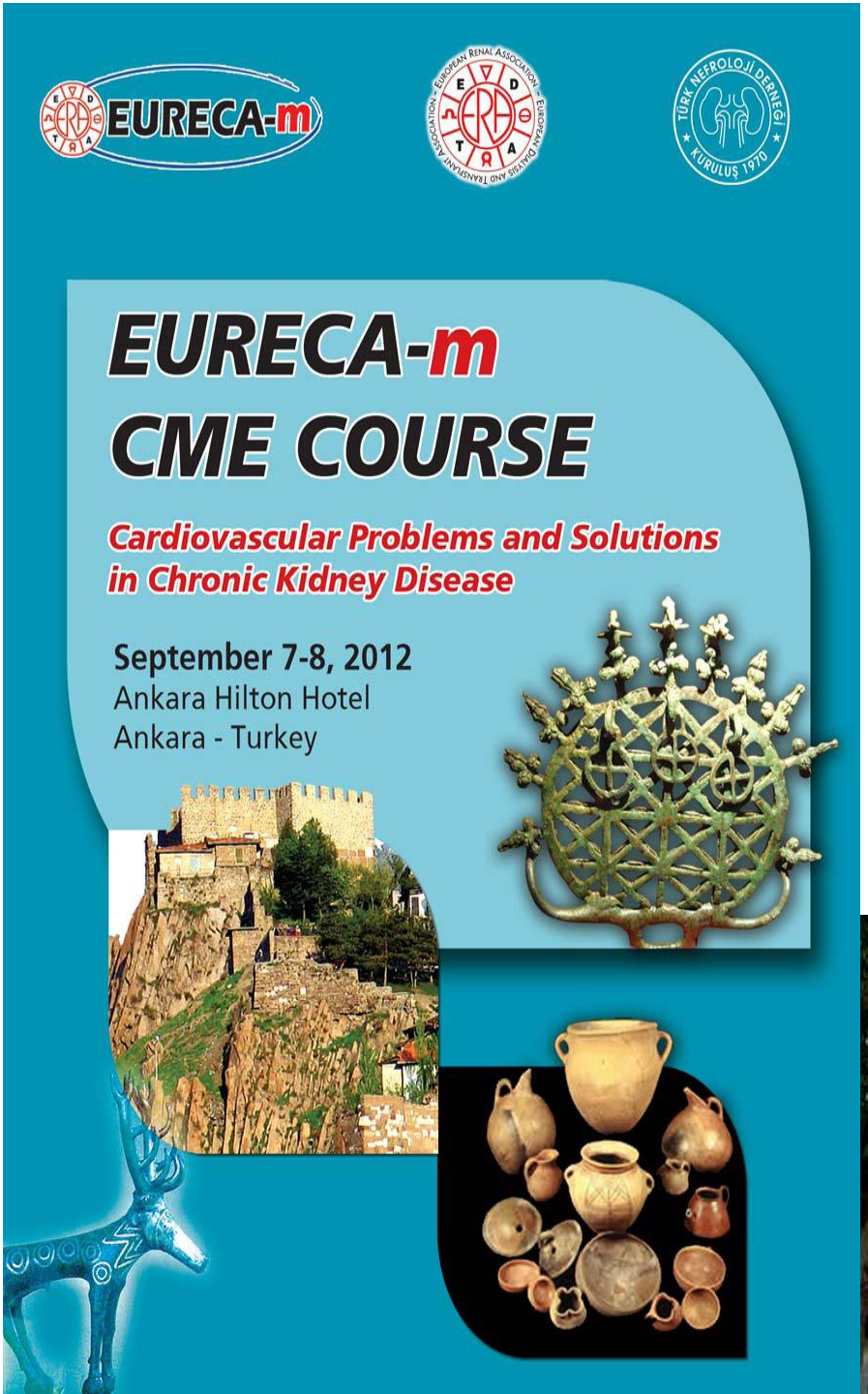


Atrial fibrillation as a cardiovascular risk factor in CKD

Adrian Covic

Content

1. *Epidemiology of atrial fibrillation*
2. *Factors associated with atrial fibrillation in CKD*
3. *Consequrences of atrial fibrillation in CKD*
4. *Treatment options:*
   - *Stroke risk and anticoagulation therapy*
   - *Heart rate control vs rhytm conversion*

Epidemiology of AF : general population

- The most common cardiac dysrhythmia;
- The prevalence rises with age from 0.4-1% app. 8% (by age 90)

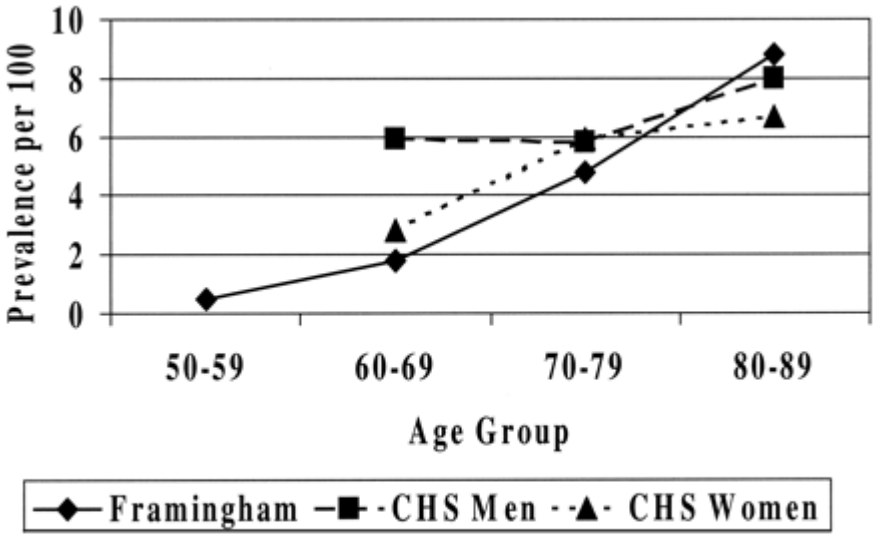


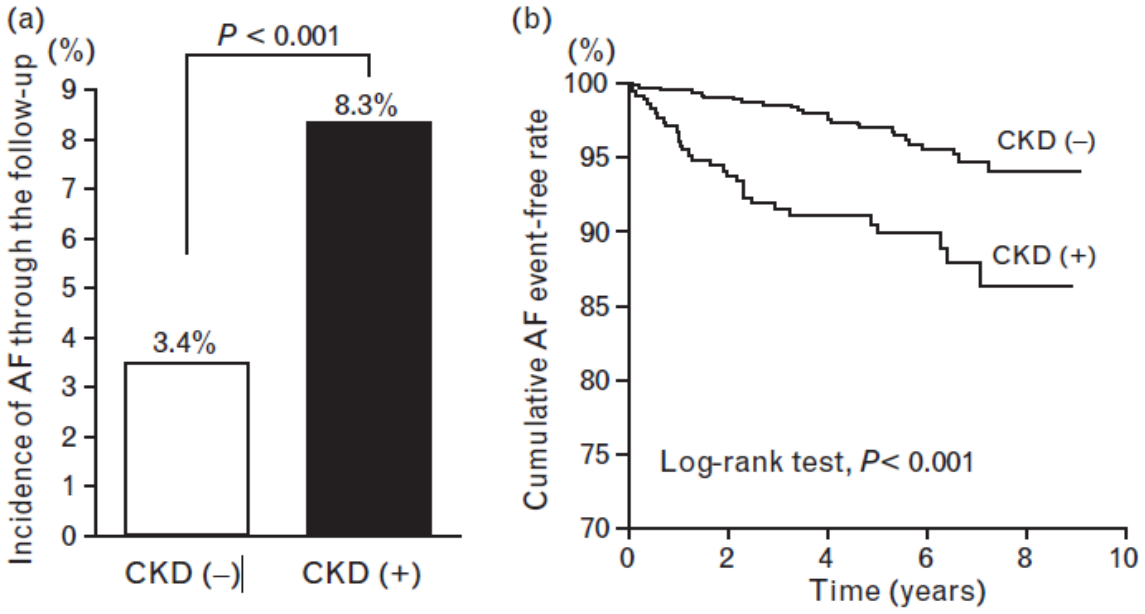
Figure 2. Prevalence of AF in 2 American epidemiological studies. Framingham indicates the Framingham Heart Study ([9]); CHS, Cardiovascular Health Study ([10]).

- In CKD and ESRD AF is common, with prevalence *several time higher* than in general population

ACC/AHA Practice Guidelines, Circulation 2001

Epidemiology of AF : CKD populations

N - 1118 hypertensive patients without previous paroxysmal AF, heart failure, MI, or valvular disease ;
The mean duration of follow-up was 4.5 years
57 cases of new-onset AF were found

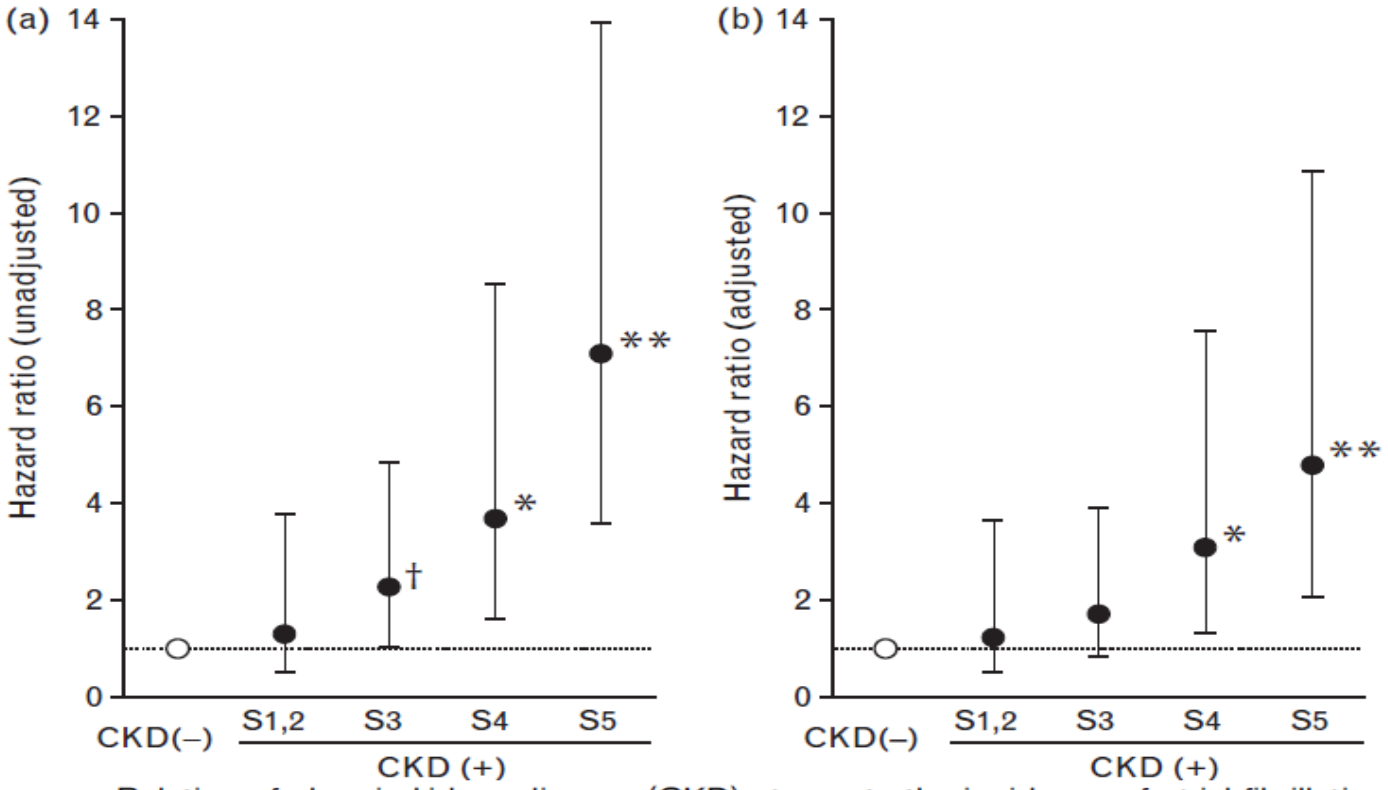


(a) Incidence of atrial fibrillation (AF) through the follow-up periods in the two groups without and with chronic kidney disease (CKD). (b) AF event-free Kaplan–Meier curves in the two groups without and with CKD.

The incidence of AF was markedly higher in the patient group with CKD

Horio, J Hypertens. 2010

Progressing renal dysfunction – a powerful predictor of new-onset AF

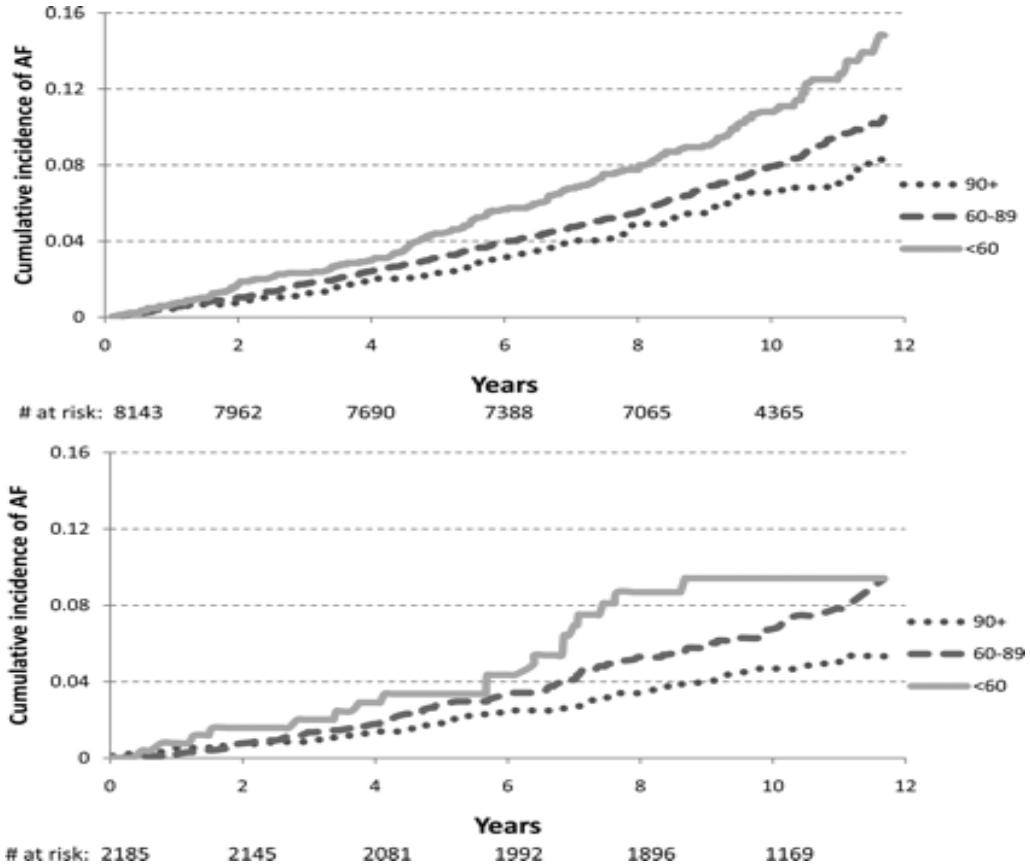


Relation of chronic kidney disease (CKD) stages to the incidence of atrial fibrillation (AF) evaluated by univariate (a) and multivariate (b) Cox regression analysis.

