

# Is there a Link between Sex and the Ablation Outcome of Atrial Fibrillation?: An Updated Systematic Review and Meta-Analysis

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## ABSTRACT

**Aim:** While females are at a higher risk of Atrial Fibrillation (AF), it is unclear whether gender differences are associated with AF recurrences after catheter ablation for AF. The goal of this study was to conduct a systematic review of the medical literature to evaluate the clinical outcomes of catheter ablation for AF in men and women.

**Methods:** A systematic review of databases (PubMed, World of Science, and Embase) was conducted to identify studies published since 2010 that reported AFCA by sex. The primary endpoints were freedom from recurrence of AF/Atrial Tachycardia (AT), and the procedure complications of interest were (1) vascular/groin complications; (2) pericardial effusion/tamponade; (3) stroke/TIA; (4) permanent phrenic nerve injury; and (5) procedural mortality. When the heterogeneity between studies was 50% (freedom from AF/atrial tachycardia), random effects models were used for meta-analysis, and fixed effects models were used for all other endpoints.

**Results:** 22 studies met the inclusion criteria, with 281872 patients undergoing AFCA, 34% of whom were women. Women were older (63.54.13 vs. 60.254.00 years), more likely to be hypertensive (46.2% vs. 44.7%), and more likely to be diabetic (18.6% vs. 16.7%) (P=0.0001 for all comparisons). Our analyses revealed that the rate of freedom from AF/AT recurrence was lower in women than men at the long year follow-up (Odds Ratio (OR): 0.67, 95% Confidence Interval (CI): 0.57-0.79; P=0.00001), but there were no statistically significant differences in all-cause mortality between men and women (OR=1.07, 95% CI 0.88-1.30, P=0.49). Other complications (pericardial effusion/tamponade, stroke/TIA, vascular complication, and hematoma) were significantly higher in women.

**Conclusion:** Women who had AF catheter ablation may have less efficacy and a higher risk of stroke/TIA and major complications than men. More in-depth research is required to better define the mechanisms of increased risk in women and to identify strategies for closing the gender gap.

Keywords: Ablation; Atrial fibrillation; Complications; Female; Gender

## INTRODUCTION

The most common type of sustained arrhythmia in the world is Atrial Fibrillation (AF) [1]. This escalating epidemic is costly and complicates the treatment of other medical conditions. In addition to an increased risk of stroke, heart failure, and cognitive impairment, atrial fibrillation is associated with a lower quality of life [2]. Several studies have been conducted to investigate the role of gender in the etiology, presentation, and prognosis of AF [3]. Women with AF are more likely than men to have a stroke and to die. The Framingham cohort study found that AF is associated with an odds ratio for death of 1.5 in men and 1.9 in women [4]. As a result, women may benefit more from maintaining sinus rhythm.

Over the last decade, catheter ablation has become a more common option for rhythm control in patients who have failed medical therapy [5]. Women are less likely than men to be referred for catheter ablation, despite the well-established role of Pulmonary Vein (PV) isolation in the treatment of symptomatic AF [6]. Several clinical scoring systems include female sex as a predictor of procedural failure or procedure-related complications, and vascular injury or cardiac tamponade after catheter ablation appear to occur

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more frequently in women [7]. However, no gender difference in outcome or complications after ablation was found in several other long-term observational studies [8]. As a result of this, we conducted an updated systematic review and meta-analysis to investigate the clinical outcomes associated with AF catheter ablation.

## METHODOLOGY

#### Data sources and searches

We conducted a thorough online search of the literature (up to December 2022) in the Medline and EMBASE databases to identify all published clinical studies that compared the outcomes of catheter ablation of AF in men and women. Relevant keywords and medical subject heading terms such as 'atrial fibrillation,' 'gender, "sex, "men,' 'women, "male,' 'female,' 'pulmonary vein isolation,' and 'ablation' were used both individually and in combination in the retrieval strategy. The bibliographies of the reviewed manuscripts were manually retrieved to avoid missing relevant data.

Studies were considered if they reported primary endpoints of interest in patients undergoing catheter ablation of AF and provided specific information on women vs. men within the main article or subgroup. Catheter ablation was used to describe an endocardial ablation procedure (radiofrequency or cryoablation). To determine which studies would be included, the following criteria were used: (i) Studies had to provide accurate information on at least one of the primary endpoints; (ii) All studies had to include at least 500 participants to reduce the risk of small-study effects; and (iii) Endpoints had to be reported as numerical events rather than just odds rates. If relevant data were not provided in the published papers, we made an effort to contact the corresponding authors to ask for more information.

### Outcomes and definitions

The primary goals were to determine the incidence rates of freedom from AF/Atrial Tachycardia (AT) recurrence. Serious complications including mortality from all causes, stroke/ Transient Ischemic Attack (TIA), pericardial effusion/tamponade and severe hemorrhage requiring transfusion were secondary outcomes. Without antiarrhythmic medication, no episode of AF, flutter, or tachycardia lasting longer than 30 seconds after a 1-or3-month break was regarded as being free from recurrence of AF/AT (AADs). All-cause mortality and the first incidence of a stroke or TIA were both referred to as these terms, as well as any deaths that happened during hospitalization or follow-up.

### Data extraction and quality assessment

Data was gathered and reported in line with the preferred reporting items for systematic reviews and meta-analyses in order to compile this article. Using a specified, standardized process and a data gathering tool, three writers abstracted data independently. From the main paper, the following details about the study, the patient, and the operation were taken. Any discrepancies were discussed and settled among the authors. The Newcastle-Ottawa Quality Assessment Scale (NOS) for observational trials was used to rate the effectiveness of the included research [9,10]. The NOS scale has a maximum score of nine and eight questions. We assessed the data based on the populations we selected, how comparable the groups were, and how a star system represented the exposure/outcome of interest [11-15].

### Data synthesis and analysis

Dichotomous data were analyzed using the Odds Ratio (OR) with

95% Confidence Intervals (CIs), whilst continuous variables were analyzed using weighted mean differences. The Cochran Q test was used to determine whether there was study heterogeneity, and the Higgins I 2 tests was used to determine how much heterogeneity was present. These tests show that there is 0-25%, 25-50%, and 50-75% heterogeneity, respectively. The pooled effects of our meta-analyses were estimated using a random-effects model due to the inherent heterogeneity in research design and demographics [16-20].

In order to demonstrate that our results were not significantly influenced by any particular study, pre-specified sensitivity analyses for the primary endpoints were carried out by systematically deleting one study at a time. To further assess the stability of our metaanalysis, numerous subgroup analyses (based on research design, study quality, and patient age) were carried out. We used a randomeffects meta-regression analysis to examine how preselected factors affected the total effect. All statistical analyses were done with STATA 12.0 and the Rev Man software suite (Review Manager, Version 5.3). Two-tailed P-values were used, and a P-value of 0.05 or above was regarded as statistically significant [21-25].

## RESULTS

22 studies met the inclusion criteria and were included in the analysis out of a total of 1316 citations that were generated by the database searches (Figure 1). A total of 281872 patients who underwent AFCA were included in these trials; 33.6% of these patients were women (94930 women) [26-31]. Table 1 lists baseline characteristics broken down by sex. Women receiving ablation had considerably higher rates of diabetes (18.6% vs. 16.7%, p=0.0001) and hypertension (46.2% vs. 44.7%), as well as significantly older ages (63.5 ± 4.13 vs. 60.25 ± 4.00 years). As a result, women had significantly higher CHADS2-VASc ratings in the studies that reported them (n=12, respectively). Left Ventricle Ejection Fraction (LVEF) was normal in the great majority of patients, regardless of gender, when reported (n=9 studies), while women had statistically higher ejection fractions (60.9 ± 4.7% vs. 58.4 ± 4.8%, PI0.0001) and more often had a paroxysmal AF pattern at enrollment. Men were more likely to have coronary artery disease, to have enlarged LA diameter, increased body mass index and less paroxysmal AF.

Table 2 describes the characteristics of the included studies and the definitions applied to each of the procedural complication endpoints. The majority of studies that documented the ablation energy source (n=17 studies) used Radio-Frequency (RF) ablation in their AFCA procedures. Only 4 studies reported using Cryoballoons (Cryo). Fifteen studies were evaluated as good quality (NOS  $\geq$  6), indicating a low risk of bias.

### Freedom from atrial fibrillation/at recurrence

Eighteen studies were included in the quantitative synthesis of freedom from AF/AT recurrence in women vs. men. Some degree of heterogeneity was present as ascertained through the heterogeneity test with I2>50. A random effects model was selected for the analysis. The sex-related difference in freedom from AF/AT recurrence was independent of follow-up time (at 1 year, OR: 0.98, 95% CI: 0.82-1.16; P=0.79; at 1-3 years, OR: 0.67, 95% CI: 0.57-0.79; P<0.00001; at  $\geq$  3 years, OR=0.78, 95% CI: 0.66–0.92; P=0.003 (Figure 2).

Although the need for intervention was not specified in all studies, efforts were made to include only pericardial effusions that required intervention (Table 2). The overall incidence of AFCA-

related pericardial effusion/tamponade was 2.4%, with women having a significantly higher incidence (2.6% vs. 2.2%, OR=1.24, 95% CI: 1.18-1.31) See Figure 3.

#### Stroke/TIA

In 24 studies, 1031 periprocedural stroke/TIA events were reported in 276420 ablations (overall incidence 0.37%). Women had 397 strokes/TIAs out of 93454 AFCA procedures (0.42%), while men had 1031 events out of 182966 procedures (0.34%), resulting in a 27% higher relative risk of stroke/TIA in women (OR: 1.26, 95% CI: 1.11-1.43), P=0.0003) (Figure 4).

#### Other complications

10 studies reported phrenic injury, three of which included outcomes with both RF and Cryo, and most studies all included only RF (Table 2). Studies that included both energy modalities

did not specify whether phrenic complications occurred with RF or Cryo. Overall, the incidence of phrenic injury was very low in both sexes, and there was no different between both groups (0.11% *vs.* 0.09%, OR: 1.44, 95% CI: 0.91-2.26, P=0.12) (Figure 3). Our analysis indicated that women undergoing catheter ablation of AF had an increased risk of vascular compliation (OR: 1.67, 95% CI: 1.56–1.78; P<0.0001), Hematoma (OR: 1.52, 95% CI: 1.43–1.62; P<0.0001).

### Procedural mortality

Mortality was reported in 12 studies, the overall mortality rate associated with AFCA was very low at 0.17% (443 deaths out of 257008 patients undergoing AFCA in 12 studies). And there was no significant difference in the risk of in hospital mortality between the two groups (OR=1.07, 95%CI 0.88-1.30, P=0.49) (Figure 5).



Table 1: Baseline characteristics of the included studies.

| Study                             | A                       | ge                      | B                       | MI                      | Hyperter           | nsion (%)          | Diabe            | tes (%)          | LA a   | irea   | CHA2D             | S2-VASc           | Eject<br>fractio | ion<br>n (%)   |
|-----------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|--------------------|--------------------|------------------|------------------|--------|--------|-------------------|-------------------|------------------|----------------|
|                                   | Female                  | Male                    | Female                  | Male                    | Female             | Male               | Fe-male          | Male             | Female | Male   | Female            | Male              | Female           | Male           |
| Alexis Her-<br>mida 2022,<br>[10] | 63 ± 9                  | 60 ± 10                 | 29 ± 6                  | 29 ± 5                  | 84 (46%)           | 254<br>(46%)       | 19 (10%)         | 66 (12%)         | 23 ± 5 | 25 ± 5 | 2.5 ± 1.2         | 1.4 ± 1.3         | 58 ± 10          | 56 ±<br>11     |
| Andrea M.<br>Russo 2021,<br>[11]  | 69.4<br>(65.3,<br>74.0) | 66.6<br>(59.8,<br>71.2) | 30.0<br>(26.1,<br>34.9) | 30.0<br>(26.8,<br>33.9) | 338/413<br>(81.8%) | 538/695<br>(77.4%) | NG               | NG               | NG     | NG     | 3.0 (3.0,<br>4.0) | 2.0 (1.0,<br>3.0) | NG               | NG             |
| Daniel W.<br>Kaiser 2016,<br>[12] | 61.9 ±<br>11.4          | 58.1 ±<br>10.5          | NG                      | NG                      | 4,061<br>(66.2%)   | 9,246<br>(61.8%)   | 1,400<br>(22.8%) | 3,097<br>(20.7%) | NG     | NG     | 2.9 ± 1.5         | 1.6 ± 1.4         | NG               | NG             |
| Fahd N.<br>Yunus 2021,<br>[13]    | 66.8 ±<br>9.6           | 63.4 ±<br>10.6          | 31.3 ±<br>7.7           | 30.8±6.0                | 1423<br>(72.3%)    | 2449<br>(72.3%)    | 360<br>(18.3%)   | 707<br>(20.9%)   | NG     | NG     | 3.4 ± 1.5         | 2.4 ± 1.6         | 57.8 ±<br>10.0   | 54.0 ±<br>11.5 |
| Moon-hyun<br>Kim 2021,<br>[14]    | 60.8 ±<br>10.2          | 56.0 ±<br>10.5          | NG                      | NG                      | 1797<br>(81.5%)    | 5320<br>(76.3%)    | 972<br>(13.9%)   | 315<br>(14.3%)   | NG     | NG     | 3.5 ± 1.7         | 2.0 ± 1.6         | NG               | NG             |

| Jim W.<br>Cheung<br>2019, [15]       | 62.2 ±<br>0.16 | 67.9 ±<br>0.16 | NG                      | NG                      | 12 459<br>(60.4%) | 19 245<br>(56.6%) | 4223<br>(20.5%) | 6854<br>(20.2%) | NG             | NG            | NG        | NG        | NG            | NG            |
|--------------------------------------|----------------|----------------|-------------------------|-------------------------|-------------------|-------------------|-----------------|-----------------|----------------|---------------|-----------|-----------|---------------|---------------|
| Claude S.<br>Elayi 2018,<br>[16]     | 65.1 ±<br>10.9 | 59.5 ±<br>10.9 | NG                      | NG                      | 16,521<br>(59.4%) | 31,433<br>(54%)   | 4705<br>(16.9%) | 8303<br>(14.3%) | NG             | NG            | 3 (2)     | 1 (2)     | NG            | NG            |
| Jonathan P.<br>Piccini 2012,<br>[17] | NG             | NG             | NG                      | NG                      | NG                | NG                | NG              | NG              | NG             | NG            | NG        | NG        | NG            | NG            |
| Hee Tae Yu<br>2018, [18]             | 50.8 ±<br>8.6  | 49.5 ±<br>7.4  | 23.8 ±<br>3.4           | 25.5 ±<br>3.1           | 58<br>(26.0%)     | 301<br>(36.0%)    | 11<br>(4.9%)    | 84<br>(10.0%)   | 39.5 ±<br>7.5  | 41.0 ± 6.2    | 1.6 ± 0.8 | 0.8 ± 1.0 | 63.8 ±<br>7.3 | 62.1 ±<br>8.5 |
| Karl-Heinz<br>Kuck 2018,<br>[19]     | 64 ± 8         | 57 ± 10        | 28 ± 5                  | 28 ± 4                  | 183<br>(62%)      | 253<br>(55%)      | 21 (7%)         | 39 (9%)         | 39.9 ±<br>6.5  | 41.2 ± 5.8    | NG        | NG        | 64 ± 6        | 62 ± 7        |
| Dimpi Patel<br>2010, [20]            | 59 ± 13        | 56 ± 19        | 28 ±8                   | 27.3 ± 9                | 286<br>(55.2%)    | 1100<br>(40%)     | 57 (11%)        | 414<br>(15%)    | NG             | NG            | NG        | NG        | 56 ± 8        | 49 ± 5        |
| XIAO-<br>Dong<br>Zhang<br>2013, [21] | 62.7 ±<br>10.6 | 61.1 ±<br>10.4 | 24.2 ± 2.6              | 24.1 ± 2.5              | 31<br>(42.5%)     | 59<br>(40.1%)     | 6 (8.2%)        | 22<br>(15.0%)   | 45.9 ±<br>4.6  | 45.5 ±<br>5.7 | NG        | NG        | 59.6 ±<br>4.2 | 58.3 ± 6.2    |
| Marielle<br>Kloostermn<br>2020, [22] | 66 (60-<br>72) | 63 (57-<br>69) | 28.0<br>(24.9–<br>32.7) | 28.4<br>(25.4–<br>31.2) | 186<br>(89.0%)    | 385<br>(90.8%)    | 22<br>(10.5%)   | 54<br>(12.7%)   | NG             | NG            | 3.2 ± 1.1 | 2.1 ± 1.1 | NG            | NG            |
| Danilo<br>Ricciardi<br>2019, [23]    | 62.4 ±<br>9.9  | 58.8 ±<br>10.6 | 27.1 ±<br>5.2           | 27.1 ± 3.6              | 298<br>(50.7%)    | 764<br>(49.6%)    | 29<br>(4.8%)    | 86<br>(5.6%)    | 40.8 ±<br>12.2 | 42.6 ± 5.9    | NG        | NG        | NG            | NG            |
| Laura<br>Ueberham<br>2020, [24]      | 69.0 ±<br>8.2  | 62.7 ±<br>10.1 | NG                      | NG                      | NG                | NG                | 160             | 233             | NG             | NG            | 3.9 ± 1.2 | 2.6 ± 1.2 | NG            | NG            |
| Masateru<br>Takigawa<br>2013, [25]   | 63.2 ±<br>9.1  | 60.0 ±<br>10.5 | 23.2 ± 3.2              | 23.7 ± 2.8              | 121<br>(46.5%)    | 372<br>(43.1%)    | 30<br>(11.5%)   | 90<br>(10.4%)   | 37.2 ± 5.0     | 38.0 ± 5.1    | 0.9 ± 1.0 | 0.8 ± 0.9 | 68.6 ± 6.2    | 65.6 ±<br>7.0 |
| Maura M.<br>Zylla 2016,<br>[26]      | 63.6 ±<br>9.6  | 59.1 ±<br>10.5 | NG                      | NG                      | 139<br>(64.4%)    | 247<br>(60.2%)    | 102<br>(8.5%)   | 186<br>(7.6%)   | NG             | NG            | NG        | NG        | NG            | NG            |
| Seung-Young<br>Roh 2018,<br>[27]     | 59 ± 10        | 59 ± 10        | 25 ± 4                  | 25 ± 3                  | 133<br>(36%)      | 124<br>(34%)      | 29 (8%)         | 35 (10%)        | 41 ± 6         | 41 ± 6        | NG        | NG        | 55 ± 6        | 56 ± 6        |
| Winkle RA<br>2011, [28]              | 65.7 ±<br>9.8  | 60.1 ±<br>10.1 | 28.7 ±<br>6.4           | 29.6 ±<br>4.8           | 117               | 245               | 17              | 47              | NG             | NG            | NG        | NG        | NG            | NG            |
| Mihaela<br>Grecu 2020,<br>[29]       | NG             | NG             | NG                      | NG                      | 709<br>(62.1%)    | 1245<br>(51.1%)   | NG              | NG              | NG             | NG            | NG        | NG        | NG            | NG            |
| Reed Mszar<br>2022, [8]              | 67.5 (9.7)     | 64.2<br>(10.4) | 31.5 (9.4)              | 31.4<br>(16.0)          | 1887<br>(9.3%)    | 3294<br>(8.6%)    | 3851<br>(18.9%) | 7912<br>(20.6%) | NG             | NG            | 3.4 (1.5) | 2.2 (1.6) | NG            | NG            |
| Nobuaki<br>Fanaka 2020,<br>[30]      | 67.9 ±<br>8.8  | 63.0 ±<br>10.6 | 23.2 ± 3.8              | 24.3 ± 3.4              | 753<br>(55.0%)    | 1881<br>(51.7%)   | 158<br>(11.5%)  | 561<br>(15.4%)  | 38.9 ± 6.8     | 40.4 ± 6.6    | 2.96      | 1.72      | 65.8 ±<br>8.4 | 62.5 ±<br>9.7 |

Note: Data are presented as mean ± standard deviation or %. Abbreviations: CHADS2:Congestive Heart Failure, Hypertension, Age > 75, Diabetes, Stroke (2 points); CHA2DS2-VASc, Congestive Heart Failure, Hypertension, Age > 75 (2 points), Diabetes, Stroke (2 points), Vascular Disease, Age 65–74, female sex.

