

Management of atrial fibrillation in patients with chronic kidney disease in Europe Results of the European Heart Rhythm Association Survey

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The purpose of this European Heart Rhythm (EHRA) Scientific Initiatives Committee EP Wire Survey was to assess 'real-world' practice in the management of patients with atrial fibrillation (AF) and chronic kidney disease (CKD) in the European Electrophysiology centres. Of 41 responding centres, 39 (95.1%) and 37 (90.2%) routinely evaluated renal function in AF patients at first presentation and during follow-up, respectively, but 13 centres (31.7%) re-assessed advanced CKD only at ≥ 1 -year intervals. While the use of oral anticoagulants (OACs) in mild-to-moderate CKD patients was mostly guided by individual patient stroke risk, 31% of the centres used no therapy, or aspirin or the left appendage occlusion in patients with advanced CKD and HAS-BLED ≥ 3 . Vitamin K antagonists (VKAs) were preferred in patients with severe CKD or under renal replacement therapy (RRT), any non-VKA in patients with mild CKD, and apixaban in patients with moderate CKD. Rhythm control was preferred in patients with mild-to-moderate CKD (48.7% of centres), and rate control in patients with severe CKD (51.2% of centres). In 20 centres (48.8%), AF ablation was not performed in advanced CKD patients. Most centres performed AF ablation on OAC, but heparin bridging was still used in $> 10\%$ of centres. Our survey has shown that the importance of renal function monitoring in AF patients is well recognized in clinical practice. In patients with mild-to-moderate CKD, AF is mostly managed according to the guideline recommendations, but more data are needed to guide the management of AF in patients with severe CKD or RRT.

Keywords

Atrial fibrillation • Chronic kidney disease • Management of atrial fibrillation • Renal replacement therapy • Stroke prevention • Anticoagulation • Non-vitamin K oral anticoagulants • Vitamin K antagonists • EHRA survey • EP wire

Introduction

Chronic kidney disease (CKD), defined as a glomerular filtration rate (GFR) of < 60 mL/min per 1.73 m² for > 3 months, is present in $> 10\%$ of adults. There is a complex interplay between kidney and cardiovascular function, and even mild CKD is associated with increased cardiovascular morbidity and all-cause mortality.¹

The presence of CKD in patients with atrial fibrillation (AF) is associated with challenging decision-making regarding specific therapies or interventions, as the risk–benefit ratio may be substantially altered [particularly in patients with end-stage renal dysfunction (ESRD)].² Since patients with advanced CKD are commonly

excluded from the randomized clinical trials on AF management, there is little high-quality evidence to guide the management of AF patients with CKD in clinical practice. The purpose of this European Heart Rhythm (EHRA) Scientific Initiatives Committee EP Wire Survey was to assess 'real-world' practice in the management of AF patients with CKD in the European electrophysiology (EP) centres.

Methods and results

Participating centres

This survey was based on a questionnaire sent via internet to the EHRA-EP Research Network centres. Of 41 responding centres,

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36 (87.8%) were university hospitals; AF ablation was not available in 4 centres (9.8%), 12 centres (29.2%) performed <100 AF ablations, 13 centres (31.7%) performed 100–199 procedures, and 12 centres (29.3%) performed ≥200 AF ablations per year.

Only one centre (2.4%) had a structured multidisciplinary team for management of AF patients with CKD, and two centres (4.9%) planned to develop such a team. In 15 centres (36.6%) AF patients with CKD were managed by cardiologists/electrophysiologists and in 19 centres (46.3%) there was a close collaboration with nephrologists (4 centres [9.8%] did not submit an answer to this question).

Renal function assessment

In most centres (39 [95.1%]) renal function was initially evaluated in all AF patients, particularly in those on OACs or with a history of CKD (37 centres, [90.2%]) and in patients taking antiarrhythmic drugs (AADs; 34 centres [82.9%]). During clinical follow-up renal function was re-assessed in 37 centres (90.2%), particularly in patients with known CKD (34 centres, 82.9%) and those taking OAC (31 centres, 75.6%) or AADs (26 centres, 63.4%).

