Restoration of Sinus Rhythm: Considerations in CKD

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Director: Center for Atrial Fibrillation
Bluhm Cardiovascular Institute
Disclosure of Interests

- Consultant: Medtronic, Biotronik, Janssen
- Speakers bureau: Medtronic, Pfizer, BMS
- Royalties: UpToDate
- Research support: NIH, Medtronic
Growth of AF

Incidence of AF in CKD: ARIC Study N=10328


AF Related Complications

- Mortality: adjusted 1-year increased by 45% for HD + AF compared to HD alone
- Stroke: CKD + AF = 49% increase in stroke risk
- CKD progression

<table>
<thead>
<tr>
<th>Event</th>
<th>Association with AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Increased mortality, especially cardiovascular mortality due to sudden death, heart failure or stroke.</td>
</tr>
<tr>
<td>Stroke</td>
<td>20–30% of all strokes are due to AF. A growing number of patients with stroke are diagnosed with ‘silent’, paroxysmal AF.</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>10–40% of AF patients are hospitalized every year.</td>
</tr>
<tr>
<td>Quality of life</td>
<td>Quality of life is impaired in AF patients independent of other cardiovascular conditions.</td>
</tr>
<tr>
<td>Left ventricular dysfunction and heart failure</td>
<td>Left ventricular dysfunction is found in 20–30% of all AF patients. AF causes or aggravates LV dysfunction in many AF patients, while others have completely preserved LV function despite long-standing AF.</td>
</tr>
<tr>
<td>Cognitive decline and vascular dementia</td>
<td>Cognitive decline and vascular dementia can develop even in anticoagulated AF patients. Brain white matter lesions are more common in AF patients than in patients without AF.</td>
</tr>
</tbody>
</table>
AF Management

Stroke Prevention

Rate Control  Rhythm Control
“Persistent symptoms associated with AF remain the most compelling indication for a rhythm-control strategy.”

Other factors that may favor attempts at rhythm control include:
• difficulty in achieving adequate rate control
• younger patient age
• tachycardia-mediated cardiomyopathy
• first episode of AF
• AF that is precipitated by an acute illness
• patient preference
Rhythm vs Rate Control on Risk of Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk Ratio (95% Cl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFFIRM</td>
<td>1.14 (1.00, 1.32)</td>
</tr>
<tr>
<td>PIAF</td>
<td>0.98 (0.14, 6.88)</td>
</tr>
<tr>
<td>STAF</td>
<td>0.50 (0.16, 1.61)</td>
</tr>
<tr>
<td>RACE</td>
<td>0.96 (0.51, 1.81)</td>
</tr>
<tr>
<td>Overall</td>
<td>1.12 (0.98, 1.28)</td>
</tr>
</tbody>
</table>

Relative Risk of Death With Rhythm Control vs Rate Control

\[ P = 0.09 \]
AF-CHF: Kaplan-Meier Estimates of Death from Cardiovascular Causes


KDIGO Controversies Conference on CKD & Arrhythmias
October 27-30, 2016 | Berlin, Germany
### Rhythm vs Rate Control on Risk of Stroke /TIA

**Study or Subgroup** | **Rate Control Events** | **Rate Control Total** | **Rhythm Control Events** | **Rhythm Control Total** | **Weight** | **Risk Ratio** | **95% CI** |
---|---|---|---|---|---|---|---|
AF CHF | 11 | 694 | 9 | 682 | 116% | 1.20 [0.85, 1.70] |
AFFIRM | 105 | 2027 | 106 | 2033 | 396% | 0.99 [0.76, 1.30] |
CARRT | 0 | 40 | 1 | 45 | 1.1% | 0.37 [0.02, 8.93] |
HOT CAFE | 0 | 101 | 3 | 104 | 13% | 0.15 [0.01, 2.81] |
J-RHYTHM | 11 | 604 | 9 | 601 | 117% | 1.27 [0.53, 3.20] |
Okumura et al. | 7 | 84 | 5 | 39 | 82% | 0.06 [0.02, 1.92] |
RACE | 14 | 256 | 21 | 266 | 176% | 0.69 [0.28, 1.73] |
STAF | 1 | 100 | 5 | 100 | 24% | 0.20 [0.03, 1.68] |
Yildiz et al. | 6 | 68 | 4 | 66 | 86% | 3.52 [1.03, 12.08] |
**Total (95% CI)** | **3772** | **3848** | **100.0%** | **0.96 [0.68, 1.34]** |
**Total events** | 155 | 163 |

