Sex differences on outcomes of catheter ablation of ventricular tachycardia in patients with structural heart disease: A real-world systematic review and meta-analysis

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BACKGROUND Sex differences have diversely affected cardiac diseases. Little is known whether these differences impact outcomes of catheter ablation of ventricular tachycardia (VT).

OBJECTIVES To assess the impact of sex differences on outcomes of catheter ablation of VT.

METHODS Databases were searched from inception through December 2021. Effect estimates from individual studies were extracted and combined using the random-effects, generic inverse variance method of DerSimonian and Laird. The outcomes of interest included VT recurrence rates, all-cause mortality, and composite outcomes of mortality, left ventricular assistant device use, and heart transplantation following VT ablation.

RESULTS Our analysis included 22 observational studies. There were 10,206 patients, of which 12.8% were women. We found no statistical difference between sexes for VT recurrence rate (pooled hazard ratio [HR] 1.04, $P = .57$, $I^2 = 14.9\%$). Similarly, there was statistical difference in neither all-cause mortality nor composite outcomes (pooled HR 0.93, $P = .75$, $I^2 = 59.1\%$ and pooled HR 0.9, $P = .33$, $I^2 = 0\%$, respectively). There was a trend toward an increase in women undergoing VT ablation in the recent registries ($P = .071$).

CONCLUSION Our contemporary analysis suggests that sex may have no impact on clinical outcomes of catheter ablation of VT in patients with structural heart disease, though women are the underrepresented. However, recent VT ablation registries have involved more women in their studies. Future studies with a higher proportion of women are encouraged to verify the current perception.

KEYWORDS Gender; Sex; Ventricular tachycardia; Ablation; Mortality; Recurrence rates; Systematic review; Meta-analysis

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The impact of sex differences on cardiac arrhythmias has been shown in many studies.[1–3] In addition to the physiological differences, several studies have shown that women were underrepresented and probably undertreated.

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KEY FINDINGS

- From recent ventricular tachycardia ablation registries, sex was associated with neither an increased risk of ventricular tachycardia recurrence nor all-cause mortality.
- Despite the underrepresentation of female participants, there was an uptrend of a higher proportion of women in recent registries from 2013 to 2021.
- Our study warrants the need of studies with greater portions of women to validate sex implications among patients who undergo ventricular tachycardia ablation.

Among patients with atrial fibrillation (AF), referrals for a rhythm control strategy were significantly lower in women compared with men.[4,5] Similarly, implantable cardioverter-defibrillators (ICDs) were less commonly used in women, though they share the same survival benefit as men.[6]

The primary pillars of ventricular tachycardia (VT) treatment comprise medications, ICDs, catheter ablation, and autonomic nervous system modulations (stellate ganglion block or thoracic sympathectomy). ICDs have been shown to improve survival in ischemic cardiomyopathy (ICM) and nonischemic cardiomyopathy (NICM),[7,8] while appropriate ICD therapies are associated with poorer psychological outcomes and increased mortality risks.[9–11] Although antiarrhythmic medications offer a noninvasive approach to suppressing VT, patient intolerance and adverse reactions remain an issue. A recent meta-analysis of pooled randomized controlled trials (RCTs) shed light on the benefits of catheter ablation over medical therapy in reducing ICD shocks and VT recurrence rate, as well as in improving composite cardiovascular outcomes.[12] Nonetheless, little is known about whether sex impacts the clinical outcomes of catheter ablation of VT and whether women are equal recipients of this therapy compared with men. We aimed to investigate sex differences in VT catheter ablation outcomes using systematic review and meta-analysis.

Methods

This study was complied with MOOSE (Meta-analysis of Observational Studies in Epidemiology) statement as described in the Supplemental File.[13] Institutional review board approval was not sought because of the use of publicly available cumulative published data.

Literature review and search strategy

A systematic literature search of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews was conducted, retrieving databases from inception to December 2021. Search terms were included “cardiomyopathy,” “ischemic,” “nonischemic,” “structural heart disease,” “gender,” “sex,” “male,” “female,” “men,” “women,” “ventricular tachycardia” and “catheter ablation,” provided in the Supplemental File.

Study selection

Citations were stored, and duplicates were removed using the EndNoteX8 software (Thomson Reuters, Toronto, Ontario, Canada). Two independent reviewers (N.P. and P.C.) screened the abstracts and titles of the studies and subsequently reviewed the full-text articles for inclusion on the Covidence.[14] No language restriction was limited. A manual search for conceivably relevant studies using references of the included articles was also performed. Authors of the included trials were contacted to clarify unclear information, if necessary. Disagreements between the reviewers were resolved by consensus-based discussions. Newcastle-Ottawa quality assessment scale was used to appraise the quality of case-control and cohort studies, and the Cochrane Collaboration’s tool for RCTs was used to appraise the quality of randomized trials, as shown in the Supplemental File.[15]

Inclusion criteria

The inclusion criteria were study type (cross-sectional study, case-control study, cohort study, or RCT), patient population (adults >18 years of age with structural heart disease undergoing catheter ablation of VT), exposure (women), control (men), and outcomes (VT recurrence and all-cause mortality).