Figure 1 shows the frequency of re-assessment during follow-up by renal function categories. In most centres, patients with initially normal GFR were re-assessed according to clinical judgement (14 centres, 34.1%) or at 1-year intervals (11 centres, 26.8%). In 13 centres (31.7%) patients with severe CKD or those on renal replacement therapy (RRT) were re-assessed only annually or at longer irregular intervals. Renal function was assessed only by serum creatinine measurements in 7 centres (17.1%). Most centres

(27 [65.9%]) estimated GFR, predominantly using the Cockcroft-Gault or Modification of Diet in Renal Disease (MDRD) equation (Figure 1). In 7 centres (17.1%) both GFR and albuminuria criteria were routinely used.

Stroke prevention and the use of oral anticoagulants

Figure 2 (upper panel) shows common strategies for stroke prevention in AF patients with CKD. The use of OAC in patients with mild or moderate CKD was mostly guided by individual patient stroke risk (estimated by the CHA2DS2-VASc score). In patients with increased risk of bleeding (HAS-BLED ≥ 3), the proportion of centres using no therapy, aspirin or the left atrial appendage occlusion instead of OAC increased with the increasing severity of CKD. The number of centres using individual shared decision-making (which involved informed patient preferences) also increased with declining renal function.

Figure 2 (middle panel) shows preferences among the centres with regard to specific OAC agents in patients with various stages of CKD. Overall, vitamin K antagonists (VKAs) were preferred to non-vitamin K oral anticoagulants (NOACs) in patients with advanced CKD or RRT, apixaban was the most commonly used OAC in patients with moderate CKD, and any NOAC was preferred to VKAs in patients with mild CKD. A minority of centres considered patient preferences regarding the choice of an OAC agent.

