Acute Rate of Transmural Lesions Induced by High-intensity Focused Ultrasounds During Peri-operative Left Atrial Ablation for Atrial Fibrillation

AMIN BENNADJI, MD, BERTRAND MARCHEIX, MD, CHRISTOPHE CRON, MD, ETIENNE GRUNENWALD, MD, ALEXANDRE DUPARC, MD, PIERRE MONDOLY, MD, ANNE ROLLIN, MD, DANIEL ROUX, MD, CAMILLE DAMBRIN, MD, BERTRAND LEOBON, MD, YVES GLOCK, MD, MARC DELAY, MD, ROMAIN NOBLEMAIRE, MD and PHILIPPE MAURY, MD

University Hospital Rangueil, Department of Cardiology, Toulouse, France

ABSTRACT. The high-intensity focused ultrasound (HIFU) based Epicor system is used for creating a linear left atrial lesion encircling both left atrial posterior wall and pulmonary veins (box lesion) for providing a long-term cure in patients with atrial fibrillation (AF) undergoing heart surgery. Whether acute complete disconnection of the box lesion is achieved by application of HIFU is poorly known. Thirteen patients (9 men, median 73 years) with AF undergoing heart surgery (8 aortic valve replacements, 4 mitral valve surgery, and 1 coronary by-pass) were concomitantly treated with HIFU. AF was paroxysmal in eight patients and persistent in five. Entrance and exit blocks into/from the box lesion were assessed using bipolar electrophysiological catheter during sinus rhythm after completion of the ablation process. Entrance block was absent in nine patients, undetermined in one and present in three. Exit block was lacking in nine patients and present in four. Entrance and exit block were both present in only two patients, while they were both lacking in eight patients. At 1 year, nine out of 12 patients were in sinus rhythm (8 on antiarrhythmic drugs) while AF was documented in three out of 12 (2 off drugs). Acute complete block of the box lesion was lacking in the vast majority of patients despite completion of the energy deliverance according to the automated ablation process. However, this did not translate into a high long-term recurrence rate. Whether block later happens, or whether supplementary applications would increase the electrophysiological and clinical success rate is unknown.

KEYWORDS. ablation, atrial fibrillation, high-intensity focused ultrasound, pulmonary vein isolation.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia carrying a substantial morbidity and mortality and is especially frequent in patients undergoing heart surgery. Surgical ablation of AF has become the standard of care in patients undergoing concomitant cardiac surgical intervention, as implemented in the latest guidelines for curative treatment of AF.1 Pulmonary vein isolation (PVI) has evolved as the cornerstone interventional treatment option for patients with AF, either percutaneously or surgically, using a variety of energy sources including radiofrequency, cryo-therapy, laser, microwave, and recently high-intensity focused ultrasound (HIFU).2,3 The rationale behind all techniques and devices is to provide complete bidirectional electrical conduction block by achieving permanent transmural tissue lesions.
which are known to be mandatory to the clinical success of AF ablation even if sometimes difficult to obtain. Initially the “cut-and-sew” technique usually led to complete and definitive linear lesions, as for example in the Maze operation or for PVIs with excellent long-term results. Incomplete lesions after non-cut-and-sew Maze operation were associated with PV reconnection and recurrence of atrial arrhythmias. Optimally, the completeness of linear lesions should be confirmed during the initial surgical procedure using electrophysiological endpoints in order to minimize the recurrence rate of atrial tachycardia, and intraoperative verification of conduction block is mandatory to assure the transmurality and contiguity of the lesions created by the ablation devices.

The Epicor™ system, based on HIFU energy, is used for creating a wide circumferential linear left atrial lesion encircling both left atrial posterior wall and PV, i.e. the “box lesion,” and is expected to provide long-term cure in patients with AF undergoing heart surgery. Limited experimental and clinical data show that HIFU may lead to transmural lesions, while variable long-term clinical results have been reported.

Whether acute complete disconnection of the box lesion is achieved by application of HIFU and if this translates in long-term maintenance of sinus rhythm is poorly known: in a limited group of 10 patients with AF undergoing mitral valve surgery and HIFU ablation, “exit block” from the PV to the atrium was lacking in any patient after surgery and at 3 weeks, contrasting with the lack of AF recurrence at 12 months.

