Journal Club - 4 marzo 2005

Fibrillazione atriale

Tony Sabatini

SOMMARIO

- Introduzione ed Epidemiologia
- Classificazione
- Eziologia
- Diagnosi
- Sintomi e conseguenze emodinamiche
- Strategie ed evidenze
- Il problema tromboembolico
- Trattamento della fibrillazione atriale

> controllo della frequenza o

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- Linee Guida
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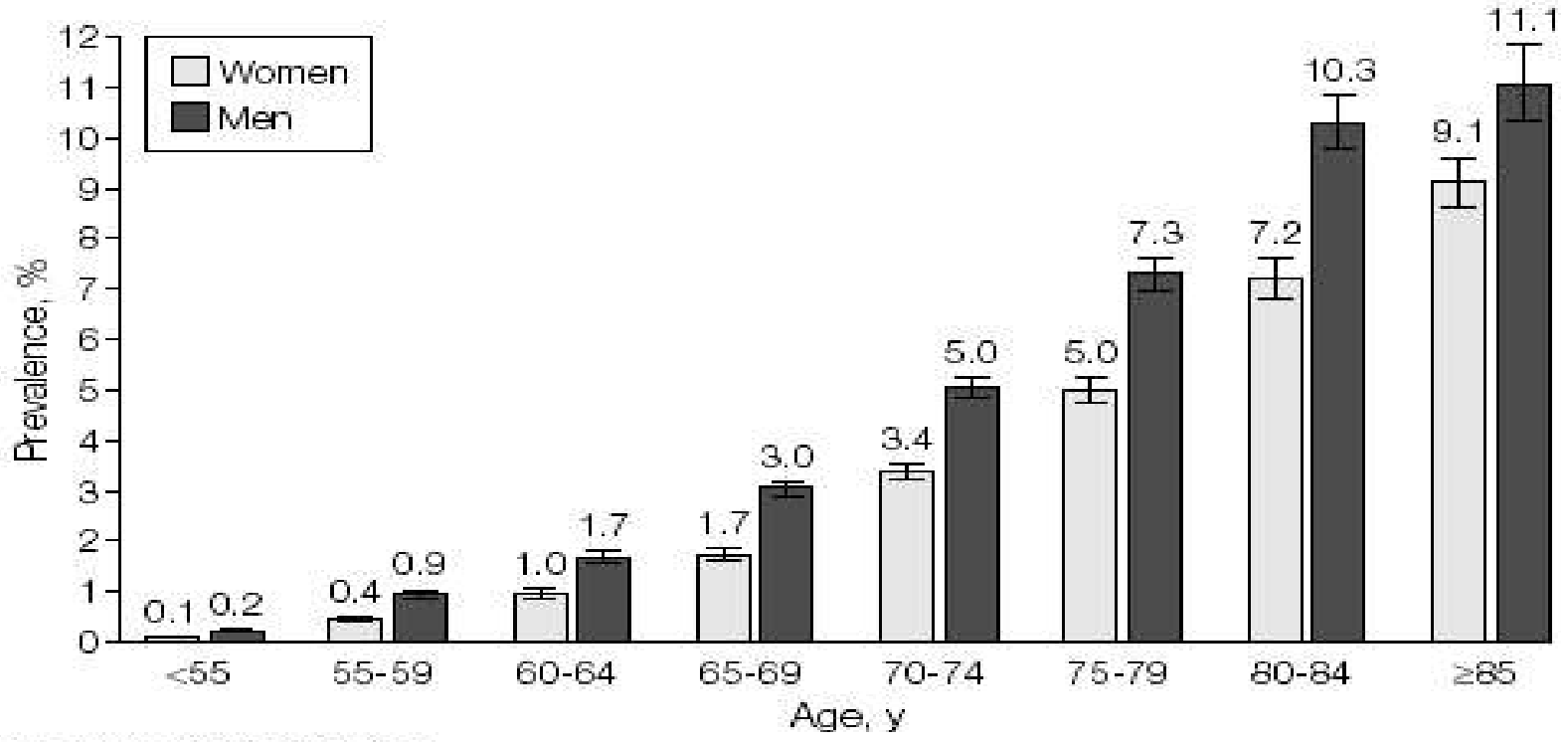
- Conclusioni

Introduzione & Epidemiologia

- La fibrillazione atriale è l'aritmia più frequente nell'anziano (9% in ultraottantenni)
- E' un'aritmia in aumento nel mondo occidentale, per l'aumento del numero di anziani

Prevalence of Atrial Fibrillation by Age and Sex



No. With Atrial Fibrillation								
Women	530	310	566	896	1498	1572	1291	1132
Men	1259	634	934	1426	1907	1886	1374	759

Data describe the community-based Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study cohort.[3] Error bars represent 95% confidence intervals. Numbers represent the number of men and women with atrial fibrillation in each age category.

Daniel E. Singer. *JAMA* October 2003

Projected age and sex distribution of adults with Atrial Fibrillation in the United States between 2000 and 2050

	Year		
	2000	2025	2050
Women	48.6	46.3	47.4
Age group, y			
<65	18.0	15.5	11.5
65-79	45.3	48.7	35.9
≥80	36.7	35.8	52.6

*Data are presented as percentage.

Alan S Go et al. JAMA 2001

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Classificazione

- **Paroxysmal** (terminates spontaneously)
- **Persistent** (needs electrical cardioversion and/or antiarrhythmic drugs to terminate)
- **Permanent** (resistant to electrical or pharmacologic conversion or accepted by the physician)

ACC/AHA/ESC Executive Summary. *JACC.* 2001

•Circa ¼ di casi diagnosticati di FA sono di tipo parossistico.

• Il 12% di pazienti con fibrillazione atriale parossistica (PAF) hanno più di un episodio al giorno, mentre un altro altro 25% riporta solo un episodio ogni 6 mesi.

•I pazienti con PAF sono in genere più giovani e con minore comorbilità rispetto a quelli con FA persistente/permanente.

•I pazienti con PAF hanno gli stessi rischi di stroke rispetto a quelli con FA persistente.

•Circa il 20% di PAF progrediscono verso una FA persistente o permanente dopo un periodo di 4 anni.

