Management of Atrial Fibrillation in Heart Failure

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Definitions

• Rate control
  • Ventricular rate is controlled both at rest and with exertion
  • No commitment to maintaining SR

• Rhythm control
  • Attempts restoration and maintenance of SR
  • Rate control required as needed

• Can switch from rhythm control to rate control, but harder to switch from rate control to rhythm control if AF has been persistent for a long period of time
Case Study: Treatment of AF in CHF

- 55 y/o man with persistent AF
- s/p MI & CABG
- NYHA functional class II-III on beta-blocker, dig, ACEI, aldo antagonist, warfarin
- Exam- BP 110/70, HR 70, no overt CHF
- Electrolytes, BUN/creat, TFT WNL
- Nuclear stress- large anteroapical scar, no ischemia, EF 0.28
- Echo- LA 46 mm, EF 30%
- ECG atrial fibrillation VR 89 bpm, q v1v2v3, QRS 118 ms no BBB
What is the most appropriate approach to therapy for this patient?

- A. Rhythm control strategy
- B. Rate control strategy
- C. Rhythm control strategy + ICD
- D. Rate-control strategy + ICD
Although many clinicians believe that maintaining sinus rhythm can improve outcomes in AF patients, all trials that have compared rhythm control and rate control to rate control alone (with appropriate anticoagulation) have resulted in neutral outcomes.
Long-term antiarrhythmic drug therapy

- Clinically successful antiarrhythmic drug therapy may reduce rather than eliminate the recurrence of AF;
- Antiarrhythmic drug therapy approximately doubles sinus rhythm maintenance compared with no therapy.
- There is no appreciable effect on mortality or cardiovascular complications, but rhythm control therapy can slightly increase the risk of hospitalizations (often for AF).

No significant differences in:

- Cardiovascular mortality (8%/yr)
- All-cause mortality (10%/yr)
- Stroke rate (~1-2%/yr)
- Worsening CHF (~7-8%/yr)
Conclusions

- A rhythm-control strategy does not improve outcomes compared to a rate-control strategy in pts with AF and CHF
- A rate-control strategy reduces the need for DCCV & hospitalization and should be considered the 1° approach for pts with AF & CHF
But!

- Many pts in rhythm control arm had AF
- Some pts in rate control arm had no AF
- Benefits of NSR may have been negated by harmful effects of rhythm-control drugs
- End points such as LVEF, LV dilatation, functional capacity not examined
The patient was treated with amiodarone for 6 weeks then underwent DC cardioversion, with successful conversion to NSR. EKG one week after DCCV NSR and holter on 2nd week NSR for 24 hrs. When seen 4 weeks later in clinic, he was again in AF. Reported significantly improved effort tolerance for 1st 3 weeks post-cardioversion. HR 75 at rest, 115/min after 1 min stair-stepping.

What Next?

A. Ablation of AF
B. Rate control strategy
C. Ablation of AF + ICD
D. Rate-control strategy + ICD
Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure

- 81 pts with AF, CHF, EF 40%
- Randomized:
  - PV isolation ± ablation lines, CFAE ablation
  - AV node ablation + BiV ICD
- Followed for 6 months after last procedure
- Weekly event monitor transmissions
- End points: EF, 6-min walk test, QoL

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

Ejection Fraction (%)

PVI

P=0.03  P<0.001

AV-node ablation+BiV

Months

0  3  6
B 6-Minute Walk

Distance (m)

Months

PVI

P < 0.001

P = 0.003

AV-node ablation + BiV

0

260

280

300

320

340

360
C Minnesota Living with Heart Failure Questionnaire

- PVI
- AV-node ablation + BiV

Score

Months

P < 0.001
Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure

• Conclusions

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

“Before choosing rate control as a long-term strategy, the clinician should consider how permanent AF is likely to affect the patient in the future”.

