The VAD Journal: *The journal of mechanical assisted circulation and heart failure*

Peer-Reviewed Systematic Review and Meta-Analysis

Impact of Atrial Fibrillation on Outcomes after Left Ventricular Assist Device Implantation: Systematic Review and Meta-Analysis

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Citation: Buttar, et al. Impact of Atrial Fibrillation on Outcomes after Left Ventricular Assist Device Implantation: Systematic Review and Meta-Analysis. *The VAD Journal*. 2022; 8(1):e2022816. https://doi.org/10.11589/vad/e2022816

Editor-in-Chief: Maya Guglin, University of Indiana

Received: March 18, 2022

Accepted: June 14, 2022

Published Online: August 3, 2022

Funding: Not applicable

Competing interests: None

Keywords: atrial fibrillation; left ventricular assist device; mechanical circulatory support; mortality; thromboembolism; bleeding

Abstract

Background: Atrial fibrillation (AF) is a common finding in patients with heart failure and is well-known for its deleterious effects on cardiac function and hemodynamics; however, there are gaps in knowledge regarding the impact of AF on patients with left ventricular assist devices (LVADs).

Methods: In this study, we searched PubMed/Medline, Embase, and Cochrane Library databases through September 2021 to find articles that assessed the outcomes of AF in patients with LVADs.

Results: A total of 12 studies that underwent systematic review evaluated the outcomes of 7853 adult patients. The meta-analysis analyzed findings from a total of 1003 patients. Pooled findings indicated a 25% higher risk of mortality in patients with AF as compared to those in sinus rhythm (P = .02). No statistically significant differences in mortality were noted between patients with paroxysmal AF or persistent AF (P = .13). No statistically significant differences were noted between the groups in terms of bleeding (P = .70). There was an increased risk of thromboembolism in patients with sinus rhythm compared to those with AF (P < .001).

Conclusion: The presence of AF was not found to be associated with an increased risk of bleeding or thromboembolism but may be associated with increased mortality.

Introduction

Left ventricular assist devices (LVADs) have become an acceptable treatment modality in patients with end-stage heart failure. Early survival rates with current generation LVADs are comparable to heart transplantation, exceeding 80% at 1 year and 70% at 2 years.[1,2] Although LVADs have significantly improved survival rates and quality of life,[3] there are several risks and adverse events associated with their use, including pump thrombosis, major infections, cerebrovascular accidents (CVA), and major bleeding.[3] LVADs have been increasingly utilized either as destination therapy or as a bridge to transplantation.[3,4] However, many patients clinically benefit from mechanical circulatory support as a bridge-to-recovery, which offers support during the acute insult, or as a bridge-to-decision.[4] Durable LVADs are considered in patients with New York Heart Association class IV symptoms despite optimal medical therapy or those deemed dependent on intravenous inotropes or temporary mechanical circulatory support.[5] A summary of current indications and contraindications is highlighted in Table 1.

Table 1. Indications and Contraindications for Left Ventricular Assist Device[4]

Indications	Contraindications
▪ New York Heart Association class III-IV despite optimal medical therapy with poor quality of life ▪ Inotrope-dependent advanced heart failure ▪ Progressive cardiac cachexia ▪ Frequent hospitalizations for heart failure with low aerobic capacity (peak VO_2 < 14 mL/kg/min or < 50% predicted) ▪ Circulatory intolerance to neurohormonal antagonists ▪ Diuretic refractoriness with worsening renal function ▪ Reversible end-organ dysfunction secondary to low cardiac output ▪ Non-responder or non-candidate for mitral regurgitation repair	▪ Irreversible neurologic injury ▪ Systemic illness or disseminated malignancy limiting survival ▪ Coagulopathy disorders or contraindications to anticoagulation ▪ Left ventricular or left atrial thrombus (that cannot be removed or treated) ▪ Aortic aneurysm or dissection ▪ Uncontrolled sepsis ▪ Severe frailty unlikely to respond to cardiac support ▪ Medication non-compliance ▪ Ventricular septal defect, severe aortic or peripheral artery disease ▪ Severe psychiatric illness

In the general population, atrial fibrillation (AF) is a known risk factor for mortality and morbidity.[6] In the United States alone, at least 3 to 6 million people have AF, and the numbers are projected to reach ~6 to 16 million by 2050.[6] The presence of atrial arrhythmias is diagnosed in approximately 21-54% of patients before LVAD implantation.[7] Several studies have demonstrated an increased risk of death and heart failure-related re-hospitalization in LVAD patients with AF with conflicting results.[8,9] This study aimed to update the findings of prior meta-analyses by exploring the clinical outcomes of patients after LVAD implantation with AF compared to patients with sinus rhythm.

