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Review

Diagnosis and Therapy of Atrial Fibrillation in Geriatric Patients

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Abstract

Atrial fibrillation is very common in most old patients who need an adapted therapy due to their comorbidities. Before initiating an antiarrhythmic therapy, possible adverse effects, especially iatrogenic proarrhythmia, and extracardiac side-effects, must be considered. In geriatric patients with atrial fibrillation, heart rate control is the most frequent therapy. Oral anticoagulation plays a vital role in the therapy, but anticoagulation in old patients, who had a bleeding or stroke event, is challenging. Available data favor the use of anticoagulation in old patients with atrial fibrillation and suggest the use of direct oral coagulants, in most cases, over the use of vitamin K antagonists. However, a gap exists in the knowledge regarding the optimal dose in very old patients, particularly in patients with mild-to-moderate renal failure, with very low or high body mass index, and in those receiving medications with a high risk of metabolic interactions.

Keywords

Atrial fibrillation; antiarrhythmic drugs; heart rate control; oral anticoagulants; rhythm control

1. Introduction

Atrial fibrillation (**AF**) is a supraventricular tachyarrhythmia with uncoordinated atrial electrical activation with consequent ineffective atrial contraction. AF may be asymptomatic (subclinical) [1-3]. Atrial high-rate episodes (**AHREs**) and subclinical AF (**SCAF**) are either markers or subtypes of AF [1].

The 2020 European Society of Cardiology (ESC) Guidelines on AF [1] provided the actual state of the art on this arrhythmia and embedded the data on geriatric patients in the general context. The current review deals with specific data for geriatric patients.

1.1 Age and AF

Age is an independent risk factor for AF and increases AF prevalence and adverse outcomes [1, 4]. The number of geriatric patients is increasing with the increasing life expectancy. Currently, in patients aged ≥80 years, the prevalence of AF is >10%; it is expected to double in the next four decades. It has also been estimated that 25% of the patients ≥40-year-old will have AF in their lifetime [5-11], and one in three individuals free of AF at index age 55 years will develop AF later in life [12]. Age affects the therapy of AF negatively as it reduces efficacy and increases adverse effects [1, 13].

1.2 Screening for AF

The 2020 ESC Guidelines on AF [1] provided some recommendations on screening for AF in old patients; in patients aged ≥65 years, AF frequently changes from paroxysmal to persistent episodes and commonly becomes permanent; the more frequent type should be used for classification. Screening can be both opportunistic or systematic. The 12-lead ECG is the gold standard for screening [1, 14, 15]. Pulse palpation, automated BP monitoring, single-lead ECG recorders, which mostly record single-point or repeated ECG [15-19], and a smartphone photoplethysmography [20] are frequently used. Previous studies reported that screening for AF highlights cases treated insufficiently and showed an increasingly high prevalence of asymptomatic AF [16-18]. Screening has also shown the potential to prevent AF-related strokes through appropriate treatment [18-20]. The 2020 ESC Guidelines on AF [1] made the following key screening recommendations:

a) in patients aged ≥65 years, opportunistic screening by recording the pulse or ECG rhythm strip (Class I Level B) should be performed;

b) intermittent ECG screening in ≥75-year-old patients;

c) monitoring pacemakers (PM) and implanted cardioverter defibrillators regularly (Class I Level C);

d) a definite diagnosis of AF in positively screened cases should be established only after a physician reviews the single-lead ECG recording of ≥30 sec, or after a 12-lead ECG confirms AF (Class I Level B); and

e) systematic ECG screening should be considered to diagnose AF in individuals aged ≥75 years, or those at high risk of stroke (Class IIa Level B).

The specificity of screening tools ranges between 70 and 100%, and the sensitivity ranges between 87 and 99%. Data on sensitivity and specificity were collected from small observational cohorts with a substantial risk of bias due to signal selection in several studies [1].

