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The 2024 ESC Guidelines for diagnosis and management of AF: A clinicians' perspective

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Abstract:
Atrial fibrillation (AF) is a complex disease requiring a multidomain and (usually) long-term management, thus posing a significant burden to patients with AF, practitioners, and healthcare system. Unlike cardiovascular conditions with a narrow referral pathway (e.g., acute coronary syndrome), AF may be first detected by a range of specialties or a general practitioner. Since timely initiated optimal management is essential for the prevention of AF-related complications, a concise, as simple as possible guidance is essential to practitioners managing AF patients, regardless of their specialty.
Guideline-adherent management of patients with AF has been shown to translate to improved patient outcome compared with guideline non-adherent treatment. To facilitate guideline implementation in routine clinical practice, a good AF Guideline document should introduce only evidence-based new recommendations, while avoiding arbitrary changes which may be confusing to practitioners. Here we discuss the main changes in the 2024 European Society of Cardiology (ESC) AF Guidelines relative to the previous 2020 ESC document.
There is a strong impression that scientific evidence appreciation was rather unbalanced across the sections of the 2024 ESC AF Guideline document. Whether the updates and new recommendations issued by the new guidelines will translate in high adherence in clinical practice (and hence improved prognosis of patients with AF) will need to be addressed in upcoming years.

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The 2024 ESC Guidelines for diagnosis and management of AF: A viewpoint from a practicing clinician's perspective

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Abstract

Atrial fibrillation (AF) is a complex disease requiring a multidomain and (usually) long-term management, thus posing a significant burden to patients with AF, practitioners, and healthcare system. Unlike cardiovascular conditions with a narrow referral pathway (e.g., acute coronary syndrome), AF may be first detected by a wide range of specialties (often non-cardiology) or a general practitioner. Since timely initiated optimal management is essential

for the prevention of AF-related complications, concise and simple as possible guidance are essential to practitioners managing AF patients, regardless of their specialty.

Guideline-adherent management of patients with AF has been shown to translate to improved patient outcome compared with guideline non-adherent treatment. To facilitate guideline implementation in routine clinical practice, a good guideline document on AF should introduce only evidence-based new recommendations, while avoiding arbitrary changes which may be confusing to practitioners.

Herein we discuss the main changes in the 2024 European Society of Cardiology (ESC) AF Guidelines relative to the previous 2020 ESC document. Whether the updates and new recommendations issued by the new guidelines will translate in high adherence in clinical practice (and hence improved prognosis of patients with AF) will need to be addressed in upcoming years.

Atrial fibrillation (AF) is associated with increased risk of major cardiovascular adverse events, including ischemic stroke/systemic embolism, heart failure, hospitalization, impaired quality of life and mortality[1]. The arrhythmia is a complex disease requiring a multidomain, integrated and (usually) long-term management, thus posing a significant burden to patients with AF, practitioners, and healthcare system.

Unlike cardiovascular conditions with a narrow referral pathway (e.g., acute coronary syndrome [ACS]), AF may be first detected by a wide range of specialties (often non-cardiology ones) or a general practitioner in primary care. Since timely initiated optimal management is essential for the prevention of AF-related complications, a concise, as simple as possible guidance is essential to practitioners managing AF patients, regardless of their specialty.

Guideline-adherent management of patients with AF has been shown to translate to improved patient outcome compared with guideline non-adherent treatment[2]. To facilitate guideline implementation in routine clinical practice, a good guideline document on AF should introduce only evidence-based new recommendations, while avoiding arbitrary changes which may be confusing to practitioners.

Herein we discuss the main changes in the 2024 European Society of Cardiology (ESC) AF Guidelines[3] relative to the previous 2020 ESC document[1] and compare the 2024 ESC document with other most recent international AF guidelines.

Integrated care for patients with AF

Approximately a decade ago, the World Health Organization had put forward the concept of integrated care models for chronic diseases in recognition of fragmentation of respective healthcare services[4]. Thereafter, a structured, patient-centred, multidisciplinary approach to the management of patients with AF (integrating healthcare professionals, patients and their family/carers and outlining the main domains of AF care) to improve patient outcomes and adherence to guidelines has been formally proposed in the 2016 ESC AF Guidelines (Class IIa, Level of Evidence [LoE] B)[5].

