Atrium Fibrillatie en Chronische Nierschade: een duivelse combinatie

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Disclosures

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Disclosure of potential conflicts of interest

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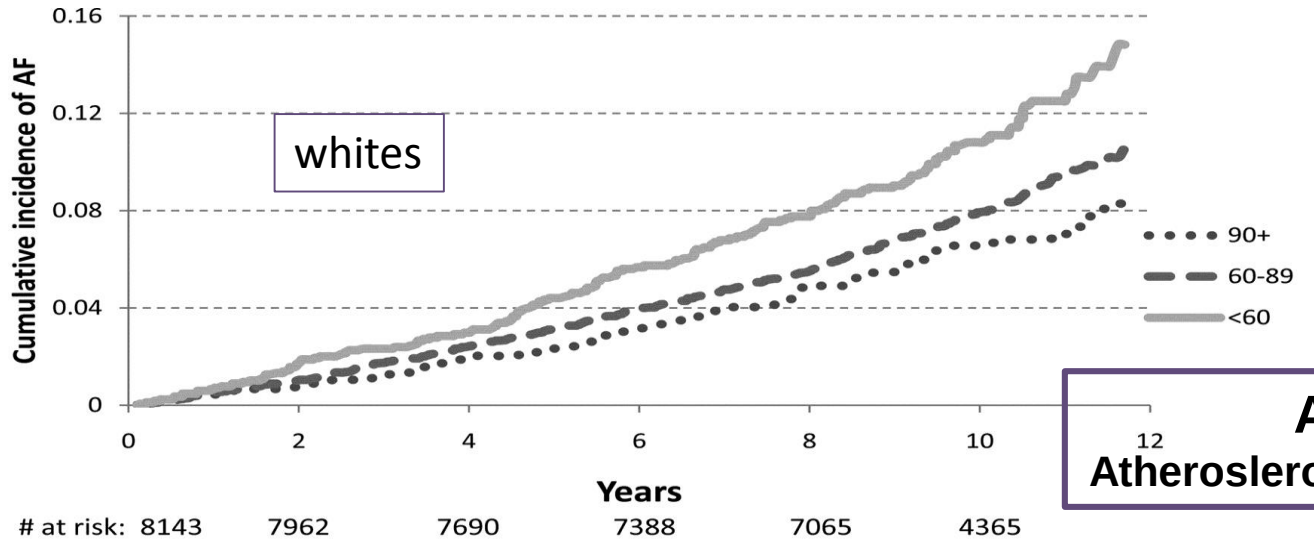
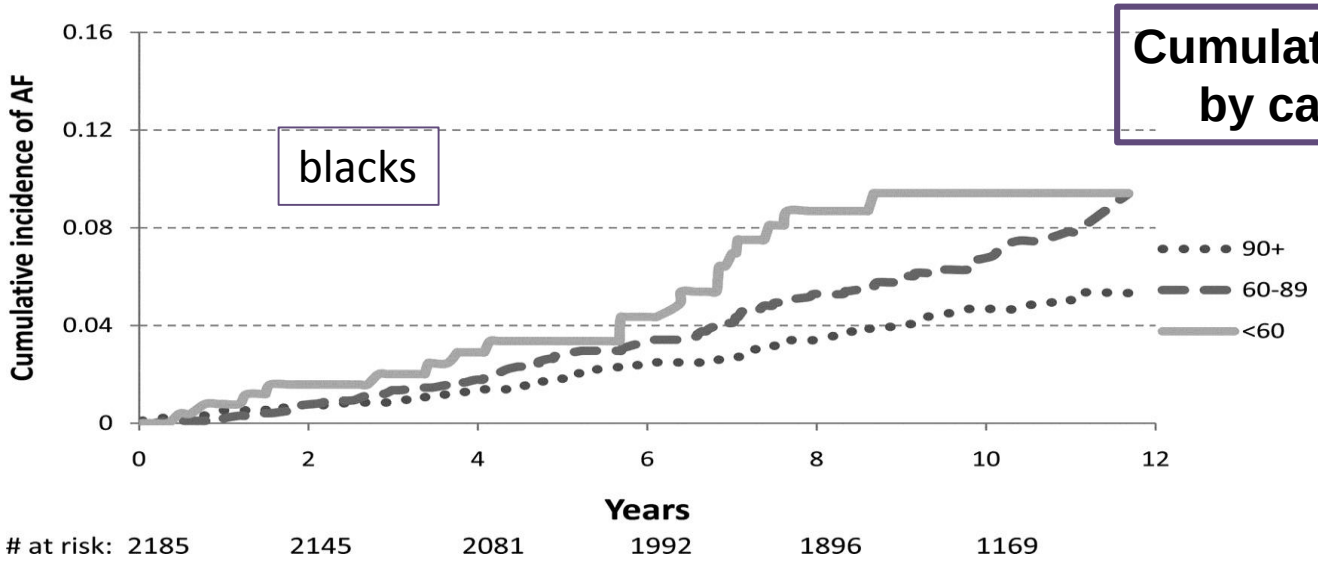
Stockholder of a healthcare company:	-None
Owner of a healthcare company:	-None
Other:	-None

Content

- Epidemiology: AF and CKD
- AF and CKD: chicken or egg?
- AF in CKD: to treat or not to treat?