Heterogeneity: Tau² = 0.08; Q(8) = 10.43, df = 8 (P = 0.24); P = 23%
Test for overall effect: Z = 0.36 (P = 0.70)

Chatterjee S; PACE 2013;36(1)
Why Isn’t Rhythm Control Superior to Rate Control?

- Long term sinus rhythm hard to achieve (particularly with AAD and particularly with persistent AF)
- Side effects / toxicity of AAD
Challenges of Rhythm Control in CKD Patients

- DCCV
- Antiarrhythmic drugs
- Ablation
Renal Dysfunction and Atrial Fibrillation Recurrence Following Cardioversion

“In patients with maintained sinus rhythm after 12-month follow-up eGFR was increased (8.46 ± 9.49 mL/min [range −7 to 43]), whereas patients with atrial fibrillation recurrence showed a decrease in eGFR over time (−5.75 ± 9.4 [range −32 to 25], P < 0.001)”

N = 159


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Challenges of Rhythm Control in CKD Patients

- DCCV
- Antiarrhythmic drugs
- Ablation
ESC 2016
AF Guidelines

KDIGO Controversies Conference on CKD & Arrhythmias
October 27-30, 2016 | Berlin, Germany
## Antiarrhythmic Drugs in CKD

<table>
<thead>
<tr>
<th>Drug</th>
<th>PK and elimination</th>
<th>Indications for CKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flecainide</td>
<td>Metabolized in liver and excreted unchanged in urine (35%)</td>
<td>Dose reduction if GFR &lt; 35 mL/min/1.73m²</td>
</tr>
<tr>
<td>Propafenone</td>
<td>95% protein bound; metabolized in liver and excreted unchanged in urine (38%)</td>
<td>Careful monitoring recommended (in hospital initiation for advanced CKD)</td>
</tr>
<tr>
<td>Sotalol</td>
<td>70% excreted unchanged in the urine</td>
<td>50% dose reduction in CKD; 75% in severe renal failure (relatively contraindicated)</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>Protein binding 60-70%; 80% excreted by kidneys</td>
<td>Dosing by GFR; contraindicated for GFR &lt; 20 mL/min</td>
</tr>
<tr>
<td>Dronedarone</td>
<td>98% protein bound; metabolized in liver; 6% excreted in urine</td>
<td>No dosing adjustment for mild to severe renal failure</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>99% protein bound; no renal elimination</td>
<td>No dosage requirements</td>
</tr>
</tbody>
</table>

EHRA Position Paper; Europace 2015(17),1169
# Antiarrhythmic Drugs in CKD

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flecainide</td>
<td>No structural heart disease</td>
</tr>
<tr>
<td>Propafenone</td>
<td>No structural heart disease</td>
</tr>
<tr>
<td>Sotalol</td>
<td>+ Contraindicated if &gt; mild CKD</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>Contraindicated if &gt; mild CKD</td>
</tr>
<tr>
<td>Dronedarone</td>
<td>EF &gt; 35%, no recent CHF</td>
</tr>
<tr>
<td>Amiodarone*</td>
<td>All</td>
</tr>
</tbody>
</table>

* Thyroid toxicity, liver failure, pulmonary fibrosis, neuropathy, optic neuritis, skin discoloration
## AFFIRM Results

### Time-Dependent Covariates Associated With Survival

<table>
<thead>
<tr>
<th>Covariate</th>
<th>P-Value</th>
<th>Hazard Ratio</th>
<th>99% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm</td>
<td>&lt;.0001</td>
<td>0.53</td>
<td>0.39-0.72</td>
</tr>
<tr>
<td>Warfarin use</td>
<td>&lt;.0001</td>
<td>0.50</td>
<td>0.37-0.69</td>
</tr>
<tr>
<td>Digoxin use</td>
<td>.0007</td>
<td>1.42</td>
<td>1.09-1.86</td>
</tr>
<tr>
<td>AAD* use</td>
<td>.0005</td>
<td>1.49</td>
<td>1.11-2.01</td>
</tr>
</tbody>
</table>

HR <1.00: decreased risk of death.
HR >1.00: increased risk of death.

