



New Directions in the Management of Atrial Fibrillation

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MANAGEMENT of atrial fibrillation (AF) was a prevalent topic at this year's European Society of Cardiology (ESC) Congress 2024. With an ever-growing rate of patients needing ablation therapy and new treatment strategies on the rise, a streamlined treatment approach is yet to be defined. Researchers came together to present timely late-breaking research and its clinical implications, but more importantly, to discuss what questions remain unanswered regarding the management of this condition.

THE EVOLVING LANDSCAPE OF RISK FACTORS

Gregory Lip, University of Liverpool, UK, opened the session by emphasising the need for a more comprehensive and integrated approach to risk assessment and management of AF, following recent findings.

In recent years, there has been a push for a streamlined approach to AF management and risk assessment, with an emphasis on the following three parameters: stroke prevention, managing symptoms with rate and rhythm control, and identification of cardiovascular risk factors and associated comorbidities. These 'three pillars' have been consistently featured in recent AF guidelines, albeit with slight variations. For example, the 2020 ESC guidelines incorporated the ABC pathway ('Avoid stroke', 'Better symptom management', 'Cardiovascular risk factor and comorbidity management'). The mAFA trial demonstrated the efficacy of a telehealth intervention based on the ABC pathway, with adherence rates above 70% and persistence over 90%, compared to standard care.¹ Furthermore, the MIRACLE-AF trial, which employed both in-person

and telehealth-based care using the ABC pathway, showed significant reductions in adverse outcomes.² Specifically, the risk of mortality was 50% lower, the risk of stroke was 36% lower, and risk of hospitalisation was 31% lower in the intervention group.² Lip noted that the outcomes achieved with an integrated care approach could ease the substantial healthcare burden associated with AF.

However, Lip also stressed that, whilst recent guidelines do feature the 'three pillars', they lack consideration of certain risk factors which have become more significant in recent years. For example, the impact of sex in AF-related stroke risk has shifted. Previous research demonstrated that female patients with AF have a 20–40% higher risk of ischaemic stroke.³ Lip explained that recent data indicate that the difference between males and females has diminished significantly, likely due to improved awareness and preventive measures for female patients.⁴ However, Lip did admit that this trend has been primarily observed in Swedish and Danish cohorts, so it may not be universally applicable, highlighting the need to regularly update risk stratification.

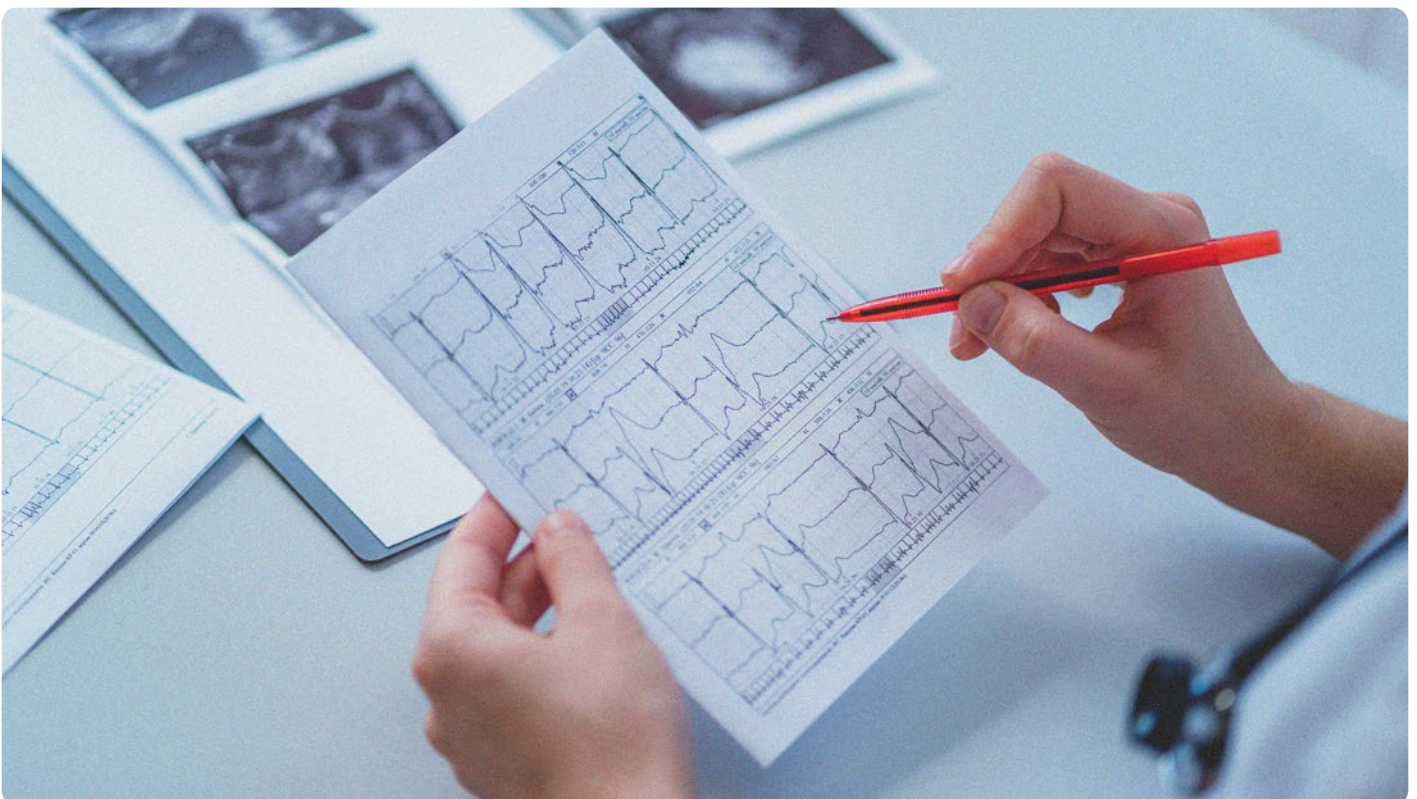
Lip also noted that current risk assessment strategies have not incorporated recent evidence that demonstrated the impact of environmental factors on AF. Lip emphasised the significance of this omission, as recent research has revealed that air pollution has a greater impact on AF onset in both female patients and those over 65 years, and is more likely to cause AF complications in younger, female patients.⁵ Overall, Lip stressed that using a simple care pathway, such as the ABC pathway, but in a holistic or integrated care manner, will improve the management, and therefore outcomes, of patients with AF. Lip stressed that new guidelines need to integrate emerging findings with traditional risk factors, such as the impact of air pollution. AF management, he concluded, is not a one-size-fits-all approach; it must be holistic and adaptable to reflect the dynamic nature of AF itself.

