The prognostic outcome of Atypical Atrial Flutter following a single electrophysiology study and ablation

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Abstract

Background: Atypical Atrial Flutter (AAFL) prevalence is increasing due to the escalating Atrial Fibrillation (AF) ablations and cardiac surgeries. We wanted to explore the outcome of the AAFL ablation, considering the recent changes in mapping and ablation. **Methods:** This study was approved by the Institutional Review Board (IRB) of Mayo Clinic hospital. We retrospectively studied 419 patients who had undergone AAFL ablation at Mayo Clinic from January 2017 to June 2022. Thirteen patients declined research authorization, and 19 patients were lost to follow-up during the 90-day blanking period, resulting in a sample size of 387. The median follow-up time for patients was 25.7 months (95% CI 23.7, 32.3). **Results:** Recurrent symptoms with documentation of atrial arrhythmia Occurred in 226/387 (58.4%) patients, of which 151/226 (66.8%) occurred within the first year. The median time to recurrence was 8.5 months (max 57.8 months). Eleven patients died during the study period, 9 of whom experienced recurrence prior to death. Overall, the median recurrence-free survival (RFS) time was 16.6 months (95% CI 13.2, 20.0) with a 1-year RFS rate of 57.2% (95% CI 52.2, 62.7%). Acute termination occurred 324/387 (83.7%) during the ablation. The 1-year RFS rate was 58.9% (95% CI 53.5%, 64.9%) for patients with acute termination and 49.0% (95% CI 37.9%, 63.4%) for those without acute termination. The rate was not significantly different based on acute termination status (p = 0.11). **Conclusions:** The one-year RFS rate of 57.2% following AAFL ablation, even though 83.7% achieved acute termination during the procedure, signifies the extent of the underlying substrate abnormalities.

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Methods: This study was approved by the Institutional Review Board (IRB) of Mayo Clinic hospital. We retrospectively studied 419 patients who had undergone AAFL ablation at Mayo Clinic from January 2017 to June 2022. Thirteen patients declined research authorization, and 19 patients were lost to follow-up during the 90-day blanking period, resulting in a sample size of 387. The median follow-up time for patients was 25.7 months (95% CI 23.7, 32.3).

Results: Recurrent symptoms with documentation of atrial arrhythmia Occurred in 226/387 (58.4%) patients, of which 151/226 (66.8%) occurred within the first year. The median time to recurrence was 8.5 months (max 57.8 months). Eleven patients died during the study period, 9 of whom experienced recurrence prior to death. Overall, the median recurrence-free survival (RFS) time was 16.6 months (95% CI 13.2, 20.0) with a 1-year RFS rate of 57.2% (95% CI 52.2, 62.7%). Acute termination occurred 324/387 (83.7%) during the ablation. The 1-year RFS rate was 58.9% (95% CI 53.5%, 64.9%) for patients with acute termination and 49.0% (95% CI 37.9%, 63.4%) for those without acute termination. The rate was not significantly different based on acute termination status ($p = 0.11$).

Conclusions: The one-year RFS rate of 57.2% following AAFL ablation, even though 83.7% achieved acute termination during the procedure, signifies the extent of the underlying substrate abnormalities.

Keywords: Atypical atrial flutter, Atypical atrial flutter ablation, Atrial fibrillation, Radiofrequency ablation, AV-nodal ablation, Pacemaker, Mitral valve repair, Surgical MAZE procedure, Structural heart defect.

Abbreviations:

AAFL: Atypical atrial flutter

AFL: Atrial flutter

AF: Atrial fibrillation

MRAT: Macro-reentrant atrial tachycardias

CTI: Cavo-Tricuspid Isthmus

EP study: Electrophysiology study

RF: Radiofrequency

AV-Node: Atrioventricular node

AAD: Anti-arrhythmic drug

RA: Right atrium

LA: Left atrium

RFS: Recurrence-free survival

IQR: interquartile range

1. Introduction:

The definition of Atypical Atrial Flutter (AAFL) includes a broad spectrum of macro-reentrant atrial tachycardias (MRAT) in which the wavefront does not include the Cavo-Tricuspid Isthmus (CTI) part of the tricuspid annulus [**1**] .

There is a substantial increase in the incidence of AAFL as an iatrogenic problem in patients who have had a catheter ablation procedure for treating AF or a surgical MAZE procedure [**2**] .