Data extraction

Comprehensive data extraction was performed to derive the following information from each study: title, year of the study, name of the first author, publication year, country where the study was conducted, demographic and characteristic data of subjects, total numbers of participants in each study, and outcomes. Studies with <100 samples were excluded to mitigate the small-study effect. To acquire the most accurate analysis, we utilized only hazard ratios (HRs) from multivariate adjustment, if they were available in the selected studies. Otherwise, HRs with univariate adjustment were chosen for our analysis. As all landmark studies relevant to VT ablation did not provide HRs when sex was subanalyzed, they were not included per our inclusion criteria.[16–18]

Outcome of interest

The outcomes of interest included VT recurrence and all-cause mortality. We performed subgroup analyses by types of cardiomyopathies, either ICM or NICM. To determine the influence of age, we stratified mean age by more than or less than 60 years in our subgroup analysis for the main outcomes of interest. Exploratory analyses of cardiac mortality and composite outcomes, including usage of left ventricular assist device, heart transplantation, and all-cause mortality, were performed if data were retrievable. Furthermore, a trend analysis was performed to determine the temporal changes in the proportion of women who underwent VT catheter ablation.

Statistical analysis

A random-effects model was used to perform meta-analysis given the anticipated between-study heterogeneity. For dichotomous data, generic inverse variance method of DerSimonian and Laird[19] was used to estimate pooled HRs and 95% confidence intervals (CIs). To assess for possible effect of modification, meta-regression was used for analysis, if suspicions were raised. The heterogeneity of effect size estimates across studies was quantified using the Mantel-Haenszel chi-square test and I^2 statistics. Substantial heterogeneity was predefined as $P < .10$ for Mantel-Haenszel chi-square test. The I^2 statistic ranges in value from 0% to 100% ($I^2 < 25\%$ indicates low heterogeneity, $I^2 = 25\%$ to 50% indicates moderate heterogeneity, and $I^2 > 50\%$ indicates substantial heterogeneity). To assess the influence of each study on overall heterogeneity, a sensitivity analysis was performed to determine the overall robustness of the study.

To analyze the temporal trends of women who underwent VT ablation, we determined the proportion of total women in relation to the total population of included studies stratified by the publication year. The percentage of women per total population in each publication year was assimilated, and the P trend test was performed using the nptrend command in the STATA package (STATA version 16; StataCorp, College Station, TX).

In accordance with the Cochrane Collaboration, publication bias was assessed by evaluation of the symmetry of a funnel plot. Egger's linear regression test and Begg's rank correlation test were used for objective evaluation, for which the presence of publication bias is defined by $P < .05$. All analysis was performed using STATA version 16.

Results

Using our search strategy through Covidence, we identified 2298 potentially eligible studies. We excluded 388 duplicate studies and 1754 studies that did not meet the inclusion criteria based on article types, methodologies, and outcomes of interest, leaving 154 studies for full-length review. Of the excluded studies, 81 had unavailable data of interest, 41 had a sample size <100, 4 provided no outcomes of interest, 2 studies had duplicate databases, 4 studies included patients with and without structural heart disease, and 2 studies were without participants of interest. Thus, our final analysis included 22 retrospective studies. The literature retrieval, review, and selection process are demonstrated in Figure 1. Characteristics and quality assessment of the included studies

