Characterization of atrial arrhythmias following mitral valve repair: incidence and risk factors

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Characterization of atrial arrhythmias following mitral valve repair: Incidence and risk factors

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Abstract

Objectives: This study aims to investigate the occurrence, type and correlation of early and late atrial arrhythmias following mitral valve repair in patients with no preoperative history of atrial arrhythmias.

Methods: Patients undergoing mitral valve (MV) repair for degenerative disease were included. Early and late postoperative electrocardiograms were evaluated for the incidence and type of atrial arrhythmia (atrial fibrillation [AF] or atrial tachycardia [AT]).

Results: The 192 patients were included. Early atrial arrhythmias occurred in 100/192 (52.1%) patients; AF in 61 (31.8%) patients, early AT in 15 (7.8%) and both in 24 (12.5%). In total 89% of patients were discharged in sinus rhythm. During a follow-up time of 7.3 years, 14 patients (7.3%) died and 49 (25.5%) patients developed late atrial arrhythmias. At 10 years, the cumulative incidence of any late atrial arrhythmia, with death as competing risk, was 64% (95% confidence interval [CI] = 55%–72%). On Fine-Gray model analysis, only early postoperative AF lasting >24 h was related to the development of late AF (hazard ratio 5.99, 95% CI = 1.78%–20.10%, $p = .004$). Early postoperative ATs were related to the development of late tachycardias, independent of their duration (<24 h hazard ratio 4.25, 95% CI = 1.89–9.57, $p = .001$ and >24 h hazard ratio 3.51, 95% CI = 1.65–7.46, $p = .001$).

Conclusions: Early and late atrial arrhythmias were common after MV repair surgery. Only early postoperative AF lasting >24 h was a risk factor for the occurrence of late AF. Conversely, any postoperative AT was correlated to the development of late ATs.

KEYWORDS
atrial arrhythmia, atrial fibrillation, cardiac surgery, mitral valve repair

Abbreviations: AA, atrial arrhythmia; AF, atrial fibrillation; AT, atrial tachycardia; CI, confidence interval; ECG, electrocardiogram; HR, hazard ratio; IQR, interquartile range; MV, mitral valve; POAF, postoperative atrial fibrillation; SD, standard deviation.

Sulayman el Mathari and Anton Tomšič shared first authorship.

1 | INTRODUCTION

Postoperative atrial arrhythmias (AAs), occurring both early and late after cardiac surgery, are common complications associated with increased morbidity and mortality.[1–3] Following valvular surgery, up to 60% of patients experience early postoperative AAs, with atrial fibrillation (AF) being the most prevalent type.[4,5]

In addition to AF, patients can experience atrial tachycardias (ATs).[5] This may be especially relevant in patients undergoing mitral valve (MV) repair by transseptal approach since the surgical incisions performed at the right atrium and the interatrial septum may facilitate the occurrence of macro-reentrant AT.[6–8] Of importance, ATs are not always self-terminating and may expose patients to thromboembolic and bleeding complications.[9,10] Moreover, the long-term clinical course of AT may differ from AF. In current literature, limited data on the precise characterization of early and late AAs after MV surgery exists.[11] As the pathophysiologic background, clinical consequences and treatment options may differ significantly between different subtypes of AAs, further research is warranted.

To address these knowledge gaps, the aims of the present study were to explore the incidence of early and late AAs following MV repair surgery in patients suffering from MV regurgitation without prior history of AAs, to characterize different types of AAs following MV repair surgery in this patient population and to investigate prognostic factors related to the occurrence and prognosis of AAs.

2 | METHODS

2.1 | Study population

Consecutive adult patients who underwent surgical repair for severe degenerative MV regurgitation between January 2010 and December 2019, at Leiden University Medical Centre, who no documented history of AAs, were included. All available clinical and rhythm documentation before surgery was reviewed. Patient characteristics and details regarding the surgical procedures were collected from patient electronic files and surgical reports.

2.2 | Study definitions

AAs were classified as AF or AT. AF was defined as an AA with no discernible repeating P waves and irregular RR intervals, and AT as a sustained regular atrial rhythm with a rate ≥100/min originating from outside the sinus node region.[12,13]

Early postoperative AF (POAF) and early ATs were defined as events that took place within a period of 30 days after surgery. Late AAs were defined as arrhythmias occurring after this period. For the purpose of this study, both POAF and early ATs were categorized based on their duration and clinical presentation:

- Lasting <24 h with either spontaneous termination or after administration of antiarrhythmic drugs,
- Lasting >24 h or needing electrical cardioversion.