A favorable cost-effectiveness profile based on pulse palpation, hand-held ECG devices, and smartphones [15, 16] was estimated for screening. For ≥65-year-old patients, opportunistic screening and systematic screening were suggested to be more cost-effective than routine practice without screening [1, 21]. In ≥65-year-old patients, intermittent ECG recording with the AliveCor heart monitor and a smartphone-based single-lead ECG system twice a week over 12 months increased new AF detection four-fold as compared to routine care without screening [22, 23]. Importantly, clinically determined AF patterns did not correspond well to the AF burden measured by long-term ECG monitoring [19, 22, 24]. AF satisfies several criteria for disease screening [25], though data are scarce on the selection of optimal screening; suitable data confirming the health benefits of screening for AF in geriatric patients are lacking in several studies [13, 21, 22, 26, 27]. Moreover, as screening might increase fear in geriatric patients, its limitations, like increased cost and false negatives, should be considered. It remains unknown whether screening would contribute to the choice of therapy of very old AF patients.

1.3 Atrial High Rate Episodes (AHREs) and Subclinical Atrial Fibrillation (SCAF)

AHREs and SCAF are very common among geriatric patients with several cardiac disorders. In 70% of the patients with implanted devices, these arrhythmias are detected, although the prevalence may be lower in the general population [28, 29]. AHREs and SCAF often change daily, and the risk of subsequent progression to longer episodes increases with the burden [29, 30]. Episodes lasting ≤20 sec/day show no significant association with an increased risk of stroke or systemic embolism, and hence, are considered clinically irrelevant [1]. Studies have shown that clinical AF develops in about 15% of the patients within 2.5 years after diagnosing AHREs and SCAF [27, 28, 31]. Data from implanted devices have shown that, with an increase in the duration, the risk of thromboembolic complications and cerebral ischemic strokes (**CIS**) increase in both AHREs and SCAF [32]. A study [33] assessed the occurrence of these arrhythmias in a patient who had a PM. When the AHREs or SCAF episodes lasted <24 hμ the risk of CIS remained the same as for patients without AF, whereas, when the episodes lasted >24 h, an increased risk of CIS was reported. Numerous studies [34-40] have shown that ≥5 min-long episodes of AHREs and SCAF are associated with an increased risk of clinical AF, cardiovascular death, and major cardiovascular events. Overall, the absolute risk of stroke associated with AHREs and SCAF might be lower than with clinical AF, though a greater risk has been reported [28, 34, 35, 38, 40]. Notably, there was a temporal dissociation between the documentation of AHREs or SCAF and the occurrence of acute strokes, and AHREs and SCAF might represent markers rather than risk factors for stroke [38, 39, 41]. Similar to that in the younger AF patients, modifiable stroke risk factors should be identified and managed in geriatric patients, and an interdisciplinary approach should be adopted to address the complexities posed by these arrhythmias [18]. The 2020 ESC Guidelines on AF [1] stated that available evidence is insufficient to justify routine oral anticoagulation (**OAC**) in patients with AHREs, but OAC might be indicated in a) select ≥75-year old patients with SCAF, who had a previous stroke, b) patients with a CHA2DS2-VASc score ≥3, and c) patients with additional stroke factors, such as spontaneous echo contrast in dilated left atrium, significant renal failure, and elevated blood biomarkers. Also, elderly female patients might have a higher risk than males.

2. Cardioversion

The 2020 ESC Guidelines on AF [1] recommended that emergency cardioversion (**CV**) could be performed in a hemodynamically unstable AF-patient, after considering the periprocedural thromboembolic risk and in the absence of a left atrial thrombus. This was also the case for geriatric patients. Synchronized direct current electric CV (**ECV**) is more effective than pharmacological CV (**PCV**) and often results in sinus rhythm (**SR**) restoration [1, 42]. ECV requires sedation which can be achieved by intravenous midazolam and/or propofol, or etomidate [43]. In geriatric patients, the dosage of the drugs must be selected after considering the concomitant morbidities. Without exception, for geriatric patients, biphasic defibrillators are more effective than monophasic defibrillators [44]. Anterior--posterior electrode positions were reported to restore SR more effectively, though few authors suggested that specific electric pad positioning was not critically important for successful ECV [45]. Maximum fixed-energy ECV was more effective than an energy-escalation strategy [46]. As skin burns might occasionally be observed, blood pressure and oxygen monitoring during the procedure should be performed routinely. Intravenous atropine or isoproterenol, or temporary transcutaneous pacing, should be provided in case of post-CV bradycardia. In the current study, in geriatric patients, troponin values were slightly above the reference values in the hours following ECV, possibly due to mild myocardial damage induced by ECV.