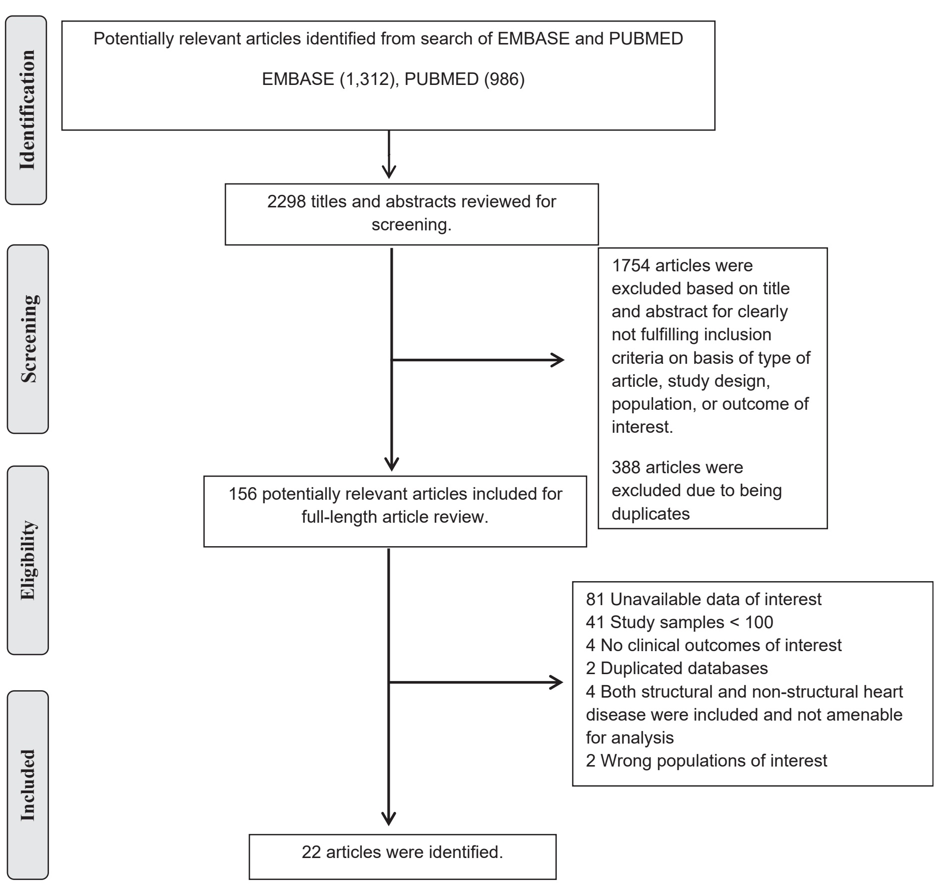

Figure 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow.

Table 1 Study characteristics

Study name	Aldhoon[20]	Baldinger (ICM)[21]	Baldinger (NICM)[21]	Darma[22]	Della Bella[23]	Di Biase[24]	Di Marco[25]	Frankel[26]	Komatsu[27]	Kumar[28]
Year	2017	2017	2017	2020	2013	2021	2017	2016	2015	2017
Study design	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective
Country	Czech	Switzerland	Switzerland	Germany	Italy	United States	Spain	Multiple	France	United States
Patient characteristics	Patients with SHD-related VT	Patients with ICM-related VT	Patients with NICM-related VT	Patients with SHD-related VT	Patients with SHD-related VT	Patients with IHD-related VT	Patients with prior MI-related VT	Patients with SHD-related VT	Patients with SHD-related VT	Patients with SHD-related VT
Single/multicenter	Single	Single	Single	Single	Single	Single	Single	Multicenter	Multicenter	Single
Years of data collection	2006–2013	2005–2015	2005–2015	2012–2015	2007–2011	N/A	2010–2013	2002–2013	N/A	1999–2014
Total population	328	485	301	309	616	134	84	2062	195	923
Female , %	11.6	9	22	12.2	11	11	4.8	12.9	8.2	12
Follow-up, y	2.5	0.75	0.75	3	2.1	2	1.6	2.1	1.9	3.6
Age, y	63.4 ± 12.1	67.6 ± 10.71	57.52 ± 14.28	64.1 ± 12	61 ± 14	66 ± 10	69 ± 10	62.4 ± 13.3	65 ± 11	68 ± 10
LVEF, %	32.5 ± 11.4	28.5 ± 11.54	38.5 ± 19.03	34 ± 13	38.5 ± 13	30.5 ± 7.7	33.5 ± 7	33.6 ± 13.2	32 ± 11	30 ± 10
ICM, %	72.3	100	0	60.1	47	100	100	53	74	60
Use of ICD, %	84.7	92	85	N/A	70.1	100	100	86.3	100	N/a
Use of CRT, %	35.1	31	25.1	N/A	N/A	N/A	N/A	25.4	N/A	N/a
NYHA functional class ≥III, %	45.5	28	22.3	34.9	24.5	50.7	36.9	33.3	28	35
NOS	6	7	7	6	7	7	7	7	7	7

Values are mean ± SD, unless otherwise indicated.
ICM = ischemic cardiomyopathy; NICM = nonischemic cardiomyopathy.

