The Late Electrophysiological Consequences Of Posterior Wall Isolation In Patients With Atrial Fibrillation

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Abstract

Introduction

There are many different lesion sets that are used for the surgical ablation of atrial fibrillation (AF). One such pattern is the ‘box set’, a single ring of scar delivered anterior to the pulmonary veins, which aims to electrically isolate the posterior wall from the rest of the heart. However it remains unclear whether posterior wall isolation (PWI) is an effective lesion set for maintenance of sinus rhythm and whether it is necessary to achieve complete bidirectional block. We investigated the long-term integrity of the ‘box set’ lesion created during surgical AF ablation by epicardial High Intensity Focused Ultrasound (HIFU). All patients had documented persistent or recurrent paroxysmal AF prior to surgery. We correlated this with subsequent success or failure in the abolition of atrial fibrillation.

Methods

With regional ethical and R&D approval, 101 patients who had previously undergone HIFU AF ablation greater than 4 years ago were screened for inclusion in the study. 17 patients agreed to late electrophysiological study: 11 with on-going AF and 6 in normal sinus rhythm. Clinical history and 7-day holters were used to define the NSR group. We performed a diagnostic EP study using a transseptal approach in fully anticoagulated patients (INR>2.0 and ACT maintained at >300s). A catheter was placed in the coronary sinus (CS) and a circular multipolar mapping catheter was used to map the left atrium and pulmonary veins. Patients in atrial fibrillation were cardioverted. We recorded whether posterior wall (PW) and pulmonary vein (PV) isolation had been achieved at the surgical procedure. In selected cases we recorded a voltage map using either CARTO (Biosense-Webster) or NavX (St Jude Medical) to identify areas of ablation scar.

Results

All 11 patients with AF had absence of PW+PV isolation with fractionated electrograms recorded across the PW. In the 6 patients with long-term freedom from AF, PW+PV isolation was confirmed in 4 (67%) and in 1 there was prolonged conduction across the box-set lesion with CS to PW activation time of around 200ms versus 45ms from mid-CS to left atrial appendage. Of the 4 patients with confirmed PW+PV isolation, 1 had dissociated spontaneous atrial potentials within the box set area and the other 3 had electrical silence throughout with inability to capture the posterior wall pacing at 10mA at multiple sites.

Conclusions

There appears to be a clear correlation between the successful restoration of long-term sinus rhythm and isolation / delayed conduction from the pulmonary veins and posterior wall. Given the advent of hybrid atrial fibrillation ablation techniques designed to deliver this lesion set, these findings are timely and highly relevant.

Introduction

The mechanism by which atrial fibrillation (AF) is initiated and sustained is complex and incompletely understood. It is clear that the majority of triggers for AF reside within the pulmonary veins (PV) but there are also influential non-pulmonary areas. These triggers are especially important for paroxysmal AF (PAF). For persistent forms of AF, a number of different mechanistic theories have been proposed involving rotors, complex fractionated atrial electrograms (CFAE) and multiple wavelets. Regardless of the mechanism underlying persistent AF (PsAF), evidence suggests that the bulk of the substrate for these mechanisms resides in the posterior wall (PW) of the left atrium (LA).1,2 Consistent with these different theories, a wide variety of different ablation techniques are currently being practiced across international centres. The majority of operators rely on a stepwise approach involving pulmonary vein isolation (PVI) followed by further substrate modification. These techniques are sometimes personalised to the individual case. Alternative ablation techniques rely on the identification and successful ablation of CFAEs, ganglionic plexi (GP), or more novel

Key Words:

Atrial Fibrillation, Surgical Ablation, High Intensity Focused Ultrasound, Persistent Atrial Fibrillation, Electrophysiology, Transseptal.
techniques involved the mapping and ablation of putative rotors. These techniques are all highly complex and rely on the skill of the operator to be able to identify all appropriate electrophysiological landmarks.

An entirely different strategy is to accept the assumption that the bulk of the substrate on which AF propagates resides within the posterior left atrium. Several groups are investigating the applicability of an empirical ablation strategy that results in posterior wall isolation. There is evidence to suggest that such an end-point may be sufficient in maintaining sinus rhythm in the majority of patients without the complexities involved in other approaches. Such techniques are already being utilised; one such involves a single ring of ablation scar being delivered anterior to the pulmonary veins with the intention of electrically isolating this entire posterior wall/pulmonary vein area. This is commonly referred to as the ‘box-set’ and may be delivered epicardially and/or endocardially.

