Atrial Fibrillation After Major Thoracic Surgery

New Insights Into Underlying Mechanisms*

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Atrial fibrillation (AF) is a common complication in patients undergoing major thoracic surgery (1–3). It is most frequently observed acutely after valve surgery and/or coronary artery bypass graft surgery (CABG), but it can also manifest after lung and heart transplantation procedures (1–7). Although mechanisms underlying this unique form of AF have not been adequately elucidated, it is likely that these involve a combination of pericardial inflammation, myocardial ischemia, catecholamine surge, autonomic imbalance, interstitial fluid mobilization, tissue rejection, and so forth (3–8). It is interesting to note that AF is observed significantly less often after cardiac transplantation than after valve surgery and/or CABG (1,2,6). This relative protection from AF after cardiac transplantation has been attributed to factors unique to this procedure, including the accomplishment of pulmonary vein (PV) isolation (because the technique involves implanting all 4 of the recipient’s PVs along with the adjacent atrial cuff into the donor’s left atrium), reduction in the arrhythmogenic substrate due to inadvertent left atrium “debulking,” autonomic denervation, and so forth (6,9). However, because of the lack of any representative animal model and/or comparative clinical outcomes, these postulations have up until now largely remained speculative. In response to this lacuna, the study by Dizon et al. (10) in this issue of the Journal provides us with some additional insights into the mechanisms that may underlie the development of AF in patients undergoing major thoracic surgery.

In this study, the investigators meticulously analyzed medical records of patients undergoing cardiac and lung transplantation procedures at their center over a 3-year period, specifically for the occurrence of post-operative AF or atrial flutter, which was defined as an electrocardiographically-documented episode that lasted ≥30 min. For patients manifesting these arrhythmias, additional data were collected on their clinical profile, echocardiographic parameters, immunosuppressive regimen, and tissue biopsy. The primary aim of this study was to assess the influence, if any, of the aforementioned variables on the occurrence of AF in patients undergoing cardiac and lung transplantation surgery. To make meaningful comparisons between expected and observed frequency of the outcome, these investigators chose to include a subgroup of patients with preserved left ventricular function who underwent CABG during the same period to serve as the control group. Using this case-control model, they found the overall occurrence of AF in patients undergoing cardiac transplantation (4.6%) to be significantly lower than that in patients undergoing lung transplantation (18.9%) and/or CABG (19.8%). It is also interesting to note that, in addition to the relatively low incidence of AF in patients undergoing cardiac transplantation, one-half of the episodes occurred beyond the first week after surgery; that was in contrast to the profile of AF observed in patients after lung transplant, for whom the majority of episodes (78%) were seen soon after the surgical procedure. Other salient findings of the study were the difference in the patient demographics between the 2 groups (patients undergoing cardiac transplantation were older and generally male) as well as the higher use of beta-blockers and antiarrhythmic agents before surgery in the cardiac transplant group. Another interesting observation was that, despite being on a similar immunosuppressive regimen, patients undergoing cardiac transplantation experienced significantly higher acute rejection rates as compared with the lung transplantation group (63% vs. 18%, respectively).

So how do we interpret these data? First and foremost, it should be acknowledged that this was a retrospective analysis of patients with diverse cardiac and pulmonary conditions. Hence, the observed differences in baseline demographics and clinical parameters are not entirely unexpected. It is also important to recognize that the actual sample size of patients manifesting AF post-operatively is quite small (8 patients in the heart transplant group vs. 23 patients in the lung transplant group). Furthermore, even though there were differences in the baseline variables between the groups, the relatively small sample size precludes determination of a cause and effect relationship. This is further compounded by the investigators limiting the evaluation of variables to patients manifesting post-operative AF or atrial
flutter and not the entire cohort. It is also worthwhile to mention that the overall occurrence of post-operative AF in all 3 groups of patients in this series, and especially among those undergoing CABG and lung transplantation, is lower than what has been previously reported (1–3,5–7,9). This raises concerns about whether the criteria used for arrhythmia screening in the current study were too specific and so may have excluded potentially eligible subjects. Having said that, the approach used for identifying AF and/or atrial flutter by these investigators, namely, electrocardiographic recordings verified by ≥1 electrophysiologist, certainly leaves little room for ambiguity in arrhythmia misclassification, and so is actually a strength of this retrospective analysis. Another strength of the study pertains to the homogeneity of surgical approach utilized in both groups. Thus, all cardiac transplants were done using the bicaval right atrial anastomosis technique, and all pulmonary surgeries utilized double lung transplant.