The aim of this study was to check the completeness of “transmural lesions” after HIFU ablation using solid electrophysiological endpoint during surgery, both entrance and exit block, and to correlate this with the recurrences of arrhythmias.

Materials and Methods

We prospectively studied 13 patients with AF undergoing perioperative HIFU ablation with Epicor™ (St-Jude Medical, Sunnyvale, CA) during heart surgery. Each patient gave informed written consent. Briefly, The Epicor™ system is designed to deliver HIFU energy on the beating heart. It consists of an ablation control system generator, which is a microprocessor-based unit that provides acoustic power to ultrasound transducers. The UltraCinch device is an array of multiple ultrasound transducers that is used to produce a continuous circumferential left atrial box lesion isolating the PVs by encompassing the whole left atrial posterior wall. According to this scheme, complete transmural lesions would lead to a complete isolation of the box lesion. Although the system is positioned epicardially in front of the four PV ostias, ablation starts at the endocardial side by focused energy delivery. The total ablation time to create a left atrial box lesion from the endocardium back up to the epicardium is approximately 10 min. The ablation cycle progressed automatically, guided by the ablation control system to generate three sequential stages of ablation. The ablation process begins with the deep ablation stage, followed by the intermediate stage, and terminates by the surface stage to eliminate any residual gap within the epicardium.

The pericardium was opened, and the pericardial reflections around both the superior and inferior vena cava were dissected. A special designed introducer sizer was used to measure the circumference of the left atrium to select the proper size of the UltraCinch LP device. After choosing the appropriate size, the Ultracinch LP device was deployed in order to isolate the posterior LA and all four PV ostias. No additional ablation line was performed in any patient. Left atrial appendage resection was performed in only one case. Control of complete isolation of the box lesion was studied using bipolar pacing and detection as performed into the box lesion using a standard electrophysiological electrode catheter (Daig Response, St Jude Medical, Sunnyvale, CA) connected to a real-time telemetry/stimulator used for testing during pacemaker implantations (Medtronic CareLink® programmer). Pacing and sensing maneuvers were performed just after completion of the ablation process on the beating heart prior to initiation of extracorporeal circulation. Sinus rhythm was present or obtained using internal cardioversion in each patient before the ablation process. Complete linear lesions were defined by the association of both entrance and exit block in/from the box lesion: 1. entrance block was defined by the lack of recorded potential into the box lesion (or dissociated slow activity) during sinus rhythm; 2. exit block was defined by the lack of capture of the remaining atrium during pacing into the box lesion at 120 bpm at the maximal output (10 V). Otherwise the lesions were defined as incomplete. Oral anticoagulation was maintained at discharge in all but one patient. Amiodarone was prescribed during the first 6 months in 10 patients and sotalol in one patient, while two patients were discharged free from any antiarrhythmic drug. Afterward, the antiarrhythmic therapy was left at the physicians’ discretion. Patients were monitored at 12 months with 12-lead ECG and 24-h ambulatory ECG monitoring without any blanking period.

Statistical analysis

Continuous data are expressed as median (range). Categorical variables were compared using the Fischer exact test, while numerical values were compared with the non-parametric Mann–Whitney test. Analysis and calculations were performed using the StatView™ program (Abacus Concepts, Inc. Berkeley, CA 1992–1996, version 5.0). A p value < 0.05 was considered statistically significant for each analysis.

Results

Patients’ characteristics

AF ablation with HIFU was performed in 13 patients (9 men) with a median age of 73 years (54–81 years)
One patient was lost to follow up. There was no short-term success rate according to the presence of acute transmural lesions because roof-dependent re-entry could not exist in the case of complete box lesion (only exit block in this patient at the time of surgery). All these three patients remain in sinus rhythm at 12 months. Nine patients were on antiarrhythmic drug at 12 months (7 on amiodarone, 2 on sotalol). At 12 months, persistent AF was present in two patients and paroxysmal AF recurred in one, while 9 of 12 patients were in sinus rhythm, leading to a 75% success rate (58% if the 2 patients undergoing percutaneous ablation during follow-up were considered as failures of the surgical HIFU ablation). Two of the three patients with recurrent AF were off drugs, while eight of the nine patients in sinus rhythm were on antiarrhythmic drugs (6 on amiodarone, 2 on sotalol). Four of five patients (80%) with acute uni- or bidirectional block were in sinus rhythm versus five of seven patients (71%) without any acute conduction block (p=0.7). For the two patients with both entrance/exit block, only one was found in sinus rhythm.