It is unclear whether freedom from AF in patients who have undergone AF ablation using the box-set pattern results from extensive debulking of the LA muscle; GP alteration / destruction; pulmonary vein isolation or from isolation of the entire PW and PV substrate.

We wished to determine whether the success of the box-set pattern was due to complete electrical isolation of the PW. One possible model to investigate this was to study the group of patients who had previously undergone AF ablation using epicardial box-set lesions delivered using High Intensity Focussed Ultrasound (HIFU). The aim of this study was to characterise the very-late electrical properties of patients in whom the ablation procedure had been a success and compare them to others with on-going AF. We sought to recruit 10 patients from each group for a diagnostic transseptal electrophysiological study. This study was performed in accordance with the Declaration of Helsinki and with the approval of the institutional research and development department and of the West of Scotland Regional Ethics Committee. This permission extended to

Figure 1: Flow diagram illustrating the recruitment process.

Figure 2: (A) With the circular mapping catheter (PV) placed flat on the posterior wall, an isolated premature atrial beat is seen showing electrical isolation of this region during sinus rhythm. (B) Circular mapping catheter (PV) in the right upper pulmonary vein and capture pacing from the coronary sinus, there is no evidence of conduction into the vein. Also seen is a non-conducted pulmonary vein potential (case 9).

Figure 3: In a patient with preoperative paroxysmal AF and freedom from any recurrent atrial arrhythmia. Pacing from CS distal demonstrates intact conduction between the coronary sinus and the posterior wall with a conduction time of 78ms (case 5).

Methods

The Patients
From the original cohort of 110, 101 patients who had previously undergone HIFU AF ablation greater than 4 years ago were screened for inclusion in the study. 17 patients agreed to late electrophysiological study, Electrophysiological data from a further 2 patients who were previously ablated for on-going AF were also included. The studies were conducted at a mean of 65 months post-surgical HIFU isolation procedure. 14 underwent HIFU concomitantly with cardiac surgery, 3 had surgical AF ablation for lone AF and have previously been described in full.

Recruitment
At routine follow up, patients were introduced to the study and invited to participate (EJD). Those who expressed an interest were given a patient information sheet (PIS) and were contacted by telephone to confirm willingness to participate 2-days later. Normal sinus rhythm (NSR) was confirmed by the absence of symptoms, a 7-day full disclosure ambulatory electrocardiogram (ECG) confirming absence of AF and a 12-lead ECG at time of recruitment. The AF group contained those patients having any documented recurrence of AF following a 3-month blanking-period post ablation. Patients with recurrences solely of atrial flutter (AFl) were included in the NSR group but described separately. The patient demographics (as at time of epicardial AF ablation) are shown in Table 1.

The Diagnostic Study
A transseptal electrophysiological study was performed in all patients. Patients with a CHA2DS2-VASc of >1 and on-going atrial arrhythmias were anticoagulated with either warfarin (target INR 2.0-3.0) or dabigatran (110mg bd) for a minimum of 3 weeks prior to the study. All diagnostic studies were performed as a day-case using IV sedation (diazemuls and diamorphine titrated to response). Access was gained via the right femoral and subclavian/internal jugular vein. A decapolar catheter was placed in the coronary sinus (CS) and a quadripoal catheter in the right ventricle. Using a standard Brock-enbrough needle, a transseptal puncture was performed to allow passage of a steerable sheath - Channel, (BARD Electrophysiology) or Agilis® (St. Jude Medical) into the LA. Punctures was facilitated using a combination of contrast injection and pressure monitoring. IV heparin was administered to maintain the activated clotting time (ACT) at >300s for the duration of LA instrumentation. Pulmonary venography was performed for all PVs. A circular mapping catheter (Expandable Lasso or AFocus II, St. Jude Medical) was sequentially placed in all four PVs and flat on the PW. For patients in sinus rhythm at the time of the study, we tested for exit and entry block and recorded the conduction times between CS and PV. Those in AF at the time of the study were cardioverted (200J biphasic AP pad position) on a maximum of two occasions to allow for conduction to be assessed.

In selected cases of apparent PW isolation (defined as the absence of electrical activity, or evidence of spontaneous isolated atrial complexes), we tested for pace/detect within the PW. We passed a second catheter alongside the steerable sheath and used it alongside the mapping catheter to test for conduction contained within the isolated posterior wall.

