Surgical treatment of atrial fibrillation using radiofrequency ablation
Khargi, K.

Citation for published version (APA):

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AF is associated with a 1.5 to 2.0 fold increase of mortality and a 2 to 5 fold increase for stroke in patients with a cardiovascular disease. AF is related to 15% of all strokes, which tend to be more fatal than the non-AF related strokes with a 30-day mortality of 25% versus 14% for the non-AF related strokes. Moreover, recurrences of strokes were more frequent and functional deficits were more likely to be severe in survivors. As a consequence, the health care costs will increase. Reports revealed that the medicare spending increased between 8.6% to 22.6% per year due to AF treatment. The estimated prevalence of AF, in the USA, is 2.3 million people. The projected number of patients, in 2050, will be 5.6 million (range 5.0- 6.3). So, the clinical importance of AF and the necessity to treat AF has gained wide spread recognition. The efficacy of the pharmacological therapy to convert AF into a stable SR is low. Even after electrical cardioversion (CV) with 100-200 Joule, the SR conversion rate was 86% after three days, 23% after 1 year and 16% after 2 years. In persistent AF the 4 year-arrhythmia free survival was less than 10% after single electrical CV without prophylactic drug therapy. If a second consecutive electrical CV was combined with medical therapy a SR conversion rate of 40% after 1 year and 33% after 2 year was anticipated. However all types of drug therapy are associated with pro-arrhythmic side effects, especially torsade des pointes adversely affecting the SR conversion rate. So, non-medical therapy modalities have emerged, such as “the cut and sew” Cox Maze III surgical procedure, which consists of a well-defined pattern of left and right atrial incisions in order to interrupt the multiple wavelet macro reentry circuits, eliminating AF. The reported SR conversion rate after the Cox-Maze III procedure is 97-99% and is therefore considered the golden standard. But, the complexity of the “cut and sew” Cox-Maze III technique is considered a drawback. Therefore, this procedure is not universally accepted as a standard practice in the surgical treatment of AF. As a consequence, alternative sources of energy (radiofrequency-, microwave-, cryoablation) have emerged to surgically treat AF. But the efficacy of the alternative energy sources is debated, because the creation of continuous linear transmural lesions, which act as an electrophysiological conduction block, is considered to be uncertain and inconsistent. This thesis describes our experience with the saline-irrigated, cooled- tip radiofrequency ablation (SICTRA) to treat AF.

Chapter 2
Surgical treatment of AF; a systematic review
In this review the efficacies of the alternative sources of energy (radiofrequency-microwave and cryoablation; group I) and the classical “cut and sew” Cox-Maze III (group II), which claims a 97-99% sinus rhythm (SR) success rate, were evaluated in the surgical treatment of atrial fibrillation (AF). A computerized search in the PubMed and Medline database was conducted. Only original, English written, clinical manuscripts on the surgical treatment of atrial fibrillation using an alternative source of energy or the classical “cut and sew” Cox-Maze III technique, citing the clinical outcome, including the postoperative sinus rhythm, were included. The data included in this review were the number and percentage of treated patients, gender distribution, the type of arrhythmia and surgery, postoperative morbidity, pacemaker implantation rate, 30-day mortality, survival- and sinus rhythm conversion
rates. Mean values for age, left atrial diameter, preoperative duration of AF and left ventricular ejection fraction were also recorded. Forty-eight studies were included comprising 3832 patients; 2279 in group I and 1553 in group II. The mean duration of AF, left atrial diameter and LVEF were 5.4 versus 5.5 years (p=0.90), 55.5 versus 57.8 millimeters (p=0.23) and 57 versus 58% (p=0.63). The postoperative SR rates for group I and II were 78.3% versus 84.9% (p=0.03). However, the “cut and sew” Cox-Maze III was conducted in younger patients (55.0 versus 61.2 years; p=0.005), more often to treat paroxysmal (22.9% versus 8.0%; p=0.05) and lone AF (19.3% versus 1.6%). Alternative sources of energy were predominantly used to treat permanent AF (92.0%), almost always as a concomitant surgical procedure (98.4%) and increasingly in combination with non-mitral valve surgery (18.5%). After correction for these variations, the postoperative SR conversion rates for group I and II did not differ significantly anymore (p=0.260). We could not identify any significant difference in the postoperative SR conversion rates between the classical “cut and sew” and the alternative sources of energy, which were used to treat atrial fibrillation.