Daniel E. Singer. *JAMA*. October 2003

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Factors predisposing to atrial fibrillation

- Age
- Alcohol
- Aortic regurgitation and stenosis
- Atrial myxoma
- Atrial septal defect
- Autonomic dysfunction
- Cardiac or thoracic surgery
- Cardiomyopathies
- Chronic lung disease
- Cocaine
- Congenital heart disease
- Coronary heart disease
- Diabets mellitus
- Drugs
- Emotional stress
- Excess coffee
- Heart failure
- Hypertension
- Hyperthyroidism
- Hypoglycemia
- Hypokaliemia
- Hypovolemia
- Hypoxia
- Left atrial enlargement
- Left ventricular dysfunction
- Left ventricular hypertrophy
- Male gender
- Mitral annular calcification
- Mitral regurgitation and stenosis
- Myocardial infarction
- Myocarditis
- Neoplastic disease
- Pericarditis
- Pneumonia
- Pulmonary embolism
- Rheumatic heart disease
- Sick sinus syndrome
- Smoking
- Systemic infection
- Wolff-Parkinson-White syndrome

Aronow. Journal of Gerontology. 2002

Eziologia

Fattori associati alla comparsa della AF	
Cardiaci	Non cardiaci
Ipertensione	Età
Cardiopatia ischemica	Abuso alcool
Valvulopatia mitralica	BPCO/pneumopatie
Scompenso cardiaco	Ipertiroidismo
Cardiomiopatia	

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Diagnosi

The patient's history and the physical examination should focus on these potential causes of atrial fibrillation.

The **"minimum evaluation"** recommended at diagnosis should include 12-lead electrocardiography, chest radiography, transthoracic echocardiography, and serologic tests of thyroid function. Echocardiographic testing is used to assess valve function, chamber size, and the peak right ventricular pressure and to detect hypertrophy and pericardial disease.

Additional tests may be warranted, including exercise testing to determine whether the patient has symptoms and to assess the heart rate with exercise, 24-hour ambulatory monitoring to evaluate heart-rate control, transesophageal echocardiography to screen for a left atrial thrombus and to guide cardioversion, and, rarely, an electrophysiological study to detect predisposing arrhythmias.

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Sintomi e conseguenze emodinamiche

La fibrillazione atriale è associata ad un aumentato rischio di morte (da 1,3 a circa 2 volte), indipendentemente da altri fattori di rischio

Benjamin EJ et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 1998;98:946-952

Sintomi e conseguenze emodinamiche

Cardiaci	Non-cardiaci
Intolleranza all'esercizio	Eventi tromboembolici
Scompenso cardiaco	Ridotta qualità di vita

Sintomi e conseguenze emodinamiche: fibrillazione atriale asintomatica

- Asymptomatic, or "silent," atrial fibrillation occurs frequently. Among patients in the Canadian Registry of Atrial Fibrillation, 21 percent in whom the condition was newly diagnosed were asymptomatic.
- The first presentation of asymptomatic atrial fibrillation may be catastrophic; in the Framingham Study, among patients with stroke that was associated with atrial fibrillation, the arrhythmia was newly diagnosed in 24 percent.
- Even among patients with documented symptomatic atrial fibrillation, asymptomatic recurrences are common. In one study of patients with symptomatic paroxysmal atrial fibrillation, asymptomatic episodes were 12 times more common than symptomatic episodes

Sintomi e conseguenze emodinamiche:

fibrillazione atriale asintomatica

- In a recent trial, among untreated patients, 17 percent had asymptomatic episodes before they noted symptoms, and the percentage was probably an underestimation, because the monitoring of these patients was intermittent.
- Some antiarrhythmic agents, by reducing conduction in the atrioventricular node, may increase the likelihood of the occurrence of asymptomatic atrial fibrillation. Both propafenone and propranolol have been associated with frequent asymptomatic atrial fibrillation, and the risk may be similar with other agents that block atrioventricular nodal conduction.
- Among patients with a pacemaker and a history of atrial fibrillation, one in six had silent recurrences lasting 48 hours or longer

Page RL, Tilsh TW, Connolly SJ, et al. Asymptomatic or "silent" atrial fibrillation: frequency in untreated patients and patients receiving azimilide. Circulation 2003;107:1141-1145

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Strategie and Evidenze

1. Il problema tromboembolico
2. Il problema aritmico

   A) Controllo della frequenza cardiaca (rate control)
   B) Controllo del ritmo (rhythm control)

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Il problema tromboembolico: Atrial Fibrillation and Stroke

- One of 6 strokes occurs in patients with AF.
- The rate of ischemic stroke among patients with nonrheumatic AF averages 5% per year, which is 2 to 7 times the rate for people without AF.
- Including transient ischemic attacs and clinically silent strokes detected radiographically, the rate of brain ischemia accompayining nonvalvular AF ecceds 7% per years.

Il problema tromboembolico: Atrial Fibrillation and Stroke

- Patients with **rheumatic heart disease and AF** have a 17-fold increased risk of **stroke** compared with age-matched controls, and the attributable risk is 5 times greater than in those with **nonrheumatic AF** (Framingham Study)

- The annual risk of **stroke** attributable to AF increases from 1.5% for those aged 50 to 59 years to 23.5% for those aged 80 to 89 years (Framingham Study).

JACC Vol. 43, No. 6, 2004
March 17, 2004:929–35

Table 1. Annual Event Rates From the Atrial Fibrillation Investigators

Age Category	Risk Category	Event Rate, % (95% CI)	
		Placebo	Warfarin
<65 yrs	No RFs	1.0 (0.3–3.1)	1.0 (0.3–3.0)
	1 or more RFs	4.9 (3.0–8.1)	1.7 (0.8–3.9)
65–75 yrs	No RFs	4.3 (2.7–7.1)	1.1 (0.4–2.8)
	1 or more RFs	5.7 (3.9–8.3)	1.7 (0.9–3.4)
>75 yrs	No RFs	3.5 (1.6–7.7)	1.7 (0.5–5.2)
	1 or more RFs	8.1 (4.7–13.9)	1.2 (0.3–5.0)

Adapted with permission (3).

CI = confidence interval; RF = risk factor, defined as history of hypertension, history of diabetes, history of prior stroke, or transient ischemic attack.