The 2020 ESC AF Guidelines reiterated this recommendation and streamlined the essential domains of care for AF patients across all healthcare levels and among different specialties into the simple ABC pathway (Figure 1), using gear wheels to emphasize the equal importance of each of the main AF care domains, as follows: 'A' Anticoagulation/Avoid stroke, 'B' Better symptom management and 'C' Cardiovascular and Comorbidity optimization[1].

The scientific evidence supporting the ABC pathway at that time was already fairly extensive[6]. There were several observational studies (from retrospective and prospective cohorts) or post-hoc analyses of randomized trial cohorts showing a significant association of the ABC pathway implementation with lower health-related costs[7], lower rates of cardiovascular adverse events, and lower risk of all-cause death and composite outcome of stroke/major bleeding/cardiovascular death and first hospitalization in comparison to usual care[8-10]. There was also one published prospective cluster randomized mAFA-II trial, which showed a significant 61% risk reduction in the composite outcome of stroke or thromboembolism, all-cause death, and rehospitalization, with ABC pathway management intervention versus usual care)[11]. The long-term extension of mAFA-II trial showed a high adherence (over 70%) and persistence (over 90%) with the intervention[12].

Subsequently, in a systematic review and meta-analysis of 285,000 patients, adherence to the ABC pathway translated to a 58% reduction in all-cause death, 63% reduction in cardiovascular death, 45% reduction in ischaemic stroke, and a 31% reduction in major bleeding[13]. A retrospective analysis of a large registry-based cohort showed that adherence to all ABC pathway domains resulted in the greatest magnitude of risk reduction and longest event-free survival, also in patients deemed as 'clinically complex'[14], and other analyses have shown the impact of the ABC pathway also on patients with multimorbidity and thus at higher baseline risk of adverse outcomes[15-17].

Most recently, the randomized MIRACLE-AF trial was presented as a Late Breaking Trial at the 2024 ESC Congress in London, and reported a cluster randomised trial comparison of ABC pathway intervention versus intensified usual care in rural villages in China - this showed a 36% lower rates of the composite outcome (cardiovascular death, stroke, hospitalization due to worsening of heart failure or ACS, and emergency visits due to AF) with the ABC intervention delivered by village doctors (previously called 'barefoot doctors') supported by telemedicine[18] (www.escardio.org/Congresses-Events/ESC-Congress/Congress-news/hot-line-9-strokestop-ii-guard-af-and-miracle-af). Secondary outcomes included a significant reduction in stroke and cardiovascular death.

Clearly, the evidence supporting the ABC pathway for integrated AF care to streamline timely optimal management of patients with AF at all healthcare levels by non-cardiologists and cardiologists has been accumulated, fulfilling LoE A. In addition, an ongoing RCT is comparing the ABC pathway versus usual care in elderly patients in Europe within the Horizon Europe funded AFFIRMO programme[19].

Notwithstanding the significant amount of evidence supporting the ABC pathway, the 2024 ESC AF Guidelines recommended a new, not previously tested acronym AF-CARE, essentially highlighting the same AF care domains as the ABC pathway, though re-arranged in a different order (Figure 1). This change in recommendation, from ABC pathway to AF-CARE, was justified mainly by a concern that the 'C' domain (Cardiovascular and Comorbidity management) could be otherwise neglected.