Additional Ablation
In 7 patients with symptomatic drug refractory atrial arrhythmia, further ablation was performed, 5 cases for AF and 2 for AFl. A voltage map was produced using either CARTO (Biosense- Webster)
or NavX (St Jude Medical). Using a contact force ablation catheter, additional lesions were delivered either around the pulmonary vein ostia and/or to complete the existing roof and floor lines created by the HIFU procedure. The ablation goal was validated PWI in the cases of AF recurrence.

Results

The Patients

Of the original 110 patients who underwent surgical AF ablation, 101 were still alive at screening follow-up. Nine had died in the interval: 4 from post-operative complications unrelated to the AF ablation procedure or use of the Epicore device, two died from malignant disease, one suffered an embolic stroke, one a traumatic intracerebral bleed and one from end-stage heart failure.

Free From Atrial Fibrillation – NSR

Of the six patients who had an absence of AF, only 3 were completely free from any atrial arrhythmia recurrence the remaining 3 had experienced episodes of documented atrial flutter. Of the 3 patients where no atrial arrhythmia had occurred since surgical ablation, two had originally experienced PsAF pre-operatively (cases 6&9) and the other infrequent PAF pre-operatively only (case 5).

In cases 6&9, there was no conduction into or out of the PW during capture pacing from the CS together with isolated atrial potentials throughout the pulmonary veins and the posterior wall (Figure 2).

Free From Atrial Fibrillation – Atrial Flutter

Of the 6 patients with freedom from AF, 3 have experienced documented recurrences of atypical paroxysmal atrial flutter. In 2 cases, the PW was found to be silent with intact block throughout the veins and posterior LA. The other one case had very delayed conduction between the PW and the CS (case 4). The area of conduction gap is identified near the RUPV (Figure 4).

In one of the cases of post-operative AFl, the patients remained symptomatic and we proceeded on to ablate a peri-mitral flutter circuit (case 16).

Atrial Fibrillation

We studied a total of eleven participants with AF following the ablation procedure.

In all instances, persistent atrial electrograms were present throughout the PW and pulmonary veins, ranging from grade 1 to 5 in degree of fractionation. Cardiovension was performed to restore NSR and allow for the conduction between the CS and the PW/PV to be assessed; rapid reversion back to AF limited assessment in 7 cases.

Where tested, the conduction times between the PW/PVs and the CS are shown in Table 2. There were no instances of conduction...
Example 1 (case 13).
During instrumentation of the LA, patient 13 developed AF with organised (grade 5) fractionated electrograms throughout the PW. Voltage mapping showed established transmural scar line along the left atrial roof and floor. We proceeded to isolate the right PV pair using a standard wide area circumferential ablation (WACA) approach resulting in rhythm organization (cycle length of 250ms). Following completion of the left PV-encircling lesion set continuous with the roof-line, spontaneous resolution of SR occurred (Figure 8A). The PW is shown to contain a flutter circuit while surface ECGs show NSR (Figure 8B). This PW block persisted during the administration of 15mg of adenosine, sufficient to caused AV block.

Example 2 (case 7).
DC cardioversion resulted in non-sustained sinus rhythm; no conduction intervals were obtained during this short window but the circular mapping catheter showed fractionated signals (Figure 9A). A voltage map was constructed using CARTO 3 (Figure 9B); established transmural scar is evident along the floor of the left atrium but was incomplete on the roof and anterior to both pairs of pulmonary veins. Bilateral PV-encircling lesions were delivered together with the completion of a roof-line (Figure 9C) resulting in spontaneous return of sinus rhythm (Figure 9D).

Outcome From Additional Ablation Cases
All cases who had additional ablation performed for post-operative AF are now in sinus rhythm (one on a class 3 antiarrhythmic) except one (case 17) in whom the posterior wall was not successfully isolated due to poorly tolerating the catheter ablation under sedation.

Discussion
Although several groups have reported on the invasive electrophysiological findings following ablation, to the best of our knowledge, this is the first study aiming to investigate the association between PW isolation and long-term (>4 years) freedom from AF. A summary of the previous knowledge gained from such studies is provided in Table 3, most of which is obtained from studies involving redo procedures. As such, there is a skew against reporting what constitutes a successful outcome.