Il problema tromboembolico: Terapia anticoagulante

- The need for anticoagulation to reduce the risk of stroke among patients with atrial fibrillation due to mitral stenosis is well recognized.

- Several randomized, prospective trials involving patients with nonvalvular atrial fibrillation have confirmed a significant reduction in the risk of stroke with warfarin.

- These studies defined the patients at greatest risk as the elderly, variably defined as those older than 60, 65, and 75 years of age, and those with a history of thromboembolism, diabetes mellitus, coronary artery disease, hypertension, heart failure, and thyrotoxicosis.

Table 3. $CHADS_2$ Risk Stratification Scheme (14)

Risk Factors	Score
C Recent congestive heart failure	1
H Hypertension	1
A Age ≥75 yrs	1
D Diabetes mellitus	1
S_2 History of stroke or transient ischemic attack	2

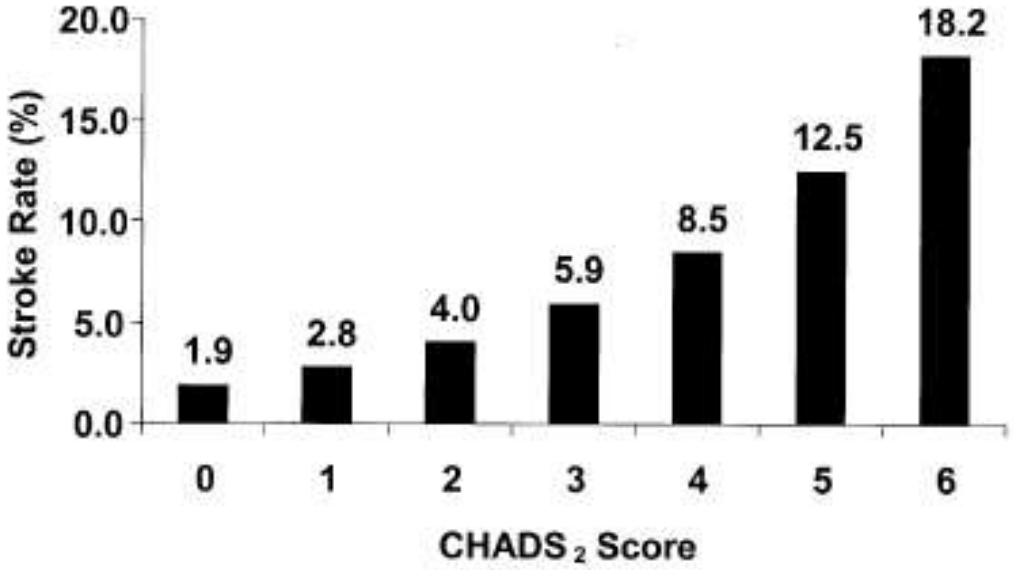

Figure 2. Relationship between the $CHADS_2$ score and the risk of stroke (14).

$CHAD_2$ SCORE

- A score of 0 to 1: low risk (ASA)
- A score of 2 to 3: moderate risk (warfarin)
- A score of 4 to 6: high risk (warfarin)

Different trials have provided a basis for two important guidelines for the use of warfarin in such patients (Table 1).

Table 1. Guidelines for Antithrombotic Therapy in Atrial Fibrillation.

Characteristic	Therapy Recommended by the ACC–AHA and ESC	Differences in ACCP Guidelines
Age		
<60 yr, no heart disease	Aspirin at a dose of 325 mg per day, or no therapy	Aspirin at a dose of 325 mg for patients <65 yr of age with no risk factor†
<60 yr, with heart disease but no risk factors*	Aspirin at a dose of 325 mg per day	No divergence
≥60–75 yr, no risk factors*	Aspirin at a dose of 325 mg per day	Option of aspirin at a dose of 325 mg per day or warfarin (INR, 2.0–3.0) for patients 65–75 yr of age
≥60 yr, with diabetes mellitus or coronary artery disease	Warfarin (INR, 2.0–3.0), aspirin optional in addition (at a dose of 81–162 mg per day)	Option of aspirin at a dose of 325 mg per day or warfarin (INR, 2.0–3.0) for patients with diabetes alone or coronary artery disease alone who are <65 yr of age
>75 yr, especially among women	Warfarin (INR, approximately 2.0; target INR, 1.6–2.5)	Warfarin (INR, 2.0–3.0), but no recommendation for INR value <2.0
Heart failure, left ventricular ejection fraction ≤0.35, thyrotoxicosis, and hypertension	Warfarin (INR, 2.0–3.0)	No divergence
Rheumatic heart disease (mitral stenosis)	Warfarin (INR, 2.5–3.5 or higher) may be appropriate	Other than for patients with mechanical valves, no INR recommended above target, 2.5 (range, 2.0–3.0)
Previous thromboembolism	Warfarin (INR, 2.5–3.5 or higher) may be appropriate	Other than for patients with mechanical valves, no INR recommended above target, 2.5 (range, 2.0–3.0)
Persistent atrial thrombus on transesophageal echocardiography	Warfarin (INR, 2.5–3.5 or higher) may be appropriate	Other than for patients with mechanical valves, no INR recommended above target, 2.5 (range, 2.0–3.0)
Prosthetic heart valves	Warfarin (INR, 2.5–3.5 or higher) may be appropriate	Depending on the type of prosthetic valve, warfarin (INR, 2.5 [range, 2.0–3.0] or INR, 3.0 [range, 2.5 to 3.5]) with or without additional aspirin, at a dose of 80 to 100 mg[34]
Warfarin recommended but contraindicated or refused	Aspirin at a dose of 325 mg per day	No divergence

* According to the guidelines of the American College of Cardiology and American Heart Association (ACC–AHA) Task Force on Practice and the European Society of Cardiology (ESC) Committee for Practice, the risk factors for thromboembolism include heart failure, a left ventricular ejection fraction of less than 35 percent, and a history of hypertension.[11] INR denotes international normalized ratio.