Methods

The study was designed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[10] The study sought articles that analyzed patients 18 years and older who underwent LVAD placement. Any patient with valvular, non-valvular, paroxysmal, persistent, and permanent atrial fibrillation was included in the study.

Selection Criteria/Search Strategy

We searched PubMed/Medline, Embase, and Cochrane Library databases for articles published before September 2021. The medical subject headings "heart-assist device," "left ventricular assist device," "atrial fibrillation," and "atrial arrhythmias" were used to extract relevant articles matching the study objective.

Two authors autonomously explored titles, abstracts, and full-text studies matching the selection criteria. The blinding of the article selection process between authors was followed by an independent assessment by a third reviewer.

We included randomized controlled trials, prospective, retrospective studies, case reports, case series, and descriptive studies. We excluded review articles, conference papers, abstracts, guidelines, systematic reviews, and meta-analyses. Studies that did not look at outcomes were excluded.

Clinical Outcomes

The outcomes of this systematic review and meta-analysis included all-cause mortality, thromboembolism, and major bleeding. Mortality is defined as either 30-day or in-hospital mortality. CVA, arterial thromboembolism, LVAD pump thrombosis, and transient ischemic attack were all classified as thromboembolism events. Major bleeding was defined in this review according to the Interagency Registry of Mechanically Assisted Circulatory Support definition or intracranial hemorrhage. Gastrointestinal bleeding was reported separately.

Data Extraction and Quality Assessment

The extracted data were exported to RevMan 5.4 to remove duplicate articles. Two independent authors used Microsoft Excel spreadsheets for data extraction.[11] Table 2 elaborates on the baseline characteristics of the included studies. All included articles were published in peer-reviewed journals. Without randomized, controlled trials, we included cohort studies (retrospective and prospective) reporting the incidence of post-operative right heart failure, unplanned right ventricular assist device, bleeding (i.e., gastrointestinal bleeds), stroke, and mortality. Clinical outcomes, study design, and sample size were extracted and listed in Table 3. Two authors assessed study quality using the Newcastle-Ottawa Scale.[12]

Table 2. Baseline Characteristics of Patients with Left Ventricular Assist Devices and Paroxysmal or Persistent Atrial Fibrillation. As available, information from studies is presented in a tabular format. Age and body mass index are presented as mean ± standard deviation, median (interquartile range), or as noted. The rest of the data is presented as the number (frequency).

	Type	Hickey et al.[7]	Enriquez et al.[8]	Oezpeker et al.[9]	Hayashi et al.[13]	Noll et al.[14]	Deshmukh et al.[15]	Hawkins et al.[22]	Kurihara et al.[23]	Pedde et al.[24]	Stulak et al.[25]	Xia et al.[17]	Xuereb et al.[26]
Total Number of Patients		249	106	322	110	418	47	1064	526	769	389	3,909	240
Number of patients	PAF	90 (36.1%)	36 (34%)		40 (36.3%)	302 (72.2%)	13 (27.7%)	121 (11.4%)	229 (43.5%)	558 (72.6%)	389 (100%)	838 (21.4%)	78 (32.5%)
	PeAF		19 (17.9%)	117 (36.3%)	19 (17.3%)								
	Others	159 (63.9%)	51 (48.1%)	205 (63.7%)	51 (46.4%)	116 (27.8%)	34 (72.3%)	943 (88.6%)	297 57.0%)	211 (27.4%)		3071 (78.6%)	162 (67.5%)
Age, years	PAF	58.0 ± 14.0	59.4 ± 9.8		61.0 ± 12.0	59.0 (52.0-67.0)	62.7 (54.5-71.0)	58.0 (52.0-64.0)	58.5 ± 11.1	60.3 (12.5)	60.0 (19.0-79.0)	485 (57.9%) > 65yrs	55.7 ± 11.4
	PeAF		61.0 ± 8.3	60.0 ± 9.3	64.0 ± 9.0								
Male	PAF	201 (81.0%)	29 (80.6%)		35 (87.5%)	83 (27.5%)	9 (69.0%)	91 (75.2%)	186 (81.2%)	463 (83.0%)	308 (79.2%)	695 (82.0%)	64 (82.1%)
	PeAF		15 (78.9%)	105 (89.7%)	17 (89.5%)								
Body Mass Index, kg/m^2	PAF							29.0 (25.0-35.0)	28 ± 6.7	26.7 ± 5.5			27.7 ± 6.1
	PeAF			21.4 ± 1.8									
Indication													
Bridge To Transplant	PAF		30 (83.3%)		8 (20.0%)				123 (53.7%)		259 (66.6%)		
	PeAF		15 (79.9%)		7 (37.0%)								
Destination Therapy	PAF		7 (19.4%)		26 (65.0%)		9 (67.0%)		106 (46.3%)		130 (33.4%)	400 (47.1%)	
	PeAF		4 (20.1%)		10 (53.0%)								
Valve Regurgitation													
Moderate/Severe Mitral Regurgitation	PAF				25 (63.0%)			62 (61.4%)	50 (21.8%)				
	PeAF				7 (37.0%)								
Moderate/Severe Tricuspid Regurgitation	PAF				15 (37.5%)			46 (45.5%)	32 (14.0%)				29 (37.2%)
	PeAF				6 (32.0%)								