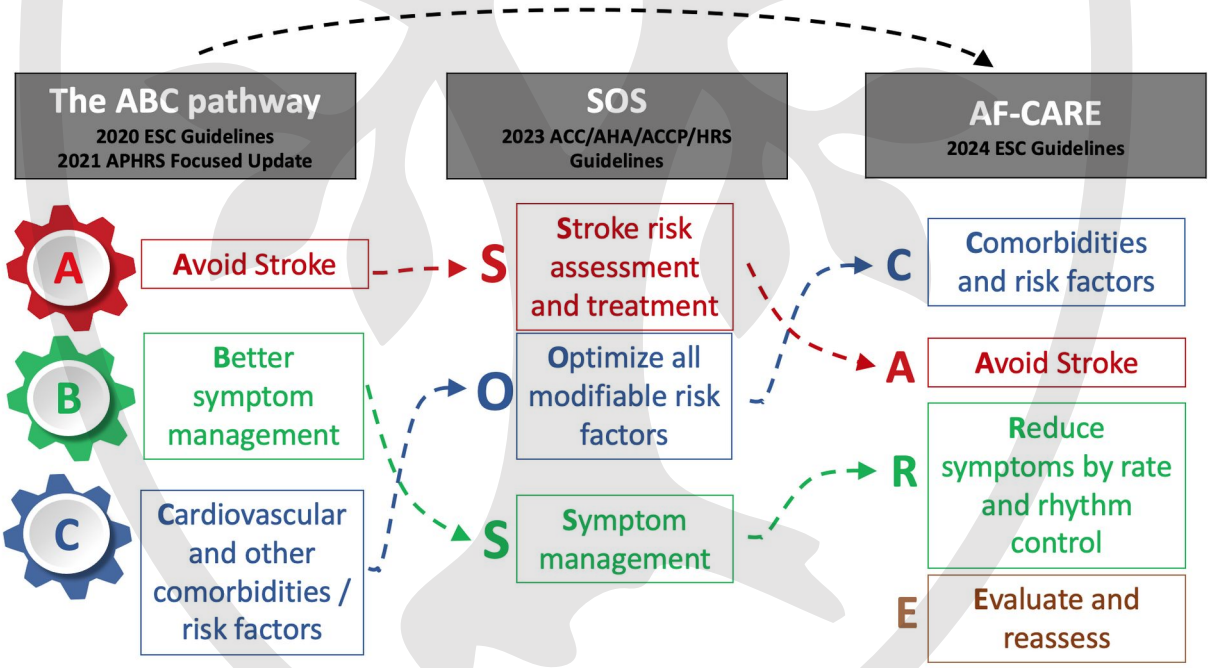
Whether this change, accompanied by a Class I LoE C formal recommendation, will really facilitate the attainment of the 'C' domain of AF care, or rather confuse practitioners

increasingly familiar with the ABC pathway and compromise guideline implementation in practice, remains to be seen. After all, when managing any cardiovascular disorder, whether AF or other non-AF conditions, it seems common sense that all cardiovascular risk factors and comorbidities should be proactively managed. Hence, the 'C' being prioritised is not unique to AF per se.

Of note, the 2023 ACC/AHA/HRS AF Guidelines[20] also provided an acronym for integrated AF care, the SOS, streamlining the AF care domains comparably to the ABC pathway (Figure 1).

Overall, the essential principles of care for AF patients worldwide remain the same, and using a particular acronym is probably only a matter of personal preference, as long as the main domains of AF care are optimally addressed.

Figure 1. Integrated management of patients with AF[1,3,20].



ESC: European Society of Cardiology; ACC/AHA/ACCP/HRS: American College of Cardiology/American Heart Association/American College of Chest Physicians/Heart Rhythm Society.

Prevention of stroke and systemic embolism

The steps essential to effective stroke prevention include: *i*) initial stroke risk assessment to identify AF patients at truly low risk of stroke, *ii*) initiation of oral anticoagulant (OAC) therapy in all AF patients with one or more stroke risk factors (preferably a non-Vitamin K antagonist oral anticoagulant [NOAC] in NOAC-eligible patients) and bleeding risk assessment, and *iii*) regular re-assessment of stroke and bleeding risk in periodic time intervals, to account for a dynamic changes in the individual patient's risk profile[1].

When tailoring stroke prevention strategy, ethnic differences in stroke and bleeding risk should also be considered[21,22].

In the 2024 ESC AF Guidelines, several changes have been made, mostly regarding stroke and bleeding risk assessment.

Stroke risk assessment

Notwithstanding that clinical risk factor-based scores generally have a modest ability to predict the clinical event of interest, most international guidelines recommend the clinical stroke risk factor-based CHA_2DS_2-VASc score for initial stroke risk assessment (Table 1), as the most validated and widely used stroke risk assessment tool to reliably identify AF patients at sufficiently low risk of stroke so that long-term OAC is not needed (i.e., as long as the score is 0 in male and 1 in female AF patients)[23,24].

Table 1. Thromboembolic and bleeding risk assessment and management in the international AF guidelines.

