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Long-term impact of catheter ablation on arrhythmia burden in low-risk patients with paroxysmal atrial fibrillation: the CLOSE to CURE study

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TITLE PAGE

Full title

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Running title

CLOSE to CURE study

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Conflict of interest statement

Mattias Duytschaever, Jan De Pooter, Milad El Haddad and Yves Vandekerckhove report personal fees from Biosense Webster, outside the submitted work. The remaining authors have nothing to disclose.

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ABSTRACT

Background: Few studies evaluated the impact of catheter ablation (CA) on atrial tachyarrhythmia (ATA) burden in paroxysmal atrial fibrillation (AF).

Objective: In the prospective, patient-controlled CLOSE to CURE study we studied longer-term impact of optimized CA on ATA burden using insertable cardiac monitors (ICM).

Methods: 105 PAF patients were implanted with an ICM 65 [61-78] days before CA. CA consisted of contact force guided pulmonary vein isolation (PVI) targeting an intertag distance ≤6mm and a region-specific ablation index. Primary endpoint was reduction in ICM-detected ATA burden, secondary endpoints were single-procedure freedom from ATA, quality of life (QOL), and adverse events.

Results: Mean age was 62±8y, CHA_2DS_2-VASc score 1[1-2], left atrial diameter 43 [39-43] mm. After PVI (1.13±0.39 procedure per patient), ATA burden decreased from 2.68 [0.09-15.02] % at baseline to 0 [0-0] % during the first year and 0 [0-0] % during the second 2-year (reduction in ATA burden 100 [100-100] %, $p<0.001$). Single-procedure freedom from any ATA was 87% at 1 year and 78% at 2-year. QOL improved significantly across all scores. Adverse events occurred in 5 (4.8%) patients.

Conclusions: CA has become an effective procedure in paroxysmal AF with a major impact on ICM-detected ATA burden. Whereas conventional survival analysis suggests progressive decline in efficacy, we observed that burden reduction is maintained at longer follow-up. These data imply that ATA burden is a more optimal endpoint for assessing ablation efficacy.

Clinical Trial Registration: CLOSE to CURE, NCT02925624

KEYWORDS

Atrial fibrillation, ablation, pulmonary vein isolation, insertable cardiac monitor, burden

TEXT

Introduction

Catheter ablation (CA) is recommended in patients with drug-resistant symptomatic paroxysmal atrial fibrillation (PAF).(1,2) In PAF, pulmonary vein isolation (PVI) results in a 65% single-procedure one-year freedom from atrial tachyarrhythmia (ATA),(3-6) with progressive decline of efficacy over time and recurrence of ATA mainly due to non-durable PV isolation.(7)

Few studies evaluated the impact of PVI on ATA burden.(8,9) ATA burden, defined as % of time spent in ATA,(1,2,10) is associated with AF-related symptoms, heart failure and stroke.(11-15)

In the prospective, patient-controlled CLOSE to CURE (C2C) study we determine the longer-term impact of PVI on ATA burden in PAF. To reliably quantify ATA burden patients were implanted with an insertable cardiac monitor (ICM) at least 2 months before PVI. Ablation consisted of a point-by-point contact force (CF)-guided RF approach aiming to enclose the PVs with contiguous, stable and optimized RF lesions.(16-19)

Methods

Study design

The C2C study (NCT02925624) is a single-center, patient-controlled, prospective cohort study. Enrollment started July 2016 until July 2017 at the St Jan Hospital Bruges. Written informed consent was obtained before patient inclusion. The study was approved by the ethics review board.

Patient population

Patients were eligible if there was a history of symptomatic ECG-proven PAF (either resistant, intolerant or unwilling to take ADT) with at least ≥3 AF episodes (anamnestic or documented) in the last 3 months.

Exclusion criteria were persistent AF, prior AF ablation, left atrial (LA) diameter >50mm, ejection fraction <35%, AF secondary to reversible causes, unstable angina or uncontrolled heart failure, myocardial infarction or CABG within the last 3 months, awaiting cardiac surgery, diagnosed atrial myxoma or thrombus, acute illness, blood clotting or bleeding abnormalities, life expectancy <12 months, pregnant or breastfeeding women, and enrollment in any other study.

Implantation and programming of the ICM

All ICMs (Reveal LINQ^{TM}, Medtronic Inc.) were insertedover the 4th intercostal space, aiming for R-wave >0.3mV. Programming of ATA detection was standardized across patients (AF/AT detection: on; sensitivity: balanced; ectopy rejection: nominal; AF/AT recording threshold: all episodes). This algorithm, based upon R-R interval stability and P-wave detection, has an overall accuracy for AF detection of 99.4%.(20,21) Because the algorithm makes a rhythm classification within a 2-min window, the minimal length of an ICM-detected ATA is 2-min. To avoid memory overflow and loss of intracardiac electrograms, patients were asked to weekly transmit ICM data to the Medtronic Care Link® Network.

Mechanical and electrical properties of the LA

All patients underwent at baseline an advanced transthoracic echocardiographic study (Vivid E9, GE-Vingmed, Milwaukee,WI) to determine LA diameter (parasternal long-axis view), LA volume (Simpson's biplane method at end-systole) and LA strain function assessed by 2-

dimensional speckle tracking (EchoPAC, GE, Norway, version 110.2). Prior to PVI, we determined atrial refractoriness, AF inducibility, electrogram voltage, and intra-atrial conduction velocity. (22) An area of low voltage was defined as an area of >1cm^2 with <0.5mV.

Catheter ablation

PVI was performed by 6 operators. The CLOSE procedure was previously described in extenso.(17) By preference the procedure was performed under general anesthesia with an esophageal temperature monitor (SensiTherm™, St Jude Medical Inc, Minnesota, US). Further set-up consisted of a contact-force (CF) catheter (Thermocool SmartTouch ®, Biosense-Webster Inc., Diamond Bar, CA, USA) and a circular mapping catheter (CMC) (Figure 1, left panel). Identification of LA-PV junction was based upon anatomy, CF, CF vector, catheter jump during pull-back maneuvers, position relative to CMC, impedance and local electrogram characteristics. Maximal intertag distance was ≤6mm. In case of (pre-)procedural documentation of typical flutter, cavotricuspid isthmus (CTI) ablation was performed.

Study visits and follow-up after CA

Clinical visits, 12-lead ECG and ICM data review were performed at enrollment, at 1, 3, 6, 12, 18 and 24 months after CA or in case of symptoms. Three months after CA, ADT was stopped whereas anticoagulation was continued according to stroke risk. Quality of life (QOL) was assessed before and every 6 months after CA via the Short Form 36 Health Survey, (23) AF Symptom Checklist,(24) and EHRA symptom score. Repeat ablation was advised in case of symptomatic ATA recurrence and consisted of re-isolation or an empirical

trigger or substrate ablation.(18)

Primary endpoint

The primary endpoint, ICM-detected ATA burden, was defined as the % of time spent in ATA (hours of ATA/hours of monitoring) (Figure 2). ATA burden before PVI was compared to ATA burden during the first (excluding a 3-month window) and second year after PVI. All ICM-detected ATA episodes and their corresponding electrograms were revised on a weekly basis by two independent investigators (JDP, MD). This allowed to adjudicate false detection of ATA due to artefact, premature atrial or ventricular beats or sinus arrhythmia (Figure 2, upper panels). For data analysis, all true episodes and their duration were exported to a custom-made database (Figure 2, lower panels). This allowed to calculate for each patient the daily burden of ATA (black bars) and the relative time spent in ATA (%).