Table 2 (Continued). Baseline Co-morbidities.

Study	Type	Hickey et al.[7]	Enriquez et al.[8]	Oezpeker et al.[9]	Hayashi et al.[13]	Noll et al.[14]	Deshmukh et al.[15]	Hawkins et al.[22]	Kurihara et al.[23]	Pedde et al.[24]	Stulak et al.[25]	Xia et al.[17]	Xuereb et al.[26]
Co-morbidities													
Diabetes Mellitus	PAF	91 (37.0%)	20 (55.6%)		10 (25.0%)	42 (13.9%)	6 (46.0%)	69 (49.6%)	107 (46.7%)		107 (28.0%)	118 (14.1%)	39 (50.6%)
	PeAF		9 (47.4%)	30 (25.6%)	7 (37.0%)								
Dyslipidemia	PAF	166 (68.0%)			27 (68.0%)						245 (63%)		
	PeAF				13 (68.0%)								
Hypertension	PAF	191 (79.0%)			25 (63.0%)	62 (20.5%)	11 (92.0%)	79 (65.3%)	147 (64.2%)		142 (37.0%)		66 (84.0%)
	PeAF			50 (42.7%)	13 (68.0%)								
Ischemic Cardiomyopathy	PAF	92 (37.0%)	16 (44.4%)		16 (40.0%)	40 (13.2%)	5 (38.0%)		112 (48.9%)	241 (43.4%)		394 (47.4%)	24 (30.8%)
	PeAF		6 (31.6%)	48 (41.0%)	9 (47.0%)								
Coronary Artery Disease	PAF					54 (17.9%)							
	PeAF												
Previous Myocardial Infarct	PAF	90 (36.1%)						50 (41.3%)					
	PeAF			8 (6.8%)									
Coronary Artery Bypass Graft	PAF						3 (23.0%)						
	PeAF												
Chronic Kidney Disease	PAF		17 (47.2%)			30 (9.9%)						352 (42%)	41 (52.6%)
	PeAF		12 (63.2%)										
Pulmonary Disease/COPD	PAF				6 (15.0%)		6 (46.0%)		33 (14.4%)				
	PeAF				2 (11.0%)								
Thyroid Disorder	PAF						4 (31.0%)					156 (18.6%)	
	PeAF				6 (32.0%)								

COPD: Chronic obstructive pulmonary disease; PAF: Paroxysmal Atrial Fibrillation; PeAF: Persistent Atrial Fibrillation

Table 3: Systematic Review of Paroxysmal and Persistent Atrial Fibrillation.

Study	Study Design	Patients	Objective	Summary of Results
Deshmukh et al.[15]	Retrospective Cohort	13	To determine the incidence, predictors, and outcomes of postoperative AF in patients undergoing LVAD implantation	Paroxysmal AF was: • Predictive of recurrent new AF within 30 days of LVAD implantation. • Associated with an increased risk of ischemic stroke and device thrombosis (P = .01). • Not associated with increased mortality, length of stay, or thrombotic complications within 30 days of device implantation.
Enriquez et al.[8]	Retrospective Cohort	55	To determine the effect of AF on outcomes in patients with HeartMate II LVAD	• Persistent AF was an independent predictor of the composite endpoint of death or HF hospitalization (HR: 3.54; 95% CI: 1.52 to 8.25; P < .01). • Paroxysmal AF was not associated with increased mortality, HF hospitalization, bleeding, or thromboembolism
Hawkins et al.[22]	Retrospective Cohort	121	To determine the risk of mortality and resource utilization of postoperative AF after LVAD placement	• Paroxysmal AF was not associated with operative mortality or stroke but was associated with major morbidity (OR, 2.5; P = .0004) and unplanned right ventricular assist device (OR, 2.9; P = .01).
Hayashi et al.[13]	Retrospective Cohort	59	To investigate the effect of AF on functional TR and cardiovascular events in patients with HeartMate 3 LVAD	• Kaplan-Meier analysis showed that patients with Persistent AF had the worst survival (no AF 98%, paroxysmal AF 98%, Persistent AF 84%, log-rank P = .038) at 1 year.
Hickey et al.[7]	Retrospective Cohort	90	To determine the prevalence of AF and its association with cardiac outcomes in patients with LVADs	• No significant differences in risk of stroke or death for patients with AF before or following LVAD insertion. • By multivariable logistic regression, female sex was associated with an increased likelihood of newly developed AF (29% vs. 9%, OR, 4.06; 95% CI, 1.61 to 10.27; P = .003).
K**urihara et al.**[23]	Retrospective Cohort	2290	To determine whether preoperative AF was associated with inferior outcomes	• After implantation, 139 patients had a stroke (78 non–preoperative AF patients [26.2%], 61 preoperative AF patients [26.6%]; P = .84). • Survival at 30 days, 6 months, 1 year, and 2 years was 89.9%, 82.5%, 75.8%, and 68.0%, respectively, for non-preoperative AF patients versus 90.8%, 78.2%, 72.5%, and 66.4%, respectively, for preoperative AF patients (P = .60 for all time points, P = .69 at 24 months).