Rate vs Rhythm Control

Current randomized studies do not demonstrate mortality differences in rate vs rhythm treatment approaches

 Patients randomized to these studies were older, relatively asymptomatic, and considered appropriate for either strategy

 QoL studies have indicated better results with SR

 Benefits of SR may be offset by AAD toxicity

Symptom-driven decisions are recommended
Caveat: symptoms may be subtle or difficult to elicit, so question patients carefully
<table>
<thead>
<tr>
<th>EHRA class</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHRA I</td>
<td>‘No symptoms’</td>
</tr>
<tr>
<td>EHRA II</td>
<td>‘Mild symptoms’; normal daily activity not affected</td>
</tr>
<tr>
<td>EHRA III</td>
<td>‘Severe symptoms’; normal daily activity affected</td>
</tr>
<tr>
<td>EHRA IV</td>
<td>‘Disabling symptoms’; normal daily activity discontinued</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation; EHRA = European Heart Rhythm Association.
Effect of AF on mortality

AF is associated with an increased long-term risk of stroke, HF, and all-cause mortality, especially among women. The mortality rate of patients with AF is about double that of patients in normal sinus rhythm and is linked to the severity of underlying heart disease (Krahn AD et al., 1995).
Electrical, contractile and structural remodeling during atrial fibrillation

- Electrical remodeling (shortening of atrial refractoriness) develops within the first days of AF and contributes to an increase in stability of AF.
- Atrial contractile remodeling (loss of contractility) leads to a reduced atrial transport function after cardioversion of AF.
- An important clinical consequence is that during several days after restoration of sinus rhythm, the risk of atrial thrombus formation is still high.
- In addition, the reduction of atrial contractility during AF may enhance atrial dilatation which may add to the persistence of AF.
- Tachycardia-induced structural remodeling takes place in a different time domain (weeks to months).
**AF in Patients With HF**

HF promotes AF, AF aggravates HF, and individuals with either condition who develop the alternate condition share a poor prognosis. Thus, managing patients with the associated conditions is a major challenge, and randomized trials are needed to investigate the impact of AF on prognosis in HF (*Wang TJ et al., 2003*).
AF in Patients With HF

• HF may develop or deteriorate with AF
  ◦ Progression of underlying cardiac disease
  ◦ Uncontrolled heart rate
  ◦ Antiarrhythmic drug toxicity

• AF may exacerbate HF symptoms due to
  ◦ Loss of atrial “kick”
  ◦ Rapid heart rate

• Patients in AFFIRM did not develop or deteriorate differently in rate vs rhythm arms

## Prevalence of AF in Heart Failure

**New York Heart Association Functional Class**

<table>
<thead>
<tr>
<th>Class</th>
<th>Annual Incidence ~ 5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4.2%</td>
</tr>
<tr>
<td>II-III</td>
<td>10.1%</td>
</tr>
<tr>
<td>III-IV</td>
<td>14.4%</td>
</tr>
<tr>
<td>IV</td>
<td>25.8%</td>
</tr>
<tr>
<td>IV</td>
<td>28.9%</td>
</tr>
<tr>
<td>IV</td>
<td>49.8%</td>
</tr>
</tbody>
</table>

From Maisel and Stevenson, AJC 2003
The aims of management

- Prevention of adverse outcomes and maintenance of a good quality of life in all patients with AF and concomitant heart failure, regardless of LVEF.
A randomised, controlled study of rate versus rhythm control in patients with chronic atrial fibrillation and heart failure: (CAFÉ-II Study)

• Conclusion

Restoring SR in patients with AF and heart failure may improve QoL and LV function when compared with a strategy of rate control.
Take-Home Points

• Heart rate control at rest and with exertion is critical for either AF strategy
• Rate vs rhythm approach should be guided by many factors, most importantly, symptoms and appropriate application of clinical trials
• It is not rate vs rhythm. It is aggressive AF management new risk factors.
• Ablation is an important option in SR maintenance
• Appropriate patient categorization is critical for management
Ventricular Rate Control, Principles

- Adequate control of the ventricular response during AF can significantly improve symptoms and is critical to avoid tachycardia-mediated cardiomyopathy.
- Most patients managed using a rhythm control strategy also require medications for rate control.

Knight, et al, Practical Rate and Rhythm Management of Atrial Fibrillation, January 2010 ed.
What Is Adequate Rate Control?