Discussion

In this short series of 13 patients undergoing left atrial ablation during heart surgery, the delivery of HIFU was not associated with acute transmural lesions as demonstrated by the lack of entrance/exit block from the box lesion in the vast majority of cases. Furthermore, this did not translate into a high long-term recurrence rate since 58% of patients were in sinus rhythm at 1 year (75% after additional percutaneous ablation during follow-up). This low rate of transmural lesions is somewhat disappointing regarding the presented technology, because the duration of HIFU application is automatically determined by the device in order to achieve transmural lesions. Even if acute transmural lesions after ultrasound ablated myocardium have been experimentally reported or speculated, a recent work however proved that conduction block was achieved in atrial tissues in only 17% of cases with a single ablation line, which furthermore resumed over the following 10 min. This study identified three potential mechanisms responsible for the failure of HIFU ablation in cardiac tissues: acoustic radiation force, acoustic cavitation and inconsistent thermal deposition, each increasing the risk of lesion discontinuity. Additional attempts to understand why transmural lesions are not achieved should be made. Our results prove in fact that acute transmural lesions are rarely achieved in clinical practice. Aside from the three suspected mechanisms enounced above, a poor contact between some of the left atrial surface and the implantation in any patient during the follow-up. One patient underwent DC shock for AF recurrence at 6 months and two patients underwent percutaneous ablation procedures for AF and perimital left atrial flutter (at 4 and 5 months): the four PVs were found connected in the first patient (no entrance or exit block in this patient at the time of surgery) while the other one presented with roof dependent macro atria re-entry: although pulmonary veins had not been checked at this occasion, this also indicates that there were no transmural lesions because roof-dependent re-entry could not exist in the case of complete box lesion (only exit block in this patient at the time of surgery). All these three patients remain in sinus rhythm at 12 months.

Postoperative management

At discharge, five patients were in sinus rhythm and recurring AF was documented in eight patients (38% short-term success rate). No atrial tachycardia was observed in any patient. There was no significant difference in short-term success rate according to the presence of acute complete transmural lesion: three of five patients with uni/bidirectional block were in sinus rhythm (60%) versus two of eight without any block (25%) (p=0.2). For the two patients with both entrance/exit block, only one was found in sinus rhythm.

Follow-up

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UltraCinch because of too large device or too short device (leading to plicatures) may be the reason of such results. We also suspected that the system itself is imperfect because of the so-called “automated” process and of the geometry of the device allowing some gaps because of non-closed contact in some part of the atrium and that repositioning the device may create more complete lesions.

The transmurality of ablation lesions has been clearly correlated to the recurrences of arrhythmias. Recurrence of atrial arrhythmias in eight patients after non-“cut-and-sew” maze operation has been shown to be associated with PV reconnection at electrophysiological study in seven of them. Using epicardial electrodes after cryo-isolation of the four PV and posterior wall, Todd et al.20

Figure 1: (a) Example of complete entrance block into the box lesion. A slow dissociated local rhythm is present in the box lesion as sensed by the real time telemetry/stimulator (middle tracing = event markers) or present on local recording (lower tracing = EGM) (*) during regular sinus rhythm seen on the ECG strip (upper tracing). (b) Example of lack of entrance block. Each P wave (ECG strip, upper tracing) is conducted with delay into the box lesion (AS on middle tracing = event markers, * on lower tracing = EGM). Of note is that these events are not QRS far-fields since they occur before QRS onset (more easily seen on the second beat, which is a premature atrial event conducted to the box lesion).
confirmed postoperatively the successful isolation in 13 of 14 patients. The only patient with recurring AF was found to have gaps in the ablation lines. Gaita et al. \(^{21}\) validated the completeness of various left atrial linear cryoablations using an electrophysiological study 3 months after surgery: surgical intent was fulfilled in only 65% of cases and this was correlated with a higher long-term success rate. Using epicardial radio-frequency ablation during open chest surgery or cardioscopic procedures, Gersak et al. \(^{22}\) acutely tested the exit block using bipolar pacing within the PV antrum in 62 patients: exit block was present in 90% and correlated with a higher long-term success rate. After HIFU ablation, all studied patients with recurring AF were shown to have incomplete box lesions. \(^{18}\)