Chapter 3
Considerations regarding energy sources to treat AF as a concomitant surgical procedure; techniques and pitfalls
Aim of the alternative source of energy is to create a conduction block without causing any tissue dehiscence. Therefore the energy application should induce a temperature between 50 and 95 degrees Celsius at a depth of 6-7 mm in the atrial wall. Irreversible cell damage occurs above 50 degrees Celsius, while tissue layer integrity is preserved beneath 95-100 Degrees Celsius.

Radiofrequency

Unipolar radiofrequency
This type of energy uses alternating electrical current of 100 KHz to 1 MHz to heat tissue, while avoiding excitation of muscles and nerves. The current is converted into thermal energy because of molecular agitation (Ohmic heating). Three types of radiofrequency application can be defined; irrigated RF, temperature controlled RF and dry RF (9).

- **Irrigated RF** creates deeper lesions than temperature RF and dry RF, because more energy can be delivered due to an improved current conductivity from the electrode to the tissue because of the irrigation.
- **Temperature controlled RF** is more effective than dry RF, but still less effective than cooled RF, because the delivered amount of energy is variable and restricted by the pre-determined temperature limit. Increase of the application time will moderately increase the size of the lesion. Temperature RF targets a temperature of 70-80 degrees Celsius. The power output is adjusted concordantly. Application time per lesion is 60 to 90 seconds. Various probes are available.
- **Dry RF** is not used intraoperatively.

Bipolar radiofrequency
The bipolar RF systems have electrodes in the jaws of an atraumatic clamp. The RF is delivered to a tissue sheet between the jaws of the clamp. Tissue conductance is monitored and will show a sudden drop, once a transmural lesion is formed.

Microwave
This energy type is a high frequency electromagnetic radiation causing oscillation of water molecules within the tissue. Electromagnetic energy is converted into kinetic energy (heat). Application is performed with an antenna mounted on a malleable shaft. As with RF, the size and depth of the produced atrial lesion is determined by the application time and output power. Although energy distribution along the
antenna probe is unequal, an effective lesion along the entire antenna can be created in approximately 25 seconds.

Cryoablation
In contrast to RF an MW, cryoablation is a hypothermic type of energy. The tip of the cryoprobe is rapidly cooled to -50 up to -90°degrees Celsius by the release and expansion of compressed nitrogen or argon gas. The tip of the probe freezes to tissue during application. Cell death occurs at -40 to -60°C. Application time per lesion is 2 to 5 minutes. Multiple applications, however, are sometimes necessary to increase the depth of the ablation lesion. Therefore this technique can be time consuming. The rigidity of the probes is a disadvantage, but more malleable probes are being developed. Cryothermal tissue injury preserves the tissue architecture and causes minimal thrombus formation. The chronic scar is made of dense fibrotic tissue that has no tendency to rupture or dilate (12).

Ultrasound
This type of energy is delivered with an ultrasonic coagulator, causing mechanical disruption of the molecular bonds.

Laser
This is a hyperthermic type of energy, which still is experimental.

SECTION II: SALINE IRRIGATED COLED TIP RADIOFREQUENCY ABLATION

Chapter 4
The saline irrigated cooled tip radiofrequency ablation was an effective technique to perform the maze procedure
Thirty patients with chronic AF and mitral valve disease were consecutively randomized to have mitral valve surgery either with a Maze procedure (group A) or without (group B). Intra-atrial linear lesions were made with an SICTRA catheter (20-32 Watt; 200-320 ml/hour saline). An echocardiography and 24-hour electrocardiogram were obtained 12 months postoperatively. The cumulative frequencies of SR in group A and B were 0.80 and 0.27 (p<0.01). Restored biatrial contraction was present in 66.7% (6/9) of the group A patients in SR. One Pt of each group received a permanent pacemaker because of a bradycardia. A fatal renal bleeding and mediastinitis occurred in 2 group A pts, 6 weeks postoperatively. One group A patient suffered from a sudden cardiac death at home, 4 months after operation. One Pt of each group had a lethal respiratory failure, 7 respectively 10 months after operation. Survival after 12 months for group A and B was 73% and 93% (p=0.131). The SICTRA appeared to be an effective technique to perform the Maze procedure.