Secondary endpoints

Secondary endpoints included alternative measures of ATA burden: ATA burden before adjudication (according to raw ICM data), proportion of patients with reduction in ATA burden (by >50%, >75%, >90% and >95%) and with residual ATA burden >0.5% after CA. In addition, we calculated for each patient the number of days characterized by ATA using different cut-offs i.e. daily burden of ≥2-min, ≥1-hour, ≥6-hours or 24-hours.

Other secondary endpoints were single-procedure freedom from any ICM-detected ATA (≥2-min) at 1 and 2 years, QOL among the different scores and ablation-related adverse events.

Sample size and statistical analysis

Normality of data distribution was tested with Shapiro-Wilk test. Continuous variables were

expressed as mean with standard deviation or medians with interquartile range throughout the manuscript. Dichotomous variables were expressed as frequency (%). Group comparisons for continuous variables were performed using the paired T test or paired Wilcoxon Signed Rank test. Group comparisons for categorical variables were performed using the Chi square test. Kaplan–Meier survival curves were used to assess time to first documented ATA recurrence.. For analysis of QOL, SF 36 data were normalized.(23-25) Statistical significance was set at 0.05 for two tailed tests.

For analysis of ATA burden, data were given for all patients (n=105) and for those patients with actual ICM-detected ATA during the baseline monitoring period (n=84). Simple linear regression models using baseline variables were calculated to predict ATA burden after PVI. A multivariable analysis was performed adjusting for potentially confounding variables by selecting variables with at least $p < 0.2$ from the univariable analysis. All analysis was performed using SPSS software (Version 23.0, IBM, Armonk, NY, US).

Results

Clinical characteristics

The study included 105 patients (Table 1). The median number of monitoring days was 65 [61-78] days. Overall, 21 patients did not reveal any ATA episode during monitoring. In these patients the time from diagnosis to CA was 9.0 [6.5-20] months and the last ECG documented-AF episode was 17 [9-28] days before enrollment.

Mechanical and electrical properties of the LA

Results are summarized in Supplemental Figure 1. In 10 patients (9.5%) we observed a low-voltage area. During premature stimulation, self-terminating ATA was induced in 8 patients

(7.6%).

Procedural characteristics of CA and follow-up

Results are given in Table 1. All patients except one were discharged the day after CA. Within the two-year follow-up period, 0 patients received a class IC or III antiarrhythmic drug or cardioversion, 14 patients received a repeat procedure at 150 [100-513] days after PVI.

Primary endpoint: ATA burden before and after ablation

Results for ATA burden for the entire study population are given in the upper panels of Figure 3. After PVI (1.13±0.39 procedure per patient throughout 2 year follow-up), ATA burden decreased from 2.68 [0.09-15.02] % at baseline to 0 [0-0] % during the first year (reduction in ATA burden 100 [100-100] %, $p<0.001$, left panel) and 0 [0-0] % during the second 2-year (reduction in ATA burden 100 [100-100] %, $p<0.001$, right panel). Burden reduction was seen both in patients without (black bars) and with any 2-min ATA recurrence (red and green bars). None of the patients progressed to persistent AF after CA. Results for the subset of 84 patients with documented ATA during the monitoring period were similar (Figure 3, lower panels).

Secondary ATA burden-related endpoints

Results for the 84 patients are given in Table 2. ATA burden without adjudication decreased from 6.61 [1.80-19.00] % to 0 [0-0.03] % during the first 12 months after PVI and to 0 [0-0.03] % during the second year ($p<0.001$ for both). The proportion of patients with >95% reduction in ATA burden was 94% and 96% at 1 and 2-y FU. Finally, throughout the first and second year after ablation, only 5 (6%) and 1 (1%) had a residual ATA burden >0.5%.

In Supplemental Figure 2, we plotted the AF calendar plots for the entire study population. Of interest, of the 14 patients with ATA during the first year, only 4 patients showed ATA during the second year. Vice versa, of the 13 patients with ATA during the second year, only 4 patients showed ATA during the first year.

A significant but weak regression was found between ATA burden after PVI and ATA burden before PVI (Supplemental Table 1). In a multivariable model during the 1st year adjusting for both ATA burden before PVI and male gender, only ATA burden before PVI remained statistically significant.

Single-procedure, off ADT freedom from ATA

In Figure 4we plotted the time to the first day with any 2-min ATA for the entire population (blue curve) and subpopulation (red curve). Single-procedure, off-ADT freedom from any ATA declined from 87% after 1 year to 78% after 2 years (p = 0.343).

Quality of Life

Results are summarized in Table 3. Physical and mental Health SF36 score, symptom frequency and severity scores, and EHRA score all improved significantly at 1 and 2 year ($p<0.001$). Improvement in QOL was comparable among patients with and without ATA recurrence.

Safety

Ablation-related adverse events were observed in 5 patients (4.7%): three patients with groin-site hematoma (all treated conservatively by mechanical pressure), one patient with femoral pseudoaneurysm (requiring surgery) and one patient with symptomatic left PV stenosis

(treated with percutaneous stenting at 104 days after PVI with resolution of symptoms throughout 2-year FU). In none of the patients undergoing repeat ablation narrowing of PVs was observed.

Discussion

Main Findings

The C2C study shows that a optimized CA results in a major overall reduction in ICM-detected ATA burden in patients with PAF. Whereas survival analysis based upon freedom from any ATA recurrence suggests progressive decline of efficacy over time, the impact of CA on ATA burden is maintained at longer-term FU. These data imply that ATA burden is a more optimal endpoint for assessing ablation efficacy. These data imply that ATA burden is a more optimal endpoint for assessing ablation efficacy.

PAF patients in the C2C study

In the present study, patients were relatively young, with limited structural heart disease, low stroke risk, near-normal left atrial diameter and relatively shorttime from diagnosis to CA. This low-risk clinical profile does not differ from the PAF patient enrolled in CA trials,(3-6) or from patients referred for CA in real-life.(26,27). Likewise ATA burden and its variation (median 2.68%) is not different from prior studies reporting on ATA burden in PAF.(8,9,14,28) Finally, C2C patients were characterized by left atrial electrical and mechanical properties in line with prior studies in PAF.(2-32). All together, above data suggest that the C2C population reflects the relatively young, symptomatic and otherwise relatively healthy patient referred for ablation of PAF both in studies and real-life.