The diagnosis of AF or AT was based on twelve-lead electrocardiogram (ECG) registrations that were obtained during the postoperative admission period, as well as during follow-up visits in the outpatient clinic. All available rhythm documentation was reviewed by experienced electrophysiologists (M.R.S. and A.P.W.).

2.3 | Surgical procedure

The MV was exposed by a transseptal approach, starting with a vertical incision of the right atrium. The type of leaflet repair and annuloplasty device implantation was left at the discretion of the operating surgeon. Anterior MV leaflet prolapse was treated predominantly by implantation of artificial neochords. For posterior MV leaflet prolapse, a combination of chordal replacement and leaflet resection techniques were used. Commissural prolapse was treated by commissural closure, chordal replacement, or papillary muscle head repositioning.

Tricuspid valve repair was performed in the presence of ≥grade 2+ tricuspid regurgitation and/or significant annular dilation. Coronary artery bypass grafting (typically performed in patients with no clinical manifestation of coronary artery disease in whom a significant stenosis was found on preoperative coronary angiography) and other concomitant procedures were performed in accordance to the respective guidelines. The type of concomitant procedures performed did not influence the surgical approach to the MV.

2.4 | Postoperative rhythm management

After surgery, continuous cardiac rhythm monitoring was applied using telemetry for the initial five postoperative days. Subsequent to this period, an ECG was performed daily or in case of symptoms suggestive for arrhythmias, until the patients' discharge from the hospital. In the absence of bradycardia, conduction abnormalities or other contraindications, patients were administered sotalol (dosage 120 milligram/day, divided in three doses) for prophylaxis of POAF from postoperative Day 1. If postoperative AAs were observed, the dosage of sotalol was increased. If conversion to sinus rhythm was not achieved within 24 h using medical treatment, electrical cardioversion (ECV) was considered. Postoperative anticoagulation regimen consisted of 3 months of vitamin K antagonist treatment with a target international normalized ratio of 2.0–3.0. Following hospital discharge, heart rhythm surveillance was continued during outpatient clinical follow-ups, utilizing either ECG or Holter, when indicated. Standard postoperative patient follow-up protocol included outpatient clinic appointments at 1 month, 3 months, and 1 year after the procedure and every 1 year thereafter.

2.5 | Study endpoints

The primary endpoint of the study was freedom from any late AAs. Secondary endpoints were overall survival, freedom from early and late AF and freedom from early and late AT.

2.6 | Statistical analysis

Continuous data are presented as mean (standard deviation [SD]) or median and interquartile ranges (IQR). The normality of distribution was tested with the Shapiro-Wilk test. Categorical data are represented as counts and percentages. Overall survival rate was calculated by means of Kaplan-Meier analysis. Between groups differences were estimated with the log-rank test. Cox proportional hazard regression survival analysis was performed to analyse risk factors for mortality. First, a univariable analysis was performed; covariates with a *p* value of <.10 at univariate analysis were included in the multivariable model with a backward selection method. Early postoperative ATs and POAF were forced into the multivariable model. A competing risk analysis, with death as a competing risk, was performed to estimate the cumulative incidence functions of AAs.

The Fine-Gray model for competing risk analysis was used to identify risk factors for late AF or ATs.[14] First, a univariable analysis was performed, including all variables reported in Table I. Covariates with a *p* value of <.10 at univariate analysis were included in the multivariable model with a backward selection method. Hazard ratios (HR) are reported with 95% confidence intervals (CI). A two-sided *p* value of <.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows) and R version 2023.03.0 (R Foundation for Statistical Computing).

TABLE 1 Baseline characteristics.

Baseline and procedural characteristics	*n* = 192
Age (years)	63 (IQR = 51–75)
Gender (male)	131 (68.2%)
Renal function (creatinine, µmol/L)	83.2 (SD = 19.1)
Obstructive sleep apnea	3 (1.6%)
Chronic lung disease	13 (6.8%)
Diabetes mellitus	9 (4.7%)
Insulin dependent	2 (1%)
Noninsulin dependent	7 (3.6%)
Impaired left ventricular function (left ventricular ejection fraction <50%)	6 (3.1%)
Pulmonary hypertension (mmHg)	80 (38.9%)
Moderate (sPAP 30–55 mmHg)	52 (27.1%)
Severe (sPAP >55 mmHg)	22 (11.5%)
Systemic hypertension	75 (39.1%)
Left atrial volume index (mL/m^2)	47 (IQR = 37–61)
NYHA class III–IV	24 (12.5%)
Concomitant procedures	109 (56.8%)
Tricuspid valve repair	67 (34.9%)
Coronary artery bypass grafting	34 (17.7%)
Aortic valve	8 (4.2%)

Note: Data are presented as *n* (%), medians with interquartile range or means (SD).