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 Table 2: Baseline demographics in the included studies for the different endpoints.

| Study                          | Study character-istics                          | Ablation energy<br>source                       | Follow-up months  | Reported primary outcomes   | NOS points |
|--------------------------------|---|---|-------------------|---|------------|
| Alexis Hermida 2022, [10]      | retrospective cohort                            | Cryoballoon abla-<br>tions                      | 26 ± 21months     | recurrence of ATa   | 5          |
| Andrea M. Russo 2021, [11]     | prospective ran-<br>domized                     | catheter ablation                               | 12months          | death, disabling stroke, serious<br>bleeding, or cardiac arrest   | 7          |
| Daniel W. Kaiser 2016, [12]    | retrospective cohort                            | catheter ablation                               | 12months          | vascular complications,<br>hematoma or hemorrhage,<br>perforation or tamponade, all-<br>cause hospitalization, stroke or<br>TIA   | 7          |
| Fahd N. Yunus 2021, [13]       | retrospective cohort                            | catheter ablation                               | NG                | hemopericardium, phrenic nerve<br>injury, perforation/tamponade<br>requiring surgery, pulmonary<br>vein stenosis, stroke/transient<br>ischemic attack)                                | 6          |
| Moon-hyun Kim 2021, [14]       | retrospective cohort                            | catheter ablation                               | 12months          | -   | 7          |
| Jim W. Cheung 2019, [15]       | Observational<br>Retrospective                  | RF  | 30days            | 30-day all-cause readmission  | 6          |
| Claude S. Elayi 2018, [16]     | Observational<br>Retrospec-tivestudy            | RF  | NG                | occurrence of at least one major<br>complica-tion during the index<br>hospitalization for the ablation<br>procedure   | 6          |
| Jonathan P. Piccini 2012, [17] | Observational<br>Retrospective                  | RF  | 12months          | diagnosis of atrial fibrillation or atrial flutter  | 5          |
| Hee Tae Yu 2018, [18]          | Observational<br>Retrospective                  | RF  | 24.5 ± 18.9months | AF recurrence   | 6          |
| Karl-Heinz Kuck 2018, [19]     | RCT secondary analysis                          | catheter abla-<br>tion+Cryoballoon<br>ablations | 12months          | recurrence of atrial arrhythmia<br>(AF >30 seconds, atrial flutter,<br>or atrial tachycar-dia), (2)<br>prescription of an antiarrhythmic<br>drug, or (3) repeat catheter<br>ablation. | 7          |
| Dimpi Patel 2010, [20]         | Observational<br>Prospective data<br>collection | RF  | 24 ± 16months     | freedom from AF/atrial<br>tachycardia   | 6          |
| XIAO-DONG ZHANG 2013,<br>[21]  | Observational<br>Retrospective                  | RF  | 19 ± 5.0months    | freedom of AF/AT recurrences  | 5          |
| Marielle Kloostermn 2020, [22] | RCT secondary analysis                          | RF+cryoballon abla-<br>tions                    | 3months           | composite all-cause death, stroke,<br>or major bleeding, Cardiac<br>tamponade   | 7          |
| Danilo Ricciardi 2019, [23]    | Observational<br>Prospective data<br>collection | Cryoballoon abla-<br>tions                      | 16.8 ± 13.9months | Freedom from atrial fibrillation<br>(AF) recur-rence.   | 7          |
| Laura Ueberham 2019, [24]      | Observational<br>Retrospective                  | catheter ablation                               | NG                | Vascular access complications (%)   | 7          |
| Masateru Takigawa 2013, [25]   | Observational<br>Retrospective                  | catheter ablation                               | 1/2/3year         | AF-recurrence   | 6          |
| Maura M. Zylla 2016, [26]      | Observational<br>Prospective                    | catheter abla-<br>tion+Cryoballoon<br>ablations | lyear             | AF-recurrence   | 5          |

| Seung-Young Roh 2018, [27] | Matched cohort<br>Retrospective                              | catheter ablation                               | 55 ± 38months | recurrence of atrial arrhythmia    | 6 |
|----------------------------|--|---|---------------|------------------------------------|---|
| Winkle RA 2011, [28]       | observational cohort<br>study                                | catheter ablation                               | 1/2/3yeas     | AF-free rates                      | 6 |
| Mihaela Grecu2020, [29]    | Observational<br>Prospective                                 | catheter abla-<br>tion+Cryoballoon<br>ablations | 12months      | AF recurrence                      | 7 |
| Reed Mszar 2022, [8]       | observational cohort<br>study, prospective co-<br>hort study | catheter abla-<br>tion+Cryoballoon<br>ablations | 10years       | A-V fistula requiring intervention | 6 |
| Nobuaki Tanaka 2020, [30]  | observational study  | catheter ablation                               | 1year/3year   | Atrial fibrillation recurrence     | 6 |

| Study or Subgroup                       | Events                    | Total              | Events     | Total                  | Weight                 | M-H. Random, 95% Cl | M-H. Random, 95% CI                   |
|---|---------------------------|--------------------|------------|------------------------|------------------------|---------------------|---------------------------------------|
| 1.1.2 1 years                           |                           |                    |            |                        |                        |                     |                                       |
| Andrea M. Russo 2021                    | 220                       | 373                | 240        | 633                    | 5.4%                   | 2.35 [1.81, 3.06]   | -                                     |
| Daniel W. Kaiser 2016                   | 5322                      | 6137               | 12759      | 14954                  | 6.8%                   | 1.12 [1.03, 1.22]   | •                                     |
| Jonathan P. Piccini 2012                | 5789                      | 6265               | 8397       | 9158                   | 6.6%                   | 1.10 [0.98, 1.24]   | -                                     |
| Karl-Heinz Kuck 2018                    | 215                       | 293                | 369        | 457                    | 4.6%                   | 0.66 [0.46, 0.93]   |                                       |
| Masateru Takigawa 2013                  | 226                       | 260                | 784        | 864                    | 3.9%                   | 0.68 [0.44, 1.04]   |                                       |
| Maura M. Zvlla 2016                     | 575                       | 1155               | 1280       | 2346                   | 6.4%                   | 0.83 [0.72, 0.95]   | -                                     |
| Mihaela Grecu2020                       | 752                       | 1146               | 1610       | 2447                   | 6.4%                   | 0.99 [0.86, 1.15]   | +                                     |
| Nobuaki Tanaka 2020                     | 919                       | 1369               | 2552       | 3641                   | 6.5%                   | 0.87 [0.76, 1.00]   | -                                     |
| Winkle RA 2011                          | 121                       | 169                | 368        | 465                    | 4.1%                   | 0.66 [0.44, 0.99]   |                                       |
| Subtotal (95% CI)                       |                           | 17167              |            | 34965                  | 50.7%                  | 0.98 [0.82, 1.16]   | <b>♦</b>                              |
| Total events                            | 14139                     |                    | 28359      |                        |                        |                     |                                       |
| Heterogeneity: Tau <sup>2</sup> = 0.05; | Chi <sup>2</sup> = 73.    | 82, df =           | 8 (P < 0.0 | 00001); I              | ² = 89%                |                     |                                       |
| Test for overall effect: Z = 0.         | 26 (P = 0.                | 79)                |            |                        |                        |                     |                                       |
| 1.1.3 1 to 3 years                      |                           |                    |            |                        |                        |                     |                                       |
| Alexis Hermida 2022                     | 74                        | 112                | 200        | 252                    | 3 4%                   | 0.51 (0.31, 0.83)   |                                       |
| Danilo Ricciardi 2019                   | 427                       | 584                | 1163       | 1541                   | 5.8%                   | 0.88 [0.71 1.10]    | -                                     |
| Dimpi Patel 2010                        | 355                       | 518                | 2129       | 2747                   | 5.9%                   | 0.63 [0.51, 0.78]   | -                                     |
| Hee Tae Yu 2018                         | 134                       | 215                | 417        | 573                    | 4.8%                   | 0.62 [0.44, 0.86]   |                                       |
| Masateru Takinawa 2013                  | 216                       | 260                | 768        | 864                    | 4.3%                   | 0.61 [0.42, 0.90]   |                                       |
| Winkle RA 2011                          | 74                        | 110                | 238        | 312                    | 3.6%                   | 0.64 [0.40, 1.03]   |                                       |
| Subtotal (95% CI)                       |                           | 1799               | 200        | 6289                   | 27.7%                  | 0.67 [0.57, 0.79]   | •                                     |
| Total events                            | 1280                      |                    | 4915       |                        |                        |                     |                                       |
| Heterogeneity: Tau <sup>2</sup> = 0.02: | Chi <sup>2</sup> = 8.0    | 8. df = 5          | (P = 0.15) | 5); I <sup>2</sup> = 3 | 3%                     |                     |                                       |
| Test for overall effect: Z = 4          | 74 (P < 0                 | 00001)             |            | ,, .                   |                        |                     |                                       |
| 1.1.4 ≥3 vears                          |                           |                    |            |                        |                        |                     |                                       |
| Alexis Hermida 2022                     | 30                        | 71                 | 120        | 298                    | 3.2%                   | 1.09 [0.64, 1.83]   | <u> </u>                              |
| Masateru Takinawa 2013                  | 206                       | 260                | 750        | 864                    | 4.5%                   | 0.58 [0.41, 0.83]   |                                       |
| Nobuaki Tanaka 2020                     | 747                       | 1369               | 2145       | 3641                   | 6.5%                   | 0.84 [0.74, 0.95]   | -                                     |
| Seung-Young Roh 2018                    | 262                       | 367                | 280        | 367                    | 4.8%                   | 0.78 [0.56, 1.08]   |                                       |
| Winkle RA 2011                          | 38                        | 59                 | 121        | 163                    | 2.6%                   | 0.63 (0.33, 1.19)   | +                                     |
| Subtotal (95% CI)                       | 00                        | 2126               |            | 5333                   | 21.6%                  | 0.78 [0.66, 0.92]   | •                                     |
| Total events                            | 1283                      |                    | 3416       |                        |                        |                     |                                       |
| Heterogeneity: Tau <sup>2</sup> = 0.01: | Chi <sup>2</sup> = 5.4    | 8. df = 4          | (P = 0.24) | 1): $ ^2 = 2$          | 7%                     |                     |                                       |
| Test for overall effect: Z = 2.         | 92 (P = 0.                | .003)              | (, ).m     | ,,                     |                        |                     |                                       |
| Total (95% Ci)                          |                           | 21092              |            | 46587                  | 100.0%                 | 0 83 [0 73 0 94]    | •                                     |
| Total events                            | 16702                     | 21002              | 36600      |                        | . 30.076               | 0.00 [0.10, 0.04]   | · I                                   |
| Heterogeneity: Tau2 = 0.08-             | Ch2 = 12                  | 1 89 44-           | 10 (P -    | 0.00004                | 12 = 86%               |                     |                                       |
| Test for overall effect: 7 = 2          | 96 (D = 0                 | 1.09, ul =<br>004) | 19 (1- 6   | 0.00001                | , i <sup>_</sup> = 00% | 0.01                | 0.1 1 10                              |
| Test for subgroup difference            | ou (P = 0.<br>e: Chil = 0 | 004)<br>361 df=    | 2 /P = 0   | 009) 18                | = 70.2%                | Fav                 | ours [experimental] Favours [control] |
| rescior suburoup difference             | a. unr = 1                | s.u i . ul i       | 2 (P = U   | .uuo). I*              | - /9.2%                |                     |                                       |

Figure 2: Forest plot of freedom from AF/AT in women vs. men at 1-, 1 to 3-, and  $\geq$  3-year follow-up after catheter ablation.

| Study or Subgroup<br>Alexis Hermida 2022 | Events |       |        | -      |        | Ouus Ratio         | Ouus Ratio        |   |
|--|--------|-------|--------|--------|--------|--------------------|-------------------|---|
| Alexis Hermida 2022                      |        | Total | Events | Total  | Weight | M-H, Fixed, 95% C  | M-H, Fixed, 95% C | l |
|  | 3      | 183   | 1      | 550    | 0.1%   | 9.15 [0.95, 88.52] |                   | • |
| Danilo Ricciardi 2019                    | 0      | 584   | 1      | 1541   | 0.2%   | 0.88 [0.04, 21.60] |                   |   |
| Seung-Young Roh 2018                     | 2      | 367   | 1      | 367    | 0.2%   | 2.01 [0.18, 22.21] |                   |   |
| XIAO-DONG ZHANG 2013                     | 1      | 73    | 2      | 147    | 0.3%   | 1.01 [0.09, 11.29] |                   |   |
| Hee Tae Yu 2018                          | 0      | 223   | 3      | 837    | 0.4%   | 0.53 [0.03, 10.36] | · · · ·           |   |
| Andrea M. Russo 2021                     | 1      | 373   | 2      | 633    | 0.4%   | 0.85 [0.08, 9.39]  |                   |   |
| Karl-Heinz Kuck 2018                     | 2      | 293   | 2      | 457    | 0.4%   | 1.56 [0.22, 11.16] |                   |   |
| Marielle Kloosterman 2020                | 0      | 209   | 2      | 424    | 0.4%   | 0.40 [0.02, 8.44]  |                   |   |
| Masateru Takigawa 2013                   | 1      | 260   | 6      | 864    | 0.7%   | 0.55 [0.07, 4.61]  |                   |   |
| Fahd N. Yunus 2021                       | 0      | 1969  | 5      | 3387   | 1.0%   | 0.16 [0.01, 2.83]  | · · · ·           |   |
| Mihaela Grecu2020                        | 4      | 1146  | 7      | 2447   | 1.1%   | 1.22 [0.36, 4.18]  |                   |   |
| Dimpi Patel 2010                         | 4      | 518   | 17     | 2747   | 1.3%   | 1.25 [0.42, 3.73]  |                   |   |
| Maura M. Zylla 2016                      | 3      | 1198  | 10     | 2454   | 1.6%   | 0.61 [0.17, 2.23]  |                   |   |
| Moon-hyun Kim 2021                       | 15     | 2206  | 39     | 6969   | 4.5%   | 1.22 [0.67, 2.21]  |                   |   |
| Laura Ueberham 2019                      | 19     | 2419  | 32     | 4024   | 5.8%   | 0.99 [0.56, 1.75]  |                   |   |
| Reed Mszar 2022                          | 42     | 20419 | 63     | 38541  | 10.5%  | 1.26 [0.85, 1.86]  |                   |   |
| Jonathan P. Piccini 2012                 | 42     | 6265  | 66     | 9158   | 12.9%  | 0.93 [0.63, 1.37]  |                   |   |
| Daniel W. Kaiser 2016                    | 52     | 6137  | 95     | 14954  | 13.2%  | 1.34 [0.95, 1.88]  |                   |   |
| Jim W. Cheung 2019                       | 57     | 20623 | 78     | 33974  | 14.2%  | 1.20 [0.86, 1.70]  |                   |   |
| Claude S. Elayi 2018                     | 146    | 27821 | 199    | 58156  | 31.0%  | 1.54 [1.24, 1.90]  | -                 |   |
| Total (95% CI)                           |        | 93286 |        | 182631 | 100.0% | 1.26 [1.11, 1.43]  | •                 |   |
| Total events                             | 394    |       | 631    |        |        |                    |                   |   |
|  |        | 0.70  | 13 00/ |        |        |                    |                   |   |

Figure 3: `Forest plot of phrenic nerve injury, vascular complications, pericardial effusion/tamponade, Hematoma in women vs men after catheter ablation.