Effect of catheter ablation on ATA burden

Efficacy of CA is commonly expressed as single-procedure freedom from any ATA (>30s).(1) This definition (in which one single, even short episode implies permanent failure) most likely underestimates clinically relevant success after CA.(1) In this regard, ATA burden, defined as % of time spent in ATA, seems a more reliable estimate of clinically relevant success after CA.(1,2,10) Indeed, prior studies suggested a dose-effect relation between ATA burden and symptoms, heart failure and stroke.(11-15) Glotzer et al showed that a ≥20% ATA burden was associated with a double stroke risk(14), whereas Go et al showed that only a ≥11.4% AF burden was associated with a >3-fold higher adjusted rate of thromboembolism in PAF patients.(13)

A limited number of prospective studies reported on patient-controlled ATA burden after CA. In the DISCERN AF study, CA reduced meanICM-detected ATA burden from 8.3% to 1.25% after 18 months.(9) In MANTRA-PAF, CA reduced estimated ATA burden from a 90th ATA burden of 30% to 13% throughout the first 24 months.(27) In the CAPTAF study, CA reduced ICM-detected ATA burden from 24.9±37% to 5.5±18.1% at 12 months ($p<0.001$), not different from medical therapy.(8)

In the present C2C study, optimized CA had a marked and maintained impact on ATA burden. (with a low number or repeat procedures and without ADT). In a PAF population in which one quarter of the patients presented with ATA burden >15.02%, median ATA burden in the 1st two years after CA was 0 [IQR 0-0] % (Figure 3) and also in patients with some ATA recurrence, ATA burden was significantly reduced (because episodes were short-lasting and isolated in nature). The good results of the C2C study, most likely, are explained by durable PV isolation,(19) rather than patient selection. Also an early intervention strategy during the first year from AF diagnosis (although performed in only 26% of patients) might

contribute to improved outcome. Whether reduction in ATA burden by CA might impact AF-related morbidity and mortality requires further study, especially in a sicker population. Marrouche et al recently showed that reduction of burden improves outcome in heart failure patients.(15) Likewise, reduction of burden might improve symptoms,(11,12) and reduce stroke.(13,14)

Single-procedure freedom from ATA, QOL, and safety after CA for PAF

In the C2C study single-procedure freedom from any ATA was ≈85% at 1-year. This relatively high success rate (in the setting of continuous monitoring)(33) is in line with 1) data from the CLOSE-PILOT study,(17) 2) prior studies reporting a ≈90% 1-year success rate after multiple PVI procedures,(3,4) and 3) the knowledge that non-PV triggers account for ≈10% of PAF.(34) The C2C data at 2-year (suggesting decline in efficacy as previosuly reported) (7) however underscore that this definition of success is not optimal to describe longer-term efficacy of CA.

Prior studies showed that CA improves QOL in AF patients, especially but not exclusively in patients free from ATA.(3,5,6) Recent studies showed that residual ATA burden (i.e. >4% assessed by Holter; or >0.5% assessed by ICM) determines poor QOL after CA.(11,12) Also in the CAPTAF study, general health was related to actual ATA burden.(8) Due to the low residual burden after CA in the C2C study, QOL significantly improved both in patients with and without ATA recurrence.

The C2C study confirms the overall safety profile of CA.(3-6) Whereas we did not observe death, stroke or tamponade, there was a limited number of groin-site hematomas, one pseudoaneurysm and one PV stenosis requiring stenting. None of the patients undergoing repeat ablation revealed PV narrowing. The safety profile is in line with prior observations after CLOSE-PVI.(17,35) Moreover, improvement in safety is underappreciated because

safety of CA also depends on the number of repeat procedures required for durable isolation.

Implications of the present study

(1) The C2C study shows that PVI, if meticulously performed, markedly impacts ATA burden on the longer-term. It suggests that any novel CA strategy resulting in durable isolation will have similar impact; (2) Despite a class I indication, despite superiority over ADT,(3,5,6) and excellent outcome after CA combined with ADT,(24) there is underutilization and late referral of ablative therapy in PAF. The current longer-term data may lower the threshold for CA; (3) Finally, C2C data suggest that ATA burden may be a more useful measure of the outcome of the ablation than to censor an ablation as a failure after a single 30-second recurrence as is currently recommended by the guidelines(1). Because of the short duration of false-positive ATA episodes, ATA burden is not sensitive to adjudication. Because of the shorter and isolated nature of late recurrences, ATA burden (in contrast to survival analysis) is more appropriate to assess longer-term efficacy of CA. In this regard, C2C analysis can serve as a methodological guide for future studies on ATA burden, either assessed by implanted or wearable devices.

Limitations

(1) Despite the importance of patient-controlled data, present results require confirmation by multi-centric large studies; (2) ATA burden is dependent on the accuracy of ICM detection. Although one can correct for false positive ATA and although adjudication did not affect results on ATA burden, one cannot correct for false negative findings (like asymptomatic AT with slow regular ventricular rate); (3) We did not advise patients to record symptoms in a

standardized diary. Therefore the C2C study is less suited to address the issue of symptomatic vs asymptomatic ATA.(9,10); (4) Finally, 21 patients did not have ICM-documented ATA during the monitoring phase. The fact that those patients had a median time from diagnosis to CA of 9.0 [6.5-20] months together with at least 3 episodes before enrollment favors the hypothesis that absence of ATA is the result of the probabilistic nature of PAF rather than spontaneous resolution of the arrhythmia.

Conclusions

We observed that CA aiming for durable pulmonary vein isolation markedly reduces ATA burden assessed by insertable cardiac monitors; in a PAF population in which one quarter of the patients presented with ATA burden >15.02%, median ATA burden in the first two years after CA was 0 [IQR 0-0] %. Finally, our data make a strong case that the "survival" approach to assessing efficacy with time to first recurrence underestimates the benefit of ablation in reducing burden.

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FIGURES LEGEND

Figure 1: Catheter ablation

Left panel: Fluoroscopic image showing position of the circular mapping catheter and ablation catheter during CA. Right panel: Tags are represented color-coded according to ablation index target.

Figure 2: Analysis of atrial tachyarrhythmia burden

Determining atrial tachyarrhythmia (ATA) burden from the insertable cardiac monitor.

Figure 3: ATA burden plot before and after catheter ablation

Plots showing the % of time spent in ATA during the first and second year compared to baseline in the entire population (upper panels) and subpopulation (lower panels). Each line represents an individual patient. Patients are arranged by recurrences during follow-up, ranging from greatest (bottom) to fewest (top). The horizontal axis is artificially truncated at 30%.

Figure 4: ATA-free survival plot

Kaplan-Meier curves depicting time to first recurrence of any ATA during the first 2 years after PVI (blue curve: entire study population; red curve: 84 patients).