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AF BURDEN OR AF RECURRENCE?

Carina Blomstrom-Lundqvist, Orebro University Hospital, Sweden, proposed that AF burden, not AF recurrence, should be the endpoint in all AF ablation trials.

Blomstrom-Lundqvist began by explaining that, historically, AF recurrence, defined as the time to the first AF episode (with a threshold of 30 seconds), has been the ‘gold standard’ endpoint in AF trials. Because this metric has been so widely used, it allows for comparisons across many studies. However, there has been a recent shift towards AF burden as a more suitable measure, and Blomstrom-Lundqvist thoroughly discussed the reasons for this, comparing studies using these two metrics. Specifically, the CIRCA-DOSE trial reported a 53% 1-year efficacy with the traditional ‘time to first AF recurrence’ endpoint, versus a much higher 98% efficacy when AF burden reduction was measured.⁶ This demonstrates that AF burden correlates better with clinically relevant outcomes, whereas AF recurrence underestimates the true impact of ablation.





Lip supported the move toward AF burden as a more meaningful endpoint, and highlighted the limitations of the 30-second threshold, noting that a 29-second AF episode does not necessarily indicate low risk. AF burden, which captures the total time a patient spends in AF, is more comprehensive, and reflects the fluctuating nature of AF and its associated comorbidities.

Unlike AF recurrence, AF burden is closely linked to hard clinical outcomes. A recent study showed that AF burden had a greater effect on quality of life than either AF duration or the number of episodes.⁷ Furthermore, recent data indicate that AF burden is associated with mortality among patients with cardiac implantable electronic devices, with the greatest risk of mortality found when weekly AF progression exceeded 24 hours.^{8,9} AF burden is also a stronger predictor of ischaemic stroke in patients with paroxysmal AF, as demonstrated by the KP-RHYTHM Study.¹⁰

Currently, the 2024 AF ablation consensus document strongly advises that AF burden be reported as the primary endpoint in AF ablation trials.¹¹