*Antiarrhythmic drug.
What if there were a better way of maintaining sinus rhythm?
Sites of 69 Foci Triggering AF in 45 Patients

AF Onset from Pulmonary Vein
Pulmonary Veins as Triggers of AF

- Intrinsic pacemaker function
- Different EP properties
- Fewer cell-cell interactions
- More susceptible to stretch and fibrosis
- Amenable to arrhythmogenesis
AF Ablation
Ablation of PV Potentials

RF

CRYO
AF Termination
Meta Analysis: Ablation vs Antiarrhythmics

<table>
<thead>
<tr>
<th>Study</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krittayaphong 2003</td>
<td>3.46</td>
</tr>
<tr>
<td>Stabile 2006</td>
<td></td>
</tr>
<tr>
<td>Pappone 2006</td>
<td></td>
</tr>
</tbody>
</table>

Favors AAD | Favors Ablation

Terasawa T: Annals Int Med; 2009; 151:191
RCT of AAD vs RF Ablation (RAAFT2)

**A** Primary efficacy outcome

- Antiarrhythmic drug
- Radiofrequency catheter ablation

Cumulative Hazard Rate vs Follow-up Since Randomization, d

No. at risk
- Antiarrhythmic drug: 61, 60, 51, 45, 38, 32, 25, 19, 13, 9, 7
- Radiofrequency catheter ablation: 66, 65, 56, 49, 42, 36, 30, 24, 18, 13, 9

HR, 0.56, 95% CI, 0.35-0.90, P = .02

**B** Time to first recurrence of symptomatic atrial tachyarrhythmias

Cumulative Hazard Rate vs Follow-up Since Randomization, d

No. at risk
- Antiarrhythmic drug: 61, 60, 51, 45, 38, 32, 25, 19, 13, 9, 7
- Radiofrequency catheter ablation: 66, 65, 56, 49, 42, 36, 30, 24, 18, 13, 9

HR, 0.56, 95% CI, 0.33-0.95, P = .03

Morillo C, JAMA 2014; 311 (7)
Correlating clinical syndrome to pathophysiology

TRIGGERING

PV PACs
OTHER PACs
AT / SVT

MAINTENANCE

LOCAL ANISOTROPY
FIBROSIS / SCARRING
REPETITIVE TRIGGERING

MODULATORS
STRETCH
AUTONOMIC TONE
ELECTRICAL REMODELING

Paroxysmal AF
Persistent AF
Permanent AF
Mechanisms/Targets of AF
Indications for AF Ablation

6.3. AF Catheter Ablation to Maintain Sinus Rhythm: Recommendations

CLASS I

1. AF catheter ablation is useful for **symptomatic** paroxysmal AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired (363,392-397). (Level of Evidence: A)

2. Before consideration of AF catheter ablation, assessment of the procedural risks and outcomes relevant to the individual patient is recommended. (Level of Evidence: C)

CLASS IIa

1. AF catheter ablation is reasonable for some patients with **symptomatic** persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication (394,398-400). (Level of Evidence: A)

2. In patients with recurrent **symptomatic** paroxysmal AF, catheter ablation is a reasonable initial rhythm-control strategy before therapeutic trials of antiarrhythmic drug therapy, after weighing the risks and outcomes of drug and ablation therapy (401-403). (Level of Evidence: B)

CLASS IIb

1. AF catheter ablation may be considered for **symptomatic** longstanding (>12 months) persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired (363,404). (Level of Evidence: B)

2. AF catheter ablation may be considered before initiation of antiarrhythmic drug therapy with a class I or III antiarrhythmic medication for **symptomatic** persistent AF when a rhythm-control strategy is desired. (Level of Evidence: C)

CLASS III: HARM

1. AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and after the procedure. (Level of Evidence: C)
Challenges of Rhythm Control in CKD Patients