Horio, J Hypertens. 2010

The same high incidence in another large cohort…

N = 10, 328 individuals free of AF participating in the Atherosclerosis Risk in Communities (ARIC) study



Caucasians

African-Americans

There was a strong association between the degree of impaired renal function and the risk of development of AF

Alonso A, Circulation 2011

Chronic kidney disease and prevalent atrial fibrillation: The Chronic Renal Insufficiency Cohort (CRIC)

Elsayed Z. Soliman, MD, MSc, MS, Ronald J. Prineas, MD, PhD, Alan S. Go, MD, Dawei Xie, PhD, James P. Lash, MD, Mahboob Rahman, MD, Akinlolu Ojo, MD, Val L. Teal, MS, Nancy G. Jensvold, MPH, Nancy L. Robinson, PhD, Daniel L. Dries, MD, MPH, Lydia Bazzano, MD, PhD, Emile R. Mohler, MD, Jackson T. Wright, MD, PhD, Harold I. Feldman, MD, MSCE, Chronic Renal Insufficiency Cohort (CRIC) Study Group

American Heart Journal
Volume 159, Issue 6, Pages 1102-1107, June 2010

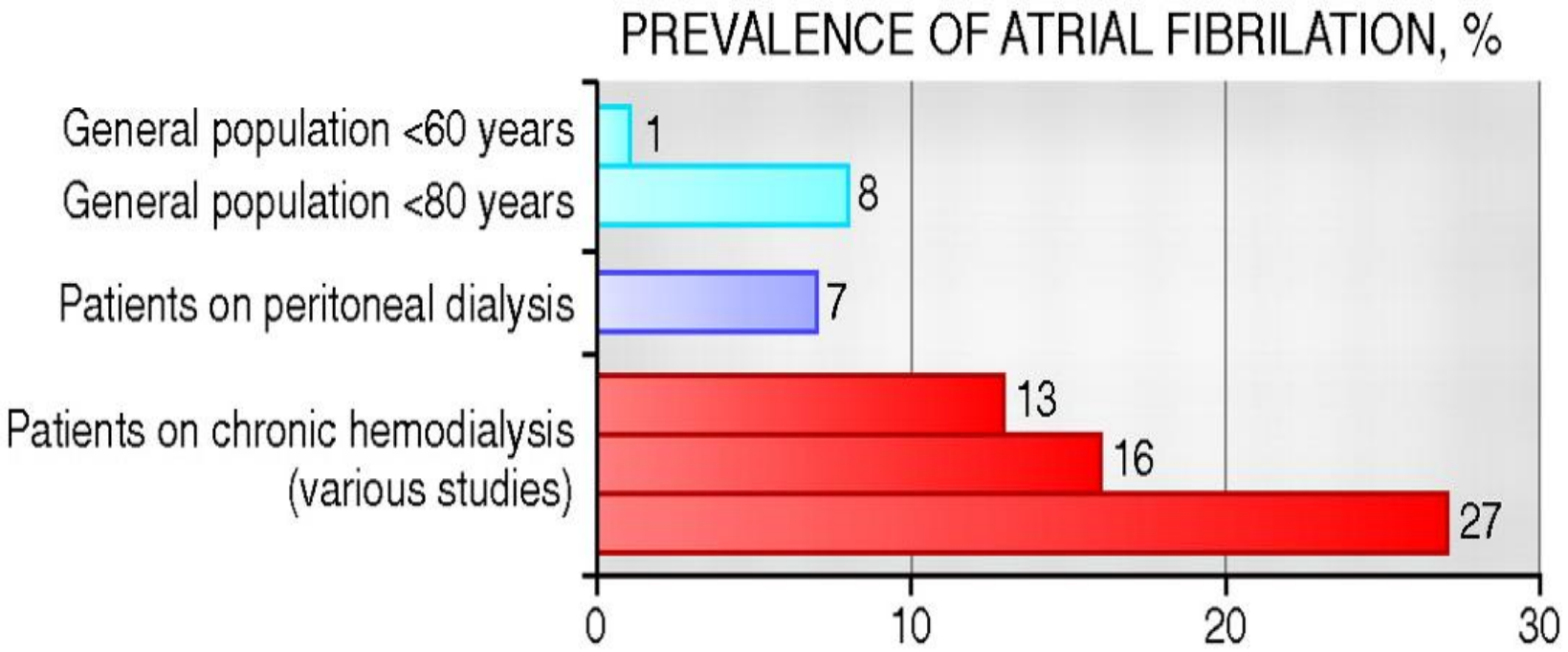
N = 3267 adult participants (50% non-Hispanic blacks, 46% females) with CKD from the Chronic Renal Insufficiency Cohort (CRIC)

Prevalence of atrial fibrillation by eGFR,

		N=3267	Atrial fibrillation N (%)	P-value
All population		3267	602 (18.4%)	
Estimated glomerular filtration rate (eGFR) (ml/min/1.73 m²)				0.0010
	< 45	1795	367 (20.4%)	
	>= 45	1472	235 (16.0%)	

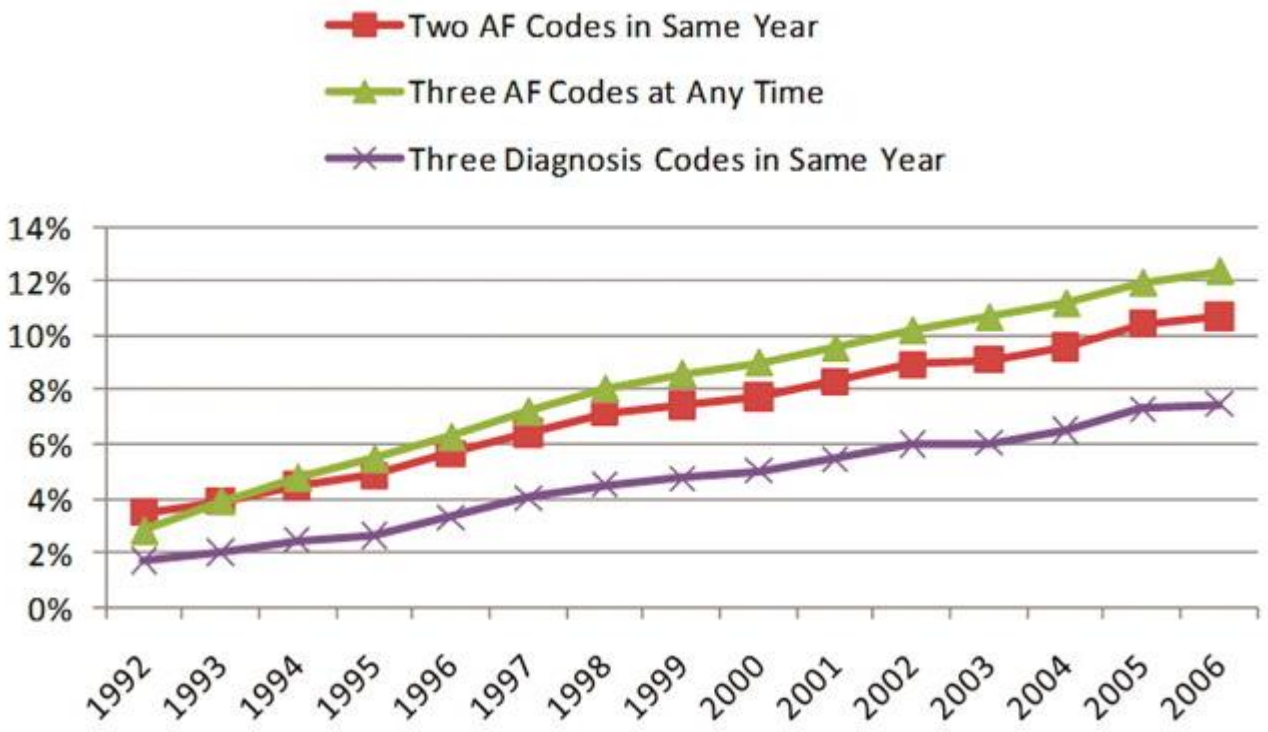
High prevalence of atrial fibrillation in a large CKD cohort

Epidemiology of AF: ESRD populations



Prevalence of atrial fibrillation in patients with ESRD seems to be 10- to 20-fold higher than in the general population

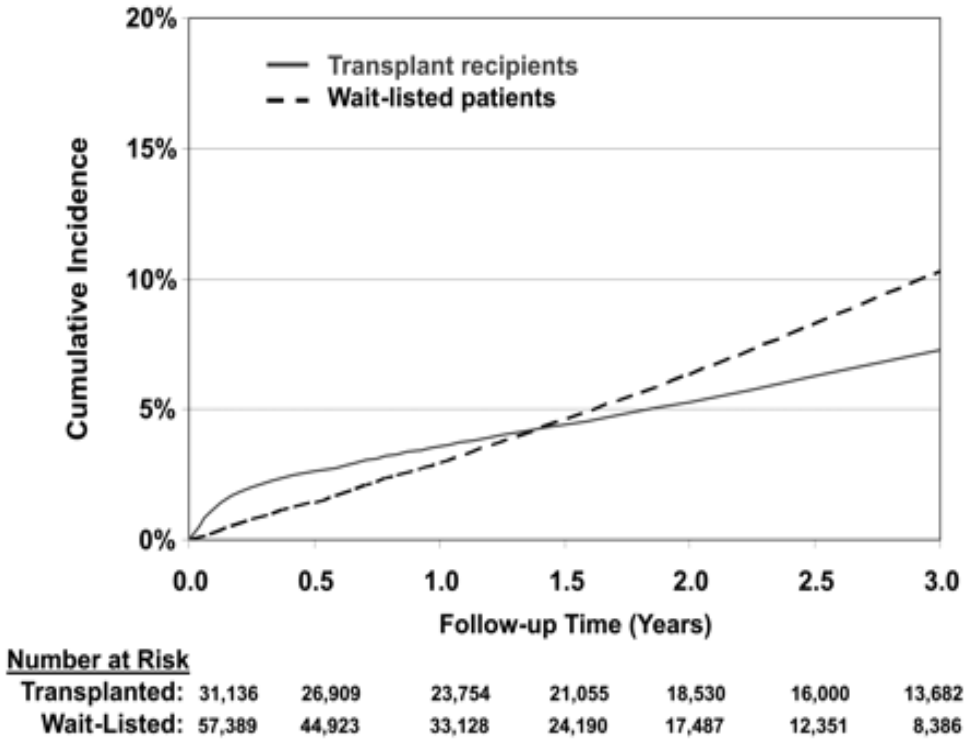
Moreover…prevalence in ESRD is increasing



In the past 15 yrs, the prevalence of diagnosed AF has tripled and the number of affected patients has increased almost 7-fold.

Winkelmayer, JASN 2011

Epidemiology of AF after renal transplantation



new-onset AF after renal transplantation is common, affecting 7% of renal allograft recipients by 3 yr posttransplantation