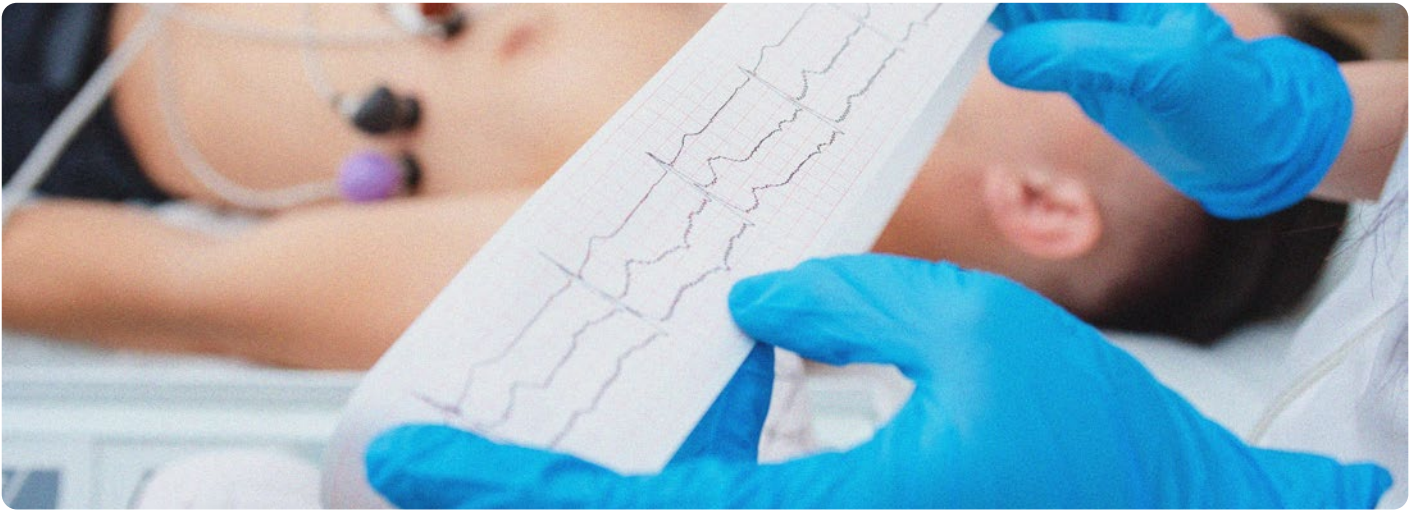
While the 30-second threshold remains in place to maintain continuity with previous research, this approach is increasingly seen as inadequate. Continuous AF burden measurements showed a more significant correlation with stroke risk than binary thresholds like AF recurrence, highlighting its direct effect on clinical outcomes.

Blomstrom-Lundqvist acknowledged that more research is needed to determine the most reliable way to measure AF burden, particularly when aiming to improve survival. Should continuous monitoring be employed? Should ablation be repeated if AF burden exceeds a certain threshold, such as 50%? These are questions that remain unanswered.

EMERGING TRENDS: PULSED FIELD ABLATION

Pulsed field ablation (PFA), a non-thermal procedure that uses high-voltage electrical pulses, is an emerging technology for the treatment of cardiac arrhythmias, and therefore the centre of many conversations on AF management. Indeed, Tom De Potter, Cardiovascular Research Center, Aalst, Belgium, joked about the current buzz around PFA, saying, “Another talk on PFA... seriously?” highlighting the increasing popularity of this modality. De Potter began his presentation by revealing that he had changed the title of his talk from “Should PFA replace radiofrequency (RF) or cryoballoon?” to “PFA will replace RF or cryoballoon.” He explained that debating whether it should replace these techniques is too philosophical, as there are currently not enough data for that discussion.

He explained that PFA is an AF ablation modality that works by damaging cell membranes using direct current. It is also called non-thermal ablation or voltage-mediated, tissue-selective ablation. De Potter noted that whilst tissue-selectivity is true in theory, it is not always perfect in practice. However, early clinical data have shown that PFA can spare vital structures such as oesophageal and phrenic nerves, which partly explains the enthusiasm for this modality.



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Whilst there aren't much data on this newer technology, De Potter highlighted recent studies that show that PFA is a straightforward and safe modality. For instance, the 5S study demonstrated that PFA has a shallow learning curve, in terms of both procedure time and ablation time, regardless of the operator's experience.¹² The study also showed that complication rates with PFA seem to lack the collateral damage seen with other ablation modalities.

On the other hand, De Potter did acknowledge concerns surrounding PFA, such as its potential link to silent cerebral injury, haemolysis, and coronary spasms, and the potential long-term effects on the autonomic nervous system. “The appeal of PFA is easy to understand,” he said, “but it's not without its own challenges.” However, he explained that the issue of silent cerebral injury in particular, appears to be a result of the ‘platform phenomenon’, meaning it is related more to procedural factors, such as fluid management and embolism avoidance, than to the thermal energy itself.

Although the data on PFA are limited, he referenced a randomised study comparing PFA to conventional thermal ablation for paroxysmal AF.¹³ The study revealed that PFA was non-inferior to conventional

ablation, and was associated with a low overall incidence of adverse events. He did note one mortality in the PFA cohort due to cardiac tamponade, but explained that, again, this is likely due to the ‘platform phenomenon’ rather than an inherent PFA energy-specific issue.

Recently, a real-world study was published which demonstrated the safety of PFA in over 17,000 patients with AF.¹⁴ The published results provide support for the ‘platform theory’, as the rate of tamponade decreased with operator experience, suggesting that with better training, procedural risks decrease, even as the energy source remains unchanged.

De Potter expanded on the growing popularity, explaining that whilst there is an increase in the number of ablation procedures worldwide, most electrophysiology centres do not fulfil the recommended requirements for ablation treatment, and the number of centres has not increased to meet the growing demand. This may thus explain the push for PFA in clinical practice, he proposed.

He argued that, whilst there are compelling arguments in favour of PFA, not all of them are entirely clinical. De Potter emphasised the importance of acknowledging the influence of industry in the drive for implementing PFA as an approach to AF management, especially as the demand for PVI and AF ablation continues to grow.

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