Society	Year	Thromboembolic risk assessment model/score	Recommendation for thrombo-embolic prevention with OAC	Bleeding Risk Assessment and recommended model/score
NHFA/CSANZ[25] (Australia, New Zealand)	2018	CHA_2DS_2-VA	CHA_2DS_2-VA ≥2 (Strong)	Identification of reversible bleeding risk factors; no
			CHA_2DS_2-VA = 1 (Strong)	

				specific score recommended
APHRS[26] (Asia-Pacific)	2021	CHA_2DS_2-VASc	CHA_2DS_2-VASc ≥2 (males) or ≥3 (females): recommended	HAS-BLED (to identify modifiable risk factors to be corrected)
			CHA_2DS_2-VASc =1 (males) or 2 (females): to be considered	
CCS/CHRS[27] (Canada)	2020	CHADS-65 ("CCS algorithm")	Score ≥1 (or 65 years) (Strong)	HAS-BLED (to identify high-risk patients and modifiable risk factors)
ESC/EACTS (Europe)[1]	2020	CHA_2DS_2-VASc	CHA_2DS_2-VASc ≥2 (males) or ≥3 (females) (Class I)	HAS-BLED (to identify high-risk patients and address modifiable risk factors)
			CHA_2DS_2-VASc =1 (males) or =2 (females) (Class IIa)	
ESC/EACTS (Europe)[3]	2024	CHA_2DS_2-VA	CHA_2DS_2-VA ≥2 (Class I)	Assessment and management of modifiable bleeding risk factors; no specific score recommended
			CHA_2DS_2-VA =1 (Class IIa)	
ACC/AHA/ACCP/HRS (United States of America)[20]	2023	CHA_2DS_2-VASc (or validated clinical risk scores)	CHA_2DS_2-VASc ≥2 (males) or ≥3 (females) (Class I)	Identify factors that indicate high risk of bleeding and possible intervention to prevent bleeding; no specific score recommended
			CHA_2DS_2-VASc = 1 (males) or 2 (females) (Class IIa)	
Chinese Expert Consensus Guidelines[28]	2024	CHA_2DS_2-VASc	CHA_2DS_2-VASc	HAS-BLED

ACC: American College of Cardiology; ACCP: American College of Chest Physician AHA: American Heart Association; APHRS: Asia-Pacific Heart Rhythm Society; CCS: Canadian Cardiovascular Society; CHS: Canadian Heart Rhythm Society; EACTS: European Association for Cardio-Thoracic Surgery; ESC: European Society of Cardiology; HRS: Heart Rhythm Society; NHFA: National Heart Foundation of Australia; CSANZ: Cardiac society of Australia and New Zealand; CHA_2DS_2-VASc: congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/TIA/thromboembolism (2 points), vascular disease, age 65–74 years and female sex.

The 2024 ESC AF Guidelines recommend using the CHA_2DS_2-VA score for stroke risk assessment (LoE C), considering that the inclusion of female sex *"complicates clinical practice both for healthcare professionals and patients"* and *"omits individuals who identify as non-binary, transgender, or are undergoing sex hormone therapy"*[3].

Indeed, female sex is a stroke risk modifier, rather than a stroke risk factor per se[29]. While earlier data showed a greater risk of stroke in female AF patients compared with males (with significant age-dependent interaction between female sex and the presence of additional clinical stroke risk factors)[30,31] and strokes tended to be more severe in female AF patients compared with males[32], more recent evidence shows that the rates of AF-related strokes are declining in both male and female patients, in the context of decreasing sex-related disparities in OAC use.

Similar observations were made by Nielsen et al. in a nationwide cohort study of 158,982 patients with incident AF not on OAC[33]. During the study period 1997-2020, the risk of stroke overall has been declining in the last two decades, and the sex difference diminished in most recent years. Whereas the likelihood of prescribing OAC was lower for female patients with AF compared with male AF patients, OAC initiation increased over time, with comparable OAC initiation patterns in male and female AF patients[33].

In a study using UK primary and secondary care data comprising 195,719 patients with AF followed between 1998-2016, there was higher thromboembolic events in women compared to men in the population with high CHA_2DS_2-VASc risk scores; however, overall stroke and thromboembolic risk prediction using the CHA_2DS_2-VA and CHA_2DS_2-VASc scores was comparable. Also, the similarity in thromboembolic risk prediction using CHA_2DS_2-VA and CHA_2DS_2-VASc scores was consistent across different ethnicities and socioeconomic status.

A most recent retrospective evaluation of temporal trends in the predictive value of the CHA_2DS_2-VASc relative to the CHA_2DS_2-VA score (using nationwide data on AF patients from all levels of care in Finland during the 2007-2018 period) showed that initial differences favouring the CHA_2DS_2-VASc score in early years (when female AF patients were at much higher stroke risk than males) gradually attenuated over time, resulting in no difference in stroke risk

prediction or reclassification between the CHA_2DS_2-VASc and CHA_2DS_2-VA scores in the 2017-2018 period[34]. Thus, recent data from Finland, Denmark and UK, found the female-male differences in AF-related strokes were removing the Sc criterion from the CHA_2DS_2VASc score did not affect its ability to discriminate thromboembolic events in the AF population[31,35,36].