In AAFL, especially in patients who had surgery or catheter ablation, an electrophysiology study (EP study) is the only way to unveil the mechanism [**3**] . An electrophysiology study, including entrainment characteristics and high-density mapping consistent with reentry, must confirm the ultimate diagnosis of AAFL [**4**] .

Catheter ablation is frequently utilized due to lack of efficacy of medications or significant symptoms and deteriorating left ventricular function [**4,5**] .

Entrainment and point-to-point map acquisition with large tip (8mm) catheter ablation was common until recently. However, in the last few years, a more comprehensive understanding of propagation and critical zones has been possible by high-density electroanatomical mapping utilizing small-diameter, multipolar catheters. Multipolar maps may have advantages over traditional point-by-point voltage maps. One such advantage is higher mapping resolution, which facilitates the detection of slow conduction zones. Additionally, multipolar maps improve the accuracy and speed of mapping procedures due to the function of smaller electrodes. Finally, pace capture can be achieved at the lower output due to increased electrical density [**6,7**]**.** Therefore, we wanted to explore the outcome of the AAFL ablation, considering the recent changes in mapping and ablation.

2. Methods:

This study was approved by the Institutional Review Board (IRB) of Mayo Clinic hospital.

Study cohort: This study is a retrospective analysis of patients that underwent AAFL ablation in the past 5 years (2017-2022) at different sites of Mayo Clinic. High-density activation sequence mapping and small-diameter multipolar catheter usage have become more prevalent in the past 5 years. Therefore, we wanted to study the impact of our contemporary practice on the overall outcome of AAFL.

Ablation and Follow-up: All included patients had Intra Cardiac Echo (ICE), a multipolar small diameter catheter used for mapping, and irrigated Radiofrequency (RF) catheter for ablation. Successful ablation was

defined as the termination of AAFL during RF energy application (either without cycle length change or lengthening) and the inability to reinduce the index AAFL. The termination was not considered successful if the index arrhythmia terminated due to a premature beat or cycle length shortening. All included patients were routinely followed up for any clinically relevant atrial arrhythmia recurrence according to the clinical standards of care. If prompted by symptoms, they were seen at the outpatient clinic or via virtual appointment. Routinely scheduled appointments were at 1, 3, and 12 months. Besides symptomatic recurrences, routine electrocardiograms and Holter monitoring were utilized to confirm recurrent events, even if unaccompanied by symptoms. The primary outcome of interest was one-year recurrence-free survival in all symptomatic event-based recordings or opportunistic, incidental routine monitoring. Early recurrent symptoms during the 90-day blanking period were excluded.

Statistical analysis: Continuous variables were summarized using median and interquartile range (IQR), and categorical variables were summarized using frequency and percentage. A Kaplan Meier curve with log-rank analysis examined the primary outcome, recurrence-free survival. Patients were censored as of the date of the last follow-up, and a p-value of <0.05 was considered significant. Statistical software R 4.1.2 was used for analysis.

3. Results:

Demographics and clinical characteristics:

A total of 419 patients had an ablation at Mayo Clinic for AAFL from January 2017 to June 2022. A total of 13 patients were excluded due to denied research authorization. Additionally, 19 patients were lost to follow-up during the 90-day blanking period and excluded, resulting in a total sample size of 387. The median follow-up time for patients was 25.7 months (95% CI 23.7, 32.3).

The demographics and clinical characteristics are given in **Table 1** . The median age was 68.0 (IQR 60.0, 74.0), and 32.6% of patients were female.

Ablation Characteristics : Bidirectional block following a linear line was confirmed at the end of the ablation in 66.06% (255/386) of the patients. In 1.2% (5/386) of the patients, only unidirectional block could be achieved. In 5.6% (22/386) of the patients, bidirectional block could not be achieved at the end of the ablation. In 26.9% (104/386) of the patients, the confirmation of the bidirectional block was not documented.

Recurrence-free survival:

Recurrent events following the ablation occurred in 226/387 (58.4%) patients after a median of 8.5 months post-ablation (max 57.8 months), of which *151/226 (66.8%) occurred within the first year* . During the study period, 11/387 patients died, 9 of whom experienced recurrence prior to death. The median recurrence-free survival (RFS) time was 16.6 months (95% CI 13.2, 20.0). The 1-year RFS was 57.2% (95% CI 52.2%, 62.7%).

Figure 1 shows the Kaplan-Meier curve for the probability of RFS over time.

