More Musing About the Inter-relationships of Atrial Fibrillation and Atrial Flutter and Their Clinical Implications

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The inter-relationship between atrial fibrillation (AF) and atrial flutter (AFL) has long been recognized both in patients and in animal models.1 There are 2 important aspects of this inter-relationship relevant to the article by Mohanty et al.2 First is the fact that AF virtually always precedes the onset of classical cavitricuspid isthmus (CTI)-dependent AFL, and second, the development of classical CTI AFL requires the development or presence of a line of block in the right atrium between the veins cavae.1 The first aspect probably was initially recognized by Sir Thomas Lewis,3 who, in studies in the normal canine heart, burst paced the right atrium, and obtained mostly transient AF, but sometimes sustained AFL. Lewis mapped the AFL and concluded that AFL was because of re-entry around the great veins (ie, the superior and inferior vena cavae). This conclusion became well accepted. The second aspect was addressed by Rosenblueth and Garcia Ramos,4 who postulated that the reason it was so difficult for Lewis et al to induce AFL was because there was short circuiting of the AFL reentrant circuit by conduction across the atria in the region between the vena cavae (from the left atrium or to the right atrium or vice versa) making the reentrant circuit impossible to sustain. Therefore, in studies in the canine heart (1947), they created conduction block between the vena cavae, either with a crush lesion (permanent block) or by painting cocaine on the atrial epicardium in the intercaval region (transient block), and, with burst atrial pacing, easily induced AFL. The latter occurred consistently in the presence of the crush lesion, but only transiently with the use of cocaine, as the effects of the cocaine wore off.

Over the years, many more studies further advanced these 2 aspects of AFL. Almost 2 decades later (1964) came the computer model studies of AF and AFL by Moe et al.,5 who demonstrated that they could not induce AFL in this model unless AF occurred first. Then, our studies of the spontaneous onset of AFL after open heart surgery in patients who had temporary epicardial atrial wire electrodes in place demonstrated that the onset of AFL was always preceded by an usually brief, but variable duration of AF.6,7 And from the 1980 studies of Watson and Josephson,8 we learned that the best way to induce AFL in the clinical cardiac electrophysiology laboratory was to perform burst atrial pacing.

In 1991, Shimizu et al,9 using high-density mapping during the induction of AFL in the canine sterile pericarditis model, demonstrated that AF of variable duration preceded the onset of AFL, and that AFL developed after the evolution of a functional line of block between the vena cavae. After the article of Shimizu et al,9 Ortiz et al10 in 1994 demonstrated in the canine sterile pericarditis model that the length of a line of functional block in the right atrial free wall was critical to the spontaneous or ATP-induced conversion of AFL to AF, and then to the spontaneous conversion of AF back to AFL. Subsequently, Chan et al11 showed that in patients who developed AFL late after repair of atrial septal defects in whom the approach for the repair was made with an incision in the right atrium between the superior and inferior vena cavae, the AFL was primarily the classical CTI-dependent type. This was attributed to the anatomic lesion created as part of the atrial septal defect repair. Then Tomita et al12 mapped the atria and showed that when an anatomic line of block was created between the vena cavae in normal canine hearts, burst atrial pacing produced AFL. Furthermore, the line of block between the vena cavae consisted not only of the anatomic line of block, but also a functional extension of the line of block to either or both of the vena cavae, thereby preventing short circuiting of the AFL reentrant circuit. In 2008, in studies in the canine sterile pericarditis model on postoperative day 2, that is, a time when burst atrial pacing induction of AFL is rare, Bui et al13 first reliably and reproducibly induced sustained AF, which was because of a reentrant driver in the left atrium. Then, after creation of a fixed line of block between the vena cavae, in all but one instance, burst atrial pacing only induced AFL. Finally, Ellis et al.,14 reported that of 363 patients who presented with only CTI-dependent AFL and who underwent only CTI ablation, long-term follow-up (mean, 39±11 months) demonstrated newly recognized AF in 82%. In short, in the latter type patients, if only CTI-dependent AFL is present, AF will ultimately become manifest. Why it takes variable periods for the AF to become manifest in patients who initially present only with AFL is of interest, in fact, of importance, but is not known. The point is that without antecedent AF, there is almost always no CTI-dependent AFL.

In summary, it seems now well established that AF of usually short but variable duration usually precedes AFL, and that the difference between development of sustained AF and AFL is
the presence or development of a line of block between the vena cavae. Hence, how does all the above relate to the article of Mohanty et al. describing the results of the APPROVAL study, a single-blinded randomized study comparing the impact of different ablation strategies on long-term procedure outcome in patients with coexistent AF and AFL? In this study, 368 patients with both AF and AFL were blindly randomized to either AF plus AFL ablation (group 1) or only AFL ablation (group 2) and followed 21±9 months to assess whether they remained arrhythmia free, and to assess quality of life, the latter using 4 self-administering survey tools. One should not be surprised that compared with the group who only underwent AFL ablation (group 2), patients who received either AF ablation alone or AFL ablation plus AFL ablation in combination (group 1) did significantly and remarkably better both in terms of arrhythmia free state and quality of life.

On the basis of our understanding of the interactions of AF and AFL, one would predict that in the APPROVAL study, patients who were randomized to the AFL ablation only arm would have a high recurrence rate of AF, and that patients randomized to the AF ablation alone or AF ablation plus AFL ablation arms would have a far better success rate. In fact, one would expect that successful AF ablation alone would also prevent recurrence of AFL, and that is basically what happened. These outcomes led Mohanty et al. to conclude that, “Our findings clearly suggested that AF±AFL ablation is more effective than [atrial] flutter ablation alone in providing high recurrence-free survival as well as causing betterment in the quality of life of patients presenting with both AF and AFL. Furthermore, between the two ablation strategies in group 1, AF ablation alone was demonstrated to be equally as effective as AF+ AFL ablation.” Of note in this regard, Wazni et al. in a randomized study comparing combined pulmonary vein–left atrial junction disconnection and CTI ablation (n=49) versus pulmonary vein–left atrial junction disconnection alone in patients presenting with typical AFL and AF concluded that, “In patients with both AFL and AF, pulmonary vein–left atrial junction disconnection alone may be sufficient to control both arrhythmias.” This certainly is a logical extension of the notion that without AF, there is rarely CTI-dependent AFL.

Finally, we should also recall that sometimes, development of AFL from AF may be desirable. Both Josephson’s laboratory16 and Wellens’ laboratory17 demonstrated long ago that when administering an antiarrhythmic drug that converts AF to AFL (usually an antiarrhythmic drug that has sodium channel blocking properties), if one ablates the AFL and keeps the patient on the drug, ~80% of the patients not only will no longer get AFL, but also will no longer get AF. This is probably one of the safest and most effective hybrid therapies (antiarrhythmic drug therapy plus ablation therapy) to treat AF. One wonders if deliberately making a line of block between the vena cavae in patients with AF would convert their recurrent episodes to AFL. And then, if one ablated the CTI and added antiarrhythmic drug therapy, would that be an effective way to successfully suppress recurrent AF? In this regard, see Bui et al.13

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References

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