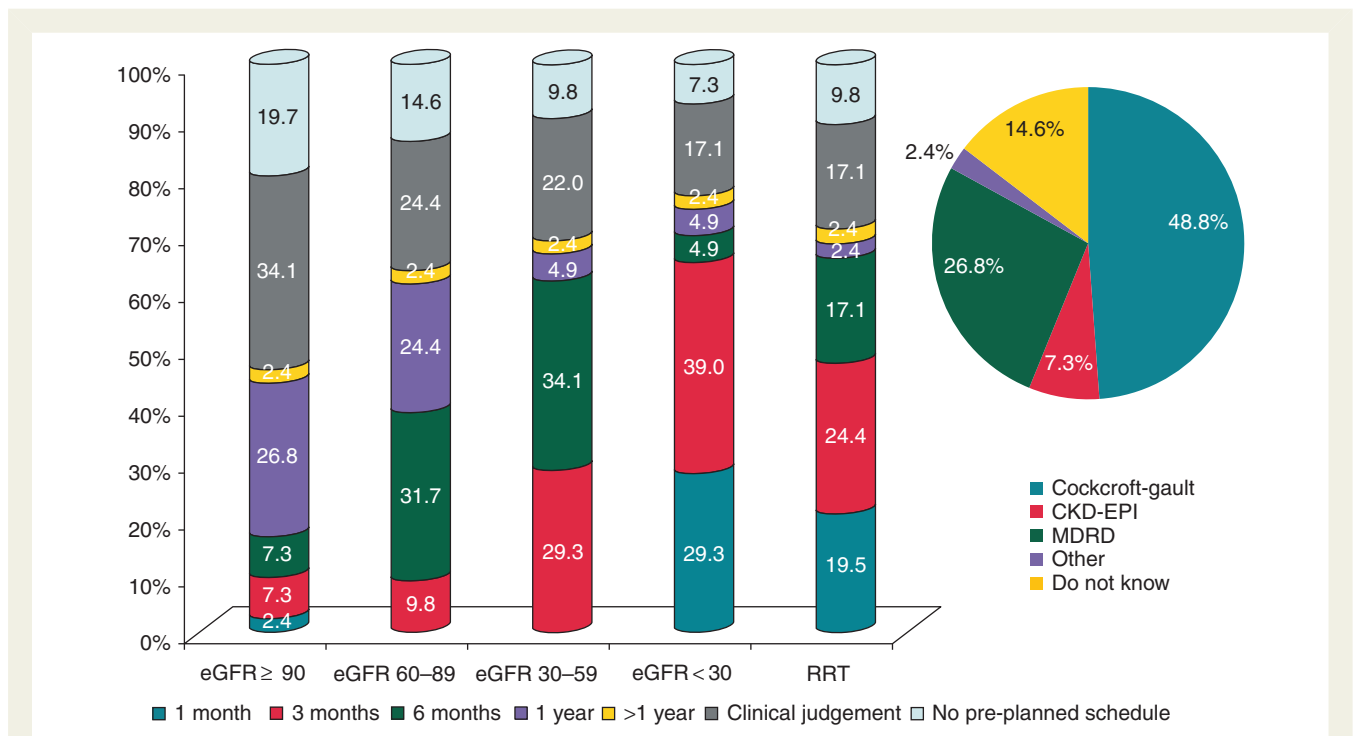


Figure 1 Follow-up renal function re-assessment by renal function categories (left); calculation of glomerular filtration rate (right). eGFR, estimated glomerular filtration rate; RRT, renal replacement therapy; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; MDRD, modification of diet in renal disease.

The patterns of OAC use by CKD category are shown in Figure 2 (lower panel). In 61% of the centres VKAs dosing was not influenced by the presence of CKD, but NOACs were used even in patients with advanced CKD (e.g. dabigatran was not used in patients with severe CKD in only 41.5% of centres).

Strategies for AF-related symptom reduction

Clinical decision on rhythm or rate control was not influenced by the presence of mild or moderate CKD in 26 (63.4%) and 22 centres (53.7%), respectively. However, shared decision-making including patients with severe CKD or RRT was employed in 21 (51.2%) and 19 centres (46.3%), respectively. In general, rhythm control was preferable in patients with less advanced CKD, and rate control in patients with more severe CKD (Figure 3, upper panel). Figure 3 (lower panel) shows patterns of AADs use by CKD category. The use of AADs such as propafenone, sotalol, amiodarone, and dronedarone was greatly heterogeneous in patients with various degrees of renal dysfunction.

In 20 centres (48.8%), catheter ablation for AF was not performed in patients with severe CKD. In further 20 centres (48.8%), only pulmonary vein isolation was performed during the first procedure, whilst 2 centres (4.9%) also performed an extensive AF substrate ablation. Re-ablation of AF was done as needed, regardless of the presence of CKD, in 20 centres (48.8%), whilst in 3 centres (7.3%) re-ablation was not considered in CKD patients. In 16 centres (39.0%) the choice of energy source was not influenced by the presence of CKD, 9 centres (22.0%) preferred radiofrequency catheter ablation for CKD patients, 2 centres (4.9%) preferred cryoablation, whilst in 6 centres (14.6%) only radiofrequency ablation was available.

Periprocedural management of oral anticoagulation

In 25 centres (61.0%) AF ablation was always performed under uninterrupted VKAs, and in 11 centres (26.8%) under uninterrupted NOACs. Due to perceived risk of bleeding, VKAs were always interrupted in 12 centres (29.3%) and NOACs in 10 centres (24.4%) but due to increased thromboembolic risk with discontinuation of

