Dear Sir,

We read with great interest the meta-analysis by Pearman et al. on the comparison between epicardial ablation for atrial fibrillation and the hybrid approach. The authors should be commended on the way they handled the data. The imbalance between the two meta-analytic cohorts – in terms of the type of atrial fibrillation and left atrial diameter – may have worked to the detriment of the hybrid arm, but the sensitivity analysis shows quite convincingly, at least from a statistical point of view, that this is probably not the case.

However, one cannot fail to note that statistics can only go so far as the quality of available data allows. An all-encompassing meta-analysis that includes not only randomised data but also small series of patients from observational and/or retrospective studies may dilute the true signals of difference between the two strategies studied. Therefore, it would be interesting to report results only from studies with a prospective design.

Furthermore, considering that clear definitions of the parameters studied are the basis of any sound analysis, one may wonder what exactly is meant as a ‘hybrid’ technique. Is it merely a combination of epicardial and endocardial ablation? Do epicardial and endocardial ablation happen at the same time or in a staged manner and, when performed simultaneously, is the confirmation of electrical isolation reliable? Aggregating different approaches – all termed ‘hybrid’ – in the same analysis may cloud the picture.

Finally, another point of concern would be the method of follow up. Considering that the minimally-invasive epicardial technique antecedes the hybrid approach, it is conceivable that in a number of the earlier studies (thus more frequently in studies of epicardial technique) follow-up was merely clinical/electrocardiographic, while in later studies (thus more frequently in studies of hybrid technique) higher-yield techniques of patient monitoring may have been used. This would result in a lower detection rate of arrhythmia recurrence in less intensively followed patients, i.e. artificially higher ‘success’ rates. Are there any data regarding these aspects of follow-up for the two patient groups?

Georgios Giannopoulos, Yale School of Medicine, New Haven, CT, USA
Spyridon Deftereos, Yale School of Medicine, New Haven, CT, USA

Dear Sir,

We thank Drs Giannopoulos and Deftereos for showing interest in our work. They wonder whether a true difference might exist between hybrid and epicardial ablation alone that may have been masked by our combining the results from retrospective observational studies with those from randomised trials.

A fine balance needs to be struck for this type of analysis. On one hand, adopting narrow inclusion criteria will ensure that

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**Authors’ Reply**

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We thank Drs Giannopoulos and Deftereos for showing interest in our work. They wonder whether a true difference might exist between hybrid and epicardial ablation alone that may have been masked by our combining the results from retrospective observational studies with those from randomised trials.

A fine balance needs to be struck for this type of analysis. On one hand, adopting narrow inclusion criteria will ensure that...
the studies within each group share very similar designs, interventions and populations, minimising the chance of dilution of a genuine difference between groups. On the other hand, using broad inclusion criteria will increase statistical power by including a larger number of studies. Previous work exploring outcomes following atrial fibrillation ablation has shown that results from observational studies match those from randomised trials and can strengthen the power of a meta-analysis. We have tried to reconcile this dilemma by presenting our primary outcome first using a broad inclusion strategy and subsequently by verifying this in sensitivity analyses designed to reduce heterogeneity. Each sensitivity analysis that was performed confirmed the initial conclusion that there was no detectable advantage associated with routine hybrid ablation.

Seven randomised trials of epicardial ablation alone were included, and the pooled estimate of 12-month survival free from atrial arrhythmias without antiarrhythmic drugs in these studies was 70.7%, similar to the result (71.5%) when all studies were included. However, it is notable that major complications were reported to occur in 31 of the 602 (5.1%) patients included in randomised trials, considerably more than the pooled estimate of 2.9% when all studies were included, suggesting that under-reporting of complications may have been present among non-randomised studies. We were unable to compare epicardial-alone with hybrid ablation in this sensitivity analysis as no randomised trials of hybrid ablation could be found that met our inclusion criteria.

Giannopoulos and Deftereos enquire about the definition used for hybrid ablation. We used the term to include all studies in which a combination of epicardial and endocardial ablation was used routinely, either simultaneously or as a staged procedure. Studies in which supplementary endocardial ablation was used only in cases of recurrent arrhythmia were not included in this group. Despite theoretical concerns that simultaneous hybrid ablation may be less effective, the single study we are aware of that has compared staged with simultaneous hybrid ablation showed no difference in success rates between these strategies. We agree that the confirmation of electrical isolation could potentially be less reliable using a simultaneous hybrid approach. Interestingly, although some studies reported performing epicardial ablation without verification of conduction block, meta-regression did not identify this as a significant predictor of arrhythmia recurrence.

The readers’ third point addresses the usage of ambulatory monitoring to detect recurrent arrhythmias. We fully appreciate that a higher prevalence of extended ambulatory monitoring is more likely to correctly identify treatment failure. In view of this, we performed a sensitivity analysis including only studies in which patients underwent at least 1 week of ambulatory monitoring in total over the follow-up period. Seventy-five per cent of patients in the epicardial-alone group remained free from atrial arrhythmias at 12 months compared to 61% of patients in the hybrid group, once again failing to find a benefit for routine hybrid ablation.

In summary, multiple sensitivity analyses aimed at decreasing heterogeneity within the treatment groups supported our initial results, leading us to conclude that evidence supporting a role for routine hybrid ablation is lacking.

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1. Pearman CM, Poon SS, Bonnett LJ, et al. Minimally invasive epicardial surgical ablation alone versus hybrid ablation for atrial fibrillation: a systematic review and meta-analysis. Arrhythm Electrophysiol Rev 2017;6:202–9. DOI: 10.15420/aer/2017.29.2; PMID: 29326836.

2. Chambers D, Rodgers M, Woolacott N. Not only randomized controlled trials, but also case series should be considered in systematic reviews of rapidly developing technologies. J Clin Epidemiol Dec 2009;62:1253–60.e1254. DOI: 10.1016/j.jclinepi.2008.12.010; PMID: 19349144.

3. Richardson TD, Shoemaker MB, Whalen SP, et al. Staged versus simultaneous thoracoscopic hybrid ablation for persistent atrial fibrillation does not affect time to recurrence of atrial arrhythmia. J Cardiovasc Electrophysiol 2016;27:428–34. DOI: 10.1111/jce.12966; PMID: 26725742.