Abbreviations: NYHA, New York Heart Association; SD, standard deviation; sPAP, systolic pulmonary artery pressure.

3 | RESULTS

3.1 | Baseline

Demographic and baseline characteristics are displayed in Table 1. Supporting Information S1: Table S1 and Table S2 show baseline characteristics for subgroups, grouped by the type and duration of postoperative AAs. In total, 192 patients were included (68% male, median age 63, [IQR = 51–75] years) (Figure 1).

3.2 | Early postoperative atrial arrhythmias

Early AAs occurred in 100 (52.1%) patients. POAF was documented in 61 (31.8%) patients, early ATs in 15 (7.8%) and both POAF and early ATs in 24 (12.5%). POAF had a duration of <24 h in half the patients with POAF. Within the group of patients with POAF lasting >24 h, 24/42 (57.1%) converted to sinus rhythm without ECV, 2/42 (4.8%) underwent successful ECV and 16/42 (38.1%) patients were discharged with AF. In the early postoperative AT group, AT lasted for <24 h in 19/39 (48.7%) patients and >24 h in 20/39 (51.3%) patients. Among the patients with early ATs lasting >24 h, 13/20 (65.0%) patients converted to sinus rhythm without ECV, 1/20 (5.0%) underwent successful ECV, 4/20 (20%) patients were discharged with AT and 2/20 (10%) patients developed AF and were discharged with AF. Figure 2 shows a detailed figure of all postoperative AAs and their clinical course.

3.3 | Long-term outcome: Mortality and late AAs

During a median follow-up of 7.3 years (IQR = 5.0–9.9), 14 (7.3%) patients died and 49 (25.5%) patients developed late AAs. In total, 8 (4.1%) patients had late AF only, 33 (17.2%) patients had late AT only and 8 (4.2%) patients had both late AF and late AT.

The estimated survival rate at 1 year was 98% (95% CI = 97%–100%), at 5 years 95% (95% CI = 91%–98%) and at 10 years 92% (95% CI = 88%–96%). The results of the competing risk analysis are presented in Figure 3. At 1, 5 and 10 years after surgery, the cumulative incidence function any late AA with death as