| Number parking         Lower         Lower         Lower         Lower         Lower         Lower         Lower         Lower         Lower           M. Russo 2021         1         373         0         633         0.0%         5.10         1.23         0.53         0.0%         5.10         1.23         0.65         0.07         3.71         0.6         0.387         0.0%         3.71         0.6         0.0%         0.01         0.13         0.00         0.04         0.01<  | or Subgroup                                | Wome<br>Evente                 | Total      | me                             | n<br>Totel | Weight   | Udds Ratio          | Odd:        | s Katio<br>ed. 95% Cl |
|---|--|--------------------------------|------------|--------------------------------|------------|----------|---------------------|-------------|-----------------------|
| non-memory 2022       7       183       15       560       0.1%       1.42 (0.57, 3.54)         nde AR, Kusso 2021       9       1966       6       337       0.1%       5.10 (0.24, 125.66)         nd N, Marso 2021       9       1966       6       337       0.0%       5.10 (0.24, 125.66)         nd N, Marso 2021       1       6.27 (0.0%)       3.77 (0.25, 0.64.47)       1.33 (0.25, 0.67.47)         nd N, Marso 2021       1       2.200       1.6       6.27 (0.0%)       1.33 (0.25, 0.67.47)         nd N, Marso 2021       1       3.00       0.0%       1.36 (0.25, 2.78)       1.42 (0.67, 1.28)         nd N, Marso 2021       1       1.30       3.00       0.0%       1.42 (0.67, 1.28)         nd N, Marso 2021       1       1.53       0.0%       3.00 (0.15, 1.28)       1.42 (0.67, 1.28)         nd N, Kanzo 2016       1.66       6.37       2.66       1.46 (0.67, 1.28)       1.46 (0.67, 1.28)       1.46 (0.67, 1.28)         new Herminal 2022       1.55       3.71       1.20 (0.14, 1.57 (1.16, 1.79)       1.42 (0.67, 1.68)       1.46 (0.67, 1.28)       1.46 (0.67, 1.28)         new Herminal 2022       1.55       3.71       1.70 (0.66, 1.20)       1.46 (0.67, 1.28)       1.46 (0.67, 1.28)       1.46 (0.67, 1.   | 3.1.1 phrenic nerve palsy                  | events                         | TOTAL      | Lvents                         | Total      | Treigilt | m-11, FIXed, 93% CI | W-E, ED     | ou. 30/0 UI           |
| between the construction of the constructio   | Alexis Hermida 2022                        | 7                              | 183        | 15                             | 550        | 0.1%     | 1.42 [0.57 3.54]    | -           | · · ·                 |
| heln V. Vuos 2021 9 1969 6 397 0.1% 229 102, 728<br>held V. Vuos 2021 1 2 200 5 804 0.0% 33 [0.2, 80, 44<br>held General 2020 5 1146 10 2247 0.1% 0.58 [0.1, 10, 51, 31, 227]<br>held General 2020 5 144 [0.3, 227] 5 264 0.0% 1.33 [0.2, 80, 44<br>held General 2020 5 144 [0.3, 227] 5 264 0.0% 1.44 [0.3, 2.27]<br>held V. Kanz 201 5 20, 00 k/ F = 0%<br>start or vent affect. 2 + 1.57 (F = 0.4) k/ F = 0%<br>start or vent affect. 2 + 1.57 (F = 0.4) k/ F = 0%<br>start or vent affect. 2 + 1.57 (F = 0.12)<br>1 2 vaccular complexition<br>work Hermids 2022 5 37 3 6 633 0.0% 3.06 [0.61, 15.27]<br>held V. Kanz 201 6 168 6 157 226 1464 0.0% 6.68 [0.60, 74.08]<br>mid V. Kanz 201 7 2 7253 1 370 8 155 4.4% 1.58 [1.53, 1.84]<br>work Hermids 2022 2 5 373 6 633 0.0% 3.06 [0.61, 15.27]<br>held V. Kanz 201 7 2 7253 1 370 8 155 4.4% 1.58 [1.53, 1.84]<br>work Hermids 2022 1 3 183 3 1 550 0.0% 3.06 [0.61, 15.27]<br>held V. Kanz 201 8 6 224 0.04% 3.34 [2.52, 6.16]<br>asater. Takipwa 2013 2 2 260 1 864 0.0% 6.68 [0.60, 74.08]<br>work Users 2013 2 2 260 1 864 0.0% 6.68 [0.60, 74.08]<br>work Hermids 2022 1 3 183 1 550 0.00% 3.06 [0.61, 15.27]<br>held works 1 1066 2028 1164 23 2447 0.35 2.06 [1.4, 3.72]<br>held works 1 1066 2028 117 227 14864 4.4% 1.33 [1.51, 158]<br>work Hermids 2020 21 3 163 1 550 0.00% 9 115 [0.55, 85.2]<br>held works 1 1066 2028 12 0 168 203 307 0.1% 1.38 [0.54, 2.63]<br>held works 2020 13 2 246 6137 427 14654 4.4% 1.33 [1.51, 158]<br>held works 2020 21 3 183 1 1 550 0.00% 9 15 [0.55, 3.46]<br>held works 2020 21 3 183 1 1 550 0.00% 9 15 [0.55, 3.46]<br>held works 2020 21 3 17 27 14654 4.4% 1.35 [1.51, 158]<br>held works 2020 21 1 1 1969 10 3377 0.1% 1.38 [0.54, 2.63]<br>held works 2020 21 2 3 183 3 1 4 200 0.00% 1.52 [1.40, 17.4]<br>held works 2020 21 1 1 1956 10 337 0.1% 1.38 [0.50, 2.78]<br>held works 2020 21 1 2 24 6137 427 [464 4.4% 1.52 [1.51, 158]<br>held works 2020 21 1 2 238 2 6 460 0.7% 1.38 [0.52, 2.03]<br>held works 2020 21 4 233 2 6 460 0.7% 1.52 [1.40, 17.6]<br>held works 2020 21 4 233 2 6 460 0.7% 1.52 [1.40, 17.6]<br>held works 2020 21 4 233 2 7 4006 40 226 5.0% 1.52 [1.40, 17  | Andrea M. Russo 2021                       | 1                              | 373        | 0                              | 633        | 0.0%     | 5.10 [0.21, 125.56] |             | <u>├</u> →            |
| e Tan Yu 2016 1 223 1 837 0.0% 3.77 [0.23, 0.0.4]<br>state Takingwork 2017 2 200 5 844 0.0% 1.35 [0.10, 10.13]<br>The add methods 2017 1 2 223 1 1 223 1 0 0 0 1 0.5 [0.5 0, 20, 20, 0.6 00]<br>the add methods 2017 1 2 223 1 1 223 1 0 0 0 1 0 1 1 0 1 0 1 0 1 0 0 1 0 0 0 0 1 0 1 1 0 1 0 1 0 0 0 0 0 0 1 1 0 0 0 0 0 0 1 0 1 0 0 0 0 0 0 1 0  | Fahd N. Yunus 2021                         | 9                              | 1969       | 6                              | 3387       | 0.1%     | 2.59 [0.92, 7.28]   |             |                       |
| asakur Tukingwa 2013 2 200 5 044 0.0% 1.31 0.28, 6.90<br>conrivus for 2021 1 2206 3 6666 0.0% 1.36 [0.31, 10.51, 31] 0.28, 6.90<br>conrivus for 2021 1 2206 3 6666 0.0% 1.36 [0.31, 10.51, 31] 1.44 [0.31, 2.26]<br>Jal events 3 1 50 0.0% 3.06 [0.51, 15.27]<br>table for 2016 166 617 227 73 6 653 0.0% 3.06 [0.51, 15.27]<br>table for 2016 166 617 227 126 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2016 166 617 227 126 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 15 32.26 17 20 126 22 2.53 17 20 58156 4.4% 1.58 [1.55, 1.58]<br>table for 2012 15 156 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 15 156 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 155 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 155 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 155 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 155 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 155 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 155 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 156 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2012 12 156 2.0623 1158 3374 15.2% 1.58 [1.55, 1.58]<br>table for 2018 12 22 733 1 70 35 0.0% 9.15 [0.36, 8.52]<br>table for 2018 12 22 733 1 70 420 25.0% 1.67 [1.5, 1.57]<br>table for 2018 12 22 733 1 70 420 25.0% 1.67 [1.5, 1.58]<br>table for 2018 12 22 733 1 10 337 0.1% 1.38 [0.04, 2.03]<br>table for 2018 1 223 11 837 1 100 10 12 127 127 [1.56, 1.58]<br>table for 2018 12 22 77 1456 4 4.4% 1.38 [1.51, 1.59]<br>table for 2018 12 22 77 1456 4 124 12.27 [1.57]<br>table for 2012 157 0.265 122 0.968 2.7% 1.16 [0.05, 8.52]<br>table for 2018 12 22 77 1456 4 114 12.21 [1.57]<br>table for 2012 157 0.256 122 0.976 13 160.267 [1.52, 2.03]<br>table for 2012 157 0.256 152 0.961 15 0.964 2.4% 1.52 [1.51, 31]<br>table for 2012 157 0.256 152 0.961 15 0.964 2.4% 1.52 [1.51, 51, 31]<br>table for 2012 157 0.256 152 0.961 15 0.964 2.4% 1.52 [1.51, 31]<br>table for 2012 157 0.256 152 0.961 15 0.967 1.53 0.2% 1.18 [0.50, 7.7]<br>table for 2016 172 77 173  | Hee Tae Yu 2018                            | 1                              | 223        | 1                              | 837        | 0.0%     | 3.77 [0.23, 60.44]  |             |                       |
| hale decad2020 5 1146 10 2247 0.1% 0.98 [0.33, 2.87]<br>deci Misza 2021 5 22410 10 2654 0.1% 0.31 [0.37, 2.78]<br>det organized and the second of   | Masateru Takigawa 2013                     | 2                              | 260        | 5                              | 864        | 0.0%     | 1.33 [0.26, 6.90]   |             |                       |
| Soch-Yun Kin 2021<br>Soch-Yun Kin   | Mihaela Grecu2020                          | 5                              | 1146       | 10                             | 2247       | 0.1%     | 0.98 [0.33, 2.87]   |             |                       |
| bed Mazz 2022 5 20419 10 38541 0.1% 0.34 [0.32, 276]<br>amount Chr = 3.46, d = 7.0 = 0.82, H = 0%<br>set for overall effect Z = 1.57 (P = 0.12)<br>1.2 vascular complication<br>exis Hermida 2022 3 163 3 553 0.0% 3.06 [0.61, 15.27]<br>thermide M. Fusico 2021 5 373 6 6136 4.4% 1.58 [1.35, 1.84]<br>mud S. Elbay 2018 278 2783 7 350 56166 4.4% 1.58 [1.35, 1.84]<br>mud S. Elbay 2018 278 2783 7 350 56166 4.4% 1.58 [1.35, 1.84]<br>mud S. Elbay 2018 278 2783 7 350 56166 4.4% 1.58 [1.35, 1.84]<br>mud S. Elbay 2018 278 2783 7 350 56166 4.4% 1.58 [1.35, 1.84]<br>mud S. Elbay 2018 228 278 2783 7 350 56166 4.4% 1.58 [1.35, 1.84]<br>mud S. Elbay 2018 2 202 1 864 0.0% 1.48 [25.2, 6.16]<br>mud S. Elbay 2018 2 202 1 864 0.0% 1.68 [0.55, 1.78]<br>mud behara 2022 2 14 6 23 2404 7.4% 3.39 [1.54, 2.57]<br>mud behara 2022 2 13 6 2208 42 6 666 0.7% 1.38 [0.34, 2.27]<br>mud behara 2022 3 3 0 2017 25 3581 0.0% 6.59 [0.56, 1.48, 372]<br>mud behara 2022 3 3 0 2017 25 3581 0.0% 6.15 [1.53, 4.53]<br>mud W. Kase 2013 2 246 017 25 25.0% 1.67 [1.54, 1.57]<br>min W. Kase 2018 234 6137 4.27 [1456 4.4% 1.35 [1.51, 1.59]<br>min W. Kase 2019 234 6137 4.27 [1456 4.23% 1.10 [10 [2.1, 1.8]<br>min W. Kase 2019 234 6137 4.27 [1456 4.23% 1.00 [1.10 [2.1, 1.8]<br>min W. Kase 2019 2 246 6137 7 427 [1456 4.4% 1.35 [1.51, 1.59]<br>min W. Kase 2019 2 246 6137 7 427 [1456 4.4% 1.35 [1.51, 1.59]<br>min W. Kase 2019 2 246 6137 7 427 [1456 4.23% 1.10 [10 [2.1, 1.8]<br>min W. Kase 2019 2 246 6137 7 427 [1456 4.24% 1.35 [1.51, 1.59]<br>min W. Kase 2019 2 247 0 10 [1 13 7 [2.56 1.27]<br>min Atala 2.50% [1 18 [2.50, 2.79]<br>min Atala 2.50% [1 2.50]<br>min Atala  | Moon-hyun Kim 2021                         | 1                              | 2206       | 3                              | 6969       | 0.0%     | 1.05 [0.11, 10.13]  |             |                       |
| Jabela (Work) C.D*         24/73         54/28         0.5%         1.44 [0.31, 2.26]           Jate oversel         affect 2 = 1.57 (P = 0.13), P = 0.8         5         0.5%         1.44 [0.31, 2.26]           Jate oversel         affect 2 = 1.57 (P = 0.13), P = 0.8         5         0.0%         3.06 [0.61, 15.27]           Jate oversel         affect 2 = 1.57 (P = 0.12), P = 0.84,   | Reed Mszar 2022                            | 5                              | 20419      | 10                             | 38541      | 0.1%     | 0.94 [0.32, 2.76]   |             |                       |
| Jale worth       31       31       90         with or wordle field: 2 = 1.5 (P = 0.12)       1         12 wascular company: (D+1 = 0.12)       1         13 words       153       0.53       0.0%       3.06 [0.61, 15.27]         wind W. Kanas 2016       128       228       1.42 [0.43, 4.86]         masher P. Pocint 2012       13       245 [1.64]       1.54 [1.61, 5.81]         masher D. Takigawa 2013       2       2.00       1       844 0.0%       6.66 [0.80, 7.406]         masher D. Takigawa 2013       2       2.01       1.64 1.03       2.52 [1.53, 4.31]   | Subtotal (95% CI)                          |                                | 26779      |                                | 54028      | 0.5%     | 1.44 [0.91, 2.26]   |             | <b>•</b>              |
| Detrogenergy Curr 3 44, dt = 10 / P = 0.48, f = 0.08, f   | Total events                               | 31                             |            | 50                             |            |          |                     |             |                       |
| abs: 0 - complexition         exit H-markal 2022       3       183       553       0.0%       3.06 [0.61, 16.27]         read M-task 2021       5       373       6       653       0.1%       1.42 (0.43, 4.68]         mude S. Elby 2016       128       278       2783       170       68166       4.4%       1.56 [1.58, 1.58]         mude S. Elby 2016       128       6266       38       9153       0.5%       1.60 [1.63, 32.20]   | Test for overall effect: 7 = 1.5           | II = 7 (P = 0)<br>57 (P = 0.12 | .84); 1* = | 0%                             |            |          |                     |             |                       |
| 12 vascular complication<br>we Hermid 202 3 183 3 553 0.0% 3.06 [0.61, 15.27]<br>where M. Russo 2021 5 373 6 633 0.1% 1.42 (0.43, 4.68]<br>we have 5. Elay 2016 1276 2773 137 0516 4.44%<br>1.42 (0.43, 4.68]<br>we have 5. Elay 2016 128 2.273 137 05186 4.44%<br>1.42 (0.43, 4.68]<br>we have 5. Elay 2016 128 2.26 1495 3.31%<br>1.38 (1.51, 1.69]<br>we have 1.06 and 2012 38 6265 38 0158 0.6% 1.46 (0.35, 2.30]<br>we have 1.06 and 2012 38 6265 38 0158 0.6% 1.46 (0.35, 2.30]<br>we have 1.06 and 2012 38 6265 38 0158 0.6% 1.46 (0.35, 2.30]<br>we have 1.06 and 2012 38 6265 38 0158 0.6% 1.46 (0.35, 2.30]<br>we have 1.06 and 2012 38 6265 38 0158 0.6% 1.46 (0.35, 2.30]<br>we have 1.00 and 2013 0 2.2 2046 2.2 2046 0.2 2.00 (0.60 (0.31, 15.17)<br>we have 2022 34 20419 2.2 3447 0.3% 2.27 (1.55, 1.78]<br>we have 1.00 and 2.0 373 1 147 0.0% 0.66 (0.30, 15.17)<br>we have 2022 3 3 0.53 1 70.420 2.25 0% 1.67 (1.56, 1.78]<br>we have 1.00 and 2.01 1 1060 2.028<br>tetre generally: Chr = 24.74, df = 11 (P = 0.010; P = 56%<br>st for overall effects and 2.21 1 1837 0.1% 0.34 (0.42, 2.8]<br>we have 1.10 and 2.01 2 518 8 2747 0.0% 1.33 (0.26, 6.27]<br>have 3.16 (0.31, 15.15)<br>minel W. Kalser 2016 1 2.23 11 837 0.1% 0.34 (0.42, 2.8]<br>we have 1.20 1 2 518 8 2747 0.0% 3.13 (0.26, 6.27]<br>we have 1.20 1 2 518 8 2747 0.0% 3.13 (0.26, 6.27]<br>we have 1.20 1 2 2.20 5 5 446 0.01% 0.35 (0.51, 7.13)<br>we have 1.20 1 2 2.21 11 837 0.1% 0.34 (0.42, 2.8]<br>we have 1.20 1 2 2.21 11 837 0.1% 0.34 (0.42, 2.8]<br>we have 1.20 1 2 2.21 12 37 0.565 12.7 0.18 0.15 (0.57, 17.30]<br>we have 2.02 1 10 7 2.27 1485 1 9.9% 1.59 (1.52, 1.67]<br>we have 2.02 1 10 7 2.27 120 3.25 (6.99 2.7% 1.16 (1.62, 2.17]<br>we have 2.02 1 172 2.22 12 11 8.37 0.2% 1.18 (1.62, 2.21]<br>we have 2.02 1.12 2.22 1.12 2.20 0.25 (1.16, 5.10]<br>we have 1.22 2.21 1.22 2.20 0.23 1.47 0.0% 0.57 (0.07, 6.52]<br>we have 2.02 1.12 2.27 2.12 1.26 4.24 0.1% 0.22 (1.14, 1.26]<br>we have 1.22 2.27 1.12 2.12 (2.00 0.00); t = 6.8%<br>st for overall effect 2.4 -8.29 (1.2, 0.000); t = 6.8%<br>st for overall effect 2.4 -8.29 (1.2, 0.0000); t = 7.8%<br>st for overall effect 2  |  | 57 (I - 0.12                   | -,         |                                |            |          |                     |             |                       |
| beis Hermida 2022 3 3 183 3 553 0.0% 3.0e [0.61, 15.27]<br>marker B. Kusao 2021 5 373 6 6 53 0.1% 1.22 (4.2 (4.3, 4.6)<br>marker D. Kusao 2015 6 276 2778 1 370 55166 4.4% 1.58 (1.3, 51, 164)<br>m W. Cheung 2019 115 20623 1155 33974 152% 1.89 (1.5, 51, 83)<br>m W. Cheung 2019 115 20623 1155 33974 152% 1.89 (1.5, 51, 83)<br>m W. Cheung 2019 12 2 265 38 6 0.6% 4.46 (0.35, 2.30)<br>m W. Cheung 2019 2 2 268 2 6669 0.7% 1.39 (0.4, 2.07)<br>con-tyun Kin 2021 36 2206 62 6669 0.7% 1.39 (0.4, 2.07)<br>con-tyun Kin 2021 37 1 147 0.0% 0.66 [0.3, 15.51]<br>Johanda M. Kusao 2013 0 73 1 147 0.0% 0.66 [0.3, 15.51]<br>Johanda M. Kusao 2010 0 733 1 0.550 0.0% 9.15 (1.5, 6, 17.6]<br>Mobel (0.5%, C) 1 57735 1770420 2.5.0%<br>stor oursail effect 2 + 15.4 (0.4 2.0, 2.00001)<br>1.39 (0.4, 2.07)<br>designed by 2.07 (1.5, 6, 1.76]<br>marker M. Kusao 2010 0 73 1 0.551 0.0% 9.15 (1.6, 5.1, 76]<br>mill Ricciar 2019 5 644 1 1451 0.0% 12.52 (1.46, 107.41]<br>mill Ricciar 2010 2 516 8 2.77 0.0% 1.59 (1.5, 6, 1.76]<br>mill Ricciar 2010 2 516 8 2.77 0.0% 1.59 (1.5, 6, 1.76]<br>mill Ricciar 2010 2 508 5 427 0.0% 1.50 (1.5, 6, 1.76]<br>mill Ricciar 2010 2 516 8 2.77 0.0% 1.50 (1.5, 6, 1.76]<br>mill Ricciar 2010 2 508 5 427 0.0% 1.50 (1.5, 6, 1.76]<br>mill Ricciar 2010 2 508 5 427 0.0% 1.50 (1.5, 6, 1.76]<br>mill Ricciar 2019 5 644 1 1451 0.0% 12.52 (1.46, 107.41]<br>mill Ricciar 2019 5 644 1 1451 0.0% 1.25 (1.7, 1.60)<br>mill Ricciar 2019 5 644 0.1% 1.50 (1.5, 6, 2.70]<br>mill Ricciar 2019 5 544 0.0% 1.50 (1.5, 1.57]<br>mill Ricciar 2019 7 12 2452 543 0.2% 1.50 (1.6, 4.21]<br>mill Ricciar 2019 7 13 625 127 9158 19.0% 1.50 (1.7, 3.0]<br>mill Ricciar 2019 7 12 2452 543 0.2% 1.50 (1.6, 4.21]<br>mill Ricciar 2010 1 1 518 2.77 0.0% 1.51 (1.47, 1.52 (1.46, 1.76]<br>mill Ricciar 2.00 1.7 146 19 2.447 0.2% 0.71 (1.3, 1.56 (1.4, 1.76]<br>mill Ricciar 2.01 11 7 2.26 85.64 0.1% 1.50 (1.7, 0.79 (1.5, 2.70)<br>mill Ricciar 2.1 12.0 (P.0.0001) F = 158%<br>stor overall effect 2 = 8.29 (P.0.00001) F = 168%<br>stor overall effect 2 = 8.29 (P.0.00001) F = 78%<br>stor overall effect 2 = 1.22 (P.0.00001) F = 78%<br>stor overall effect 2   | 3.1.2 vascular complication                | ı                              |            |                                |            |          |                     |             |                       |
| Index J. Busics 2021       5       373       6       633       0.1%       1.42 (0.43, 4.68)         Intel W. Kalew 2016       168       6137       2.26       1495.43       3.1%       1.38 (1.5.16)         Intel W. Cheung 2019       1155       2.062       1155       3.87       1.58 (1.5.16)  | Alexis Hermida 2022                        | 3                              | 183        | 3                              | 553        | 0.0%     | 3.06 [0.61, 15.27]  | -           |                       |
| aude 5. Elay 2018 276 27831 370 58166 4.4% 1.58 (1.3, 1.44)<br>m V. Chenug 2019 155 20823 1155 33974 152% 1.58 (1.3, 1.44) 1.48 (1.9, 9.2, 20)<br>aura Usberham 2010 65 2419 28 4024 0.4% 3.54 (2.5, 6.16)<br>aura Usberham 2010 65 2419 28 4024 0.4% 3.54 (2.5, 6.16)<br>aura Usberham 2010 22 34 2004 1 28 4024 0.4% 3.54 (2.5, 6.16)<br>aura Usberham 2010 23 2004 1 28 4024 0.4% 3.54 (2.5, 6.16)<br>aura Usberham 2010 23 2004 1 28 4024 0.4% 3.54 (2.5, 6.16)<br>aura Usberham 2010 23 40419 25 326 466 0.00, 7.4 0.69 (0.0, 7.4 0.69)<br>ADO-DON 274AN2 2013 0 73 1 1.47 0.0% 0.66 (0.0, 7.4 0.69)<br>ADO-DON 274AN2 2013 0 733 1 0.473 1 0.075 0.66 (0.0, 7.4 0.69)<br>ADO-DON 274AN2 2013 0 733 1 0.472 1.4984 4.46% 2.271 (1.5, 6, 1.78)<br>auto 40 Kaze 2020 3 1 683 0 0.0% 9.15 (0.95, 68.52)<br>Not estimable<br>tate organeity: Chi = 24.74, df = 11 (P = 0.010; P = 55%<br>st for overall effect: Z = 15.48 (P < 0.00001)<br>1.3 pericardial effusiontamponade<br>ens Harvia 2012 1 17 665 127 31423 4 5.00% 0 .915 (0.96, 68.52)<br>mel W. Kazer 2016 22 3 1 183 1 550 0.0% 9.15 (0.96, 68.52)<br>mel W. Kazer 2016 1 20 2215 1 230 25.66 23.3% 1 1.01 (0.2, 1.16)<br>mel W. Kazer 2016 2 24 6137 427 14984 4.46% 22.1571<br>mel W. Kazer 2016 1 20 223 1 183 7 0.1% 1.90 (1.80, 4.48)<br>aura 42.3(1.80, 2021 1 11 1969 10 3.387 0 1.% 1.36 (1.61, 1.56)<br>mel W. Kazer 2016 1 20 229 5 424 0.1% 0.56 (1.05, 1.56) (1.5, 4.21, 1.56)<br>mel W. Kazer 2016 1 20 220 5 15 684 0.1% 1.36 (1.61, 0.44)<br>mel M. Kazer 2012 1 17 6265 127 9158 1.9%, 1.56 (1.63, 1.54)<br>mel Maxer 2020 7 1146 19 2447 0.2% 0.79 (0.33, 1.57]<br>mel Haiza W. Kazer 2016 1 16 718 2.27 2747 0.2% 0.20 (1.00, 5.16)<br>mel M. Kazer 2016 1 16 718 2.27 2747 0.2% 0.20 (1.00, 5.16)<br>mel M. Kazer 2016 1 19 6.37 2.27 1.485 0.25% 0.27 (1.16, 5.34)<br>mel Maxer 2021 1 17 2.20 2.25 6.26 (60, 2.7%, 1.18 (0.50, 2.79)<br>mater Kazer 2016 1 19 6.37 2.27 1.496 0.20 (1.14, 1.40, 2.21)<br>mel Maxer 2010 1 1 5.18 2.27 2.774 0.2% 0.20 (1.00, 5.16)<br>mel Maxer 2010 1 1 5.18 2.7 2.774 1.90 0.00 (1.14, 1.90, 2.14)<br>mel Maxer 2016 1 19 6.37 2.27 1.496 0 4.20 (1.5% 0.27 (1.16, 5.36)<br>mel  | Andrea M. Russo 2021                       | 5                              | 373        | 6                              | 633        | 0.1%     | 1.42 [0.43, 4.68]   |             |                       |
| anial W. Kaiser 2016 168 6137 226 14954 3.1% 1.39 (1.15, 169)<br>matham P. Pacim 2012 138 6265 38 9158 0.6% 1.46 (1.98, 2.30)<br>sasterior Takigawa 2013 2 240 244 0.4% 1.46 (1.98, 2.30)<br>sasterior Takigawa 2013 2 240 244 0.4% 1.46 (1.98, 2.30)<br>matham General/2012 146 2.3 2440 0.5% 0.56 (1.14, 3.72)<br>con-tyun Kim 2021 23 0 25 98641 0.7% 1.57 (1.56, 1.78)<br>table of the constraint of the const  | Claude S. Elayi 2018                       | 278                            | 27831      | 370                            | 58156      | 4.4%     | 1.58 [1.35, 1.84]   |             | -                     |