Table 3 (continued): Systematic Review of Paroxysmal and Persistent Atrial Fibrillation.

Study	Study Design	Patients	Objective	Summary of Results
Noll et al.[14]	Retrospective Cohort	302	To describe the burden of AF/Atrial Flutter in patients with LVADs and to evaluate the impact of rhythm control strategies	• AF/AFL patients had fewer thromboembolic events (13% vs. 23%; P < .01). • Paroxysmal or persistent AF/AFL was present in 238 patients (57%), and rhythm control exposure (n = 166, 70%) was not associated with decreased mortality (39% vs 43%; P = .57), thromboembolism (13% vs 17%; P = .41), or bleeding (49% vs 39%; P = .16). • Patients with AF/AFL had similar mortality as those without. AF/AFL had no association with the risk of death, thromboembolism, or bleeding.
Oezpeker et al.[9]	Retrospective Cohort	117	To compare the risk of thrombotic and hemorrhagic complications as well as overall survival during a 2-year follow-up period in patients with LVADs with or without permanent AF	• Two-year survival was 65.4% (n = 134) in the SR group and 51.3% (n = 60) in the AF group. • Right heart failure was a more frequent cause of death in the AF group than in the SR group (P = .008). • The propensity score-adjusted two years HR of TE and bleeding events were similar in both groups.
Pedde et al.[24]	Retrospective Cohort	558	To determine if preoperative AF in patients with LVADs exhibit a higher rate of pump thrombosis and TE than those in SR	• The cumulative incidence of TE was 8.4% (95% CI 6.0–10.7%) after one year and 10.7% (95% CI 8.0–13.4%) after two years. The difference in the incidence between the SR and AF groups was not significant (P = .163)
Stulak et al.[25]	Retrospective Cohort	389	To identify and examine the effect of preoperative AF patients who underwent implantation of CF-LVAD and had preoperative AF	• TE events for patients with no preoperative AF and no GI bleeding was 17%, preoperative AF and no GI bleeding was 24%, no preoperative AF and GI bleeding was 36%, and preoperative AF and GI bleeding was 45% (P < .001).
Xia et al.[17]	Retrospective Cohort	485	To evaluate the association of preoperative AF with thromboembolic events and patient survival	• Patients with AF had a higher rate of bleeding events; 617 bleeding events occurred in 323 (38.5%) patients with AF. • AF was not significantly associated with TE (adjusted HR, 0.95; 95% CI, 0.91-1.31)
Xuereb et al.[26]	Retrospective Cohort	78	To determine the impact of preoperative AF on stroke, device thrombosis, and survival	• There was a similar incidence of stroke in patients with and without AF: 12.8% versus 16%, (P = .803). • Survival was also similar with 1-, 6-, 12- and 24-months survivals of 96.2%, 91.7%, 84.5%, & 69.2%, respectively, in AF patients compared to 93.1%, 85%, 79.4% and 74.1% for non-AF, respectively (P = .424).

AF: Atrial Fibrillation; AFL: Atrial Flutter; CF-LVAD: continuous flow- LVAD; CI: confidence interval; GI: Gastrointestinal; HR: hazard ratio; LVAD: left ventricular assist device; OR: Odds Ratio; SR: Sinus Rhythm; TE: Thromboembolism

Statistical Analysis

A meta-analysis of the clinical outcomes was performed by calculating the odds ratios (ORs) and 95% CIs (confidence intervals). The risk ratios (RRs) assessment was performed through random effects methods to assess the risk of respective outcome variables in the AF and sinus rhythm groups. Forest plots from included studies reflected total patients versus those with reported clinical endpoints. The I-square values indicated the heterogeneity of the study outcomes. Minimal, moderate, and high heterogeneity were defined by the I-square ranges of 0-30%, 31-60%, and 61-100%, respectively. A P-value of ≤ .05 was considered statistically significant.