Previous Studies On The Box Set.
Possibly the first group to attempt a box pattern using catheters was Ernst et al. in 1999. The limited technology available at that time resulted in failure to achieve PWI in all of their cases. Todd et al. describes the initial 2003 experience following the combined open-chest surgical and catheter cryoablation box pattern for AF. At 6-days post procedure, all cases had persistently intact posterior wall isolation, determined through epicardial wires. Late recurrent of atrial arrhythmias in one patient resulted in EP restudy - a gap was found in the posterior wall isolation, closure of which restored sinus rhythm. Todd demonstrated that the isolated PW was able to sustain atrial arrhythmia independent of the remaining atria; this finding has been replicated in our study.

Lim et al. provides a comprehensive assessment of the mechanisms of arrhythmia recurrence following single ring ablation delivered by catheter. In 100 patients with an end-point of validated PWI, 69% experienced recurrence of an atrial arrhythmia (35% AF and 34% flutter). In those patients that underwent a redo procedure for recurrent AF, all had gaps in the ablation ring with conduction in and out of this region. In six of the patients, a flutter circuit was established through two gaps in the ring. Four patients had atrial flutter without
Pre-op = Preoperative; AF = Atrial Fibrillation; LSP = Longstanding Persistent Atrial Fibrillation; PsAF = Persistent Atrial Fibrillation; AAD = Antiarrhythmic drug; LA = Left Atrial; AP = Anterioposterior; cm = centimetre; EF = Ejection Fraction; DM = Diabetes Mellitus; HTN = Hypertension; CVE = Cerebrovascular Event; BMI = Body Mass Index; CAD = Coronary Artery Disease; CTI = Concomitant Isthmus Ablation; DCCV = DC Cardioversion

Table 1: Study participant demographics and operative data

<table>
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<th>Participant Number</th>
<th>Pre-op AF category</th>
<th>Pre-op AF duration (months)</th>
<th>Pre-op AAD failed</th>
<th>Operation</th>
<th>Op to EP duration (months)</th>
<th>LA size (AP)/(cm)</th>
<th>EF (%)</th>
<th>NTH</th>
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Table 2: Conduction times expressed as exit and entry between the pulmonary veins / posterior wall and coronary sinus

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<th>RUPV</th>
<th>RLPV</th>
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Evidence of atrial fibrillation and were found to have intact isolation of the posterior wall. The authors conclude that “electrically isolating the posterior LA may thus prevent the initiation and perpetuation of AF”. This agrees with the findings in our patients to mean follow-up of 63-months.

Tamborero et al.13 randomised patients undergoing AF ablation to receive PV-encircling lesions and roof-line alone or supplemented with a floor line to complete PWI. A redo procedure was performed.
in 20% of their patients and in 67% of initial PWI group, conduction across the roof-line was seen, suggesting that failure of the PWI model was in part due to reconnection. They found no advantage to PWI attempted through the addition of a floor line compared to PV-encircling lesions and roof-line only. Sanders et al. provide a rare example of AF recurrence in one of 27 patients following box isolation in whom the PWI remained intact at restudy.14 That index patient required additional “substrate modification” to restore sinus rhythm.

Kumagai et al.15 studied a purely paroxysmal group who, at mean follow-up of 13 months following catheter box-set ablation, showed a 95% rate of freedom from AF. Six of these patients required a redo procedure, three for recurrences of AF and the others from organised/focal arrhythmia. In all cases of recurrence, gaps in the lesions lines were seen. In none of these cases of recurrence was the PW isolated.

A recent resurgence in interest in the box set pattern has come about as a result of the development of hybrid AF ablation techniques, combining epicardial ablation using a variety of platforms with catheter-based endocardial ablation. This has resulted in reported outcomes in the region of 90%. These studies have the potential to offer some further insight into the electrical consequences of a single ring approach.5 To date, little has been published on the association between on-going AF prior to the second (catheter) stage of the hybrid pathway and the subsequent EP findings. As technology matures, this is a key opportunity to gaining a greater appreciation into the mechanisms of PsAF.

Comments On The Box Set.
While it is clear that many features of the posterior LA wall mark it out as a key area of substrate for the propagation and perpetuation of AF, other areas of the atria may also be involved. Such sites as the superior vena cava, LA appendage base, interatrial septum and the anterior LA wall have all been implicated in AF propagation to a lesser extent.16 In addition, CFAEs,17 rotors and right atrial autonomic ganglia18 have also been shown to reside in the non-isolated area.

Oesophageal injury and fistulae formation is a rare but potentially
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