AF & CKD: Epidemiology



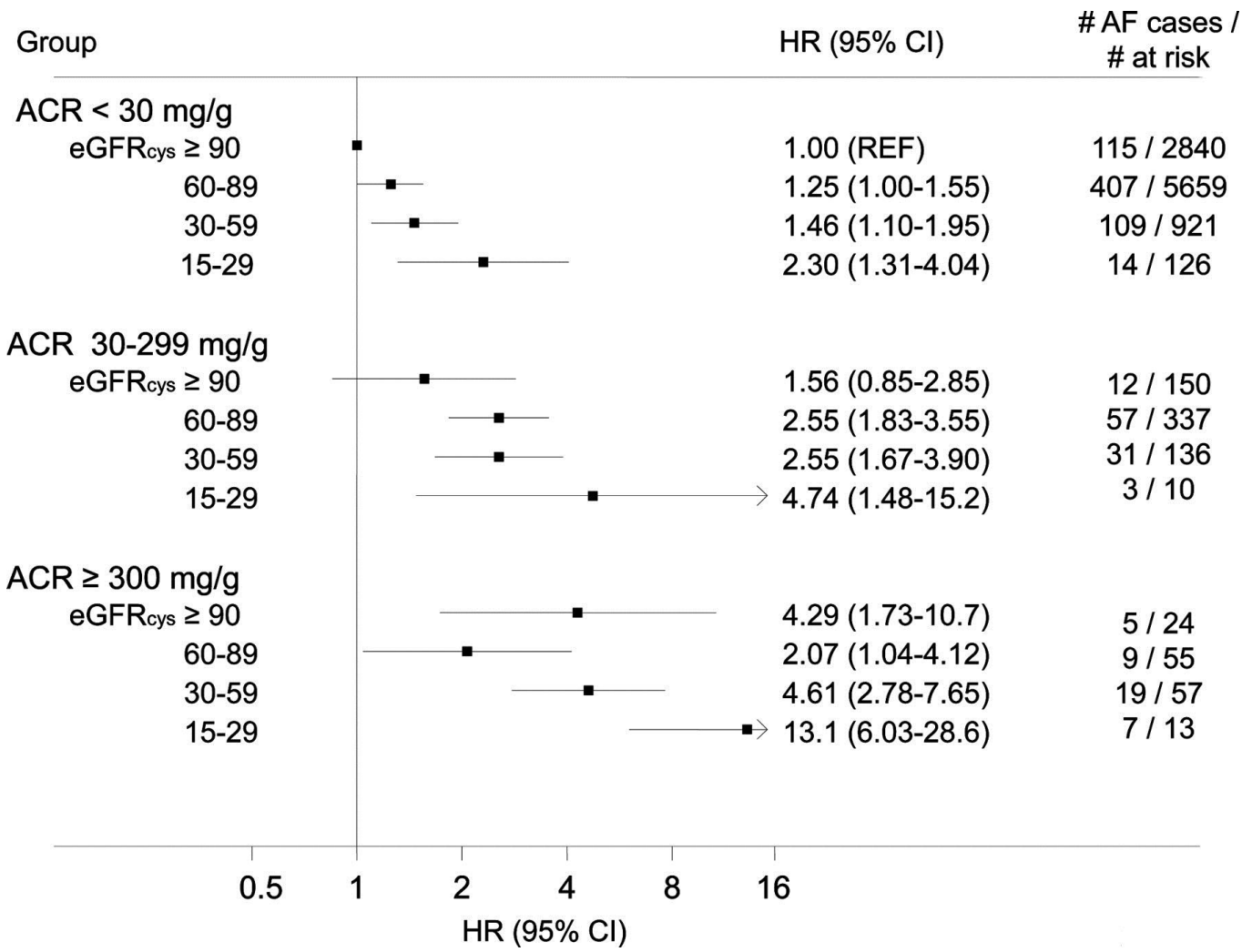


ARIC study
Atherosclerosis Risk in Community

Cumulative incidence of AF by categories of eGFR

Alonso A et al. Circulation. 2011;123:2946-2953

AF & CKD: Epidemiology



ARIC study

Adjusted HR of AF increases with:

lower eGFR
higher albuminuria

Alonso A et al. Circulation. 2011;123:2946-2953

AF & CKD: Epidemiology

CKD is associated with an increased prevalence of AF among US adults (>45 yr).

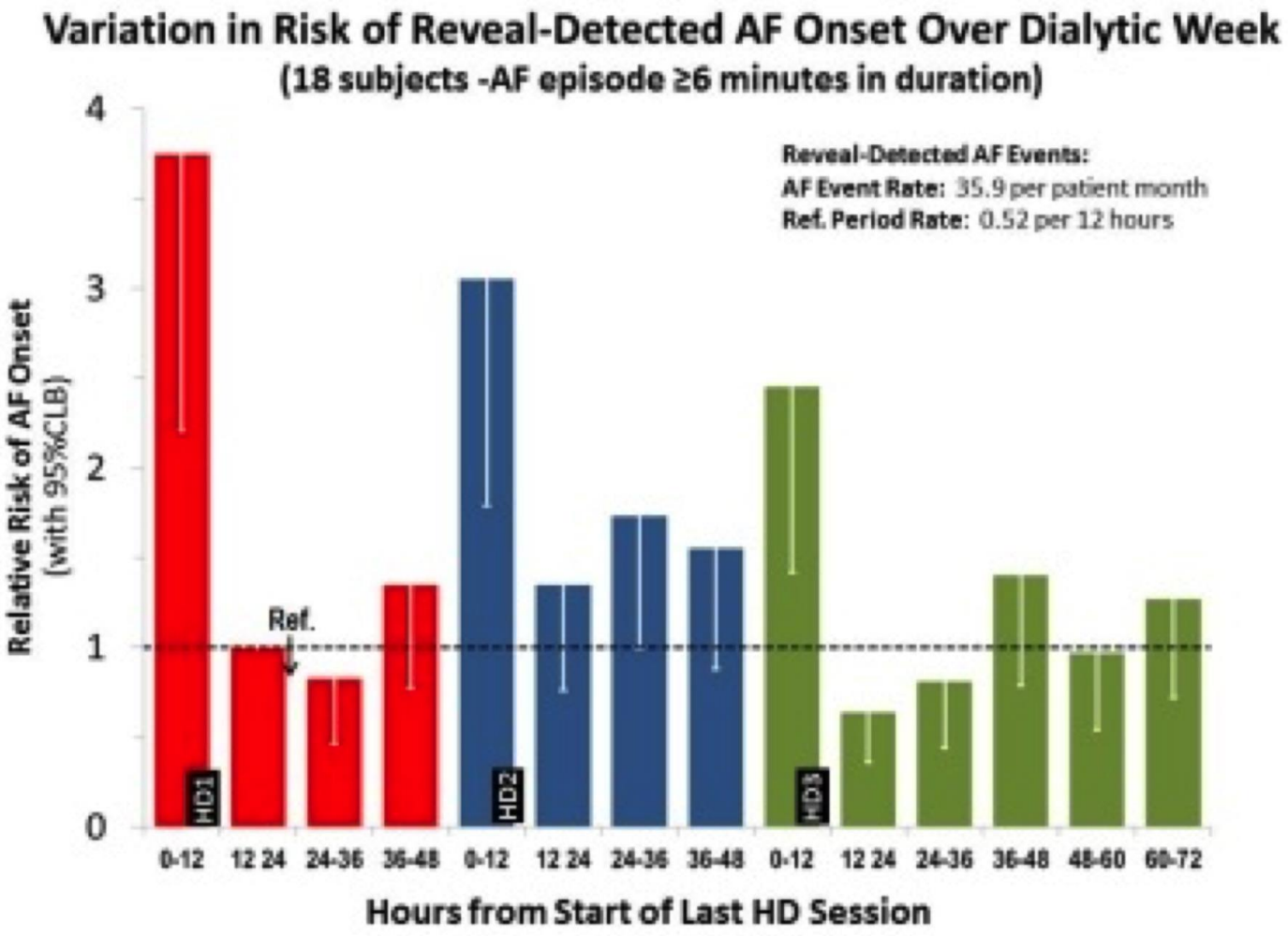
REGARDS
26 917 participants
ECG detected AF

	Number	Prevalence of AF	OR for AF (adjusted)
No CKD	21.081	1%	
CKD stage 1-2	2938	2.8%	2.67
CKD stage 3	2638	2.7%	1.68
CKD stage 4-5	215	4.2%	3.52

Albuminuria was strongly associated with AF
Hypertension was not associated with AF
African-Americans have lower risk of AF
RAS blockade does not protect for AF