Recurrence-free survival based on acute termination status:

Acute termination occurred in 324/387 (83.7%) during the ablation.**Figure 2** shows the Kaplan-Meier curve for the probability of RFS over time-based on acute termination or lack of termination during ablation. For patients with acute termination, the 1-year RFS rate was 58.9% (95% CI 53.5%, 64.9%). For patients without acute termination, the 1-year RFS rate was 49.0% (95% CI 37.9%, 63.4%). The RFS was not significantly different based on acute termination status ($p = 0.11$).

Recurrence:

For patients who experienced recurrence following the ablation, 48.7% experienced a different AAFL, and 40.7% experienced AF. 51.8% of patients were cardioverted, 14.6% had an AV node ablation, 35.0% underwent a repeat ablation **(Table 2), and** 44.7% were on anti-arrhythmic drugs after index ablation.

4. Discussion:

Cause of AAFL: Table 1 shows 66.1% had undergone prior ablation for AF/typical AFL; 6.5% had a surgical correction for congenital heart disease; 15.2% had mitral/ aortic valve repair/replacement; 7.8% had undergone surgical MAZE procedure and the rest 7% with other cardiac interventions. This cohort is representative of the referral patterns seen in many centers that frequently deal with AAFL.

This is the largest cohort of patients who underwent the contemporary AAFL mapping and ablation practice. Ablation of AF begets more AAFL is the new norm.

Outcome:

1. Acute: 83.7% achieved acute termination of the flutter during the ablation, and the rest required electrical cardioversion to achieve sinus status at the end of the ablation. The recurrence-free survival rate was not significantly different based on acute termination status (p = 0.11), as mentioned in **Figure 2** . Acute termination and lack of inducibility are the common standards to determine success in the EP lab, particularly for reentrant arrhythmia[**8,9,10**] . The most important finding is that the index macroreentrant arrhythmia's termination does not predict recurrence-free survival. Lack of inducibility is not an indicator of recurrence-free survival is another significant finding as it is commonly used as an endpoint for ablation.

2. Follow-up:

Recurrence: For patients with acute termination, the 1-year recurrence-free survival rate was 58.9% (95% CI 53.5%, 64.9%). For patients without acute termination, the 1-year recurrence-free survival rate was 49.0% (95% CI 37.9%, 63.4%). During the study, 58.4% had recurrent arrhythmic symptoms following ablation, not including the immediate blanking phase (90-day period). Index arrhythmia was terminated in most patients, but significant recurrent other atrial arrhythmias were noticed. AAFL is the most common form of arrhythmic recurrence, followed by AF. As the recurrence was assessed only by surface recording, it is difficult to discern whether it is due to the original or new arrhythmia mimicking the pattern. Based on the replication of morphology from pre-procedural flutter tracings, the recurrence of the targeted flutter is extremely low (2.7%). Ongoing follow-up beyond 1-year showed higher rates of recurrences. Recurrence is not due to recently ablated AAFL is the other useful finding.

Recurrences of new arrhythmia suggest progressive substrate changes from the native disease or additional new substrate due to the ablation. Utilizing linear lines to connect to electrically inert or anatomical barriers may influence the recurrence rate. Any non-transmural lesion in a linear line can become a substrate for reentrant arrhythmia. Assessing the block across a linear line is operator-dependent. Most of the block across a linear line was confirmed with a multipolar catheter time delay and or activation reversals. After the procedure, recovery of conduction across the line may contribute to recurrence.

Management of recurrent arrhythmias: The recurrences were managed by anti-arrhythmic drugs, electrical cardioversion, repeat ablation, or as the final resort, AV-node ablation. Repeat ablation was required in 35% of the cases. AV-Nodal ablation is the last resort in some patients (14.6%) who failed to achieve sinus rhythm despite the flutter ablation. Achieving sinus rhythm was difficult in a small number of patients, and they were counseled to accept that the arrhythmia was likely their new normal if the rate was under control.

5. Limitations:

A blanking period of 90 days is utilized for post-AAFL ablation, similar to AF ablation, where the arrhythmia recurrences within the period are disregarded. This blanking interval is debatable for a reentrant arrhythmia,

but the period was chosen for consistency with AF studies. Any interventions in this period, such as repeat procedures and AV-nodal ablation, are not considered.

Besides symptom-based recording, routine Holter monitoring at periodic intervals and snapshot ECGs were used as markers of recurrence. However, continuous recording with a loop recorder or implanted device such as a pacemaker may have detected a higher recurrence rate.

