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RATE VERSUS RHYTHM CONTROL OF ATRIAL FIBRILLATION: SPECIAL CONSIDERATION IN ELDERLY

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NO CONFLICT OF INTEREST TO DECLARE

Relationship Between Atrial Fibrillation and Age



Go AS, et al. JAMA. 2001; 285:2370-2375.

10 Most Common Comorbid Chronic Conditions Among Medicare Beneficiaries With AF

Beneficiaries ≥65 y of Age (N=2,426,865)			Beneficiaries <65 y of Age (N=105,878)		
(Mean Number of Conditions=5.8; Median=6)			(Mean Number of Conditions=5.8; Median=6)		
	N	%		N	%
Hypertension	2,015,235	83.0	Hypertension	85,908	81.1
Ischemic heart disease	1,549,125	63.8	Ischemic heart disease	68,289	64.5
Hyperlipidemia	1,507,395	62.1	Hyperlipidemia	64,153	60.6
HF	1,247,748	51.4	HF	62,764	59.3
Anemia	1,027,135	42.3	Diabetes mellitus	56,246	53.1
Arthritis	965,472	39.8	Anemia	48,252	45.6
Diabetes mellitus	885,443	36.5	СКD	42,637	40.3
СКD	784,631	32.3	Arthritis	34,949	33.0
COPD	561,826	23.2	Depression	34,900	33.0
Cataracts	546,421	22.5	COPD	33,218	31.4

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Management of AF

- Rhythm control
 - Antiarrhythmic drugs
 - Direct current cardioversion
 - PV isolation

- Rate control
 - Beta-blockers
 - Calcium antagonists
 - Digoxin
 - AVN ablation + PM



AV, atrioventricular: NYHA, New York heart association class: LVH, left ventricular hypertrophy

FIGURE 3: Decision tree for the therapy of AF in the elderly integrating pharmacological treatment and catheter ablation, modified from the galdelines for the management of AF proposed by the European Society of Candiology [63].

Physiological changes in the geriatric population

 The myocardium experiences electrical and structural changes, such as increased fibrosis resulting in decreased ventricular compliance, as a direct consequence of aging.

Pharmacokinetics, pharmacodynamics, and pharmacogenetics in the elderly

- Age-related changes in pharmacokinetics and pharmacodynamics make the elderly more prone to the development of adverse drug reactions, especially when incremental comorbidities are taken into account.
- Consequently, many elderly patients suffer from Polypharmacy, making drug interactions more likely.
- The altered pharmacokinetics of aging change the effects of absorption, bioavailability, distribution, and clearance of drugs.

ATHENA Trial: Study Design

4,628 patients \geq 75 years with atrial fibrillation or 70-75 years with atrial fibrillation and at least one additional cardiovascular risk factor prior to randomization. Double blind. Randomized. Placebo controlled. International multicenter. Mean follow-up 21 months.



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JCE 2008; 19.1/Heart Rhythm 2008

ATHENA Trial: Baseline Characteristics

Characteristic	Incidence/Mean Value
Patient age	
<65 years	19%
65-74 years	40%
≥75 years	42%
Female gender	47%
Hypertension	86%
Mean systolic blood pressure	134 mmHg
AF at baseline*	25%
History of cardioversion	34%
*AF at baseline: according to the stratification factor at randomiza	tion.

JCE 2008; 19.1 /Heart Rhythm 2008

ATHENA Trial: Primary Endpoint Results

Multaq[®] (dronedarone) decreased the risk of cardiovascular hospitalizations or death from any cause by 24% (p<0.001).

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	Placebo (n = 2875)	Dronedarone 400 mg twice daily (n = 3282)
Gastrointestinal		
Diarrhea	6%	9%
Nausea	3%	5%
Abdominal pain	3%	4%
Vomiting	1%	2%
Dyspeptic signs and symptoms	1%	2%
General		
Asthenic conditions	5%	7%
Cardiac		
Bradycardia	1%	3%
Skin and subcutaneous tissue		
Including rashes (generalized, macular, maculopapular,	3%	5%
erythematous), pruritus, eczema, dermatitis, dermatitis allergic		

Data from Touboul P, Brugada J, Capucci A, Crijns HJ, Edvardsson N, Hohnloser SH. Dronedarone for prevention of atrial fibrillation: a dose-ranging study. Eur Heart J. 2003;24(16):1481–1487.