Lentine, cJASN 2006

Content

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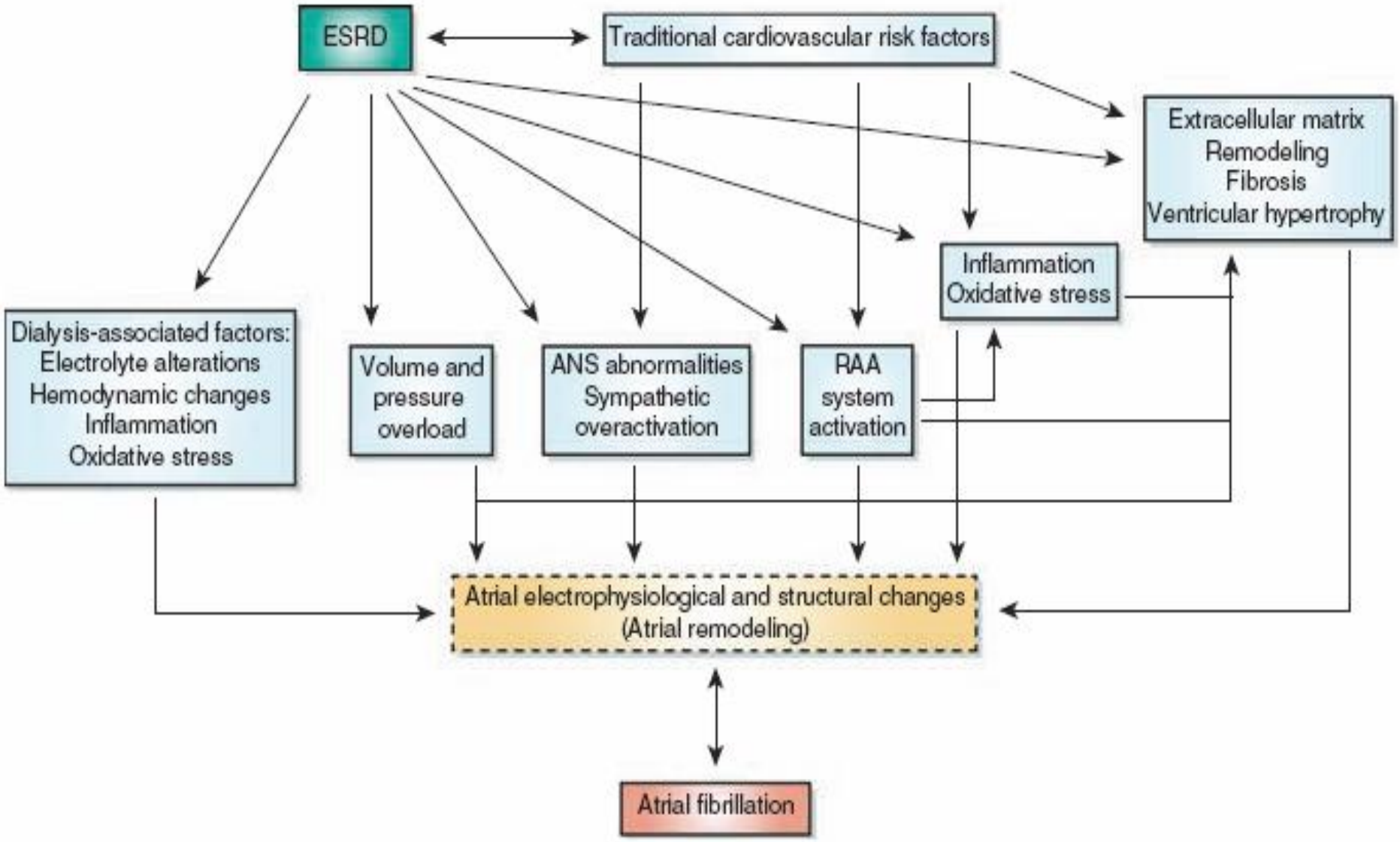
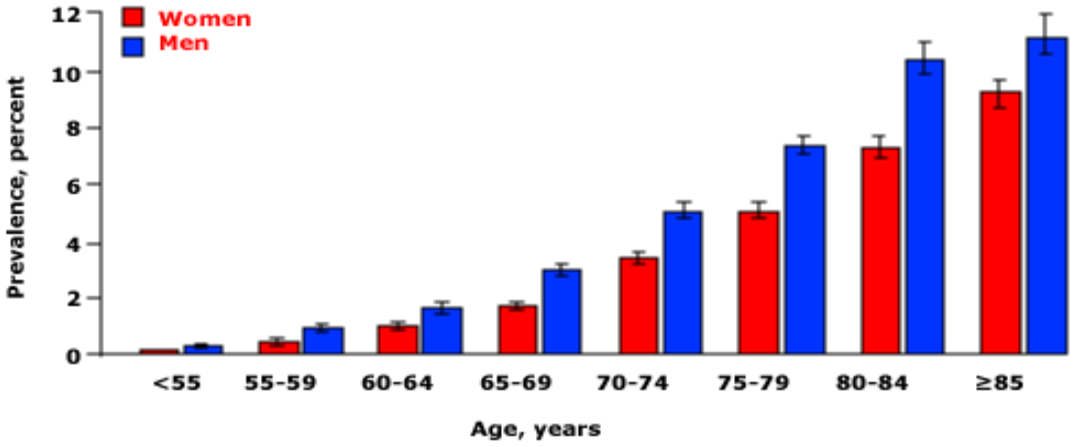
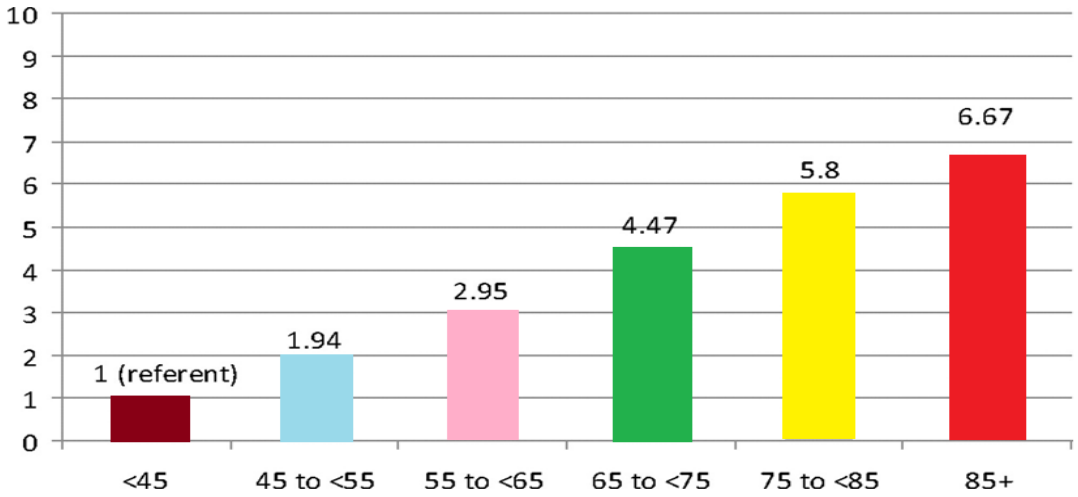

ESRD
Traditional cardiovascular risk factors
Extracellular matrix
Remodeling
Fibrosis
Ventricular hypertrophy
Inflammation
Oxidative stress
Dialysis-associated factors:
Electrolyte alterations
Hemodynamic changes
Inflammation
Oxidative stress
Volume and pressure overload
ANS abnormalities
Sympathetic overactivation
RAA system activation
Atrial electrophysiological and structural changes
(Atrial remodeling)
Atrial fibrillation

Factors Associated with AF: age



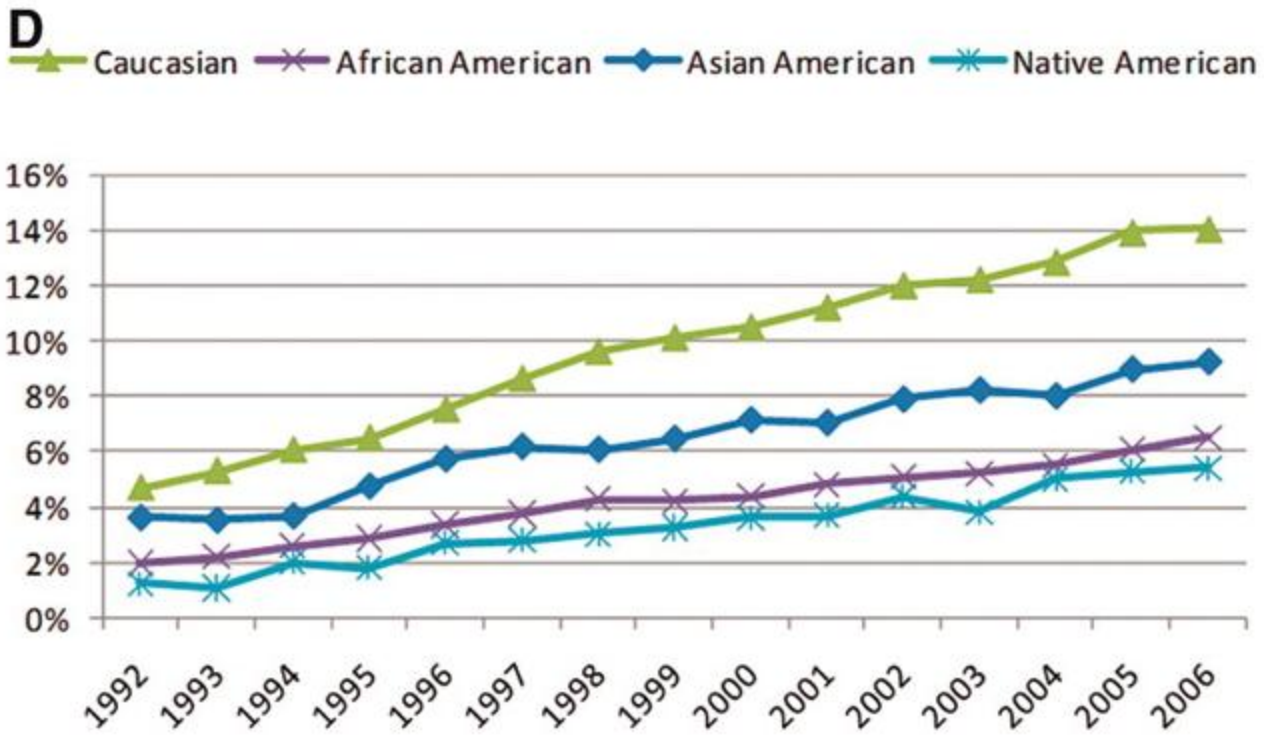
general population



ESRD

Go AS, JAMA 2001
Winkelmayer, JASN 2011

Factors Associated with AF: race

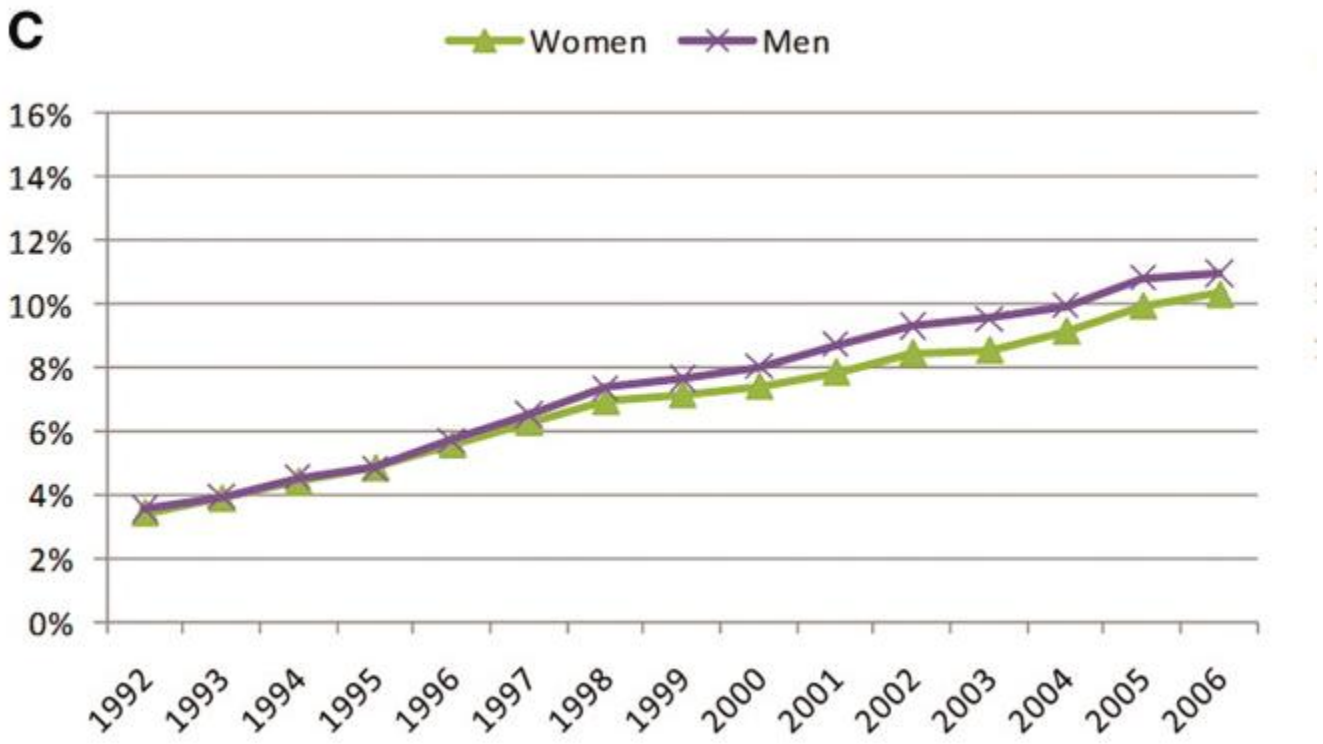


Compared with Caucasians, African Americans had a 39% lower prevalence of AF, whereas the prevalences were 18% lower for Asians and almost half for Native Americans

These racial differences may be due to genetic polymorphisms that code for intrinsic differences in atrial membrane stability and/or conduction pathways, resulting in different susceptibilities to development of AF

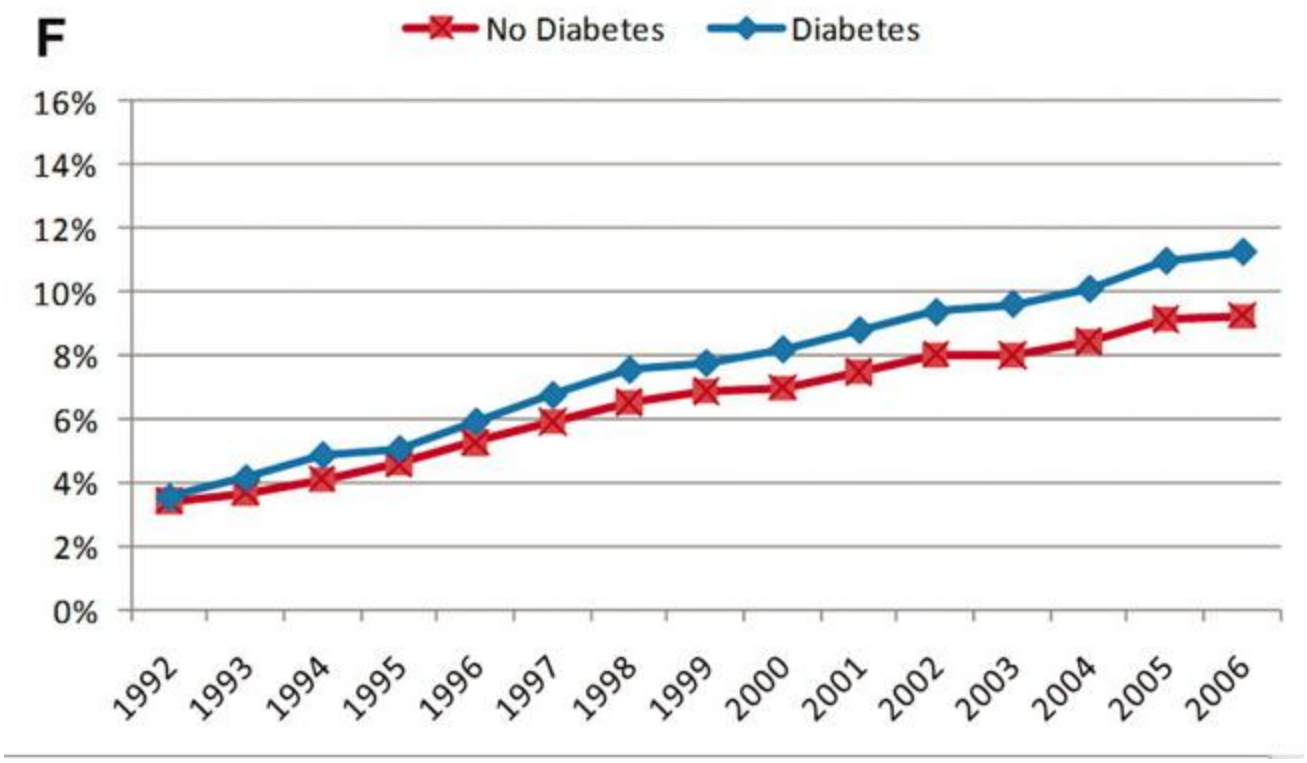
Winkelmayer, JASN 2011

Factors Associated with AF: gender



Winkelmayer, JASN 2011

Factors Associated with AF: diabetes



Patients with diabetes have an accelerated AF risk compared with patients without diabetes, at least in more recent years