Circulation: Arrhythmia and Electrophysiology. 2011; 4: 26-32

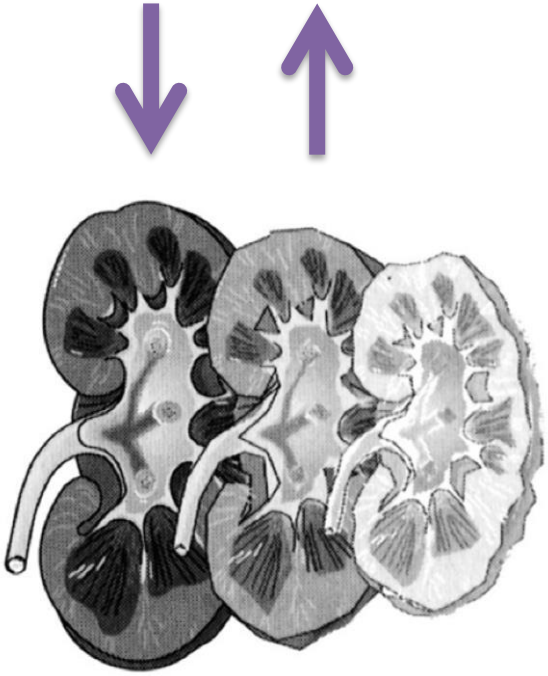
AF & CKD: Epidemiology

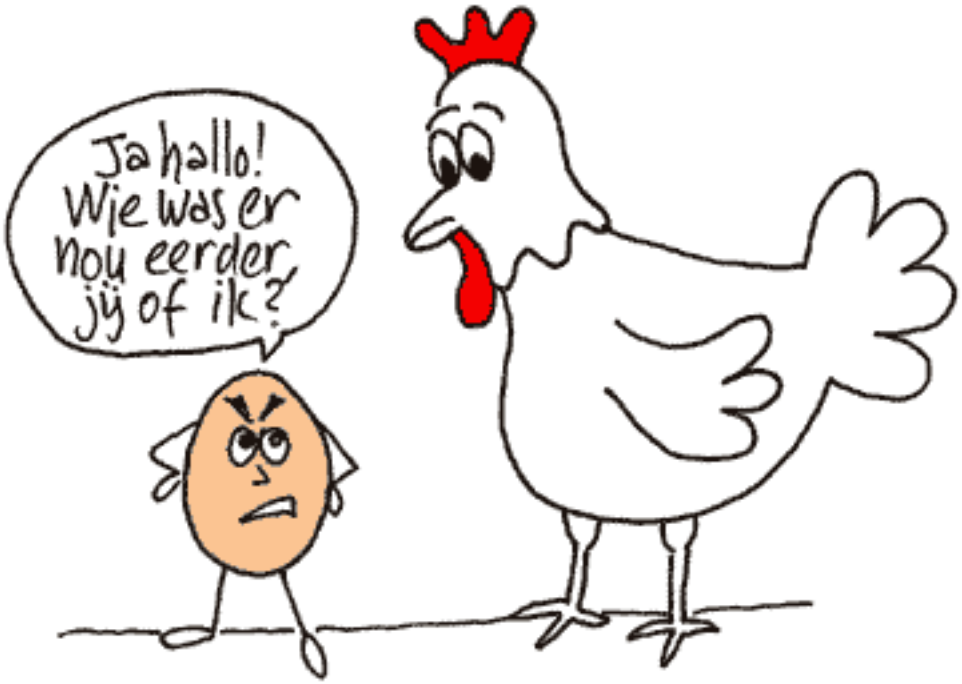


TH-OR144
J. Tumlin et al

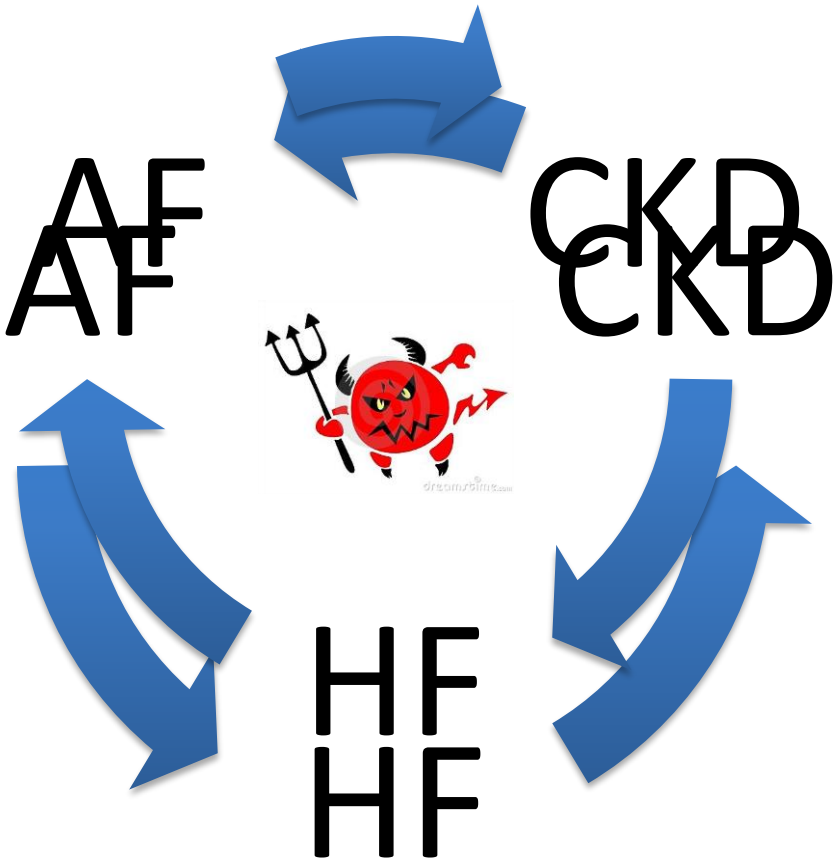
In 40% of 45 HD patients AF is seen,
with greatest incidence in 12 hours after initiation of dialysis

AF & CKD: chicken or egg?





AF & CKD: chicken or egg?



AF & CKD: chicken or egg?

CRIC study
Chronic Renal Insufficiency Cohort
3091 participants without AF at baseline

Association between incident AF (self-reported and/or ECG confirmed) and ESRD during mean follow up of 5.9 years

Incident AF indepently increases the risk of developing ESRD:

4.23 per 100 p-y (with AF)
3.54 per 100 p-y (without AF)

Abstract FR-OR022
N.Bansal et al

AF & CKD: chicken or egg?

- 206.229 adults with eGFR < 60

  (members of Kaiser Permanente Northern California)

- Follow up 5 yr

⇒Incident AF (based on primary hospital discharge diagnoses) is associated with 67% increased risk for development of ESRD

⇒AF may contribute to an accelerated progression of CKD to ESRD independent of other known risk factors.

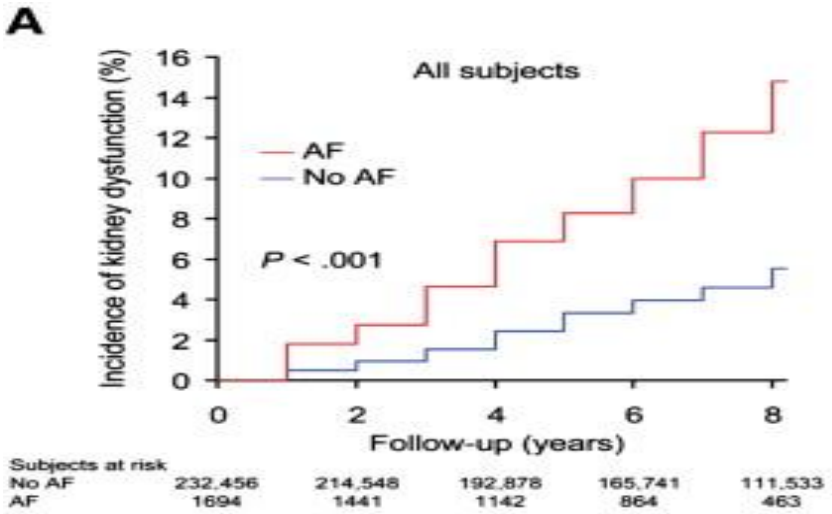
Bansal, Circulation 2013; 127:569-574

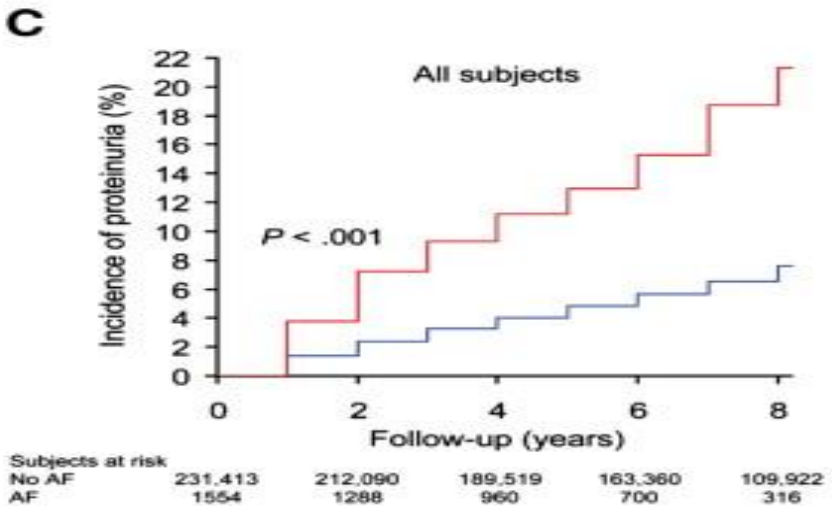
AF & CKD: chicken or egg?