Of note, an analysis from the same Finish dataset and time period showed how female sex was initially associated with lower use of OAC, while sex-based disparities attenuated during the study, and were finally resolved at the end of the observation.[37] Other studies have also shown an increase in the use of OAC among female patients over the last decade.[38] This evidence suggests that improved use of OAC in females may have contributed to the decreasing sex-based difference in the incidence of AF-related stroke.

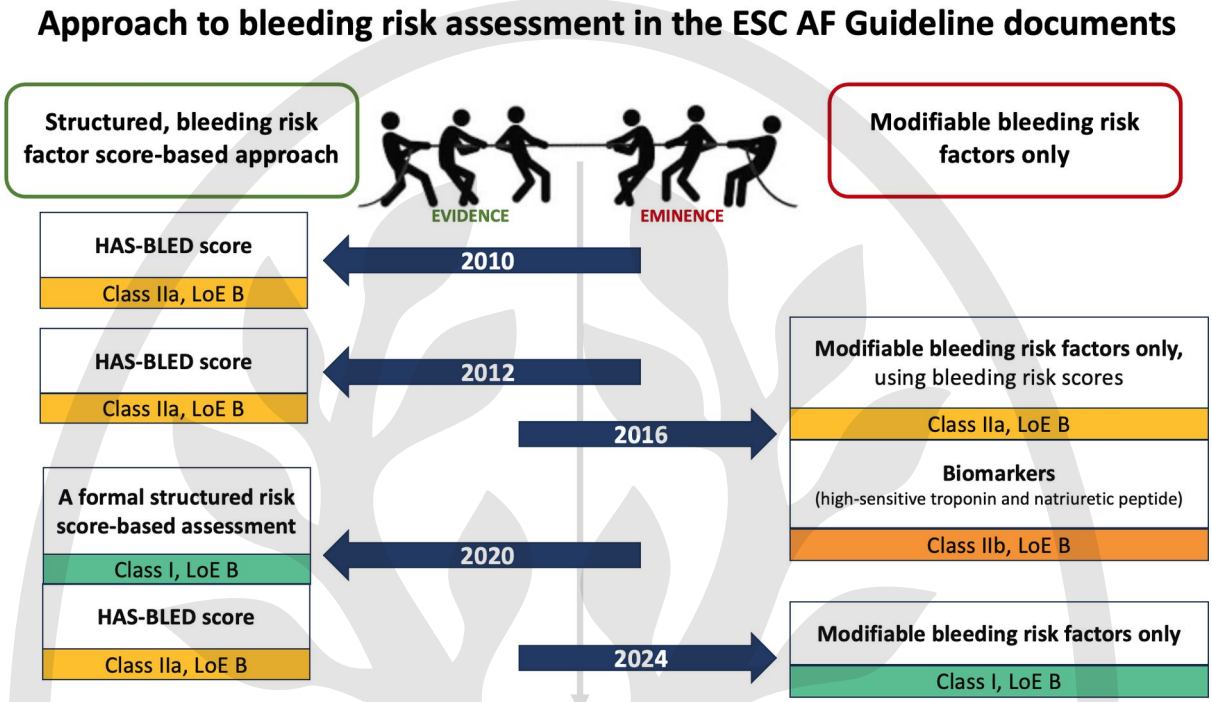
Although the concept of not considering female sex in AF-related stroke risk assessment is not new (the CHA_2DS_2-VA score was first proposed in the 2018 Australian/New Zealand AF Guidelines[39] albeit with limited evidence then), the evidence supporting the CHA_2DS_2-VA score remained extremely scarce. Fortunately, the subsequently reported most recent data suggests that adopting the CHA_2DS_2-VA score could potentially simplify stroke risk assessment in AF patients.

Still, some caution is needed, as it is very likely that the use of CHA_2DS_2-VASc score contributed to draw attention to the risk of stroke in women risk and improved OAC use in female AF patients, in addition to improved overall management of concomitant cardiovascular risk factors and underlying comorbidities. Also, the patterns seen in Finland, Denmark and UK may not be evident in other healthcare systems. Hence, it could still be too early to replace the CHA_2DS_2-VASc score with CHA_2DS_2-VA when assessing the risk of stroke in AF patients.