| m W. Chenug 2016 1155 2063 1155 33974 152% 1.46 [0.83, 2.00]<br>wara Uberham 2019 65 2419 28 4024 0.4% 334 [2.52, 6, 16]<br>safetim Takigawa 2013 2 240 1 26 4024 0.4% 334 [2.52, 6, 16]<br>wara Uberham 2019 65 2419 28 4024 0.4% 334 [2.52, 6, 16]<br>wara Uberham 2013 2 1206 1 264 0.0% 6.68 [0.0, 7, 40]<br>wara Uberham 2013 2 1206 1 264 0.0% 0.66 [0.03, 16.51]<br>Uberham 2013 2 2 2019 2 5 2668 0.7% 1.36 [1.54, 7.69]<br>wara Uberham 2013 0 73 1 147 0.0% 0.66 [0.03, 16.51]<br>Uberham 2013 2 2 2019 2 5 20%<br>1.37 [1.56, 1.78]<br>valae exemit 1006 2028<br>wara Uberham 2016 2 2010 1 7 7 10420 2 5.0%<br>1.37 [1.56, 1.78]<br>valae exemit 1006 2 2028<br>wara Uberham 2016 2 24 6130 427 1 4454 44%<br>1.39 [1.56, 1.78]<br>valae exemit 2016 1 224 6131 427 1 4454 44%<br>1.39 [1.56, 1.78]<br>valae Stage 2011 1 203 2781 2 204 5155 2 2.3%<br>valae Stage 2011 1 203 2781 2 204 5156 2 2.3%<br>valae Stage 2011 1 223 211 1 397 0 1%<br>1.39 [1.56, 1.78]<br>valae Stage 2016 1 223 613 3974 7 47%<br>1.39 [1.26, 1.57]<br>valae Stage 2016 1 223 1 233 2 457 0.0%<br>3.15 [0.57, 17.30]<br>within X-taker 2016 1 2 209 5 424 0.1%<br>valae Stage 2011 1 2 239 1 1387 0.1%<br>valae Stage 2015 1 203 27 158 1.9%<br>valae Stage 2015 1 203 27 158 1.9%<br>valae Stage 2015 1 8 129%<br>valae Stage 2015 1 97 227 1 4954 2.5%<br>valae Stage 2015 1 97 37 1 3 633 0.2%<br>1.18 [0.50, 2.79]<br>valae Stage 2015 1 97 227 14954 2.5%<br>valae ward X-2 120 2016 1 1 518 27 2747 0.2%<br>valae ward X-2 120 2016 1 1 518 27 2747 0.2%<br>valae ward X-2 120 2016 1 1 518 27 2747 0.2%<br>valae ward X-2 120 2016 1 1 518 27 2747 0.2%<br>valae ward X-2 120 2016 1 1 518 27 2747 0.2%<br>valae ward X-2 120 2016 1 1 518 27 2747 0.2%<br>valae ward X-2 120 2016 1 1 1 2.96 2.466 99 2.1%<br>valae wa  | Daniel W. Kaiser 2016                      | 168                            | 6137       | 296                            | 14954      | 3.1%     | 1.39 [1.15, 1.69]   |             |                       |
| Inatham Practini 2012       38       6265       38       9158       0.6%       1.46       1.93, 2.30         saskert Takgawa 2013       2       200       1       664       0.0%       6.68       0.0%       6.68       0.0%       6.70, 00         saskert Takgawa 2013       2       200       1       664       0.0%       6.68       0.0%       6.68       0.0%       6.68       0.0%       6.68       0.0%       6.68       0.0%       0.67       0.00       0.06       0.05       0.05       0.05       0.05       0.05       0.05       0.05       0.05       0.05       0.05       0.06       0.05 <t< td=""><td>Jim W. Cheung 2019</td><td>1155</td><td>20623</td><td>1155</td><td>33974</td><td>15.2%</td><td>1.69 [1.55, 1.83]</td><td></td><td></td></t<>  | Jim W. Cheung 2019                         | 1155                           | 20623      | 1155                           | 33974      | 15.2%    | 1.69 [1.55, 1.83]   |             |                       |
| Lura Userham 2019 e5 2419 28 4024 0.4% 334 [252, 5, 16]<br>hale a Gracu 2020 22 1146 23 2447 0.3% 2.06 [1.14, 3.72]<br>deel Mazar 2022 34 2241 25 38541 0.3% 2.26 [1.5, 3, 43]<br>deel Mazar 2022 34 2241 25 38541 0.3% 2.26 [1.5, 3, 43]<br>deel Mazar 2022 34 2241 [1.6] = 0.010; F 56%<br>stor overall effect: Z = 15.48 (P < 0.00001)<br>1.3 percental effect: Z = 15.48 (P < 0.00001)<br>1.4 percental effect: Z = 15.48 (P < 0.0001)<br>1.4 percental effect: Z = 15.29 (P < 0.00001)<br>1.4 percental effect: Z = 15.29 (P < 0.00  | Jonathan P. Piccini 2012                   | 38                             | 6265       | 38                             | 9158       | 0.6%     | 1.46 [0.93, 2.30]   |             |                       |
| satelin Jacquana 2013 2 2 116 2 2 247 0 3% Exp [0.00, 4 0.09]<br>don-hyun Kin 2021 38 2206 82 6969 0.7% 1.39 [0.94, 2.07]<br>J. 206 [1.14, 7.2]<br>J. 206 [1.14, 7.2]<br>J. 207 [1.14, 7.2]<br>J. 20  | Laura Ueberham 2019                        | 65                             | 2419       | 28                             | 4024       | 0.4%     | 3.94 [2.52, 6.16]   | -           |                       |
| Landen Grundback<br>Landen Grundback<br>Devel Macro 2022<br>Bill A 2 419<br>Bill A 2 417<br>Bill  | Masateru Takigawa 2013                     | 2                              | 260        | 22                             | 2447       | 0.0%     | 0.09 [0.00, 74.08]  |             |                       |
| Numeric 2022         34         2019         25         354         0.3%         2.271         1.53         4.47           AD-DONG 27406 2013         0         73         1         147         0.0%         0.66 [0.03.66 51]           abhotal (19% C1)         97335         170420         25.0%         1.67 [1.56, 1.76]           abhotal (19% C1)         9733         1         550         0.0%         9.15 [0.95, 85.52]           ofter overall effect: Z = 15.48 (P < 0.00001)   | Moon-byun Kim 2021                         | 36                             | 2206       | 23                             | 6060       | 0.3%     | 1 30 [0 04 2 07]    |             | -                     |
| AD-DOMS 224-AUG 2013<br>bit of the constraints of the  | Rood Mezar 2022                            | 34                             | 20410      | 25                             | 38541      | 0.3%     | 2 57 [1 53 4 31]    |             |                       |
| $\begin{aligned} \begin{array}{c} \text{biscus} & (10) & \text{cm}^2 & 3733 & 170420 & 25.0\% & 1.67 [15.6, 1.78] \\ \text{aterogeneyby: Ch2 = 24.74, df = 11 (P = 0.010); P = 56\% \\ \text{sat for overall effect Z = 15.48 (P < 0.0001) \\ \text{outs} for overall effect Z = 15.48 (P < 0.0001) \\ \text{outs} for overall effect Z = 15.48 (P < 0.0001) \\ \text{outs} for overall effect Z = 15.29 (2.13) \\ \text{outs} S = 1000 \\ \text{outs} S = 10000 \\ \text{outs} S = 10000 \\ \text{outs} S = 100000 \\ \text{outs} S = 100000 \\ \text{outs} S = 1000000 \\ \text{outs} S = 10000000 \\ \text{outs} S = 1000000 \\ \text{outs} S = 1000000 \\ $ | XIAO-DONG ZHANG 2013                       | 0                              | 73         | 1                              | 147        | 0.0%     | 0.66.0.03 16.511    | · · · · · · |                       |
| Tale events 1006 2028<br>energoneity: Ch <sup>2</sup> = 2.47, df = 11 ( $P = 0.010$ ); $P = 65\%$ ,<br>sat for overall effect: $Z = 15.48$ ( $P < 0.00001$ )<br>1.3 pericardial effusiontamponade<br>events Hermida 2021 3 183 1 550 0.0% 9.15 [0.95, 88.52]<br>ndrea M. Russo 2021 0 373 0 633 0.10 [10.2, 118]<br>antel W. Kaiser 2016 1232 4 6137 427 14954 4.4% 135 [1.15, 1.59]<br>antel W. Kaiser 2016 1232 4 6137 427 14954 4.4% 135 [1.25, 1.69]<br>antel W. Kaiser 2016 1232 4 6137 427 14954 4.4% 135 [1.25, 1.69]<br>antel W. Kaiser 2016 1 223 11 837 0.1% 0.348 [0.04.26.3]<br>mp Patel 2010 2 518 8 2747 0.0% 1.33 [0.28, 6.27]<br>anthel N. Yuna 2011 1 1269 10 3387 0.1% 0.34 [0.04.26.3]<br>mp V. Cheurg 2019 4 54 20623 56.51 33974 7.74 (1.39 [1.25, 2.03]<br>4.44 1.95 (1.25, 2.03]<br>artelen Koosterman 2020 2 209 5 424 0.1% 0.31 [0.16, 4.21]<br>asteru Takgma 2013 6 260 15 864 0.1% 0.31 [0.16, 4.21]<br>asteru Takgma 2013 6 120 17 18 2145 0.2% 2.05 [1.06, 3.95]<br>antel W. Cheurg 2019 2 117 2.05 325 6869 2.7% 1.14 [1.08, 2.21]<br>artelen Koosterman 2020 2 198 2447 0.2% 0.29 [0.13, 3.167]<br>con-hyuu Kim 2021 117 2.06 325 6869 2.7% 1.14 [0.32, 1.42]<br>and M. Xyla 2016 18 1057 18 2145 0.2% 2.05 [1.06, 3.95]<br>antel W. Kaiser 2016 13 0.57 18 2145 0.2% 2.05 [1.06, 3.95]<br>antel W. Kaiser 2016 13 0.57 18 12448 0.2% 1 124 [1.18, 1.34]<br>and M. Xyla 2016 18 1057 18 2447 0.0% 0.67 [1.07, 6.52]<br>and V. Kaiser 2016 137 237 1495 44 2.5% 1.44 [1.16, 1.78]<br>antel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>antel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>antel W. Kaiser 2016 139 2.33 1 457 0.0% 0.57 [0.07, 6.52]<br>4.44 0.33 1.52 [1.43, 3.28]<br>4.44 0.3% 1.52 [1.43, 3.28]   | Subtotal (95% CI)                          | °.                             | 87935      |                                | 170420     | 25.0%    | 1.67 [1.56, 1.78]   |             | •                     |
| eterogeneity: Ch <sup>2</sup> = 24.74, df = 11 (P = 0.010); P = 56%<br>set for overall effect: 2 = 15.48 (P < 0.00001)<br>tail of overall effect: 2 = 15.48 (P < 0.00001)<br>1.3 pericardial effusion/tamponade<br>exis Hermida 2022 3 183 1 550 0.0% 9.15 [0.95, 88.52]<br>note estimable<br>made S. Elayi 2018 1203 27831 2304 58156 28.3% 1.10 [1.02, 1.18]<br>andie N. Caiser 2016 234 6137 427 14956 44.4% 1.35 [1.15, 15 9]<br>andie N. Caiser 2016 234 6137 427 14956 44.4% 1.35 [1.15, 15 9]<br>andie N. Caiser 2016 234 6137 427 14956 44.4% 1.35 [1.16, 15, 15 9]<br>andie N. Caiser 2016 234 6137 427 14956 44.4% 1.35 [1.22, 16.17, 11<br>mit Pictual 2010 2 518 8 2747 0.0% 1.31 (0.28, 6.27)<br>andia N. Cuiser 2013 1 1 1969 10 3387 0.1% 1.39 (0.28, 6.27)<br>analthar P. Piccini 2012 137 6265 127 9156 1.9% 1.55 [1.25, 2.03]<br>arkHainz Kuck 2018 1 223 517 9156 1.9% 1.59 [1.25, 2.03]<br>arkHainz Kuck 2018 1 203 27 6265 127 9156 1.5 844 0.1% 0.81 (0.16, 4.21]<br>araile Notostemma 2020 2 209 5 424 0.1% 0.81 (0.16, 4.21]<br>araile Notostemma 2020 2 209 5 424 0.1% 0.91 (0.51, 3.48]<br>araina N. Xija 2016 18 1057 18 2145 0.2% 0.79 (0.33, 1507)<br>araile Notostemma 2020 2 19 0 38541 2.0% 0.79 (0.33, 1507)<br>araile Notostemma 2020 1 7 1146 19 2447 0.2% 0.27 (0.33, 1.57)<br>araile Notostemma 2020 1 77 0 38541 2.5% 1.141 (1.4, 2.21]<br>araile Notostemma 2020 1 77 3 13 633 0.2% 1.18 (0.50, 2.79]<br>anale W. Kaiser 2016 139 6137 237 14954 2.5% 1.201 (1.46, 1.78]<br>anale W. Kaiser 2016 139 6137 237 14954 2.5% 2.10 (1.03, 1.66]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.10 (1.03, 1.66]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.10 (1.03, 1.66]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.10 (1.03, 1.66]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.40 (1.03, 3.86]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.40 (1.03, 3.86]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.40 (1.30, 3.66]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.40 (1.30, 3.66]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.40 (1.30, 3.67]<br>araile W. Kaiser 2016 139 6137 237 14954 2.5% 2.40 (1.03, 3.8  | Total events                               | 1806                           |            | 2028                           |            |          |                     |             |                       |
| st for overall effect: Z = 15.48 (P < 0.00001)<br>1.3 portaardial effusion/Tamponade<br>weis Hermida 2022<br>ande S. Elwy 2018<br>1.3 portaardial effusion/Tamponade<br>weis Hermida 2012<br>1.3 portaardial effusion/Tamponade<br>weis Hermida 2018<br>1.3 portaardial effusion/Tamponade<br>weis Hermida 2018<br>1.3 portaardial effect: Z = 0.76 (P < 0.00001); P = 73%,<br>st for overall effect: Z = 13.22 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.3 portaal effect: Z = 0.27 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.3 portaal effect: Z = 0.27 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.3 portaal effect: Z = 0.27 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.4 portaardial effect: Z = 0.27 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.4 portaal effect: Z = 0.29 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.4 portaal effect: Z = 0.29 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.4 portaal effect: Z = 0.29 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 71 (P < 0.0001); P = 94.4%.<br>1.4 portaal effect: Z = 0.29 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.<br>1.4 portaal effect: Z = 0.29 (P < 0.00001); P = 94.4%.<br>1.4 portaal effect: Z = 0.29 (P < 0.00001); P = 73%,<br>st for overall effect: Z = 0.76 (P < 0.00001); P = 73%,<br>st for subtoru offleerenese: Chif = 53.76 . df = 3 (P < 0.00001); P = 94.4%.  | Heterogeneity: Chi2 = 24.74, d             | df = 11 (P =                   | = 0.010);  | <sup>2</sup> = 56%             |            |          |                     |             |                       |
| 1.3 pericardial effusion/tamponade         exis Hermida 2022       3       163       1       550       0.0%       9.15 [0.95, 88.52]         hordea M. Russo 2021       0       373       0       633       Not estimable         naude S. Elayi 2018       1203       27831       2304       85156       26.3%       1.10 [1.02, 1.18]         namic Nicolardi 2019       5       584       1       1451       0.0%       1.25 [1.46, 107.41]         mpi Patel 2010       2       588       2.271       1456       4.4%       1.35 [1.52, 2.03]         andha P. Flocinol 2012       17       6265       127       9156       1.39 [1.52, 2.03]         art-Heinz Kuck 2018       4       2.209       5       424       7.0%       3.15 [0.57, 17.30]         art-Heinz Kuck 2018       4       2.209       5       6464       1.34 [1.61, 63.35]       1.46 [1.62, 2.03]         art-Hainz Nicolardi 2016       18       2.477       0.48       0.28       0.26 [1.61, 2.01]       1.38 [1.62, 0.27]         art-Max Z020       7       1.14 [1.62, 2.13]       0.33 [1.61, 2.1]       0.33 [1.61, 2.1]       0.33 [1.61, 2.2]       1.41 [1.61, 2.7]         art-Max Z016       18       2.427       0.26 <td< td=""><td>Test for overall effect: Z = 15.</td><td>.48 (P &lt; 0.0</td><td>0001)</td><td></td><td></td><td></td><td></td><td></td><td></td></td<>  | Test for overall effect: Z = 15.           | .48 (P < 0.0                   | 0001)      |                                |            |          |                     |             |                       |
| 1.3 portarial enturision developments in the series Hermida 2022 3 183 1 550 0.0% 9.15 [0.95, 88.52]<br>more al. Russo 2021 0 373 0 6 633 Not estimable<br>and W. Russo 2018 120 2783 1204 58156 28.5% 1.10 [1.02, 1.16]<br>aniel W. Kaiser 2016 234 6137 427 14964 4.4% 1.35 [1.15, 1.59]<br>mip Fatel 2010 2 518 8 2747 0.0% 12.52 [1.46, 107.41]<br>mip Fatel 2010 2 518 8 2747 0.0% 12.52 [1.46, 107.41]<br>mip Fatel 2010 1 2 518 8 2747 0.0% 12.52 [1.46, 107.41]<br>mip Fatel 2010 1 2 518 8 2747 0.0% 13.60 [0.51, 3.48]<br>areal W. Cheung 2019 454 20623 554 11 8 87 0.1% 0.34 [0.04, 2.63]<br>mathan P. Piccini 2012 137 6265 127 9158 1.9% 1.59 [1.22, 1.57]<br>mathan P. Piccini 2012 137 6265 127 9158 1.9% 1.59 [1.22, 1.57]<br>mathan P. Piccini 2012 137 6265 127 9158 1.9% 1.59 [1.22, 1.57]<br>mathan P. Piccini 2012 137 6265 127 9158 1.9% 1.59 [1.22, 2.57]<br>arielle Kloosterman 2020 2 2.09 5 424 0.1% 0.81 [0.16, 4.21]<br>arielle Kloosterman 2020 2 2.09 5 424 0.1% 0.81 [0.16, 4.21]<br>arielle Kloosterman 2020 2 1.09 5 424 0.0% 3.16 [0.51, 3.48]<br>arielle Kloosterman 2020 2 1.09 5 7.7% 1.14 [1.09, 1.42] [1.49, 2.21]<br>arielle Kloosterman 2020 2 1.09 0736 1178208 46.4% 1.24 [1.18, 1.53]<br>AC-DORK 2HANG 2013 1 7.3 3 147 0.0% 0.57 [0.07, 6.52]<br>AC-DORK 2HANG 2013 1 7.3 3 1470 0.0% 0.57 [0.03, 1.67]<br>mino Ricciardi 2019 1 2.419 8 4024 0.1% 0.21 [0.13, 1.67]<br>aniel W. Kaiser 2016 139 6137 22.7 14854 2.7% 1.14 [1.48, 1.31]<br>tatl events 247 4036<br>tetrogenetiy: Chi* 52.97, df = 1/9 C 0.00001) I* 6 803 0.2% 1.18 [0.50, 2.79]<br>arielle Kloosterman 2020 19 203 244 0.3% 0.7% 0.52 [0.02, 1.27]<br>arielle Kloosterman 2020 19 2.09 2.3 440 0.3% 0.7% 0.52 [0.02, 1.27]<br>arielle Kloosterman 2020 19 2.09 2.44 0.3% 0.7% 0.52 [0.02, 1.27]<br>arielle Kloosterman 2020 19 2.09 2.44 0.3% 0.7% 0.52 [0.02, 1.27]<br>arielle Kloosterman 2020 19 2.09 2.44 0.3% 0.7% 0.52 [0.02, 1.27]<br>arielle Kloosterman 2020 19 2.09 2.44 0.68% 0.33 [0.18, 0.61]<br>arielle Kloosterman 2020 19 2.09 2.44 0.3% 0.7% 0.52 [0.02, 1.27]<br>arielle Kloosterman 2020 19 2.09 2.44 0.68% 0.33 [0.18, 0.6   |  |                                |            |                                |            |          |                     |             |                       |
| exis Hermida 2022 3 183 1 550 0.0% 915 [U35, 88.52]<br>midre M. Russo 2021 0 373 0 633<br>Note stimulate S. Elayi 2018 1203 27831 2304 58156 26.3% 1.10 [102, 118]<br>anilo Ricciardi 2019 5 554 1 1451 0.0% 12.52 [146, 107.41]<br>migr Patel 2010 2 518 8 2747 0.0% 1.33 [0.28, 6.27]<br>anilo Ricciardi 2019 5 554 1 1451 0.0% 12.52 [146, 107.41]<br>anilo Ricciardi 2019 5 554 1 1451 0.0% 12.52 [146, 107.41]<br>anilo Ricciardi 2019 2 518 8 2747 0.0% 1.33 [0.28, 6.27]<br>anthen P. Pictol 2012 137 6256 512 9158 19% 1.55 [145, 159]<br>anthen P. Pictol 2012 137 6256 512 9158 19% 1.55 [145, 123]<br>antel N. Kaiser 2020 2 209 5 424 0.1% 0.81 [0.16, 4.21]<br>antel N. Kaiser 2020 7 1146 19 2447 0.0% 0.33 [162, 153]<br>antel N. Kaiser 2020 7 1146 19 2447 0.2% 0.79 [0.33, 187]<br>antel N. Kaiser 2020 7 1146 19 2447 0.2% 0.79 [0.33, 187]<br>antel N. Kaiser 2020 19 373 13 647 0.2% 2.50 [148, 5.30]<br>AO-DNOK 2HANK 2013 173 3 147 0.0% 0.67 [0.07, 6.52]<br>and N. Caiser 2016 1372 27021 1866 58156 21.1% 1.56 [146, 1.68]<br>anilo N. Kaiser 2016 139 6137 22 71484 58156 21.1% 1.56 [146, 1.68]<br>anilo N. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>anilo N. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>anilo N. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>anilo N. Kaiser 2016 139 6137 22 7124 19 8 4024 0.1% 0.21 [10.3, 1.68]<br>anilo N. Kaiser 2016 19 209 23 424 0.1% 0.2% 0.79 [1.88, 4.43]<br>anilo N. Kaiser 2016 139 6137 22 714954 2.5% 1.44 [1.16, 1.78]<br>anilo N. Kaiser 2016 139 6137 22 714954 2.5% 1.44 [1.16, 1.78]<br>anilo N. Kaiser 2016 139 633 1.457 0.0% 0.52 [0.02, 12.77]<br>anilo N. Kaiser 2016 139 6137 22 71 4954 2.0.5% 0.33 [0.18, 0.61]<br>anilo N. Kaiser 2016 139 6137 22 757 1486 58156 2.1.1% 1.50 [148, 4.43]<br>anilo N. Kaiser 2016 139 633 1.457 0.0% 0.52 [0.02, 12.77]<br>anilo N. Kaiser 2016 19 209 2.54 2.64 66669<br>anilo N. Kaiser 2016 19 200 24.66 6666 2.1% 1.403 3.28 [1.41, 1.52 [1.43, 1.62]<br>anilo N. Kaiser 2016 1.20 1197 12 2452 0.1% 1.45 [1.43, 1.62]<br>anilo N. Kaiser 2016 1.20 0.10(1); I= 78%<br>stor overall effect: Z = 13.22 (IP < 0.00001);   | 3.1.3 pericardial effusion/ta              | imponade                       | 100        |                                |            | 0.00/    | 0 45 10 05 00 501   |             |                       |
| Under J. Nulsso 2021       0       3.73       0       0.33       2034       58156       26.3%       1.101 [02, 118]         aniel W. Kaiser 2016       234       6137       427       14954       4.4%       1.35 [11.5, 159]         aniel W. Kaiser 2016       2       5584       1       1451       0.0%       1.25 [14.6, 107.41]         mpi Patel 2010       2       518       8       2747       0.0%       1.33 [0.28, 6.27]         mathen N. Ynus 2021       11       1969       0       3387       0.1%       0.34 [10.21, 118]         w. Cheung 2019       454       2062       3533       1.50 [122, 157]       *         and Heinz Kuck 2018       4       293       2       457       0.0%       315 [0.57, 17.30]         and M. Zyla 2016       18       1057       18       2146       0.2%       0.76 [10.6, 3.98]         asateru Takigawa 2013       6       260       15       864       0.1%       1.34 [14.92, 2.17]       *         unary-Kuung Koho 2118       17       206       255       666       27%       1.16 [0.92, 1.18, 1.30]       *         vang-Young Koho 2118       1.72       2782       1466       58165       2.11.16       1.26   | Alexis Hermida 2022                        | 3                              | 183        | 1                              | 550        | 0.0%     | 9.15 [0.95, 88.52]  |             |                       |
| and $23$ Log $2013$ (1) (1) (1) (1) (1) (1) (1) (1) (1) (1)   | Claudo S. Elavi 2018                       | 1202                           | 3/3        | 2204                           | 69166      | 26 20/   | 1 10 /1 02 1 191    |             |                       |
| anish in Kikadir 2010       2.4       4.2       4.24       4.24       1.53 [14.01, 13.5]         mpi Patel 2010       2       518       8       2.747       0.0%       1.33 [0.28, 6.27]         mpi Patel 2010       1       1.283       1.33 [0.28, 6.27]   | Dapiel W. Kaiser 2016                      | 224                            | 6127       | 2304                           | 14054      | 20.3%    | 1.10[1.02, 1.10]    |             | -                     |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $  | Danilo Ricciardi 2019                      | 2.54                           | 584        | 421                            | 1451       | 0.0%     | 12 52 [1 46 107 41] |             |                       |
