Management of atrial fibrillation in patients with chronic kidney disease in clinical practice: a joint European Heart Rhythm Association (EHRA) and European Renal Association/European Dialysis and Transplantation Association (ERA/EDTA) physician-based survey

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The European Heart Rhythm Association (EHRA) and European Renal Association/European Dialysis and Transplantation Association (ERA/EDTA) jointly conducted a physician-based survey to gain insight into the management of atrial fibrillation (AF) in patients with chronic kidney disease (CKD) and adherence to current European Society of Cardiology AF Guidelines in contemporary clinical practice. Physician-based survey conducted during an 8-week period using an internet-based questionnaire sent to all EHRA and ERA/EDTA members, with voluntary and anonymous responses. Among 306 physicians (160 EHRA and 146 ERA/EDTA members; 56 countries), a multidisciplinary team for management of AF-CKD patients was available to only 20/300 respondents (6.7%) and 132/295 (44.7%) routinely screened CKD patients for AF. Oral anticoagulation (OAC) use was based on individual stroke risk in mild/moderate CKD but on shared decision-making in advanced CKD. The CHA2DS2-VASc score-based decisions were more common among cardiologists, with substantial intra- and inter-specialty heterogeneity in the use and dosing of specific OAC drugs across CKD stages, heterogeneous strategies for OAC monitoring (especially among nephrologists) and a modest impact of CKD on rate and rhythm control treatment decisions. The HAS-BLED score was generally not a determinant of OAC prescribing. Our survey provided important insights into contemporary management of AF patients with CKD in clinical practice, revealing certain differences between nephrologists and cardiologists and highlighting shared and specific knowledge gaps and unmet needs. These findings emphasize the need for streamlining the care for AF patients across different specialties and may inform development of tailored education interventions.

Keywords
European Heart Rhythm Association survey • European Renal Association/European Dialysis and Transplantation Association • Atrial fibrillation • Chronic kidney disease • Dialysis • Oral anticoagulant therapy

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What’s new?

- This is the first physician-based survey jointly conducted by European Heart Rhythm Association and European Renal Association/European Dialysis and Transplantation Association to gain insight into the management of atrial fibrillation (AF) in patients with chronic kidney disease (CKD).
- The survey revealed a suboptimal interdisciplinary collaboration in the management of patients with AF and CKD, low utilization of screening for AF, substantial intra- and inter-specialty heterogeneity in the use and dosing of specific oral anticoagulant (OAC) drugs across CKD stages, heterogeneous strategies for monitoring of patients taking OAC, especially among nephrologists, and a modest impact of CKD severity on arrhythmia-directed treatment decisions.
- Our survey provided important insights into contemporary management of AF patients with CKD, highlighting shared and specific knowledge gaps and unmet needs. These findings emphasize the need for streamlining the care for patients with AF across different specialties and may inform development of tailored education interventions.

Introduction

Atrial fibrillation (AF) and chronic kidney disease (CKD) share common risk factors and are increasingly prevalent globally. The two conditions often co-exist: 20% of patients with CKD have symptomatic AF, whereas around 50% of patients with AF will have some degree of renal impairment. Patients with both conditions have a higher risk of stroke, cardiovascular morbidity, and all-cause mortality compared with patients who only have either AF or CKD. The presence of CKD is also associated with increased risk of bleeding, owing to the CKD-related platelet dysfunction. Thromboembolic events associated with AF can be effectively prevented using oral anticoagulant therapy (OAC), either a non-vitamin K antagonist oral anticoagulant (NOAC) or vitamin K antagonists (VKAs). However, the risks and benefit of specific therapies or interventions may be substantially altered in the presence of advanced CKD. For example, the risk of OAC-related bleeding increases with increasing severity of CKD. Reduced renal function may also facilitate the occurrence of drug adverse effects, owing to slower drug elimination resulting in increased plasma levels, and patients with AF and CKD have increased risk of peri-procedural complications with cardiovascular invasive procedures such as, for example, percutaneous coronary intervention or AF catheter ablation.

Patients with end-stage CKD are commonly excluded from randomized clinical trials (RCTs) of OAC for stroke prevention in AF, and the high-quality evidence to inform the management of such patients in daily clinical practice is missing. The European Heart Rhythm Association (EHRA) and European Renal Association/European Dialysis and Transplantation Association (ERA/EDTA) jointly conducted a physician-based survey with the aim to gain insight into the management of AF in patients with CKD and adherence to current European Society of Cardiology (ESC) Guidelines for AF management in contemporary clinical practice.