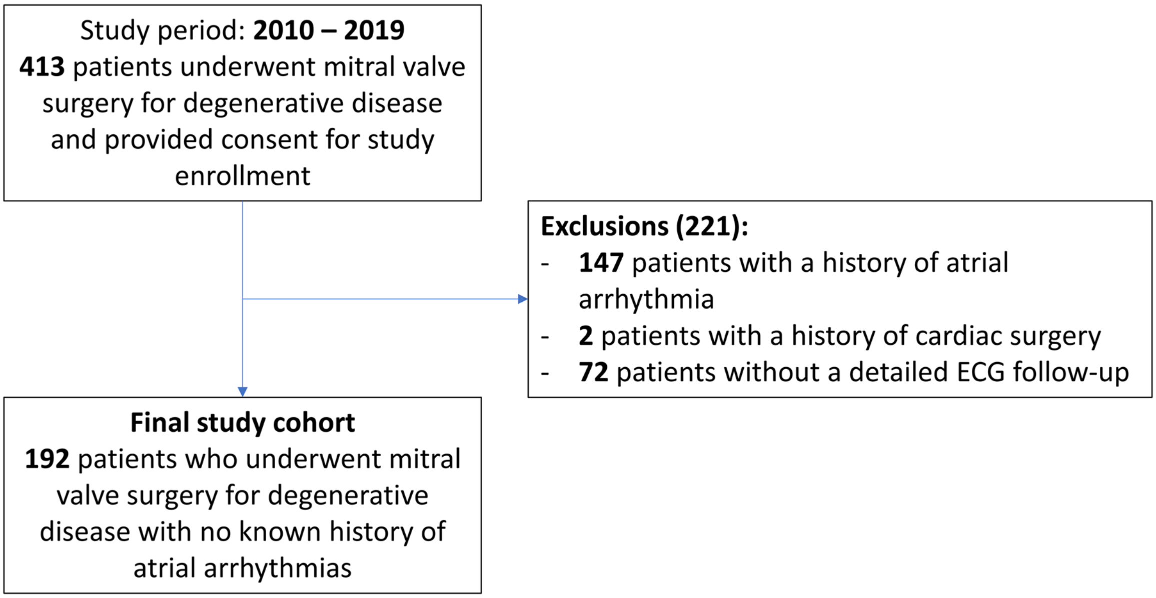

FIGURE 1 Consort diagram of total mitral valve surgery cohort, exclusions by criteria and the final study cohort.

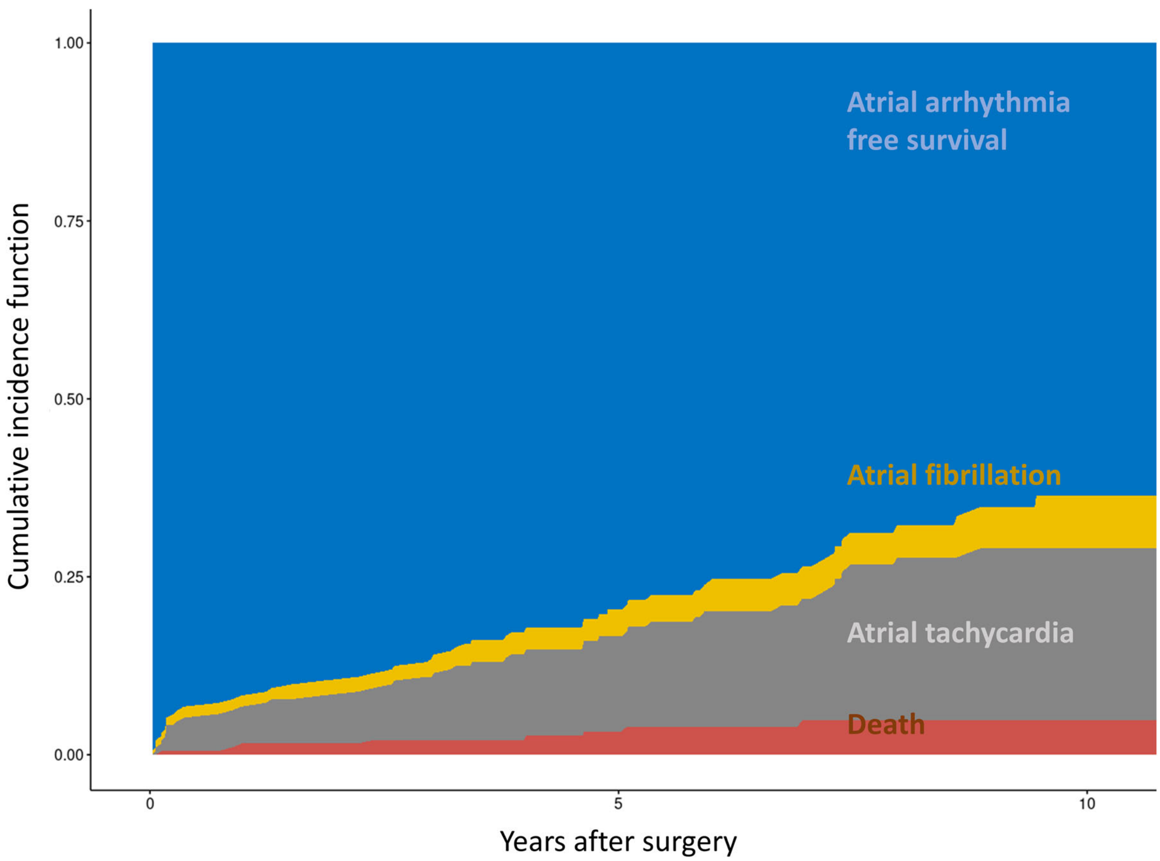

FIGURE 2 Alluvial plot from inclusion of total study cohort to hospital discharge with results and course of postoperative cardiac arrhythmias.

competing risk was 92% (95% CI = 88%–96%), 80% (95% CI = 74%–86%) and 64% (95% CI = 55%–72%), respectively.