† According to the American College of Chest Physicians (ACCP), moderate risk factors include an age of 65 to 75 years, diabetes mellitus, and coronary artery disease with preserved left ventricular function; high risk factors include previous stroke, transient ischemic attack, or systemic embolus; a history of hypertension; poor left ventricular systolic function; an age of 75 years or older; rheumatic mitral-valve disease; and the presence of a prosthetic heart valve.[33]

Il problema tromboembolico: Terapia anticoagulante

- An international normalized ratio (INR) value in the range of 2.0 to 3.0 is recommended. The risk of stroke doubles when the INR falls to 1.7, although values up to 3.5 do not convey an increased risk of bleeding complications.
- INR values of 2.0 or greater are associated with a reduced severity of stroke and, if stroke occurs, a lower likelihood that it will result in death (§).
- Certain patients are at relatively low risk for a thromboembolic event and do not require intensive anticoagulant therapy. Aspirin is often recommended for these patients, although their risk is so low that even aspirin may not be necessary. Alternative antiplatelet agents, such as clopidogrel, have not been tested adequately in this clinical situation.

§ Hylek EM, Go AS, Chang Y, et al. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. N Engl J Med 2003;349:1019-1026

Risk Factors for Bleeding Complications with Oral Anticoagulation

Risk factor	Potential clinical characteristic
History of bleeding	Gastrointestinal blood loss, epistaxis, haematuria
Drugs which cause bleeding	Non-steroidal anti-inflammatory drug therapy
Drugs which potentiate warfarin effect	Erythromycin, amiodarone
Co-morbid health problems	Heart failure, liver disease
Poor compliance	Cognitive impairment, lack of carer support
Psycho-social problems	Excess alcohol
Trauma	Recurrent falls

The specificity of prescription patterns in stroke prevention

Giuseppe Bellelli and Marco Trabucchi. JNNP, February 2004

In elderly patients, a geriatric assessment including a evaluation of the psychosocial conditions may guide physicians in the selection of the correct treatment, thus avoiding the risks related to anticoagulants in subjects at high risk of falls or with presumed inability to comply with repeated blood monitorings

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Trattamento della fibrillazione atriale

- **Rate control** (ensure that the ventricular rate is controlled)

- **Rhythm control** (to restore and maintain sinus rhythm)

Rate Control

•Current guidelines recommend a ventricular rate during atrial fibrillation of 60 to 80 beats per minute at rest and 90 to 115 beats per minute during exercise.

•A number of pharmacologic agents are available to control the heart rate and rhythm . Digoxin has been replaced as first-line therapy for rate control by beta-adrenergic blockers and calcium-channel blockers, largely owing to improved rate control during exertion with the use of these alternative agents.

•In one study, during peak exercise, the mean heart rate was 175 beats per minute in patients receiving digoxin, as compared with 130 in those receiving a beta-adrenergic blocker and 151 in those receiving a calcium-channel blocker.

Rate Control

- Digoxin is useful in combination with other agents or when beta-adrenergic-blocking agents and calcium-channel blockers are not tolerated.
- In some patients, particularly the elderly, the ventricular rate during atrial fibrillation may be intrinsically controlled, so that no atrioventricular nodal–blocking agent is required.
- Among patients with a pause that causes symptoms after the spontaneous conversion of atrial fibrillation, or those whose symptoms are due to low heart rates in spite of their having high heart rates at other times, a pacemaker may be necessary to permit therapy with atrioventricular nodal–blocking agents (as in the "tachy-brady" or the sick sinus syndrome).

Rhythm Control

1. **Cardioversion** (electrical or pharmacologic)

5. **Maintenance of Sinus Rhythm**

1. Cardioversion

- The risk for thromboembolic events does not seem to differ between electrical and pharmacologic conversion
- In trials comparing the conventional approach of 3 weeks of anticoagulation before cardioversion followed by 4 weeks of anticoagulation after cardioversion and transesophageal echocardiography-guided early cardioversion with up to 3 weeks of anticoagulation after cardioversion, **no differences in the end point of stroke, transient ischemic attack, or peripheral embolism have been seen.**
- The absence of detectable thrombus not preclude thromboembolism after cardioversion if patients do not receive anticoagulation therapy
- Long-term warfarin therapy should be offered for patients who undergo rhythm control if they have associated risk factors for stroke.

Amar M Salam et al. JAGS. December 2003

Management of Atrial Fibrillation. Robert L McNamara et al. Annals of Internal Medicine. December 2003

2. Maintenance of Sinus Rhythm

- A number of agents may maintain sinus rhythm . The use of beta-adrenergic agents may be effective in paroxysmal atrial fibrillation (although the effects may be related to the conversion of symptomatic atrial fibrillation into asymptomatic atrial fibrillation).

- With the exception of the beta-adrenergic–blocking agents, **most antiarrhythmic drugs carry a risk of serious adverse effects**. Antiarrhythmic therapy should be chosen on the basis of the patient's underlying cardiac condition. Antiarrhythmic agents classified according to the Vaughn Williams system as class IC are reserved to treat patients without a structural cardiac abnormality,

- Agents in classes IA and III should be avoided by patients with prolongation of the QT interval or left ventricular hypertrophy because of the potential for torsades de pointes. On the one hand, amiodarone, which has a low risk of proarrhythmia (less than 1 percent per year), causes substantial noncardiac toxic effects and is therefore generally reserved for second-line therapy except in the treatment of patients with severe cardiomyopathy. On the other hand, it is the most effective antifibrillatory agent; in one trial, 65 percent of patients treated with amiodarone were free from recurrence after 16 months of therapy (as compared with 37 percent of those who were treated with propafenone