| and N. Yunus 2021 11 1 1969 10 3387 0.1% 190 [0.8.0.4.46]<br>m W. Cheung 2019 454 20623 543 33974 7.4% 1.39 [1.22, 1.57]<br>m W. Cheung 2019 454 20623 543 33974 7.4% 1.39 [1.22, 1.57]<br>m H-Henz Kuck 2018 4 293 2 457 0.0% 3.15 [0.57, 17.30]<br>antelle Kloosterman 2020 2 2.09 5 424 0.1% 0.81 [0.57, 17.30]<br>antelle Kloosterman 2020 2 2.09 5 424 0.1% 0.81 [0.57, 17.30]<br>antelle Kloosterman 2020 2 2.09 5 424 0.1% 0.81 [0.57, 17.30]<br>antelle Kloosterman 2020 7 1146 19 2447 0.2% 0.79 [0.33, 1.87]<br>antelle Kloosterman 2020 7 1146 19 2447 0.2% 0.79 [0.33, 1.87]<br>antelle Kloosterman 2020 7 1146 19 2447 0.2% 0.79 [0.33, 1.87]<br>antelle Kloosterman 2020 7 38541 2.6% 1.81 [1.49, 2.21]<br>antelle Xloosterman 2020 7 38541 2.6% 1.81 [1.49, 2.21]<br>antelle Xloosterman 2020 7 38541 2.6% 1.81 [1.49, 2.21]<br>antelle Xloosterman 2020 7 373 1 3 633 0.2% 1.18 [0.50, 2.79]<br>antelle Kloosterma 2016 19 237 14564 2.5% 1.44 [1.18, 1.31]<br>antelle Xlooster 2016 19 237 14564 2.5% 1.44 [1.16, 1.68]<br>antelle Xlooster 2016 19 237 14564 2.5% 1.44 [1.16, 1.68]<br>antelle Xlooster 2016 19 231 427 0.00001; P = 68%<br>est for overall effect: Z = 8.29 (P < 0.00001; P = 68%<br>est for overall effect: Z = 8.29 (P < 0.00001; P = 68%<br>est for overall effect: Z = 8.29 (P < 0.00001; P = 68%<br>est for overall effect: Z = 8.29 (P < 0.00001; P = 68%<br>est for overall effect: Z = 8.29 (P < 0.00001; P = 68%<br>est for overall effect: Z = 8.29 (P < 0.00001; P = 78%<br>antel N.Kaise 2016 19 20 23 424 0.3% 0.74 (1.63, 7.69]<br>antel N.Kaise 2016 19 20 23 424 0.8% 0.33 (0.18, 0.61]<br>antelle Xloosterma 2020 19 209 2.46 6660 2.1% 1.18 [0.50, 2.79]<br>antelle Xloosterma 2020 19 209 2.46 6660 2.1% 0.11 (0.93, 3.28]<br>antelle Xloosterma 2020 19 209 2.46 6660 2.1% 0.14 (1.23, 9.367]<br>antelle Kloosterma 2020 19 2.20 2.46 6660 2.1% 0.14 (1.23, 9.367]<br>antelle Kloosterma 2020 19 2.20 2.46 6660 2.1% 0.14 (1.23, 9.367]<br>antelle Kloosterma 2020 19 2.20 2.46 6660 2.1% 0.16 (1.23, 9.367]<br>antelle Kloosterma 2020 19 2.20 2.46 6660 2.1% 0.16 (1.23, 9.367]<br>antelle Kloosterma 2020 19 2.20 2.46 6660 2.1% 0.14   | Dimpi Patel 2010                           | 2                              | 518        | 8                              | 2747       | 0.0%     | 1.33 [0.28, 6.27]   |             | · · · · ·             |
| ee Tae Yu 2018 1 223 11 837 0.1% 0.34 [0.04, 263]<br>mathan P. Piccini 2012 137 6265 127 9158 1.9% 1.59[1.22, 157]<br>art-Heinz Kuck 2018 4 2023 543 33074 7.4% 1.39[1.22, 157]<br>art-Heinz Kuck 2018 4 2023 542 2 457 0.0% 3.15 [0.57, 17.30]<br>art-Mark 2012 2 209 5 424 0.1% 0.31 [0.16, 4.21]<br>asateu Takigawa 2013 6 260 15 864 0.1% 1.34 [0.51, 3.48]<br>art M. Zyla 2016 18 1057 18 2145 0.2% 2.05[1.66, 3.95]<br>thaela Grecu2020 7 1146 19 2447 0.2% 0.79 [0.33, 1.87]<br>aread M. Zyla 2016 18 205 18 2.05 0.2% 2.05[1.16, 5.30]<br>aread M. Zyla 2016 13 2016 18 207 38541 2.6% 18[1 (1.49, 2.21]<br>aread M. Zyla 2016 17 2026 325 6666 2.7% 1.14 [0.92, 1.42]<br>aread M. Zyla 2016 17 207 38541 2.6% 18[1 (1.49, 2.21]<br>aread M. Zyla 2016 17 207 38541 2.6% 18[1 (1.49, 2.21]<br>aread M. Zyla 2016 17 3 3 147 0.0% 0.67 [0.07, 6.52]<br>abtotal (95% CI) 90736 178208 46.4% 1.24 [1.16, 1.31]<br>all events 2427 4036<br>eterogeneity: Ch <sup>2</sup> = 52.97, df = 17 (P < 0.0001); P = 68%<br>stof roverall effect Z = 8.29 (P < 0.00001)<br>14 Hematoma<br>driea M. Russo 2021 9 373 13 633 0.2% 1.18 [0.50, 2.79]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.31]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.36]<br>aniel W. Kaiser 2016 139 6137 237 14954 0.1% 0.25 (0.22, 12.77]<br>aniel W. Kaiser 2016 120 9 120 9 2.42 (2.11% 1.56 [1.46, 1.68]<br>aniel W. Kaiser 2016 120 119 12 2429 0.0% 0.05 (0.52 (0.22, 12.77]<br>aniel W. Kaiser 2016 120 119 12 2429 0.0% 0.5% (0.52 (0.22, 12.77]<br>aread M. Zyla 2016 20 1197 12 24252 0.1% 3.46 [1.68, 7.09]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.68, 7.09]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.68, 7.09]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aread M. Zyla 2016 20 1197 12 2462 0.1% 1.43 [1.38, 1.48]<br>aread H   | Fahd N. Yunus 2021                         | 11                             | 1969       | 10                             | 3387       | 0.1%     | 1.90 [0.80, 4.48]   |             |                       |
| m W. Cheung 2019 454 2023 543 33974 7.4% 1.39 [1.22, 1.57] * * * * * * * * * * * * * * * * * * *  | Hee Tae Yu 2018                            | 1                              | 223        | 11                             | 837        | 0.1%     | 0.34 [0.04, 2.63]   |             |                       |
| nathan P. Piccini 2012       137       6265       127       9158       1.9%       1.59 [1.25, 203]  | Jim W. Cheung 2019                         | 454                            | 20623      | 543                            | 33974      | 7.4%     | 1.39 [1.22, 1.57]   |             | *                     |
| arl-Heinz Kuck 2018 4 293 2 457 0.0% 3.15 [0.57, 17.30]<br>asateur Takigawa 2013 6 260 15 864 0.1% 0.81 [0.16, 4.21]<br>asateur Takigawa 2013 6 260 15 864 0.1% 0.81 [0.16, 4.21]<br>asateur Takigawa 2013 6 260 15 82445 0.2% 2.05 [1.63, 3.95]<br>haela Grecu2020 7 1146 19 2447 0.2% 0.79 [0.33, 1.87]<br>aura M. Zyla 2016 18 245 260 2.7% 1.14 [0.92, 1.42]<br>aura Y. Zyla 2016 18 24 367 10 367 0.2% 2.50 [1.18, 5.30]<br>AD-DONG ZHANK 2013 173 3 147 0.0% 0.67 [1007, 6.52]<br>abtotal [95% C] 90736 172206 46.4% 1.24 [1.18, 1.31]<br>tale vents 2427 4036<br>terrogeneity: Ch <sup>2</sup> = 5.2.97, d = 17 (P < 0.0001); P = 68%<br>stof or verall effect: Z = 0.76 (2.11% 1.56 [1.46, 1.68]<br>anial W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.18, 1.31]<br>anio Ricairdi 2019 1 2419 8 4024 0.1% 0.21 [0.03, 1.66]<br>anial W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.68]<br>anial W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.68]<br>anial W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.68]<br>anial W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.68]<br>anial W. Kaiser 2016 129 1 2419 8 4024 0.1% 0.21 [0.03, 1.66]<br>anial W. Kaiser 2016 129 209 21 427 0.0% 0.52 [0.02, 12.77]<br>anial Ricairdi 2019 1 2419 8 4024 0.1% 0.21 [1.03, 4.27]<br>anial Ricairdi 2019 1 22 4249 0.0% 0.32 [0.02, 12.77]<br>anial Kaiser 2016 20 1197 12 2452 0.1% 3.46 [1.68, 7.09]<br>aura M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.68, 7.09]<br>aura M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aura M. Zyla 2016 20 1197 12 2462 0.1% 3.46 [1.69, 7.16]<br>aura M. Zyla 2016 20 1197 12 2462 0.1% 1.15 [0.92, 1.50]<br>aura M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>aura M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.16]<br>aura M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.16]<br>aura M. Zyla 2016 20 1197 12 2452 0.1% 3.45 [1.69, 1.40]<br>aura M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.16]<br>aura M. Zyla 2016 20 1197 12 246 6060<br>aura M. Zyla 2016 20 1197 12 2452 0.1% 3.45 [1.69, 7.16]<br>aura M. Zyla 2016 20 1197 12 246 6060<br>at letrogeneity: Ch <sup>2</sup> = 13.3.  | Jonathan P. Piccini 2012                   | 137                            | 6265       | 127                            | 9158       | 1.9%     | 1.59 [1.25, 2.03]   |             | -                     |
| arielle Kloosterman 2020 2 2099 5 424 0.1% 0.81 [0.16, 4.21]<br>aura M. Zylla 2016 18 1057 18 2145 0.2% 0.79 [0.33, 1.87]<br>aura M. Zylla 2016 18 1057 18 2145 0.2% 0.79 [0.33, 1.87]<br>con-hyun Kim 2021 117 2206 325 6969 2.7% 1.14 [0.92, 1.42]<br>aura M. Zylla 2016 24 367 10 367 0.2% 2.50 [1.14, 5.30]<br>aura M. Zylla 2017 3631 173 3 147 0.0% 0.67 [0.07, 6.52]<br>aura M. Zylla 2018 24 367 10 367 0.2% 2.50 [1.18, 5.30]<br>AbcODNG 2HANK2 0213 1 73 3 147 0.0% 0.67 [0.07, 6.52]<br>autor Start 216 139 247 4006 46.4% 1.24 [1.18, 1.31]<br>autor Start 216 139 247 4026 46.4% 1.24 [1.18, 1.31]<br>autor Start 216 139 27 2721 1866 58156 2.11% 1.56 [1.46, 1.68]<br>anilo K.ciaire 216 139 27 2737 14954 2.5% 1.44 [1.61, 7.78]<br>autor Start 216 139 27 2737 14954 2.5% 1.44 [1.61, 7.78]<br>autor Start 216 139 2419 8 4024 0.1% 0.21 [1.03, 1.66]<br>autor 11 518 27 247 0.0% 0.57 [1.08, 4.42]<br>autor 11 518 27 247 0.0% 0.57 [1.08, 4.42]<br>autor 11 518 27 247 0.2% 2.19 [1.08, 4.42]<br>autor 11 518 27 247 0.2% 2.19 [1.08, 4.42]<br>autor 11 518 27 247 0.2% 2.19 [1.08, 4.42]<br>autor 14 Hematoma<br>antio K.ciaire 216 139 20 13 2419 8 4024 0.1% 0.21 [0.03, 1.66]<br>autor 14 Hematoma<br>antio K.ciaire 216 139 20 23 424 0.1% 0.21 [0.03, 1.66]<br>autor 14 Hematoma 2019 12 2419 60 4024 0.8% 0.33 [0.18, 0.61]<br>autor 4.2018 0 293 14 457 0.0% 0.52 [0.02, 12.77]<br>autor 4.2018 0 293 424 0.1% 0.33 [0.18, 0.61]<br>autor 4.2018 0 293 424 0.1% 0.33 [0.18, 0.61]<br>autor 4.2018 0 293 424 0.1% 0.33 [0.18, 0.61]<br>autor 4.2018 0 293 424 0.3% 1.74 [0.93, 3.28]<br>autor 4.2018 0 293 424 0.1% 0.33 [0.18, 0.61]<br>autor 4.2018 0 21 91 4206 426 6660<br>autor 4.2018 0 20 1197 12 2452 0.1% 1.48 [1.93, 3.26]<br>autor 4.2018 0 20 197 12 2452 0.1% 1.48 [1.93, 3.26]<br>autor 4.2018 0 20 197 12 2452 0.1% 1.45 [1.43, 1.48]<br>autor 4.2018 0 20 197 12 2452 0.1% 1.45 [1.43, 1.48]<br>autor 4.2018 0 20 197 12 2456 21% 1.41 [1.93, 3.267]<br>autor 4.  | Karl-Heinz Kuck 2018                       | 4                              | 293        | 2                              | 457        | 0.0%     | 3.15 [0.57, 17.30]  |             | 1. Cl.,               |
| asateru Takigawa 2013 6 2200 15 864 0.1% 1.34 [0.51, 3.48]<br>minaela CreuX0200 7 1146 19 2447 0.2% 0.79 [0.33, 1.87]<br>minaela CreuX0200 7 1146 19 2447 0.2% 0.79 [0.33, 1.87]<br>minaela CreuX0200 7 1146 19 2447 0.2% 0.79 [0.31, 1.87]<br>minor 201 17 2206 325 6666 2.7% 1.14 [0.92, 1.42]<br>minor 201 17 2206 325 6666 2.7% 1.14 [0.92, 1.42]<br>minor 201 17 2206 325 6666 2.7% 1.14 [0.92, 1.42]<br>minor 201 17 206 326 6666 2.7% 1.14 [0.92, 1.42]<br>minor 201 17 206 326 6666 2.7% 1.14 [0.92, 1.42]<br>minor 201 17 206 366 581 50 0.2% 2.50 [1.18, 5.30]<br>minor 201 17 206 363 0.2% 1.18 [0.50, 2.79]<br>minor 201 17 2720 18 137 13 633 0.2% 1.18 [0.50, 2.79]<br>minor 201 17 2720 186 581 50 21.1% 1.56 [1.46, 1.68]<br>minor 201 19 373 13 633 0.2% 1.18 [0.50, 2.79]<br>minor 201 17 2721 1866 581 50 21.1% 1.56 [1.46, 1.68]<br>minor 201 19 201 237 14954 2.5% 1.44 [1.16, 1.78]<br>minor 201 11 518 27 2747 0.2% 2.19 [1.03, 1.68]<br>minor 201 11 518 27 2747 0.2% 2.19 [1.03, 1.42]<br>minor 201 11 518 27 2477 0.2% 2.19 [1.03, 1.42]<br>minor 201 11 518 27 2477 0.2% 2.19 [1.03, 1.42]<br>minor 201 11 518 27 2477 0.2% 2.19 [1.03, 1.42]<br>minor 201 19 209 23 424 0.1% 0.32 [0.02, 1.27]<br>minor 201 19 209 23 424 0.3% 0.3% 0.161 [1.2, 3.467]<br>minor 201 19 200 24 424 0.3% 0.3% 0.174 (0.93, 3.28]<br>minor 201 19 200 24 424 0.3% 0.3% 0.161 [1.2, 3.467]<br>minor 201 19 200 24 424 0.3% 0.3% 0.174 (0.93, 3.28]<br>minor 201 19 200 24 424 0.3% 0.3% 0.174 (0.93, 3.28]<br>minor 201 19 200 24 424 0.3% 0.3% 0.174 (0.93, 3.28]<br>minor 201 19 200 24 424 0.3% 0.3% 0.174 (0.93, 3.28]<br>minor 201 19 200 246 6660 3 136915 28.1% 1.52 [1.43, 1.62]<br>minor 201 19 200 246 6660 3 136915 28.1% 1.52 [1.43, 1.62]<br>minor 201 19 200 246 6660 3 136915 28.1% 1.52 [1.43, 1.62]<br>minor 201 19 200 246 6660 3 136915 28.1% 1.52 [1.43, 1.62]<br>minor 201 19 200 246 6660 3 136915 28.1% 1.52 [1.43, 1.62]<br>minor 201 19 100 women men  | Marielle Kloosterman 2020                  | 2                              | 209        | 5                              | 424        | 0.1%     | 0.81 [0.16, 4.21]   | 1.1         | 10                    |
| aura M. Zylia 2016 18 1057 18 2145 0.2% 2105 [1.06, 3.95]<br>oon-hyun Kim 2021 117 2206 325 6969 2.7% 1.14 [0.92, 1.42]<br>aura M. Zyla 2016 24 367 10 367 0.2% 2.50 [1.48, 5.30]<br>aura M. Zyla 2016 24 367 10 367 0.2% 2.50 [1.48, 5.30]<br>Abbotal (95% CI) 90736 178208 46.4% 1.24 [1.18, 1.31]<br>aubotal (95% CI) 90736 1737 27621 1866 58156 2.1.1% 1.56 [1.46, 1.66]<br>auto S. Elayi 2018 1372 27621 1866 58156 2.1.1% 1.56 [1.46, 1.66]<br>auto S. Elayi 2018 1372 27621 1866 58156 2.1.1% 1.56 [1.46, 1.66]<br>auto S. Elayi 2018 1372 27621 1866 58156 2.1.1% 1.56 [1.46, 1.66]<br>auto S. Elayi 2018 1372 27621 1866 58156 2.1.1% 1.56 [1.46, 1.66]<br>auto S. Elayi 2018 1372 27621 1866 58159 2.1.1% 1.56 [1.46, 1.66]<br>auto S. Elayi 2018 1372 27621 1866 58159 2.1.1% 1.56 [1.46, 1.66]<br>auto N. Caisar 2016 139 6137 2.37 14954 2.25% 1.44 [1.68, 7.69]<br>auto M. Caisar 2016 13 22 419 60 4024 0.8% 0.33 [0.18, 0.61]<br>auto M. Caisar 2016 19 209 23 424 0.3% 0.74 (0.93, 3.28]<br>auta M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.68, 7.09]<br>auto M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.62, 7.09]<br>auto M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.62, 7.09]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 7.09]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 7.09]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 7.09]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 7.09]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 1.50]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 1.50]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 1.50]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 1.50]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 1.50]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 1.50]<br>auto M. Zyla 2016 20 [197 12 2452 0.1% 3.46 [1.62, 1.50]<br>auto M. Zyla 2016 20 [197 12 2456 0.00001)<br>bat [65% CI) 271503 539571  | Masateru Takigawa 2013                     | 6                              | 260        | 15                             | 864        | 0.1%     | 1.34 [0.51, 3.48]   |             | 1 m                   |
| named SecU2020 1 1 1140 19 2447 0.2% 0.19 [0.53, 107]<br>deed Mszar 2022 198 20419 207 38641 2.6% 1.81 [1.49, 2.21]<br>aung-Young Roh 2018 24 367 10 367 0.2% 2.50 [1.8, 5.30]<br>AO-DONG ZHANG 2013 1 7.3 3 147 0.0% 0.67 [0.07, 6.52]<br>blottal (95% CI) 90736 178208 46.% 1.24 [1.18, 1.31]<br>aude S. Elay (216 1372 2.7821 1866 58156 21.1% 1.56 [1.46, 1.68]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6437 2.37 (1.1954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6437 2.37 (1.1954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6437 2.37 (1.1954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6437 2.37 (1.1954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6437 2.37 (1.1954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6437 2.37 (1.1954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 64 3387 0.2% 2.19 [1.08, 4.43]<br>ath N- Yunus 2021 11 518 27 2477 0.2% 2.19 [1.08, 4.43]<br>ath Heinz Kuck 2018 0 293 1 4.57 0.0% 0.52 [0.02, 1.277]<br>ath Heinz Kuck 2018 0 293 1 4.57 0.0% 0.52 [0.02, 1.277]<br>ath Heinz Kuck 2018 0 293 1 4.57 0.0% 0.52 [1.03, 3.28]<br>atra M. Zyla 2016 20 1197 12 2452 0.1% 3.46 [1.68, 7.09]<br>on-hyun Kim 2021 91 2206 246 6666 1.1% 1.474 [0.33, 3.28]<br>atra M. Zyla 2016 20 1197 12 2452 0.1% 1.52 [1.43, 3.67]<br>blottal (95% CI) 600001); P = 76%<br>est for overall effect: Z = 0.76 (0.00001); P = 76%<br>est for overall effect: Z = 0.76 (0.00001); P = 75%<br>blottal (95% CI) 271503 539571 100.0% 1.43 [1.38, 1.48]<br>4 Jatle vents 1750 2546<br>berogoneity: Ch <sup>2</sup> = 4.98 (d = 1.2 (P < 0.00001); P = 75%<br>est for overall effect: Z = 0.76 (P < 0.00001); P = 73%<br>blottal (95% CI) 6.1 (2.71503 539571 100.0% 1.43 [1.38, 1.48]<br>4 Jatle vents 1750 2546<br>berogoneity: Ch <sup>2</sup> = 1.   | Maura M. Zylla 2016<br>Mihoolo Creeu 2020  | 18                             | 1057       | 18                             | 2145       | 0.2%     | 2.05 [1.06, 3.95]   |             |                       |
| 0.00-m/gmtm.2021         111         2.00         0.23         0.000         1.14         0.021         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         1.14         0.221         0.000         0.07         0.071 </td <td>Moon-buun Kim 2021</td> <td>117</td> <td>2206</td> <td>325</td> <td>2447</td> <td>2 7%</td> <td>0.79 [0.33, 1.87]</td> <td></td> <td>-</td>  | Moon-buun Kim 2021                         | 117                            | 2206       | 325                            | 2447       | 2 7%     | 0.79 [0.33, 1.87]   |             | -                     |
| sung Young Pion 2018       24       367       10       367       22%       2.50 [118, 5.30]         AQ-DONG ZHANG 2013       1       73       3       147       0.0%       0.67 [0.07, 6.52]         Jala events       2427       4036       404%       1.24 [1.18, 1.51]       1         Jala events       2427       4036       404%       1.24 [1.18, 1.51]       1         Jala events       2427       4036       4056       1.24 [1.18, 1.51]       1         Mides M, Russo 2021       9       373       13       633       0.2%       1.18 [0.50, 2.79]         aude S. Elayi 2018       1372       27821       1866       58150       21.1%       1.56 [14.61, 168]       -         auld Nusso 2021       9       373       149642       0.2%       1.16 [106, 4.42]       -         aude S. Elayi 2016       132       2747       0.2%       2.19 [108, 4.43]       -       -         aude S. Elayi 2010       11       518       2727       0.0%       0.52 [0.02, 1277]       -         aura M. Zylla 2016       203       1457       0.0%       0.52 [0.02, 1277]       -       -         aura M. Zylla 2016       20       19       22       42   | Reed Mszar 2022                            | 198                            | 20419      | 207                            | 38541      | 2.6%     | 1 81 [1 49 2 21]    |             | -                     |
| AC-DONG 2HANC 2013 1 73 3 147 0.0% 0.67 [0.07, 6.52]<br>ubtotal (95% CI) 90736 178208 46.4% 1.24 [1.16, 1.31]<br>all events 2427 4036<br>teterogeneity: Ch <sup>2</sup> = 52.97, df = 17 (P < 0.0001); P = 68%<br>stor overall effect: Z = 8.26 (P < 0.0001)<br>1.4 Hematoma<br>ndrea M. Russo 2021 9 373 13 633 0.2% 1.18 [0.50, 2.79]<br>aniel W. Kaiser 2016 137 22 77821 1866 58165 21.1% 1.56 [1.46, 1.68]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>aniel W. Kaiser 2016 139 6137 237 14954 0.1% 0.2% 2.19 [1.03, 1.68]<br>aniel W. Kaiser 2016 129 20 21 71 1969 14 3387 0.2% 2.19 [1.03, 1.42]<br>and N. Yunus 2021 17 1969 14 3387 0.2% 2.19 [1.03, 1.42]<br>aniel W. Kaiser 2016 20 1197 12 2452 0.1% 0.58 [0.02, 1.277]<br>aniel M. Kaiser 2016 20 1197 12 2452 0.1% 3.46 [1.68, 7.09]<br>on-hyun Kim 201 91 220 24 66 6969 1.2% 1.18 [0.59, 1.70]<br>aura M. Zylia 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.10]<br>aura M. Zylia 2016 20 1197 12 2452 0.1% 1.43 [1.23, 1.62]<br>aura M. Zylia 2016 20 1197 12 2452 0.1% 1.45 [1.43, 1.62]<br>aura M. Zylia 2016 20 1197 71 2564<br>eterogeneity: Ch <sup>2</sup> = 49.98, df = 12 (P < 0.00001); P = 76%<br>stor overall effect: Z = 0.76 (P < 0.00001)<br>batal (95% CI) 271503 539571 100.0% 1.43 [1.38, 1.48]<br>bitotal (95% CI) 271503 539571 100.0% 1.43 [1.38, 1.48]<br>bitotal (95% CI) 0 10 271503 539571 100.0% 1.43 [1.38, 1.48]<br>bitotal (95% CI) 0 10 271503 539571 100.0% 1.43 [1.38, 1.48]<br>bitotal (95% CI) 0 10 271503 539571 100.0% 1.43 [1.38, 1.48]<br>bitotal (95% CI) 0 291 53.79, df = 3 (P < 0.00001); P = 94.4%  | Seung-Young Roh 2018                       | 24                             | 367        | 10                             | 367        | 0.2%     | 2.50 [1.18, 5.30]   |             |                       |
| bibbotal (95% CI) 90736 178208 46.4% 1.24 [1.18, 1.31]<br>1.4 levents 2427 4036<br>eterogeneity: Ch <sup>2</sup> = 52.9 (P < 0.0001); P = 68%<br>set for overall effect: Z = 8.29 (P < 0.0001); P = 68%<br>set for overall effect: Z = 8.29 (P < 0.0001); P = 68%<br>set for overall effect: Z = 7.82 (P < 0.0001); P = 68%<br>set for subroub differences: Ch <sup>2</sup> = 8.29 (P < 0.0001); P = 9.4%<br>1.4 levents 2010 11 518 27 247 0.02% 2.19 [1.08, 4.43]<br>1.4 levents 2010 11 518 27 247 0.2% 2.19 [1.08, 4.43]<br>1.4 levents 2010 11 518 27 244 0.2% 2.10 [1.03, 1.66]<br>1.4 levents 2010 11 2419 60 4024 0.8% 0.33 [0.18, 0.61]<br>1.4 levents 2019 20 23 424 0.1% 0.2% 0.19 [1.08, 4.42]<br>1.4 levents 2019 12 2419 60 4024 0.8% 0.33 [0.18, 0.61]<br>1.4 levents 2019 12 2419 60 4024 0.8% 0.33 [0.18, 0.61]<br>1.4 levents 2019 12 2046 6969 2.1% 1.18 [0.92, 1.50]<br>4.4 ODW 24.4 N218 0.2% 1.10 (1.03, 3.28]<br>1.4 or 00% 10.74 [1.23, 39.67]<br>1.4 Jevents 21 01 200 254 24019 38 38541 0.5% 2.69 [1.77, 4.07]<br>AO-DONG 24.4 D2 < 0.00001); P = 75%<br>set for overall effect: Z = 13.22 (P < 0.00001); P = 75%<br>set for overall effect: Z = 13.22 (P < 0.00001); P = 75%<br>set for overall effect: Z = 13.50 (P < 0.00001); P = 75%<br>set for overall effect: Z = 13.50 (P < 0.00001); P = 94.4%  | XIAO-DONG ZHANG 2013                       | 1                              | 73         | 3                              | 147        | 0.0%     | 0.67 [0.07, 6.52]   |             |                       |
| hall events     2427     4036       eterogeneity: Ch <sup>2</sup> = 43.9, (P < 0.00001); P = 68%,   | Subtotal (95% CI)                          |                                | 90736      |                                | 178208     | 46.4%    | 1.24 [1.18, 1.31]   |             | •                     |
| eterogeneity: Ch <sup>2</sup> = 52.97, df = 17 (P < 0.0001); P = 68%<br>set for overall effect: Z = 0.5 (P < 0.0001)<br>1.4 Hematoma<br>drae M. Russo 2021 9 373 13 633 0.2% 1.18 [0.50,2.79]<br>anicl Russo 2021 9 373 1272 1866 58156 21.1% 1.56 [1.46, 1.66]<br>anicl W. Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]<br>anicl Russo 2021 1 1 2419 8 4024 0.1% 0.21 [0.03, 1.66]<br>anicl Russo 2021 1 1 518 27 2747 0.2% 2.19 [1.06, 4.43]<br>anicl Russo 2021 1 1 518 27 2747 0.2% 2.19 [1.06, 4.43]<br>anicl Russo 2021 1 7 1969 14 3387 0.2% 2.10 [1.06, 4.42]<br>art Heinz Kuck 2018 0 293 1 467 0.0% 0.52 [0.02, 12.77]<br>art Heinz Kuck 2018 0 293 424 0.3% 1.74 (0.93, 3.28]<br>arr Al-Heinz Kuck 2018 0 293 424 0.3% 1.74 (1.03, 3.26]<br>arr Al-Heinz Kuck 2018 0 293 424 0.3% 1.74 (1.03, 3.28]<br>arr Al-Heinz Kuck 2018 0 293 424 0.1% 3.46 [1.68, 7.09]<br>arr Al-Heinz Kuck 2018 0 21 91 220 246 6969 2.1% 1.18 [0.92, 1.50]<br>arr Al-Heinz Kuck 2018 0 253 136915 28.1% 1.52 [1.43, 1.62]<br>bit of powerall effect: Z = 13.22 (P < 0.00001); P = 76%<br>set for overall effect: Z = 0.76 (P < 0.00001); P = 73%<br>bit for overall effect: Z = 0.76 (P < 0.00001); P = 73%<br>bit for overall effect: Z = 0.76 (P < 0.00001); P = 94.4%  | Total events                               | 2427                           |            | 4036                           |            |          |                     |             |                       |