- Adequate rate control is critical to avoid tachycardia-mediated cardiomyopathy
- Criteria vary with age
- May be evaluated using 24-hour Holter recording
- 60-80 beats per minute at rest.
- 90-115 beats per minute with exertion

A resting heart rate of <110 bpm (i.e. lenient rate control) should be considered as the initial heart rate target for rate control therapy.
AF guidelines vs HF guidelines

- It is worthwhile to note that many ‘adequately rate-controlled’ patients (resting heart rate 60 – 100 b.p.m.) are severely symptomatic, calling for additional management. Nonetheless, lenient rate control is an acceptable initial approach, regardless of heart failure status, unless symptoms call for stricter rate control.
Cardiac Pacing guidelines

- The minimum rate should be programmed higher (e.g. 70 bpm) than for SR patients in an attempt to compensate for loss of active atrial filling and
- The maximum sensor rate should be programmed restrictively (e.g. 110–120 bpm), in order to avoid ‘overpacing’, i.e. pacing with a heart rate faster than necessary, which can be symptomatic, especially in patients with coronary artery disease.
Ventricular Rate Control: Drugs

LVEF <40%

- Beta-blocker
- Digoxin

Consider early low-dose combination therapy

- Add digoxin
- Add beta-blocker
Ventricular Rate Control: Drugs

• Compared with placebo, beta-blockers are associated with a reduced risk of new-onset AF in patients with HFrEF and sinus rhythm.

• Beta-blockers have also been reported to reduce symptomatic AF recurrences, but this finding may be driven by the beneficial effect of rate control, which will render AF more often asymptomatic.

Ventricular Rate Control: Drugs

- A combination of a beta blocker and digoxin may be needed to control the HR.
- The choice of medication should be individualized and the dose modulated to avoid bradycardia.
- AV nodal blocking drugs at doses required to control the ventricular response can cause symptomatic bradycardia that requires pacemaker therapy.
Ventricular Rate Control: Drugs

- Digitoxin is a suitable alternative to digoxin, where available.
- Bisoprolol, carvedilol, long-acting metoprolol, and nebivolol.

Paulus Kirchhof et al, ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. European Heart Journal (2016) 37, 2893–2962
Ventricular Rate Control: Drugs

Despite this lack of prognostic benefit in HFrEF, beta- blockers still considered as a useful first-line rate control agent across all AF patients, based on

- The potential for symptomatic.
- Functional improvement as a result of rate control.
- Lack of harm from published studies.
- Good tolerability profile across all ages in sinus rhythm and in AF.

Paulus Kirchhof et al, ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. European Heart Journal (2016) 37, 2893–2962
Ventricular Rate Control: AV Nodal Ablation

- Ablation of the AV conduction system and permanent pacing (the “ablate and pace” strategy) is an option for patients who have rapid ventricular rates despite maximum medical therapy and often yields remarkable symptomatic relief.

- There is growing concern about the negative effects of long-term RV pacing.

- Biventricular pacing, on the other hand, may overcome many of the adverse hemodynamic effects associated with RV pacing and is preferred when systolic dysfunction is present.

- Catheter ablation of the AV node should not be attempted without a prior trial of medication to control the rate.
Cardiac contractility modulation (CCM)

- Is similar in its mode of insertion to CRT, but it involves non-excitatory electrical stimulation of the ventricle during the absolute refractory period to enhance contractile performance without activating extra systolic contractions.
- CCM has been evaluated in patients with HFrEF in NYHA Classes II–III with normal QRS duration (<120 ms).
- An individual patient data meta-analysis demonstrated an improvement in exercise tolerance and quality of life. Thus CCM may be considered in selected patients with HF. The effect of CCM on HF morbidity and mortality remains to be established.
Clinical Considerations for Management Strategy

- Duration and patterns of AF
- Type and severity of symptoms
- Associated cardiovascular disease
- Potential for changes in cardiac function over time
Does Underlying Rhythm Matter?

- The major clinical trials that led to FDA approval for CRT enrolled only patients in NSR.
- The benefit of CRT may be mediated in part by optimization of AV timing in patients with NSR; not relevant for AF.
- The benefit of CRT may be dependent on ventricular rate control in patients with AF, independent of resynchronization.
The only prospective and randomized trial truly dedicated to patients with permanent AF and severe HF
Conclusion of MUSTIC study

- They found a favorable one-year results of BiV pacing in patients with severe HF and major intraventricular conduction disturbances in either SR or AF.

- And significant sustained benefit in exercise tolerance quality of life from BiV over a 12-month follow-up period.

- A reduction in mitral regurgitation and an improvement in ejection fraction were also observed.