In hemodynamically stable AF patients of any age, treatment of potentially modifiable conditions (e.g., electrolyte disturbances) should be considered, and an elective CV should be planned [1, 18]. PCV is a possible choice. It is less effective than ECV but requires no sedation and is usually effective in recent-onset AF. It should be considered that in patients with recent-onset AF who are aged ≥65 years, spontaneous conversion to SR occurs: within 3 h in up to 18%, within 4 - 8 h in 69%, within 24 h in up to 66%, and within 48 h in up to 83% of the patients [47, 48]. Hence, in these patients, a “wait-and-watch” approach, with rate control (**RaCo**) only and PCV when needed within 48 h of symptom onset, is as safe as and non-inferior to immediate PCV [48]. However, in general, geriatric patients have long-standing and persistent AF, and consequently, the spontaneous conversion to SR is rare, and the chances for an effective CV are also low.

3. Antiarrhythmic Drugs

Pretreatment with antiarrhythmic drugs (**AADs**) can enhance the efficacy of CV [48]. The choice of the drug is based on the type and severity of the heart disease. This is especially important in geriatric patients with multiple morbidities. As in younger patients, in geriatric patients, class IC antiarrhythmic drugs (AADs), such as flecainide, are prescribed in the absence of significant left ventricular hypertrophy, systolic dysfunction, or ischemic heart disease. These AADs result in prompt (3−5 h) and safe restoration of SR in >50% of AF patients aged ≥65 years [47]. In patients treated with class IC AADs, especially flecainide, an atrioventricular node blocking drug should be prescribed to avoid the transformation of AF to atrial flutter with 1:1 conduction [49]. Intravenous amiodarone is primarily indicated in geriatric patients with left ventricular dysfunction; it has a limited and delayed effect but can reduce heart rate within 12 h [50]. Intravenous vernakalant is the most rapid cardioversion drug, including for patients with mild heart failure and ischemic heart disease, and is more effective than flecainide [51] or amiodarone [52]; however, no study could be found on the use of vernakalant in geriatric patients. We could not find any paper in geriatric patients on the rare use of Dofetilide. In some patients with rare paroxysmal AF episodes, a self-administered oral dose of flecainide or propafenone was slightly less effective than PCV, but these drugs might be offered, provided that the safety and efficacy of these drugs are first established in a specialized setting [53]. However, geriatric patients usually have a long-standing permanent AF, and consequently, this therapy is rarely useful. Old age, combined with an increased size of the left atrium, is one of the factors associated with a greater risk of AF recurrence after CV [1, 54, 55]. In younger patients, in case of AF recurrence after PCV, an early re-cardioversion might prolong the subsequent duration of SR [56]. However, no specific data on geriatric patients was available.

Though several authors [57] had reported that CV did not halt the progression of AF and did not improve the quality of life (**QoL**), others [58] found a significant improvement of QoL in patients who maintained SR after CV. Notably, most studies have reported data from patients aged ≥65 years, and data on very old AF patients are lacking. Because of the multiple medical conditions and the need for treatment with other drugs, geriatric patients might experience more side effects than young patients when treated with AADs [13].

4. Rhythm Control

Based on the available literature, in patients aged <65 years, rhythm control (**RC**), which attempts to maintain SR, is aimed to reduce AF-related symptoms and improve QoL [1]. RC requires a combination of different treatment approaches, including cardiovascular prophylactic medications, treatment for sleep apnea, lifestyle, AADs, OAC [1, 54-58], and catheter ablation (**CA**) [1]. No established evidence exists currently for younger patients, which shows that RC improves the outcome of AF [1]. In geriatric patients, factors against the possibility of reaching RC must be considered. Very old age predicts AF progression, and AF becomes less amenable to treatment and often remains irreversible [1, 4, 53, 59]. In real-world settings, in the very old AF patients, concomitant morbidities and the presence of long-standing AF reduces the possibility of RC. Furthermore, geriatric patients are more prone to experience iatrogenic adverse effects than younger ones.

The registry Record-AF Trial [59] reported an association of physician-directed treatment with either RC over an average follow-up period of one year with improvement in health-related QoL in recent-onset AF patients. Although the overall difference was not significant, a subset of patients experienced a better improvement in their quality of life (QoL). After adjusting for baseline factors, the degree of improvement in QoL was minimally higher in patients treated with RC compared to those treated with RaCo. This paper is based on data from patients with recent-onset AF and usually younger than 65 years.