Selection of Antiarrhythmic Agents in Patients With Certain Cardiac Diseases

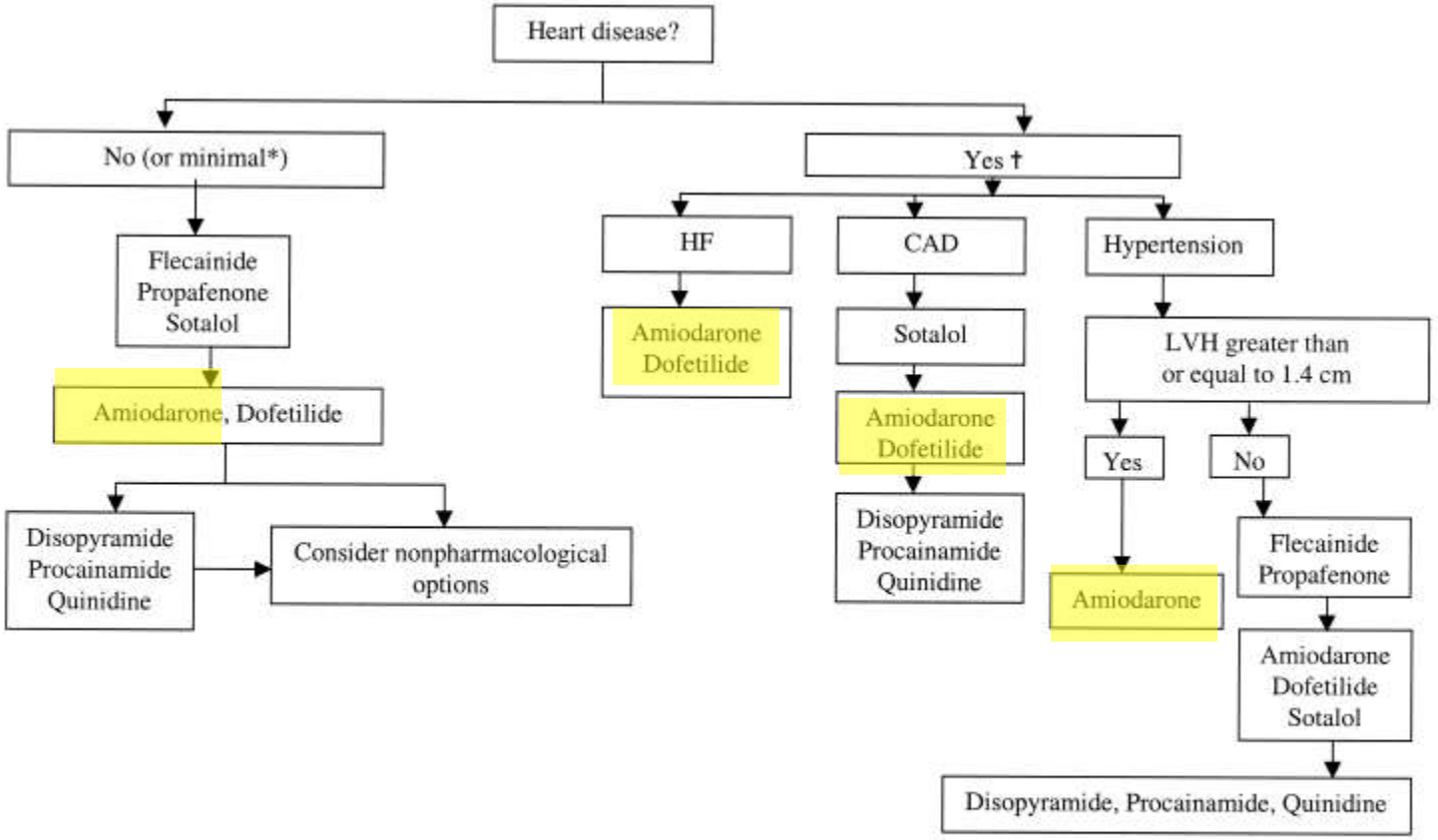

Figure 11. Antiarrhythmic drug therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation. Drugs are listed alphabetically and not in order of suggested use. *For adrenergic atrial fibrillation, beta-blockers or sotalol are the initial drugs of choice. †Consider nonpharmacological options to maintain sinus rhythm if drug failure occurs. HF indicates heart failure; CAD, coronary artery disease; and LVH, left ventricular hypertrophy.

ACC/AHA/ESC Executive Summery. Fuster and Rydèn, et al. *JAAC.* 2001

REVIEW ARTICLE

Rate vs Rhythm Control in Patients With Atrial Fibrillation

A Meta-analysis

Simon de Denus, MSc; Cynthia A. Sanoski, PharmD; Jörg Carlsson, MD; Grzegorz Opolski, MD; Sarah A. Spinler, PharmD

Conclusions: In patients with persistent AF or with AF that is likely to be recurrent, a strategy of ventricular rate control, in combination with anticoagulation in appropriate patients, appears to be at least equivalent to a strategy of maintaining sinus rhythm by using currently available antiarrhythmic drugs in preventing clinical outcomes.

Arch Intern Med. 2005;165:258-262

Managing Atrial Fibrillation in Older People: Comparison of Two Treatment Strategies

Because the two approaches seem equivalent in the long term, physicians must modify the management of AF for the individual patient.

For patients presenting with minimal or no symptoms, rate control should now be considered first-line strategy, but patients who have disabling palpitations during episodes of paroxysmal AF are more appropriately candidates for rhythm control.

Amar M Salam et al. *JAGS*. December 2003

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Guidelines

- The **American College of Cardiology** and **American Heart Association (ACC–AHA) Task Force on Practice** and the **European Society of Cardiology (ESC) Committee for Practice** have published guidelines for the management of atrial fibrillation that recommend the "minimum evaluation" of newly discovered atrial fibrillation, mentioned earlier, and advise on the use of antiarrhythmic agents .
- These guidelines suggest that there is **"no clear advantage"** to a strategy of **rate control** as compared with **rhythm control**.
- Their recommendations for antithrombotic therapy are similar to, but not identical with, those published by the **American College of Chest Physicians (ACCP).**
- A third set of guidelines, proposed by the **American Academy of Family Physicians (AAFP)** and the **American College of Physicians (ACP),** recommend less aggressive anticoagulant therapy with warfarin. This set of guidelines defines patients who have no history of stroke or transient ischemic attack and have only a single risk factor for stroke (e.g., an age of 75 years or older, congestive heart failure, hypertension, or diabetes) as at low risk (i.e., not in need of warfarin therapy).

Clinical Guidelines Management of Newly Detected Atrial Fibrillation: A Clinical Practice Guideline from the American Academy of Family Physicians and the American College of Physicians.

Vincenza Snow et al.

Ann Intern Med. 16 December 2003

Recommendation 1*: *Rate control with chronic anticoagulation* *is the recommended strategy for the majority of patients with atrial fibrillation.