ATHENA Trial: Adverse Events



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JCE 2008; 19.1/Heart Rhythm 2008

Elderly with AF: challenges to disease management

- Co-morbid illness: Hypertension, congestive heart failure, LVH
- Age-related degenerative changes in the cardiac conduction system: sick-sinus syndrome and tachycardia-bradycardia syndrome
- Age-related pharmacologic and pharmacodynamic changes in the antiarrhythmic drugs (AAD): increase the predilection for side effects and pro-arrhythmias.

Am J Geriatr Cardiol 2002;11:357–364 Br J Cardiol 2003;10:373–378. Am J Geriatr Cardiol 2002;11:370–375. Am J Med 2007;120:481–487 Fig 2 Cumulative incidence of atrial fibrillation in relation to thyroid dysfunction at baseline thyroid screening (age >65 years).



Rate versus rhythm control

FAVOURING RATE CONTROL	FAVOURING RHYTHM CONTROL
Persistent AF	Paroxysmal AF or newly detected AF
Less symptomatic	More symptomatic
Age ≥65 y	Age < 65 y
Hypertension	No hypertension
No history of HF	HF clearly exacerbated by AF
Previous failure of antiarrhythmic drug	No previous failure of antiarrhythmic drug
Patient preference	Patient preference

Can J Cardiol 2011;27(1):47-59.

Major studies on rhythm v/s rate control

These studies have shown that primary rate control is not inferior to rhythm control. Therefore, first-line therapy in the elderly patient population with symptomatic AF is usually a primary rate control approach

True	7941		Prenary End Point	HR (Rute ve Rhythen Caribati	
PWP ¹	2900	292	improvement AF symptome	1.10	1.11
AFTEM".	2002	4000	Overall murtality	0.67	1.08
RACE ¹	2002	522	Composite	0.73	8.11
STAFE	2900	700	Composite	1.00	0.99
HOT OWN	2004	205	Composite	1.98	>471
M-OF	2908	1376	Cardiovascular mortality	0.84	0.59
Pable-Orf"	2008	*	Composite	Wullgie (nee better)	<3.001

New England Journal of Medicine, vol. 347, no. 23, pp. 1834–1840, 2002. Journal of the American College of Cardiology, vol. 41, no. 10, pp. 1690–1696, 2003 Chest, vol. 126, no. 2, pp. 476–486, 2004. Circulation, vol. 109, no. 12, pp. 1509–1513,2004.

AFFIRM



Source: Am J Geriatr Cardiol © 2005 Le Jacq Communications, Inc.

AFFIRM

 A post hoc analysis of the AFFIRM data revealed that although maintenance of sinus rhythm was associated with better survival, this benefit was neutralized by increased mortality resulting from antiarrhythmic drug use.

Circulation. 2004;109:1509-1513.



European Heart Journal (2010) 31, 2369-2429 doi:10.1093/eurheartj/ehq278



Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

Recommendations	Class ^a	Level®	Ref. ^c
late control should be the initial pproach in elderly patients with VF and minor symptoms (EHRA core 1).	1	A	86–87, 90



2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

Elderly

Because AF is often associated with minimal or no symptoms in this population and the clearance of antiamhythmic medications is diminished, sensitivity to proarrhythmic effects, including bradyarrhythmias, is often increased. Therefore, a rate-control strategy is often preferred (30), and direct-current cardioversion is less often warranted (456). Typically, rate control can be achieved with beta blockers or nondihydropyridine calcium channel antagonists. Care must be taken in these patients because they are often more susceptible to orthostatic hypotension or bradyarrhythmias and when AF is paroxysmal and sinus node dysfunction is more common. Comorbidities should also be considered. Digoxin can be useful for rate control in the relatively sedentary individual, but there are concerns about its risks (Section 5.1.3).