Methods

This physician-based survey was conducted during an 8-week period starting from 18 January 2019, using an internet-based questionnaire that was jointly developed by the EHRA Scientific Initiatives Committee (SIC) and ERA/EDTA European Renal and Cardiovascular medicine (EURECA-m) working group. The link to questionnaire containing 26 single- or multiple-choice questions (see Supplementary material online) was sent to all EHRA and ERA/EDTA members, and the response was voluntary and anonymous. The respective members’ responses were collected by the EHRA-SIC and EURECA-m, and then pooled together for analysis.

Statistical analysis

The values are shown as numbers and percentages. In case of missing data for a particular question, the number of available responses is shown as n/N, where N is the total number of respondents. Owing to the observational survey design, only descriptive statistical analyses were conducted, and two-sided P-value of <0.05 was considered as statistically significant.

Results

Study population

A total of 306 physicians (160 EHRA and 146 ERA/EDTA members) from 56 countries participated in the survey (see Figure 1).

Overall, most participants were affiliated to a university-based public hospital, although affiliations of the ERA/EDTA responding members were more heterogeneous compared with the EHRA participants (Table 1). Most respondents were specialists (266/306, 86.9%), either nephrologists or cardiologists. Among EHRA respondents, 106/160 (66.3%) were electrophysiologists/arrhythmologists. More ERA/EDTA respondents had a working experience of >20 years, whereas more EHRA respondents were fellows in training.

The EHRA respondents were more frequently seeing AF patients with CKD not on dialysis, whereas ERA/EDTA respondents were more commonly seeing patients on renal replacement therapy (i.e. dialysis or renal transplant), Table 1.

Interdisciplinary collaboration in the management of patients with atrial fibrillation and chronic kidney disease

A structured multidisciplinary team for the management of patients with AF and CKD was available to only 20/300 respondents (6.7%), but 160 respondents (53.3%) were closely collaborating with physicians of another specialty (Figure 2A). Overall, 73 respondents (24.3%) stated that a multidisciplinary team was neither available nor planned, and this response was significantly more frequent among ERA/EDTA respondents (Figure 2A).

The means of renal function assessment in routine practice

For the purpose of routine assessment of renal function, most EHRA respondents were using the Cockcroft-Gault equation to estimate creatinine clearance (CrCl), whereas ERA/EDTA respondents mostly
preferred the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to estimate glomerular filtration rate (eGFR), Figure 2B. Similar preferences were observed in the assessment of renal function for OAC-related decision-making (e.g. eligibility for NOACs, dose selection), Figure 2C.

Screening for atrial fibrillation among chronic kidney disease patients

Overall, 132/295 respondents (44.7%) would routinely screen for the presence of AF in all CKD patients at their first presentation, 68/295 (23.1%) would screen for AF only in selected CKD patients, and 95/295 respondents (32.2%) would not screen for AF among CKD patients (Figure 3A). Compared with ERA/EDTA respondents, EHRA respondents would more frequently screen for AF only in selected CKD patients (Figure 3A). The approaches to screening for AF during follow-up were broadly similar to those selected for patient’s first presentation (Figure 3B). Overall, screening for AF was most likely in patients with symptoms suggestive of a cardiac arrhythmia or those with a history of arrhythmias (Figure 3A and B). More ERA/EDTA respondents would screen for AF among patients on dialysis or those with a working kidney transplant compared with EHRA respondents (Figure 3A and B).

The most common screening techniques were a single 12-lead electrocardiogram (ECG) recording (240/288 respondents, 83.3%) or ≥24-h Holter monitoring (181/288, 62.8%), see Figure 3C. The ERA/EDTA respondents more frequently chose pulse palpation, whereas EHRA respondents more frequently opted for a cardiac rhythm monitoring strategy using a handheld device, telemetry, Holter-monitoring, an implantable cardiac monitor, or cardiac implantable electronic device memory readings (Figure 3C).