- DCCV
- Antiarrhythmic drugs
- Ablation
Catheter Ablation in CKD Patients: Meta-Analysis (RF)

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Year</th>
<th>Total no. of patients</th>
<th>Ablation strategy</th>
<th>Method of AF detection</th>
<th>Definition of CKD</th>
<th>Follow up period [months]</th>
<th>Blanking period [months]</th>
<th>Risk estimate</th>
<th>Study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berkowitsch</td>
<td>2012</td>
<td>702</td>
<td>PVI</td>
<td>12-lead ECG, 24-h Holter</td>
<td>eGFR &lt; 68 mL/min/1.73 m²</td>
<td>Median follow up time of 15.6</td>
<td>3</td>
<td>aHR</td>
<td>9</td>
</tr>
<tr>
<td>Chao</td>
<td>2011</td>
<td>232</td>
<td>PVI</td>
<td>Clinical symptoms, 12-lead ECG, 24-h Holter and 1 week cardiac event recordings</td>
<td>eGFR &lt; 60 mL/min/1.73 m²</td>
<td>25.4 ± 13.3</td>
<td>2</td>
<td>HR</td>
<td>8</td>
</tr>
<tr>
<td>Naruse</td>
<td>2011</td>
<td>221</td>
<td>PVI</td>
<td>12-lead ECG, 24-h Holter, portable ECG</td>
<td>eGFR &lt; 60 mL/min/1.73 m²</td>
<td>31.9 ± 7.6</td>
<td>3</td>
<td>aHR</td>
<td>9</td>
</tr>
<tr>
<td>Tokuda</td>
<td>2011</td>
<td>224</td>
<td>PVI</td>
<td>Patients' symptom, ECG, 24-h Holter monitor</td>
<td>eGFR &lt; 60 mL/min/1.73 m²</td>
<td>37.4 ± 24.4</td>
<td>3</td>
<td>HR</td>
<td>9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study of subgroup</th>
<th>log [hazard ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard ratio IV, Random. 95% CI</th>
<th>Hazard ratio IV, Random. 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berkowitsch</td>
<td>0.3577</td>
<td>0.1576</td>
<td>34.3%</td>
<td>1.43 [1.05–1.95]</td>
<td></td>
</tr>
<tr>
<td>Chao</td>
<td>1.1982</td>
<td>0.2864</td>
<td>22.3%</td>
<td>3.31 [1.89–5.81]</td>
<td></td>
</tr>
<tr>
<td>Naruse</td>
<td>0.7367</td>
<td>0.2452</td>
<td>25.8%</td>
<td>2.09 [1.29–3.38]</td>
<td></td>
</tr>
<tr>
<td>Tokuda</td>
<td>0.5306</td>
<td>0.3537</td>
<td>17.7%</td>
<td>1.70 [0.85–3.40]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>100%</td>
<td>1.96 [1.35–2.85]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.08; Chi² = 7.07; df = 3 (p = 0.07); I² = 58%
Test for overall effect: Z = 3.52 (p = 0.0004)

“CKD was associated with higher AF recurrence rate following single catheter ablation (HR = 1.96, 95% CI 1.35–2.85, p = 0.0004)”

Li M, Cardiology Journal 2014, Vol. 21, No. 1, pp. 89–95
No patients developed contrast-induced nephropathy after the catheter ablation procedure.

The presence of non-PV ectopic beats (with isoproterenol) was significantly increased in patients with impaired renal function.
Mean changes in estimated glomerular filtration rate (eGFR) from baseline to 1 year after ablation of atrial fibrillation (AF)

White and black bars represent patients free from arrhythmias and patients who had recurrences of atrial tachyarrhythmia, respectively.