6. Conclusions:

The one-year RFS rate of 57.2% following AAFL ablation, even though 83.7% achieved acute termination during the procedure, signifies the extent of the substrate abnormalities.

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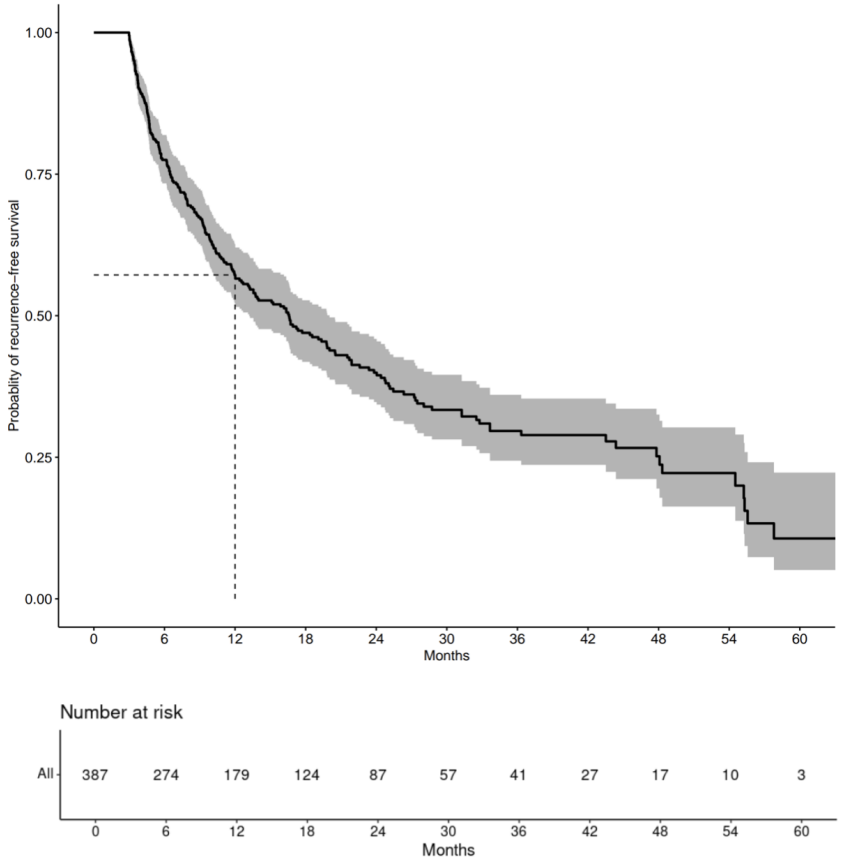