The indications, techniques, advantages, and complications of CA are listed in the 2020 ESC Guidelines on AF [1]. In young patients without long-standing AF, an early CA performed by appropriately trained operators is a safe therapy for RC, showing symptom improvement, and should halt the progressive pathoanatomical changes associated with AF [1, 60, 61]. In real-world settings, CA is seldom used in geriatric patients [62]. However, in identified old FA patients, CA is effective, with better success rates comparable to younger ones [62-69] and with acceptable complication rates [61-69]. Nevertheless, age was a predictor of complications in CA [68-76], and some studies [77, 78] suggested an age-related increase in multivariable-adjusted risks for AF recurrence, death, and major adverse cardiac events. Finally, it should also be considered that in some young AF patients a successful RC with CA can fail to reduce the pathological atrial changes associated with AF [73, 74].

The 2020 ESC Guidelines presented data on surgery and hybrid surgical/CA procedures on AF [1], but the use of these procedures is quite unlikely in very old AF patients.

5. Rate Control

When RC is neither feasible nor suggested, RaCo becomes an integral part of management and is often sufficient to improve AF-related symptoms [79]. However, the best intensity of RaCo treatment is not known [80] because, in two large trials [81, 82], no difference was observed in a composite of clinical events, NYHA class, or hospitalizations between the 'strict' (target heart rate <80 bpm at rest and <110 bpm during moderate exercise) and 'lenient' heart rate arm (heart-rate target <110 bpm). Therefore, lenient RaCo could be an acceptable approach, though, in geriatric patients with multiple pathologies, tachycardic AF may induce a hemodynamic deterioration. In this case, the target heart rate intensity must be lowered to a strict value. For RaCo, either β-blockers calcium antagonists, diltiazem, or verapamil are better than digoxin and are usually effective in case of a high sympathetic tone [83-85]. However, in geriatric patients, verapamil might induce hypotension and constipation, and diltiazem might induce edemas and worsen cardiac function. In AF patients with reduced left ventricular function, amiodarone can be used [85, 86], although in the long term, especially in elderly patients, amiodarone is problematic due to its many side effects. In case of insufficient effect, combination therapy might be required with β-blockers and digoxin [87, 88].

AADs are used to improve several symptoms related to AF [1]. The comparative efficacy of available AADs remains unknown [88], and AAD therapy is less effective than CA [88-93]. In geriatric patients with multiple pathologies and medications, AADs have shown frequent proarrhythmic and extracardiac side effects [1, 8, 16].

6. Antiarrhythmic Drugs after Catheter Ablation

Compared to no therapy, AADs should approximately double SR maintenance after CA [1] and, after being used for a short time, should decrease the occurrence of recurrent AF [94-97], although no consensus exists on the benefits of AADs [94, 95]. CA is less often used in geriatric AF patients than in younger ones; in old patients treated with CA, management of the underlying cardiovascular conditions is pivotal to reduce AF symptom burden and facilitate the maintenance of SR [98-101]. Several AADs have been shown to reduce AF recurrence in patients aged <70 years, but all available AADs may be proarrhythmic [1]. Furthermore, quinidine and disopyramide (class IA AADs), and sotalol have been associated with increased overall mortality [101]. Frequent risk factors for the occurrence of a proarrhythmic effect are detailed in the 2020 ESC Guidelines on AF [1], and old age is one of these risk factors [101, 102]. The impact of multimorbidity on treatment effects is poorly understood [103] because most clinical trials enroll younger and healthier patients than geriatric ones and rarely systematically account for patient multimorbidity. Furthermore, treatment effect heterogeneity is usually tested across different subgroups of patients based on the presence or absence of individual variables, not based on summative risk scores that account for multimorbidity.

7. Atrionodal Catheter Ablation (ANCA) and PM Implantation

ANCA and PM implantation is used as the last option for drug-resistant and poorly tolerated tachycardic AF. The treatment has proven to be very effective, relatively simple, and with a low complication rate and low long-term mortality risk [1, 104, 105], especially when the PM is implanted a few weeks before the ANCA, and the initial pacing rate after ablation is set at 70-90 bpm [105-107]. The choice of pacing therapy (right ventricular or biventricular pacing) depends on the characteristics of the patients [107-109]. In geriatric AF patients, ANCA+PM has proven useful as it does not worsen [105] and may even improve the left ventricular function [105-109]. However, in younger AF patients ANCA+PM should be considered only if there is a serious need for RaCo and all other treatment options have been exhausted.