Table 1a Study characteristics (part 2)

Study name	Kuo[29]	Kulchetscki[30]	J. Liang[31]	E. Liang[32]	Maury[33]	Muser[34]	Muser[35]	Okubo[36]	Peretto[37]	Santangeli[38]
Year	2021	2021	2017	2020	2014	2017	2019	2020	2020	2014
Study design	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective
Country	Taiwan	Brazil	United States	China	Europe	United States	United States	Italy	Italy	United States
Patient characteristics	Patients with scar-related VT	Patients with Chagas disease–related VT	Patients with SHD-related VT	Patients with ARVD-related VT	Patients with SHD with LVEF >30% with VT	Patients SHD with drug resistant VT storm	Patients with NIDCM and VT	Patients with NICM-related VT	Patients with history of myocarditis-related VT	Patients with SHD scar–related VT
Single/multicenter	Single	Single	Single	Single	Multicenter	Single	Single	Single	Single	Single
Years of data collection	2010–2013	2013–2018	2008–2011	2000–2019	2005–2010	2005–2014	1999–2014	2010–2016	2010–2019	2010–2011
Total population	317	121	231	284	166	267	282	403	125	193
Female, %	12.9	35.6	10	18.7	16	8	20	13	7	11.90
Follow-up, y	3.3	1	1.7	3	3	3.7	4	6.8	5.2	1.5
Age, y	64 ± 13	58.9 ± 10.2	63.4 ± 12.9	38.2 ± 13.3	62 ± 15	65 ± 13	59 ± 15	57.2 ± 15.6	51 ± 14	62.4 ± 14.7
LVEF, %	33 ± 13	35 ± 9.5	31.4	60.8 ± 8.7	50 ± 10	29 ± 13	36 ± 13	41.8 ± 15.5	52 ± 9	35 ± 15
ICM, %	55	0	53.7	9.86	81	73.4	0	0	0	56
Use of ICD, %	55.2	61.9	94.8	14.4	12	N/A	85	77	78	54
Use of CRT, %	33.1	5.7	43.2	N/A	N/A	N/A	23	77		36
NYHA functional class ≥III, %	25.2	23	25.5	0.3	6	37	30	20.5	0	20
NOS	8	5	7	7	6	7	7	7	7	7

Table 1b Study characteristics (part 3)

Study name	Silberbauer[39]	Tung[40]	Wolf[41]
Year	2014	2015	2018
Study design	Retrospective	Retrospective	Retrospective
Country	Italy	Multiple	France
Patient characteristics	Patients with post–MI-related VT	Patients with SHD-related VT	Patients with post–MI-related VT
Single/multicenter	Single	Multicenter	Single
Years of data collection	2010–2012	2002–2013	2006–2015
Total population	160	2061	159
Female, %	3.75	12.80	4.40
Follow-up, y	1.54	1	3.9
Age, y	70.0 ± 8.1	63.5 ± 13.2	65 ± 11
LVEF, %	34.1 ± 9.2	30.9 ± 14.9	34 ± 11
ICM, %	100	53.10	100
Use of ICD, %	94	84	92
Use of CRT, %	21.9	24.90	26
NYHA functional class ≥III, %	29.60	31.40	20
NOS	6	7	7

ARVD = arrhythmogenic right ventricular dysplasia; CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; ICM = ischemic cardiomyopathy; IHD = ischemic heart disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; N/A = not available; NICM = nonischemic cardiomyopathy; NIDCM = nonischemic dilated cardiomyopathy; NOS = Newcastle-Ottawa Scale; NYHA = New York Heart Association; SHD = structural heart disease; VT = ventricular tachycardia.

are presented in Table 1. In summary, Newcastle-Ottawa Scale ranged from 5 to 8, indicating moderate to high quality of the included studies (Supplemental File).

Study characteristics and quality assessment

The population in our study was 10,206 patients in total, with women comprising 12.8%. In general, the proportion of women in studies that met our inclusion criteria ranged from 3.75% to 35.6%. The average age of patients in our study was 62.5 ± 12.8 years. Most VT ablation registries were from North American or European centers (19 studies), 2 studies were from Asia (China and Taiwan),[29,32] and 1 study was from South America (Brazil).[30] The Frankel and colleagues[26] and Tung and colleagues[40] studies were from an international registry (International VT Ablation Center Collaborative Group), which comprised multiple centers from Europe, the United States, and Japan. The majority of patients who underwent VT ablation had ICM (52.8%), while the remaining 47.2% had NICM. The use of ICD in each study ranged from 12% to 100%. Mean follow-up time ranged from 0.75 to 6.8 years (Table 1).

VT recurrence rates

From 16 studies, our analysis demonstrated no statistically significant difference in VT recurrence between women and men (pooled HR 1.04, 95% CI 0.9–1.22, $P = .57$, $I^2 = 14.9\%$) (Figure 2A) A subgroup analysis was performed by cardiomyopathy types (ICM, NICM) and from 10 studies, no statistically significant difference in VT recurrence was observed (pooled HR 0.79, 95% CI 0.58–1.1, $P = .16$, $I^2 = 0\%$ in ICM and pooled HR 1.02, 95% CI 0.78–1.33, $P = .89$, $I^2 = 26.9\%$ in NICM). A subgroup analysis stratified by age group did not show a statistical association ($P = .627$ in age >60 years and $P = .890$ in age <60 years) (Supplemental File).