CAD and HF important comorbidities associated with new onset atrial fibrillation

Table 3. *Factors related to the presence of atrial fibrillation*

	Univariate analysis		Multivariate analysis	
Factors	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
Age (per 10 years increase)	1.49 (1.27–1.74)	<0.0001	1.39 (1.17–1.64)	<0.0001
Smoking	0.58 (0.39–0.87)	0.009	0.60 (0.39–0.92)	0.020
Previous stroke/TIAs	1.93 (1.08–3.46)	0.027		
Coronary artery diseases	2.14 (1.44–3.19)	<0.0001		
Heart failure	2.68 (1.78–4.04)	<0.0001	2.11 (1.35–3.28)	0.001
β-blockers use	1.94 (1.29–2.89)	0.001	1.81 (1.18–2.79)	0.007
α-calcidol	1.59 (0.96–2.62)	0.071	1.73 (1.02–2.96)	0.044
Left ventricular end systolic diameter	1.03 (0.99–1.05)	0.078		
Intraseptal wall width	1.13 (1.01–1.27)	0.034		
Posterior wall width	1.16 (1.04–1.31)	0.009		
Left atrial diameter	1.14 (1.10–1.19)	<0.0001	1.07 (1.02–1.13)	0.008
Aortic root diameter	1.06 (1.02–1.11)	0.002	1.10 (1.03–1.18)	0.005
Ejection fraction	0.97 (0.96–0.99)	<0.0001		
Valvular heart calcification	5.70 (3.76–8.64)	<0.0001	6.72 (3.23–13.98)	<0.0001

Ananthapanyasut, Cjasn 2010

CAD and HF associated with AF

N = Combined DOPPS I and II data (1996–2004), among respective phase-specific prevalent cross-sections (n=17,513 overall);

Table 2 | Associations with pre-existing and newly diagnosed atrial fibrillation

	Pre-existing AF			Newly diagnosed AF		
Characteristics	OR[a]	95% CI	*P*-value	HR[b]	95% CI	*P*-value
Summary comorbid conditions (yes vs no)						
Coronary artery disease	**1.56**	**(1.39–1.75)**	**<0.001**	1.12	(0.89–1.41)	0.341
Heart failure	**2.08**	**(1.84–2.35)**	**<0.001**	1.14	(0.90–1.45)	0.283
Cerebrovascular disease	1.11	(0.98–1.25)	0.090	0.87	(0.65–1.18)	0.374
Hypertension	1.08	(0.95–1.23)	0.232	1.19	(0.89–1.58)	0.239
Peripheral vascular disease	1.02	(0.90–1.16)	0.762	1.03	(0.80–1.34)	0.805
Recurrent cellulitis	**1.23**	**(1.04–1.46)**	**0.017**	1.11	(0.70–1.75)	0.665
Diabetes mellitus	0.89	(0.79–1.00)	0.053	0.88	(0.69–1.13)	0.325
GI bleed	1.18	(0.97–1.44)	0.094	0.97	(0.64–1.46)	0.875
Lung disease	1.15	(1.00–1.32)	0.050	1.15	(0.84–1.56)	0.392
Neurological disorder	1.09	(0.93–1.27)	0.281	1.00	(0.68–1.46)	0.997
Psychiatric disorder	**1.15**	**(1.01–1.30)**	**0.031**	1.07	(0.82–1.39)	0.602
Cancer, other than skin	0.96	(0.83–1.11)	0.585	1.09	(0.81–1.45)	0.575
HIV/AIDS	0.70	(0.26–1.88)	0.484		No events	

Wizemann, kidney Int 2010

AF and hTA

Table 6. Univariate logistic regression analyses for the presence of AF among nondialysis patients with CKD

Variable	OR	95% CI	*P*
Age (yr)	1.08	1.06 to 1.09	<0.001
Age ≥65 yr	5.76	3.94 to 8.44	<0.001
White race	6.34	4.57 to 8.79	<0.001
CHF	5.20	3.77 to 7.17	<0.001
Mean SBP (mmHg)	0.38	0.26 to 0.56	<0.001

Table 7. Multivariate logistic regression analyses for the presence of AF among nondialysis patients with CKD

Variable	Adjusted OR	95% CI	*P*
Age (yr)	1.04	1.03 to 1.06	<0.001
Age ≥65 yr	3.00	1.88 to 4.80	<0.001
White race	2.06	1.32 to 3.21	0.001
SBP (mmHg)	0.98	0.97 to 0.99	0.005

lower SBP is an independent predictor of AF

Ananthapanyasut, CJASN 2010

AF and echocardiographic parameters

Table 4. Echocardiographic data of nondialyhsis patients who have CKD with and without AF

Echocardiographic Data	AF	Non-AF	*P*
LVEF (%; mean ± SD)	50.7 ± 15.6	56.8 ± 13.6	<0.001
LV systolic dysfunction (%)	37.2	20.0	<0.001
LVH (%)	64.8	61.5	0.423
LA diameter (mm; mean ± SD)	46.4 ± 25.4	40.8 ± 6.5	<0.001
VHD (%)	26.6	6.0	<0.001
Pulmonary artery systolic pressure (mmHg; mean ± SD)	44.1 ± 10.4	43.9 ± 13.2	0.241

Patients with AF have significantly lower LVEF, increased LA diameter, and increased frequencies of VHD and LV systolic dysfunction

Ananthapanyasut, CJASN 2010

Factors Associated with AF: bundle branch block

Table 4 | Factors independently associated with the presence of atrial fibrillation over the clinical course of dialysis

Variable	Odds ratio	95% CI	*P*
Valvular calcifications	5.23	1.74–15.67	0.003
Bundle branch block at start of dialysis	5.92	2.22–15.77	0.000
Previous ischemic stroke or transient ischemic attack	3.53	1.12–11.12	0.031
Left ventricle ejection fraction	0.05	0.91–0.99	0.021
Pulse pressure	1.02	1.00–1.03	0.018
Hemoglobin concentration	0.71	0.52–0.97	0.036

Bundle branch block at the start of dialysis increases the probability of developing the arrhythmia over the clinical course of the dialysis by sixfold

Wizemann, kidney Int 2010

Biochemical parameters and AF

Patients with AF have lower serum potassium, calcium, phosphorus, creatinine, albumin, cholesterol, and triglyceride levels and higher serum bicarbonate levels.

Laboratory Data	AF	Non-AF	*P*
Hemoglobin (g/dl)	11.6 ± 1.76	11.3 ± 1.8	0.062
Sodium (mEq/L)	138.8 ± 4.3	139.2 ± 3.4	0.211
Potassium (mEq/L)	4.1 ± 0.6	4.4 ± 0.6	<0.001
Bicarbonate (mEq/L)	25.4 ± 4.8	24.2 ± 4.0	<0.001
BUN (mg/dl)	41.9 ± 22.1	40.3 ± 20.3	0.523
Creatinine (mg/dl)	2.0 ± 0.9	2.7 ± 1.7	<0.001
Calcium (mg/dl)	8.7 ± 0.7	8.8 ± 0.7	<0.001
Magnesium (mg/dl)	2.1 ± 0.3	2.1 ± 0.4	0.660
Phosphorus (mg/dl)	3.7 ± 1.1	3.9 ± 1.1	0.003
Albumin (g/dl)	2.9 ± 0.7	3.4 ± 0.8	<0.001
hsCRP (mg/L)[a]	4.3 ± 5.7	5.7 ± 8.2	0.420
Parathyroid hormone (pg/ml)[b]	172.9 ± 132.5	173.4 ± 167.4	0.680
Ferritin (ng/L)	389.0 ± 671.6	272.8 ± 366.7	0.240
HbA_{1c} (%)	7.0 ± 1.8	6.9 ± 1.7	0.700
Total cholesterol (mg/dl)	141.0 ± 42.9	167.4 ± 46.2	<0.001
LDL cholesterol (mg/dl)	81.3 ± 33.6	95.6 ± 36.8	<0.001
HDL cholesterol (mg/dl)	35.1 ± 11.3	42.4 ± 13.9	<0.001
Triglyceride (mg/dl)	126.7 ± 111.7	150.6 ± 89.0	<0.001
Urine protein (g/d)[c]	1.9 ± 3.3	2.1 ± 3.0	0.140

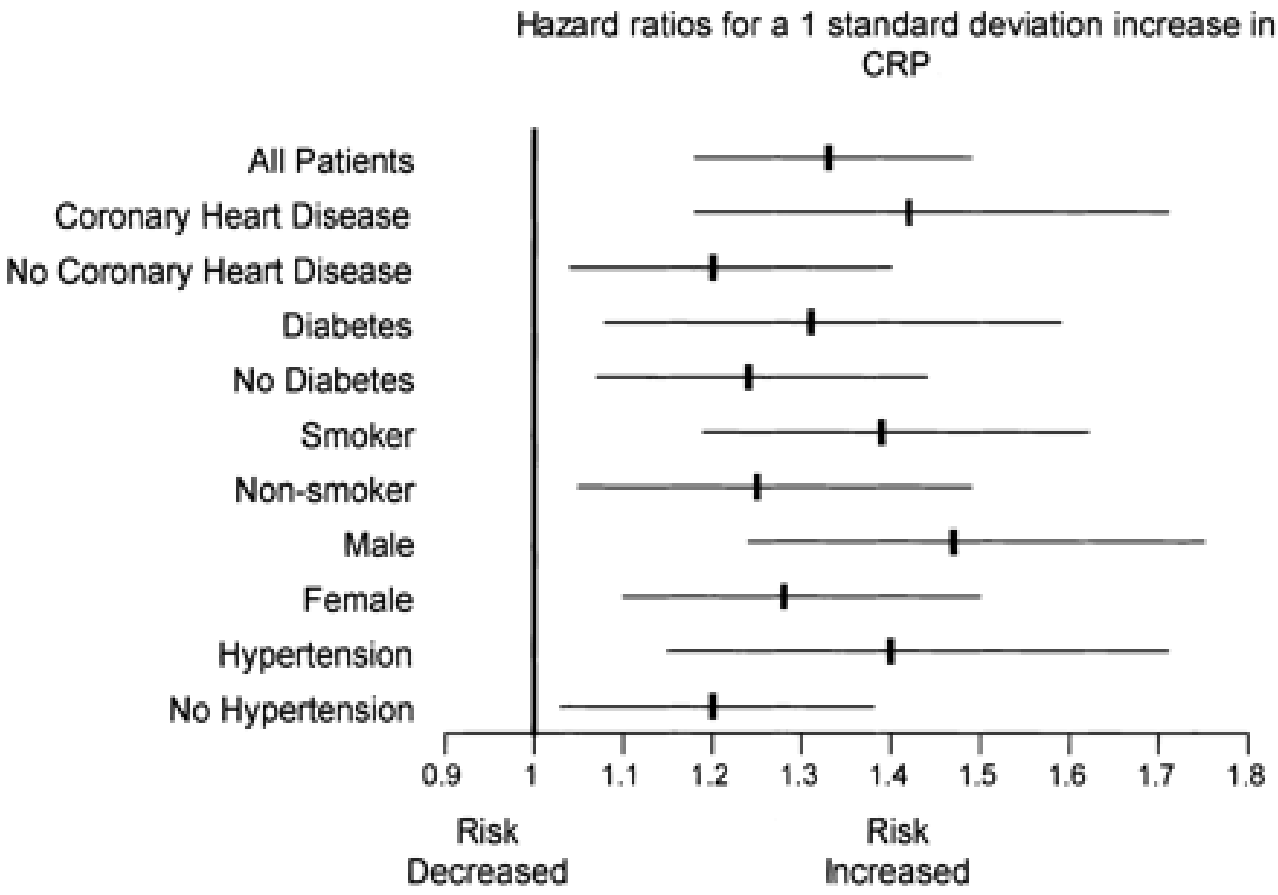
Inflammation and AF in CKD

Variable	OR	95% CI	*P*
Age (yr)	1.08	1.06 to 1.09	<0.001
Age ≥65 yr	5.76	3.94 to 8.44	<0.001
White race	6.34	4.57 to 8.79	<0.001
eGFR (ml/min per 1.73 m^2)	1.01	1.00 to 1.02	0.014
Potassium (mEq/L)	0.45	0.34 to 0.59	<0.001
Calcium (mg/dl)	0.73	0.60 to 0.90	0.003
Phosphorus (mg/dl)	0.81	0.67 to 0.98	0.028
Albumin (g/dl)	0.48	0.39 to 0.58	<0.001
hsCRP (mg/L)	0.97	0.90 to 1.04	0.446

Although serum hsCRP levels were elevated, in CKD population levels did not correlate with the presence of AF

Ananthapanyasut, Cjasn 2010

IN CONTRAST...
elevated CRP predicted increased risk for developing future AF in the GENERALPOPULATION



Aviles, Circulation 2006

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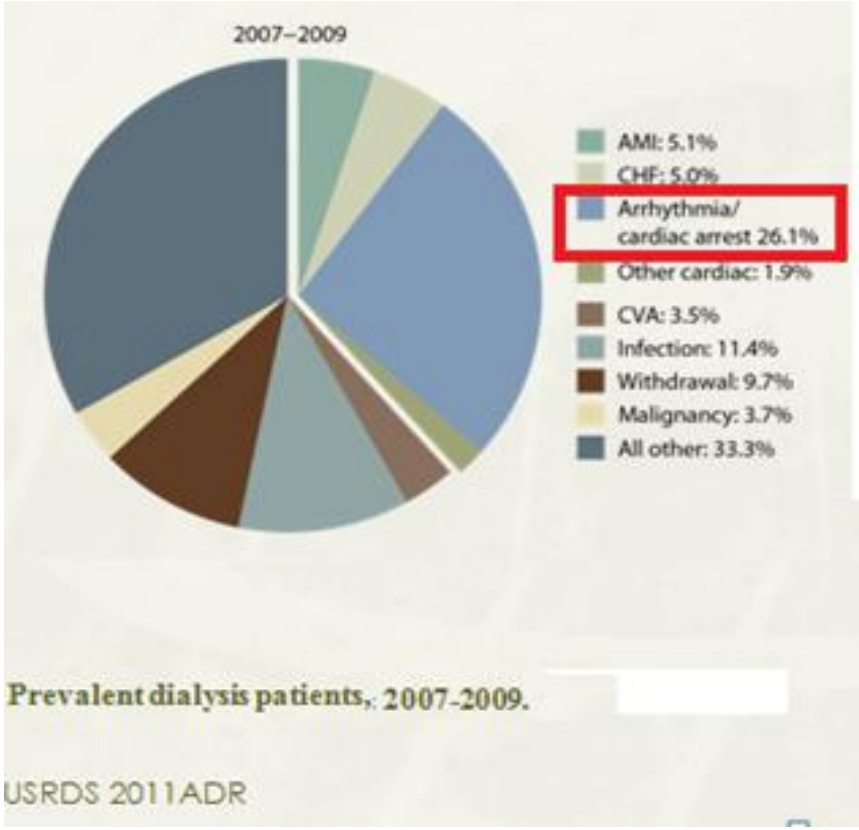
Consequences of arrhythmias in ESRD populations

- US dialysis population mortality (2004): 230/1000 patient years = 23%/yr

- Arrhythmic death:
  - 58% of cardiac deaths

    (25% all cause) in CAPD

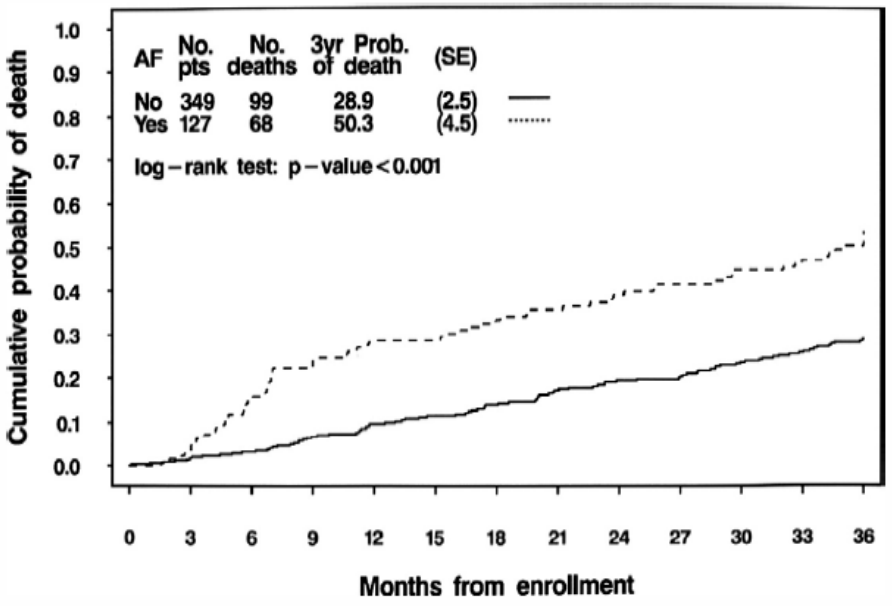
    (27% all cause) in HD



Cheung AK et al. Kidney Int 2004;65:2380-0
Wanner C et al. N Engl J Med 2005;353:238-48

AF is associated with greater total and cardiovascular mortality risk in prevalent HD pts.