On adjusted Cox proportional hazard regression survival analysis, POAF was associated with an increased risk of mortality (HR = 6.93, 95% CI = 1.21–39.82, p = .03; Table 2). This was not the case for early ATs (HR = 0.17, 95% CI = 0.20–1.47, p = .11). During follow-up, recurrent mitral regurgitation (≥grade 2+ regurgitation) was seen in 14 patients. Out of these 14 patients, 2 developed late AF and 5 developed late AT. The incidence of AAs in this patient group was comparable to the group of patients who did not develop AAs during follow-up.

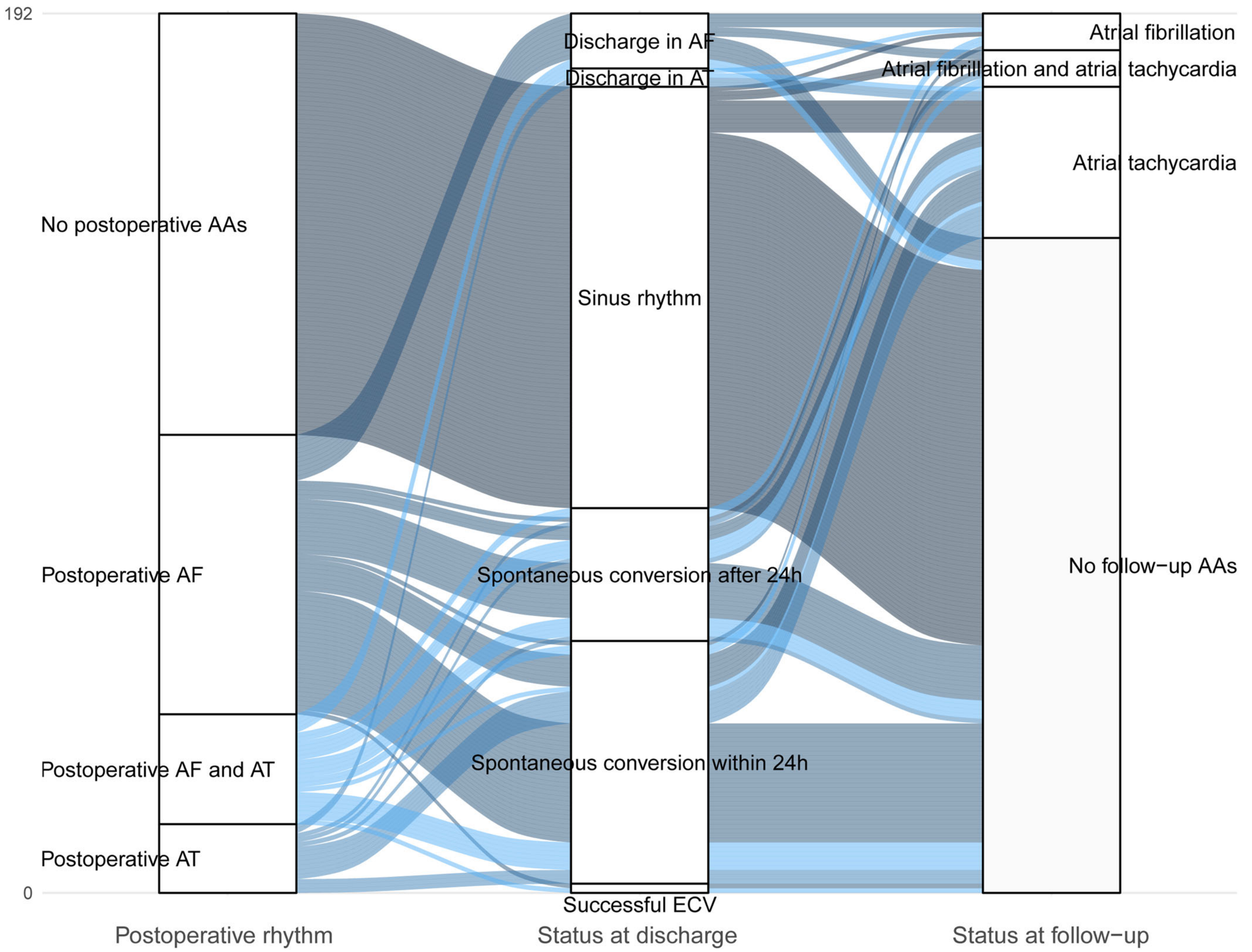

FIGURE 3 Cumulative incidence function of freedom from any late postoperative atrial arrhythmias, with death as competing risk.