Stroke prevention strategies in patients with atrial fibrillation and chronic kidney disease

A small proportion of respondents of both specialties would routinely use OAC for the prevention of AF-related stroke in all AF patients irrespective of estimated individual patient stroke risk and CKD severity (Figure 4). Increased individual stroke risk (as estimated by the CHA2DS2-VASc score value of ≥1 in males or ≥2 in females) was the most common threshold for OAC use in AF patients with a CKD of Stage 2 (68.0% of the cardiologist and 27.4% of the nephrologists). With increasing severity of CKD, the use of OAC was more commonly based on shared informed decision-making than the stroke risk alone, especially for patients on renal replacement therapy (i.e. dialysis), Figure 4, bottom panel. Overall, treatment decision-making regarding OAC use was more often based on the patient’s CHA2DS2-VASc score value among cardiologists compared with nephrologists.

The risk of bleeding, as estimated by the HAS-BLED score, was generally not a determinant of OAC prescribing among most physicians of both specialties, whereas only a few respondents would consider using aspirin or left atrial appendage occlusion for stroke prevention in patients with a HAS-BLED score of ≥3.

Regarding AF patients on haemodialysis, 12.2% of the responding cardiologists and 4.3% of nephrologists would refrain from treatment decision-making for stroke prevention, and as many as 32.4% of
cardiologists and 24.8% of nephrologists would do so for AF patients on peritoneal dialysis (Figure 4, bottom panel, the 'not applicable' bars).

**The use of specific oral anticoagulation drugs**
The use of specific OAC per CKD category is shown in Figure 5.

**Vitamin K antagonists**
When using VKAs, a similar proportion of cardiologists and nephrologists (50.7% and 49.5%, respectively) would not consider any CKD-related dose adjustment, whereas others stated different values of eGFR/CrCl as a cut-off for reduced dose of a VKA and only a very small proportion of cardiologists (2.2%) and nephrologists (8.3%) would never consider using a VKA in AF patients with severe CKD or on dialysis (Figure 5).

**Dabigatran**
In AF patients with severe CKD or on dialysis, 38.8% of cardiologists and 43.1% of nephrologists would never consider using dabigatran, whereas a small proportion of cardiologists and nephrologists would use dabigatran 110 mg bid in patients with eGFR/CrCl <30 mL/min not on dialysis, and 3% of cardiologists (but none of the responding nephrologists) would use dabigatran 110 mg bid in patients on dialysis (Figure 5).

**Rivaroxaban**
In AF patients with severe CKD or on dialysis, 23.1% of cardiologists and 39.5% of nephrologists would never consider using rivaroxaban,
whereas the renal function cut-off for using reduced dose rivaroxaban (15 mg once daily) varied among both specialties (Figure 5).

Apixaban
Only 17.9% and 22.0% of responding cardiologists and nephrologists, respectively, would never consider using apixaban in AF patients with severe CKD or on dialysis, whereas 38.8% of the cardiologists and 33.9% of the nephrologists would use reduced dose apixaban (2.5 mg bid) only in patients with eGFR/CrCl of <30 mL/min not on dialysis (Figure 5).

Edoxaban
Overall, a half of the respondents would refrain from treatment decisions regarding edoxaban because of the lack of experience with the drug; 15.7% of the cardiologists and 25.7% of the nephrologists would never consider using edoxaban in AF patients with severe CKD or on dialysis (Figure 5).

A very small proportion of responding cardiologists and nephrologists would consider no CKD-related dose adjustment of NOACs.

Monitoring of patients taking a non-vitamin K antagonist oral anticoagulant
When choosing a NOAC for patients with AF and CKD, 39.6% of responding cardiologists and 24.1% of nephrologists would schedule these patients for more frequent clinical follow-up visits, 75.4% of the cardiologists and 29.6% of nephrologists would more frequently reassess renal function in patients taking a NOAC, and 10.5% of cardiologists and 33.9% of nephrologists would manage these patients as any other patient with AF.

A small proportion of responding cardiologists (6.7%) and nephrologists (11.1%) would regularly assess specific coagulation tests in their patients taking a NOAC, whereas 4.5% of cardiologists and 1.9% of nephrologists would measure NOAC plasma levels in these patients (Figure 5).

The choice between rate and rhythm control strategy
More than a half of responding cardiologists (53.4%) and 34.5% of nephrologists stated that the presence of CKD would not influence their treatment decision about rate or rhythm control strategy for their AF patients, while more nephrologists (20.2%) than cardiologists (9.8%) would opt for rate control as a first-line therapy for AF in all patients with CKD. Only 13.5% of nephrologists and 6.8% of cardiologists would choose rate control as a first-line treatment for AF in patients on dialysis (Figure 6).