Results

Included Studies

The initial search across PubMed/Medline, Embase, and Cochrane Library resulted in the selection of 896 articles matching the inclusion criteria. After excluding duplicate articles, 844 unique studies underwent further screening based on their titles and abstracts. Sixty-five studies were retained after the screening process, requiring further assessment based on the full-text articles. Twelve studies were included in the systematic review, and five studies were used for meta-analysis. A total of 12 studies that underwent systematic review evaluated the outcomes of 7853 adult patients. The meta-analysis analyzed findings from a total of 1003 patients.

All-Cause Mortality: Atrial Fibrillation Versus Sinus Rhythm

All-cause mortality was examined in 521 patients in the AF group and 457 in the sinus rhythm group from five studies (Noll, et al., Enriquez, et al., Oezpeker, et al., Deshmukh, et al., and Hayashi, et al.).[8,9,13-15] The pooled findings indicated a 25% higher mortality risk in patients with AF compared to those with sinus rhythm (RR, 1.25; CI, 1.04-1.50; P = .02) (Figure 1A). There was minimal heterogeneity in findings from respective studies (I-square =0%; P = .53), which was not statistically significant. The asymmetry of the funnel plot indicated a risk of publication bias in these reported findings (Figure 1B).

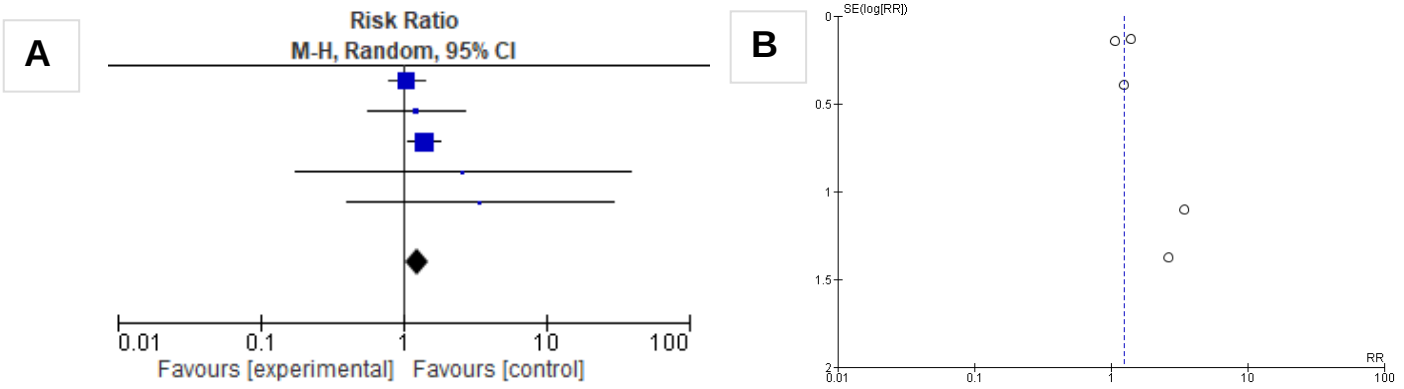

Figure 1. All-cause Mortality. A) Forest Plot; B) Funnel Plot

All-Cause Mortality: Paroxysmal Atrial Fibrillation Versus Persistent Atrial Fibrillation

All-cause mortality was examined further in three studies (Enriquez, et al., Hayashi, et al., Noll, et al.) comparing persistent AF and paroxysmal AF.[8,13,14] The pooled findings from these studies indicated an 85% higher risk of mortality in patients with persistent AF compared to those with paroxysmal AF (RR, 1.85; CI, 0.84-4.08; P = .13) (Figure 2A); however, this increased risk was found to be statistically insignificant. There was moderate heterogeneity in the included studies (I-square = 52%; P = .13). The asymmetrical funnel plot indicated a risk of publication bias in the findings related to all-cause mortality (Figure 2B).