Figure 1. Recurrence-free survival

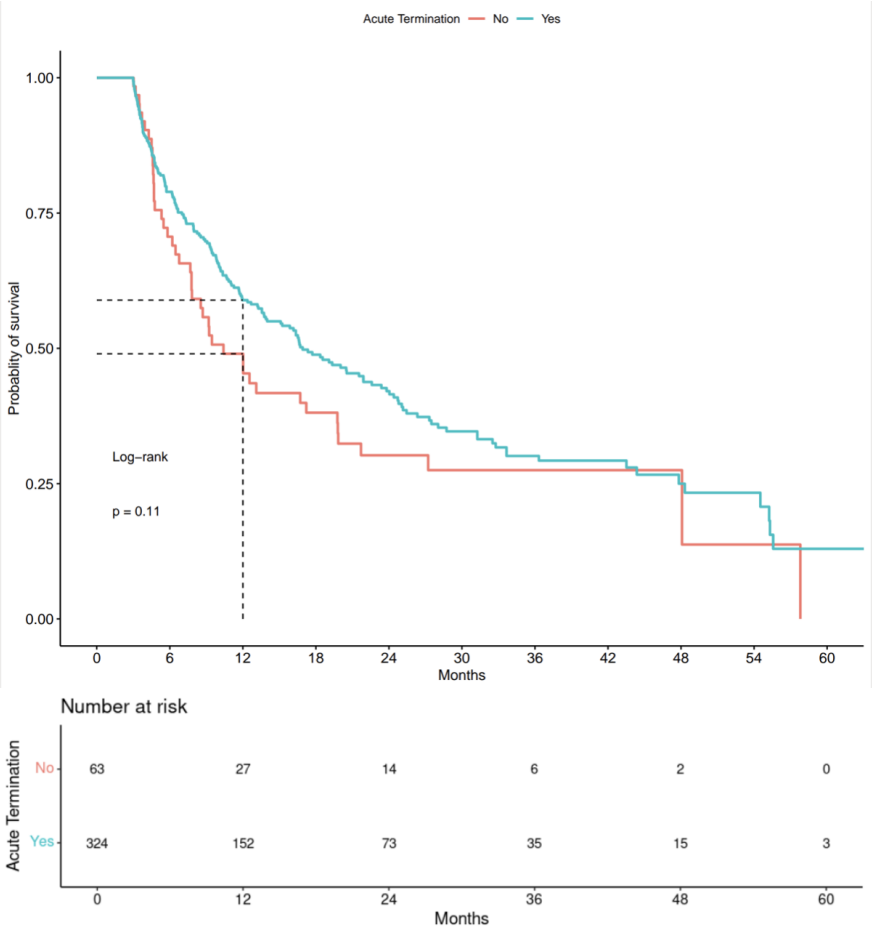


Figure 2. Recurrence-free survival based on acute termination status

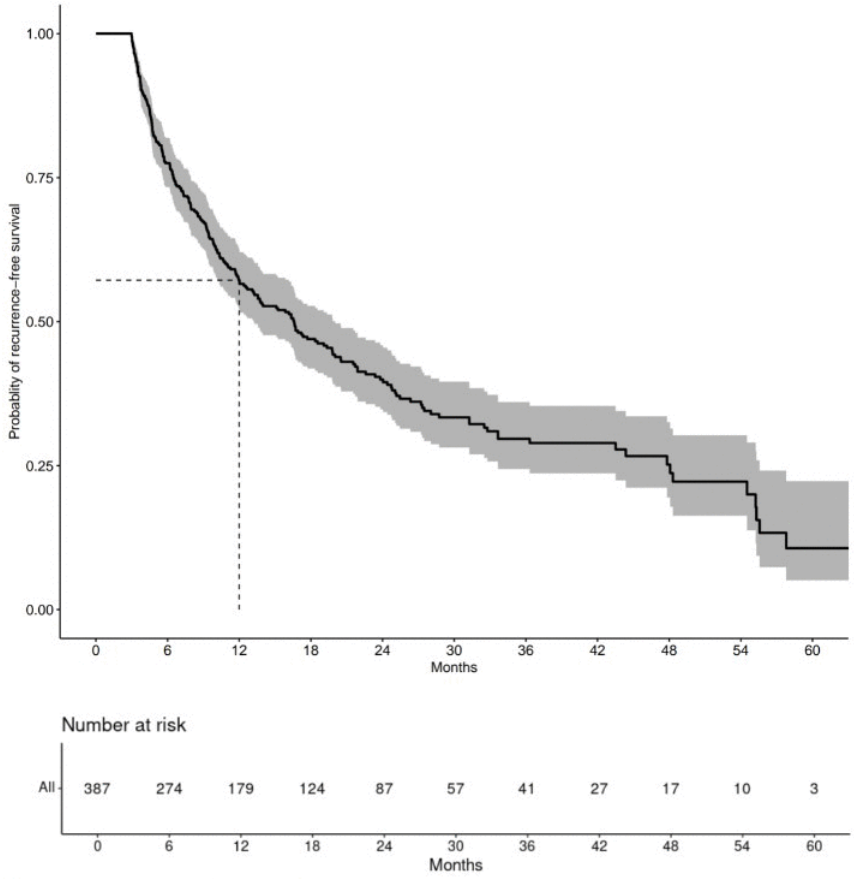
Table 1. Demographics and Clinical Characteristics

	Overall (N=387)
Sex (Male)	261 (67.4%)
Age at procedure	
Median (Q1, Q3)	68.0 (60.0, 74.0)
Range	27.0 - 87.0
Hypertension	280 (72.4%)
Diabetes Mellitus (Type II)	47 (12.1%)
Coronary artery disease	74 (19.1%)
Congestive heart failure	152 (39.3%)
Dyslipidemia	244 (63.0%)
Thyroid status	
Amiodarone Induced Hyper	1 (0.3%)
Hyper	2 (0.5%)
Hypo	63 (16.3%)
None	317 (81.9%)
Subclinical Hypo	4 (1.0%)
Obstructive sleep apnea	185 (47.8%)