3.4 | Risk factors for late AF

The estimated freedom from late AF rates at 1, 5 and 10 years after surgery were 98% (95% CI = 96%–99.9%), 93% (95% CI = 90%–97%) and 89% (95% CI = 83%–94%), respectively. Fine-Gray model analysis revealed that POAF lasting >24 h was related to the development of late AF (HR = 5.99, 95% CI = 1.78–20.10, *p* = .004) whereas this was not the case for POAF lasting <24 h (HR = 2.24, 95% CI = 0.49–10.20, *p* = .30; Supporting Information S1: Figure S1 and Table 3). Early ATs was not related to an increased risk of developing late AF.

3.5 | Risk factors for late ATs

The estimated freedom from late AT rates at 1, 5 and 10 years after surgery were 94% (95% CI = 91%–98%), 85% (95% CI = 80%–90%) and 74% (95% CI = 66%–81%), respectively. On Fine-Gray analysis, early AT was a risk factor for the development of late AT, both in case of early postoperative AT lasting <24 h (HR = 4.25, 95% CI = 1.89–9.57, *p* = .001) or >24 h (HR = 3.51, 95% CI = 1.65–7.46, *p* = .001; Supporting Information S1: Figure S2 and Table 4). Moreover, age (HR = 1.03, 95% CI = 1.00–1.96, *p* = .050) and male gender (HR = 2.99, 95% CI = 1.29–6.95, *p* = .011) were related to the development of late ATs. POAF lasting <24 h or >24 h were both not related to the development of late postoperative ATs.

Of the 41 patients who developed late ATs during follow-up, 5 (12.2%) underwent an ablation procedure due to recurrent symptomatic ATs. Of the five patients, (multiple) ATs were inducible in four patients, including a cavo-tricuspid isthmus dependent flutter (*n* = 2), an intra-atrial re-entrant tachycardia in the right atrium related to the right atriotomy scar (*n* = 2) and for a focal left sided AT (*n* = 1). The patient with no inducible AT underwent an empirical cavo-tricuspid isthmus ablation.

4 | DISCUSSION

In this study, we systematically evaluated the incidence, type, timing and impact on long-term prognosis of AAs after surgical repair for degenerative MV disease. Early AAs were very frequent, affecting >50% of all patients with POAF occurring in 45% of cases and early

TABLE 2 Cox proportional hazard regression survival analysis on risk factors for mortality.

	Univariable			Multivariable		
Variable	HR	*p* value	95% CI	HR	*p* value	95% CI
Age	1.10	.006	1.03–1.17	1.08	.024	1.01–1.16
Gender (male)	2.78	.19	0.61–12.53			
Renal function (creatinine)	1.03	.003	1.01–1.05			
Left atrial volume index	1.00	.011	1.00–1.01			
Chronic lung disease	3.97	.037	1.09–14.43			
Diabetes mellitus	7.32	.003	2.01–26.67	24.42	.001	3.51–169.78
Impaired left ventricular function	N/A	N/A	N/A			
Pulmonary hypertension						
Moderate	1.38	.62	0.39–4.90			
Severe	2.56	.18	0.64–10.24			
Hypertension	1.40	.55	0.47–4.16			
Tricuspid valve repair	1.50	.46	0.51–4.48			
Coronary artery bypass grafting	1.91	.28	0.59–6.20			
Aortic valve procedure	N/A	N/A	N/A			
Postoperative atrial fibrillation	2.89	.078	0.89–9.38	6.93	.030	1.21–39.82
Postoperative atrial tachycardia	0.33	.28	0.04–2.50			

Abbreviations: CI: confidence interval; HR: hazards ratio; NYHA: New York Heart Association.

ATs in 20%. Most of these AA's converted spontaneously, some after ECV, resulting in a discharge rate in sinus rhythm of 89%. Late AAs were a common complication within the first 10 years after surgery with late ATs seen more common than late AF. Only POAF lasting >24 h was related to the occurrence late AF, while early postoperative ATs, regardless of their duration, were associated with the occurrence of late ATs. Lastly, POAF was associated with late mortality, while this was not the case for AT.