Cumulative risk of developing kidney disease and proteinuria by baseline AF.

Japanese cohort 235.818 subjects
Follow up 5.9 yr

Watanabe et al. American Heart Journal, 2009, 629 - 636





CKD increased risk of new onset AF

AF increased the risk of development of CKD
HR for kidney dysfunction 1.77 (1,5-2,2)
HR for proteinuria 2.2 (1,95-2,5)

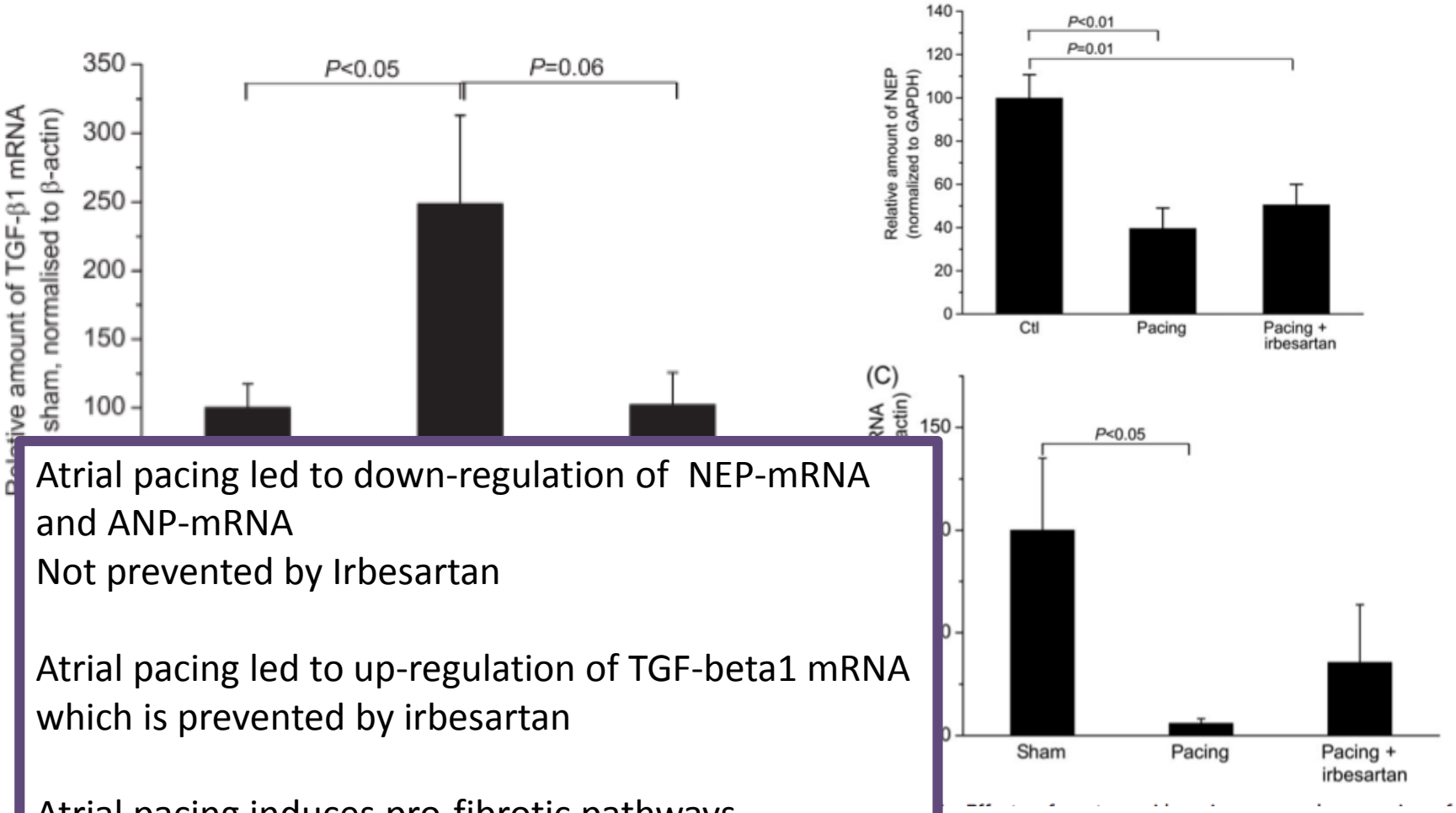
AF & CKD: chicken or egg?

Potential mechanisms of AF causing CKD:

- Profibrotic effects
- Renal hemodynamic changes
- Activation RAS
- Microthrombi
- Alterations of cardiac hemodynamics

AF & CKD: chicken or egg?

Effects of rapid atrial pacing on renal gene expression patterns in pigs



Atrial pacing led to down-regulation of NEP-mRNA and ANP-mRNA
Not prevented by Irbesartan

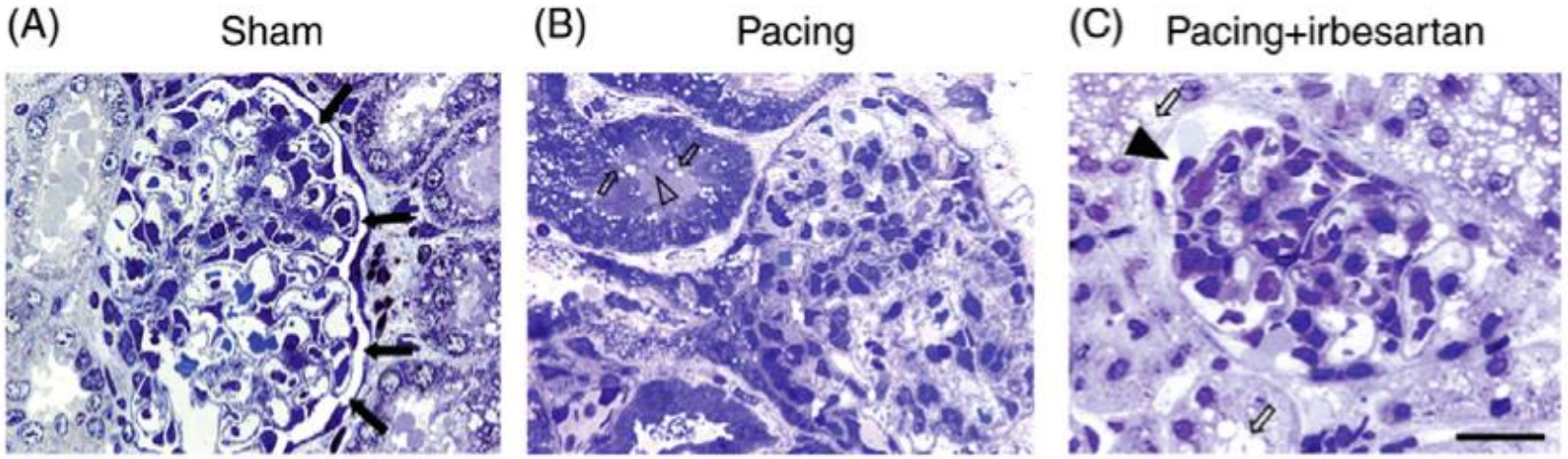
Atrial pacing led to up-regulation of TGF-beta1 mRNA which is prevented by irbesartan

Atrial pacing induces pro-fibrotic pathways

Bukowska et al. Eurospace 2008

AF & CKD: chicken or egg?