So, factoring in these pros and cons of the study design and methodology, what can we infer from observed differences in the outcomes between the 2 groups? Certainly, these data are consistent with previous studies that have found lower post-operative AF among patients undergoing cardiac as compared with patients undergoing lung transplantation surgery (5,6,9,11). Thus, as far as the development of post-operative AF is concerned, clearly, cardiac transplantation surgery is less pro-arrhythmic. Why that is the case may perhaps be better answered by the observations made in this series. Indeed, as these investigators suggest, autonomic modulation may have been an important factor. There is emerging literature supporting the role of the autonomic nervous system in the genesis of clinical AF, and although the precise mechanism of how different autonomic inputs contribute to the development of AF remains elusive, both the sympathetic and parasympathetic arms have been implicated (12,13). Since heart transplantation achieves complete cardiac autonomic denervation acutely (9), that could certainly underlie its less pro-arrhythmic profile. This hypothesis can also explain the late occurrence of AF (up to 9 months after heart transplant) observed in the study that may be attributed to long-term partial regeneration of the cardiac autonomic nerve supply, which is a known phenomenon (14). A more definitive assessment of this hypothesis could perhaps have been made if the investigators had provided additional data on heart rate variability, substantiating the evolving autonomic profile of these patients. In the absence of this information, another possible but perhaps less plausible explanation for the observed differences in AF occurrence between patients undergoing heart and lung transplantation may pertain to the type of PV isolation achieved by the 2 techniques. As Dizon et al. (10) show nicely in the illustrations accompanying this paper, for patients undergoing cardiac transplant, all 4 veins and the surrounding common atrial cuff (which is essentially the left atrial posterior wall) are anastomosed to the donor heart by a single atriotomy. In contrast, for patients undergoing double-lung transplant, this involves anastomosing ipsilateral PVs with the adjacent atrial cuffs from the donor onto the recipient’s left atrium, through 2 separate atriotomies. Thus, in the latter approach, more of the recipient’s left atrial posterior wall is left intact, which is a well-known site for AF triggers (15). Additionally, the 2 atriotomies, by creating a protected zone between them, could serve as a substrate for re-entrant organized atrial tachyarrhythmias, not unlike our experience with catheter-based wide-area circumferential PV ablation (16). Furthermore, chronic lung disease has also been shown to cause alterations in atrial cellular electrophysiology and/or the development of fibrosis, both of which have been implicated as factors underlying its association with the development of atrial tachyarrhythmias (5,11,17). Thus, the higher incidence of AF observed after lung transplant in this study is not entirely unexpected, since the electrophysiologically-altered entire right atrium and the majority of the left atrium in the recipient’s heart were left intact. In support of this hypothesis, it is interesting to note that the majority of AF events occurred in these patients within the first week of lung surgery, with decreasing incidence beyond this period. Such a time course of AF occurrence after lung transplantation may be coincident with the normalizing electrophysiologic profile of the recipients’ atria in response to successful lung transplantation.

So, how do these data enhance our understanding of AF encountered after major thoracic surgery? Clearly, this form of AF has diverse underlying mechanisms as reflected in its variable occurrence and time course vis-à-vis the type of surgical procedure. The lower incidence of post-operative AF among patients undergoing cardiac transplantation as compared with lung transplantation, despite both procedures essentially achieving PV isolation, albeit with some variation of technique, makes a strong case that PV triggers are likely not responsible for AF in this setting. Alternative explanations for observed difference in AF occurrence between the 2 groups include autonomic denervation and/or left atrial “debulking,” neither of which can be conclusively proven or disproven from the results of this study. Nevertheless, these investigators are to be congratulated because they have largely accomplished the goals of a well-done retrospective study, namely, provided us with intriguing data that have generated interesting questions that may be better answered by prospective studies.

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