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Research article

Acute and Mid-Term results of Superoseptal Versus Inferolateral Mitral Isthmus Linear Ablation for Left Atrial Substrate Modification

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Abstract

Background: In patients with paroxysmal or persistent atrial fibrillation (AF) and diseased left atrium (LA) substrate modification might increase efficacy of pulmonary vein (PV) isolation. LA linear lesions effectively modify the substrate, but have been largely abandoned because bidirectional block at the mitral isthmus (MIL, left inferior PV to mitral annulus) is difficult to achieve. We therefore aimed to compare safety, acute and mid-term efficacy of MIL vs. an alternative superoseptal line (SSL, right superior PV to mitral annulus).

Methods and Results: patients were alternatively assigned to MIL or SSL in addition to PV isolation and linear ablation at the LA roof and at the cavotricuspid isthmus. Conventional criteria were used to confirm bidirectional block. Seventy patients [median 64 years, 84% persistent and 16% ≥48hours episodes of long paroxysmal AF] were enrolled. Bidirectional block was achieved in 94% of MILs vs. 83% of SSLs (P = .2595). Most (5/6) failed SSLs occurred in the first half of the study period. All PVs were isolated, bidirectional block was 96% and 100% at the LA roof and cavotricuspid isthmus. No difference in procedural or complication rate was found. At follow-up, a trend toward better success rate was found for the SSL (86% vs. 74%; P = .2293).

Conclusion: After completion of a short learning curve, the SSL is a good alternative, showing equal safety/acute efficacy and a trend for better midterm success rates.

Keywords: *Atrial Fibrillation; Left Atrial Linear Ablation; Mitral Isthmus Ablation; Inferolateral Mitral Isthmus; Superoseptal Mitral Isthmus.*

Introduction

Modification of the electrical and anatomical substrate in addition to pulmonary vein (PV) isolation has been showed to increase the success rate of catheter ablation for patients with atrial fibrillation (AF) [1-4] and left atrial (LA) linear ablation, mostly at the roof and at the inferolateral mitral isthmus (MIL, between the left inferior PV and the mitral annuls) proved to be an effective way to modify the substrate [5-11]. Due to anatomical reasons [12,13], bidirectional block at the MIL is sometimes difficult to achieve [5,7-9,11,12] and

this might explain why a recent randomized study did not find a better outcome when linear ablation was added to PV isolation [14]. Nevertheless, anatomy in other LA areas might be more favourable and bidirectional block easier to achieve. Ablation between the right superior PV and the mitral annulus, an area that often exhibits complex fractionated electrograms during AF [4] and lower voltages during sinus rhythm [1,2], often leads to organization and/or termination of AF [4,15,16]. Therefore, a superoseptal line (SSL, between the right superior PV and the mitral annulus) might be an attractive alternative for patients undergoing LA linear ablation for substrate modification. Aim of this study was to compare safety, acute and mid-term efficacy of these 2 linear ablation strategies at the mitral isthmus in patients with persistent or long episodes of paroxysmal (> 48 hours under antiarrhythmic drugs) AF.

Methods

Patient population

In this prospective interventional study, consecutive patients with either persistent, or long episodes of paroxysmal (defined for this study as ≥ 48 hours under antiarrhythmic therapy) AF undergoing atrial substrate modification with linear lesions in the left and right atrium in addition to PV isolation were alternatively and in equal numbers, assigned to either MIL or SSL (Figure 1). In all patients, additional linear ablation was performed at the roof of the LA and at the cavotricuspid isthmus.

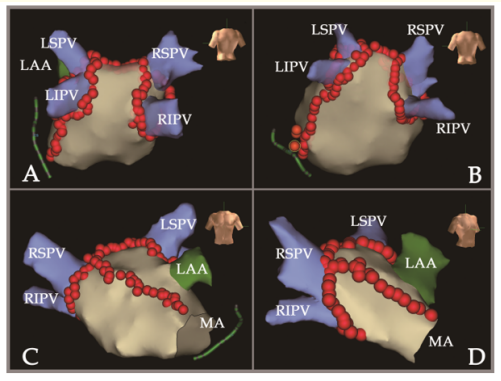

Figure 1: *Linear ablation between the mitral annulus and the left inferior (A and B, posteroanterior view) or the right superior (C, anteroposterior view, and D, right anterior oblique view) pulmonary vein (PV) in 4 different patients. LS (left superior), LI (left inferior), RS (right superior), RI (right inferior) PV; LAA= left atrial appendage; MA= mitral annulus; Red Lesion= endocardial lesion; Orange Lesion= lesion inside the coronary sinus (B).*

Patients with paroxysmal AF were included only in the presence of significant LA dilatation and if antiarrhythmic drug therapy with amiodarone was not effective or not possible or AF was recurrent after previous PV isolation. Previous LA linear and/or complex fractionated atrial electrogram ablation were considered exclusion criteria.

