Stroke, major bleeding and mortality in newly diagnosed atrial fibrillation with moderate-to-severe chronic kidney disease: Results from GARFIELD-AF

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BACKGROUND

- Atrial fibrillation (AF) is associated with a five-fold increase in the risk of stroke[1].
- Concomitant chronic kidney disease (CKD) further increases the risk of thromboembolism[2,3] and also increases the risk of bleeding[2] in patients with AF.
- Currently, there are no clear guidelines on how to achieve a good balance of risk when treating patients at different stages of CKD with antithrombotic agents.

PURPOSE

- To study outcomes in AF patients with moderate-to-severe CKD vs no/mild CKD under real-world antithrombotic therapy in the Global Anticoagulant Registry in the FIELD–Atrial Fibrillation (GARFIELD-AF).

METHODS

- GARFIELD-AF is an ongoing, international, observational registry of consecutively recruited patients aged ≥18 years with newly diagnosed (≤6 weeks' duration) non-valvular AF and ≥1 additional investigator-determined stroke risk factor(s)[4].
- Patient demographics – including age and presence of comorbid conditions – were recorded and clinical outcomes were reported after 1 year of follow-up.
- Renal function was assessed according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative classification by investigators at baseline, and is reported as moderate-to-severe CKD (stage ≥3) vs no/mild CKD (stage <3).
- Clinical outcomes were the incidences of stroke/systemic embolism (SE), all-cause mortality, cardiovascular mortality and major bleeding.
- Hazard ratios (HRs) were estimated using a Cox proportional hazards model and adjusted for components of CHA_2DS_2-VASc, race, antithrombotic therapy, smoking and AF type.

RESULTS

- A total of 17,162 patients with AF were enrolled prospectively at 858 sites in 30 countries between March 2010 and June 2013.
- 17,159 patients had data on CKD stage and 1-year outcomes: 1760 were stage ≥3 patients and 15,399 were stage <3 patients.
- Stage ≥3 patients were older than stage <3 patients and more often female (Table 1).
- Stage ≥3 patients also had more comorbidities and higher CHA_2DS_2-VASc and HAS-BLED scores (Table 1).

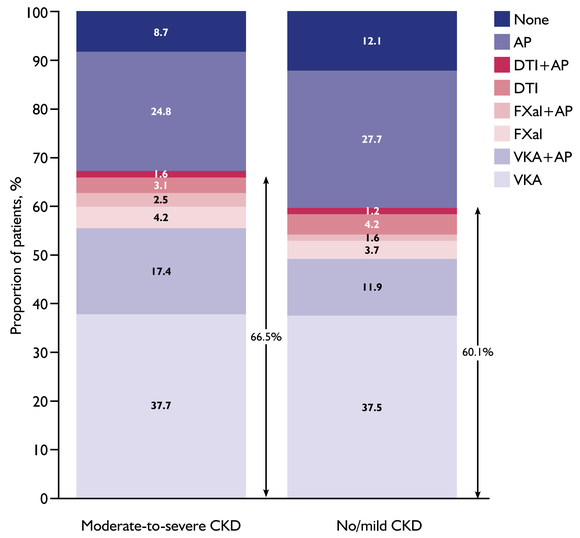
Table 1. *Patient baseline characteristics according to renal function*

	Moderate-to-severe CKD (n=1760)	No/mild CKD (n=15,399)
Female, %	49.5	43.2
Age, years, mean (SD)	76.5 (9.1)	69.0 (11.4)
Medical history, %		
Congestive cardiac failure	29.4	19.6
Coronary artery disease	27.7	19.0
Acute coronary syndromes	15.3	8.7
Systemic embolism	0.9	0.6
Bleeding	4.8	2.7
Hypertension	84.4	77.3
Diabetes mellitus	29.7	21.0
Risk score, mean (SD)		
CHA_2DS_2-VASc	4.2 (1.5)	3.2 (1.6)
HAS-BLED	2.6 (0.8)	1.3 (0.8)

CKD, chronic kidney disease; SD, standard deviation.