Chapter 5
Irrigated radiofrequency ablation is a safe and effective technique to treat chronic AF
The safety of intraoperative non-irrigated--temperature- controlled radiofrequency ablation, to treat AF, is a matter of debate, because esophageal- and circumflex artery injuries have been reported. This study evaluates a different operative technique using saline-irrigated-cooled-tip radiofrequency ablation to treat AF. Between 1997- 2002, 124 concomitant anti-arrhythmic procedures, using irrigated-cooled-tip radiofrequency ablation (20-32 Watt and 200-320 ml/hour saline irrigation speed) were performed; 113 to treat chronic AF (> 6 months) and 11 to cure paroxysmal AF. Type of procedures were 28 MVP-, 42 MVR-, 17 AVR- and 6 double valves with or without CABG, 1 ASD closure and 30 solitary CABG were performed. The mean (SD) left atrial diameter, preoperative duration of AF, aortic cross clamp
time were 50.5 mm (9.8), 57 months (64) and 99 minutes (21). Thirty-day mortality was 4.8% (6/124; euroscore 17, 11, 8, 8, 6, 5). The cause of death was a cerebral stroke, an atrial-ventricular dehiscence, a cardiac failure and low cardiac output (n=3). Autopsies did not reveal any esophageal-, pulmonary orifice-, or circumflex artery injuries. No ablation related bleeding was observed. Mean follow up (SD) is 19.7 months (14.4). Fourteen patients died during follow-up; cerebral stroke (1), coumadine related bleedings (2), COPD (4), cardiac failure (1), mediastinitis (2), sudden cardiac death (2), endocarditis (1), unknown (1). The cumulative postoperative SR at 6 and 12 months was 60% and 70%. The cumulative survival at 1 and 2 years was 86% and 83%. Irrigated radiofrequency ablation was effective. It was not associated with procedural complications, in our series.

Chapter 6
Left atrial versus biatrial Maze surgery using intraoperatively cooled-tip radiofrequency ablation in patients undergoing open heart surgery; safety and efficacy
Is a left atrial only Maze surgery encircling each of the pulmonary vein foci using cooled-tip radiofrequency ablation as effective as a biatrial approach? Prospective, non-randomized analysis of patients with chronic AF undergoing open heart surgery adding a Maze surgery using intraoperatively cooled-tip radiofrequency ablation either in the left atrium alone (group A) or in both atria (group B). Follow-up included ECG, holter-ECG and Doppler echocardiography. Patients in group A (n = 21) and group B (n = 49) did not differ in regard to baseline patient characteristics. Concomitant open heart surgical procedure was MVR (3 versus 25), MVP (0 versus 2), MVR and AVR (1 versus 1), AVR (4 versus 6) and CABG (13 versus 15). Follow-up ranked from 1 to 50 months postoperatively. Overall cumulative rates of SR were 0.816 in group A and 0.745 in group B without a statistically significant difference (p=0.571). Biatrial contraction documented in transthoracic Doppler echocardiography was revealed in 92.3% of patients in SR in group A and 79.2% in group B. Cumulative survival was 90.5% in group A and 77.9% in group B (p = 0.880). The addition of a left or biatrial Maze surgery using intraoperative cooled tip radiofrequency ablation can safely be combined with an open heart surgical procedure. In our small series of patients a left atrial Maze surgery is as effective as a biatrial procedure and restores SR in 82% of patients with a biatrial contraction in 92% of these patients.

SECTION III; PATIENTS' INDICATION AND SELECTION

Chapter 7
Concomitant anti-arrhythmic procedures to treat permanent AF in CABG and AVR patients are as effective as in mitral valve patients
Concomitant anti-arrhythmic procedures, to treat permanent AF, are not routinely performed in non-mitral valve surgery (e.g. CABG and AVR). This study evaluated the SR conversion rate of a concomitant anti-arrhythmia procedure in non-mitral valve surgery compared to mitral valve surgery. Between 1997 and 2002, 128 patients with a documented permanent AF had a concomitant anti-arrhythmic procedure using unipolar endocardial radiofrequency ablation; 65 mitral valve surgery (group I) and 63 aortic valve surgery or CABG (group II). Follow up was complete and included standard ECG and echocardiogram at 3, 6, 12 months and each consecutive year. Stability of SR was confirmed with a 24 hour ECG registration. Group II patient were distinctly older (69.3 versus 64.8 years; p= 0.04), but the size of the left atrium was smaller (45.9 versus 52.4 millimeters; p= 0.0001) and the aortic cross clamp time was shorter (91 versus 99 minutes; p=0.05). The cumulative SR rates are similar. A concomitant ant arrhythmic procedure in CABG and AVR patients is as effective as in mitral valve patients, although these patients tend to be older, but with a smaller left atrial size.

Chapter 8
Concomitant anti-arrhythmia surgery, using irrigated-cooled-tip radiofrequency ablation, to treat chronic permanent AF in CABG patients; expansion of the indication?