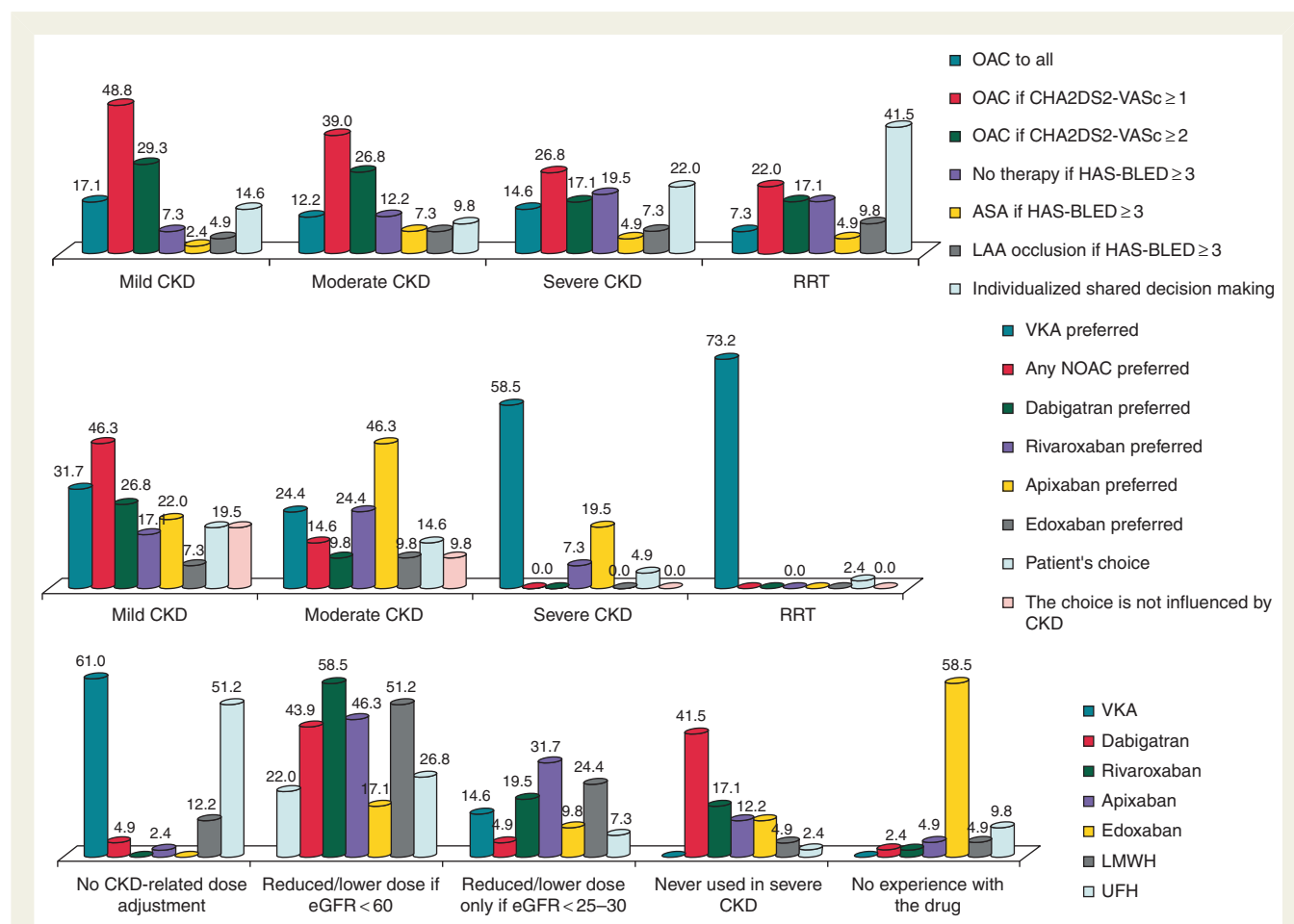
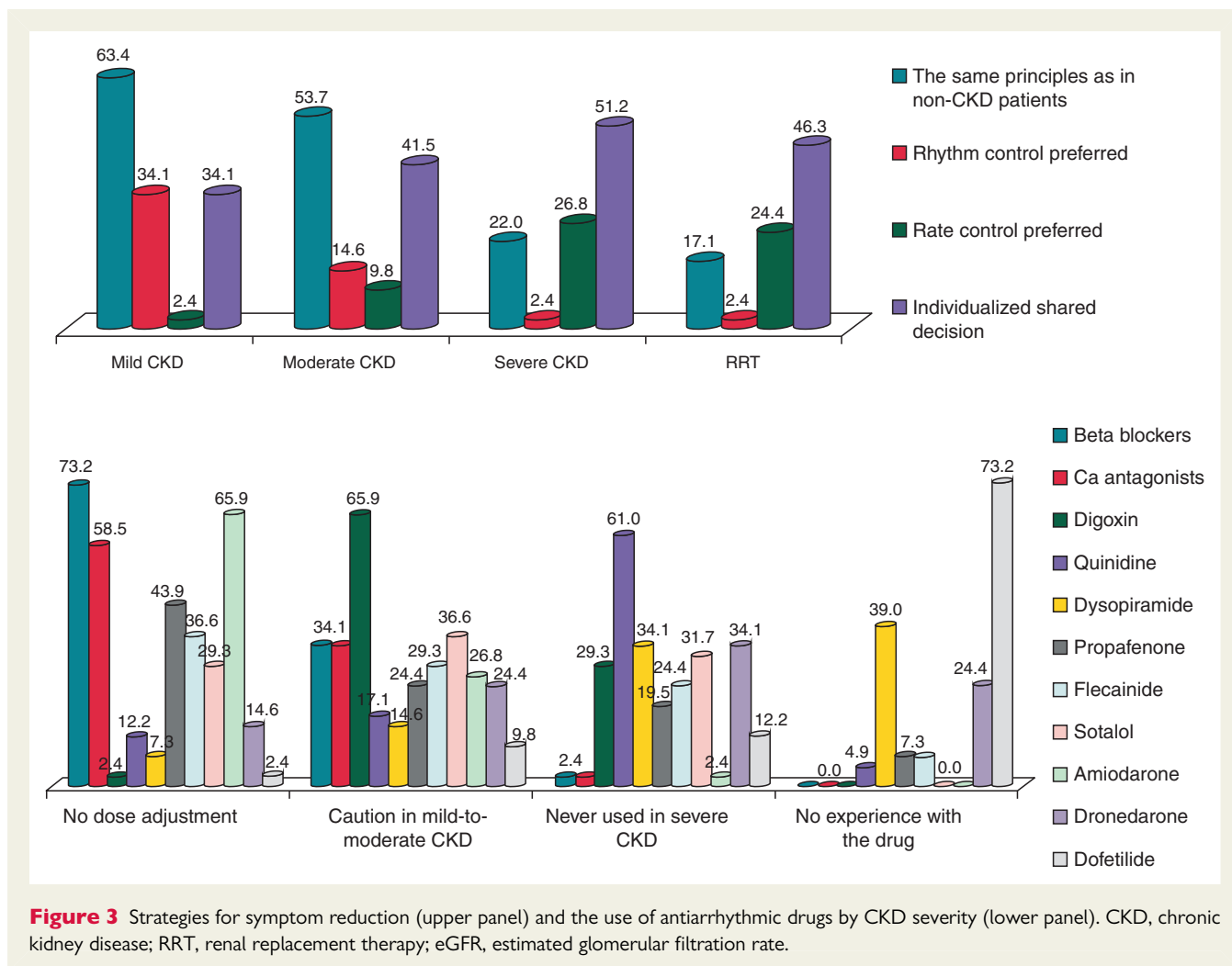