# AF Ablation in CKD*

<table>
<thead>
<tr>
<th></th>
<th>CKD (N=1593)</th>
<th>No CKD (N=19498)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64 ± 11</td>
<td>59 ± 11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Comorbidity Index</td>
<td>2.7</td>
<td>0.92</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CHADSVASC</td>
<td>3.2</td>
<td>1.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>57%</td>
<td>32%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Prior MI</td>
<td>11%</td>
<td>5%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PAD</td>
<td>11%</td>
<td>4%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DM</td>
<td>42%</td>
<td>20%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Dialysis</td>
<td>3.8%</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Using MarketScan® Commercial Claims and Medicare Supplemental Databases,
### AF Ablation in CKD: 1-Year Outcomes

<table>
<thead>
<tr>
<th></th>
<th>CKD (N=1593)</th>
<th>No CKD (N=19498)</th>
<th>Adjusted P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause hospitalization</td>
<td>42.7%</td>
<td>27.1%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AF Hospitalization</td>
<td>13.1%</td>
<td>12.4%</td>
<td>0.79</td>
</tr>
<tr>
<td>Cardioversion</td>
<td>21.5%</td>
<td>20.1%</td>
<td>0.87</td>
</tr>
<tr>
<td>Repeat AF Ablation</td>
<td>11.6%</td>
<td>14.4%</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Ullal; HRS 2016
# AF Ablation in Dialysis Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>HD/non-HD</th>
<th>Follow-Up</th>
<th>Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sairaku</td>
<td>30/60 (matched)</td>
<td>2.2 years</td>
<td>54% v 78%</td>
</tr>
<tr>
<td>Hayashi</td>
<td>16 / 111</td>
<td>5.5 years</td>
<td>25% v 41%</td>
</tr>
<tr>
<td>Takigawa</td>
<td>32 / 1332</td>
<td>5 years</td>
<td>20% v 62%</td>
</tr>
</tbody>
</table>

Panel: Multiple Procedures
81% in HD v 83% non-HD

Sairaku A. J Cardiovasc Electrophysiology 2012; 23:1289
Hayashi M. Nephrol Dial Transplant 2014; 29:160
Takigawa M. Europace 2014; 16.327
Quebec, Canada: Population-based Study of Patients with AF; N=26,130

Impact of AF Ablation

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Bunch TJ et al. Heart Rhythm 2010; 7: 433
Summary

- AF common in CKD and is associated with increased morbidity and mortality

- Scant data on benefits of rhythm control in patients with CKD (improved GFR?) and no data on ESRD

- Limited antiarrhythmic drug options

- Ablation possibly less successful based on degree of CKD

- Ideal energy (RF vs cryo) source unknown

- More study needed
Mean changes in estimated glomerular filtration rate (eGFR) from baseline to 1 year after ablation of atrial fibrillation (AF) across quartiles of baseline eGFR.
Prevalence of AF:
No CKD: 1.0%
stage 1 to 2: 2.8%
stage 3: 2.7%
stage 4 to 5 CKD: 4.2%

Adjusted OR for AF:
Stage 1-2: 2.7
Stage 3: 1.7
Stage 4-5: 3.5
AF Risk Factors: Classical and Novel

- Age
- HTN (less so in ESRD)
- Valvular disease
- Cardiomyopathy
- DM
- CAD
- Genetic factors
- Obesity
- OSA
- LA enlargement
- Systemic inflammation (CRP, IL2, IL6, IL8, TNFα, fibrinogen)
- Low serum / dietary Mg
- Hypokalemia
Mechanisms of AF in CKD

- Chronic volume overload
  - LA size
- RAAS activation
  - Fibrosis
  - Electrical remodeling
- Sympathetic activation
- Dialysis
  - More AF during HD
AF Ablation in Dialysis Patients

First Report: N = 30 HD, 60 non-HD (matched on age/gender)

HD Patients:
- Larger LA
- Longer procedures
- More fluoroscopy
- Long RF times

![Graph showing freedom from AF recurrence](image-url)
# AF Prevalence by CKD Stage, Age, Race, Diabetes, HTN, CHF Status