Bleeding risk assessment

All international AF Guidelines recognise the need for bleeding risk assessment (and regular re-assessment) in AF patients taking OAC and agree that the estimated bleeding risk itself should not preclude OAC prescription (Table 1). However, the approach to bleeding risk assessment has varied over time in the ESC AF Guideline documents (Figure 2).

Figure 2. Bleeding risk assessment in the ESC AF Guidelines 2010-2024[1,3,5,40,41].



ESC: European Society of Cardiology; AF: Atrial fibrillation; LoE: Level of Evidence; HAS-BLED: Hypertension (uncontrolled, systolic blood pressure >160mmHg), Abnormal renal and/or hepatic function, Stroke, Bleeding history or predisposition, Elderly (>65 years), Drugs or excessive alcohol intake.

Bleeding risk factors are classified to non-modifiable (e.g., age >65 years, prior stroke or bleeding), partially modifiable (e.g., renal impairment, anaemia) and modifiable (e.g., hypertension, concomitant antiplatelet therapy, alcohol intake)[1]. In interaction with modifiable bleeding risk factors, non-modifiable factors are important drivers of bleeding events[42], hence should not be overlooked.

The importance of reviewing both modifiable and non-modifiable bleeding risk factors to mitigate bleeding risk has been acknowledged in most international AF Guidelines (Table 1), and the 2020 ESC AF Guidelines explicitly recommended a structured, clinical risk factor-based bleeding risk assessment (Figure 2), since relying solely on modifiable bleeding risk consideration has been shown to be inferior to formal bleeding risk assessment using a

bleeding risk score inclusive of both modifiable and non-modifiable bleeding risk factors[43-45], such as the HAS-BLED score[23,36,45,46], for example (Table 1, Figure 2).

From the practical perspective, any bleeding (major or minor) is 'red flag' for subsequent ischaemic events, yet OAC is often discontinued for the bleeding event[47]. Nevertheless, the guidance on consideration of individual patient bleeding risk in the 2024 ESC AF Guidelines may be confusing, especially for non-expert clinicians managing AF patients. While the document mentions that patients with non-modifiable bleeding risk factors should be reviewed more often, or even referred to a multidisciplinary team, the formal recommendation for bleeding risk assessment refers only to the assessment and management of modifiable bleeding risk factors (Class I, LoE B), while the use of bleeding risk scores is not recommended (Class III, LoE B), to avoid under-use of OAC[3]. Of note, none of the three references cited in support of the latter examined the effects of bleeding risk scores on OAC underuse[48,49], and one was the 2014 AHA/ACC/HRS AF Guideline document[50].

Transcatheter left atrial appendage closure

The evidence supporting non-pharmacological prevention of AF-related stroke using transcatheter left atrial appendage closure (LAAC)[51] has not changed much since consideration of LAAC was recommended in AF patients with a high risk of stroke and contraindications to long-term OAC (Class IIb, LoE B) in the 2012 ESC AF Guideline Update[41], hence the recommendation remained unchanged in the 2016 and 2020 ESC AF Guideline documents[1,5].

In the 2024 ESC AF Guidelines, the same recommendation is downgraded to LoE C, with the rationale that the available evidence does not refer to patients with contraindications to OAC [3]. From the clinicians' practical perspective, the approach proposed in the 2023 ACC/AHA/HRS AF Guideline could be more helpful, as the recommendation referring to LAAC is divided to the recommendation on patients with a contraindication to long-term OAC (Class IIa, LoE B-NR) and another one referring to patients with a high risk of both stroke and bleeding (Class IIb, LoE B-R)[20].

It is very likely that numerous ongoing randomized trials will change the LAAC landscape soon [51].

Rhythm and rate control

It is widely accepted that appropriate rate control is important background therapy in all AF patients. In addition, a large body of evidence supports consideration of rhythm control in symptomatic patients with AF to improve symptoms and quality of life (Class I, LoE A in the 2020 ESC AF Guidelines[1] and Class IIa, LoE B-R in the 2023 ACC/AHA/ACCP/HRS AF Guidelines [20]), but such formal recommendation is missing in the 2024 ESC AF Guideline document, being mentioned only in the text[3].