The study was approved by the institutional review board of the hospital. All patients gave written informed consent and underwent transoesophageal and transthoracic echocardiogram to exclude the presence of intracardiac thrombi and to determine cardiac dimension and function as well as valvular abnormalities.

Raw data of a pre-procedural 64-slice dual source computed tomography of the heart (Somatom™ Definition, Siemens AG, Munich, Germany) were used to reconstruct the LA (Verismo™, EnSite NavX™, St. Jude Medical, St. Paul, MN, USA). LA and PV morphology was assessed on the three-dimensional image and the length of each hypothetical LA linear ablation (i.e. at the level of both the MIL and the SSL between the mitral annulus and the ostium of the inferior left and superior right PVs, respectively and at the roof between the ostium of the 2 superior PVs) was measured.

Electrophysiological study

Antiarrhythmic drugs were continued peri-operatively, the electrophysiological study was performed in a fasting state and with an INR ≤ 3.0. Intravenous midazolam, fentanyl and propofol were administered for deep sedation throughout the procedure. Surface ECG leads and bipolar intracardiac electrograms were digitally recorded using an electrophysiology workstation (CardioLab System, Prucka Engineering, GE Healthcare, Milwaukee, WI, USA). Vascular access was obtained via the internal jugular and right femoral vein. Using biplane fluoroscopy (Philips Healthcare, Best, the Netherlands), two decapolar catheters (6Fr CSL and 4Fr steerable Inquiry, both St. Jude Medical, St. Paul, MN, USA) were positioned in the coronary sinus and at the His bundle, respectively. After placing 2 long sheaths (steerable Agilis and SL1, St. Jude Medical, St. Paul, MN, USA) in the LA via single or double transseptal puncture, systemic anticoagulation with intravenous heparin was started with an initial bolus of 100U/kg (max 10.000 Units). Activated clotting time was measured every 20 min and additional doses of heparin were administered to achieve and maintain a value of ≈ 350s.

Pulmonary vein isolation

Antral or ostial PV isolation was carried out during AF or in sinus rhythm with an irrigated catheter (Celsius ThermoCool, D-Type, Biosense Webster, Diamond Bar, CA, USA) at 25 to 35 Watts (43 - 45° Celsius, 17 ml/min) for the posterior/anterior aspect of the PVs or with the Pulmonary Vein Ablation Catheter (PVAC, Medtronic Ablation Frontiers LLC, Carlsbad, CA, USA). Using entry- and exit block as the endpoint, electrical isolation was proved with a circular mapping catheter (Lasso™, 15 mm, Biosense Webster, Diamond Bar, CA, USA). As standard practice in our laboratory [17], all adenosine-induced PV reconnections were treated with further ablation until the drug response was no longer seen.

Left and right atrial linear ablation

If patients were in AF after PV isolation, electrical cardioversion was done and linear ablation started at the roof, where radiofrequency (RF) energy was limited to 35 Watts (43 - 45° Celsius, 17 ml/min). Power was eventually increased to 40 Watts (43 - 45° Celsius, 17 ml/min) for the SSL and the ventricular portion of the MIL. An ablation time of 30 to 50 sec for each lesion was employed before changing the position of the ablation catheter. If endocardial ablation at the MIL was not successful and/or preferential epicardial conduction was suspected, ablation was continued in the coronary sinus (20 - 25 Watts, 43° Celsius, 17 - 35 ml/min). Ablation at the cavotricuspid isthmus was performed thereafter (40 - 50 Watts, 45 - 48° Celsius, 17 ml/min). Success for linear ablation was defined by the presence of a corridor of widely split double potentials, differential pacing and changes of the activation sequence while pacing on each side of the line. Maps collected with the EnSite NavX™ system were also used to confirm the change in activation sequence. A waiting time of at least 30 and 20 min was observed for left and right atrial linear ablation, respectively. No pre-specified procedural or RF time was used to define failure of linear ablation. It was rather the combination of total procedural time, time spent mapping a specific target, as well as total and specific RF time that would advocate termination of treatment and acceptance of failure.

In addition, detailed sinus rhythm activation maps of the LA and an echocardiographic evaluation to study the mitral inflow and exclude pericardial effusion were performed in each patient after PV isolation and at the end of the study. These data, aiming at describing the electrophysiological and hemodynamic effect on the LA of each linear ablation, will be presented in a separate manuscript, as the combined amount of data would make the current manuscript too long.

Complications, in hospital and mid-term follow-up

Complications were classified as related to transseptal puncture, RF therapy or vascular access. Patients were kept in hospital for at least 48 hours after the procedure with continuous 2-lead ECG monitoring. A 24-hours-Holter was suggested at 3, 6, 12 months and yearly thereafter. Patients were seen at 6 months at our outpatient clinic, or by the referring physician. Any arrhythmic event lasting more than 30 sec was defined as recurrence. A blanking period of 3 months was observed, unless the clinical situation related to intra-hospital post-operative recurrences required alterations in treatment.