In severely symptomatic patients with permanent AF and at least one hospitalization for heart failure, ANCA combined with cardiac resynchronization therapy (**CRT**) might be preferred [1]. In a small trial, the primary composite outcome (death, hospitalization for heart failure, or worsening of heart failure) was significantly less common in the ANCA+CRT group compared to the outcome for the drug arm group, and ANCA+CRT patients showed a significant (36%) decrease in symptoms and physical limitations at 1-year follow-up [110, 111]. However, published data are available on AF patients aged ≥65 years, but data on geriatric patients is scarce.

Lastly, data from young AF patients showed that His-bundle pacing after ANCA might evolve as an attractive alternative pacing mode [112, 113].

8. Thromboembolic Risk

To sum up, AF increases the risk of stroke up to fivefold, especially when permanent. AF is responsible for up to 30% of CIS [1, 5, 6, 114]. However, this risk is not homogeneous and varies depending on the presence of specific stroke risk factors and modifiers [1]. Guideline-recommended scoring systems are used to assess ischemic and hemorrhagic risks [1, 115]. These scoring systems incorporate age for assessing the risks. However, it should be noted that the scoring systems were developed and validated not specifically for guiding OAC in the elderly, and thus, have many limitations when applied to very old patients [116]. The HAS-BLED score chiefly predicts the major bleeds, at least 80% of which are extracranial hemorrhages (particularly gastrointestinal), carry <6% mortality rates and are manageable. However, it does not help to identify old patients with AF in whom the risk of fatal or disabling intracranial hemorrhage (**ICH**), which is the worst concern in the elderly patients, might increase the risk of fatal CIS. Furthermore, the risk is not static and particularly in the case of bleeding, many potentially dangerous conditions can be addressed [12, 116, 117]. Therefore, some cardiologists [116] have proposed that it would be beneficial to develop a novel scoring system for geriatric AF patients, encompassing all the risk factors specific to this population. Physicians should recognize early and minimize the impact of each modifiable risk factor such as inadequate blood pressure control, deteriorated renal function, hematologic disorders, suboptimal nutritional status, and lack of social support. Close periodic re-evaluation of the very old patient is essential due to frequent changes in the clinical status to assess treatment adherence, verify the need for dose adjustment, and educate the patient continuously about the importance of OAC. Unfortunately, the new scoring system proposed is not feasible for routine therapy.

The CHA2DS2-VASc scoring system considers patient's age, but studies of the CHA2DS2-VASc score report a broad range of stroke rates depending on study setting, methodology, ethnicity, and prevalence of specific stroke risk factors in the study population [1, 117-119].

Despite being beneficial, OAC remains underused in ≥80-year-old patients due to the concerns of bleeding complications, comorbidities (mainly renal failure), and poor functional autonomy [1, 13, 115-119] and, finally, it must be acknowledged that a high HAS-BLED score should not withhold OAC, as the net clinical benefit of OAC is even greater for such patients [1, 12, 13].

9. Antiplatelets

In the case of AF, antiplatelets are less effective and less safe than vitamin K antagonists (**VKAs**), are ineffective for stroke prevention, and are potentially harmful, especially among elderly AF patients. Additionally, dual antiplatelet therapy is associated with a bleeding risk similar to OAC therapy. Therefore, antiplatelet therapy should not be used for stroke prevention in AF patients [1, 120, 121].

10. Vitamin K Antagonists

VKAs are currently recommended for AF patients with rheumatic mitral valve stenosis or with a mechanical heart valve only. Compared to the placebo, in AF, VKAs mitigate stroke risk by 64% and mortality by 26% [119, 122, 123]. Especially in geriatric patients, their use is limited by the narrow therapeutic interval and many drug interactions, thus necessitating frequent international normalized ratio monitoring and dose adjustments [1].

