 ± 2.1	47.6 ± 1.5	50 ± 0.8	NS
LVES diameter (mm)	29.5 ± 2.4	29.9 ± 1.3	30.9 ± 1.0	NS
LV FS (%)	39 ± 3.5	37.6 ± 3	38.6 ± 1.7	NS

FS = fractional shortening; LA = left atrium; LV = left ventricular; LVED = left ventricular end-diastolic; LVES = left ventricular end-systolic.

Kistler PM, et al. J Am Coll Cardiol 2004;44:109-16

Electrophysiologic and Electroanatomic Changes in the Human Atrium Associated With Age



Coronary sinus node recovery times ($CSNRT_{max}$) were significantly longer in group A patients at all cycle lengths. Solid bars group A; spotted bars group B; open bars group C. *p 0.05 for groups A vs. C

Kistler PM, et al. J Am Coll Cardiol 2004;44:109-16

Electrophysiologic and Electroanatomic Changes in the Human Atrium Associated With Age

Table 2. Conduction

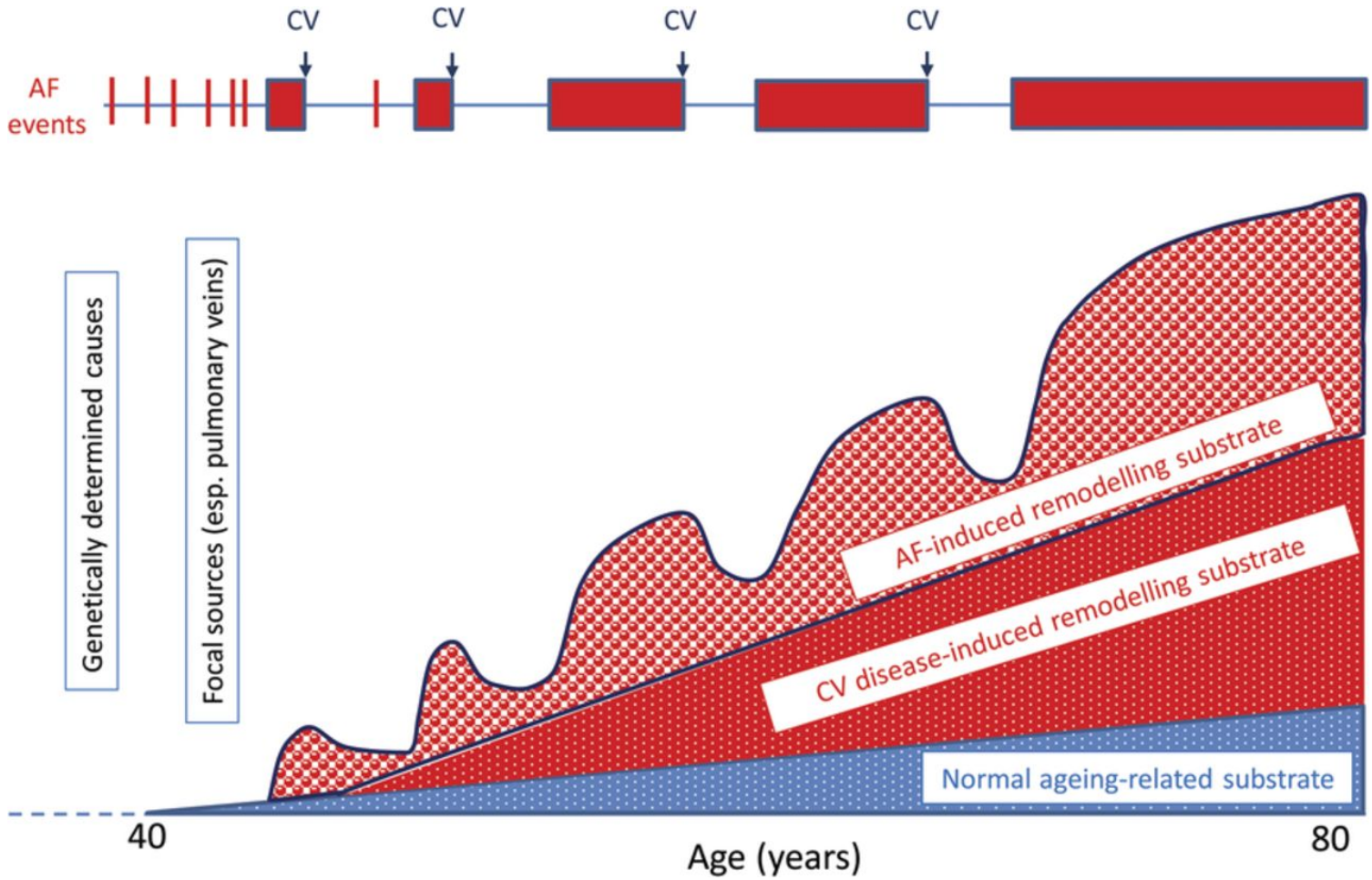
Conduction Times	Group A (ms)	Group B (ms)	Group C (ms)	p Value ANOVA
CS				
600	36.3 ± 1.5	33.7 ± 1.4	29.5 ± 1.3	< 0.01*
500	35.9 ± 1.6	33.2 ± 0.9	30.9 ± 1.7	< 0.01*
400	34.8 ± 1.7	33.4 ± 1.1	30.8 ± 1.3	< 0.05*
LRA				
600	41.3 ± 3.4	40.3 ± 1.5	35.7 ± 1.3	NS
500	37.7 ± 2.3	39.7 ± 1.0	35.8 ± 1.5	NS
400	40.4 ± 3.8	39.2 ± 1.1	33.6 ± 1.9	< 0.05*
Number of Bipoles With Double Potentials at CT				
HLRA				
S1 600	1.5 ± 0.9	0 ± 0	0 ± 0	< 0.05*†
S1 500	2 ± 1.2	0 ± 0	0 ± 0	< 0.01*†
S1 400	1.5 ± 0.9	0 ± 0	0 ± 0	< 0.05*†
S2 600	4.7 ± 1.0	1.3 ± 0.4	1 ± 0.4	< 0.01*†
S2 500	4.5 ± 0.5	1.4 ± 0.6	1.3 ± 0.4	< 0.01*†
S2 400	4.8 ± 0.8	0.7 ± 0.3	0.9 ± 0.1	< 0.01*†