| set for overall effect: Z = 8.29 (P < 0.00001)  | Heterogeneity: Chi <sup>2</sup> = 52.97, o | df = 17 (P <                   | < 0.0001)  | l <sup>2</sup> = 68%           | b          |          |                     |             |                       |
| 1.4 Hematoma         Indrea M. Russo 2021       9       373       13       633       0.2%       1.18 [0.50, 2.79]         Indrea M. Russo 2021       9       373       13       633       0.2%       1.18 [0.50, 2.79]         Indrea M. Russo 2021       139       6137       237       14954       2.5%       1.46 [1.46, 1.68]         Indrea M. Russo 2016       139       6137       237       14954       2.5%       1.44 [1.16, 1.78]         Impl Patel 2010       1       2419       8       4024       0.1%       0.21 [1.03, 1.66]   | Test for overall effect: Z = 8.2           | 29 (P < 0.00                   | 001)       |                                |            |          |                     |             |                       |
| La Hematoma<br>direa M. Russo 2021 9 373 13 633 0.2% 1.18 [0.50, 2.79]<br>aude S. Elayi 2018 1372 27821 1866 58156 2.11% 1.56 [1.46, 1.68]<br>aude S. Elayi 2018 1372 27821 1866 58156 2.11% 1.56 [1.46, 1.68]<br>anilo Ricciardi 2019 1 2419 8 4024 0.1% 0.21 [0.03, 1.66]<br>anilo Ricciardi 2019 1 2419 8 72 474 0.2% 2.19 [1.08, 4.43]<br>anilo Ricciardi 2010 11 518 27 2474 0.2% 2.19 [1.08, 4.42]<br>auta M. Yunus 2021 17 1969 14 3387 0.2% 2.10 [1.08, 4.42]<br>auta M. Zyula 2016 220 1197 12 2452 0.0% 0.52 [0.00, 1.67]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 3.46 [1.68, 7.09]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>auta M. Zyula 2016 20 2.1% 1.18 [0.92, 1.50]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>auta M. Zyula 2016 (200 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>auta M. Zyula 2016 20 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>auta M. Zyula 2016 20 2.19 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>auta M. Zyula 2016 20 2.19 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>auta M. Zyula 2016 20 2.19 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>auta M. Zyula 2016 20 2.10 1197 12 2456 2.1% 1.50 [1.77, 4.07]<br>bat devents 1750 2546<br>beterogeneity: Ch* = 49.6, d = 1.02 <0.00011)<br>bat (95% Cl) 271503 539571 100.0% 1.43 [1.38, 1.48]<br>auta M. Zyula 2016 0.1 0.1 0.1 0.1 0.1 0.1 0.0 0.0 0.1 0.1   |  |                                |            |                                |            |          |                     |             |                       |
| nurea m, ruusso cv.z i 9 3/3 13 63 0.2% 1.16 [0.30, 2/9]  aniel W, Kaiser 2016 132 27821 1866 58156 2.11% 1.56 [1.46, 1.68]  aniel W, Kaiser 2016 139 6137 237 14954 2.5% 1.44 [1.16, 1.78]  mipi Patel 2010 11 518 27 2747 0.2% 2.19 [1.08, 4.43]  mipi Patel 2010 11 518 27 2747 0.2% 2.19 [1.08, 4.43]  ark-Hoinz Kuck 2018 0 283 1 457 0.0% 0.52 [0.02, 1277]  ark-Hoinz Kuck 2018 0 283 1 457 0.0% 0.52 [0.02, 1277]  ark-Hoinz Kuck 2018 0 283 1 457 0.0% 0.52 [0.02, 1277]  ark-Hoinz Kuck 2018 0 283 1 457 0.0% 0.52 [0.02, 1277]  ark-Hoinz Kuck 2018 0 2419 60 4024 0.8% 0.33 [0.18, 0.61]  ark-Hoinz Kuck 2018 0 2419 60 4024 0.1% 0.21 [0.92, 1.50]  ark-Hoinz Kuck 2018 0 266 6660 2.1% 1.18 [0.92, 1.50]  art M-00-Nyu Kim 2021 91 220 4246 6660 2.1% 1.18 [0.92, 1.50]  atorhyun Kim 2021 91 220 426 6660 3 136915 28.1% 1.52 [1.43, 1.62]  atol events 1750 2546  berogonehiy: Chi <sup>2</sup> = 4.98, df = 12 (P < 0.00001); P = 76%  est for overall effect: Z = 0.16 (P < 0.00001); P = 76%  est for overall effect: Z = 0.16 (P < 0.00001); P = 76%  est for overall effect: Z = 0.16 (P < 0.00001); P = 78%  befor year and the 2 = 53.79. df = 3 (P < 0.00001); P = 94.4%  women men   | 3.1.4 riematoma                            | c                              | 070        | 40                             | 000        | 0.001    | 4 40 10 50 0 701    |             | 21                    |
| autue 5. Lawy 2010 13/2 27/22/1 1805 35150 27.1.7% 1.55 [1-46, 1.56]<br>anilo Ricairdi 2019 1 2419 8 4024 0.1% 0.21 [0.03, 1.66]<br>anilo Ricairdi 2019 1 2419 8 4024 0.1% 0.21 [0.03, 1.66]<br>anilo Ricairdi 2019 1 2419 8 4024 0.1% 0.21 [1.08, 4.43]<br>anilo Ricairdi 2010 11 518 27 2747 0.2% 2.19 [1.08, 4.43]<br>and N. Yunus 2021 17 1969 14 3387 0.2% 2.10 [1.03, 4.27]<br>and N. Yunus 2021 17 1969 14 3387 0.2% 2.10 [1.08, 4.43]<br>ant A. Yunus 2021 17 1969 14 2387 0.2% 0.33 [0.18, 0.61]<br>ant A. Yunus 2021 19 209 23 424 0.8% 0.33 [0.18, 0.61]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.68, 7.09]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.09]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.32, 1.40]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.32, 1.40]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.32, 1.40]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.32, 1.40]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.32, 1.40]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.34, 1.48]<br>ant A. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.38, 1.48]<br>ant A. Yula 2016 20 1197 12 2452 0.00001); F = 73%<br>ast for overall effect: Z = 13.22 (P < 0.00001); F = 73%<br>bat overall s 6014 8600<br>betrogeneity: Ch <sup>2</sup> = 184.33, df = 50 (P < 0.00001); F = 73%<br>bat for overall effect: Z = 0.50 (P < 0.00001); F = 73%<br>bat for overall effect: Z = 0.51 (P < 0.00001); F = 73%<br>bat for suboroup differences: Ch <sup>2</sup> = 53.79. df = 3 (P < 0.00001); F = 94.4%  | Andrea M. Russo 2021                       | 4070                           | 373        | 13                             | 633        | 0.2%     | 1.18 [0.50, 2.79]   |             |                       |
| attern tr., hases 2010     1.59     0.137     2.37     1.4954     2.35%     1.44     [1,10, 1,76]       mpi Patel 2010     11     518     27     2747     0.2%     2.19     [1,03, 1,66]       mpi Patel 2010     11     518     27     2747     0.2%     2.19     [1,03, 1,67]       arH-binz Kuck 2018     0     293     1     457     0.2%     2.19     [1,03, 4,43]       arH-binz Kuck 2018     0     293     1     457     0.0%     0.52     [0,02, 1,27]       aura M. Zylla 2016     20     2197     12     2459     0.49%     0.35     [0,18, 0.61]       arielle Kloosterman 2020     19     2209     23     424     0.3%     1.74     [0,33, 1.26]       aura M. Zylla 2016     20     1197     12     2452     0.1%     3.46     [1,68, 7.09]       oorhyun Kim 2021     91     200     23     424     0.3%     2.69     [1,77, 4.07]       Ab-DONG ZHANN 2013     5     73     147     0.0%     1.52     [1,43, 1.62]       atel events     1750     2546     2566     1.52     [1,43, 1.48]     4       atel events     6014     8660     466     6060     4.00001); P = 73%  | Daniel W. Keiser 2016                      | 13/2                           | 2/821      | 1866                           | 14054      | 21.1%    | 1.56 [1.46, 1.68]   |             | -                     |
| and PLAULADIN 2013 1 2119 6 4024 0.1% 0.21 [0.05, 1.66]<br>min PLAUL2D1 11 518 27 2747 0.2% 2.19 [1.68, 4.43]<br>and N. Yunus 2021 17 1969 14 3387 0.2% 2.10 [1.68, 4.42]<br>and N. Yunus 2021 17 1969 14 3387 0.2% 2.10 [1.68, 4.42]<br>and N. Yunus 2021 17 1969 14 3387 0.2% 2.10 [1.68, 4.42]<br>and N. Yunus 2021 17 1969 14 3387 0.2% 2.10 [1.68, 4.42]<br>and N. Yunus 2021 19 209 24 424 0.8% 0.33 [0.18, 0.61]<br>and N. Yunus 2020 19 209 23 424 0.8% 0.33 [0.18, 0.61]<br>and N. Yunus 2016 20 1197 12 2452 0.1% 3.46 [1.68, 7.09]<br>and N. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.16]<br>and N. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.16]<br>and N. Yula 2016 20 1197 12 2452 0.1% 3.46 [1.69, 7.16]<br>and N. Yula 2016 20 1197 12 2452 0.1% 1.41 [1.23, 9367]<br>and N. Yula 2016 20 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>and N. Yula 2016 20 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>and N. Yula 2016 20 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>and N. Yula 2016 20 1197 12 2452 0.1% 1.52 [1.43, 1.62]<br>and N. Yula 2016 20 1197 12 2452 0.1% 1.43 [1.38, 1.48]<br>and on the substrained of the subs  | Daniel W. Kalser 2016                      | 139                            | 0137       | 237                            | 14954      | 2.5%     | 1.44 [1.16, 1.78]   |             |                       |
| Implementation       III       516       27       2747       0.25%       2.15 [1.66, 4.45]         ant-Heinz Kuck 2018       0       293       1       4367       0.2%       2.10 [1.03, 4.27]         ant-Heinz Kuck 2018       0       293       1       457       0.0%       0.52 [0.02, 12.77]         ant-Heinz Kuck 2018       0       293       1       457       0.0%       0.52 [0.02, 12.77]         arielle Kloosterman 2020       19       209       23       424       0.8%       0.33 [16, 0.61]         arielle Kloosterman 2020       19       209       23       424       0.8%       0.32 [16, 0.7, 4.07]         oon-hym Kim 2021       91       22.06       246       6669       2.1%       1.18 [0.92, 1.50]         oon-hym Kim 2021       91       22.06       246       6669       2.6% [1.77, 4.07]       A.O-ONG 274ANS 2013       5       7.3       1       1.47       0.5%       2.69 [1.77, 4.07]       A.O-ONG 274ANS 2013       5       7.3       1       1.52 [1.43, 1.62]       I.52 [1.43, 1.62] </td <td>Danilo Ricciardi 2019</td> <td>1</td> <td>2419</td> <td>27</td> <td>4024</td> <td>0.1%</td> <td>0.21 [0.03, 1.06]</td> <td></td> <td></td>  | Danilo Ricciardi 2019                      | 1                              | 2419       | 27                             | 4024       | 0.1%     | 0.21 [0.03, 1.06]   |             |                       |
| an R + Truits 2021<br>The R + Mark K 2016<br>1 457 027<br>1  | Eabd N. Xupus 2021                         | 11                             | 1060       | 21                             | 2/4/       | 0.2%     | 2.19 [1.08, 4.43]   |             |                       |
| Minimum Value Value Value       0.0       0.03 [0.18, 0.61]         arrielle Kloosterman 2019       12       2419       60       4024       0.8%       0.03 [0.18, 0.61]         arrielle Kloosterman 2020       19       209       23       424       0.3%       0.03 [0.18, 0.61]         arrielle Kloosterman 2020       19       209       23       424       0.3%       0.03 [0.18, 0.61]         arrielle Kloosterman 2020       19       2206       246       6869       2.1%       1.74 [0.93, 3.28]         oon-hyun Kim 2021       91       2206       246       6869       2.1%       1.18 [0.92, 1.50]         oon-hyun Kim 2021       5       73       1       147       0.0%       10.74 [1.23, 93.67]         Alo-DONKO 2HANG 2013       5       73       1       147       0.0%       10.74 [1.23, 93.67]         abtotal (95% Cl)       271503       539571       100.0%       1.43 [1.38, 1.48]       4         staf (95% Cl)       271503       539571       100.0%       1.43 [1.38, 1.48]       4         staf (95% cl)       271503       539571       100.0%       1.43 [1.38, 1.48]       4         staf overall effect: Z = 20.76 (P < 0.00001); P = 73%   | Karl-Heinz Kuck 2018                       | 0                              | 203        | 1                              | 457        | 0.2%     | 0.52 [0.02 12 77]   |             |                       |
| aura M. Ostonian I. 2010<br>aura M. Zyla 2016<br>aura M. Zyla 2016<br>2019<br>2020<br>213<br>244<br>2452<br>201%<br>2452<br>201%<br>2452<br>2452<br>2452<br>2454<br>201%<br>246<br>246<br>246<br>246<br>246<br>246<br>246<br>246  | Laura Lleberbarn 2019                      | 12                             | 293        | 60                             | 4024       | 0.0%     | 0.32 [0.02, 12.77]  |             |                       |
| Label At Value All Arg 16     20     1197     12     2425     0.1%     3.64 [1.68, 7.09]       Joon-Hyun Kim 2021     91     2206     246     6665     2.1%     1.16 [0.92, 1.50]       Joon-Nyun Kim 2021     91     2206     246     6665     2.1%     1.16 [0.92, 1.50]       JAO-DONG ZHANG 2013     5     7.3     1     147     0.0%     10.74 [1.23, 93.67]       Jobtal (95% Cl)     2546     59515     28.1%     1.52 [1.43, 1.62]       Jala events     1750     2546     2549       stof rowarall effect: Z = 13.22 (P < 0.00001); P = 76%  | Marielle Kloosterman 2020                  | 10                             | 2419       | 23                             | 4024       | 0.3%     | 1 74 [0 93 3 28]    |             |                       |
| con-hyun Kim 2021         91         2206         246         6969         2.1%         1.18 [0.92, 1.50]           eed Mazar 2022         54         20019         38         38541         0.5%         2.69 [1.77, 4.07]           AO-DONG ZHANG 2013         5         73         1 47         0.0%         10.74 [1.23, 93.67]           ubtotal (95% CI)         66053         139915         28.1%         1.52 [1.43, 1.62]           atal events         1750         2546           eterogeneity: Ch <sup>2</sup> = 49.96, df = 12 (P < 0.00001); P = 76%,<br>sast for overall effect: Z = 13.22 (P < 0.00001); P = 76%,<br>bate events         6014         8660           ateoremeity: Ch <sup>2</sup> = 184.33, df = 50 (P < 0.00001); P = 73%,<br>bat for overall effect: Z = 20.76 (P < 0.00001); P = 73%,<br>bat for suboroup differences: Ch <sup>2</sup> = 53.79. df = 3 (P < 0.00001); P = 94.4%,  | Maura M Zvlla 2016                         | 20                             | 1197       | 12                             | 2452       | 0.5%     | 3 46 [1 68 7 09]    |             |                       |
| beed Mazar 2022         54         20419         38         38841         0.5%         2.69 [1.77, 407]           AboDONG 2HARQ 2013         5         7.3         1.47         0.0%         1074 [12.3, 93.67]           Jablotal (95% Cl)         66053         136915         28.1%         1.52 [1.43, 1.62]         1           Jale vents         1750         2546         2546         2546         2546         2546           set for overall effect:         2 1.52 [1.43, 1.62]         1         1.52 [1.43, 1.62]         1         1           st for overall effect:         2 1.52 [1.60,00001); IF = 75%         1.43 [1.38, 1.48]         1         1         1           st for overall effect:         2 3.00 [0.10,00001); IF = 73%         1.43 [1.38, 1.48]         1         1           st for overall effect:         2 3.00 [0.4 0,00001); IF = 73%         0.01         0.1         1         100           st for overall effect:         2 3.00 (0.4 0,00001); IF = 73%         0.01         0.1         1         100           st for overall effect:         2 3.00 (0.4 0,00001); IF = 73%         0.01         0.1         1         100           st for overall effect:         2 3.79 of f = 3 (P < 0.00001); IF = 94.4%   | Moon-hyun Kim 2021                         | 91                             | 2206       | 246                            | 6969       | 2.1%     | 1.18 [0.92, 1.50]   |             | -                     |
| AQ-DONK 2HANG 2013 5 73 1 147 0.0% 10.74 [1:23, 93.67]<br>Jubitotal (95% CI) 2546<br>teterogeneity: Ch <sup>2</sup> = 49.96, df = 12 (P < 0.00001); P = 76%<br>stof overall effect: Z = 13.22 (P < 0.00001); P = 76%<br>stof overall effect: Z = 13.22 (P < 0.00001); P = 73%<br>teterogeneity: Ch <sup>2</sup> = 184.33, df = 50 (P < 0.00001); P = 73%<br>stof overall effect: Z = 07.6 (P < 0.00001); P = 73%<br>stof overall effect: Z = 07.6 (P < 0.00001); P = 94.4%<br>women men   | Reed Mszar 2022                            | 54                             | 20419      | 38                             | 38541      | 0.5%     | 2.69 [1.77, 4.07]   |             |                       |
| biblotal (95% Cl) 66053 136915 28.1% 1.52 [1.43, 1.62]<br>talle vents 1750 2546<br>eterogeneity: Chi <sup>2</sup> = 4.98, df = 12 (P < 0.00001); P = 76%<br>est for overall effect: Z = 13.22 (P < 0.00001); P = 76%<br>est for overall effect: Z = 13.22 (P < 0.00001); P = 73%<br>tall events 6014<br>8660<br>eterogeneity: Chi <sup>2</sup> = 184.33, df = 50 (P < 0.00001); P = 73%<br>to for overall effect: Z = 20.76 (P < 0.00001); P = 73%<br>st for overall effect: Z = 20.76 (P < 0.00001); P = 94.4%<br>women men  | XIAO-DONG ZHANG 2013                       | 5                              | 73         | 1                              | 147        | 0.0%     | 10.74 [1.23, 93.67] |             |                       |
| tale events       1750       2546         eterogeneity: Ch <sup>2</sup> = 49.96, df = 12 (P < 0.00001); I <sup>2</sup> = 76%,       141 events         stof roverall effect: Z = 13.22 (P < 0.00001);   | Subtotal (95% CI)                          |                                | 66053      |                                | 136915     | 28.1%    | 1.52 [1.43, 1.62]   |             | •                     |
| eterogeneity: Ch <sup>2</sup> = 49.96, df = 12 (P < 0.00001); P = 76%<br>sst for overall effect: Z = 13.22 (P < 0.00001);<br>sst for overall effect: Z = 13.22 (P < 0.00001);<br>btal events 6014 8660<br>btal events 6014 8660<br>st for overall effect: Z = 20.76 (P < 0.00001); P = 73%<br>st for overall effect: Z = 20.76 (P < 0.00001); P = 73%<br>sst for overall effect: Z = 20.73, ff < 0.00001); P = 94.4%<br>women men   | Total events                               | 1750                           |            | 2546                           |            |          |                     |             |                       |
| set for overall effect: Z = 13.22 (P < 0.00001)<br>btal (95% CI) 271503 539571 100.0% 1.43 [1.38, 1.48]<br>tal events 6014 8660<br>eterogeneity: Chi <sup>2</sup> = 184.33, df = 50 (P < 0.00001); l <sup>2</sup> = 73%<br>est for overall effect: Z = 20.76 (P < 0.00001); l <sup>2</sup> = 73%<br>0.01 0.1 1 10 100<br>set for suboroup differences: Chi <sup>2</sup> = 53.79. df = 3 (P < 0.00001); l <sup>2</sup> = 94.4%   | Heterogeneity: Chi <sup>2</sup> = 49.96, 0 | df = 12 (P <                   | < 0.00001  | ); I <sup>2</sup> = 76         | %          |          |                     |             |                       |
| stal events         6014         8660         1.43 [1.38, 1.48]         I           sterogeneity: Ch <sup>2</sup> = 184.33, df = 50 (P < 0.00001); l <sup>2</sup> = 73%         0.01         0.1         1         10         100           stof or suborous differences: Ch <sup>2</sup> = 53.79. df = 3 (P < 0.00001); l <sup>2</sup> = 94.4%         women         men         100   | Test for overall effect: Z = 13.           | .22 (P < 0.0                   | 0001)      |                                |            |          |                     |             |                       |
| tate (vars v-y) 2/1303 333971 100.07% 1.43 [1.36, 1.46] T<br>tate versits 6014 8660<br>teterogeneity: Chi² = 184.33, df = 50 (P < 0.00001); l² = 73%<br>stof overall effect Z = 20.76 (P < 0.00001)<br>stof suboroup differences: Chi² = 53.79. df = 3 (P < 0.00001); l² = 94.4%<br>women men   | Total (05% CI)                             |                                | 74602      |                                | E20E74     | 100.08/  | 4 42 14 20 4 403    |             | 1                     |
| Jail events         CO14         CO00           berogeneity:         Chi² = 184.33, df = 50 (P < 0.00001); l² = 73%   | Total (95% CI)                             | 6014                           | 2/1503     | 9660                           | 539571     | 100.0%   | 1.43 [1.38, 1.48]   |             | 1                     |
| Star overall effect: Z = 20.76 (* 0.00001), 'F = 53.79. df = 3 (P < 0.00011), I² = 94.4%  | Heterogeneity: Chi2 = 194 33               | 0014<br>df = 50 /P             | < 0.0000   | 0000<br>1)· l <sup>2</sup> = 7 | 3%         |          |                     | H           |                       |
| st for subaroup differences: Chi <sup>2</sup> = 53.79. df = 3 (P < 0.00001), l <sup>2</sup> = 94.4% women men   | Test for overall effect: 7 = 20            | 76 (P < 0.0                    | - 0.0000   | 1, 1 - 7                       | J 70       |          |                     | 0.01 0.1    | 1 10 100              |
|   | Test for subaroup differences              | s: Chi <sup>2</sup> = 53       | 79. df = 1 | B (P < 0 0                     | 0001). 12  | = 94.4%  |                     | women       | men                   |
|   |  |                                |            |                                |            |          |                     |             |                       |