This prospective study included 36 CABG patients, who had a concomitant anti-arrhythmic procedure using irrigated, cooled-tip radiofrequency ablation. Follow-up included a 24-hour EKG and ultrasound examination at 3, 6, 12 months. The mean (SD) age was 68.7 years (8.0), left atrial diameter 44.9 millimeters (6.7), preoperative duration of AF 67 months (73), left ventricular ejection fraction 54% (14), euroscore 5.5 (2.6), number of distal anastomoses 3.3 (1.2), aortic cross-clamp time 90 (19) minutes, extra corporeal bypass time 156 (38) minutes. Thirty-day mortality was 2.8% (1/36). Mean (SD) follow-up was 25.3 months (17.9). Cumulative survival rates (SE) at 12 and 24 months were 0.94 (0.04) and 0.90 (0.06). Cumulative postoperative SR rates (SE) at 6 and 12 months were 0.60 (0.08) was 0.75 (0.08). Restored bi-atrial contraction occurred in 73% (19/26) of all SR patients. As a consequence coumadine was stopped, after the 6th postoperative month, in 76% (16/21) in this subset of patients, corresponding with 44% (16/36) of all study group patients. One patient experienced a sick sinus syndrome 12 months postoperatively, for which a DDD pacemaker was implanted. Three out of 5 patients with a preexistent VVI pacemaker regained a stable postoperative SR with bi-atrial contraction, obviating the need of any pacemaker support. Concomitant anti-arrhythmia surgery in CABG patients with chronic permanent AF was safe, effective and beneficial.

Chapter 9
Concomitant anti-arrhythmic procedure in combined valve(s) and CABG high risk patients

Is a concomitant anti-arrhythmic procedure to treat AF in combined valve(s) and CABG surgery efficacious? A concomitant anti-arrhythmic procedure using unipolar endocardial radiofrequency ablation was performed in 203 patients; 45 (group I) had a combined valve(s) and CABG procedure (mitral valve with CABG n=30, non-mitral valve with CABG surgery n=10, multiple valve surgery n=5) and 158 patients (group II) had a solitary valve or CABG surgery (non-mitral valve surgery n=82, mitral valve surgery n=76). Permanent AF occurred in 67.6% (30/45) group I and 80.4% (127/158) group II patients (p=0.07). Mean age for group I and II was 71.3 versus 67.0 years (p=0.001), euro score 7.4 versus 5.9 (p=0.03). Thirty-day mortality rates for group I and II were 13.3% (6/45) versus 3.8% (6/158) (p=0.027). Left ventricular ejection fraction below 44% was a risk factor for death (p=0.03). Cumulative SR for patients with permanent AF (group I, n=30; group II, n=127) at 12 months was 84% and 75% (p=0.814). Left atrial diameter above 52.1 millimeter was a risk factor for SR conversion failure (p=0.03). Survival rates for SR and AF patients with a minimum 3 months follow-up were 83% versus 95% (p=0.189). Concomitant anti-arrhythmic surgery is safe and effective in combined valve(s) and CABG procedures, except in patients who have an impaired LVEF (lower than 44%) and an enlarged left atrium (above 52.0 mm).

SECTION IV; POSTOPERATIVE CARE AND COMPLICATIONS

Chapter 10
Morphology of intraoperatively induced linear radiofrequency ablation lesions in patients with chronic AF

We studied 58 ablation lesions from 7 patients who had died 2 to 22 days after open heart surgery plus successful intraoperative cooled-tip radiofrequency ablation to treat chronic permanent AF (mean of 4 years). Hearts were dissected to study the morphology and transmurality of the linear ablations both macroscopically and histologically. Radiofrequency ablation produces clearly delineated coagulation necrosis, bordered by an irregular zone of fresh bleeding and incomplete necrosis. No superficial charring, thrombotic deposition or perforation was documented. The necrotic core consisted of homogenized,
swollen myocardial cells without nuclear staining reaching up to a depth of 5.5mm. Endocardium and subendocardium displayed edematous loosening, swelling and micro fragmentation of connective tissue fibers. In the early phase (2 to 6 days) interfibrillar disseminated bleeding and non-reactive necrosis was found. In the mid-term phase (21 and 22 days) mild inflammatory removal reaction and granulation tissue was seen along the border of the necrotic core. 24% of all lesions in patients with documented postoperative SR were non-transmural. Multiple nervous fibers with different degrees of thermal injury were detected in the vicinity of the pulmonary ostium. Intraoperative cooled-tip radiofrequency ablation in AF results in coagulation necrosis of endocardium, subendocardium and the atrial myocardial layer to a depth of about 5.5 mm, bordered by an irregular zone of incomplete thermal damage. Transmurality of the lesions was found only in 76% of intraoperatively applied lesions.