Catheter ablation for atrial fibrillation
In general, the consideration of catheter ablation for AF would not be influenced by concomitant CKD in 32.3% of responding cardiologists and 53.3% of nephrologists, but a greater proportion of cardiologists (37.6% vs. 13.3%) would not consider catheter ablation if CrCl was below 30 mL/min in non-dialysis patients. In addition, 11.3% of cardiologists and 5.7% of nephrologists would not consider catheter ablation for AF in patients on dialysis (Figure 6).
First-line antiarrhythmic drugs
Overall, most participants would use a beta blocker or amiodarone as the first-line therapy (Figure 6, bottom panel). Cardiologists would also consider using dronedarone (23.3%), flecainide (15.0%), or propafenone (17.3%). A small proportion of cardiologists (6.8%) would consider using sotalol as the first-line antiarrhythmic drug. An overwhelming majority of nephrologists would never consider dronedarone, flecainide, or sotalol.

Discussion
The main findings of this physician-based survey jointly conducted among ERA/EDTA and EHRA members (mostly nephrologists and cardiologists–electrophysiologists working in a university-based hospital) are as follows: (i) a suboptimal interdisciplinary collaboration in the management of patients with AF and CKD, (ii) low utilization of screening for AF among CKD patients (most cardiologists and nephrologists would never consider screening for AF among CKD patients).
nephrologists rather opted for various case finding strategies in selected CKD patients with symptoms or history of arrhythmia), (iii) OAC treatment decisions being driven by individual patient stroke risk and patient’s preferences (i.e. shared decision-making) rather than the estimated risk of bleeding, (iv) substantial intra- and inter-specialty heterogeneity in the use and dosing of specific OAC drugs across the CKD stages, (v) heterogeneous strategies for monitoring of patients taking a NOAC, especially among nephrologists, and (vi) a modest impact of the presence and severity of CKD on rate and rhythm control treatment decisions.

Only 6.7% of participants in our survey had a multidisciplinary team available for treatment decisions and management of patients with AF and CKD. Although 53% of participants were closely collaborating with another specialty, there was still a significant proportion of cardiologists and nephrologists (40% overall) not having any structured collaboration. A recent EHRA/ESC survey of cardiologists, neurologists, and general practitioners or family physicians managing patients with AF in six European countries also showed that >50% of participants regarded the interdisciplinary collaboration suboptimal.5

In a recent prospective study, a multidisciplinary pathway in the management of patients with AF was associated with reduced hospital admission and length of hospitalization compared with usual care,6 and management of patients with AF was associated with reduced hospital admission compared with usual care,6 and in 2016 ESC AF Guidelines (Class I, Level of Evidence B), whereas systematic ECG screening for AF may be considered in patients aged >75 years, or those at high stroke risk (IIb, B).8 Nevertheless, 32% of physicians in our survey would not routinely screen for AF in CKD patients and 23% would screen for AF only in CKD patients with symptoms or a history of arrhythmia. When screening for AF, nephrologist most commonly opted for pulse palpation or a single ECG recording, whereas cardiologists predominantly used a single ECG recording or Holter monitoring, likely owing to different availability of heart rhythm monitoring tools.

The use of OAC for stroke prevention in our survey was generally guided by patient’s stroke risk and CKD severity, and not the risk of bleeding, in line with all major international AF guidelines.9 The HAS-BLED score was generally not a determinant of OAC prescribing, consistent with contemporary studies.9,10 Indeed, the HAS-BLED score was designed to draw attention to modifiable bleeding risk factors and to flag up the ‘high risk’ patients for early follow-up.11

The proportion of physicians who would prefer shared decision-making increased with increasing severity of CKD (Figure 4), and there was a preference towards the use of VKAs and apixaban or edoxaban (and, to some extent, rivaroxaban) over dabigatran in patients with severe CKD or on dialysis. Similar to an earlier EHRA electrophysiology network centre-based survey conducted in 2015,15 the thresholds for lower/reduced NOAC doses were highly variable in the present study, altogether reflecting a persistent knowledge gap regarding NOAC dosing in patients with mild to moderate CKD and lack of high-quality evidence to inform the use of (N)OAC.