Using HIFU, the presence of PV disconnection was only once evaluated: Pozzoli et al. \(^{17}\) using epicardial electrodes in 10 patients demonstrated that exit block from the box lesion was never obtained either acutely or at 3 weeks. This contrasted with the good clinical success rate, since all patients were found in sinus rhythm at 1 year, although half were on antiarrhythmic drugs. \(^{17}\) This is in accordance with our results.

This discrepancy between the poor acute electrophysiological success and the rather good long-term clinical success was also found in our study and deserves further comments.

First, most patients in this study were still on antiarrhythmic drugs at 1-year follow-up and two has undergone additional percutaneous ablation, thus the true success rate is probably lower than reported and thus potentially more in accordance to the lack of transmural lesions.

Second, the evolution of HIFU-based lesions is said to be different from those observed with radiofrequency for example, where recovery of conduction happens in 15% of patients at 3 weeks. \(^{23}\) Even if tissue samples from autopsied human hearts have shown transmural chronic HIFU-induced lesions, according to some authors, it could be hypothesized that HIFU lesions may take time to lead to definitive scarring because cell death with this energy source may differ from that of radio-frequency and may not be instantaneous. \(^{16}\) This phenomenon is believed to occur in approximately 3 months. \(^{13}\) However to the best of our knowledge, this remains speculative, even if it has been reported that only subtle changes happen in acute lesions in rabbit muscle using HIFU, while variable amounts of scar and fat are found in the chronic phase. \(^{24}\) In humans, no disconnection was found either acutely or at 3 weeks in the study by Pozzoli et al., \(^{17}\) while data from unpublished work show that only a minority of patients will present with complete transmural lesions and box isolation when reinvestigated 6 months after the surgery whether they presented with recurrences or not. \(^{25}\) In our study, there was no sign of transmural lesion in the only two patients reinvestigated for recurring arrhythmias.
On the other hand, experimental examples of acute transmural lesions after ultrasound ablated myocardium have been reported, while Villamizar et al. have speculated that HIFU ablation may acutely achieve 100% transmurality in humans due to the thickness of the atrial wall, based on their experiments on calf hearts where acute transmural lesions were observed for left atrial thickness up to 6 mm. These findings argue against the hypothesis of a delayed completeness of the lesions. Proving that efficiency of HIFU is in fact delayed due to the possible evolution of lesions deserves further studies including control of disconnection at later phases. Finally, if achievement of acute complete lesions is believed to be mandatory, determination of entrance/exit block in clinical practice may allow delivery of additional HIFU energy in patients lacking complete block and possibly enhance the long term success rate of HIFU ablation. Further studies are needed to answer this issue.

Limitations

This is a short series of 13 patients, and our findings need to be confirmed in larger populations. Some loss of capture may have happened due to a high pacing threshold, but this could not explain the lack of electrical dissociation often seen during sensing maneuvers. We did not look at the lesions as present visually on the epicardial surface after the ablation. Checking the lesions would possibly help in locating the gaps and to further close them. We did not perform late electrophysiological studies in our patients. This would have demonstrated whether late build-up of incomplete lesions to transmural lesions would occur after HIFU. However, this was already partially reported by Pozzoli et al., showing the lack of exit block at 3 weeks and only a minority of patients will present with complete box isolation when reinvestigated 6 months after the surgery in an unpublished work. We did not check autonomic nervous damage as shown after extensive atrial surgery, which may have contributed to the better than expected long-term success rate. However such lesions are probably minimal without atrial incision. Finally, the largest proportion of patients were still on antiarrhythmic drugs at 12 months, and the methods used for determining the long-term success rate clearly lack sensitivity. However, most of the previous studies about surgical AF ablation share the same limitations.

References


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