4.1 | Incidence of early postoperative AA after MV surgery

AAs are frequently observed in the early postoperative phase after MV surgery and their development is attributed to a combination of factors, including a pre-existing atrial substrate, inflammation, cardiac ischemia, alterations in fluid balance/electrolytes and a disbalance in the cardiac autonomic nervous system.[15] The addition of atrial scarring by surgical incisions in the right atrium and the interatrial septum, as made in case of a trans-septal approach to the MV, may contribute to the creation of areas of slow conduction and unidirectional conduction block, predisposing to the occurrence of macro-reentry.[16]

The characterization of postoperative AAs following MV surgery is seldomly reported in the literature and, typically, postoperative AAs are defined as a single entity and not specified as either AF and AT. However, a comparison study on the clinical course of patients undergoing MV surgery using either the transseptal or left atrial approach, suggested that AAs other than AF might be even more common after MV surgery.[8] Consistent with previous findings, a substantial proportion of our patients developed POAF, which emerged as the most prevalent form of early postoperative AAs. The incidence of early ATs observed in our study aligns with previously reported rates.[8] Of the POAF episodes lasting >24 h, 50% terminated spontaneously, suggesting a connection solely with transient physiological factors, despite their prolonged duration. Conversely, the remaining half of POAF episodes lasting >24 h did not exhibit spontaneous termination, potentially implicating pre-existing atrial abnormalities capable of sustaining AF for an extended duration. Of all early AT cases lasting >24 h, 65% terminated spontaneously.

4.2 | Incidence of late postoperative AAs after MV surgery

To the best of our knowledge, only few studies differentiated between various types of late AAs following MV surgery.[3,8] Our results demonstrate that the incidence of late ATs in patients undergoing MV surgery by transseptal approach might be even higher than the incidence of late AF.

In addition to the differentiation between different types of late AAs, we have divided early AAs based on their clinical course early

TABLE 3 Uni- and multivariable Fine-Gray model analysis on predictors of late atrial fibrillation.

	Univariable			Multivariable (I)			Multivariable (II)		
Variable	HR	*p* value	95% CI	HR	*p* value	95% CI	HR	*p* value	95% CI
Age	1.03	.21	0.98–1.08						
Gender (male)	3.78	.065	0.92–15.50				3.39	.095	0.81–14.20
Renal function (creatinine)	1.02	.023	1.00–1.04	1.02	.023	1.00–1.04			
Chronic lung disease	3.12	.08	0.82–11.20						
Diabetes mellitus	1.98	.32	0.52–7.59						
Hypertension	1.30	.60	0.49–3.46						
Impaired left ventricular function	3.08	.31	0.36–26.7						
Pulmonary hypertension									
Moderate	1.86	.22	0.69–5.02						
Severe	0.65	.68	0.08–5.26						
Left atrial volume index	1.01	.30	0.99–1.03						
Tricuspid valve repair	1.06	.92	0.39–2.88						
Coronary artery bypass grafting	1.95	.22	0.67–5.71						
Aortic valve procedure	1.58	.65	0.23–11.00						
Postoperative atrial fibrillation									
<24 h	1.97	.38	0.44–8.9				2.24	.30	0.49–10.20
>24 h	6.39	.002	1.95–21.00				5.99	.004	1.78–20.10
Postoperative atrial tachycardia									
Duration <24 h	1.71	.49	0.37–7.90						
Duration >24 h	3.01	.053	0.99–9.22						

Note: Two models were built, one (I) including only preoperative variables and the other (II) including various types of postoperative AAs.
Abbreviations: CI, confidence interval; HR, hazards ratio.

after surgery. Interestingly, a shorter duration and spontaneous conversion of early POAF was not related to the development of late AF. On the other hand, early POAF lasting >24 h was strongly related to the occurrence of late AF. This suggests that early POAF might not be a homogenous clinical entity. POAF lasting <24 h might be a temporary arrhythmia related to acute reversible changes in the postoperative phase (inflammation, anemia, ischemia, electrolyte imbalance). On the other hand, patients with POAF > 24 h might already have a pre-existing substrate in a remodeled atrium and preoperative changes will not regress despite correction of mitral regurgitation.

Early ATs were related to the occurrence of late ATs, regardless of the duration and clinical course early after surgery. This comes to little surprise as ATs after MV surgery are more likely related to surgical scars and anatomical structures and are thus related to macro re-entrant pathways. It has previously been shown that right atriotomy incisions can be proarrhythmogenic early after surgery, especially in case of the transseptal approach.[7,16] The findings from electrophysiologic studies performed during follow-up provide further support these observations. While only a minority of patients experiencing ATs underwent an ablation procedure, the majority of ATs were right sided, either a cavo-tricuspid isthmus dependent flutter or an intra-atrial re-entrant tachycardia, both facilitated by the introduction of scar by the right atriotomy.