Figure 4: Forest plot of stroke/TIA in women vs. men in-hospital after catheter ablation.

|  | Experin    | nental   | Cont     | rol    |        | Odds Ratio          | Odds Ratio |            |          |     |
|--|------------|----------|----------|--------|--------|---------------------|------------|------------|----------|-----|
| Study or Subgroup                        | Events     | Total    | Events   | Total  | Weight | M-H, Fixed, 95% C   |            | M-H, Fixed | , 95% CI |     |
| Claude S. Elayi 2018                     | 73         | 27821    | 103      | 58156  | 33.2%  | 1.48 [1.10, 2.00]   |            | - -        | -        |     |
| Daniel W. Kaiser 2016                    | 4          | 6137     | 3        | 14954  | 0.9%   | 3.25 [0.73, 14.53]  |            | +          |          |     |
| Fahd N. Yunus 2021                       | 0          | 1969     | 1        | 3387   | 0.6%   | 0.57 [0.02, 14.08]  |            |            |          |     |
| Jim W. Cheung 2019                       | 21         | 20623    | 68       | 33974  | 25.7%  | 0.51 [0.31, 0.83]   |            |            |          |     |
| Jonathan P. Piccini 2012                 | 52         | 6265     | 68       | 9158   | 27.4%  | 1.12 [0.78, 1.61]   |            | -          | -        |     |
| Karl-Heinz Kuck 2018                     | 1          | 293      | 1        | 457    | 0.4%   | 1.56 [0.10, 25.06]  |            |            | •        | _   |
| Laura Ueberham 2019                      | 2          | 2419     | 4        | 4024   | 1.5%   | 0.83 [0.15, 4.54]   |            |            |          |     |
| Marielle Kloosterman 2020                | 1          | 209      | 1        | 424    | 0.3%   | 2.03 [0.13, 32.67]  |            |            | •        |     |
| Mihaela Grecu2020                        | 1          | 1146     | 0        | 2447   | 0.2%   | 6.41 [0.26, 157.47] |            |            |          |     |
| Moon-hyun Kim 2021                       | 1          | 2206     | 5        | 6969   | 1.2%   | 0.63 [0.07, 5.41]   |            |            |          |     |
| Nobuaki Tanaka 2020                      | 1          | 1369     | 3        | 3641   | 0.8%   | 0.89 [0.09, 8.53]   |            |            |          |     |
| Reed Mszar 2022                          | 10         | 20419    | 19       | 28541  | 7.9%   | 0.74 [0.34, 1.58]   |            |            | -        |     |
| Total (95% CI)                           |            | 90876    |          | 166132 | 100.0% | 1.07 [0.88, 1.30]   |            | •          |          |     |
| Total events                             | 167        |          | 276      |        |        |                     |            |            |          |     |
| Heterogeneity: Chi <sup>2</sup> = 18.48, | df = 11 (P | = 0.07); | l² = 40% |        |        |                     |            |            | 10       | 100 |
| Test for overall effect: Z = 0.6         | 9 (P = 0.4 | 9)       |          |        |        |                     | 0.01       | 0.1 1      | 10       | 100 |