Statistical analysis

Using our personal success rate during MIL for the 35 procedures preceding this study (91%) and previously published studies on ablation at the superior septum [18,19], detection of a difference between groups with a two-sided α-value of 0.05 and a power of 80% required inclusion of 70 (35 per group) patients. Categorical variables are presented as numbers and percentages. Continuous variables are summarized as mean and standard deviation or median, first and third interquartile ranges, depending on normality of distribution. Comparisons for categorical variables were made with χ^2 or Fisher's exact test, as appropriate. The t-test or the Wilcoxon-Mann-Whitney test were used to compare continuous variables, as appropriate. A probability value < .05 was considered statistically significant.

Results

Patient characteristics

Between June 2010 and April 2012, 70 consecutive patients [64 (56, 68) years old, 26% (18) female] with persistent (90%, 63/70) or long lasting episodes (> 48 hours) of paroxysmal AF (7 patients, 10%: 3 patients with recurrent AF, 2 patients with side effects on amiodarone, 1 patient with marked sinus bradycardia and 1 patient refusing drug therapy) were enrolled. Ten (14%) patients had recurrent AF after ≥ 1 previous PV isolation (4 patients underwent 2 procedures). Recurrent AF was paroxysmal in 3 and persistent in 7 patients.

A CHA_2DS_2-VASc Score of 0, 1, 2 and ≥ 3 was seen in 7% (5/70), 27% (19/70), 36% (25/70) and 30% (21/70) of patients, respectively. A left ventricular ejection fraction < 50% was found in 2 patients with idiopathic dilated cardiomyopathy and in 13 patients with tachycardiomyopathy. One patient in the SSL group previously underwent biological aortic valve replacement. An increased echocardiographic LA dimension (parasternal long axis view; female > 38 mm; male > 40 mm) was seen in 68% (13/19) and 84% (43/51) of female and male patients, respectively. The clinical characteristics of both groups were similar except for a slightly, clinically not-significant, lower ejection fraction in the SSL group (Table 1).

Ablation at the inferolateral vs. superoseptal mitral isthmus

Bidirectional block was achieved in 94% (33/35) and 83% (29/35) of patients in the MIL and SSL groups (P = .2595), respectively. Temporary block, considered as failure, was achieved in 1 patient in each group. Delivery of RF lesions inside the coronary sinus was necessary to achieve success in 85% (28/33) of MIL ablation. In 2 patients assigned to MIL, stable bidirectional block (temporary block in 1 of them) could not be achieved despite endocardial and epicardial ablation. In the SSL group, failure to achieve bidirectional block was mainly limited to the first half of the study period (5/6 patients) and temporary block was achieved in the last patient without success. When block was not achieved, the site of residual conduction was always at the LA insertion of the Bachmann's bundle and continuous electrical activity was recorded in this area whereas a corridor of narrowly split double potentials was seen along the rest of the line (Figure 2).

Longer mapping and RF times were seen when linear ablation was not successful (Table 2). In 1 of the 2 patients in whom bidirectional block at the MIL could not be achieved, a SSL was performed and bidirectional block was achieved after 100 and 53 additional min of mapping and RF time.

Although the SSL compared to the MIL is anatomically longer (Table 1), a trend toward shorter time to achieve block (27 (20, 32) vs. 41 (20, 82) min; P = .0645) and RF time (21 (15, 30) vs. 31 (16, 50) min; P = .568) was seen for successful SSL vs. MIL lines and the length of each line in both group did not influence success (Table 2). Further, to prove the absence of bias in the MIL or SSL group assignment, the length of each MIL and SSL was assessed in all patients and no difference was found for the inferolateral ["MIL group": 38 (33, 44) vs. "SSL group": 39 (35, 42) mm; P = .7109] and superoseptal ["MIL group": 60 (55, 66) vs. "SSL group": 58 (52, 62) mm; P = .1263] line between groups.