All-cause mortality

For 10 studies, our analysis did not demonstrate a statistically significant difference in all-cause mortality rate between sexes (pooled HR 0.93, 95% CI 0.58–1.47, $P = .75$, $I^2 = 59.1\%$) (Figure 2B). A subgroup analysis was performed by cardiomyopathy type (ICM, NICM). Only 5 available studies met our inclusion criteria and, in a similar trend, did not show a statistically significant difference in all-cause mortality (pooled HR 1.06, 95% CI 0.61–1.85, $P = .84$, $I^2 = 0\%$ and pooled HR 1.82, 95% CI 0.23–14.46, $P = .57$, $I^2 = 83.9\%$, respectively). In a subgroup analysis stratified by age group, there was also no statistical association ($P = .697$ in age >60 years and $P = .573$ in age <60 years) (Supplemental File).

Composite outcomes

Available composite outcomes, including all-cause mortality, transplantation rates, and usage of left ventricular assist device, were available in 5 studies. Again, we found no statistically significant sex differences on composite outcomes (pooled HR 0.9, 95% CI 0.72–1.2, $P = .33$, $I^2 = 0\%$) (Figure 3A).

Cardiac mortality

From 3 available studies, we found no statistically significant sex differences in cardiac mortality despite a trend toward higher cardiac mortality in women (pooled HR 2.0, 95% CI 0.88–4.5, $P = .1$, $I^2 = 58.1\%$) (Supplemental File).

Meta-regression

Considering age as a continuous variable, we further performed a meta-regression analysis to assess the potential effect modification by age. Our analysis suggested that age did not confer a significant impact on the main outcomes, both