N = 488 patients in 5 dialysis centers in Lombardia, Italy; follow-up – 3 yrs; 127 patients had atrial fibrillation at enrollment; New-onset atrial fibrillation occurred in 35 pts;



	Atrial Fibrillation		
	Yes (n = 127)	No (n = 349)	Total
Total deaths	68 (53.5)	99 (28.4)	167
Cardiovascular deaths	30 (23.6)	36 (10.3)	66
Sudden	16	15	31
Other	14	21	35
Noncardiovascular deaths	38 (29.9)	63 (18.1)	101
Infections	10	25	35
Cachexia	11	15	26
Neoplasms	7	8	15
Other	10	15	25

Note: Values expressed as number (percent).

Genovesi, AJKD 2008

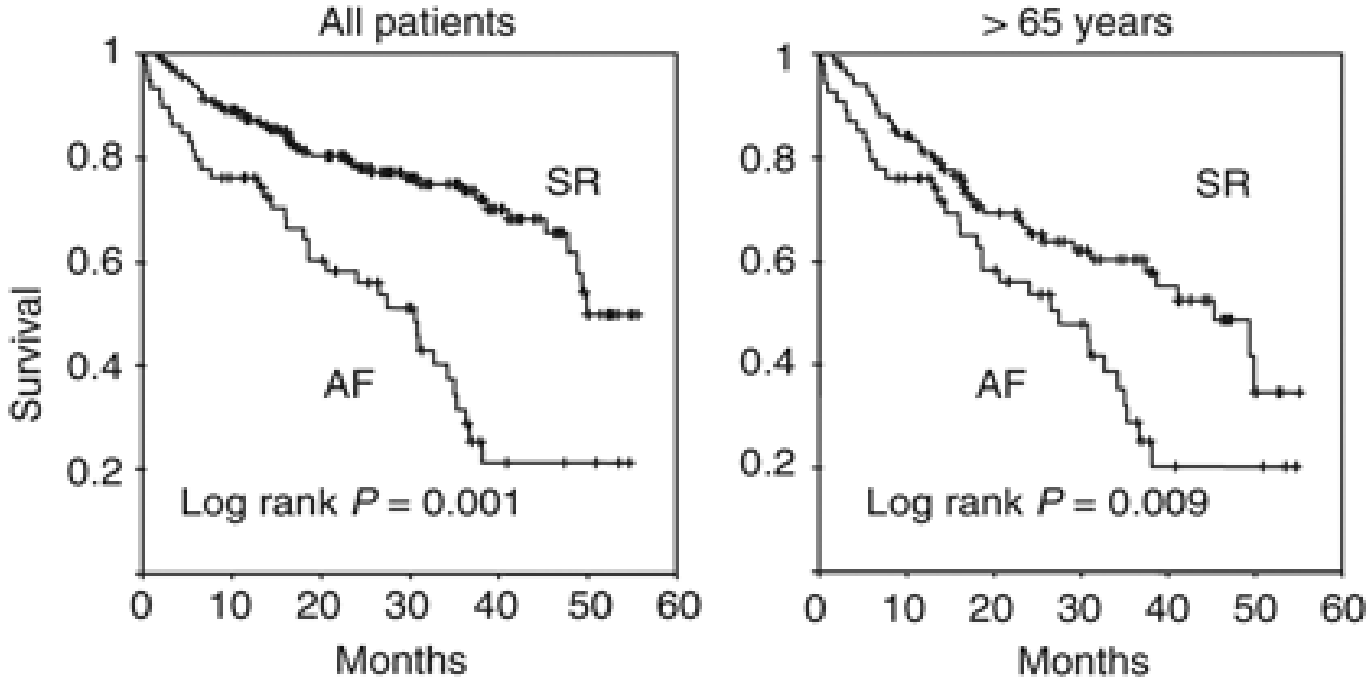
original article

http://www.kidney-international.org

Atrial fibrillation in incident dialysis patients

Eduardo Vazquez[1], Carmen Sanchez-Perales[2], Francisco Garcia-Garcia[1], Patricia Castellano[1], Maria-Jose Garcia-Cortes[2], Antonio Liebana[2] and Cristobal Lozano[1]

N = 256 patients studied, 31 had atrial fibrillation at the start of dialysis; 8 developed atrial fibrillation during a mean follow-up time of 2 years.



AF is associated with greater mortality risk also in incident HD patients

AF is associated with increased hospitalization

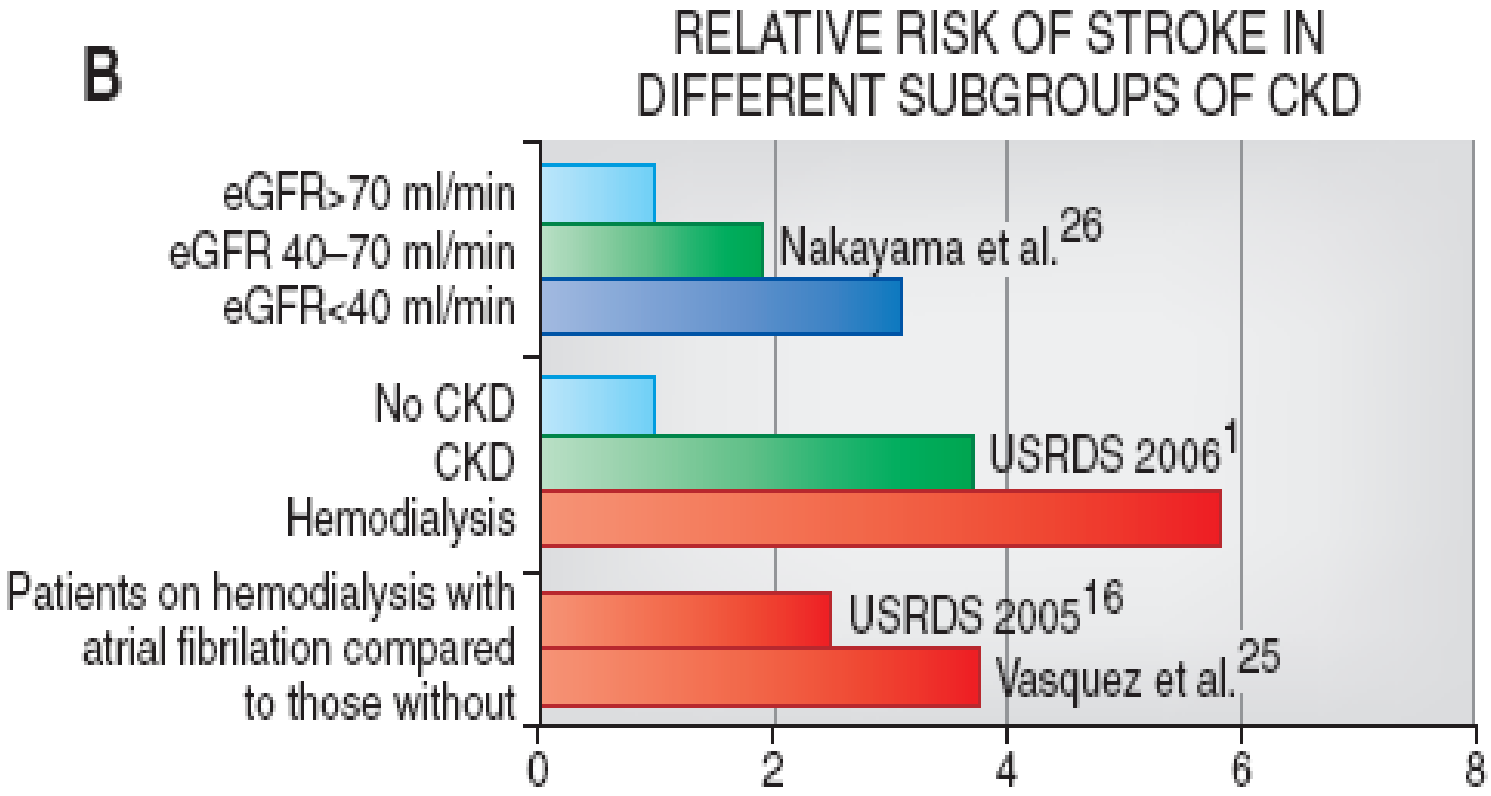
Table 5. Multivariate Analysis of 476 Patients Evaluating the Impact of Prognostic Factors on Time to First Hospitalization (265 events)

Variables	First Hospitalization	
	Hazard Ratio (95% confidence interval)	*P*
Atrial fibrillation		
Yes *v* no	1.54 (1.18-2.01)	<0.01
Age (y)		
61-70 *v* <61	1.30 (0.93-1.82)	0.06
>70 *v* <61	3.22 (1.97-5.26)	
Duration of hemodialysis (mo)		
>36 *v* ≤36	1.05 (0.82-1.34)	0.7

Patients with atrial fibrillation were hospitalized more frequently than patients without atrial fibrillation

Genovesi, AJKD 2008

Increase risk of stroke in CKD population



AF and ischemic stroke: controversial results

Table 7 | Differences between patients with and without ischemic stroke in the course of the dialysis period

	Ischemic stroke	No stroke
Age (years)		
Platelets ($n \times 10^3/\mu l$)		
Hematocrit (%)		
Previous ischemic stroke (		
(n (%))		
AF in the course of dialys		
AF at any time (n (%))		

AF, atrial fibrillation; TIA, tran
Univariate analysis. Student's
and Pearson's χ^2-test for qual

IN CONTRAST, IN GENOVESY STUDY...

Atrial Fibrillation, Stroke, and Hospitalization

Frequencies of patients who experienced a stroke were 15.4% (n = 25) in 162 patients who had atrial fibrillation either at enrollment or during follow-up and 12.4% (n = 39) in the remaining 314 patients ($P = 0.4$).

Table 8 | Factors indep
of ischemic stroke in the course of the dialysis period

	Odds ratio	95% CI	*P*
Previous stroke or transient ischemic attack	6.98	1.24–39	0.027
AF at any time	17.3	1.99–150	0.010

The presence of AF increased the probability of developing an ischemic stroke

Vazquez, Kidney International (2009

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Clinical management of patients with AF involves the following five objectives:

1. Prevention of thromboembolism
2. Optimal management of concomitant cardiovascular disease
3. Symptom relief
4. Rate control
5. Correction of the rhythm disturbance

AF = atrial fibrillation; i.v. = intravenous.

European Heart Journal (2010) 31, 2369-2429

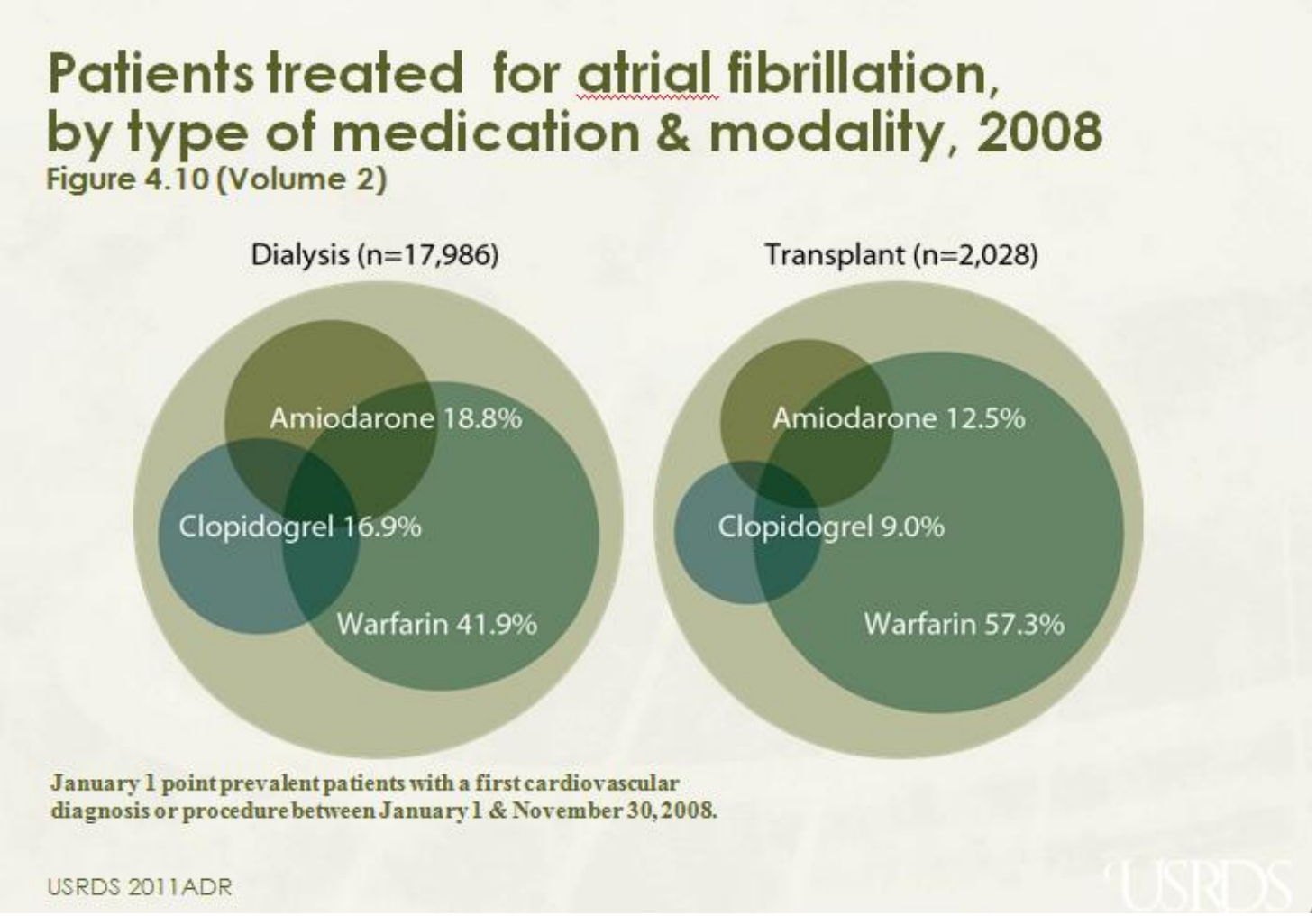
- **Inthe general population…many RCT have shown net clinical benefit of oral anticoagulation therapy for primary and secondary prevention of stroke in patient populations with AF**