Figure 2 Strategies for stroke prevention in AF patients with CKD (upper panel), preference for specific oral anticoagulant drug (middle panel) and dosing by CKD severity (lower panel). AF, atrial fibrillation; CKD, chronic kidney disease; RRT, renal replacement therapy; OAC, oral anticoagulant; ASA, aspirin; LAA, left atrial occlusion; eGFR, estimated glomerular filtration rate; VKA, vitamin K antagonists; LMWH, low molecular weight heparin; UFH, unfractionated heparin.



OAC, bridging with heparin was used in 8 (19.5%) and 5 centres (12.2%), respectively. Four centres (9.8%) had a centre-specific protocol for periprocedural management of VKA therapy, and 10 centres (24.4%) had such a protocol for NOACs.

Discussion

This EP Wire provided an insight into the European clinical practice in management of AF in patients with CKD. The survey mostly reflects the clinical practice of arrhythmologists, and the low response rate is a limitation. The main findings of this survey are (i) an awareness of the relevance of renal function in AF patients, (ii) a heterogeneity in stroke prevention strategies and clinical follow-up in AF patients with severe CKD or RRT, (iii) an inconsistent approach to NOACs use and dosing relative to the presence and severity of CKD, (iv) variable effects of the presence and severity of CKD on the choice of AF-related symptom reduction strategies, including the use (and dosing) of AADs and AF ablation, and (v) variations in periprocedural management of OAC therapy (particularly NOACs).

Renal function assessment

Renal function and albuminuria should be monitored at least annually, or more frequently in patients at risk of CKD progression or in

whom indices of renal function would impact treatment decisions.¹ In our survey, most centres monitored renal function over time, but <20% of the centres routinely measured albuminuria, and in 31% of the centres patients with severe CKD or RRT were monitored less frequently than recommended or were left without a monitoring plan. A recent update of the EHRA Practical Guide on NOACs use in AF patients suggests that renal function re-assessment intervals can be simply determined by dividing CrCl value by 10 in patients with a creatinine clearance (CrCl) of <60 mL/min.³

Compared with Cockcroft-Gault or MDRD, CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation is less biased, offers a greater accuracy in GFR estimation and is increasingly used.¹ Less than 10% of centres in our survey used CKD-EPI equation for the estimation of GFR.