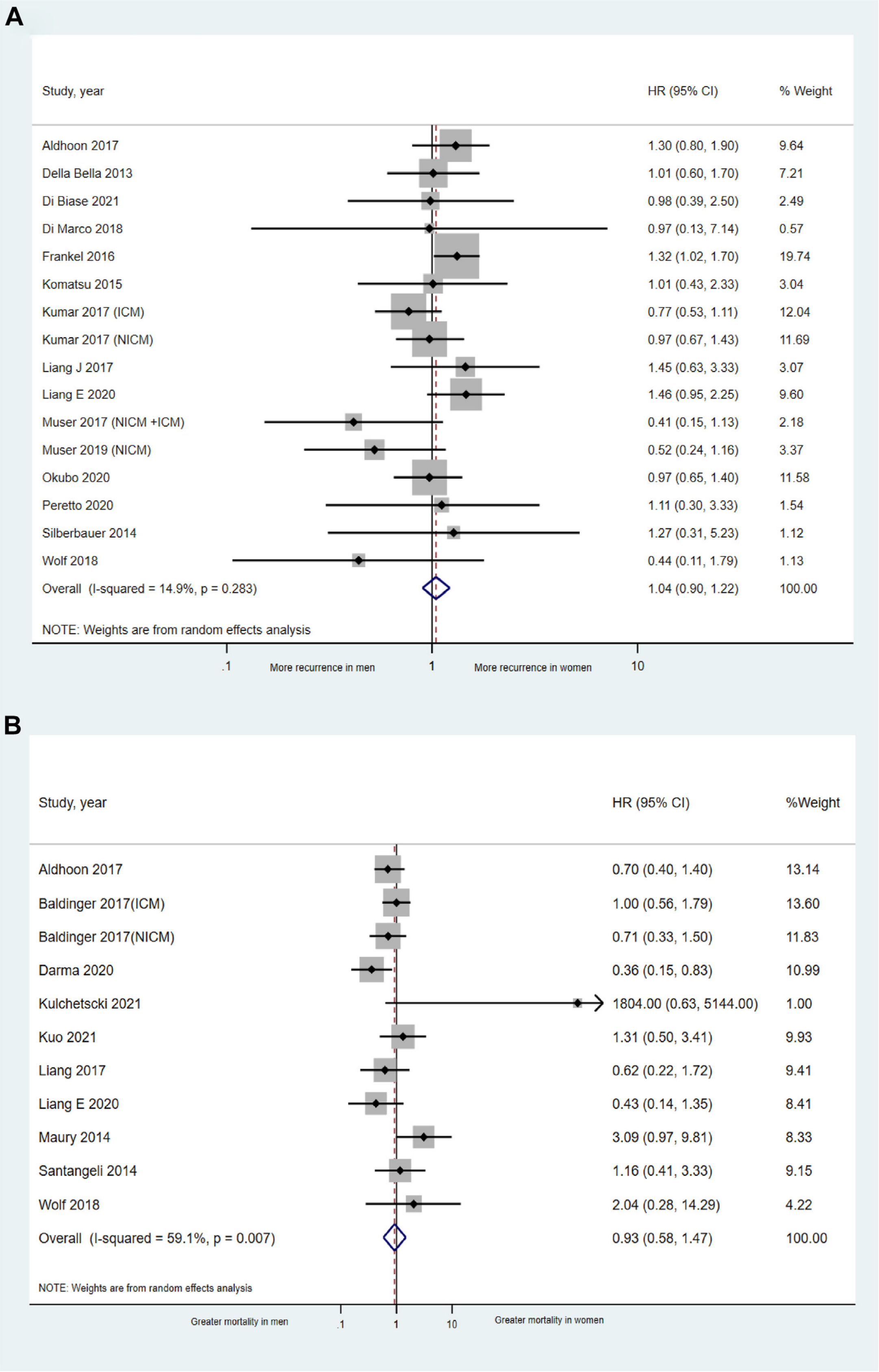

Figure 2 Forest plot including studies that compared women and men for **A:** ventricular tachycardia (VT) recurrence and **B:** all-cause mortality. ICM = ischemic cardiomyopathy; NICM = nonischemic cardiomyopathy.