Rhythm control* *has not been shown to be superior to* *rate control (with chronic anticoagulation)* *in reducing morbidity and mortality and may be inferior in some patient subgroups to rate control.

Rhythm control* *is appropriate when based on other special considerations, such as* *patient symptoms, exercise tolerance, and patient preference*. *Grade: 2A

Clinical Guidelines Management of Newly Detected Atrial Fibrillation. Vincenza Snow et al. *Ann Intern Med*. 16 December 2003

***Recommendation 2*:**

Patients with atrial fibrillation should receive chronic anticoagulation with adjusted-dose warfarin, unless they are at low risk of stroke or have a specific contraindication to the use of warfarin (thrombocytopenia, recent trauma or surgery, alcoholism). Grade: 1A

Recommendation 3:

For patients with atrial fibrillation, the following drugs are recommended for their demonstrated efficacy in rate control during exercise and while at rest: atenolol, metoprolol, diltiazem, and verapamil (drugs listed alphabetically by class).

Digoxin is only effective for rate control at rest and therefore should only be used as a second-line agent for rate control in atrial fibrillation. Grade: 1B

Clinical Guidelines Management of Newly Detected Atrial Fibrillation. Vincenza Snow et al. *Ann Intern Med*. 16 December 2003

Recommendation 4:

For those patients who elect to undergo acute cardioversion to achieve sinus rhythm in atrial fibrillation, both direct-current cardioversion* (Grade: 1C+) *and pharmacological conversion* (Grade: 2A) *are appropriate options.

Recommendation 5:

***Both transesophageal echocardiography with short-term prior anticoagulation followed by early acute cardioversion (in the absence of intracardiac thrombus) with postcardioversion anticoagulation versus delayed cardioversion with pre- and postanticoagulation are appropriate management strategies for those patients who elect to undergo cardioversion.* Grade: 2A**

Clinical Guidelines Management of Newly Detected Atrial Fibrillation. Vincenza Snow et al. *Ann Intern Med*. 16 December 2003

Recommendation 6:

Most patients converted to sinus rhythm from atrial fibrillation should not be placed on rhythm maintenance therapy since the risks outweigh the benefits.

In a selected group of patients whose quality of life is compromised by atrial fibrillation, the recommended pharmacologic agents for rhythm maintenance are amiodarone, disopyramide, propafenone, and sotalol (drugs listed in alphabetical order). The choice of agent predominantly depends on specific risk of side effects based on patient characteristics. **Grade: 2A**

Clinical Guidelines Management of Newly Detected Atrial Fibrillation.
Vincenza Snow et al. *Ann Intern Med*. 16 December 2003

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Areas of Uncertainty

- Approaches to prevent the development of atrial fibrillation warrant further attention. Recent randomized trials involving patients with left ventricular dysfunction suggest that angiotensin-converting–enzyme inhibitors reduce the risk of atrial fibrillation. These data emphasize the importance of treatment for hypertension and cardiovascular disease in such patients.

- The role of ablation, as compared with antiarrhythmic therapy, remains uncertain; its use may increase as tools and techniques are improved.

- The role of new oral anticoagulant agents that are currently in development, which might obviate the need for dose adjustment and the measurement of INR values, needs to be determined. The direct thrombin inhibitor ximelagatran appears to be as effective as warfarin in the prevention of stroke and systemic embolism in patients with atrial fibrillation. However, clinical use of ximelagatran may be limited by its hepatic toxicity; the elevation of levels of alanine aminotransferase to more than three times the upper limit of normal occurred in 6 percent of the patients taking ximelagatran, as compared with 1 percent of those taking warfarin, and hepatic failure leading to death has been reported with the use of ximelagatran.

Ximelagatran vs Warfarin for Stroke Prevention in Patients With Nonvalvular Atrial Fibrillation: A Randomized Trial

SPORTIF Executive Steering Committee for the SPORTIF V Investigators*
JAMA. 2005;293:690-698.

The results establish the efficacy of fixed-dose oral ximelagatran without coagulation monitoring compared with well-controlled warfarin for prevention of thromboembolism in patients with atrial fibrillation requiring chronic anticoagulant therapy, but the potential for hepatotoxicity requires further investigation.

Areas of Uncertainty

- Recently, the use of anatomical ablation with lesions placed circumferentially around the right and left veins, with or without additional left atrial linear lesions, has been successful in patients with paroxysmal atrial fibrillation and those with persistent atrial fibrillation. In an observational study of 1171 patients, those who underwent ablation had significantly lower rates of recurrence after one year (16 percent) than those receiving antiarrhythmic drugs (39 percent); among the patients who underwent ablation, mortality and morbidity also were lower and the quality of life was better *Pappone C, et al. J Am Coll Cardiol 2003;42:185-197* .
- However, data are needed from a randomized trial to establish whether these differences are attributable to the therapy or to other factors. Early series primarily enrolled patients with normal left ventricular function, but in a recent study of 377 patients, one quarter had an ejection fraction below 40 percent, and 73 percent of this group had no recurrence during a follow-up period of 14 months (as compared with 87 percent of the patients with a left ventricular ejection fraction of 40 percent or greater). *Chen MS et al. J Am Coll Cardiol 2004;43:1004-1009*

SOMMARIO

- Introduzione ed Epidemiologia
- Classificazione
- Eziologia
- Diagnosi
- Sintomi e conseguenze emodinamiche
- Strategie ed evidenze
- Il problema tromboembolico
- Trattamento della fibrillazione atriale

> controllo della frequenza o

> ripristino del ritmo

- Aree di incertezza
- Linee Guida
- Casi clinici
- Conclusioni

CASO CLINICO 1

- **Uomo, di 66 anni, in ottime condizioni motorie e cognitive**
- **Pregresso infarto miocardico (2 anni fa) in terapia con ASA ed ACE-I**
- **Dopo cena con amici con eccessivo consumo di alcolici, episodio di tachiaritmia da FA,sintomatica per cardiopalmo, regredita spontaneamente dopo 4 ore**
- **L'ecocardiogramma mostra un atrio sinistro di 44 mm ed una funzione sistolica conservata (FE=62%)**
- **E' indicata profilassi antiaritmica?**
- **Se sì con quale farmaco?**
- **Terapia anticoagulante?**