	Inferolateral mitralisthmus line (35)	Superoseptal mitralisthmus line (35)	P
Age (years)	64 (56, 68)	61 (56, 68)	.7511
Gender (F/M)	11/24 (31%/69%)	7/28 (20%/80%)	.2740
Paroxysmal/Persistent AF	5/30 (14%/86%)	2/33 (6%/94%)	.4283
Time since first AF Diagnosis (months)	48 (22, 108)	60 (25, 96)	.9532
Duration of Persistent AF (months)	12 (5, 27)	14 (7, 38)	.3894
Previous pulmonary vein isolation	6 (17%)	4 (11%)	.7343
Previous cavotricuspid ablation	9 (26%)	7 (20%)	.5692
Previous electrical cardioversion	24 (68%)	30 (86%)	.0877
No. of previous cardioversions (1/≥2)	10/14 (42%/58%)	13/17 (43%/57%)	.9020
No. of ineffective antiarrhythmic drugs	1 (1, 3)	1 (1, 2)	.8326
CHA_2DS_2-VASc Score	2 (1, 3)	2 (1, 2)	.6698
Congestive heart failure	7 (20%)	10 (29%)	.4030
Hypertension	30 (86%)	31 (89%)	1.000
Age (65 - 74/≥75years)	14/3 (40%/9%)	13/2 (37%/6%)	.8427
Diabetes	4 (11%)	6 (17%)	.7343
Previous stroke, TIA or embolism	1 (3%)	0 (0%)	1.000
Vascular Disease	2 (6%)	0 (0%)	.4928
Sex category (i.e. female sex)	10 (29%)	7 (20%)	.4030
Presence of structural heart disease	19 (54%)	21 (57%)	.6291
Hypertensive heart disease	14 (40%)	16 (46%)	.6290
Ischemic heart disease	3 (9%)	2 (6%)	1.000
Idiopathic dilated cardiomyopathy	1 (3%)	1 (3%)	1.000
Tachycardiomyopathy	5 (20%)	8 (14%)	.3457
LA antero-posterior (mm; TTE, PLAX)	43 (39, 45)	42 (41, 45)	.6776
LA medial-lateral (mm; TTE, A4C)	44 (41, 48)	43 (42, 45)	.6634
LA superior-inferior (mm; TTE, A4C)	59 (54, 65)	64 (59, 69)	.0952
LA volume (ml) [1]	133 (113, 160)	132 (111, 158)	.6832
LV ejection fraction (%)	60 (55, 60)	55 (45, 60)	.0385
LV end diastolic diameter (mm; TTE)	51 (47, 54)	51 (48, 55)	.6213
LV end systolic diameter (mm; TTE)	35 (31, 38)	33 (30, 36)	.4629
Mitral insufficiency (No/mild/moderate)	4/27/4 (11%/77%/11%)	4/25/6 (11%/71%/17%)	.7878

Table 1: *Patient Characteristics (n = 70).*

Data are presented as median, first and third interquartile range or numbers and percentages. Hypertensive heart disease was defined by significant left ventricular hypertrophy (left ventricular mass >95g/m² for female and >115g/m² for male). 1= left atrial volume was obtained from the three-dimensional reconstruction with the Verismo™ software (St. Jude Medical); A4C= apical four chambers view; LA= left atrium; LV= left ventricle; PLAX= parasternal long axis view; TIA= transient ischemic attack; TTE= transthoracic echocardiography.

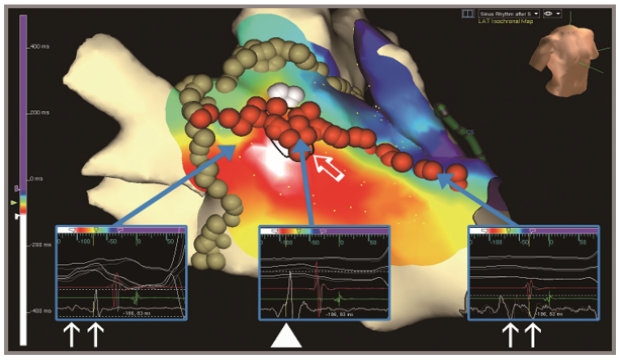

Figure 2: *Sinus rhythm activation mapping in a patient with incomplete linear ablation at the superior septum (right anterior oblique view). The left and the right electrogram samples show the presence of a split double potentials on the tracing of the ablation catheter (upright arrows), whereas the central panel, in the area of the left atrial insertion of the Bachmann's Bundle, shows a continuous electrogram (triangle). Lesions were deployed above the insertion of Bachmann's bundle, extending also in the anterior wall (white lesions). The black circle (empty white arrow) shows the first 10 msec activation of the left atrium before deployment of the linear lesion.*

	Successful Ablation	Non-successful Ablation	P
Superoseptal Mitral Isthmus line	29 (83%)	6 (17%)	
Conduction time pacing superior (from the LAA, msec)	190 (173, 206)	126 (122, 135)	.0002
Isthmus conduction time pacing inferior (from the right atrial septum, msec)	185 (171, 216)	115 (94, 141)	.0004
Mapping time (min)	27 (20, 32)	75 (47, 102)	.0241
Radiofrequency time (min)	21 (16, 30)	40 (32, 79)	.0048
Length of the line (mm)	58 (50, 62)	53 (46, 56)	.1196
Inferolateral Mitral Isthmus line	33(94%)	2 (6%)	
Conduction time pacing superior (from the LAA, msec)	155 (148, 168)	89 (74, 105)	.0208
Conduction time pacing inferior (from the inferolateral coronary sinus, msec)	161 (151, 176)	99 (69, 130)	.0301
Mapping time (min)	41 (20, 82) min	190 (141, 239)	.0251
Radiofrequency time (min)	31 (16, 50)	94 (64, 125)	.0360
Length of the line (mm)	43 (36, 51)	38 (33, 43)	.3925
Roof line	67 (96%)	3 (4%)	
Conduction time pacing anterior (from the LAA, msec)	157 (145, 177)	120 (105, 126)	.0059
Conduction time pacing posterior (from the posterior left atrial wall, msec)	153 (139, 170)	110 (107, 114)	.0192
Mapping time (min)	21 (12, 33)	67 (66, 101)	.0084
Radiofrequency time (min)	22 (14, 33)	39 (38, 54)	.0065
Length of the line (mm)	36 (31, 40)	36 (31, 47)	.6629

Table 2: *Successful vs. non-successful left atrial linear ablation (n = 70).*

Data are presented as median, first and third interquartile range or numbers and percentages. LAA= left atrial appendage.