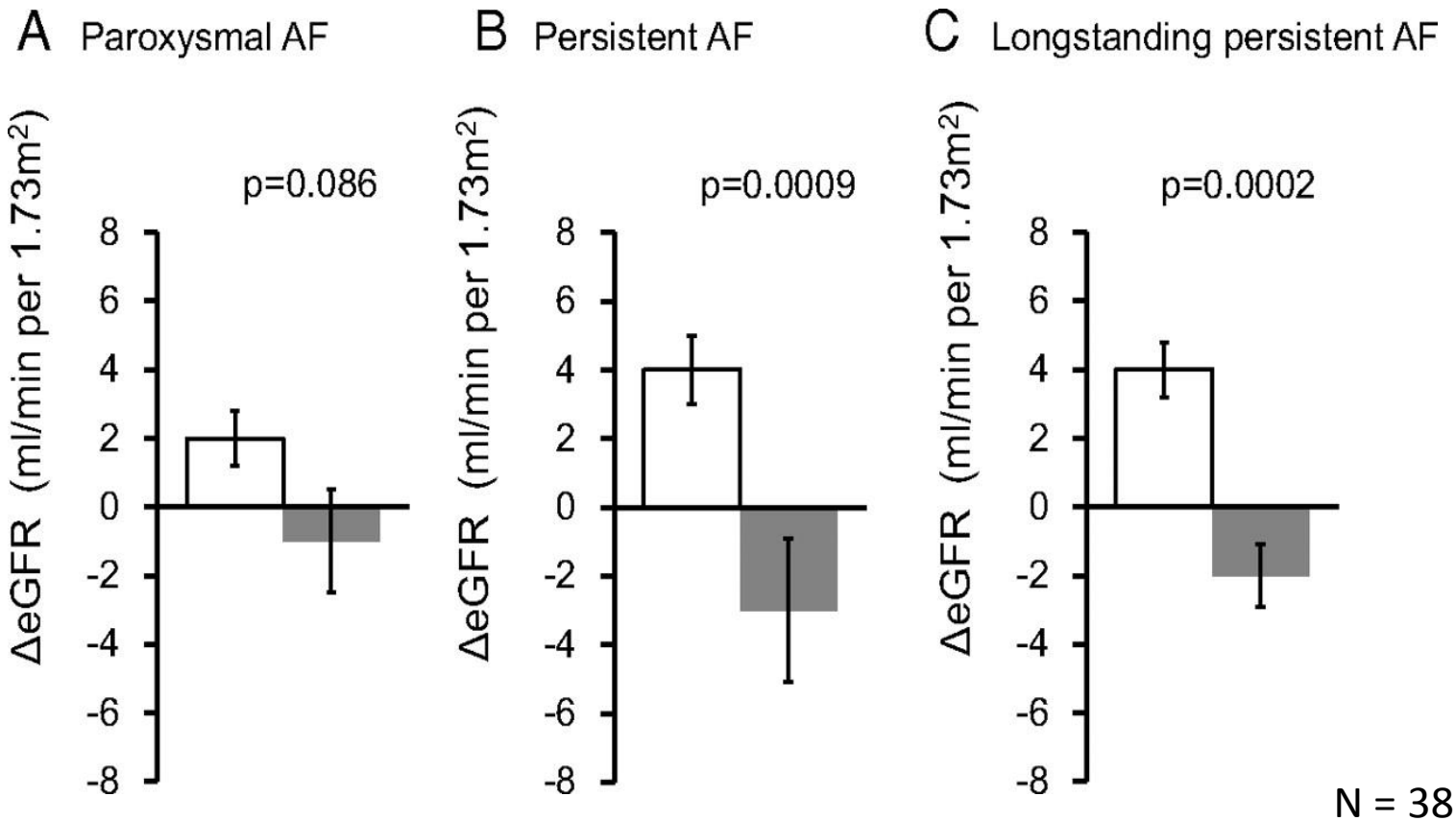
Histomorphology of the kidney is affected by AF



Disintegrated Bowman's capsules
Vacuoles in proximal tubules
Segmental attachments of glomerular tufts
Protein casts

AF & CKD: chicken or egg?

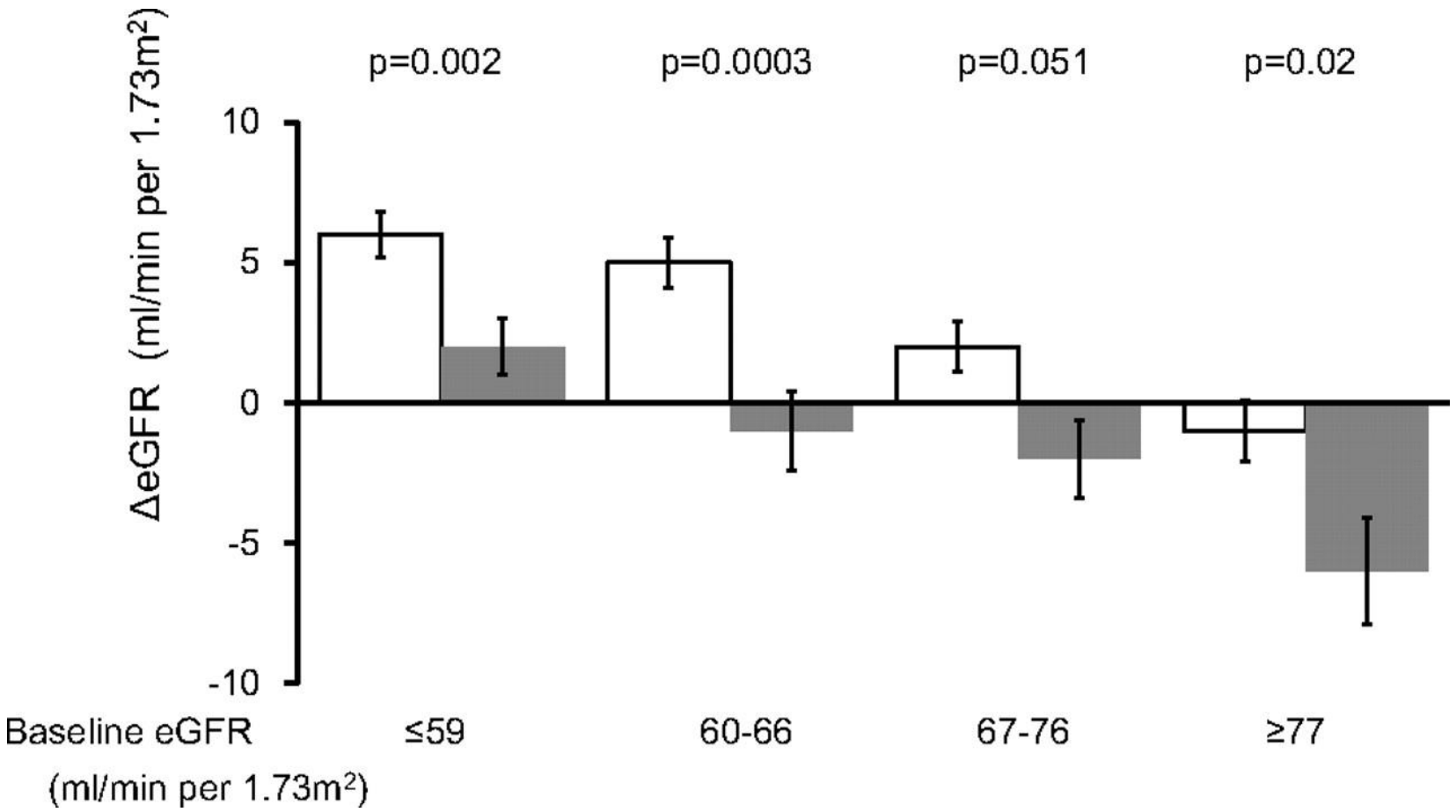
Renal function 1 year after catheter ablation for AF



Takahashi Y et al.
Circulation. 2011;124:2380-2387

AF & CKD: chicken or egg?

Improvement in eGFR after catheter ablation best in lowest eGFR group



Takahashi Y et al. Circulation. 2011

AF & CKD: chicken or egg?