RISPOSTA CASO 1

- **Per il primo paziente (robusto) non è indicata profilassi antiaritmica per vari motivi (uno perchè è il primo episodio di FA, con fattore scatenante ben individuato, secondo per la difficoltà a scegliere antiaritmico: non possibile usare antiaritmici della classe I ma sono possibili solo sotalolo ed amiodarone)**
- **Utile proseguire con ASA (non con warfarin) essendo la aritmia durata poche ore ed eventualmente aggiungere beta-bloccante**
- **Evitare fattori scatenanti (eccessivo consumo di alcolici)**

CASO CLINICO 2

- **Uomo, di 78 anni, in buone condizioni motorie e cognitive**
- **Ipertensione arteriosa da 16 anni**
- **Atrio sinistro di 47 mm**
- **Riscontro casuale , durante controllo della PA (effettuata mensilmente), di polso aritmico con ECG indicativo di FA**
- **E' indicata cardioversione ?**
- **E' indicata profilassi antiaritmica?**
- **Se sì con quale farmaco?**
- **Oppure mantenere adeguata la frequenza ventricolare?**
- **Terapia anticoagulante?**

RISPOSTA CASO 2

Per il secondo paziente (robusto) sono possibili due approcci:

2. **Cardioversione (elettrica o farmacologica), previa terapia anticoagulante per almeno 3 settimane con INR tra 2 e 3, con o senza esecuzione di ecotransesofageo, seguita da anticoagulazione con WARFARIN (per 4 settimane) e profilassi antiaritmica (classe IC o III);**
3. **Controllo della frequenza cardiaca ed anticoagulazione con WARFARIN**

CASO CLINICO 3

- **Donna, di 89 anni, in scadenti condizioni motorie (cadute a terra recidivanti per instabilità posturale) e cognitive (decadimento cognitivo di grado moderato)**
- **Vive sola con assistenza di badante straniera**
- **Ipertensione arteriosa da 30 anni circa**
- **Ricoverata per polmonite; al momento del ricovero riscontro di aritmia da FA parzialmente sintomatica (scompenso cardiaco)**
- **E' indicata cardioversione ?**
- **E' indicata profilassi antiaritmica?**
- **Se sì con quale farmaco?**
- **Mantenere adeguata la frequenza ventricolare?**
- **Terapia anticoagulante?**

RISPOSTA CASO 3

- **Per la terza paziente (disabile e demente) non è indicata cardioversione acuta perchè non è databile la aritmia**
- **Se si considera una FA permanente è necessario il solo controllo della frequenza ventricolare**
- **Sarebbe indicato il WARFARIN ma potrebbe essere più appropriata antiaggregazione con ASA (325mg/die) (difficoltà ad eseguire i controlli dell'INR, somministrazione del farmaco fatto da badante, cadute a terra)**

CASO CLINICO 4

- **Donna, di 78 anni, in ottime condizioni generali nonostante pregresso minor stroke cardioembolico (2001- in assenza di esiti neurologici) e di IMA complicato da FV (1998)**
- **Vive con il marito in assenza di deficit motori e cognitivi**
- **FA permanente (in terapia con WARFARIN dal 2001)**
- **Ricoverata nel Ns Reparto il 15/2/05 per emorragia capsulare dx con emiplegia sin**
- **L'INR del 15/2 era 7.2 (in passato sempre tra 2 e 3)**

Prevenire un ictus cardioembolico
ha portato ad un ictus emorragico

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Newly Diagnosed Atrial Fibrillation

Richard L. Page, M.D.

N Engl J Med 2004;351:2408-16.

CASO CLINICO

- **Donna di 77 anni**
- **Ipertensione da 7 anni (terapia con metoprololo)**
- **Al controllo annuale, in assenza di sintomi, il medico rileva irregolarità del polso**
- **L'ECG mostra fibrillazione atriale con frequenza ventricolare media di 75 bpm**
- **Non storia di aritmie, coronaropatia, valvulopatia, diabete, etilismo, TIA o stroke**
- **Nei mesi predenti la paziente aveva praticato esercizi con cyclette senza lamentare disturbi, fatta eccezione per il riscontro di irregolarità nel battito al cardiofrequenzimetro**

CASO CLINICO

La paziente descritta si presentava con FA asintomatica forse presente da mesi (come evidenziato dalla irregolarità del battito al cardiofrequenzimetro)

La valutazione della paziente dovrebbe includere ECG, ecocardiogramma, Rx torace e funzione tiroidea

Sulla base dei dati provenienti da trial randomizzati la sopravvivenza della nostra paziente non sarebbe migliorata da strategie volte alla cardioversione con il successivo mantenimento del ritmo sinusale; d'altra parte nessuna strategie potrebbe migliorarne i sintomi dal momento che ella non ne ha

CASO CLINICO

“Pertanto io proseguirei con la terapia di controllo della frequenza ventricolare (heart-rate–control therapy) proseguendo il betabloccante che già assumeva”.

“ L’età della paziente e la presenza di ipertensione la pongono ad elevato rischio di tromboembolismo, pertanto è indicata una terapia anticoagulante, con target di INR tra 2 e 3”.

“Poichè la FA è un marker di rischio per malattia aterosclerotica e stroke, io controllerei nella paziente gli altri fattori di rischio per malattie cardiovascolari e li tratterei aggressivamente” (NDT paziente robusta)