Pulmonary vein isolation

PV isolation was achieved in all patients after 90 (62, 123) min and 22 (21, 26) and 64 (46, 87) min of RF energy with the PVAC® and the irrigated catheter, respectively, including the time for mapping and treatment of spontaneous (8 patients, 10 PVs) and adenosine-induced (18 patients, 24 PVs) reconnections. At the beginning of the procedure, 90% (9/10) of patients with recurrent AF had reconnection of 1 (5 patients) or ≥ 2 (4 patients) PVs. No differences in anatomical LA characteristics and procedural parameters were found between MIL and SSL groups (Table 3).

	Inferolateral mitralisthmus line (35)	Superoseptal mitralisthmus line (35)	P
Total Procedural time (min)	365 (328, 401)	357 (338, 430)	.7467
Total Radiofrequency Time (min)	125 (94, 150)	114 (92, 135)	.2645
X-Ray time (min)	32 (20, 46)	34 (27, 48)	.5067
Dose area product (µGy/m^2)	5504 (3548, 10017)	7495 (4674, 9318)	.4076
Pulmonary Vein Isolation			
Time to PV isolation (min)	86 (62, 120)	99 (72, 127)	.3430
Radiofrequency time "cooled tip" (min)	62 (46, 91)	64 (44, 87)	.7478
Radiofrequency time "PVAC" (min)	20 (18, 23)	29 (22, 36)	.6985
Inferolateral vs. Superoseptal Mitral Isthmus line			
CT-derived length of the inferolateral vs. superoseptal mitral isthmus line (mm)	38 (33, 44)	58 (52, 62)	<.0001
Time to line completion (min)	41 (21, 86)	30 (22, 67)	.1356
Achievement of block	33 (94%)	29 (83%)	.2595
Radiofrequency time (min)	31 (17, 50)	24 (18, 34)	.1297
DP spacing pacing superior (msec)[1]	105 (97, 123)	131 (115, 152)	<.0001
Conduction time pacing superior (msec) [1]	155 (148, 168)	190 (173, 206)	<.0001
DP spacing pacing inferior (msec) [1]	121 (101, 138)	131 (118, 152)	.0330
Conduction time pacing inferior (msec) [1]	161 (151, 176)	185 (171, 216)	.0006
Roof line			
CT-derived length of the roof line (mm)	37 (33, 42)	34 (30, 39)	.0815
Time to line completion (min)	21 (13, 32)	21 (11, 43)	.8194
Achievement of block	34/35 (97%)	33/35 (94%)	1.000
Radiofrequency time (min)	17 (13, 23)	12 (10, 24)	.1215
DP spacing pacing anterior (msec) [1]	107 (87, 113)	96 (86, 117)	.6623
Conduction time pacing anterior (msec) [1]	166 (147, 186)	155 (137, 172)	.1102
Conduction time pacing posterior (msec) [1]	156 (140, 177)	151 (135, 163)	.1453
Complications			
Pericardial effusion	20 (57%)	14 (40%)	.1513
Groin hematoma	2 (6%)	1 (3%)	1.000
Neck hematoma	2 (6%)	0 (0%)	.4928
Arteriovenous fistula	2 (6%)	1 (3%)	1.000
Signs of post-procedural hypervolemia	0 (0%)	2 (6%)	.4928

Table 3: *Procedural, complication and in hospital arrhythmia recurrence data (n = 70).*

Data are presented as median, first and third interquartile range or numbers and percentages. PV: Pulmonary Vein; PVAC: Pulmonary Vein Ablation Catheter; Ado: Adenosine; DP: double potentials; 1= comparison between successful ablation only.

Ablation at the roof of the left atrium

After 21 (12, 33) min, bidirectional block at the LA roof was achieved in 96% (67/70) of patients with 14 (11, 22) min of RF energy. Bidirectional block at the roof was not achieved in 1 and 2 patients in the MIL and SSL groups, respectively. No difference in success rate, electrophysiological parameter and procedural time were observed between MIL and SSL groups (Table 3).

Ablation at the cavotricuspid isthmus

After 11 (7, 17) and 8 (6, 12) min of mapping and RF time, bidirectional block was achieved in all patients. Seven of the 16 patients who previously underwent cavotricuspid isthmus ablation showed a gap in the line.

Procedure length, X-ray exposure and complication rate

No differences in total length of the procedure, total RF time, X-ray time, X-ray exposure and complication rate were found between the 2 groups (Table 3).