- **current stroke risk stratification schemes are based on studies that have deliberately excluded patients with severe renal impairment**

- **there are no large randomized controlled trials that assess the real risk/benefit of full intensity anticoagulation in patients with severe renal impairment**

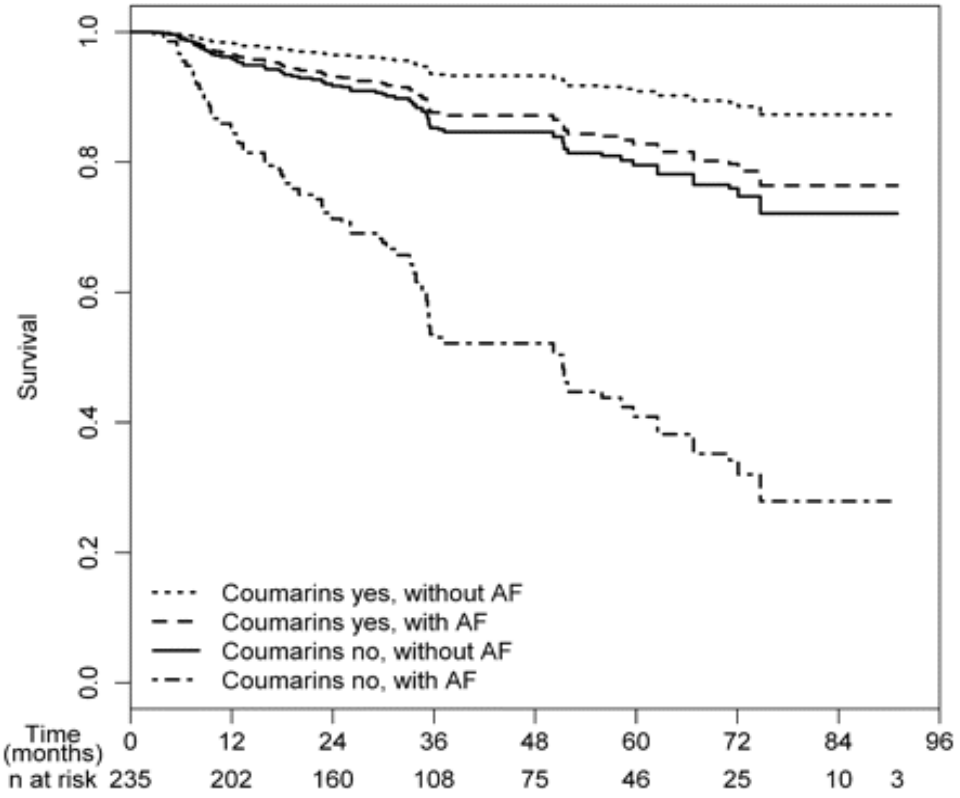
- ***SHOULD WE USE ORAL ANTICOAGULATION THERAPY???***

Prescription drug therapy in patients with atrial fibrillation and ESRD



Coumarins and survival in incident dialysis patients

Florian Knoll[1,*], Gisela Sturm[2,*], Claudia Lamina[2], Emanuel Zitt[1,3], Friederike Lins[3], Otto Freistätter[3], Florian Kronenberg[2], Karl Lhotta[1,3] and Ulrich Neyer[1,3]



Survival of the two coumarin-treated groups was slightly better than the reference group without reaching statistical significance

ORIGINAL ARTICLE

Stroke and Bleeding in Atrial Fibrillation with Chronic Kidney Disease

Jonas Bjerring Olesen, M.D., Gregory Y.H. Lip, M.D.,

N = 132,372 patients with a diagnosis of AF; 3587 (2.7%) had CKD stage 2-4 and 901 (0.7%) required dialysis

observational cohort design

Characteristic	Total Population (N=132,372)		No Renal Disease (N=127,884)†		Non–End-Stage Chronic Kidney Disease (N=3587)†		Disease Requiring Renal-Replacement Therapy (N=901)†	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
All participants			1.00		1.49 (1.38–1.59)	<0.001	1.83 (1.57–2.14)	<0.001
Antithrombotic therapy								
None	1.00		1.00		1.00		1.00	
Warfarin	0.59 (0.57–0.62)	<0.001	0.59 (0.56–0.61)	<0.001	0.84 (0.69–1.01)	0.07	0.44 (0.26–0.74)	0.002
Aspirin	1.11 (1.07–1.15)	<0.001	1.10 (1.06–1.14)	<0.001	1.25 (1.07–1.47)	0.01	0.88 (0.59–1.32)	0.54
Warfarin and aspirin	0.70 (0.65–0.75)	<0.001	0.69 (0.64–0.74)	<0.001	0.76 (0.56–1.03)	0.08	0.82 (0.37–1.80)	0.62

warfarin therapy was associated with a significant reduction in the risk of stroke or thromboembolism among patients with CKD

Olesen, NEJM 2012

Warfarin and high risk of bleeding

N = 132,372 patients with a diagnosis of AF; 3587 (2.7%) had CKD stage 2-4 and 901 (0.7%) required dialysis

Table 4. Hazard Ratios for Bleeding.*

Characteristic	Total Population (N=132,372)		No Renal Disease (N=127,884)†		Non–End-Stage Chronic Kidney Disease (N=3587)†		Disease Requiring Renal-Replacement Therapy (N=901)†	
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All participants			1.00		2.24 (2.10–2.38)	<0.001	2.70 (2.38–3.07)	<0.001
Antithrombotic therapy								
None	1.00		1.00		1.00		1.00	
Warfarin	1.28 (1.23–1.33)	<0.001	1.28 (1.23–1.33)	<0.001	1.36 (1.17–1.59)	<0.001	1.27 (0.91–1.77)	0.15
Aspirin	1.21 (1.16–1.26)	<0.001	1.21 (1.16–1.26)	<0.001	1.12 (0.96–1.30)	0.14	1.63 (1.18–2.26)	0.003
Warfarin and aspirin	2.15 (2.04–2.26)	<0.001	2.18 (2.07–2.30)	<0.001	1.63 (1.32–2.02)	<0.001	1.71 (0.98–2.99)	0.06

The risk of bleeding is increased in CKD patients

Olesen, NEJM 2012

OXFORD JOURNALS

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ABOUT THIS JOURNAL CONTACT THIS JOURNAL SUBSCRIPTIONS CURRENT ISSUE

Warfarin in haemodialysis patients with atrial fibrillation: what benefit?

Table 3
Studies of warfarin in dialysis patients with atrial fibrillation

Study (year, design)	Number of dialysis patients with AF (no. of patients with AF on warfarin)	Mean follow-up	Major findings
To *et al.*[9] (2007, retrospective)	40 (10)	26 months	Cerebrovascular events did not differ between patients with AF from those without AF (5.0%/year vs. 2.4%/year; NS)
Genovesi *et al.*[46] (2008, prospective multicentre)	127 (31 at enrolment)	36 months	No difference in stroke incidence when comparing an undertreated population of dialysis patients with AF (only 24% of AF patients were on warfarin at enrolment) compared with patients without AF (15.4 vs. 12.4%; $P = 0.4$).
DOPPS[3] (2010, retrospective)	3245 (509)	Not reported	Warfarin use was associated with higher stroke risk; significantly in patients >75 years of age (HR = 2.17; 95% CI 1.04–4.53, $P = 0.04$).
Chan *et al.*[42] (2010, retrospective)	1671 (746)	19 months	Warfarin use increased haemorrhagic stroke risk (1.2%/year among warfarin users vs. 0.5%/year among non-users) and ischaemic stroke risk (5.8%/year among warfarin users vs. 2.3%/year among non-users) without increasing all-cause mortality or hospitalization

Warfarin may actually increase stroke risk

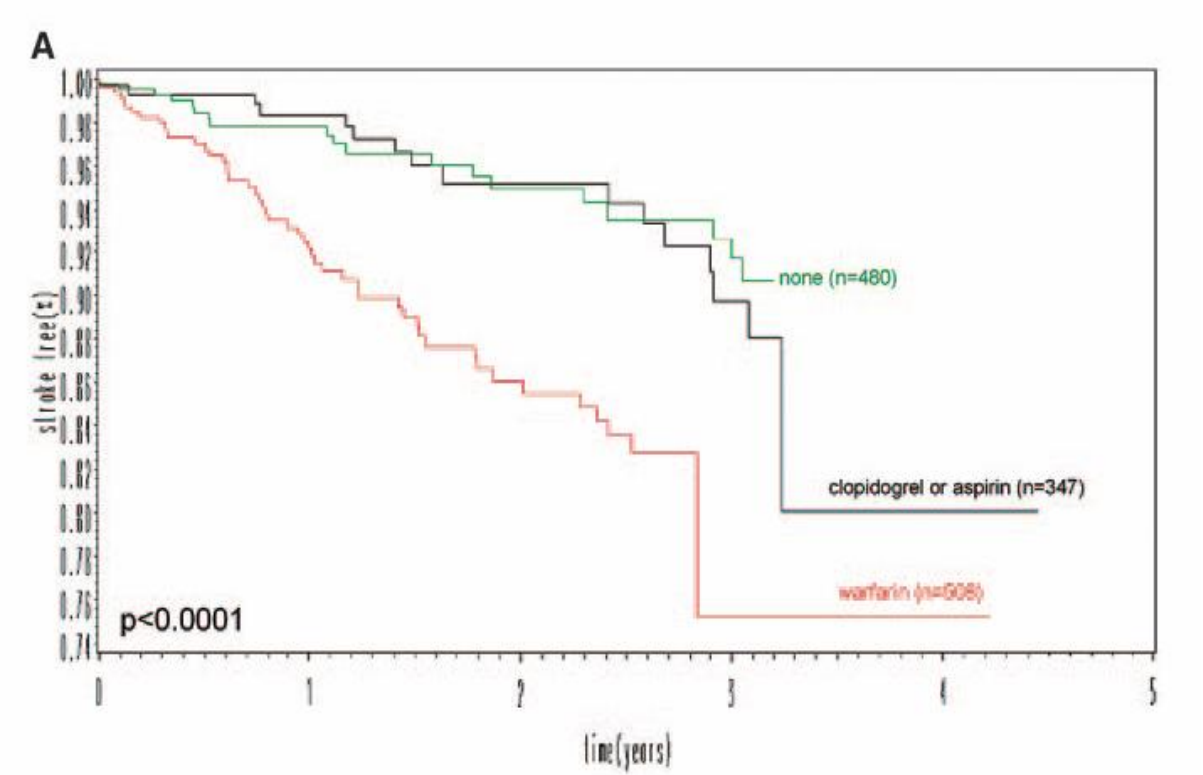
CLINICAL EPIDEMIOLOGY www.jasn.org

Warfarin Use Associates with Increased Risk for Stroke in Hemodialysis Patients with Atrial Fibrillation

Kevin E. Chan,* J. Michael Lazarus,* Ravi Thadhani,† and Raymond M. Hakim*

*Fresenius Medical Care NA, Waltham, Massachusetts; and †Nephrology Division, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts

N = 1671 patients who already had AF when starting HD and survived 90 days from initiation



The risk of any stroke was double among pre-existing users of warfarin at initiation of dialysis

CLINICAL EPIDEMIOLOGY www.jasn.org

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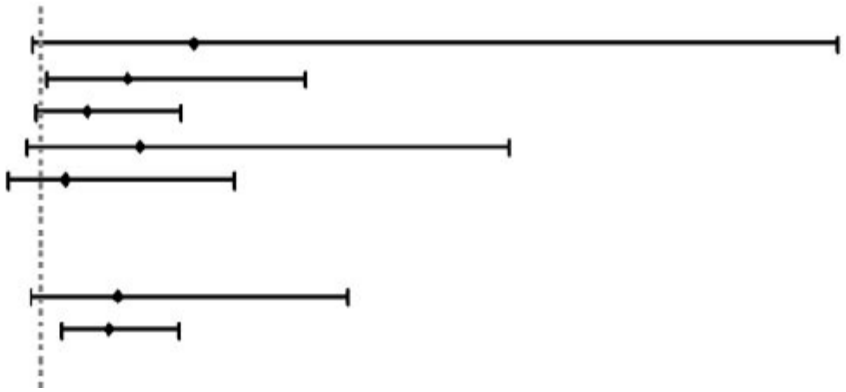
N = 1671 patients who already had AF when starting HD and survived 90 days from initiation

	warfarin use (%)	mean INR in warfarin users (%)	warfarin users with no INR monitoring (%)
-$CHADS_2$ 0-1 (n=262)	39	2.3	76
-$CHADS_2$ 2 (n=496)	44	2.2	67
-$CHADS_2$ 3 (n=552)	47	2.3	76
-$CHADS_2$ 4 (n=235)	44	2.2	74
-$CHADS_2$ 5 (n=126)	50	2.3	71
-past history of stroke/TIA (n=221)	49	2.3	70
-no history of stroke/TIA (n=1,450)	44	2.3	73



Even patients with the highest CHADS2 scores or those with a history of stroke or TIA DID NOT BENEFIT from warfarin.

