A meta-analysis of the comparative efficacy of ablation for atrial fibrillation with and without ablation of the ganglionated plexi

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CRD summary
This review found that combined ablation of the ganglionated plexi with pulmonary vein isolation or the Maze procedure was more effective for treatment of atrial fibrillation than Maze or pulmonary vein isolation alone. The results and authors’ conclusion should be interpreted with some caution because of the small number of patients included in the review.

Authors' objectives
To evaluate the comparative efficacy of ablation for atrial fibrillation with and without ablation of the ganglionated plexi.

Searching
PubMed, EMBASE, Cochrane Central Register Controlled Trials (CENTRAL) and ClinicalTrials.gov were searched for relevant studies to January 2011; search terms were reported.

Study selection
Eligible studies were clinical trials of patients who received ablation of the ganglionated plexi alone or in combination with pulmonary vein isolation or the Maze procedure and that reported sufficient information for the calculation of summary data. Control groups in the eligible trials were required to receive pulmonary vein isolation or the Maze procedure without ablation of the ganglionated plexi. The primary outcome was freedom from atrial fibrillation or other sustained arrhythmia recurrence (including atrial fibrillation, atrial flutter and atrial tachycardia). Studies in which the experimental group received ganglionated plexi ablation and Marshall or complex fractionated atrial electrograms were excluded from the review.

The patients presented with persistent atrial fibrillation or paroxysmal atrial fibrillation. Where reported, mean age of patients ranged from 51.7 to 65 years and the proportion of male patients in the trials ranged from 35% to 84%. The evaluations made in the review were ganglionated plexi ablation and pulmonary vein isolation compared to pulmonary vein isolation alone, ganglionated plexi ablation compared to pulmonary vein isolation and ganglionated plexi ablation plus Maze procedure compared to Maze procedure alone. Anatomic ganglionated plexi ablation was performed in three trials based on empiric high density ablation at anatomic sites with frequent location of ganglionated plexi clusters. Selective ganglionated plexi ablation was performed in the remaining trials where target sites were identified as places where vagal reflexes were defined as sinus bradycardia, atrioventricular block or transient hypotension occurring during or immediately after onset of circumferential radiofrequency ablation. Follow-up ranged from one month to 37 months and in most trials was 12 months.

Two reviewers independently performed the study selection.

Assessment of study quality
Methodological quality was assessed by two reviewers in terms of sequence generation, allocation concealment, attrition of less than 15%, use of blinded assessments and intention-to-treat analyses, completeness of follow-up and whether monitoring of atrial fibrillation was adequate.

Data extraction
Two independent reviewers extracted data to calculate odds ratios (OR) and 95% confidence intervals for the outcomes. Any disagreements between the reviewers were resolved by discussion.

Methods of synthesis
Pooled odds ratios and 95% CIs were calculated using a Mantel-Haenszel fixed-effect model. The authors evaluated statistical heterogeneity using Cochran's Q and I². Results were stratified according to treatment because of the presence
of significant heterogeneity across the trials in procedure methods ($I^2=84\%$) for the primary outcome. The first subgroup comprised ganglionated plexi ablation plus pulmonary vein isolation or Maze compared to pulmonary vein isolation or Maze. In the second subgroup ganglionated plexi ablation was compared to pulmonary vein isolation.

**Results of the review**
Six controlled trials (342 patients, range 32 to 75) were included in the review. One trial reported adequate sequence generation. None of the trials reported allocation concealment or blinded assessments of outcomes. Attrition was less than 15% in all the studies. Intention-to-treat analyses were performed in all the trials. Follow-up was complete in five trials. Monitoring of atrial fibrillation was adequate in all the trials.

Freedom from atrial fibrillation or other sustained arrhythmia at 12 months was significantly improved in patients who received ganglionated plexi ablation in addition to pulmonary vein isolation or the maze procedure compared to patients who received pulmonary vein isolation or Maze without ganglionated plexi ablation (OR 5.66, 95% CI 2.97 to 10.82; four trials; $I^2=0\%$). Ablation of the ganglionated plexi was associated with statistically significant aggravation of atrial fibrillation or sustained atrial arrhythmia recurrence compared to pulmonary vein isolation alone (OR 0.32, 95% CI 0.14 to 0.73; two trials; $I^2=0\%$).

Early recurrence of atrial arrhythmia was significantly higher in patients treated with ganglionated plexi ablation alone compared with pulmonary vein isolation alone (OR 2.75, 95% CI 1.20 to 6.27; two trials; $I^2=0\%$). There were no differences in early recurrence between patients treated with ganglionated plexi ablation plus pulmonary vein isolation or Maze procedure (four trials).

Two studies (145 patients) assessed complications. One study reported no deaths during hospitalisation and no ablation device-related complications. One study reported one case of cardiac tamponade. One trial had non-significant narrowing of both superior pulmonary veins in patients who received ganglionated plexi ablation. Among patients treated with pulmonary vein isolation, one had significant left superior pulmonary vein stenosis diagnosed four months post-ablation and one had significant upper respiratory tract bleeding 25 months post procedure.

**Authors’ conclusions**
Combined ablation procedures (pulmonary vein isolation or the Maze procedure plus ablation of the ganglionated plexi) produced superior outcomes compared to pulmonary vein isolation or Maze without ablation of the ganglionated plexi for atrial fibrillation. However ablation of the ganglionated plexi alone did not decrease early and long-term recurrence of atrial fibrillation compared with pulmonary vein isolation alone.

**CRD commentary**
The review addressed a clear question. Criteria for the inclusion of studies were defined and reproducible. Appropriate databases were searched for relevant studies and some attempts were made to identify unpublished studies. Steps were taken to minimise errors and bias at each stage of the review process. Methodological quality was assessed and the overall quality of the included studies was average. The authors’ decision to summarise the results in stratified analyses by treatment type appeared justified because of the differences in procedure types. There were some discrepancies between results presented in the text and those presented in the figures. The results of the review were based on a small number of studies that had very small sample sizes.

The review was well conducted but the small numbers of included patients means that the results should be interpreted with some caution and the reliability of the authors’ conclusions is unclear.

**Implications of the review for practice and research**
**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that future research was necessary to establish and standardise targeting sites, endpoints and methods of ablation of the ganglionated plexi.

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