The type of concomitant procedures performed showed no correlation to the occurrence of AAs during follow-up, suggesting a predominant influence of preoperative atrial remodeling and surgical incisions for valve exposure on the occurrence of these AAs. Interestingly, older patient age and male gender were associated with the development of late ATs. These factors can be used to identify patients at particular risk of developing AAs during follow-up after MV surgery.

4.3 | Late mortality

Consistent with recent studies, early POAF was associated to a higher risk of late mortality after surgery in our cohort.[17,18] Conversely, early postoperative ATs did not exhibit a significant association with late mortality. This discrepancy suggests that early POAF

TABLE 4 Uni- and multivariable Fine-Gray model analysis on predictors of late postoperative atrial tachycardia.

	Univariable			Multivariable (I)			Multivariable (II)		
Variable	HR	*p* value	95% CI	HR	*p* value	95% CI	HR	*p* value	95% CI
Age	1.03	.025	1.00–1.06	1.04	.020	1.01–1.07	1.03	.050	1.00–1.06
Gender (male)	3.30	.006	1.41–7.69	3.54	.003	1.54–8.14	2.99	.011	1.29–6.95
Renal function (creatinine)	1.01	.051	1.00–1.03						
Chronic lung disease									
Diabetes mellitus	2.04	.12	0.82–5.04						
Hypertension	1.32	.59	0.48–3.63						
Impaired left ventricular function	1.50	.20	0.81–2.78						
Pulmonary hypertension	1.09	.94	0.13–9.05						
Moderate									
Severe	1.37	.36	0.70–2.68						
Left atrial volume index	0.92	.88	0.32–2.65						
Tricuspid valve repair	1.00	.58	0.99–1.02						
Coronary artery bypass grafting	1.94	.034	1.05–3.58						
Aortic valve procedure	1.31	.49	0.61–2.84						
Postoperative atrial fibrillation	0.59	.59	0.09–4.04						
<24 h	1.36	.42	0.64–2.90						
>24 h	1.49	.30	0.70–3.19						
Postoperative atrial tachycardia									
<24 h	4.48	<.001	2.18–9.19				4.25	.001	1.89–9.57
>24 h	3.30	<.001	1.49–7.29				3.51	.001	1.65–7.46

Note: Two models were built, one (I) including only preoperative variables and the other (II) including various types of postoperative AAs.
Abbreviations: CI, confidence interval; HR, hazards ratio.

likely serves as an indicator of advanced MV disease and/or patients in worse clinical status, which in turn contribute to a less favorable prognosis. On the other hand, early postoperative ATs appear to be more closely tied to myocardial tissue damage resulting from surgical incisions. This is a known problem following MV surgery that might necessitate additional ablation procedures after surgery.[19] The fact that early ATs were not related to worse survival seems reassuring.

4.4 | Limitations

Our study has inherent limitations due to its retrospective cohort design. Furthermore, the results presented in our study are specific to patients who underwent MV repair surgery using the transseptal approach. The detection of late AAs may be affected by detection biases and lack of uniform protocols for its diagnosis, as no clinical indication existed for strict rhythm surveillance during follow-up. With intermittent ECGs used to determine the outcome, one of the limitations is that asymptomatic and short episodes of AF/AT will most likely not be recorded. For this reason, there is a possibility that the actual incidence of late AF/AT is higher than reported. The indication for Holter monitoring performed during follow-up was at the discretion of the attending cardiologist and the results were not available for reassessment.

5 | CONCLUSION

Early and late AAs are common after MV repair surgery in patients without a history of preoperative AAs. In our experience, POAF was associated with worse prognosis whereas early AT was not. POAF lasting >24 h was a risk factor for late AF and carried a different prognosis than POAF lasting <24 h. Lastly, early ATs are a risk factor for late ATs, regardless of their duration in the early preoperative phase.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The local institutional ethics committee of the Leiden University Medical Center, Leiden, Netherlands (number P16.003, date of approval 14-06-2021) approved this study. Written patient consent was obtained to allow for pseudoanonymous data collection and analysis.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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