11. Direct Oral Anticoagulants

For old and frail AF patients, the dosages of apixaban, dabigatran, edoxaban, and rivaroxaban must be administered and reduced [1]. Idarucizumad is available as an antidote for dabigatran, and andexanet alfa is available in some countries as an antidote for all Direct Oral Anticoagulants (DOACs) [1]. Additionally, we lack data on the use of DOACs, especially on apixaban and rivaroxaban, in very old patients. Despite an abundance of data on DOACs, no randomized controlled trials targeting this age group have been performed, and concerns regarding their use in the elderly are unavailable. A recent meta-analysis [124] reported data on DOACs from 30,655 elderly patients (≥75-year old) with AF and venous thromboembolism events based on 3,720 publications. DOACs show similar or greater efficacy than VKAs. Of note, it is sometimes incorrectly apperceived that a correct OAC is not a 100% warranty for no ICH. Some differences in safety profiles among DOACs were observed, and individual differences in terms of safety profile cannot be excluded based on current evidence. However, direct head-to-head comparisons are necessitated to investigate possible divergence in pharmacological profiles among DOACs. Also, the global ETNA-AF program with edoxaban [125, 126] assessed the rate of ICH events in old patients with and without a history of ICH. There were low ICH in both groups, but unexpectedly, the ICH risk was greater in patients without a previous ICH than in those with a previous ICH, and consequently, edoxaban was more effective in patients with a previous ICH than in patients without an ICH. Additionally, edoxaban was found non-inferior to warfarin in patients with bioprosthetic cardiac valves, with similar bleeding complications [127]. Another trial [128] in patients with AF and bioprosthetic mitral valves reported that rivaroxaban was not inferior to warfarin. Further studies conducted in real-world settings and the frail elderly are ongoing and should provide specific data on this particular patient group.

Overall, DOACs are not inferior to VKAs, and the thromboembolic risk with their use is associated with a significantly smaller risk of ICH and cardiac mortality, with smaller bleeding risk and risk of all complications [1, 129-131]. DOACs are preferable, and their few contraindications include active serious bleeding if the source remains untreated, associated comorbidities (e.g., severe thrombocytopenia <50 platelets/µL and severe anemia), or a recent high-risk bleeding event such as Intracerebral Hemorrhage (ICH).

12. OAC in SCAF

Efficacy and safety of OAC remain poorly understood in SCAF [1]. The RE-SPECT-ESUS [132, 133] compared the administration of aspirin 100 mg once a day (oad) to rivaroxaban 15 mg/day, and the NAVIGATE-ESUS study [134] compared the administration of aspirin 100 mg oad to dabigatran (110 or 150 mg bid). In both the studies, the DOACs were not superior to aspirin, and the bleed risk was higher than that with aspirin. Nonetheless, the ESC recommends DOACs in patients with AHREs (heart rate >180 bpm) or with an anamnesis of SCAF, following the CHA2DS2-VASc score [1].

13. OAC in Geriatric AF Patients with Cognitive Impairment and Frailty

In geriatric patients, frailty and increased risk of falls can be problematic for administering OAC. However, sufficient evidence supports the use of OAC in this population [1, 13], but these patients are less likely to receive OAC [1, 135-138].

Dementia impacts treatment adherence to OAC [1, 13, 139-141]. Evidence regarding effective prevention of cognitive impairment in AF is derived primarily from observational studies and suggests that OAC could protect geriatric AF patients from stroke, not only by preventing stroke but also by preventing cognitive decline [139-141]. The type and quality of OAC seem to play an additional role. Indeed, with VKAs, therapeutic values below or above the necessary INR values were associated with a higher risk of dementia [141-143]. Limited evidence suggests that DOACs might be superior to VKAs in preventing cognitive impairment [144-146], but several studies have shown different results [140, 141]. Currently, the role of OAC for prevention of cognitive impairment in AF is unknown [147], but a recent meta-analysis [13] in geriatric AF patients reported that treatment with OAC was also useful in geriatric patients with cognitive impairment and that the higher absolute stroke risk resulted in a larger absolute risk reduction by using DOACs instead of VKAs, thus resulting in a lower value needed in geriatric AF patients for treatment compared to treatment for younger AF patients.

