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**Recovery of left atrial contractile function after maze surgery  
in persistent longstanding atrial fibrillation: a matched cohort study**

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Atrial fibrillation (AF), the commonest dysrhythmia, affects nearly 4.5 million people in Europe and 2.2 million in the US. Prevalence increases with age (4% over 60 years and 9% over 80) and impact on quality of life and health resources is considerable. Fibrillating atria have no contractile function. The most serious complication is thromboembolic stroke (12500 strokes attributed to AF annually in the UK). To reduce thromboembolism, patients are anticoagulated, increasing bleeding risk. AF also exacerbates heart failure and is a rising public health burden as the population ages.

The maze procedure creates lesions in the atria to obstruct the macro-re-entry circuits essential to sustain AF. Maze is most commonly performed as an adjunct to major cardiac surgery and significantly increases 12-month freedom from AF, restoring sinus rhythm (SR) in 44% - 94% of treated patients compared to 5% - 33% of controls (1). Restoring SR does not guarantee return of atrial contractile function, and both thromboembolism and heart failure exacerbation are related to the loss of contractile function (2).

Studies of atrial transport after maze are limited by small samples, selection bias and lack of matched controls. The HESTER (Has Electrical Sinus Translated into Effective Remodelling?) matched cohort study, compared atrial transport in patients whose SR was restored by maze with those in SR before and after cardiac surgery. The maze cohort were in SR at least one year after receiving maze for persistent longstanding AF as an adjunct to cardiac surgery. The control cohort were patients in SR both before and at least one year after cardiac surgery, matched one-to-one for time since procedure ( $\pm 6$  months), age ( $\pm 5$  years), sex, type of surgery, left ventricular function, and risk profile (logistic EuroSCORE). The aim was to assess whether the two cohorts had equivalent LA function, primarily active LA ejection fraction (ALAEF).

$$ALAEF = 100 \times \frac{LAV_{preA} - LAV_{min}}{LAV_{preA}}$$

Secondary outcomes were LA volume measurements, active and passive stroke volume and LA ejection fraction.

LA function evaluation was by transthoracic echocardiography and multislice MRI. For each modality, a single operator blinded to the cohort performed the test and interpreted the findings. A mixed effects linear regression model was fitted, including treatment and matching variables (fixed effects) and matched pairs (random effects). An unconstrained covariance model was assumed, with residuals at both levels presumed independent and normally distributed. The estimated treatment coefficient was taken as the mean ALAEF difference. In normal subjects in SR, the standard deviation in ALAEF was 18.2% (3). This was taken as the minimum clinically important ALAEF difference.

Between 2013 to 2015, 22 patients were recruited per cohort and had LA functional measurements. Maze patients had lower mean ALAEF (18.4%) than controls (26%). One-to-one comparison shows that controls had higher ALAEF in all but three pairs (Figure 1A). After adjusting for the paired design and matching variables, mean ALAEF was 8.03% lower in maze than controls (95% CI -12.43%, -3.62%,  $p=0.0015$ ), but the confidence interval was entirely contained within the standard deviation of normal subjects ( $\pm 18.2\%$ ). This study demonstrates no clinically important difference in ALAEF between patients in SR after maze procedure and matched controls who were in SR before and after cardiac surgery but average ALAEF was lower in maze than controls. Results of regression analyses for secondary outcomes are shown in Figure 1B.

Patients with chronic AF may have persistent LA dysfunction, even after restoration of SR by ablation. Buber et al reported that absence of LA contraction, despite SR restoration, is associated with a significant increase in the risk of thromboembolic stroke after maze. Global and regional atrial dysfunction may be the result of a combination of injury from the ablation process and pre-existing disease (2). The two adverse features of asymptomatic AF, thromboembolism and impact on cardiac function, are both directly related to atrial function. Restoring SR without restoring function is unlikely to be of clinical benefit. HESTER provides evidence that function is indeed restored after adjunct maze with potential clinical benefits in reducing thromboembolic and heart failure risk. Whether patients can safely stop taking anticoagulants after SR is restored by a maze procedure requires long-term follow-up

and stroke surveillance, and HESTER does not answer this question. The varying rates of LA functional recovery after maze mean that it would be prudent to measure atrial function before considering anticoagulation withdrawal.