In line with recently published data[52,53], the 2024 ESC AF Guidelines recommended implementation of a rhythm control strategy within 12 months of diagnosis in *selected* AF patients at risk of thromboembolism to reduce the risk of cardiovascular death or hospitalization (Class IIa, LoE B)[3]. However, how to select patients in practice is less clear.

On the contrary, the 2023 ACC/AHA/ACCP/HRS AF Guidelines provide a helpful set of goals with rhythm control therapy including *i)* evaluation of AF contribution to the reduced left ventricular (LV) function in patients with reduced LV function and persistent (high burden) AF (Class I, LoE B-R), *ii)* symptom improvement in patients with symptomatic AF, *iii)* reduction in hospitalization, stroke and mortality in patients recently diagnosed with AF (<1 year), *iv)* improvement of symptoms and outcomes in patients with AF and heart failure (all Class IIa, LoE B-R) and *v*) reduction in AF progression (Class IIa, LoE B-NR)[20].

Catheter ablation of AF

The recommendation for catheter ablation of AF as the first-line therapy for paroxysmal AF has been upgraded from Class IIa, LoE B[1] to Class I, LoE A[3] in the 2024 ESC AF Guidelines, whereas the recommendations regarding AF ablation in patients with heart failure remained unchanged. This is in contrast to the 2023 ACC/AHA/ACCP/HRS AF Guidelines, wherein AF ablation is recommended in appropriate patients with AF and HFrEF to improve symptoms, quality of life, ventricular function and cardiovascular outcomes (Class I, LoE A)[20]. A missed

opportunity to upgrade the role of AF ablation in patients with heart failure in the 2024 ESC AF Guidelines could result in the therapy being delayed or withheld from patients who would most benefit from it[54,55].

While providing a new recommendation on repeat AF ablation (Class IIa, LoE B), the 2024 ESC AF Guidelines have not addressed AF ablation in asymptomatic AF patients, unlike the 2023 ACC/AHA/ACCP/HRS AF Guidelines where AF ablation may be considered for reducing progression and complication of AF in younger patients with few comorbidities and moderate-to-high burden of AF (Class IIb, LoE B-NR)[20].

Other considerations

Optimal management of patients with so-called 'subclinical' AF remains debatable, after the two randomised trials (i.e., ARTESiA and NOAH-AFNET 6) showed reduction in ischemic stroke, at the cost of increased risk of (non-fatal) major bleeding with NOAC versus control (either aspirin in ARTESiA, or placebo in NOAH-AFNET 6) in patients with subclinical AF of short duration[56-58]. The 2024 ESC AF Guidelines provided a Class IIb, LoE B recommendation for considering a NOAC in such patients, excluding those at high risk of bleeding[3]. Questions remain on how to stratify thromboembolic risk and to individualize treatment strategies in these patients.

Concluding remarks

Overall, the 2024 ESC AF Guidelines claimed 57 new recommendations, of which 17 (29%) were supported with LoE C. Of the latter, some appear rather unlikely to aid management of AF patients in daily practice (for example, the Class I recommendation, LoE C that "a transthoracic echocardiogram is recommended in patients with an AF diagnosis where this will guide treatment decisions").

There is a strong impression that scientific evidence appreciation was rather unbalanced across some sections, ranging from shifting from an established approach with a significant amount of support evidence (e.g., the ABC pathway) to a new approach (i.e. AF-CARE) which is

still to be validated, to meticulous scrutinization of current evidence (e.g, percutaneous LAAC). Whether the updates and new recommendations issued by the new guidelines will translate in high adherence in clinical practice (and hence improved prognosis of patients with AF) will need to be addressed in upcoming years, also taking into account the other changes proposed from previous guidelines (e.g., the ABC pathway vs. the new AF-CARE acronym, CHA_2DS_2-VASc vs. CHA_2DS_2-VA, and removal of the HAS-BLED score).

Clearly, the most striking aspect of the 2024 ESC AF Guideline document is the strong emphasis on the importance of concomitant comorbidity and risk factor management, supported by changing from the ABC pathway to AF-CARE acronym. It remains to be seen whether this change will translate into better guideline implementation in practice and improved patients' outcome, also considering current knowledge on barriers to guidelines implementations in clinical practice[59]. However, it is simply common sense that all cardiovascular risk factors and comorbidities should be proactively managed, and regular review implemented, in patients with heart disease.

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