The 2020 ESC Guidelines on AF [1] recommended that OAC should be considered for very old AF patients with a CHA2DS2-VASc score of 1, and OAC should be provided to patients with a score of ≥ 2. Old age and frailty per se do not form absolute exclusion criteria for OAC in AF. According to current data, DOACs are the preferred choice for geriatric AF patients without mitral stenosis or a metal prosthetic valve, even if there are no “one-size-fits-all” direct anticoagulants, and this applies to the elderly, particularly to the vulnerable patients [147, 148].

14. Left Atrial Appendage Occlusion

Some AF patients might have absolute contraindications of OAC independent of age, and in such cases, the left atrial appendage occlusion (LAAO) might be a valuable choice. LAAO devices had been listed in the 2020 ESC guidelines on AF [1]. Only the Watchman device had been compared to VKAs therapy in a few controlled trials [149-154]. In AF patients with moderate stroke risk, the LAAO was found to be non-inferior to VKAs in stroke prevention, with a possibility of lower bleeding rates on longer follow-up [150]. Notably, the most common justification for LAAO in clinical practice is a perceived high bleeding risk or, less often, contraindications of OAC [154, 155], but LAAO has not been randomly tested in such populations. Most patients, who would be considered unsuitable for therapy with VKAs many years ago, now seem to do relatively well on DOACs; LAAO has not been compared to surgical or DOAC therapy in patients at risk of bleeding [156, 157]. Most of those patients were treated with warfarin [149-154], and with proper knowledge, DOAC therapy would be a better strategy. There is no data to indicate LAAO or DOAC therapy in patients with relative or absolute contraindications of OAC, in those suffering from a hemorrhagic cerebral stroke on OAC, and for the assessment of the appropriate antithrombotic therapy after LAAO. In summary, available findings corroborate the use of LAAO to reduce the risk of stroke in patients with contraindications of OAC [158-161]; additionally, a large European registry on LAAO reported a 98% success rate with a 4% procedure-related complication rate at 30 days [162]. Nevertheless, LAAO can cause serious complications. Higher event rates were reported in real-world analyses compared to that in industry-sponsored studies, possibly identifying some reporting bias. Furthermore, device-related thrombosis is not benign [160-163], and incomplete LAAO might be associated with an increased risk of stroke [163].

15. Discussion

Since age is a relevant risk factor for AF, this arrhythmia is very frequent in geriatric patients and induces many adverse effects. Screening for AF is now recommended; however, its utility in very old AF patients is less conspicuous than in younger patients. The therapeutic approach in geriatric AF patients differs from that in younger patients. Geriatric patients should be regularly monitored for progression of the disease and changes in their thromboembolic risk. Close periodic re-evaluation of very old patients is essential due to frequent changes in the clinical status, to evaluate treatment adherence, and to verify the need for dose adjustment. Physicians should recognize early and minimize the impact of each modifiable risk factor such as suboptimal nutritional status, inadequate blood pressure control, deteriorated renal function, hematologic disorders, and lack of social support.

RC by CA is useful in younger AF patients, although it is less useful in geriatric patients with long-standing AF and concomitant morbidities. Consequently, in geriatric AF patients, the most frequent therapy is RaCo, even if it is currently unclear which heart rate should be the best. It is important to consider that, in geriatric AF patients, the decision to initiate long-term AAD therapy needs to balance thromboembolic risk and symptom burden against possible adverse drug reactions, particularly iatrogenic proarrhythmia or extracardiac side effects. OAC in old AF patients plays a vital role in therapy, but OAC use in these patients after a bleeding or stroke event is challenging. We require high-quality data on this situation, and the use of OAC is currently based on expert consensus. An elevated bleeding risk should not automatically lead to withholding OAC in geriatric AF patients with stroke risk. Instead, it is suggested to address modifiable bleeding risk factors and high-risk patients scheduled for a more frequent clinical review and follow-up. Available data suggest that DOACs should be preferred to VKAs in geriatric AF patients without rheumatic mitral stenosis or with a valvular prosthesis. Nonetheless, a gap in knowledge exists regarding optimal DOAC dose in very old AF patients, especially in patients with mild-to-moderate renal failure, with very low or high body mass index, and in those receiving medications with a high risk of metabolic interactions.

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G. Cocco selected the references, wrote the paper and discussed the changes with the reviewers. Ph. Amiet discussed the paper and worked on the corrections for the reviewers.

Competing Interests

The authors have declared that no competing interests exist.

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