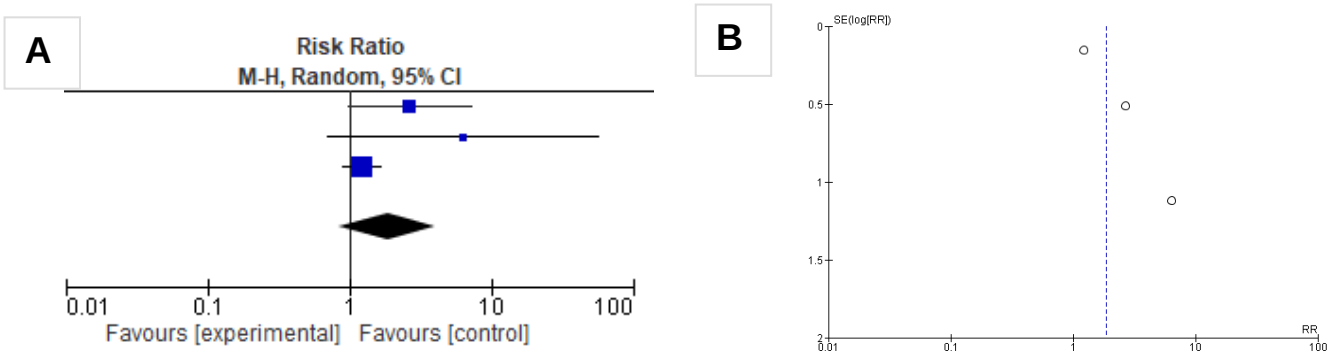

Figure 2. All-cause Mortality between Paroxysmal and Persistent Atrial Fibrillation. A) Forest Plot; b) Funnel Plot.

Thromboembolism Analysis for Sinus Rhythm versus Atrial Fibrillation

Thromboembolism was evaluated in 218 patients in the sinus rhythm group and 416 patients in the AF group from the same three studies.[8,13,14] The pooled outcomes indicated an increased risk of thromboembolism in patients with sinus rhythm compared to those with AF (RR, 2.04; CI 1.38-3.02; P < .001) (Figure 3A). There was minimal heterogeneity (I-square = 7%; P = .34) that lacked statistical significance. The asymmetrical funnel plot did not rule out the risk of publication bias (Figure 3B).

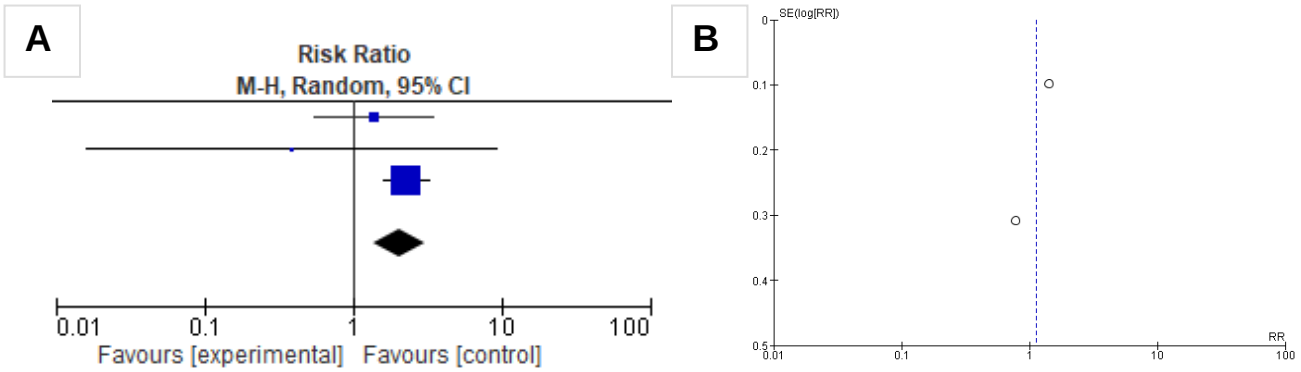

Figure 3. Risk of Thromboembolism in Atrial Fibrillation versus Sinus Rhythm. A) Forest Plot; b) Funnel Plot.

Risk of Thromboembolism in Paroxysmal AF versus Persistent AF

Thromboembolism was evaluated in 226 patients in the paroxysmal AF group and 126 patients in the persistent AF group.[8,13,14] Pooled results from three studies indicated a 35% reduced risk of thromboembolism in patients with paroxysmal AF as compared to those with persistent AF (RR, 0.65; CI, 0.15-2.82; P = .57) (Figure 4). The pooled results lacked statistical significance. There was moderate heterogeneity in findings from these studies (I-square = 58%; P = .09).