- Hospitalizations for HF were fewer during BiV pacing.
The Question raised

- Whether these favorable results translate into an improved survival or not.
CRT Employed in AF: Outcomes From Observational Study
Outcomes for AF patients After CRT

Comparison of Kaplan–Meier estimates of overall (A), cardiac (B), and heart failure (C) survival between AF patients who underwent AVJ ablation and AF patients treated only with anti-arrhythmic drugs. The p-values presented derive from the adjusted hazards ratio analysis stratified according to the corresponding cause of death. Reproduced from M. Gasparini, A. Auricchio, M. Metra, F. Regoli, C. Fantoni, B. Lamp, et al. 2008 Long-term survival in patients undergoing cardiac resynchronization therapy: the importance of performing atrio-ventricular junction ablation in patients with permanent atrial fibrillation. European Heart Journal. 2916441652
ESC-Cardiac Pacing guidelines 2013

Figure 10: Indication for atrioventricular junction (AVJ) ablation in patients with symptomatic permanent atrial fibrillation (AF) and optimal pharmacological therapy. BiV = biventricular; CRT = cardiac resynchronization therapy; EF = ejection fraction; HR = heart rate; ICD = implantable cardioverter defibrillator; NYHA = New York Heart Association.
Problems Associated with Achieving CRT in Patients with AF

- If AV conduction is not severely impaired (intrinsic or pharmacologic), the goal of continuous resynchronization therapy may be disturbed.
- Programmed pacing rate may be set higher than desired in an effort to ensure consistent capture.
- Medical therapy to block AV nodal conduction is often unsuccessful.
- Pacing algorithms that attempt to assure pacing have no proven benefit.
Challenges to Achieving Consistent BV Capture in Patients With AF

- Higher intrinsic heart rate necessitates higher programmed pacing rate
- Frequent fusion beats
- Frequent pseudofusion beats
- Inaccurate assessment of BV capture by device counters
Inconsistent Capture During AF
12-lead Holter Assessment

- Patients selected on basis of >90% pacing capture on CRT interrogation
- Patients were instructed to wear an ambulatory 12-lead Holter for 24 hours
- Template matching analysis software was used to record percentages of fusion, pseudofusion and complete capture beats

- Intrinsic
- Paced beat
- Fusion beat
- Pseudofusion beat
Holter Data Analyses

- Ineffective pacing (N=10), 56%
- Effective pacing (N=8), 44%
ESC-Cardiac Pacing guidelines 2013

- There is evidence, from small randomized trials, of an additional benefit of performing CRT pacing in patients with reduced EF, who are candidates for AV junction ablation for rate control, in order to reduce hospitalization and improve quality of life.
- However, the quality of evidence is moderate and discordance of opinion exists among experts.
Complete atrioventricular block does not reduce long-term mortality in patients with permanent atrial fibrillation treated with cardiac resynchronization therapy

José M. Tolosana, Emilce Trucco, Malek Khatib, Adelina Doltra, Roger Borras, M. Àngeles Castel, Antonio Berruezo, Elena Arbelo, Marta Sitges, Maria Matas, Eduard Guasch, Josep Brugada, and Lluís Mont

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Received 20 February 2013; revised 5 June 2013; accepted 7 June 2013; online published ahead of print 11 July 2013

Conclusion:
Atrioventricular junction block did not improve survival for patients in AF treated with CRT. Basal NYHA functional class IV, poor renal function, and LVEF were the independent predictors of mortality.
Discussion

- A meta-analysis described a positive effect of AVJ ablation in CRT-AF patients, with a reduction in all-cause mortality
  1. Ferreira et al.
  2. Dong et al.
  3. Gasparini et al.
I-Ferreira et al.

- mortality results must be carefully interpreted due to the small sample size of patients with permanent AF included in the study [25/53 (47%)] and the percentage of ventricular pacing achieved in the non-AVJ ablation group (87%), which was lower than in our series.
2-Dong et al.

- The AF non-AVJ ablation group in that study were older, with worse NYHA functional class, lower LVEF, and higher plasma creatinine levels compared with patients in the AF + AVJ ablation group.
3-Gasparini et al.

- The low percentage of ventricular pacing prior to AVJ ablation (74 ± 4.2%) despite programming the trigger by right ventricular sense algorithm ‘on’ suggests that the study by Gasparini et al. may have included a high percentage of patients in AF with very fast and uncontrolled heart rate in the AF + AVJ ablation group, thus explaining the very low mortality and the excellent prognosis of these patients after AVJ ablation.

- The percentage of ventricular pacing achieved by the AF non-AVJ ablation group: this was 90% in the study by Gasparini et al. but 94% in our study.
Thank You!