<table>
<thead>
<tr>
<th>Stage of CKD</th>
<th>Stages 1-2</th>
<th>Stage 3</th>
<th>Stages 4-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFIB (Overall)</td>
<td>20.8</td>
<td>24.5</td>
<td>26.6</td>
</tr>
<tr>
<td>Age:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>66-69</td>
<td>11.3</td>
<td>14.7</td>
<td>16.8</td>
</tr>
<tr>
<td>70-74</td>
<td>14.9</td>
<td>18.0</td>
<td>20.8</td>
</tr>
<tr>
<td>75-84</td>
<td>22.6</td>
<td>25.1</td>
<td>26.6</td>
</tr>
<tr>
<td>85+</td>
<td>31.3</td>
<td>32.9</td>
<td>32.9</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>23.0</td>
<td>27.3</td>
<td>29.3</td>
</tr>
<tr>
<td>Female</td>
<td>18.8</td>
<td>22.0</td>
<td>24.4</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>22.9</td>
<td>26.3</td>
<td>29.3</td>
</tr>
<tr>
<td>Black/African American</td>
<td>12.9</td>
<td>15.4</td>
<td>14.2</td>
</tr>
<tr>
<td>Other race</td>
<td>11.7</td>
<td>16.1</td>
<td>18.6</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-diabetes</td>
<td>20.5</td>
<td>24.0</td>
<td>25.9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21.1</td>
<td>25.1</td>
<td>27.3</td>
</tr>
<tr>
<td>Non-hypertension</td>
<td>10.3</td>
<td>15.0</td>
<td>17.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21.7</td>
<td>25.2</td>
<td>27.0</td>
</tr>
<tr>
<td>No Heart Failure (CHF)</td>
<td>12.5</td>
<td>14.2</td>
<td>13.5</td>
</tr>
<tr>
<td>Heart Failure (CHF)</td>
<td>47.8</td>
<td>49.8</td>
<td>46.7</td>
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</table>

*Data Source: Special analyses, Medicare 5 percent sample. Patients aged 65 and older, alive, without end-stage renal disease, and residing in the U.S. on 12/31/2013 with fee-for-service coverage for the entire calendar year. Totals of patients for the study cohort: N=88,241; Stages 1-2=13,271; Stage 3=61,466; Stages 4-5=13,504. Abbreviations: AFIB, atrial fibrillation; CHF, congestive heart failure; CKD, chronic kidney disease.*
Risk of Stroke by AF Type: ACTIVE-A / AVERROES ASA Arms

**Figure 1** Kaplan–Meier cumulative hazard rates of embolic events according to the pattern of atrial fibrillation occurrence.

Vanassche et al. Eur Heart J 2014
1 Year Mortality: 39% versus 19%

What about other neurologic sequelae of AF?
Lower Mortality with Rate Control

Lower Mortality with Rhythm Control

Quebec, Canada populaion-based Study of Patients with AF

Mechanism of AF

Focal Triggers
1947

Multiple Wavelets
1959

PV Anatomy
Catheter in Pulmonary Vein: Pre-Ablation
Catheter in Pulmonary Vein: Post-Ablation
<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Rate Control</th>
<th>Rhythm Control</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>CRRAFT</td>
<td>5</td>
<td>40</td>
<td>0</td>
<td>46</td>
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<tr>
<td>Okou et al.</td>
<td>36</td>
<td>84</td>
<td>6</td>
<td>39</td>
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<tr>
<td>PIAF</td>
<td>2</td>
<td>125</td>
<td>2</td>
<td>127</td>
</tr>
<tr>
<td>Yildiz et al.</td>
<td>5</td>
<td>68</td>
<td>2</td>
<td>156</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>315</td>
<td></td>
<td>366</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Total events 48

Heterogeneity: Tau² = 0.00; Chi² = 2.85, df = 3 (P = 0.42); I² = 0%

Test for overall effect: Z = 3.38 (P = 0.0007)
Hazard ratios (HR) and 95% confidence intervals (CI) of atrial fibrillation (AF) according to urinary albumin-to-creatinine ratio (ACR) and estimated glomerular filtration rate from blood cystatin C (eGFRcys), Atherosclerosis Risk in Communities (ARIC), 1996 to 2007.

AF And Cognitive Impairment

Cognitive Function Evaluation

Scores

Immediate memory  Visuo-spatial  Language  Attention  Delayed memory

Controls  Paroxysmal  Persistent

AF And Cognitive Impairment

Incidence of Dementia by AF Status (n=37,026)

- **No AF**
- **AF**

Incidence (%)
- Non-specific
- Alzheimer's
- Senile
- Vascular

Bunch TJ et al. Heart Rhythm 2010; 7: 433