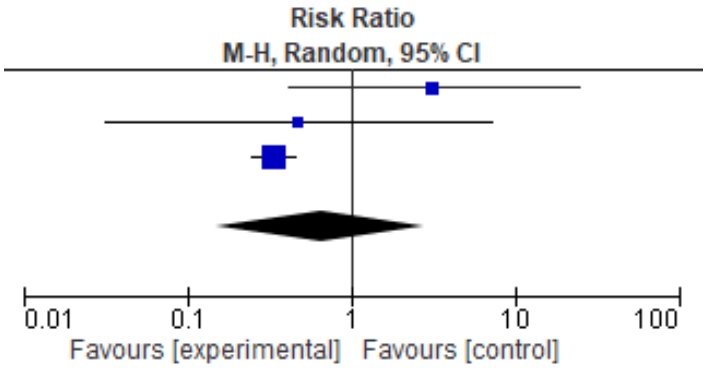

Figure 4. Forest Plot of Risk of Thromboembolism in Paroxysmal versus Persistent Atrial Fibrillation

Bleeding Risk in Sinus Rhythm versus Atrial Fibrillation

Bleeding risk was assessed in 167 patients in the sinus rhythm group and 293 patients in the AF group.[8,14] The pooled results from two studies revealed a 12% higher risk of general bleeding in patients with AF compared to those with sinus rhythm (RR, 1.12; CI, 0.63-2.00; P = .70) (Figure 5). This result, however, lacked statistical significance. The pooled outcomes revealed moderate heterogeneity (I-square = 72%) that lacked statistical significance (P = .06).

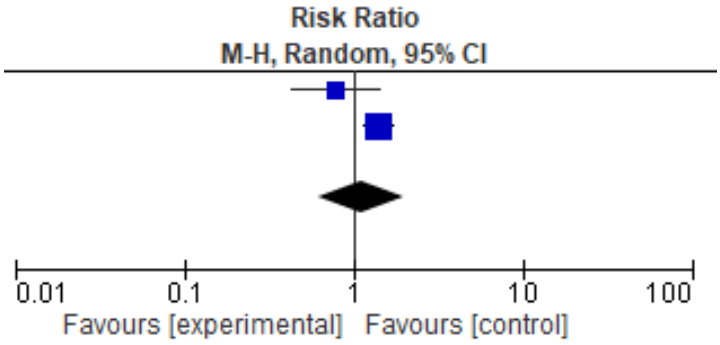

Figure 5. Forest Plot of General Bleeding in Sinus Rhythm versus Atrial Fibrillation

Bleeding Risk for Paroxysmal AF versus Persistent AF

Bleeding risk was assessed in two studies comparing paroxysmal AF and persistent AF.[8,14] The pooled results indicated an 8% higher risk of general bleeding in patients with paroxysmal AF compared to those with persistent AF (RR, 1.08; CI, 0.82-1.42; P = .58) (Figure 6). This finding was statically insignificant. The outcomes revealed minimal heterogeneity (I-square = 0%) that lacked statistical significance (P = .57).

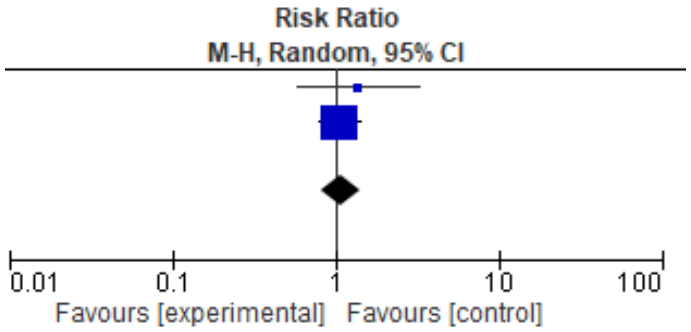

Figure 6. Forest Plot of General Bleeding Risk in Paroxysmal versus Persistent Atrial Fibrillation

Risk of Gastrointestinal Bleeding

Gastrointestinal bleeding was assessed in 167 patients in the sinus rhythm group and 293 patients in the AF group.[8,14] The pooled outcome from two studies indicated a 24% lower risk of gastrointestinal bleeding in patients with sinus rhythm compared to those with AF (RR, 0.76; CI, 0.41-1.43; P = .40) (Figure 7). The results were statistically insignificant. The pooled findings revealed moderate heterogeneity (I-square = 70%) but lacked statistical significance (P = .07).

