# Development of Atrial Fibrillation After Atrial Flutter Ablation: More a Question of When Than Whether

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## Editorial Comment

The relationship between atrial fibrillation (AF) and cavotricuspid isthmus (CTI)-dependent atrial flutter (AFL) has long been recognized in clinical practice. The development of both is favored by the presence of common triggers and substrate, particularly in the setting of structural heart disease with its attendant electrical and structural remodeling. Conditions associated with atrial remodeling, including heart failure, hypertension, increasing age and valvular heart disease, predispose to both fibrillation and flutter.

The nature of the "peri-tricuspid" macroreentry circuit, constrained by structural and functional barriers to electrical propagation, is now well understood. Experimental and clinical studies have demonstrated that CTI-dependent AFL is most frequently preceded by a period of short cycle length atrial activation, and in particular by a period of AF.[1-4] Such activity induces regions of functional conduction block and slowed conduction that are necessary for the transition from multiple unstable wavefronts to a single organized circuit.[5,6] The development of functional conduction block along the crista terminalis seems particularly important in the pathogenesis of CTI-dependent AFL.[7-9] Thus the same pulmonary vein (PV) and non-PV triggers that initiate AF are also responsible, via transitional AF, for onset of the great majority of AFL episodes.

This background is of prime importance when considering the accumulated literature evaluating the incidence of AF late after AFL ablation. This incidence is clearly time-dependent with reported rates of 17–22% at 6 months, increasing to 50% at 2 years and 63% at 4 years.[10,11] The most consistently identified risk factor for the development of post-ablation AF is documented pre-ablation AF, the prevalence of which varies according to the intensity of monitoring,[10-14] Other identified risk factors have included left ventricular (LV) systolic dysfunction,[12,14] significant mitral regurgitation,[10] left atrial (LA) enlargement,[11,15] and the failure of multiple antiarrhythmic drugs (AADs).[14] All are associated with LA remodeling and an elevated risk of incident AF regardless of AFL ablation. Importantly, the incidence of AF after AFL ablation is also proportional to the intensity of monitoring. In a small study of patients who had loop recorders implanted after flutter ablation, 55% developed new AF within the first year of follow-up.[16] It seems probable that the variability in the reported incidence of post-ablation AF is related in large part to varying intensities of monitoring.

In this issue of the *Journal*, Brembilla-Perrot and colleagues[17] further explore the incidence of and risk factors for AF following ablation of AFL. They present a large single-center series of 1,121 consecutive patients undergoing catheter ablation of CTI-dependent AFL, with data retrospectively extracted by chart review. A history of AF before AFL ablation was present in 31.8% of patients, but the nature of pre-ablation monitoring to determine this is not described. It is probable that the real AF incidence before ablation was much higher. Follow-up was continued for a mean of 2.1 ± 2.7 years, and included ECG and 24-hour Holter monitoring at 1 month but thereafter only at annual intervals or for investigation of symptoms. Using this approach, new AF was observed during follow-up in 19.3% of patients without pre-ablation AF, but ongoing AF was only detected in 31.5% of patients who did have pre-ablation AF. The study thus observed a fall in the overall AF incidence post-ablation (23.2%) compared with pre-ablation (31.8%), with a particularly marked fall in the group with AF before AFL ablation. This result should be viewed in the context of the limited post-ablation monitoring performed. Nevertheless, the ongoing involvement with the healthcare system remained significant with 8% developing permanent AF, 7% requiring electrical cardioversion, 7% atrio-ventricular node ablation and 15% pacemaker implantation. These data certainly make it difficult to argue that AFL ablation in this population provides a definitive result.

Only AF history and female gender were significant predictors of AF occurrence post-ablation. Other established markers of AF risk such as age, hypertension, diabetes and various forms of structural heart disease were not associated with post-ablation AF in this study. Importantly, at the time of ablation 50.5% had a $CHADS_2$ score $\geq 1$ and although only 2 strokes occurred during follow-up both were in patients who were not anti-coagulated and who had AF recurrence. The authors have acknowledged the significant limitations of this study, most notably its retrospective nature conducted by chart review and, importantly, the relatively minimal amount

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of monitoring performed both before and following AFL ablation to detect AF.

This study raises some important questions regarding the contemporary management of patients with CTI-dependent AFL. Is there still a role for isolated AFL ablation in the era of AF ablation? If so, in which patients and what is the appropriate post-ablation anti-coagulation strategy?

In patients with both AF and AFL, various ablation strategies have been evaluated. Studies testing the hypothesis that a hybrid combination of CTI ablation plus continuation of AADs would prevent further AF showed initial promise. One study observed a lower incidence of AF episodes with combined therapy compared with AAD therapy alone over $11 \pm 4$ months.[18] However, more recent studies with longer follow-up and more intensive monitoring have demonstrated that this strategy has limited longer-term efficacy. AF recurrence rates have been reported to be as high as 27% by 16 months[19] and 93% by 5 years.[20] In a randomized study of 108 patients with both AF and AFL, Wazni and colleagues demonstrated no additional long-term benefit from the addition of linear CTI ablation to pulmonary vein isolation (PVI), when compared to PVI alone. There was no reduction in AF recurrence, the need for AADs or the requirement for repeat AF ablation beyond 8 weeks.[21] In a subsequent study, also in patients with coexistent AF and AFL, the same group demonstrated that PVI alone was vastly superior to CTI ablation alone for prevention of recurrent atrial arrhythmias.[22] Finally, in patients with a mitral isthmus-dependent macroreentry tachycardia after AF ablation, repeat PVI and trigger ablation has been shown to be significantly superior to performing linear ablation of the mitral isthmus alone for prevention of recurrent atrial arrhythmias.[23] These studies emphasize the importance of AF in the initiation of stable flutter circuits and, taken together, arguably demonstrate the limited efficacy of AFL ablation in the management of atrial arrhythmias in general, and of AF in particular.

Nevertheless, we continue to believe that isolated AFL ablation, without simultaneous AF ablation, does have a clinical role in appropriately selected patients. Such patients may include those with chronic AFL or those with a rapid and difficult to control ventricular response rate. When consenting patients for this procedure it is important for them to be made aware that it is largely palliative, with an incidence of late AF that is high and which increases over time. In patients with paroxysmal AFL, careful monitoring will invariably reveal coexistent fibrillation, and in this group PVI provides better long-term outcomes.

Of course a key question, given the high probability of developing AF after AFL ablation, is whether it is ever safe to stop systemic anticoagulation. Observational studies describing stroke risk following AFL ablation have reported rates of 6% over 40 months despite a large proportion of participants being anticoagulated.[24] Many of the identified risk factors for post-ablation AF such as heart failure, hypertension, and structural heart disease are also key risk factors for embolic events. Although specific guidelines for anticoagulation following AFL ablation are lacking general guidelines, including relating to management after cardioversion, recommend treatment as for AF. As AFL ablation cannot be viewed as definitive atrial arrhythmia therapy, it seems prudent to guide ongoing anticoagulation decisions according to $CHADS_2$ or CHA2DS2-VASc scores. The alternate suggested approach of intensive monitoring should be viewed with caution in light of evidence from the TRENDS study demonstrating a lack of temporal relationship between stroke and episodes of atrial tachyarrhythmia.[25]

Although perhaps an overused expression, it is nevertheless true that AFL and AF represent 2 sides of the same coin.[26] Can you really have flutter without fibrillation? In considering the risk of AF after AFL ablation it is more a question of when than whether.

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