Immediately after the procedure, minimal (≤ 5 mm) pericardial effusion was seen in 11% (8/70) of patients. On the following day, an effusion was found in 49% (34/70) of patients and this was moderate (> 5 but ≤ 20 mm) in 14% (10/70) of patients. Pericardial drainage was never required and spontaneous resolution was observed in all. Four patients required treatment due to pericarditis symptoms (colchicine 0,5mg bid for 3 weeks) without associated electrocardiographic changes. Pericardial effusion was not associated with the need for epicardial lesions during MIL ablation [16/28 (57%) vs. 4/7 (57%); P = 1.000].

Two (3%) patients in the SSL developed signs (at chest radiograph) of post-procedural hypervolemia. This rapidly resolved with a short course of diuretic therapy and patients were discharged 9 and 12 days after ablation. An antibiotic was also started and continued for 5 and 7 days, although the observed raise of the C reactive protein, without increase in white blood cells or fever, is most likely direct consequence of the procedure and not reflecting an active infective process.

Arteriovenous fistula occurred in 3 patients, resolved spontaneously in 2 and surgery (performed 18 months after the procedure) was necessary in 1 patient. Hematoma rate was similar in both groups and resolved without need for specific therapy in all (Table 3).

In hospital follow-up

During a median post-procedural hospital stay of 5 (4, 7) days, 3 patients had persistent episodes of AF (n = 1) or AT (n = 2) requiring electrical cardioversion. Of those, 2 had undergone successful MIL ablation whereas the third patient with persistent AT had undergone unsuccessful SSL ablation. No difference in sustained [12 (34%) vs. 10 (29%); P = .8060], persistent [2 (6%) vs. 1 (3%); P = 1.000] or any [22 (63%) vs. 21 (60%); P = .6066] post-procedural recurrences was found when MIL and SSL groups were compared.

Due to repeated highly symptomatic long lasting/persistent post-procedural arrhythmic recurrences and personal preference, 2 patients with successful MIL and SSL ablation eventually underwent minimally invasive Cryo-MAZE.

A blanking period of 3 months was observed except for the 2 patients who subsequently underwent minimally invasive Cryo-MAZE operation (both were counted as treatment failures). After a median follow-up of 185 (171, 193) days, 30 (86%) and 26 (74%) of patients assigned to SSL and MIL ablation were free from any arrhythmic recurrence (P =. 5723, Figure 4). At this time, antiarrhythmic drug had been stopped in 40% (14) of patients in both groups. Due to freedom from arrhythmia, drug therapy was stopped at the time of the last visit in 11 (31%) and 8 (23%) additional patients in the SSL and MIL groups, respectively.

At follow-up, 4 patients in the SSL group had paroxysmal episode of AT and in 2 of them paroxysmal AF was documented in addition to the regular AT. Persistent AT was documented in 1 patient. Eight patients in the MIL group developed recurrences, 4 had paroxysmal episodes of AT and 4 had AF recurrence (paroxysmal in 3 and persistent in 1).

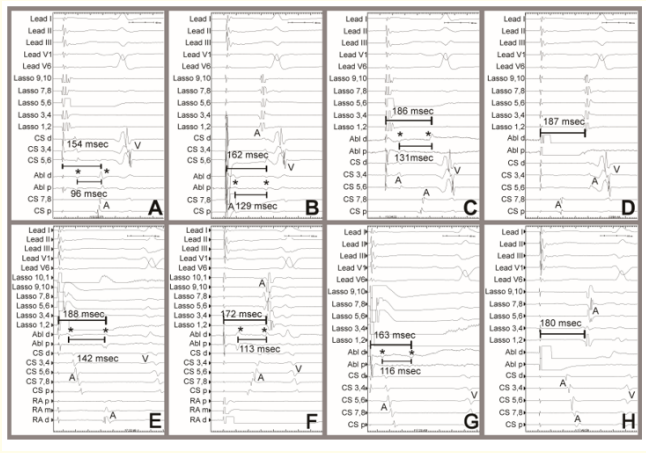

Figure 3: *Intracardiac recording of patients assigned to inferolateral (A to D) and superoseptal (E to H) linear ablation. Block pacing anterior (from the appendage) after ablation at the "standard" (A) and superoseptal (E) mitral isthmus. Block pacing inferior after ablation at the "standard" (B, pacing from the proximal coronary sinus) and SSL (F, pacing from the mid right atrial septum) mitral isthmus. Block at the left atrial roof pacing anterior (from the appendage, C and G) and posterior of the line (D and H) during "standard" and SSL mitral isthmus linear ablation, respectively. Lead I to V6 = surface EKG; Abl, Lasso, CS, and RA = intracardiac recordings from the ablation, the LassoTM, coronary sinus and right atrial catheter, respectively; A and V = atrial and ventricular signal; p, m and d = proximal, medial and distal. * = indicates double potential. Paper speed 20 0mm/s.*