Chapter 11 and 12
Esophageal perforation during left atrial radiofrequency ablation. A possible surgical technique to avoid esophageal- and circumflex artery injuries using radiofrequency ablation to treat AF
SICTRA creates deep, non-thrombogenic, atrial wall lesions, however without causing any collateral damage. The keystones of this surgical technique are: mobilization of the left atrium, lifting up the atrial tissue during ablation, oscillating movements using a hand-held RF pen-catheter the occurrence of yellow- white blistering endocardium lesions.

Chapter 13
Antiarrhythmic surgery to cure AF – subgroups and postoperative management
The use of antiarrhythmic surgical procedures to cure AF is widely spread in specialized centers of cardiac surgery. Whereas the Cox Maze procedure remains the gold-standard with high efficacy a variety of different antiarrhythmic procedures aim at reducing extent and duration of the procedure. Especially in patients with mitral valve disease SR is established significantly more often by an antiarrhythmic procedure added to mitral valve surgery. In 110 patients with chronic-permanent AF undergoing different surgical procedures SR was reestablished in 75%. There is no subgroup of patients or underlying cardiac procedure that benefits more from an antiarrhythmic procedure. Because conversion usually occurs spontaneously within the first 6 months and antiarrhythmic medication does not increase conversion it seems feasible to wait for spontaneous occurrence of SR in these patients. In specialized and experienced cardio-surgical centers patients with permanent AF should be rendered eligible for additional antiarrhythmic procedures proven to not increase morbidity or mortality.

SECTIONS V; CONCLUSIONS AND RECOMMENDATIONS
The surgical therapy of AF is still evolving and is influenced by various factors such as the patient's selection, the indication, the type of AF, the lesion pattern and the energy source. The safety and efficacy of the surgical treatment of AF are the two most important short-term considerations in the evaluation of this therapy. The hypothetic sequence of events after the surgical treatment of AF includes the abolition of AF, enabling the sinus node to regain its activity, permitting the restoration of the atrial contractility with associated atrial kick which will subsequently improve the left and right ventricular filling during the late diastolic phase, optimizing the cardiac output and performance. As a consequence, an improved quality of life and survival and a decrease in cerebral vascular events can theoretically be anticipated. Each preceding element of the described sequence is a prerequisite for a successful next consecutive step.
Recommendations

1. SICTRA is an effective and safe energy source to treat AF. The intraoperative handling of the SICTRA probe is practicable and versatile, because the malleable shaft enables an optimal tissue-surface contact, without exertion of any manual pressure while making an oscillating movement in order to create an ablation line.

2. A left atrial SICTRA lesion pattern is an effective blueprint to abolish AF. So, the extent of the anti-arrhythmic surgical procedure can be limited to a solitary left atrial ablation pattern, except in patients who additionally have an atrial flutter or patients in whom tricuspid valve surgery is anticipated.

3. Histological transmural lesions are an important but not an unique prerequisite to abolish AF. Histological examination of patients who died within 33 days postoperatively in our series, revealed histological transmurality in only 76% of the specimens. The ablation lines from the left inferior pulmonary orifice to the mitral valve annulus were rarely transmural. Nevertheless SR could be established in most of the patients during the early postoperative period.

4. CABG and AVR patients with AF should have a concomitant anti-arrhythmic procedure, even if the left atrium has to be opened intentionally to perform the ablation lines. The postoperative SR conversion rate, in this subset of patients in our series, was 79%. These patients were older, although the mean size of the left atrium was smaller. In 44% of the treated CABG patient, coumadine was stopped 6 months postoperatively, contributing to a potential reduction of the long-term morbidity.

5. In cardiac failure patients with a high anticipated operative risk, the treatment of AF should be incorporated in an overall surgical strategy comprising of restoration of SR, reversing of any myocardial ischemia and correction of any mitral valve regurgitation. In our study a SR conversion rate of 84% was observed. But the indication for an anti-arrhythmic procedure in patients with an impaired LVEF, lower than 40%, and an enlarged left atrium, above 52 mm, should be made with caution.

6. A beta blocker such as metoprolol should be started on the 1st postoperative day, except in patients with a severe impaired left ventricular function or severe COPD. A cardioversion is only performed at 6 month postoperatively, if AF perpetuates.