Rate control is typically a simpler strategy than rhythm control

- The use of generally less toxic medications
 - Beta-blockers
 - Digoxin
 - Calcium-channel blockers
- Fewer medical procedures
- Rate control strategies can result in adverse drug side effects and toxicities and, in some cases, may require interventions such as pacemaker implantation and atrioventricular (AV) nodal ablation

Tachy-Brady syndrome



ADVANTAGES OF AV NODAL ABLATION IN ELDERLY PATIENTS

- Avoidance of polypharmacy in a population with several comorbidities and medications
- Decreasing risk of drug-drug interactions
- Greater incidence of hepatic and renal insufficiency increases risk for drug toxicity
- Side effects of antiarrhythmics such as bradycardia, orthostatic hypotension, urinary retention and falls is greater
- Permanent safe solution for controlling rate in AF. Low incidence of repeat procedures compared to PVI procedures
- Elderly patients commonly have long standing AF with atrial dilatation, hence they are poor candidates for PVI procedures
- Possibility of improvement in cognitive symptoms

Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure (PABA-CHF)

Characteristic	Pulmonary-Vein Isolation (N=41)	AV-Node Ablation with Biventricular Pacing (N=40)
Age (yr)	60±8	61±8
Male sex (%)	95	88
Coronary artery disease (%)	73	68
Type of atrial fibrillation (%)		
Paroxysmal	49	54
Persistent or long-standing persistent	51	46
Duration of atrial fibrillation (yr)	4.0±2.4	3.9±2.8
Ejection fraction (%)	27±8	29±7
Left atrial internal diameter (cm)	4.9±0.5	4.7±0.6
Heart rate (beats/min)	80±12	82±11
Duration of QRS interval (msec)	92±9	90±10
Distance on 6-minute walk test (m)	269±54	281±44
MLWHF score†	89±12	89±11

N Engl J Med 2008;359:1778-85.

Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure

Journal of Cardiovascular Electrophysiology May 2005

Pulmonary-vein isolation was superior to atrioventricular-node ablation with biventricular pacing in patients with heart failure who had drug-refractory atrial fibrillation

100-



Figure 2. Freedom from Atrial Fibrillation in Patients Undergoing Pulmonary-Vein Isolation with or without Antiarrhythmic Drugs (AAD).

Catheter Ablation of Atrial Fibrillation Versus Atrioventricular Junction Ablation Plus Pacing Therapy for Elderly Patients with Medically Refractory Paroxysmal Atrial Fibrillation

- 71 elderly patients with medically refractory paroxysmal AF were included; group 1 included 32 patients with successful AV junction ablation plus pacing therapy and group 2, 37 patients with successful catheter ablation of AF.
- *Results:* After a mean follow-up of more than 52 months, the AF was better controlled in the group 1 patients than group 2 (100% vs 81%, P = 0.013), however, they had a significantly higher incidence of persistent AF (69% vs 8%, P < 0.001) and heart failure (53% vs 24%, P = 0.001). Furthermore, the incidence of ischemic stroke and cardiac death was similar between the 2 groups. Compared with the preablation values, a significant increase in the NYHA functional class ($1.7 \pm 0.9 \text{ vs } 1.4 \pm 0.7$, P = 0.01) and significant decrease in the left ventricular ejection fraction ($44 \pm 8\% \text{ vs } 51 \pm 10\%$, P = 0.01) were noted in the group 1 patients, but not in the group 2 patients.
- Conclusions: Although AV junction ablation plus pacing therapy better controlled the AF in elderly patients with medically refractory paroxysmal AF, that method was associated with a higher incidence of persistent AF and heart failure than catheter ablation of AF in the very long-term followup.

Journal of Cardiovascular Electrophysiology , May 2005

Conclusion

- The incidence and prevalence of AF increase with age
- Rate control strategy was recommended in most guidelines
- AVN ablation plus pacemaker could be a solution for rate control complication
- Whether AVN ablation is better than PV isolation in elderly patients needs to be evaluated in more randomized clinical trials

Conclusion I

If you can't be good . . .

Conclusion II

... be careful!

 "Say not I have found the truth, but rather I have found a truth"

Khalil Gebran – Lebanese poet