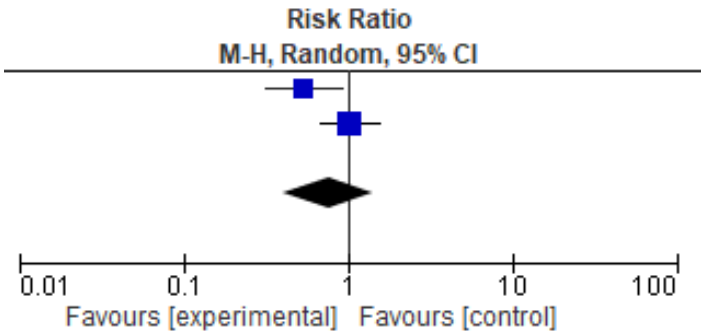

Figure 7. Forest Plot of Gastrointestinal Bleeding

Discussion

Our study reports that AF is associated with an increased risk of all-cause mortality but not with thromboembolism or bleeding. This study builds on the results from a prior meta-analysis by Usman et al.[16], who examined studies that attributed the increased risk of mortality in patients with LVADs to the presence of AF. We add to their findings by including all patients with reported AF both pre-operatively and post-operatively. Our findings support those of Oezpeker et al.[9] and Xia et al.[17], who reported a higher mortality rate in patients with AF. A study by Hickey et al.[7] found no significant differences in mortality in patients with AF before and after LVAD implantation. However, more of Hickey's study patients were taking amiodarone (35%) or beta-blockers (43%) before LVAD implantation for documented ventricular arrhythmia, which may have suppressed the development of AF or AF with rapid ventricular rate.

Only three studies were found that categorized outcomes by the type of AF. Enriquez et al.[8] confirmed an increase in mortality in patients with persistent AF, suggesting that there may be an arrhythmic burden. A more recent study by Noll et al.[14] found no difference in all-cause mortality between patients with paroxysmal or persistent AF. In our study, although there was a trend toward increased mortality in the persistent AF group, it did not reach statistical significance. Many studies in our meta-analysis did not provide subgroup analysis between the types of AF to conclude if rhythm burden could potentially affect the outcome of LVAD implantation. Future studies should include a subgroup analysis of the types of AF to evaluate further the discrepancy found among these studies.

Potential mechanisms to explain why AF might be associated with increased mortality risk in patients with LVADs include the development of right ventricular failure because of AF with rapid ventricular rates.[9,18] Although our current study does not provide direct evidence of this, Oezpeker et al. did find a significantly higher incidence of right heart failure as a cause of death in the AF group. Hottiguader et al.[18] reported from a case series that catheter ablation led to the resolution of right heart failure in these patients and improved survival.

Our study found no difference in the incidence of thromboembolism between the patients with paroxysmal and persistent AF. This supports the findings from the meta-analysis by Usman et al.16 and Tantrachoti et al.[19], who reported no association between pre-operative AF and thromboembolism. Similarly, our results are inconsistent with the additive effect theory that therapeutically anticoagulated LVAD patients with AF are at an increased risk of thromboembolic events. Other studies suggested a reduced association.[8] To date, there is no clinical trial available to support decision-making regarding target international normalized ratio, rhythm control strategies, or left atrial appendage procedures in this subgroup of patients.[20] The study by Enriquez et al.[8] found that patients with AF were on a higher intensity of anticoagulation (INR goal of 2.0–2.5) compared to those without AF (INR goal of 1.5–2.0), and the patients with AF developed thromboembolic complications despite higher INR levels (2.7 versus 1.54; P =

.003).[8] Hickey et al. noted that the majority of individuals who suffered a stroke in their study did so in the setting of subtherapeutic INR levels.[7] The optimal INR goal in LVAD-treated patients with AF has not yet been established.[21]

Our study did not find a significant difference in the risk of bleeding between the two groups. Interestingly, Usman et al. reported an increased risk of gastrointestinal bleeding in patients with pre-operative AF. The absence of this association in our results suggests that other factors may have contributed to this increased risk. The age differences, risk of bleeding, and comorbidities were not accounted for in prior studies.

Limitations

Our study has several limitations. Most of the pooled studies were retrospective and observational and likely have residual confounding; this results in studies being prone to bias. Several discrepancies in baseline demographics and clinical characteristics may have also affected the results. All patients with AF after LVAD implantation were included regardless of having AF before implantation or after. In addition, there are variations between the studies in terms of anticoagulation protocols, median follow-up time, and the type of LVAD implanted.

Conclusion

This meta-analysis showed that AF in patients with LVADs is associated with an increased mortality rate and is not associated with increased bleeding or thromboembolism. However, as previously mentioned, interpretation of our results is limited by the potentially confounding factors from retrospective studies. Our observations highlight the current uncertainty regarding arrhythmias in patients with LVADs and the need for future research as well as larger prospective studies. Given the complexity of the LVAD population, the clinical implications and management strategies of AF can be challenging in clinical practice. Important knowledge gaps about arrhythmias in LVAD recipients remain, and determining the benefit of any particular treatment remains challenging given the paucity of data available.

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