- Use of anticoagulant ± antiplatelet was more frequent in patients with moderate-to-severe CKD than in those with no/mild CKD (Figure 1).

Figure 1. *Antithrombotic therapy initiated at atrial fibrillation diagnosis according to renal function*



AP, antiplatelet; CKD, chronic kidney disease; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist.

- The risks of all-cause mortality, cardiovascular mortality and stroke/SE were higher in patients with moderate-to-severe CKD (Table 2 and Figure 2).
- The risk of major bleeding was also higher in patients with moderate-to-severe CKD (Table 2 and Figure 2).

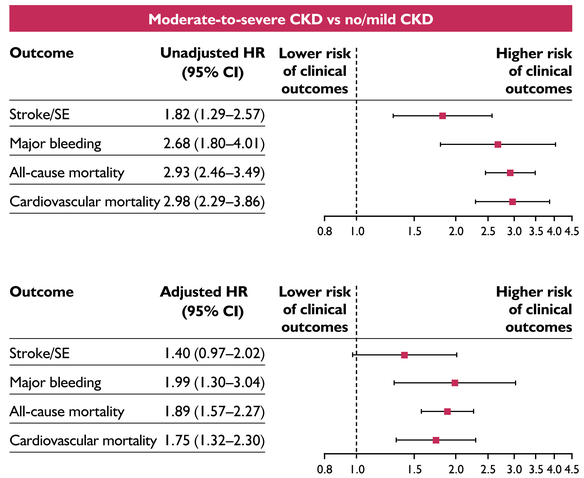
Table 2. *Event rates in patients with atrial fibrillation according to renal function*

	Moderate-to-severe CKD (n=1760)	No/mild CKD (n=15,399)
Outcome	**Rate, % per person-year (95% CI)**	**Rate, % per person-year (95% CI)**
Stroke/SE	2.4 (1.8–3.3)	1.3 (1.2–1.5)
Major bleeding*	1.9 (1.4–2.7)	0.7 (0.6–0.9)
All-cause mortality	10.2 (8.8–11.9)	3.5 (3.2–3.8)
Cardiovascular mortality	4.6 (3.7–5.8)	1.5 (1.4–1.8)

CI, confidence interval; CKD, chronic kidney disease; SE, systemic embolism.

**Seven of these patients died during 1-year follow-up. The cause of death for five of them cannot be assigned to intracranial haemorrhage.*

Figure 2. *Hazard ratios for clinical outcomes through 1-year follow-up for patients with atrial fibrillation and moderate-to-severe chronic kidney disease versus patients with atrial fibrillation and no/mild chronic kidney disease*



Hazard ratios were estimated using a Cox proportional hazards model and adjusted for CHA_2DS_2-VASc components (age, gender, congestive heart failure, hypertension, previous stroke/transient ischaemic attack/systemic embolism, vascular disease and diabetes mellitus), race, antithrombotic therapy, smoking and type of atrial fibrillation.

CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; SE, systemic embolism.

CONCLUSIONS

- Moderate-to-severe CKD is associated with a nearly two-fold higher rate of all-cause mortality, cardiovascular mortality and major bleeding, and a 1.4 times higher rate of stroke/SE in patients with AF compared with no/mild CKD, after adjustment for other risk factors
- Moderate-to-severe CKD is a poorly modifiable risk factor for adverse clinical outcomes in patients with newly diagnosed AF
- Further interrogation of mortality and bleeding event rates in the ongoing GARFIELD-AF registry may provide greater insight into balancing the benefits and risks of anticoagulant therapy for patients with newly diagnosed AF at different stages of CKD

DECLARATION OF INTEREST

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J-PB: no conflicts to declare.

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AF Garfield
global anticoagulant registry in the field

TRI Thrombosis Research Institute

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