In summary, return to SR after adjunct maze is associated with recovery of LA function, with an ALAEF smaller than controls but within the predetermined clinically acceptable range of variation. This functional recovery and the variability observed have important implications for survival, heart function and clinical decisions on long-term anticoagulation.

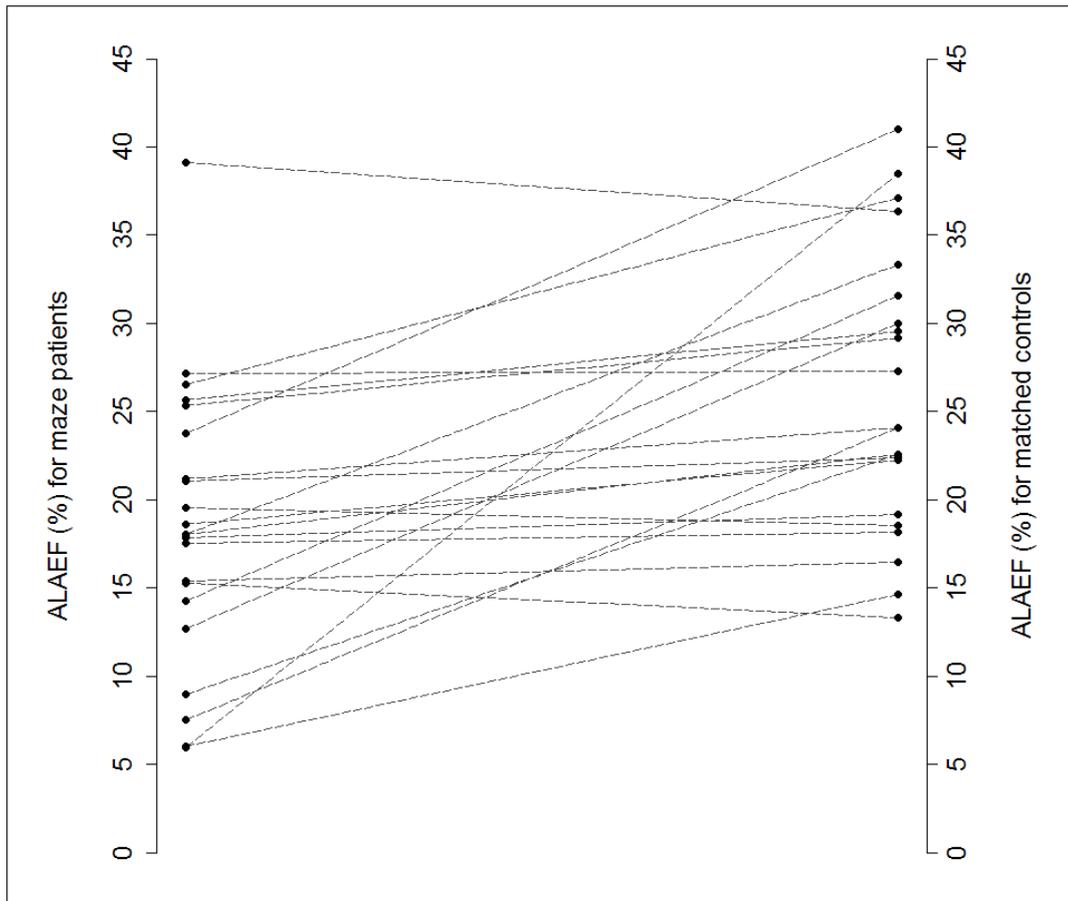
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**Figure 1**

**A.**

ALAEF measurements for individual patients undergoing the maze procedure and their matched controls



**B.**

Forest plots showing estimated treatment effects (maze-control) and 95% confidence intervals for secondary outcomes