Stroke prevention and the use of oral anticoagulants

Patients with AF and CKD are at increased risk of both stroke and bleeding,^{1,2} but warfarin (and not aspirin) use has been associated with a positive net clinical benefit and lower all-cause mortality even in patients with ESDR or on RRT.⁴ In our survey, a total of 14.6, 28.3, 31.5 and 31.8% of the centres used alternatives to OAC (i.e. no therapy, aspirin or the LAA occlusion) in patients

with mild, moderate, or severe CKD or on RRT and an HAS-BLED score of ≥ 3 , respectively. In a recent EP Wire, patient preferences were of the highest relevance for clinical decision on OAC therapy in nearly 70% of centres.⁵ In the present survey, however, shared decision on OAC for patients with mild CKD was used in only 14.6% of centres, but the proportion increased to 41.5% when deciding on OAC therapy in RRT patients. In a recent meta-analysis, NOACs had a consistent efficacy and safety compared with warfarin in patients with mild-to-moderate CKD, and the reduction in bleeding with apixaban relative to warfarin was even more pronounced in patients with moderate CKD compared with those with normal renal function.⁶ However, patients with severe CKD were not included in the major NOACs trials, and the use of NOACs is currently not recommended in patients with eGFR < 25 – 30 mL/min.^{1,3} In our survey, warfarin was clearly preferred to NOACs in patients on RRT, but in 26.8% of the centres NOACs (mostly apixaban) would be given to patients with severe CKD without RRT. Interestingly, only 41.5% of the centres stated that they would never give dabigatran to patients with severe CKD (i.e. eGFR < 30 mL/min). Dabigatran is 80% renally eliminated and should not be used in patients with a CrCl of < 30 mL/min.³

Whilst only a small proportion of centres in our survey did not consider renal function when choosing the NOAC dose, there was a considerable heterogeneity in NOAC dosing in patients with moderate-to-severe CKD. Generally, NOAC dose should not be reduced in patients with moderate CKD in the absence of additional bleeding risk factors (excluding rivaroxaban, which should be reduced to 15 mg if CrCl is < 50 mL/min). However, dabigatran is not recommended in patients with CrCl < 30 mL/min in Europe, and other NOACs should be used in reduced doses in patients with CrCl 15–29 mL/min.^{1–3} Of note, a post-hoc analysis of the RE-LY dataset showed superior efficacy and safety of dabigatran when used according to the European label.⁷

Strategies for atrial fibrillation-related symptom reduction

Renal dysfunction promotes arrhythmogenic substrate development and alters drug pharmacokinetics.¹ Heterogeneity in AADs use in our survey emphasizes the need for more data on AADs safety relative to renal function (e.g. although sotalolol is 70% renally eliminated, no CKD-related dose adjustments was required in nearly 30% of centres, whilst in 26.8% of centres amiodarone was used with caution in patients with mild-to-moderate CKD, although amiodarone is not renally eliminated).¹

In our survey, the choice between rate and rhythm control was influenced by the presence of more advanced CKD. Rhythm control was preferred in patients with less severe CKD, likely due to the lower expected success rate and limited data on safety of AADs in patients with more advanced CKD. However, AF ablation is increasingly performed in patients with advanced CKD.¹ Recent data suggest that persistent sinus rhythm was associated with improvement in renal function, whilst multiple re-ablations yielded similar efficacy as in non-CKD patients at 5 years.^{1,8} In our survey, nearly half the centres did not perform AF ablation in patients with advanced CKD, and the majority of the centres which

performed AF ablation in CKD patients would perform re-ablation as needed, regardless of the CKD stage.

Periprocedural management of oral anticoagulation

The risk of procedure-related vascular complications is increased in CKD patients compared with those without CKD.¹ Although majority of centres in our survey performed AF ablation per current recommendations (i.e. under uninterrupted VKAs or with brief temporary NOACs discontinuation),⁹ around 30% of centres temporarily discontinued VKAs, and half of those centres used bridging with heparin, despite clear evidence of increased bleeding and no reduction in stroke rate with bridging.⁹

Conclusion

Our survey showed that the importance of renal function monitoring in AF patients is well recognized in clinical practice. In patients with mild-to-moderate CKD, AF is mostly managed according to the guideline recommendations, but more data are needed to guide the management of AF in patients with severe CKD or on RRT. Close collaboration of cardiologists and nephrologists (as in nearly half the centres in our survey), or multidisciplinary AF teams may improve management of AF patients with advanced CKD.

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