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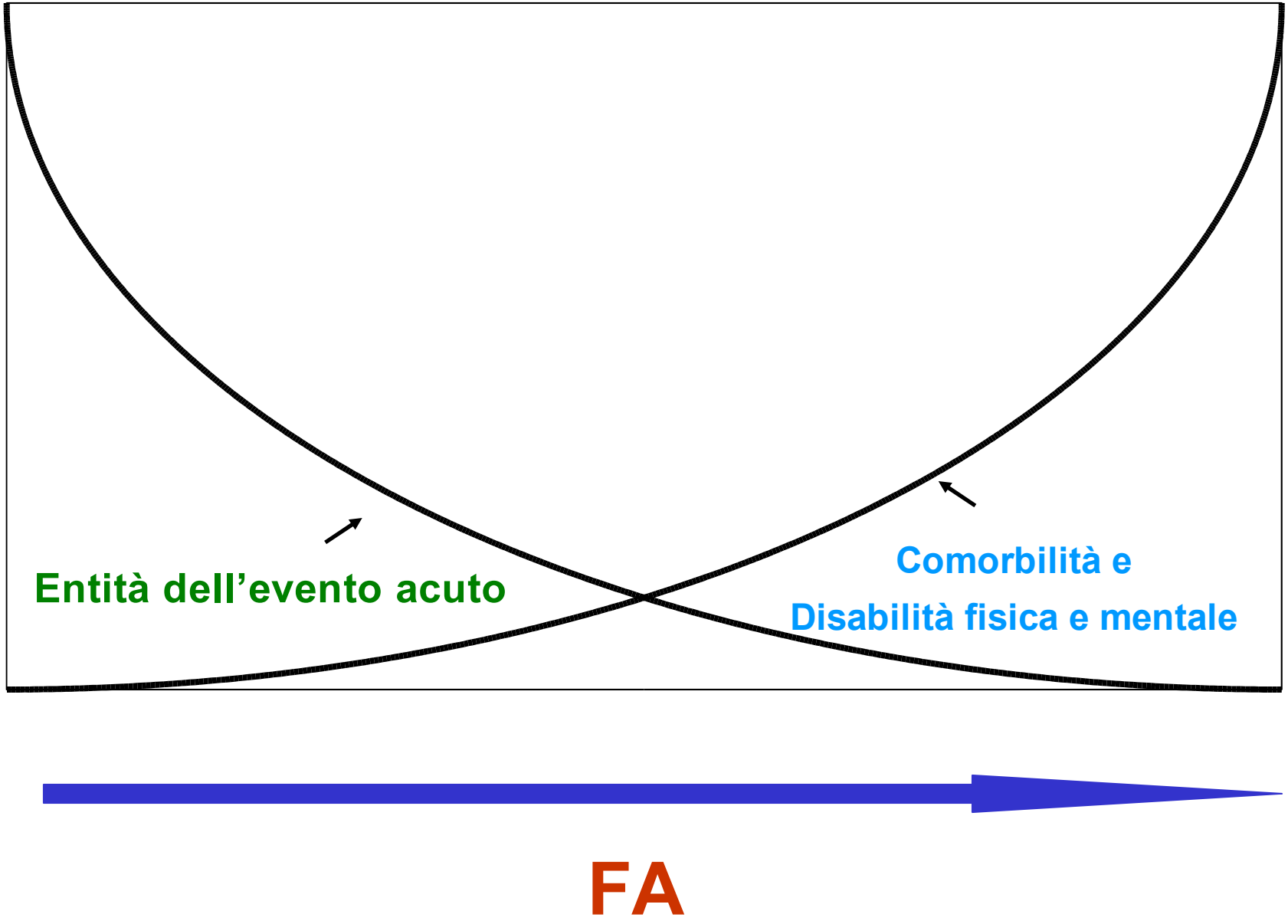
Conclusioni

In futuro vedremo sempre più fibrillazioni atriali

La FA è una diagnosi "povera"

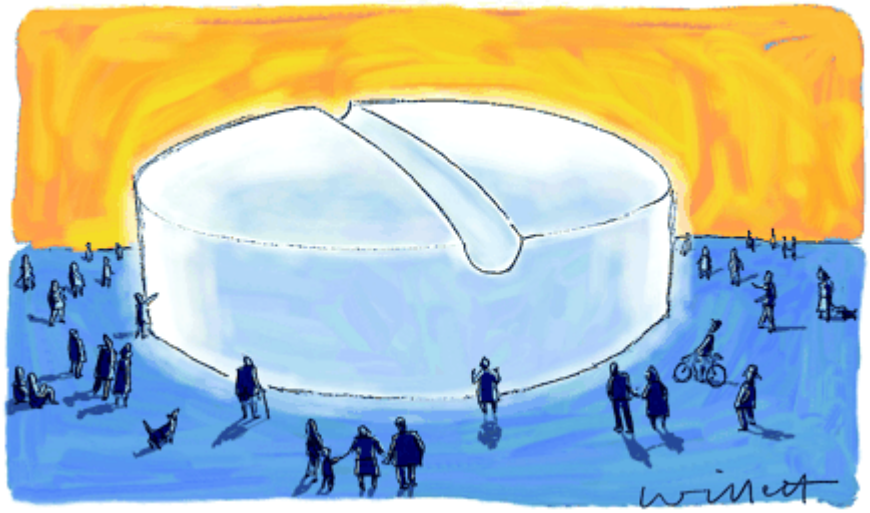
La FA sembra essere, oltrechè un fattore di rischio di scompenso cardiaco e di complicanze tromboemboliche, un **marker di un evento clinico acuto (cardiologico o non) su una base di comorbilità**


Entità dell'evento acuto
Comorbilità e
Disabilità fisica e mentale
FA

Conclusioni

Probabilmente la strategia che adotteremo più frequentemente nei nostri pazienti (disabili, molto disabili, dementi) sarà il solo controllo della frequenza cardiaca e la terapia anticoagulante (magari con farmaci che non necessitano monitoraggio come lo ximelatagran o antiaggreganti come il clopidogrel) lasciando la cardioversione ed il controllo del ritmo ai soli pazienti robusti (più esposti al rischio emorragico della terapia anticoagulante per la loro vita più attiva: auto, bicicletta, hobbies)

La presenza di molte **comorbilità protrombotiche** (come scompenso cardiaco, BPCO, neoplasie) in nostri pazienti (disabili, molto disabili, dementi), spesso allettati o poco mobilizzati per le notevoli disabilità motorie (ad esempio per artrosi, di per sé non protrombotica), renderà forse in futuro più ragionevole l'uso cronico "sine die" di anticoagulanti o antiaggreganti



bmj.com

"Polypill" to fight cardiovascular disease

Polypill cardiovascolare per il robusto: ASA, ACE-I, statina,ac folico, etc

Polypill cardiovascolare per il fragile: anticoagulante, ACE-I

Ask me no questions,

I'll tell you no lies

T. (Costa)Turner