Restoration of arrythmia after ablation increases eGFR in stage 3 CKD

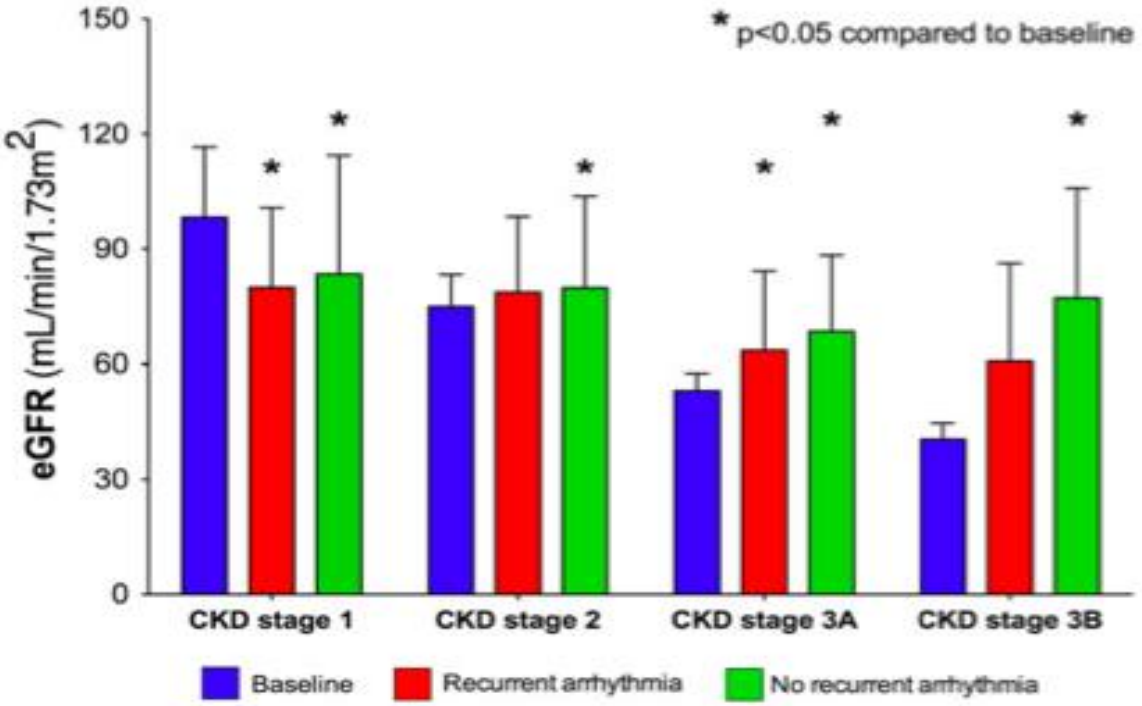
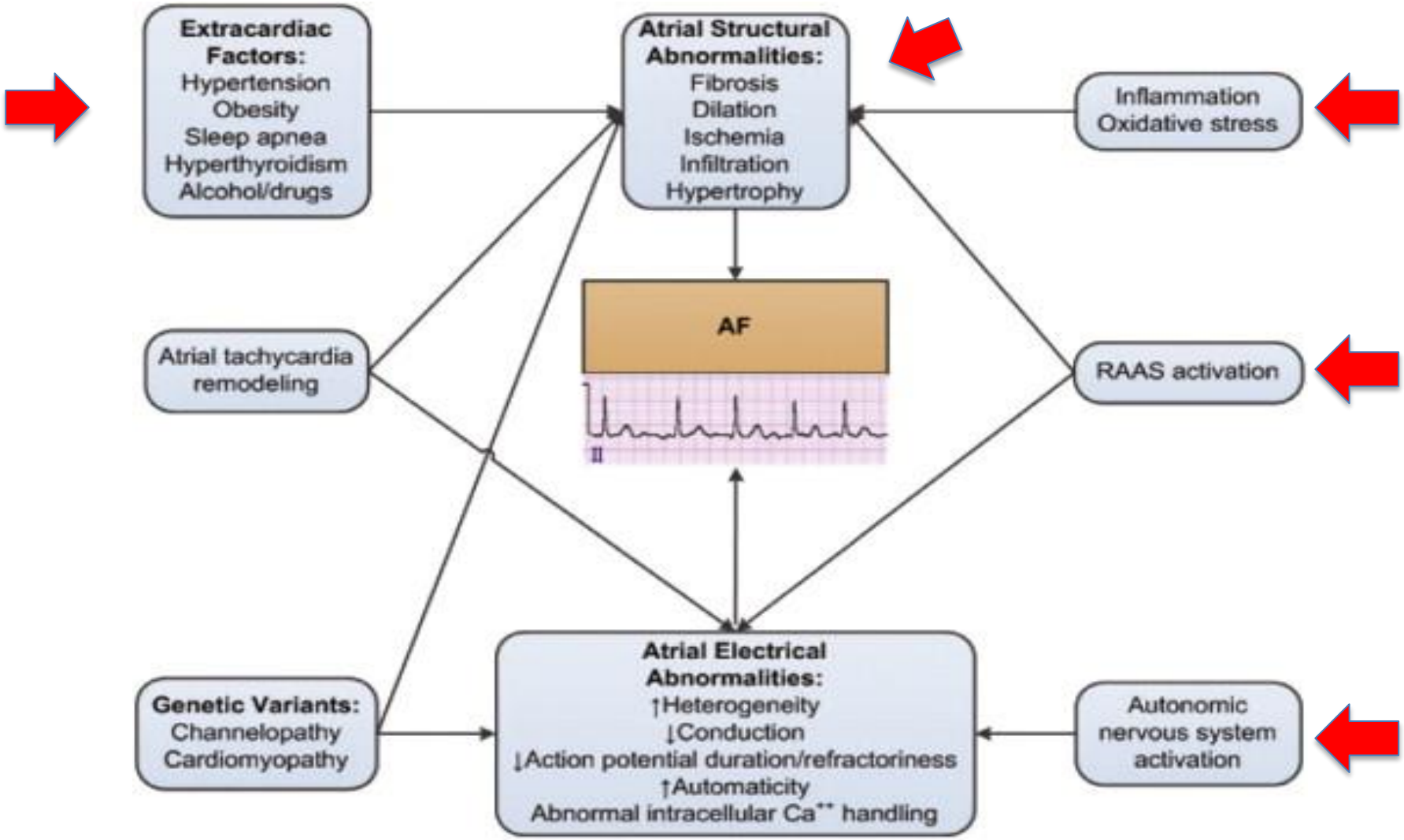


Figure 4. *Bar graphs of eGFRs at baseline (blue) and after ablation in patients with (red) and without (green) arrhythmia recurrence across the different stages of CKD.*