TABLES

Table 1: Baseline and procedural characteristics (n = 105)

Baseline characteristics	
Age, yrs	62±8
Male gender, n(%)	65(62)
BMI, kg/m2	27±4
CHA_2DS_2-VASc-score, median[IQR]	1[1,2]
Arterial hypertension, n(%)	35(33)
Diabetes, n(%)	8(8)
Structural heart disease, n(%)	13(12)
Coronary artery disease, n(%)	11(10)
Valvular heart disease, n(%)	2(2)
Paroxysmal AF, n(%)	105(100)
Time from 1st AF episode to PVI (months), median[IQR]	15[9,28]
Left atrial diameter (mm), median[IQR]	43[39,43]
Left atrial volume, ml	84±22
ADT resistant, n(%)	63(60)
ADT intolerance or unwillingness, n(%)	42(40)
Procedural characteristics	
General anaesthesia, n(%)	102(97)
Procedure duration, min	143±31
Isolation of all PVs, n(%)	105(100)
Additional ablation of CTI, n(%)	6(6)
First pass isolation right circle, n(%)	98(93)
First pass isolation left circle, n(%)	101(96)
Adenosine challenge performed, n(%)	97(92)
Adenosine proof isolation, n(%)	93(96)
RF energy, number of applications	59±11
RF energy, total time of delivery, min	28±6
DAP, mGy/cm²	4769±3378

Table2: ATA burden before and after PVI (n=84)

	ATA burden before PVI	ATA burden throughout 3-12 months after PVI	ATA burden throughout 12-24 months after PVI	P value
ATA burden (relative time spent in ATA), unadjudicated %	6.61 [1.80, 19.00]	0 [0, 0.03]	0 [0 0.03]	<0.001*
ATA burden (relative time spent in ATA), %	6.56 [1.71, 17.24]	0 [0, 0]	0 [0, 0]	<0.001*
Reduction in ATA burden, %	-	100 [100, 100]	100 [100, 100]	
Proportion of patients with reduction in ATA burden, n (%)				
By >50%	-	82/84 (98)	82/84 (98)	-
by >75%	-	81/84 (96)	81/84 (96)	-
by >90%	-	79/84 (94)	81/84 (96)	-
by >95%	-	79/84 (94)	81/84 (96)	-
Proportion of patients with ATA burden after PVI, n (%)				
> 0.5 and ≤1 %	-	1 (1)	0 (0)	-
> 1 and ≤5 %	-	3 (3)	1 (1)	-
> 5 and ≤10 %	-	0 (0)	0 (0)	-
> 10%	-	1 (1)	0 (0)	-

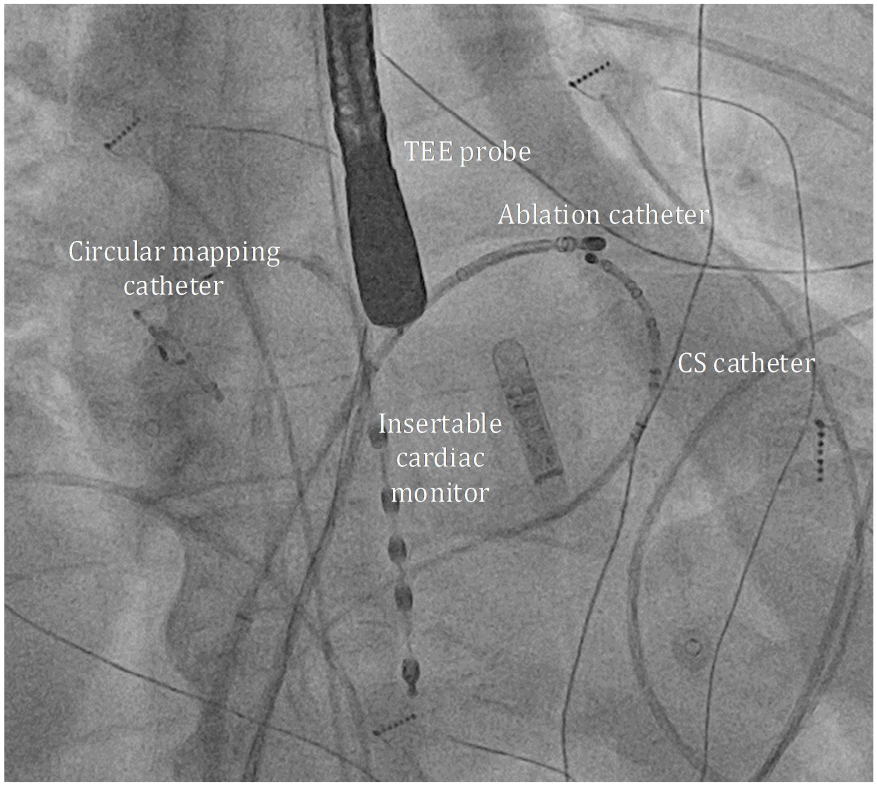
*** Applies to ATA before PVI vs 3-12M and to ATA before PVI vs 12-24M. Data is given as median [IQR].**

Table 3: Quality of Life assessment before vs after PVI

	At baseline before PVI	At 12 months after PVI	P value	At 24 months after PVI	P value
SF 36 normalised scores					
Physical health score	47.6±7.4	51.0±6.8	<0.0001	49.45±7.96	0.192
N of fully completed forms	97	95		96	
Mental health score	48.7±9.1	52.1±7.9	0.002	52.16±8.31	<0.001
N of fully completed forms	97	95		96	
Symptoms scores					
Symptoms frequency score	18.3±8.7	9.8±7.4	<0.0001	10.76±8.50	<0.0001
N of fully completed forms	102	99		102	
Symptoms severity score	13.9±7.4	7.12±7.0	<0.0001	7.81±7.30	<0.0001
N of fully completed forms	95	93		96	
EHRA score					
Median score [IQR]	3[2,3]	1[1,1]	<0.001	1[1,1]	<0.001

FIGURES

Figure 1:



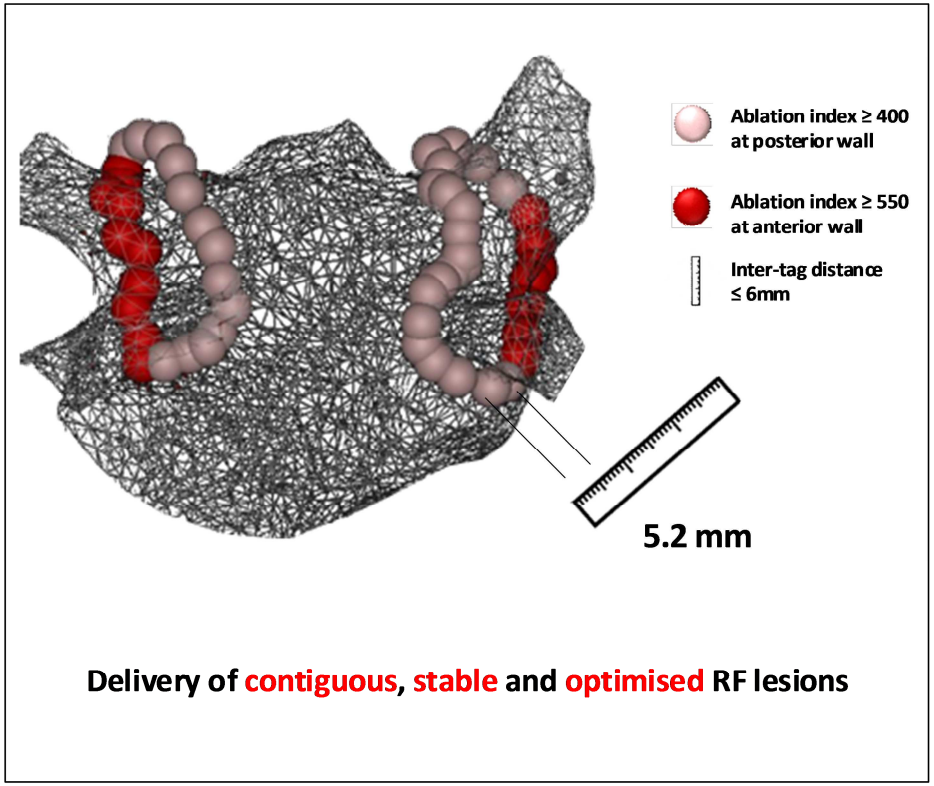


Figure 2:

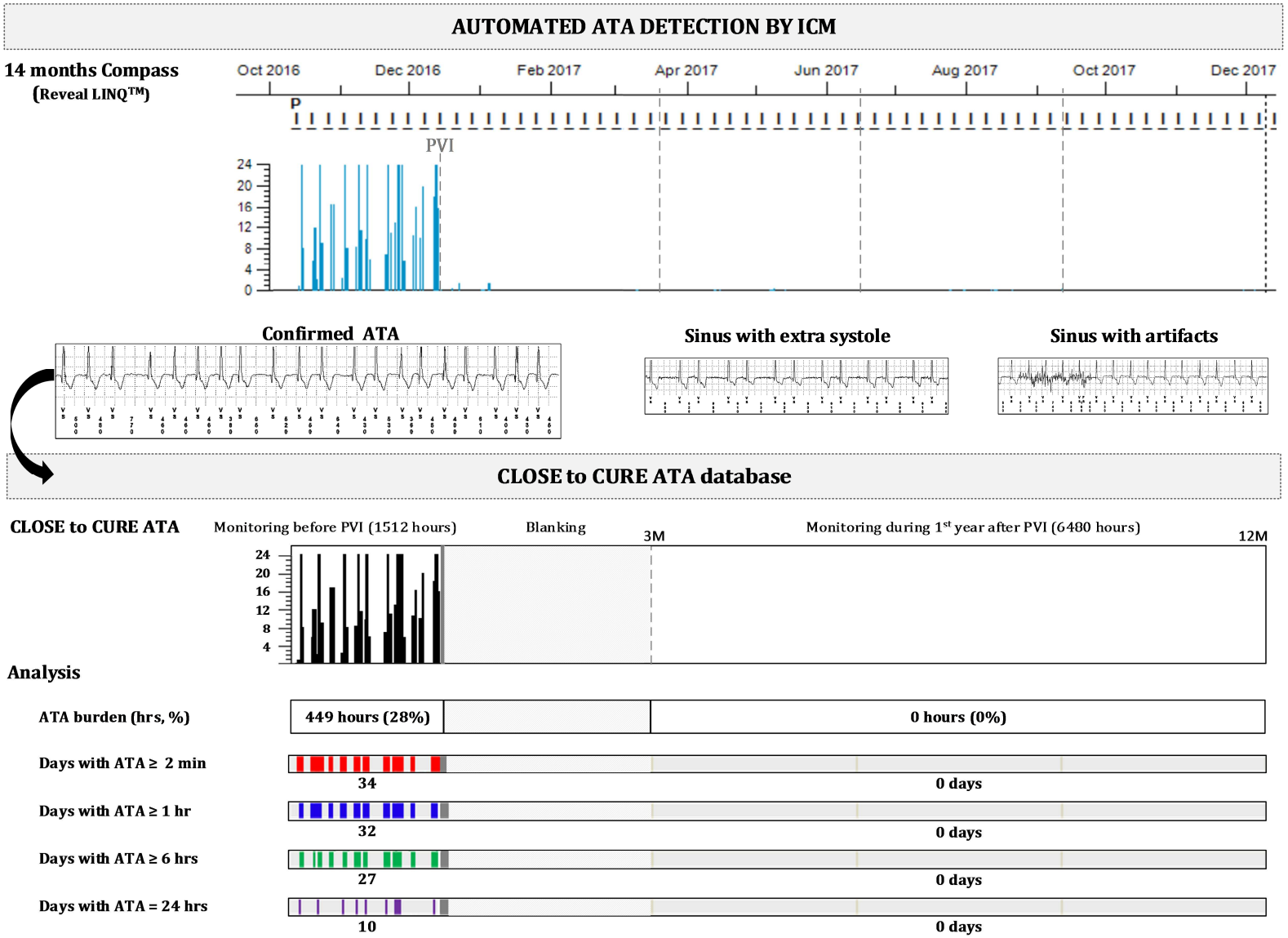

AUTOMATED ATA DETECTION BY ICM
14 months Compass
(Reveal LINQ™)
Oct 2016
Dec 2016
Feb 2017
Apr 2017
Jun 2017
Aug 2017
Oct 2017
Dec 2017
P
PVI
24
20
16
12
8
4
0
Confirmed ATA
Sinus with extra systole
Sinus with artifacts
CLOSE to CURE ATA database
CLOSE to CURE ATA
Monitoring before PVI (1512 hours)
Blanking
3M
Monitoring during 1st year after PVI (6480 hours)
12M
Analysis
ATA burden (hrs, %)
449 hours (28%)
0 hours (0%)
Days with ATA ≥ 2 min
34
0 days
Days with ATA ≥ 1 hr
32
0 days
Days with ATA ≥ 6 hrs
27
0 days
Days with ATA = 24 hrs
10
0 days

Figure 3:

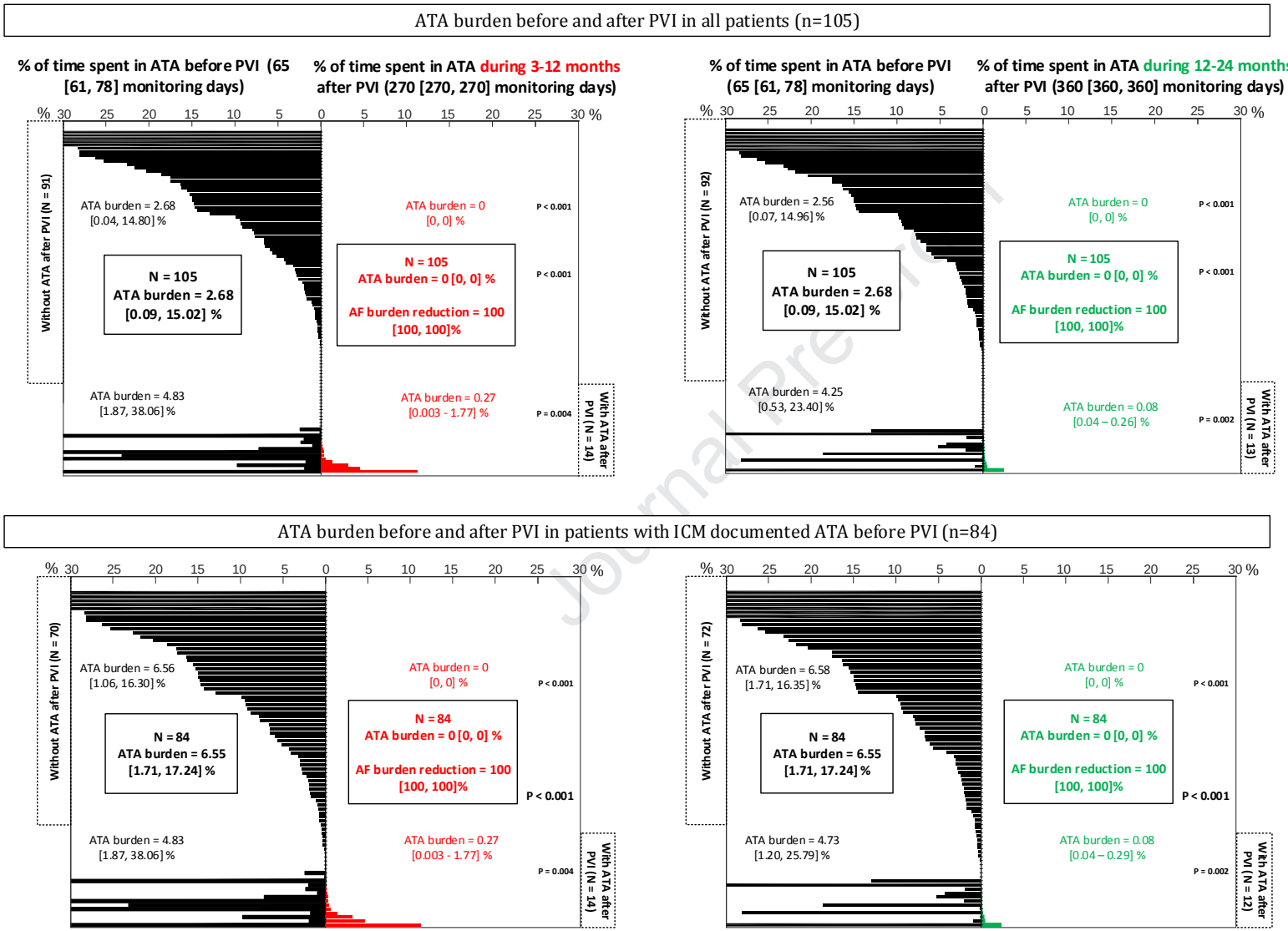
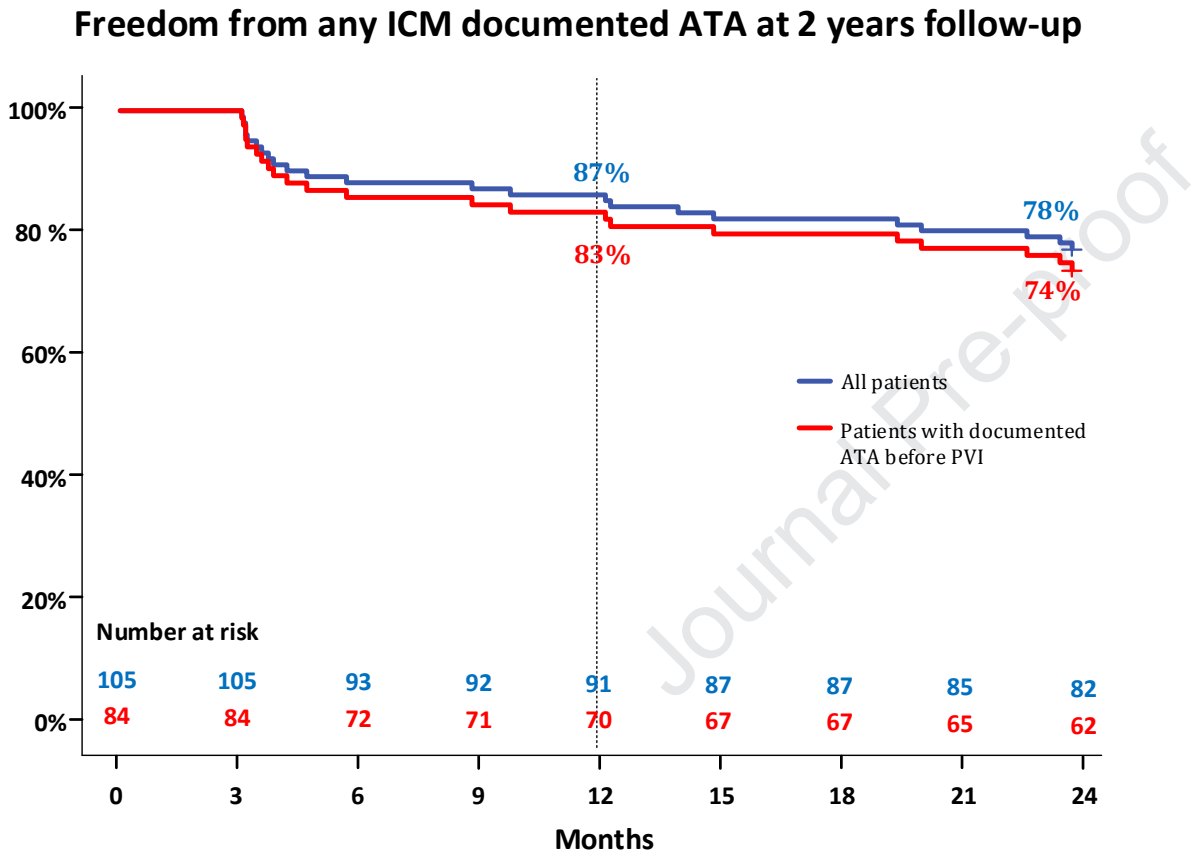
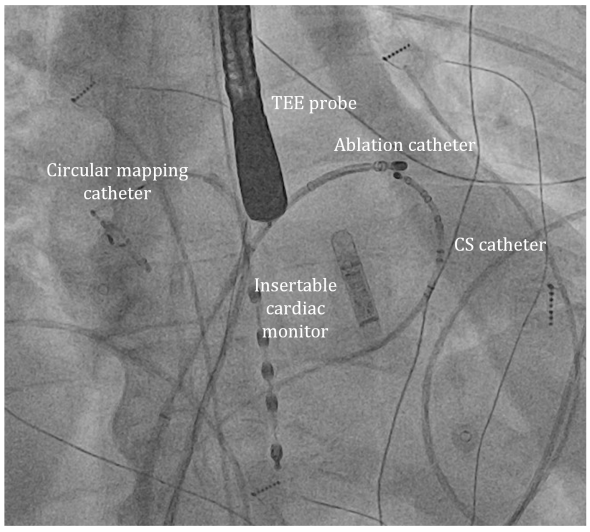
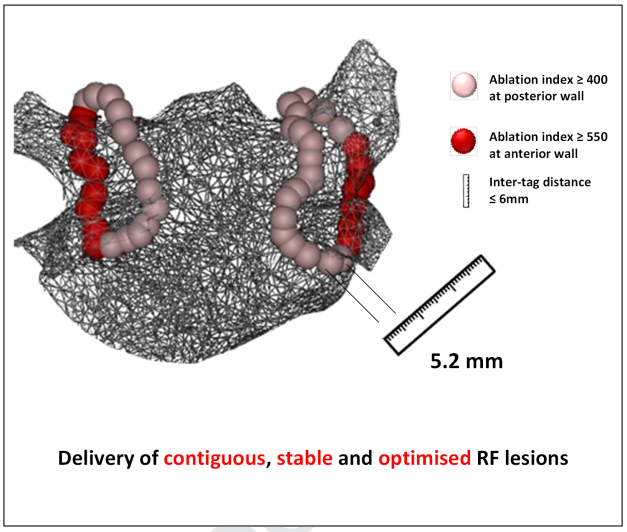
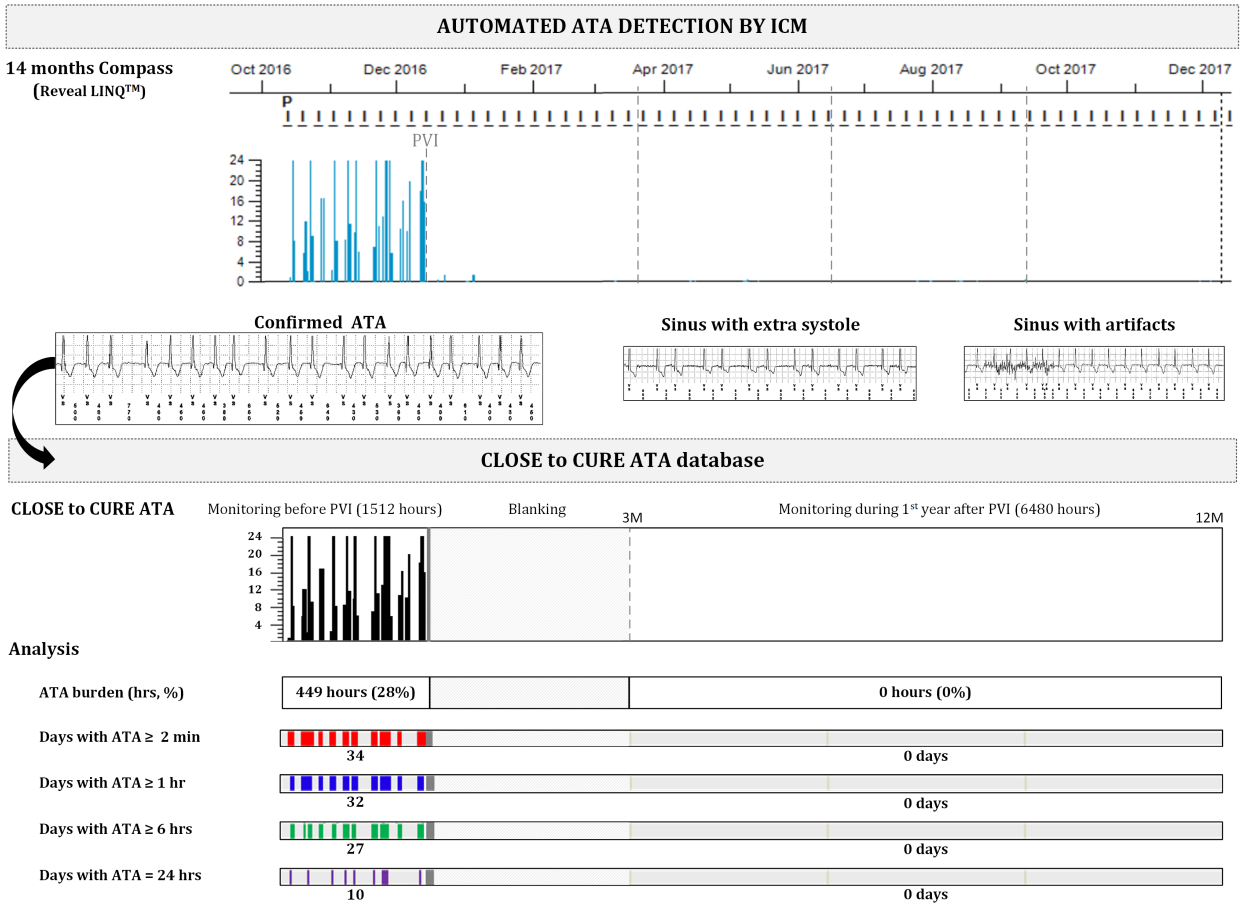