*Group A vs. C; †group B vs. C.

ANOVA = analysis of variance; CS = coronary sinus; CT = crista terminalis; HLRA = high lateral right atrium; LRA = lateral right atrium.

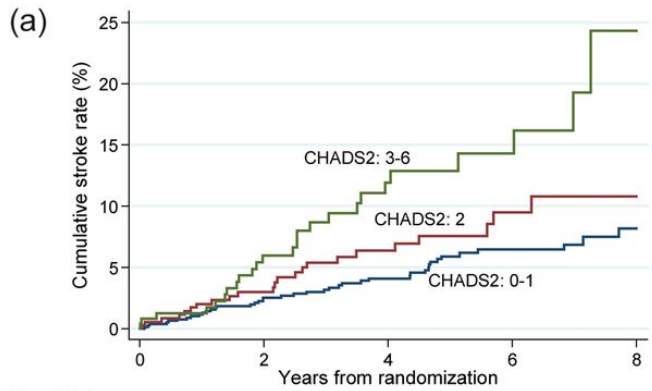
Kistler PM, et al. J Am Coll Cardiol 2004;44:109-16

A conceptual model of atrial fibrillation events in relationship to underlying substrate

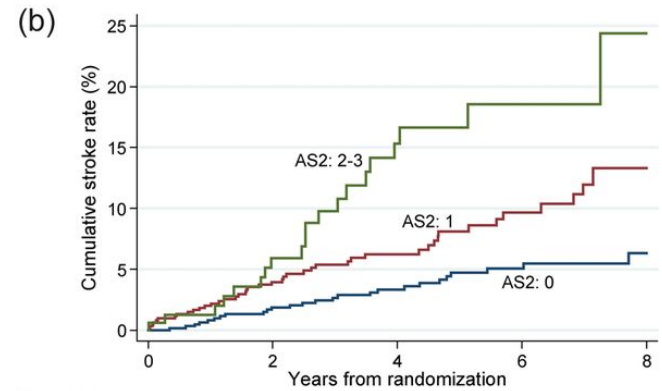


Stanley Nattel et al. Eur Heart J 2014;eurheartj.ehu028

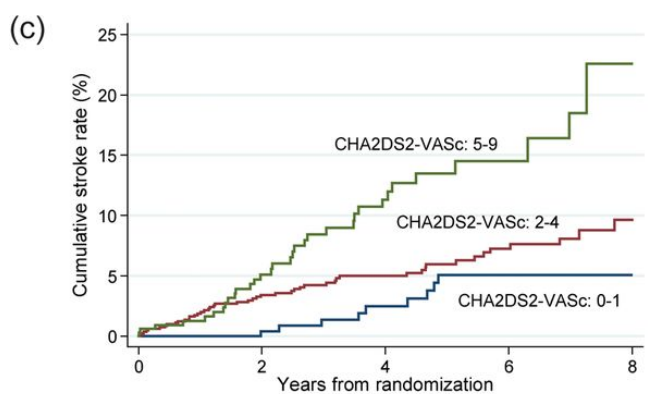
Cumulative stroke rate



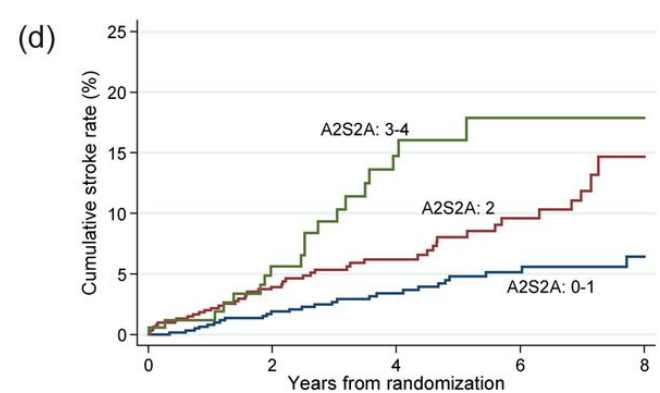
No. at Risk					
Score 0-1	802	679	490	305	103
Score 2	363	281	184	84	26
Score 3-6	250	161	100	51	12



No. at Risk					
Score 0	627	545	398	250	85
Score 1	625	464	307	153	45
Score 2-3	163	112	69	37	11



No. at Risk					
Score 0-1	256	232	170	103	35
Score 2-4	829	662	460	267	92
Score 5-9	330	227	144	70	14



No. at Risk					
Score 0-1	618	536	393	246	84
Score 2	625	465	310	156	46
Score 3-4	172	120	71	38	11