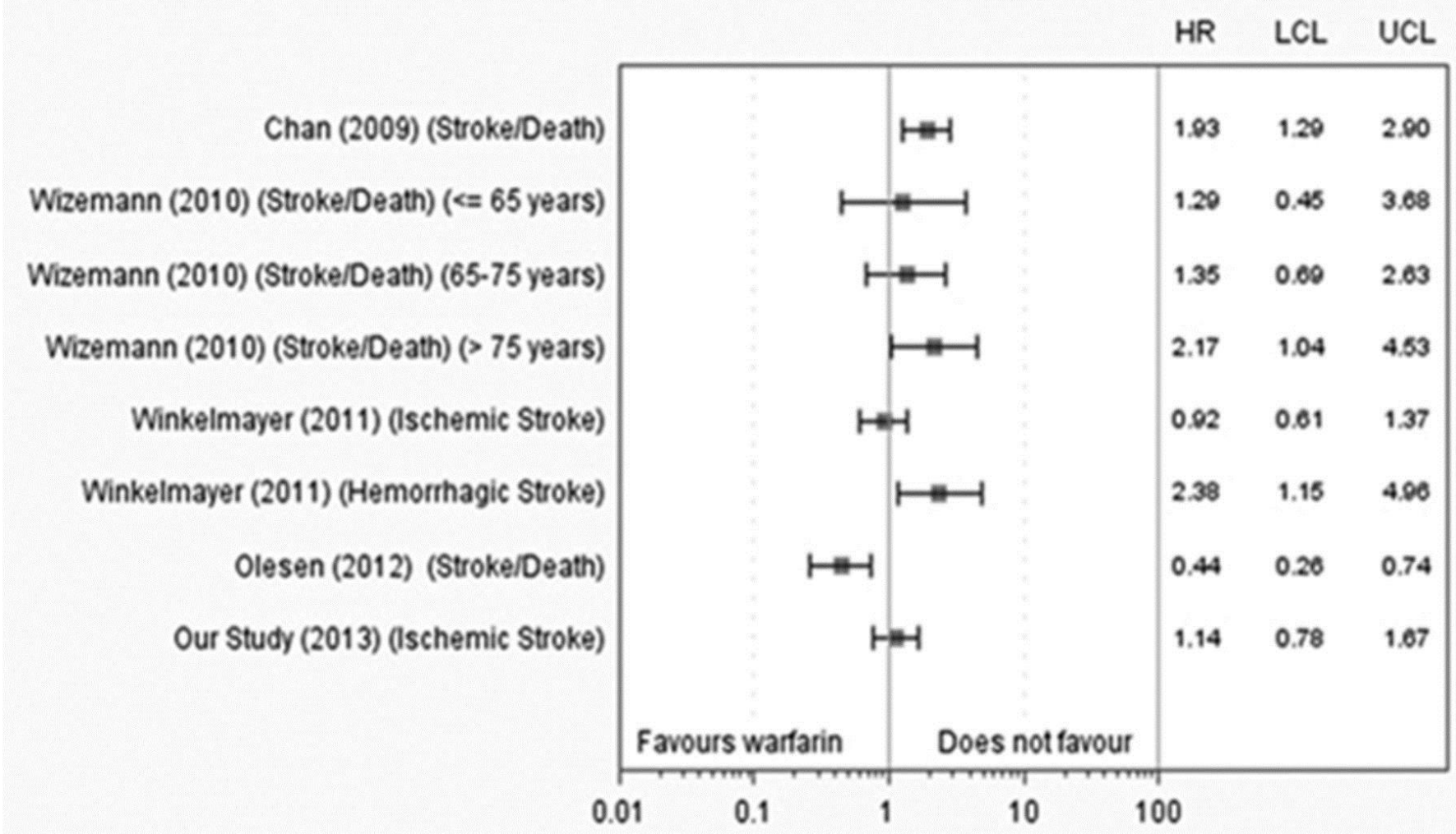
Navaravong, J Cardiovasc Electrophysiol 2014

AF & CKD: chicken or egg?



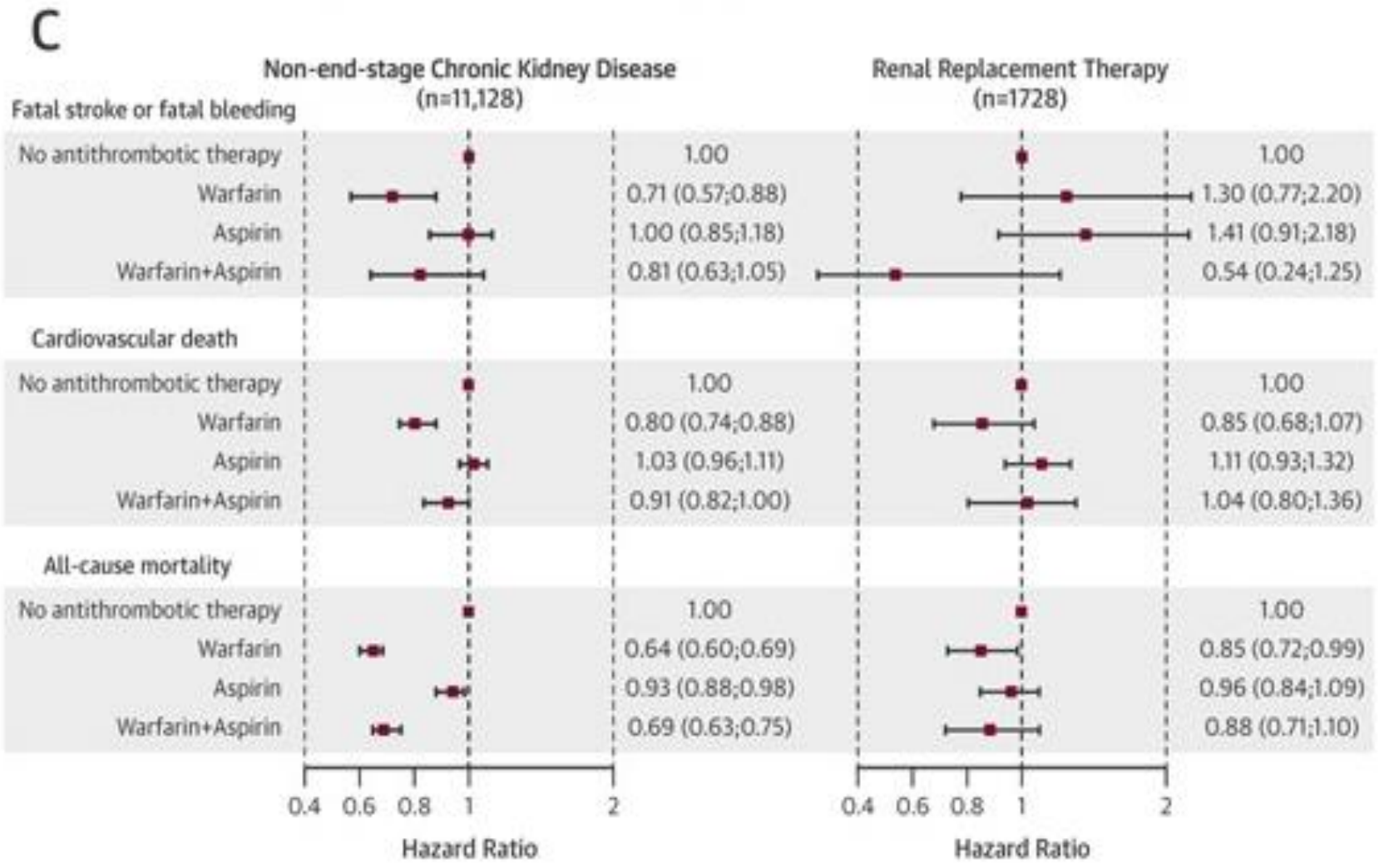
AF in CKD:To treat or not to treat?

Warfarin use and the risk for stroke in patients with atrial fibrillation undergoing dialysis.