CLINICAL EPIDEMIOLOGY www.jasn.org

Warfarin Use Associates with Increased Risk for Stroke in Hemodialysis Patients with Atrial Fibrillation

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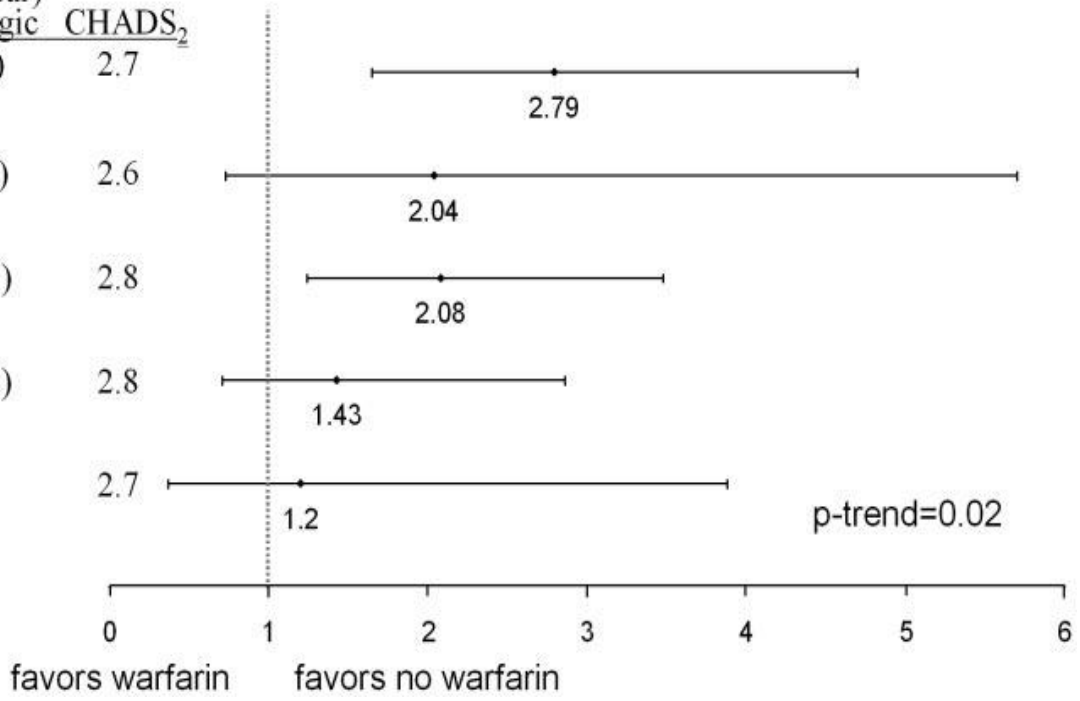
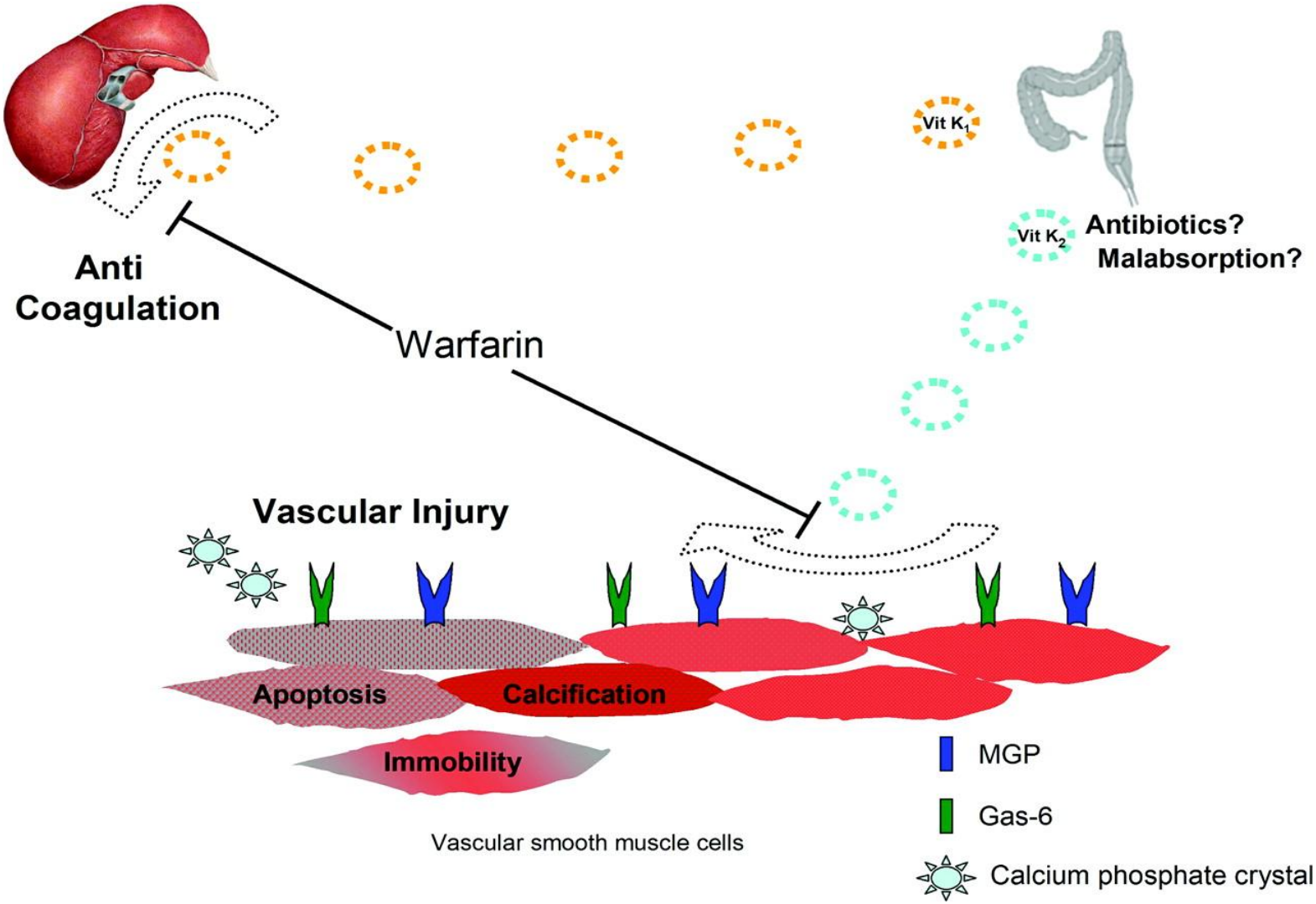
	N	strokes (strokes per pt year) ischemic	hemorrhagic	$CHADS_2$
No INR monitoring available	204	23 (0.068)	6 (0.017)	2.7
INR>3	60	3 (0.031)	1 (0.011)	2.6
INR=2-3	272	19 (0.038)	6 (0.012)	2.8
INR=1.5-1.9	155	9 (0.029)	4 (0.013)	2.8
INR<1.5	56	3 (0.027)	0 (-)	2.7



Higher INR levels resulted in a significantly higher stroke risk

Warfarin and vascular calcification



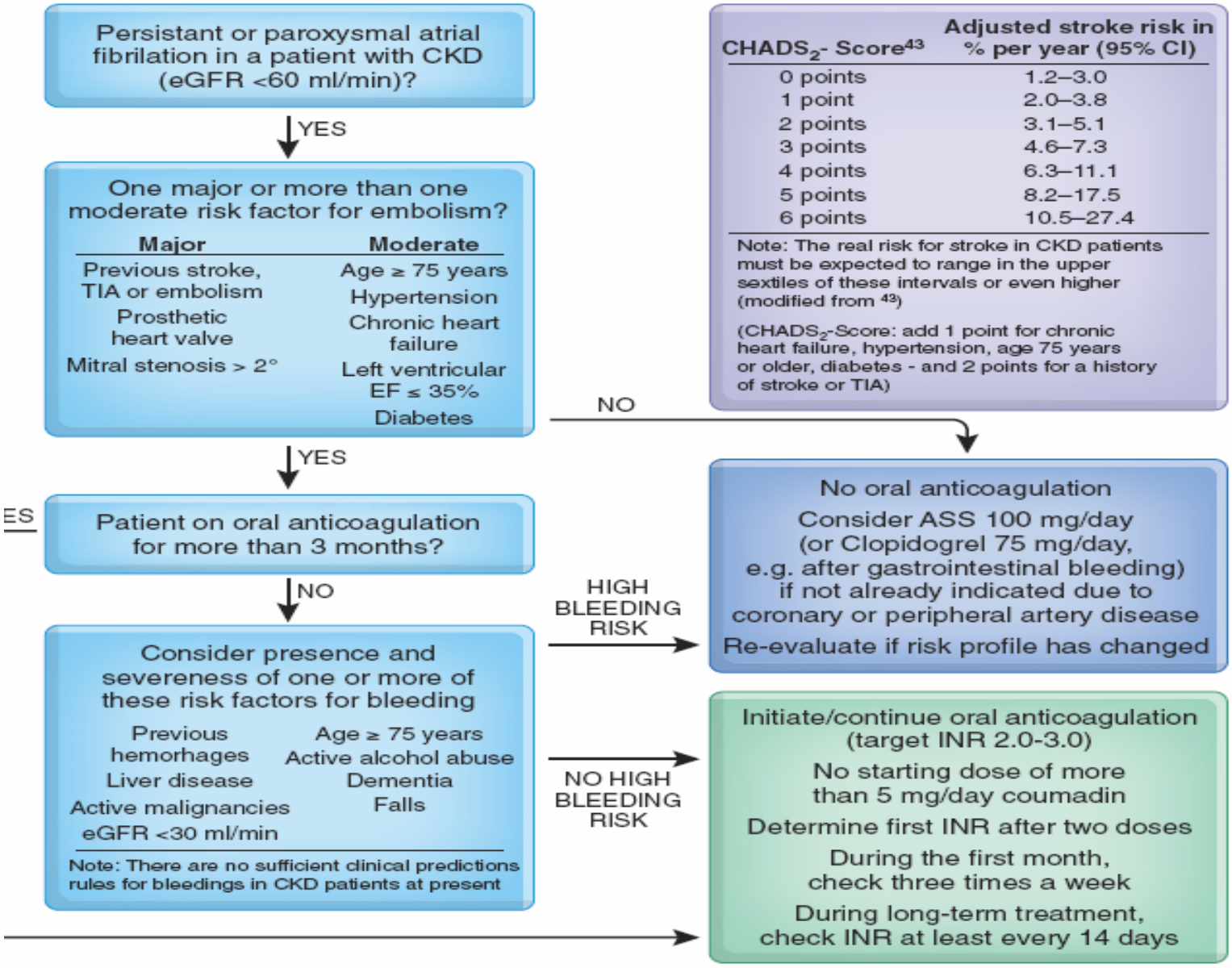
Danziger J CJASN 2008;3:1504-1510

IN CONCLUSION...therapy should only be reserved for dialysis patients at high risk for thrombo-embolic stroke and carefully monitored if implemented.

Table 4
Risk stratification for warfarin use in stroke prevention in dialysis patients with atrial fibrillation

Risk stratification	Description
Favours warfarin	Known atrial thrombus
	Prosthetic heart valve
	$CHADS_2$ score greater than or equal to the OBRI score by two points
	Mitral stenosis
	Previous TIA or stroke
	Patient preference
Favours no warfarin[a]	Age <65 years with no risk factors
	Uncontrolled hypertension
	Concurrent antiplatelet use
	History of active calciphylaxis
	Previous life-threatening haemorrhage
	Severe malnutrition
	Non-compliance
	Frequent falls

Yang, Europace. 2010

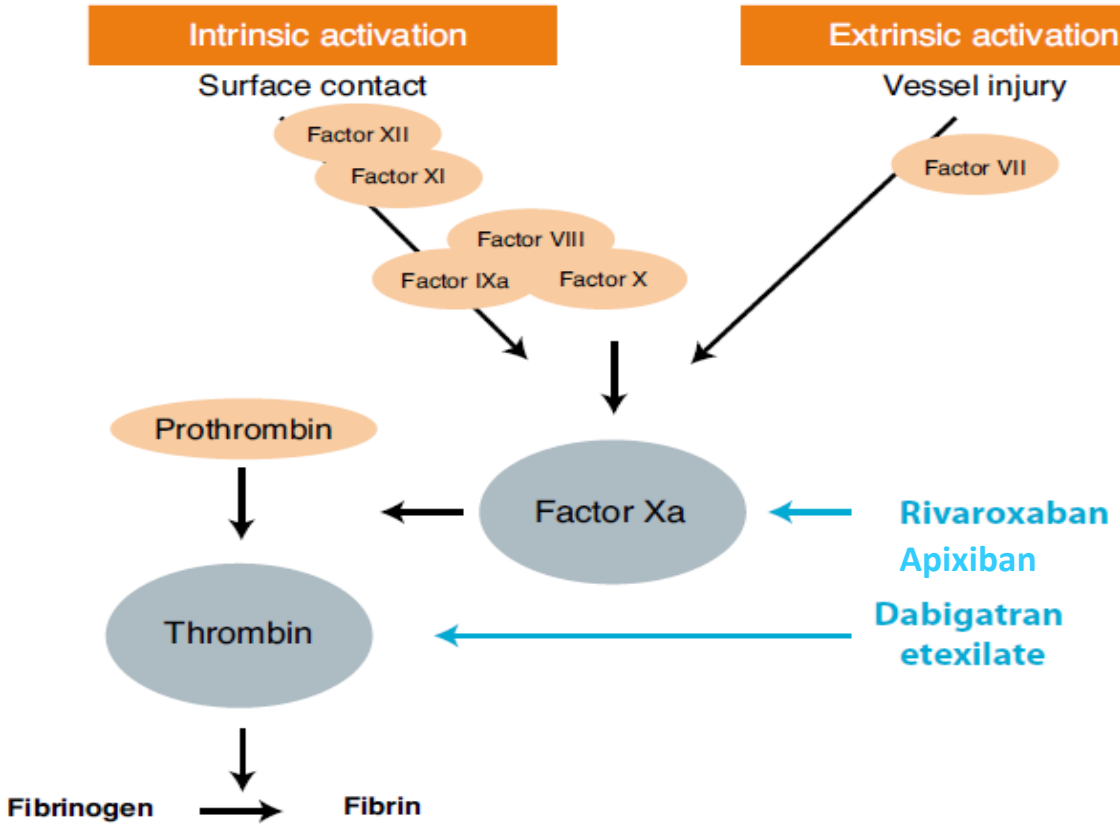


Reinecke, JASN 2009

New therapeutic options

Fig. 1

Site of action of new anticoagulant drugs



New therapeutic options

Trial (reference)	Stroke/SEE in patients without CKD (eGFR ≥50 mL/min)		HR, 95% CI	Stroke/SEE in patients with CKD (eGFR 30–49 mL/min)		HR, 95% CI	*P*-value for interaction
	Intervention	Control		Intervention	Control		
RELY[8]	Dabigatran 110 mg b.i.d., 1.35%/year	Warfarin, 1.51%/year	0.90, 0.71–1.14	Dabigatran 110 [illegible]			0.60
	Dabigatran 150 mg b.i.d., 1.02%/year	Warfarin, [illegible]					54
AVERROES[9]	Apixaban 5 [illegible]					[illegible], 0.24–0.77	0.87
R[illegible]				[illegible] o.d., [illegible] year	Warfarin, 2.77%/year	0.84, 0.57–1.23	0.76

rivaroxaban, dabigatran, and apixaban were not associated with higher bleeding rates in CKD.