Figure 4 Stroke prevention strategies in patients with AF and CKD. AF, atrial fibrillation; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; EHRA, European Heart Rhythm Association; ERA, European Renal Association; f, female; m, male; OAC, oral anticoagulation; SPAF, stroke prevention in AF.
in patients with severe CKD or on dialysis. Also, in the previously mentioned EHRA/ESC physician-based survey, 36% of cardiologists and >50% of other participants declared insufficient skills to manage NOAC therapy in AF patients with renal issues.5

Patients with AF and end-stage CKD/on dialysis were excluded from landmark NOAC trials of stroke prevention in AF patients, but the efficacy and safety of NOACs in AF patients with mild to moderate CKD13 and those with declining renal function1 is consistent to NOACs effects in patients with normal renal function. Since all NOACs are eliminated via kidneys to some extent (especially dabigatran), appropriate NOACs dosing (as per the drug label) in patients with renal dysfunction is essential for their optimal effects.14 Owing to the lack of high-quality data, the use of NOACs in patients with CrCl <30 mL/min (dabigatran), CrCl 15 mL/min (rivaroxaban, apixaban, and edoxaban), or on dialysis (all NOACs) is not recommended in European guidelines.8,14 A meta-analysis of observational studies of

Figure 5 The use of VKAs and NOACs in patients with AF and CKD. AF, atrial fibrillation; CKD, chronic kidney disease; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; NOAC, non-vitamin K antagonist oral anticoagulant; VKA, vitamin K antagonist.
VKAs in patients with AF on dialysis showed a neutral net effect of VKAs, whereas two recent observational studies suggested that apixaban and rivaroxaban could be safer than VKAs in AF patients with end-stage CKD or on dialysis, and several ongoing RCTs may inform optimal OAC use in AF patients on dialysis in the future. Despite some limitations of estimated CrCl as a measure of renal function, most cardiologists in our survey would use CrCl to monitor renal function. Since patients in the four landmark NOAC trials of stroke prevention in AF were stratified by estimated CrCl values, using CrCl may be more convenient for (N)OAC-related treatment decision-making, especially for cardiologists. However, prior analyses have disclosed inconsistent knowledge about the similarities and differences between estimated CrCl and eGFR, including the fact that they are expressed in different units. In this regard, the automatic reporting of eGFR but not estimated CrCl by biochemistry laboratories in some countries may also impact the use of one or the other. In general, cardiologists would more closely follow AF patients with CKD taking a NOAC compared with nephrologists, whereas 10.5% of cardiologists and 33.3% of nephrologists would routinely manage AF patients with CKD as any other patients. A small proportion of participants would routinely measure specific blood coagulation tests or even NOAC plasma levels, although such an approach is not recommended.

The choice between rate and rhythm control strategies was not influenced by the presence and severity of CKD in our survey. However, cardiologists were more reluctant to opt for catheter ablation in patients with severe CKD or on dialysis, likely owing to increased risk of peri-procedural complications and recurrent AF. Overall, beta blockers and amiodarone were the most commonly used first-line antiarrhythmic drugs, whereas very few nephrologists would use other antiarrhythmic drugs, probably owing to a lack of experience with those therapies.

**Limitations**

Voluntary participation and self-reporting could have introduced a selection and reporting bias in our survey, thus influencing the generalizability of our findings. In addition, most participating physicians were affiliated to a university hospital, thus limiting the information about management of patients with AF and CKD in other healthcare settings. Nevertheless, a wide geographical representation is a strength of our survey. Additionally, some of the questions may have had limited granularity accounting for potential differences between cardiologists and nephrologists [e.g. sotalol is contraindicated in patients with a CrCl <10 mL/min, thus limiting the information about management of patients with AF and CKD in other healthcare settings].

**Conclusion**

Our survey provided important insights into contemporary management of patients with AF and CKD in clinical practice, revealing certain differences between nephrologists and cardiologists and highlighting shared and specific knowledge gaps and unmet needs. These findings emphasize the need for streamlining the care for
patients with AF across different specialties and may inform development of tailored education interventions.

**Supplementary material**

Supplementary material is available at Europace online.

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**Conflict of interest:** none declared.

**References**


**Corrigendum**

**Corrigendum to: 2019 HRS/EHRA/AFHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias [Europace 2019;21:1143–4]**

In this expert consensus statement, Figure 5 has been modified for clarity to illustrate the inner loop and to include a supporting reference in the figure legend. Please refer to the text of subsection 8.3.1 “Entrainment Mapping: Overview” and the references for further discussion. The figure is shown correctly below and has been corrected online.

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