Jesper Hastrup Svendsen et al. Heart 2013;99:843-848

ORIGINAL ARTICLE

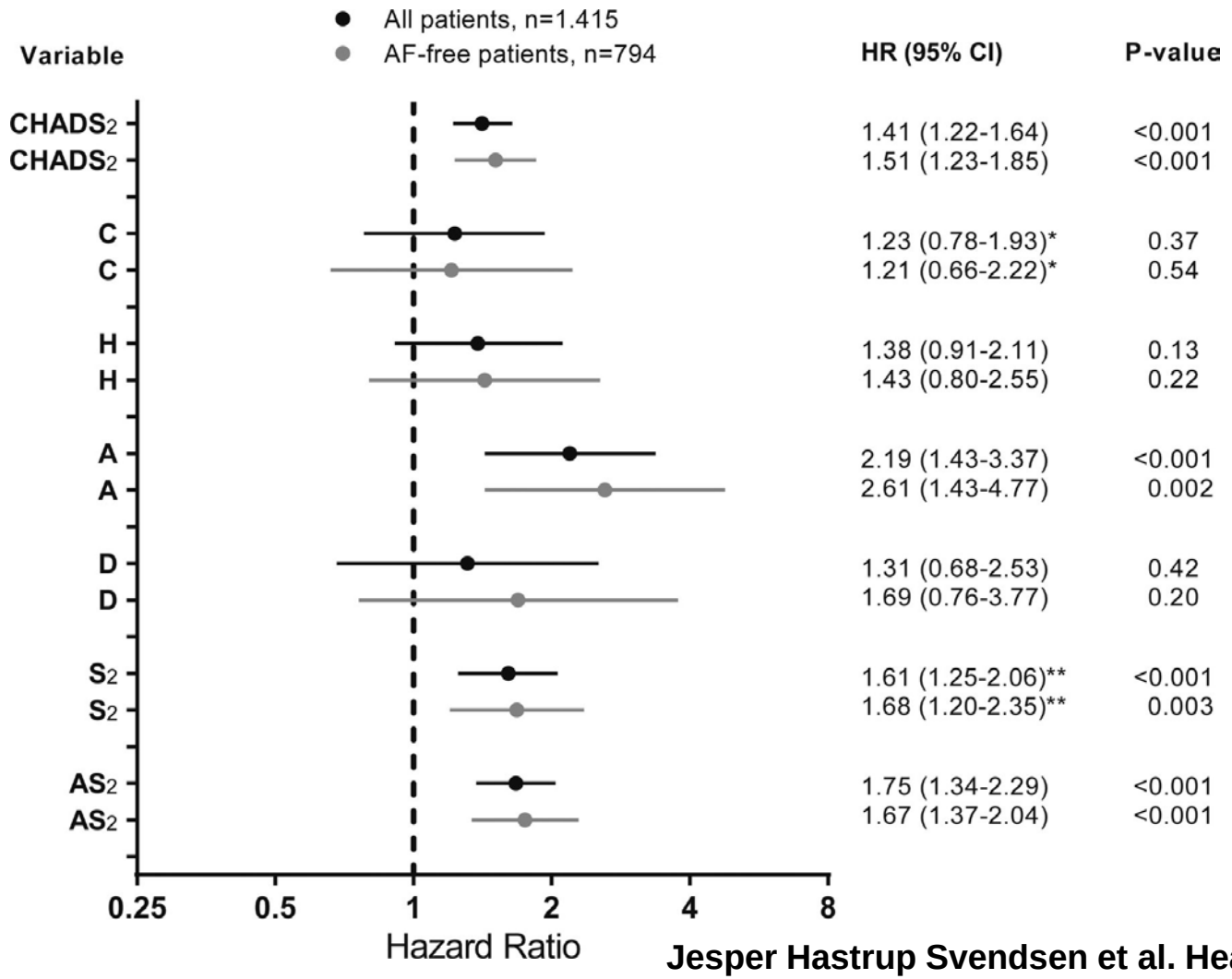
ORIGINAL ARTICLE

$CHADS_2$ and CHA_2DS_2-VASc score to assess risk of stroke and death in patients paced for sick sinus syndrome

Jesper Hastrup Svendsen,[1,2,3] Jens Cosedis Nielsen,[4] Stine Darkner,[1]
Gunnar Vagn Hagemann Jensen,[5] Leif Spange Mortensen,[6] Henning Rud Andersen,[4]
on behalf of the DANPACE Investigators

Jesper Hastrup Svendsen et al. Heart 2013;99:843-848

HRs for CHADS2 score and its association with stroke for all patients and patients without a history of atrial fibrillation (AF) at baseline (AF-free patients).