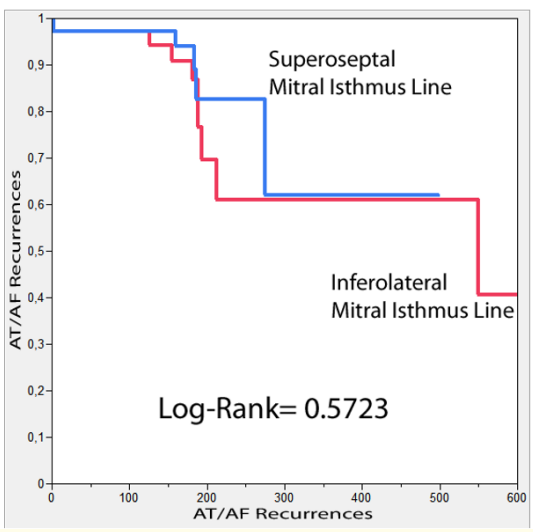

Figure 4: *The graph shows Kaplan–Meier estimates of freedom from documented atrial fibrillation or tachycardia more than 30 seconds. There were no significant differences between patients assigned to the standard inferolateral vs. the superoseptal mitral isthmus line (P = 0.5723).*

Ten patients, including the 2 patients who underwent minimally invasive Cryo-MAZE, underwent a second procedure (6 MIL and 4 SSL). In all patients, bidirectional block was achieved for each linear ablation during the first procedure. Due to scarce symptoms, 4 additional patients (3 MIL and 1 SSL) were managed conservatively, with 3 of them kept on antiarrhythmic drugs.

All 4 patients undergoing a redo procedure and initially assigned to the MIL group had bidirectional block at the MIL, 2 patients had reconnection of ≥ 1 PV and 2 and 1 patients had a gap at the left atrial roof and at the tricuspid line, respectively. One patient with short but highly symptomatic runs of AF, decided to undergo minimally invasive Cryo-MAZE.

Both patients undergoing a redo procedure an initially assigned to the SSL group who underwent a second catheter ablation were found to have bidirectional block at each left and right atrial linear ablation lines. Reconnection of 1 PV was seen in both patients. One additional patient underwent a redo procedure in an outside hospital, all veins were found to have recovery of conduction, but no information about left and right atrial linear ablation was provided.

Discussion

Main findings

This prospective interventional study comparing an equal and consecutive number of patients alternatively assigned to "standard" MIL vs. SSL ablation shows several important findings: 1) acute success rates were similar in both groups and as high (94%) as in the most successful previously reported studies for MILs and higher (83%) for SSLs; 2) 85% of patients undergoing MIL ablation required RF lesions inside the coronary sinus; 3) total procedural and RF times were similar between groups, but a trend towards shorter mapping and RF times was observed for the SSL linear ablation, although this line was anatomically longer; 4) complication and acute recurrence rates were similar in both groups, but a trend towards better mid-term success was seen in the SSL group.

Linear ablation at the mitral isthmus: inferolateral and superoseptal approaches

In the presence of a diseased atrium PV isolation alone is unlikely to achieve satisfactory results in patients with paroxysmal or persistent AF, therefore additional LA substrate modification to increase success rates is gaining new interest [1-3]. LA linear ablation is one of the means to effectively modify anatomical and electrical substrate and has been showed to achieve good long-term result in a number of study [5-11,18,19]. Although a recent randomized study in patients with persistent AF found no benefit of left atrial linear (or complex atrial electrograms) ablation in addition to PV isolation, the trial was underpowered to show that a strategy of pulmonary-vein isolation alone is superior to a combined strategy [14]. Besides, only achievement of a high rate (> 80% and ideally > 95%) of bidirectional block can definitely prove if additional substrate modification by means of LA linear ablation can further increase the success rate of PV isolation for persistent AF.

Because the reported acute success rate for mitral isthmus linear ablation varies widely (31% to 92%) [5,7,9-11,20] and only a few studies report success rates > 85% [5,10], sometime with the use of high energy and a steerable sheath [20], alternative treatment strategies needs to be evaluated. In our study, very good results at the MIL (94%) and SSL (83%) were achieved by (1) extensive ablation (median 31 min of RF), (2) the use of a steerable sheath and (3) careful mapping. Of importance, the length of both ablation lines was assessed in all patients and for each line there was no difference between groups. This rules out an hypothetical bias in patients assignment to 1 of the 2 ablation strategies because of the presumed anatomical length of the planned ablation.

Performing the ablation in sinus rhythm leads to prompt recognition of preferential epicardial conduction after initial endocardial ablation at the MIL and due to epicardial fibers and/or increased thickness of the myocardium close to the mitral annulus [13] ablation inside the coronary sinus is often necessary [5,7]. In addition, a relatively quick switch from endocardial to epicardial ablation avoids unnecessary creation of endocardial edema that might render subsequent lesions ineffective.