Shah M et al. Circulation. 2014;129:1196-1203

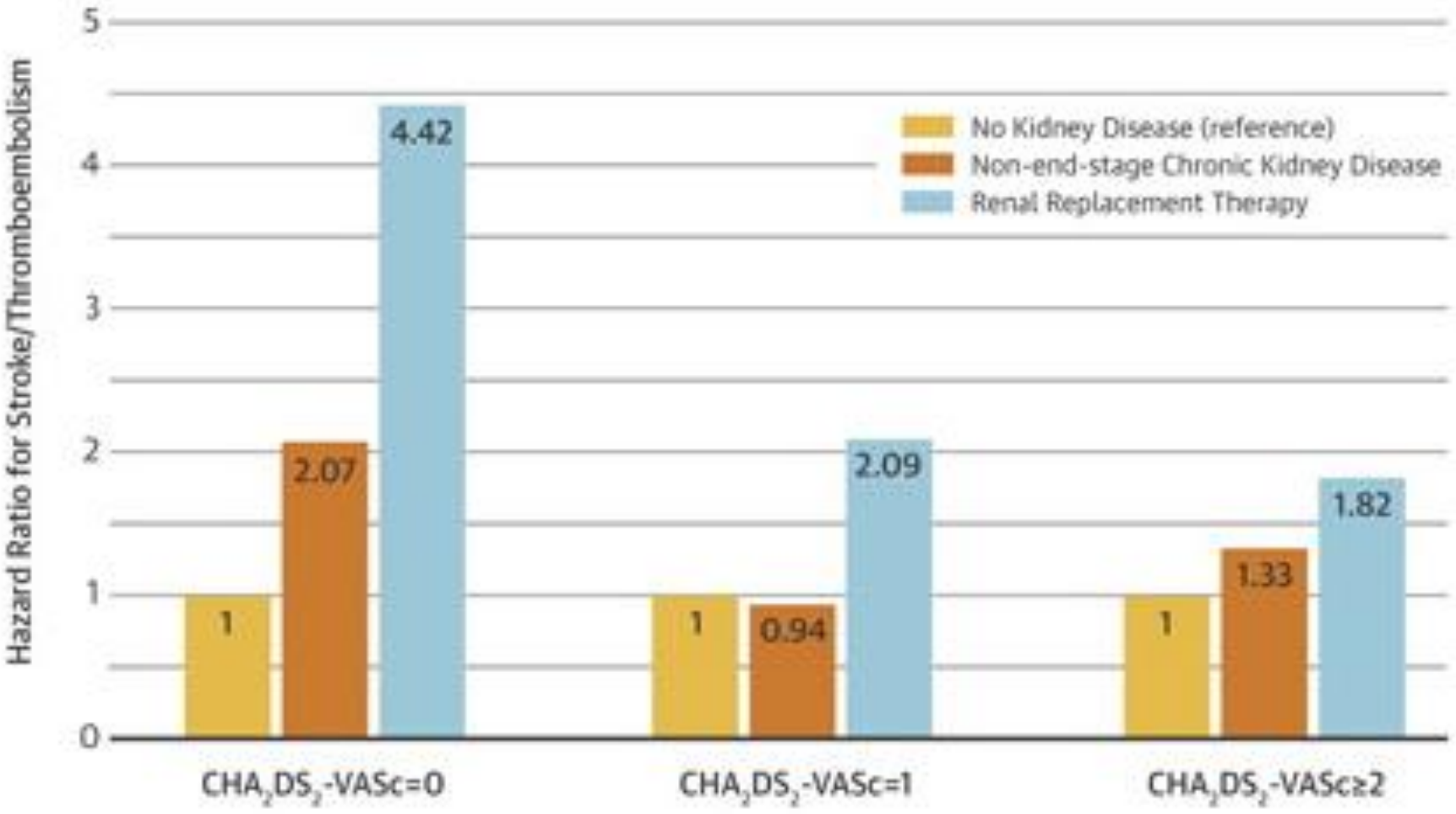
AF in CKD:To treat or not to treat?



Bonde, A.N. et al. J Am Coll Cardiol. 2014; 64(23):2471-82.

AF in CKD:To treat or not to treat?

AF in RRT is associated with higher risk of stroke, especially in low risk patients



Bonde, J Am Coll Cardiol, 2014

AF in CKD:To treat or not to treat?

Risk of onset stroke is increased in incident HD patients,
and associates with CV risk factors but not with prevalent AF

- 1382 HD patients
- Age 62.9 yrs
- Prevalence of AF 21,2% (59,4% incident)
- Stroke incidence 39,7/1000 patient years (prevalent pt) and 54,3/1000 patient years (incident patients).

- No correlation between AF and stroke
- No difference in stroke in patients with AF treated with warfarin or not

- Factors associated with high risk of stroke:
  - Incident AF
  - Hypo albuminemia
  - DM
  - Age
  - Prior CeVD

Abstract FR-PO1031
M D Findlay

AF in CKD:To treat or not to treat?

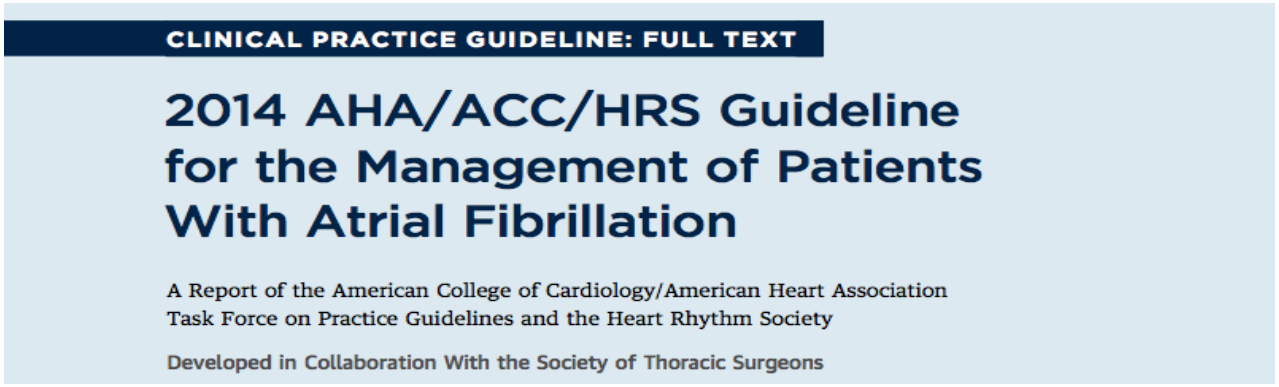
USRDS data
443.890 incident HD patients
39.387 with diagnosis of AF at incident date of dialysis

Mortality following anticoagulation therapy (OAT) for AF in ESRD

Table 1			
Patients with AF (39,387); with AF and OAT (5,048)			
	<90d from IDD	>90d from IDD	none
Stroke (3,129)	5.3%	2.6%	92.1%
OAT with Stroke (446)	6.0%	2.9%	91.1%
Death (27,632)	50.8%	19.3%	29.8%
OAT with Death (3,837)	57.4%	18.6%	24.0%
OR for Death Controlling for OAT (95% CI)	1.31 (1.21-1.42)	1.09(0.99-1.20)	

Conclusion:
AF in incident HD patients carries a high mortality
OAT increases risk of death in first 3 months of dialysis

Abstract FR-PO1029
MJ Diamond et al



For patients with nonvalvular AF with a CHA2DS2-VASc score of 2 or greater and who have end-stage chronic kidney disease (CKD) (creatinine clearance [CrCl] <15 mL/min) or are on hemodialysis, it is reasonable to prescribe warfarin (INR 2.0 to 3.0) for oral anticoagulation (Level of Evidence: B)

For patients with nonvalvular AF and moderate-to-severe CKD with CHA2DS2-VASc scores of 2 or greater, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (e.g., dabigatran, rivaroxaban, or apixaban), but safety and efficacy have not been established.

(Level of Evidence: C)

The direct thrombin inhibitor dabigatran and the factor Xa inhibitor rivaroxaban are not recommended in patients with AF and end-stage CKD or on dialysis because of the lack of evidence from clinical trials regarding the balance of risks and benefits

(Level of Evidence: C)

Take home messages

- CKD and albuminuria are associated with higher risk of AF, especially in whites

- AF can cause deleterious effects on kidney function and albuminuria by both hemodynamic and pro-inflammatory effects

- Treatment of AF by ablation can be beneficial for kidney function especially in stages CKD 3-5

Take home messages

- CKD increases risk for thrombo-embolic events among patients with AF
- Treatment with warfarin (and NOAC's) seems beneficial in patients with CKD stages 1-3
- Treatment with aspirin does not show any benefit in any group of CKD patients
- There are still conflicting data on benefit of treatment with warfarin for AF in patients with ESRD