Chronic obstructive pulmonary disease	40 (10.3%)
Chronic kidney disease	78 (20.2%)
Pre-procedure creatinine	
Median (Q1, Q3)	1.1 (0.9, 1.2)
Range	0.6 - 4.9
Atrial fibrillation/flutter status	
History of atrial fibrillation/flutter without intervention	89 (23.0%)
No history of atrial fibrillation/flutter	42 (10.9%)
Previous ablation for atrial fibrillation/flutter	256 (66.1%)
Congenital heart disease	25 (6.5%)
Valve repair/replacement	59 (15.2%)
MAZE	30 (7.8%)
VT11Ventricular tachycardia/PVC22Premature ventricular contraction ablation	6 (1.6%)
AVNRT33Atrioventricular nodal reentrant tachycardia ablation	5 (1.3%)
HOCM44Hypertrophic obstructive cardiomyopathy s/p myectomy	12 (3.1%)
WPW55Wolff-Parkinson-White ablation	1 (0.3%)
Other cardiac symptoms	1 (0.3%)
Ablation success	323 (83.5%)
Acute termination	324 (83.7%)
Lack of inducibility	385 (99.5%)
Use of DCCV66Direct current cardioversion during procedure	
None	322 (83.2%)
Hemodynamic Instability	2 (0.5%)
Failure of termination	63 (16.3%)

Table 2. Nature of recurrence and interventions for patients with recurrence

	Overall (N=226)
Nature of recurrence	
Atrial fibrillation	92 (40.7%)
Different atypical flutter	110 (48.7%)
Same and different atypical flutter	4 (1.8%)
Same atypical flutter	6 (2.7%)
Typical flutter	6 (2.7%)
Unspecified	8 (3.5%)
Direct current cardioversion	104 (46.0%)
AV Node ablation	33 (14.6%)
Repeat ablation	79 (35.0%)



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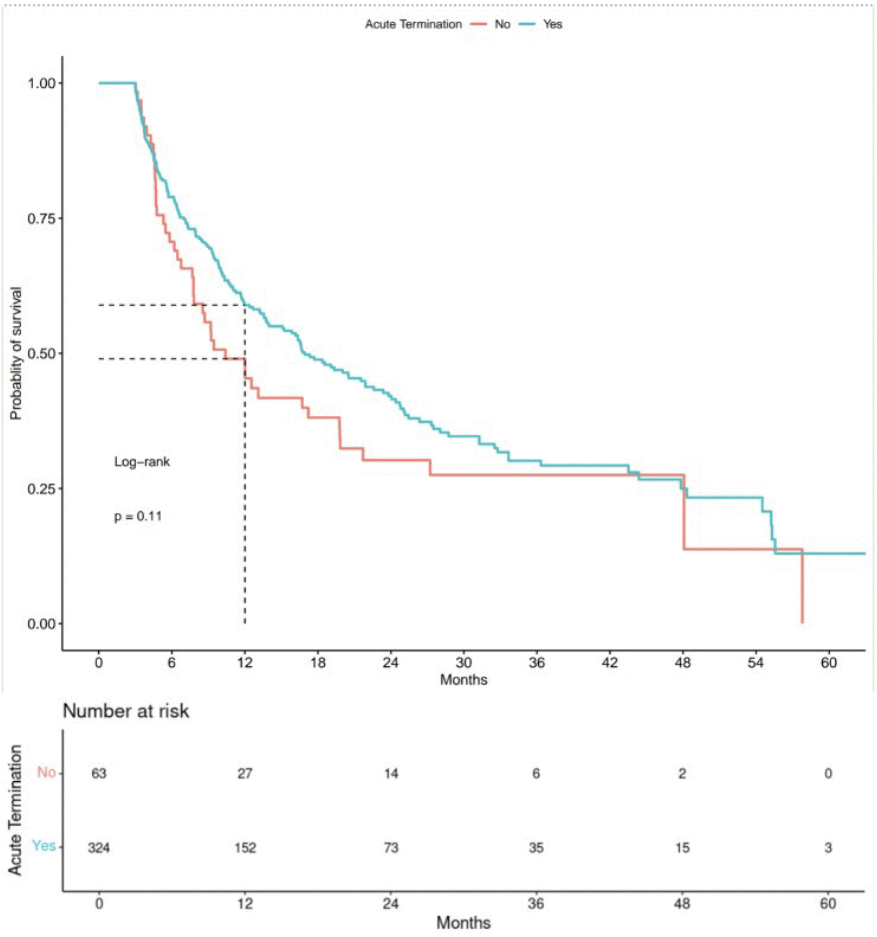

Figure 2. Recurrence-free survival based on acute termination status