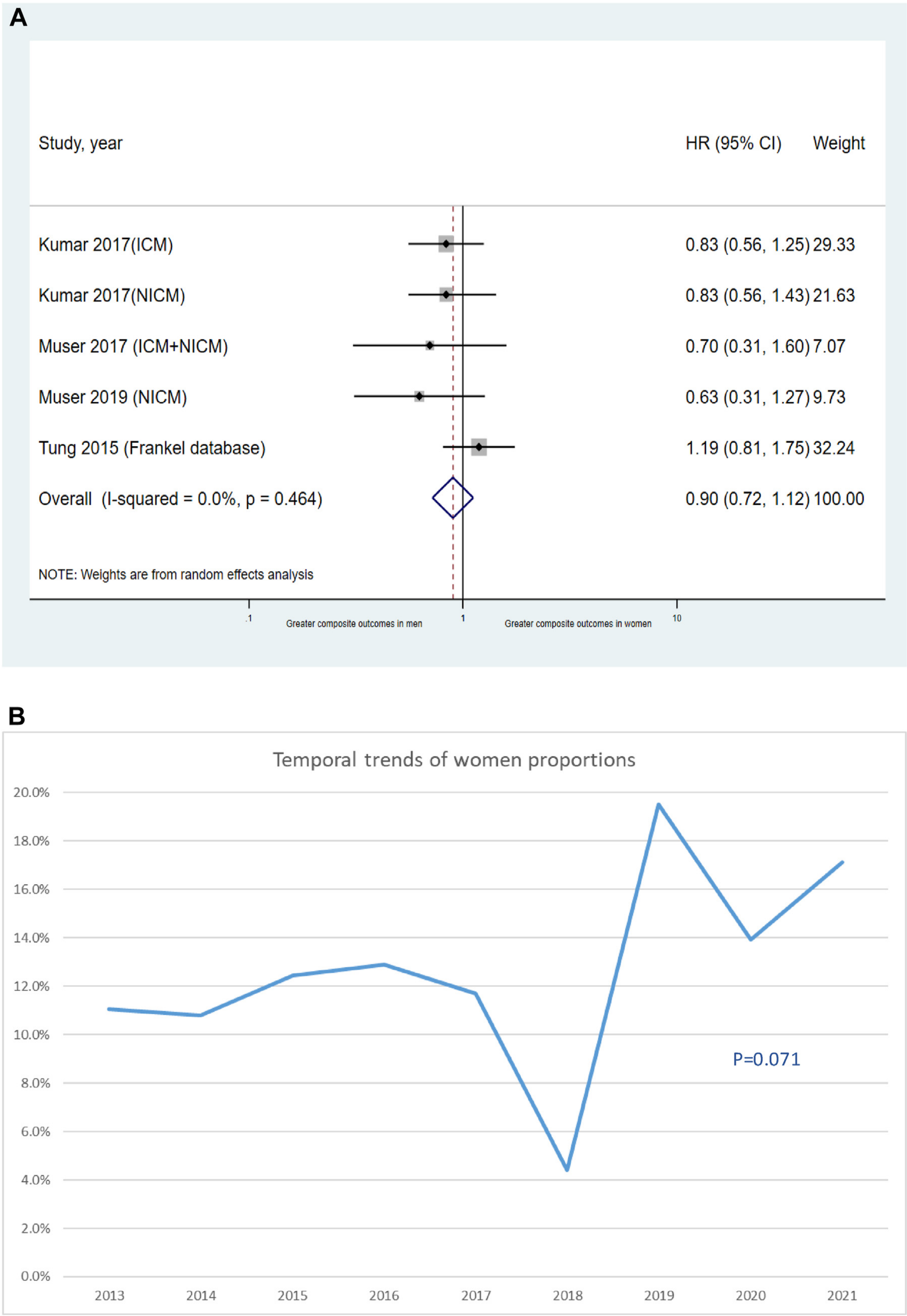

Figure 3 Forest plot including studies that compared women and men for **A:** composite outcomes and **B:** temporal trend of women who underwent ventricular tachycardia (VT) catheter ablation. ICM = ischemic cardiomyopathy; NICM = nonischemic cardiomyopathy.

VT recurrence and mortality (P = .541 and .245, respectively) (Supplemental File).

Trend analysis

We further performed P trend analysis to assess the temporal trends of women who underwent VT catheter ablation by the year of study publication. There was a trend toward a yearly increment in the proportion of women, with a P value of .071 (Figure 3B).

Publication bias and sensitivity analyses

Publication bias was not found from funnel plots and Egger's linear regression test for VT recurrences and all-cause mortality analyses (Supplemental File). Sensitivity analyses are provided separately in the Supplemental File.

Discussion

Our systematic review and meta-analysis found that fewer women were referred for VT ablation compared to men, and that these data with suboptimal representation of women appear to show no difference in both sexes on VT recurrence, all-cause mortality, cardiac mortality, or composite outcomes. In our subgroup analysis by cardiomyopathy types (ICM vs NICM) and age groups (stratified by more than or less than 60 years), there was no statistical difference in VT recurrence and all-cause mortality. Nevertheless, we found a trend toward higher proportions of women undergoing VT catheter ablation during the publication year from 2013 to 2021.

From our analysis, women remained underrepresented among patients who underwent VT ablation. Women comprised only 12.8% of the study population, which is in line with other RCTs in which women made up 7% to 13% of participants.[16–18] Limited evidence exists to explain this notion. One speculation is that men tend to have a higher rate of ventricular arrythmia when compared with women in both ICM and NICM.[42] As a result, the proportion of men being referred for VT ablation is more than women. Previous studies have also shown that women had a lower risk of ICD therapies and VT inducibility among ICM patients.[43,44] In NICM, women had significantly lower VT or ventricular fibrillation rates but higher noncardiac death compared with men, despite a similar composite outcome of VT or ventricular fibrillation and death between sexes.[43]

Sex disproportionality in our analysis could denote a possibility of selection bias, especially referral bias. As previously discussed, men were transferred for VT ablation, owing to higher ventricular arrythmia burdens and ICD therapies. Of note, female participants from certain registries[26,21] were younger and had fewer comorbidities. This observation implies that sicker patients may be managed conservatively and resulted in less presentation in registries.

The slow enrollment of VT registries may partly affect our results as only retrospective studies met our inclusion criteria. Because the slow recruitment process has substantially limited the number of study participants in prospective studies,[45] insufficient data may preclude further subanalyses on sex aspects. More bodies of evidence are needed to establish firm conclusions, knowing a scant female portion from prior studies.

In contrast to a study by Frankel and colleagues,[26] our study did not find any sex differences in VT recurrence. Frankel and colleagues demonstrated that female sex portended a higher risk of VT recurrence for several reasons, such as shorter ablation time and a higher proportion of nonischemic substrates. The perceivably thinner myocardial wall in women may cause the operators to perform less aggressive ablation compared with male patients.[45,22] A recent meta-analysis including 4 cohort studies demonstrated higher rates of ventricular arrythmia recurrences and procedure failure in NICM compared with ICM substrates.[46] The modification and progression of substrates over time, difficulty in isthmus identification, inefficient energy delivery to midmyocardium, and more intricate VT circuits in NICM were regarded as potential mechanisms.[47,48]