ATA burden before and after PVI in all patients (n=105)
% of time spent in ATA before PVI (65 [61, 78] monitoring days)
% of time spent in ATA during 3-12 months after PVI (270 [270, 270] monitoring days)
% of time spent in ATA before PVI (65 [61, 78] monitoring days)
% of time spent in ATA during 12-24 months after PVI (360 [360, 360] monitoring days)
Without ATA after PVI (N = 91)
With ATA after PVI (N = 14)
Without ATA after PVI (N = 92)
With ATA after PVI (N = 13)
ATA burden = 2.68 [0.04, 14.80] %
N = 105
ATA burden = 2.68 [0.09, 15.02] %
ATA burden = 0 [0, 0] %
N = 105
ATA burden = 0 [0, 0] %
AF burden reduction = 100 [100, 100]%
ATA burden = 4.83 [1.87, 38.06] %
ATA burden = 0.27 [0.003 - 1.77] %
ATA burden = 2.56 [0.07, 14.96] %
N = 105
ATA burden = 2.68 [0.09, 15.02] %
ATA burden = 0 [0, 0] %
N = 105
ATA burden = 0 [0, 0] %
AF burden reduction = 100 [100, 100]%
ATA burden = 4.25 [0.53, 23.40] %
ATA burden = 0.08 [0.04 – 0.26] %
P < 0.001
P < 0.001
P = 0.004
P < 0.001
P < 0.001
P = 0.002
ATA burden before and after PVI in patients with ICM documented ATA before PVI (n=84)
Without ATA after PVI (N = 70)
With ATA after PVI (N = 14)
Without ATA after PVI (N = 72)
With ATA after PVI (N = 12)
ATA burden = 6.56 [1.06, 16.30] %
N = 84
ATA burden = 6.55 [1.71, 17.24] %
ATA burden = 0 [0, 0] %
N = 84
ATA burden = 0 [0, 0] %
AF burden reduction = 100 [100, 100]%
ATA burden = 4.83 [1.87, 38.06] %
ATA burden = 0.27 [0.003 - 1.77] %
ATA burden = 6.58 [1.71, 16.35] %
N = 84
ATA burden = 6.55 [1.71, 17.24] %
ATA burden = 0 [0, 0] %
N = 84
ATA burden = 0 [0, 0] %
AF burden reduction = 100 [100, 100]%
ATA burden = 4.73 [1.20, 25.79] %
ATA burden = 0.08 [0.04 – 0.29] %
P < 0.001
P < 0.001
P = 0.004
P < 0.001
P < 0.001
P = 0.002

Figure 4:





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Analysis
ATA burden (hrs, %)
449 hours (28%)
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Days with ATA = 24 hrs
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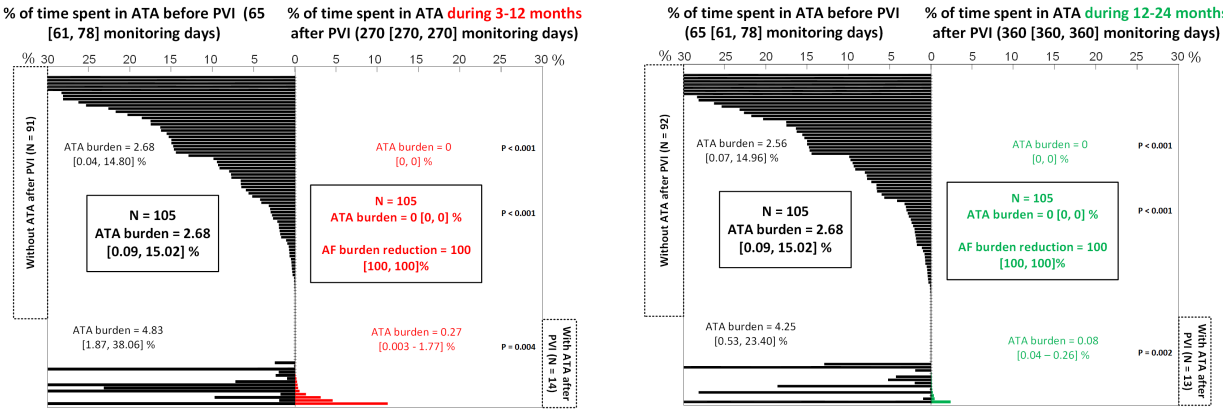
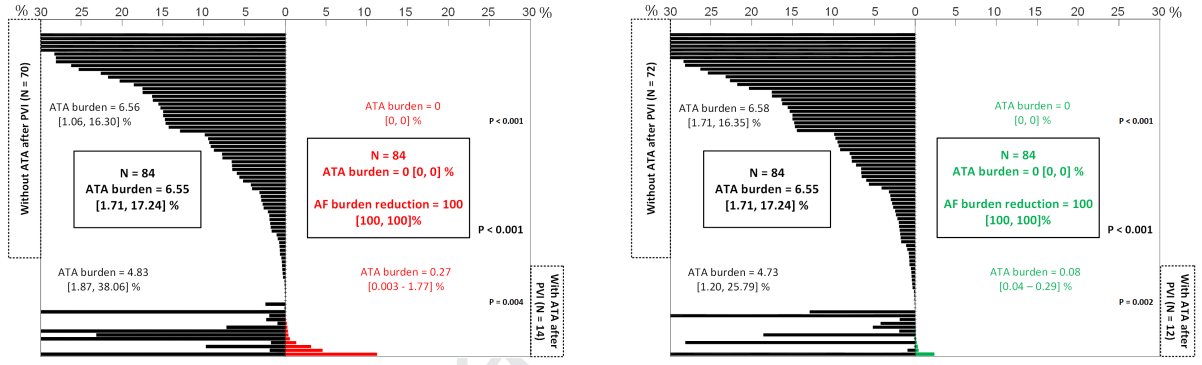
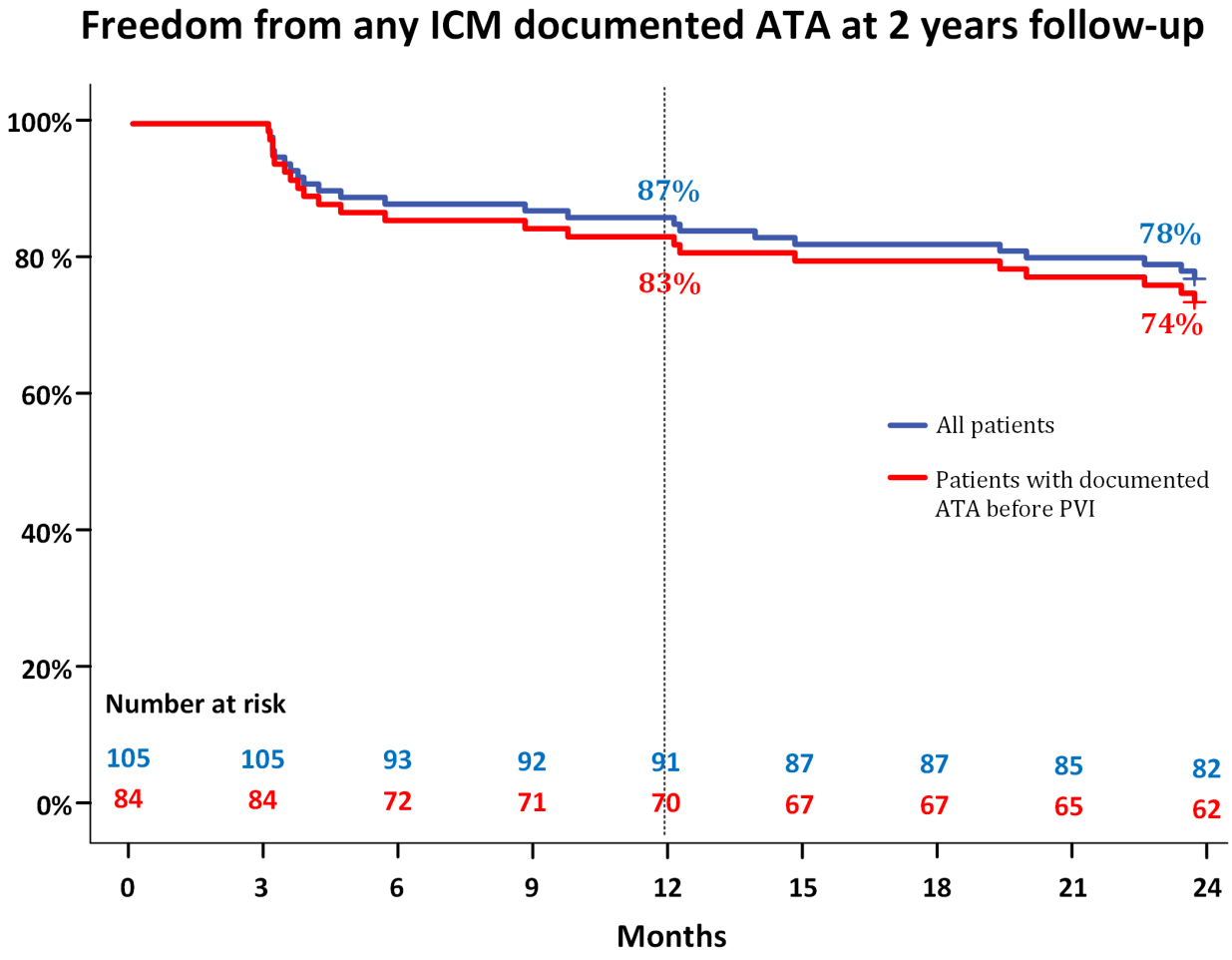
0 days

ATA burden before and after PVI in all patients (n=105)



ATA burden before and after PVI in patients with ICM documented ATA before PVI (n=84)




Freedom from any ICM documented ATA at 2 years follow-up
100%
80 %
60%
40%
20%
0%
87%
78%
83%
74%
All patients
Patients with documented ATA before PVI
Number at risk
105 105 93 92 91 87 87 85 82
84 84 72 71 70 67 67 65 62
0 3 6 9 12 15 18 21 24
Months