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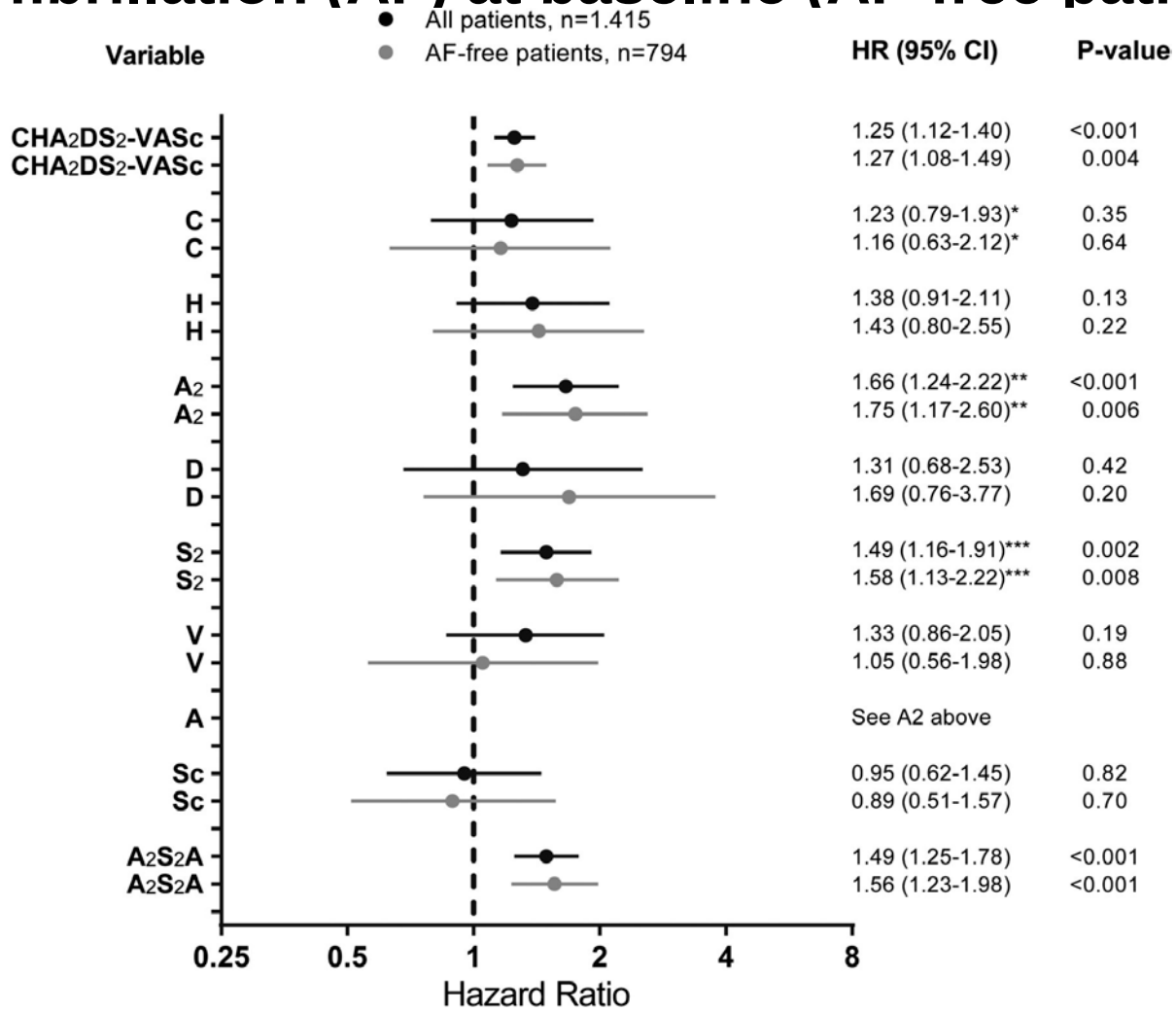

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Gunnar Vagn Hagemann Jensen,[5] Leif Spange Mortensen,[6] Henning Rud Andersen,[4]
on behalf of the DANPACE Investigators

Conclusions; CHADS2 and CHA2DS2-VASc score are associated with increased risk of stroke and death in patients paced for SSS irrespective of the presence of AF.

Jesper Hastrup Svendsen et al. Heart 2013;99:843-848

EDITORIAL

Should Catheter Ablation be the Preferred Approach for Treatment of Atrial Fibrillation Related Symptomatic Sinus Node Dysfunction?

Each patient needs to be examined on a case-by-case basis.

Clearly catheter ablation would not be the best option in a 93-year-old with tachybrady syndrome. And similarly it would be difficult too offer catheter ablation alone to a patient with atrial fibrillation-induced tachybrady syndrome who has experienced syncope with no warning, especially if it resulted in injury or occurred while driving. But for many patients with this syndrome, especially those who are less than 70 years of age and have less severe symptoms, catheter ablation of atrial fibrillation appears to be a far better treatment strategy.

HUGH CALKINS. PACE 2014; 37;401-402