On the other hand, similar results have not been reproducible in other studies.[21,22] In a study by Baldinger and colleagues,[21] a subgroup analysis observed no difference in VT recurrence rates despite a shorter ablation time in women with NICM. Darma and colleagues[22] conducted a case-control study to examine sex differences in VT ablation. Women had a longer referral time for VT ablation, suboptimal goal-directed medical therapy, and a higher rate of inducible VT during electrophysiology study. Nevertheless, similar recurrence rates were noted in both sexes and were similar in ICM and NICM.[21,22] These findings resemble our subgroup analyses, which showed no difference in VT recurrence regardless of sex or cardiomyopathy type. These suggest that the efficacy of VT ablation is equivalent between sexes. Furthermore, state-of-the-art ablation technologies, including high-density mapping systems, ablation techniques, and advancements in goal-directed medical therapies for heart failure with reduced ejection fraction, might render more reliable lesion formation and limit the progression of VT substrates.[49–51]

In addition, our analysis did not find statistically significant sex differences in all-cause mortality or transplantation rates after VT ablation. Subgroup analysis demonstrated similar trends in cardiomyopathy types (ICM and NICM) and age groups (more or less than 60 years of age). Dedicated studies that focused on the impact of sex and post–VT ablation outcomes discovered similar results to our study.[21,22] Nonetheless, little is known about whether cardiac and noncardiac mortality are disparate between women and men. From the best available data, we did not find any differences in cardiac mortality (P = .1). Indirectly, from previous meta-analyses,[52,53] the rates of appropriate ICD intervention were significantly lower in women compared with men, while total mortality rates were similar. One would estimate that women experience more noncardiac death than men. Whether VT ablation would modify the nonarrhythmic clinical course is unknown, and there is a lack of pertinent data.

There remain caveats despite exhaustive analyses. It is possible that selection bias may play a role in nullifying the impacts of sex in VT catheter ablation. Inadequate statistical power to detect a significant difference in outcome could ensue because of the small number of women. As we previously discussed, women with low-risk clinical profiles may be intentionally included. Thereby, a healthy population effect may assuage the true clinical outcomes. In parallel, the effect modification with age and types of cardiomyopathies may be offset by the lower-risk participants in studies and statistical limitations of a subgroup analysis itself. Nonetheless, these are only our presumptions. These observations may, in fact, reflect a natural course of VT and its epidemiology. This knowledge gap deserves more in-depth investigations in future studies with a larger proportion of women to ensure studies are not underpowered. In fact, the BIO-LIBRA study (Analysis of Both Sex and Device Specific Factors on Outcomes in Patients With Non-Ischemic Cardiomyopathy) (NCT03884608) is purposefully targeting 40% female enrollment and examining device outcomes, including VT in NICM patients. We anticipate that this study will provide much more meaningful insights, as inequalities in sex proportions are mitigated.

Despite the underrepresentation of women, we found that the recent studies recruited higher percentages of female patients. The improvement in heart disease awareness among women was reported in American Heart Association National Survey in 2012.[54] In the future, specific protocols to ensure optimal sex representation are vital. It will enhance the study generalizability and explore the potential sex-specific effect.

Limitation

There are several limitations to our study. First, as essential information was not available in RCTs or prospective trials, only retrospective studies were thus included. Thereby, typical biases from a retrospective design are inevitable. As described, we cannot deny the possibility that selection bias may play a role in abating the sex effects on VT catheter ablation, disfavoring the representativeness of women in this meta-analysis. Thus, the interpretation of our data must be cautiously exercised. However, to our knowledge, this is the largest and most up-to-date pooled analysis. We only included studies with available HRs to account for time-to-event endpoints. Second, substantial heterogeneity was found in our analysis, which can be explained by the diversities in demographic data, methodologies, follow-up time, procedural aspects, and other unexplorable factors. As anticipated, we utilized an a priori random-effects model to justify the appropriate assumption. The sensitivity analyses were performed, showing the consistency in results. Third, we were not able to appraise whether sex had any impact on noncardiac mortality given the unavailable data. Complication rates and procedural aspects were not analyzed, owing to the same reasons. Last, our study is liable to referral bias for VT ablation in women because of the small proportion in included studies, ranging from 3.75% to 35.6% (Table 1). Whether women were preferentially excluded from the clinical trials and prior observational studies is unclear. Future investigations are warranted to determine the reasons that women are underrepresented.

Conclusion

From real-world experiences, our study demonstrated that women are underrepresented for VT ablation referral. Nonetheless, we observed an uptrend of a higher proportion of women in the recent registries with the publication year from 2013 to 2021. There was no statistical difference in VT ablation outcomes, including VT recurrence and all-cause mortality between men and women. Further studies with a higher women proportion will improve our conceptions of the roles of sex.

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Ethics Statement: This study was compiled with MOOSE (Meta-analysis of Observational Studies in Epidemiology) statement as described in the Supplemental Data. Institutional review board approval was not sought because of the use of publicly available cumulative published data.

Disclaimer: Given his role as Associate Editor, Nazem Akoum had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Jeffrey S. Healey.

Appendix Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hroo.2022.09.009.

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