Reported success rates for linear ablation at the superior LA septum (58 - 68%) [18,19] are lower than the ones observed in our study. In addition, most (5/6) failures in our study were seen in the first half of the study period and a relatively steep learning curve was seen

with a success rate that rose from 58% (7/12 pt) to 96% (22/23 patients) in the second half of the study period. The thickness and insertion width of Bachmann's bundle can represent a major challenge for catheter ablation, but understanding the importance of careful sinus rhythm mapping of its LA breakthrough, which always represented the area of residual conduction when bidirectional block was not achieved, significantly increased success. In fact, difficulties in achieving block can be overcome by moving the ablation line slightly more superolateral, above the insertion of the bundle (i.e. where a delay of at least 10 - 15 msec from the earliest activation point is seen in the sinus rhythm). The superior septum is often an area of lower voltage in sinus rhythm [1,2,18] and AF can frequently be terminated when RF lesions target complex fractionated electrograms at this level [15,16], therefore, ablation in this area should, in our opinion, increase success rates.

Successful ablation at the superior septum produces significant delay of LA appendage activation in sinus rhythm and a detailed electrophysiological (with activation mapping) and hemodynamic (with echocardiography) analysis of this phenomenon will be presented in a future manuscript. Whether this has consequences for long term arrhythmia recurrence or atrial function needs to be investigated.

Pulmonary vein isolation, linear ablation at the roof of the left atrium

Electrical isolation of all PVs, including adenosine-induced recovery of conduction, was achieved in all patients. The success rate of linear ablation at the LA roof was high (96%) and comparable to the most successful previous studies [6-10,14].

Procedure length

Our median procedure and RF times of 6 and 2 hours, respectively, are longer than in most recently published series (2 - 5 and 1 to 1½ hours, respectively) [8,9,11,18,19,21]. This is partly explained by (1) the study protocol which included the detailed collection of sinus rhythm activation maps of the LA before and after linear ablation and an echocardiographic evaluation to study the mitral inflow after PV isolation (median of 19 min to collect the maps and ≈ 10 min for the echocardiographic evaluation) and (2) the longer RF delivery approach for each anatomical site. However, for each step of the procedure, at least 60% and often 75% of the time was used for the ablation itself, making this approach time-effective. In addition, the median X-Ray time of 34 minutes is less than previously reported (39 - 73 min) in studies with shorter total procedure duration (2 to 5 hours) [8,9,11,18].

In hospital follow-up and complications

Before hospital discharge, only a minority of patients (4%, 3/70) required electrical cardioversion due to persistent episodes and treatment strategy did not influence the acute outcome. A pericardial effusion was common (49%, 34/70), although this was moderate (>5 but ≤ 20 mm) in only a minority (14%, 10/70) of patients, drainage was never necessary and only 4 patients required therapy (colchicine 0.5mg bid) due to pericarditis symptoms. The rapid clinical and echocardiographic resolution of the effusion without therapy in most suggests a reactive origin. Signs of post-procedural of hypervolemia, likely due to fluid overload during the procedure, were seen in 2 patients in the SSL group.

Mid-term follow-up

Despite the somewhat higher number of patients free from arrhythmic episodes in the SSL group, the difference between groups was not statistically different. Therefore, definitive conclusions about the superiority of 1 of the 2 lines cannot be drawn.

None of the 6 patients undergoing a second catheter ablation procedure at our institution was found having a gap at the SSL or MIL, presumably due to the ablation strategy combining extensive RF-delivery together with mapping/ablation carried out in sinus rhythm. Gaps at the roof line (n = 2) or at the cavotricuspid isthmus (n = 1) were seen and reconnection of ≥ 1 PV was relatively common. Interestingly, AT was the reason for recurrence in 64% (9/14) of patients. Four of them underwent a second procedure at our hospital and PV dependent AT was proved in 1 and suspected (absence of gaps at linear lesions) in 3 patients. This suggests that recurrence of ATs, following substrate modification with LA linear ablation and a high rate for bidirectional block, are not necessarily related to recovery of conduction and pro-arrhythmia (due to slow conduction) rate after the index procedure might be lower than previously thought.

Limitations

This was not a randomized study. However, 1:1 alternation for MIL and SSL was respected for all except 4 patients. Of importance, the absence of a bias in the assigned treatment strategy is demonstrated by similar length of each line between groups.

In addition, the study protocol included the collection of a detailed sinus rhythm activation map of the LA before and after linear ablation and all patients underwent echocardiography to study the mitral inflow after PV isolation. This has prolonged the procedure duration by ≈ 45 min and might have influenced the complication rate. In clinical practice, sinus rhythm activation mapping before SSL in order to localize and characterize Bachmann's bundle insertion might be limited to the anterior and septal wall and should then require less time.

The follow-up is still short, and this precludes definitive conclusions about which line should be preferred.

Conclusion

Ablation of the MIL shows a somewhat higher initial success but often requires extensive endo- and epicardial (within the coronary sinus) ablation. After completion of a relatively short learning curve, the SSL line is a good alternative for atrial substrate modification, showing equal acute and a trend for better midterm success rates, shorter RF/mapping time and avoiding epicardial ablation.

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