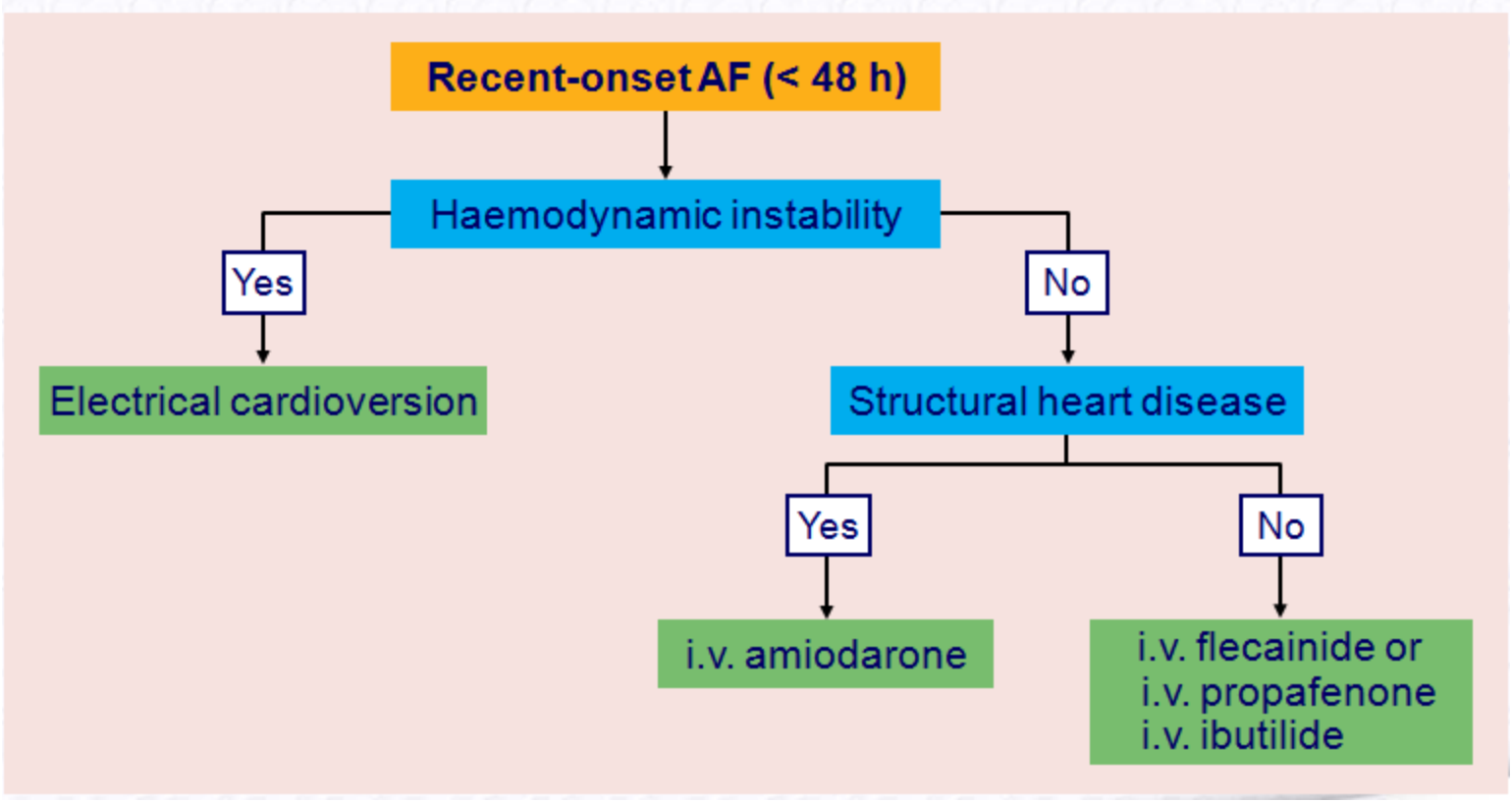
[illegible], and apixaban were not associated with higher bleeding rates in CKD.

Hohnloser, European Heart Journal 2011

Content

1. *Epidemiology of atrial fibrillation*
2. *Factors associated with atrial fibrillation in CKD population*
3. *Consequrences of atrial fibrillation in CKD;*
4. *Treatment options:*
   - *Stroke risk and anticoagulation therapy*
   - *Heart rate control vs conversion*

DCC and pharmacological conversion recent-onset AF



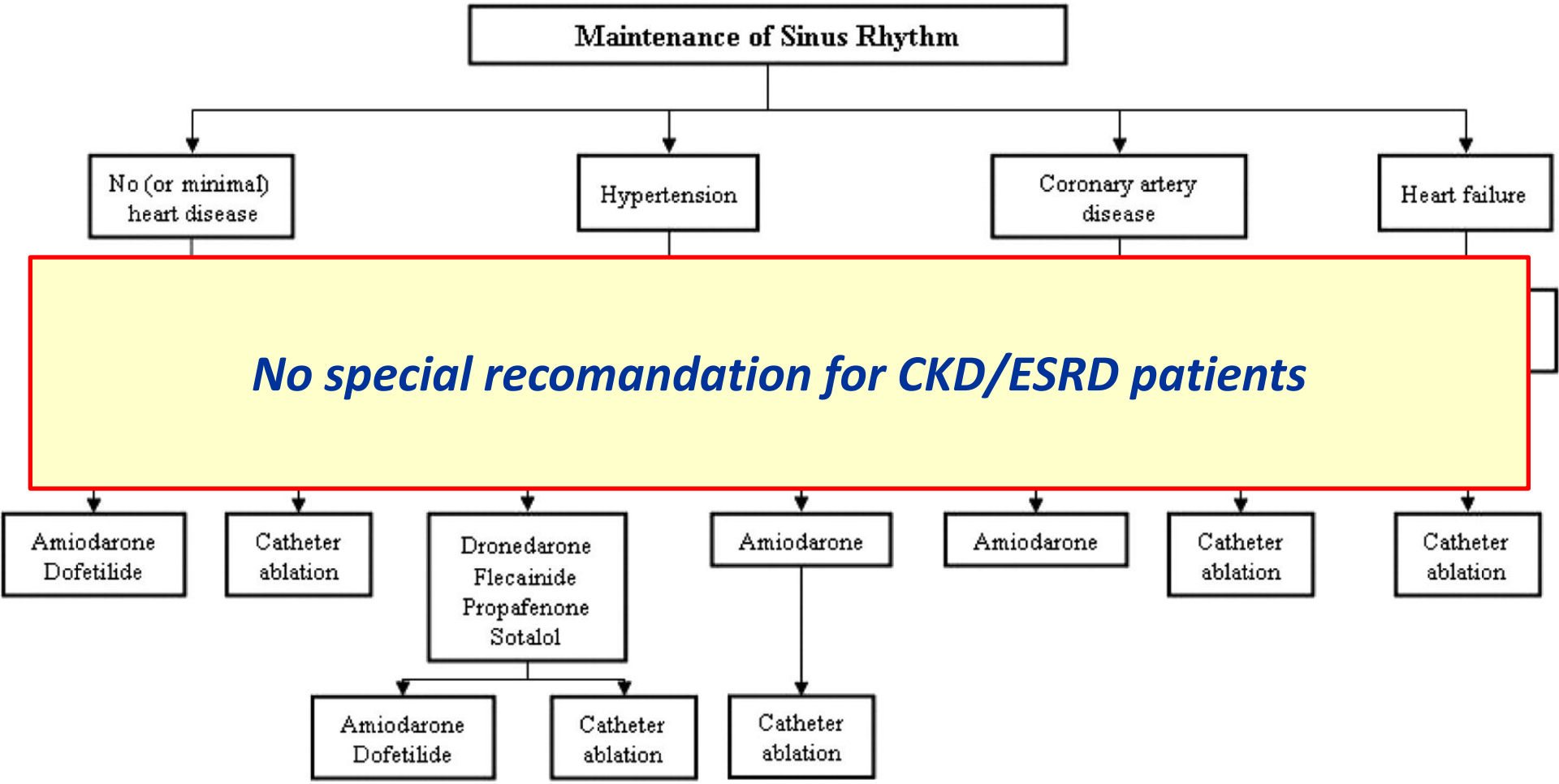
AF = atrial fibrillation; i.v. = intravenous.

www.escardio.org/guidelines

European Heart Journal (2010) 31, 2369-2429

EUROPEAN SOCIETY OF CARDIOLOGY®

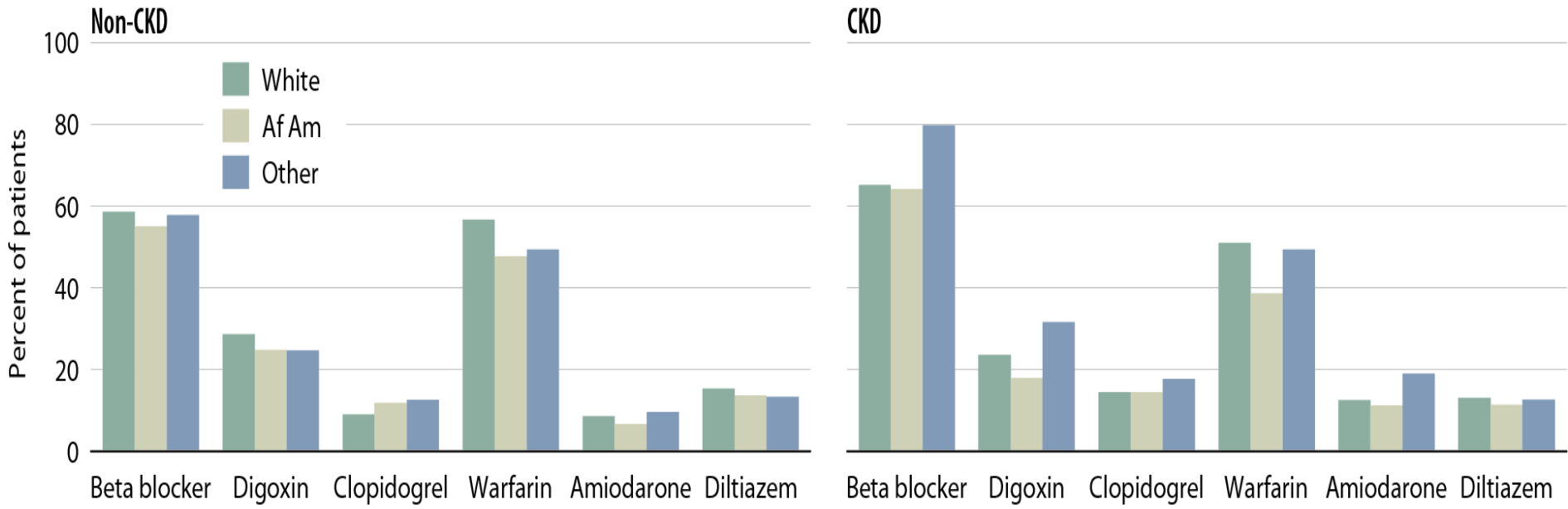
Therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation.



2011 Writing Group Members et al. Circulation 2011;123:104-123

American Heart Association
Learn and Live

THE REAL LIFE:
Prescription drug therapy in patients with atrial fibrillation, by CKD status, 2008



kidney INTERNATIONAL
Official journal of the International Society of Nephrology

Atrial fibrillation: the beat is faster than the answers

Kidney International (2012) **81,** 432–433; doi:10.1038/ki.2011.430

Lynda A Szczech

The ability to extrapolate these somewhat counterintuitive results to patients with kidney disease is again, however, limited. The differences in blood vessel compliance as measured by pulse pressure[13] and the complexity of the associations between hemodynamic changes on dialysis and mortality[14] in comparison with people with normal kidney function may modify the effect of whether rhythm control is achieved and of to what extent

Finally, future directions in the treatment of atrial fibrillation include catheter-based oblation for symptomatic paroxysmal atrial fibrillation that has failed one or more drugs.

There are no data for patients with ESRD. But given the real lack of data on safety for any of the agents recommended for use in rate and rhythm control (amiodarone, dofetilide, dronedarone, propafenone, sotalol, and flecainide) and the risk associated with anticoagulation, perhaps this will be the most therapeutic option.

Review: Perioperative statins reduce perioperative MI and AF in statin-naïve patients

Reitze Rodseth, MD; and P.J. Devereaux, MD, PhD

[+] Article and Author Information

Ann Intern Med. 19 June 2012;156(12):JC6-2

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Article | References | Comments

Question: Does perioperative statin treatment improve clinical outcomes in adults having surgery and not using long-term statins?

Review scope: Included studies evaluated perioperative statin treatment in patients≥ 18 years of age who were having surgery and were not maintained on long-term statin treatment before surgery (statin-naïve). Exclusion criteria included percutaneous coronary interventions and cardioversions. Studies had to report≥ 1 of the following outcomes: perioperative death, myocardial infarction (MI), atrial fibrillation (AF), length of hospital stay, or length of intensive care unit (ICU) stay.

Review methods: MEDLINE, EMBASE/Excerpta Medica, Biosis, Cochrane Central Register of Controlled Trials, Conference Proceedings Index, Web sites (ClinicalTrials.gov, International Federation of Pharmaceutical Manufacturers, and Pharmaceutical Research and Manufacturers of America), and reference lists were searched to April 2011 for published and unpublished randomized controlled trials (RCTs). Experts and study authors were contacted. 15 RCTs ($n = 2292$, 59% to 90% men) met inclusion criteria. Studies enrolled patients having cardiac surgery (11 RCTs, $n = 1056$), noncardiac surgery (2 RCTs, $n = 1030$), and vascular surgery (2 RCTs, $n = 206$). 14 studies used a placebo control, and 1 study compared high-dose with low-dose atorvastatin. Statins assessed were atorvastatin (8 RCTs, $n = 852$), fluvastatin (3 RCTS, $n = 1076$), simvastatin (2 RCTs, $n = 121$), rosuvastatin (1 RCT, $n = 200$), and pravastatin (1 RCT, $n = 43$). 7 studies were at low-risk for bias (Cochrane Statistical Methods Group criteria).

Main results: Compared with controls, perioperative statins reduced risk for MI in patients having any surgery and AF in patients having cardiac surgery; groups did not differ for mortality in patients having any surgery (Table). Perioperative statins reduced length of hospital stay, but not length of ICU stay, more than controls (Table).

Conclusion: Perioperative statins reduce risk for myocardial infarction and atrial fibrillation in statin-naïve patients.

What did he say?

Table 4. Hazard Ratios for Bleeding.*

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Aspirin	1.21 (1.16–1.26)	<0.001						0.003
Warfarin and aspirin	2.15 (2.04–2.26)							0.06

NEWER OPTIONS - POSSIBLY BETTER FOR CKD:

1) Catheter ablation +

2) rivaroxaban, dabigatran, and apixaban - not associated with higher bleeding