Figure 5: Forest plot of all-cause mortality in women *vs.* men after catheter ablation.

## DISCUSSION

To the best of our knowledge this is the largest study evaluating sex difference in the characteristics and outcomes between females and males following catheter ablation of AF. (i) Females AF patients experienced higher AF recurrence rates after the initial RFCA procedures; and (ii) Females experienced more frequent incidence of procedure-related complications.

It is still difficult to identify people who are at risk for arrhythmia recurrence after AF ablation. There have been reports of several prediction models based on clinical, anatomical, imaging, and serological traits [32]. A residual non-PV arrhythmogenic substrate after the PVI and the restoration of isolated PV potentials were the two main mechanisms of recurrence following AF ablation [33]. The PVI techniques were not well defined in the past, and PV re-conduction was common. The impact of patient variables, particularly gender, may have been muted in earlier research since PV re-conduction was such a significant factor influencing recurrence [34]. Today, PVI is more durable and the influence of patient features on the success of the ablation may be revealed advancements in the PVI technique like 3D mapping systems, irrigation catheters, contact force catheters, consequently, emphasis is gradually being directed to sexy differences [35].

Numerous inflammatory reactions, including oxidative stress, calcium overload, and myofibroblast activation, are brought on by prolonged atrial stimulation [36]. These inflammatory responses, which may be more severe in women than in males, may result in deformation of the extracellular matrix and of the electrophysiological characteristics of the atria [37]. Inflammatory markers like high-sensitivity C-reactive protein, soluble intercellular adhesion molecule-1, and fibrinogen have been linked to incident AF in women even when established risk factors have been taken into account, according to the women's health study [38]. Higher frequency of non-pulmonary triggered activity, longer action potential duration in female atria, and more pronounced AF-associated fibrotic remodeling result in higher AF recurrence in females than in males [39]. Females in this study who were scheduled for ablation were older, had less paroxysmal AF, and had more comorbid conditions; these factors were linked to more advance structural remodeling and resulted in poorer success rates.

Women undergoing AFCA have a higher risk of pericardial effusion tamponade [40]. According to previous research, tamponade is more common in women than in men. Our research backs up this finding. Pericardial effusion is a risk with both transseptal puncture and catheter manipulation, with left atrial perforation being the most common complication [41]. Despite the fact that routine use of ICE is associated with a significantly lower rate of pericardial complications, cost considerations limit its routine use [42]. Patients receiving continuous oral anticoagulation may be at increased risk of refractory bleeding despite pericardiocentesis and protamine administration [43]. And exanet alfam idarucizumab can be used to reverse dabigatran, rivaroxaban, or apixaban in such cases, and to lower the danger of pericardial effusion/tamponade, numerous innovative catheter ablation techniques have been deployed, including ultra-low temperature cryoablation catheters and extremely high-power short-duration catheter ablation [44-46].

Vascular surgeries were relatively infrequent in this study's reported vascular access problems [47]. A higher percentage of obese women, a known risk factor for more difficult vascular access, smaller vascular diameter in women than in men, and the close anatomic relationship between the femoral artery and its branches, which makes veins in women more difficult to puncture and increases the risk of unintentional arterial puncture [48,49]. This gap could be filled by using vascular ultrasonography for femoral venous access on a regular basis.

Even after controlling for other risk factors, females with AF have an increased risk of stroke compared to males. In line with previous findings, our study reported 0.37% in-hospital stroke/TIA. Our findings are consistent with a previous meta-analysis of AFCA outcomes stratified by gender, which found that women had significantly higher rates of stroke/TIA and mortality after AFCA [50]. However, the precise mechanism of gender and procedural stroke is unknown, and there are several possible explanations. First, it is assumed that procedural strokes/TIAs are primarily caused by thrombus formation, though non-thrombotic mechanisms may also contribute to neurologic events associated with AFCA [51]. Second, differences in heparin pharmacokinetics between men and women may contribute to the higher rate of stroke/TIA observed in women. More research is needed to identify optimal peri and intra-procedural anticoagulation strategies in women that balance not only thrombotic risk but also the increased risk of bleeding complications [52]. Third, differences in genetic, vascular biology, hormonal between men and women may increase the risk of stroke [52]. Physicians must discuss the ongoing risks and benefits of anticoagulant therapy, especially when combined with a high CHA2DS2-VASc score and a high likelihood of AF recurrence.

The risk of in-hospital mortality in the current study was extremely low (0.14%). These findings matched the 0.06-0.60% estimated death risk for AF catheter ablation. Our research looked at over 257008 patients and discovered that there was no difference in in-hospital mortality between male and female patients. Campbell found that women had significantly higher rates of mortality after AFCA [52]. However, one significant difference between our analysis and Campbell's is that we included five newly published studies totaling 75230 patients. Patients were included in a larger sample size, resulting in a different conclusion.

Our analysis included 22 studies from various institutions and countries. It is the largest study aimed at providing real-world information about sex-specific catheter ablation outcomes to physicians and their patients. This meta-analysis, however, has several limitations. First, the majority of the included studies are retrospective in nature, potentially biasing our findings. Despite our efforts to overcome this limitation by conducting multiple sensitivity and subgroup analyses, as well as meta-regression analyses, selection bias could not be ruled out. Second, most studies did not provide detailed information on AF type, ablation strategy, and perioperative medication use (AAD, b-blocker, platelet inhibitors, and anticoagulant). As a result, unmeasured confounders could exist in our findings. Finally, the study data did not allow for a separate analysis of cardiac and non-cardiac death, haemorrhagic and non-haemorrhagic stroke.

### CONCLUSION

In conclusion, updated analysis of our study's data revealed that women may have a lower percentage of patients who experience no AF/AT recurrence following catheter ablation of AF. Furthermore, female sex was linked to a higher risk of stroke/TIA. Major problems also occurred more frequently in the female sex. Further research is required to determine the causes of these sex-related variations in catheter ablation of AF and more ways to reduce the recurrence rate of atrial fibrillation caused by gender differences.

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### REFERENCES

- Fabritz L, Obergassel J. Artificial intelligence for early atrial fibrillation detection. Lancet. 2022;400(10359):1173-1175.
- Davidson KW, Mangione C, Ogedegbe G. US preventive services task force recommendation statement on screening for atrial fibrillation-reply. JAMA. 2022;327(20):2022.
- 3. Compagnucci P, Guerra F, Capucci A. Early or delayed cardioversion in recent-onset atrial fibrillation. N Engl J Med. 2019;381(4):386.
- Vinter N, Huang Q, Fenger-Grøn M, Frost L, Benjamin EJ, Trinquart L. Trends in excess mortality associated with atrial fibrillation over 45 years (framingham heart study): Community based cohort study. BMJ. 2020;370:m2724.
- Kistler PM, Chieng D, Sugumar H, Ling LH, Segan L, Azzopardi S, et al. Effect of catheter ablation using pulmonary vein isolation with vs without posterior left atrial wall isolation on atrial arrhythmia recurrence in patients with persistent atrial fibrillation: The CAPLA randomized clinical trial. JAMA. 2023;329(2):127-135.
- Packer DL, Mark DB, Robb RA, Monahan KH, Bahnson TD, Poole JE, et al. Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation: The CABANA randomized clinical trial. JAMA. 2019;321(13):1261-1274.
- Bollmann A, Ueberham L, Schuler E, Wiedemann M, Reithmann C, Sause A, et al. Cardiac tamponade in catheter ablation of atrial fibrillation: German-wide analysis of 21 141 procedures in the helios atrial fibrillation ablation registry (SAFER). Europace. 2018;20(12):1944-1951.
- 8. Mszar R, Friedman DJ, Ong E, Du C, Wang Y, Zeitler EP, et al. Sex-based differences in atrial fibrillation ablation adverse events. Heart. 2022.
- Oremus M, Oremus C, Hall GB, McKinnon MC, ECT & Cognition Systematic Review Team. Inter-rater and test-retest reliability of quality assessments by novice student raters using the Jadad and Newcastle-Ottawa Scales. BMJ open. 2012;2(4):e001368.
- Hermida A, Burtin J, Kubala M, Fay F, Lallemand PM, Buiciuc O, et al. Sex differences in the outcomes of cryoablation for atrial fibrillation. Front Cardiovasc Med. 2022;9:893553.
- Russo AM, Zeitler EP, Giczewska A, Silverstein AP, Al-Khalidi HR, Cha YM, et al. Association between sex and treatment outcomes of atrial fibrillation ablation versus drug therapy: Results from the CABANA trial. Circulation. 2021;143(7):661-672.
- Kaiser DW, Fan J, Schmitt S, Than CT, Ullal AJ, Piccini JP, et al. Gender differences in clinical outcomes after catheter ablation of atrial fibrillation. JACC Clin Electrophysiol. 2016;2(6):703-710.
- 13. Yunus FN, Perino AC, Holmes DN, Matsouaka RA, Curtis AB, Ellenbogen KA, et al. Sex differences in ablation strategy, lesion sets, and complications of catheter ablation for atrial fibrillation: An analysis from the GWTG-AFIB Registry. Circ Arrhythm Electrophysiol. 2021;14(11):e009790.
- 14. Kim MH, You SC, Sung JH, Jang E, Yu HT, Kim TH, et al. Safety and long-term outcomes of catheter ablation according to sex in patients with atrial fibrillation: A nationwide cohort study. Int J Cardiol. 2021;338:95-101.
- 15. Cheung JW, Cheng EP, Wu X, Yeo I, Christos PJ, Kamel H, et al. Sex-based differences in outcomes, 30-day readmissions, and costs following catheter ablation of atrial fibrillation: The united states nationwide readmissions database 2010-2014. Eur Heart J. 2019;40(36):3035-3043.
- Elayi CS, Darrat Y, Suffredini JM, Misumida N, Shah J, Morales G, et al. Sex differences in complications of catheter ablation for atrial fibrillation: Results on 85,977 patients. J Interv Card Electrophysiol. 2018;53:333-339.

- 17. Piccini JP, Sinner MF, Greiner MA, Hammill BG, Fontes JD, Daubert JP, et al. Outcomes of medicare beneficiaries undergoing catheter ablation for atrial fibrillation. Circulation. 2012;126(18):2200-2207.
- Yu HT, Yang PS, Kim TH, Uhm JS, Kim JY, Joung B, et al. Poor rhythm outcome of catheter ablation for early-onset atrial fibrillation in womenmechanistic insight. Circ J. 2018;82(9):2259-2268.
- Kuck KH, Brugada J, Fürnkranz A, Chun KJ, Metzner A, Ouyang F, et al. Impact of female sex on clinical outcomes in the fire and ice trial of catheter ablation for atrial fibrillation. Circ Arrhythm Electrophysiol. 2018;11(5):e006204.
- 20. Patel D, Mohanty P, Di Biase L, Sanchez JE, Shaheen MH, Burkhardt JD, et al. Outcomes and complications of catheter ablation for atrial fibrillation in females. Heart Rhythm. 2010;7(2):167-172.
- 21. Zhang XD, Tan HW, Gu J, Jiang WF, Zhao L, Wang YL, et al. Efficacy and safety of catheter ablation for long-standing persistent atrial fibrillation in women. Pacing Clin Electrophysiol. 2013;36(10):1236-1244.
- Kloosterman M, Chua W, Fabritz L, Al-Khalidi HR, Schotten U, Nielsen JC, et al. Sex differences in catheter ablation of atrial fibrillation: Results from AXAFA-AFNET 5. Europace. 2020;22(7):1026-1035.
- 23. Ricciardi D, Arena G, Verlato R, Iacopino S, Pieragnoli P, Molon G, et al. Sex effect on efficacy of pulmonary vein cryoablation in patients with atrial fibrillation: Data from the multicenter real-world 1STOP project. J Interv Card Electrophysiol. 2019;56:9-18.
- 24. Ueberham L, König S, Hohenstein S, Mueller-Roething R, Wiedemann M, Schade A, et al. Sex differences of resource utilization and outcomes in patients with atrial arrhythmias and heart failure. Heart. 2020;106(7):527-533.
- 25. Takigawa M, Kuwahara T, Takahashi A, Watari Y, Okubo K, Takahashi Y, et al. Differences in catheter ablation of paroxysmal atrial fibrillation between males and females. Int J Cardiol. 2013;168(3):1984-1991.
- 26. Zylla MM, Brachmann J, Lewalter T, Hoffmann E, Kuck KH, Andresen D, et al. Sex-related outcome of atrial fibrillation ablation: Insights from the german ablation registry. Heart Rhythm. 2016;13(9):1837-1844.
- 27. Roh SY, Shim J, Lee KN, Ahn J, Kim DH, Lee DI, et al. Gender-related difference in clinical outcome of the patient with atrial fibrillation after radiofrequency catheter ablation. Korean Circ J. 2018;48(7):605-618.
- Winkle RA, Mead RH, Engel G, Patrawala RA. Long-term results of atrial fibrillation ablation: The importance of all initial ablation failures undergoing a repeat ablation. Am Heart J. 2011;162(1):193-200.
- 29. Grecu M, Blomström-Lundqvist C, Kautzner J, Laroche C, Van Gelder IC, Jordaens L, et al. In-hospital and 12-month follow-up outcome from the ESC-EORP EHRA atrial fibrillation ablation long-term registry: Sex differences. Europace. 2020;22(1):66-73.
- Tanaka N, Inoue K, Kobori A, Kaitani K, Morimoto T, Kurotobi T, et al. Sex differences in atrial fibrillation ablation outcomes: Insights from a large-scale multicenter registry. Europace. 2020;22(9):1345-1357.
- Schmidt M, Dorwarth U, Straube F, Daccarett M, Rieber J, Wankerl M, et al. Cryoballoon in AF ablation: Impact of PV ovality on AF recurrence. Int J Cardiol. 2013;167(1):114-120.
- 32. Özlem K, Selçuk K. High ABSI values and association with AF recurrence after AF ablation: A prospective single-center study. Eur Rev Med Pharmacol Sci. 2022;26(19):7151-7160.
- 33. Jian B, Li Z, Wang J, Zhang C. Correlation analysis between heart rate variability, epicardial fat thickness, visfatin and AF recurrence post radiofrequency ablation. BMC Cardiovasc Disord. 2022;22(1):65.
- 34. Huang Z, Liang X, Wang W, Mao Z, Lin Y, Zhang L, et al. Relationship between plasma Cancer Antigen (CA)-125 level and one-year recurrence of atrial fibrillation after catheter ablation. Clin Chim Acta. 2020;502:201-206.
- 35. Gomez SE, Parizo J, Ermakov S, Larson J, Wallace R, Assimes T, et al. Evaluation of the association between circulating IL-11 and other inflammatory cytokines and incident atrial fibrillation in a cohort of postmenopausal women. Am Heart J. 2023.

- 36. Zhou Y, Song X, Ma J, Wang X, Fu H. Association of inflammation indices with left atrial thrombus in patients with valvular atrial fibrillation. BMC Cardiovasc Disord. 2023;23(1):9.
- 37. Cong X, Tian B, Zhu X, Zhang X, Gu W, Zhao H, et al. Interleukin-11 is elevated in patients with atrial fibrillation, correlates with serum fibrosis markers, and represents a therapeutic target for atrial fibrosis. Cerebrovasc Dis. 2023;1-12.
- 38. Zhang T, Wang Y, Liang Z, Zhao H, Han Z, Wang Y, et al. Effect of combined pulmonary vein and superior vena cava isolation on the outcome of second catheter ablation for paroxysmal atrial fibrillation. Am J Cardiol. 2020;125(12):1845-1850.
- 39. Zghaib T, Allison JD, Barrett C, Arkles J, D'Souza B, Luebbert J, et al. Multicenter experience with andexanet alfa for refractory pericardial bleeding during catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol. 2023.
- 40. Mo BF, Wu CQ, Wang QS, Li YG. Case report: Intrapericardial thrombus aspiration in early stage of pericardial thrombosis for cardiac tamponade complicating percutaneous left atrial appendage closure. Front Cardiovasc Med. 2022:924570.
- 41. Tsai J, Chishinga N, Mannil SV, Schaffer R, Kuchciak A, Gomez SI, et al. Acute cardiac tamponade as a complication of pulmonary vein isolation ablation. Cureus. 2021;13(11): e19572.
- 42. Wu C, Li X, Lv Z, Chen Q, Lou Y, Mao W, et al. Second-generation cryoballoon versus contact force radiofrequency ablation for atrial fibrillation: An updated meta-analysis of evidence from randomized controlled trials. Sci Rep. 2021;11(1): 17907.
- 43. Kurdziel M, Hudzik B, Kazik A, Piegza J, Szkodzinski J, Gąsior M. Idarucizumab for dabigatran reversal in cardiac tamponade complicating percutaneous intervention in ST elevation myocardial infarction. Advances in Interventional Cardiology/Postępy w Kardiologii Interwencyjnej. 2021;17(1):129-130.
- 44. Tohoku S, Schmidt B, Bordignon S, et al. Initial clinical experience of pulmonary vein isolation using the ultra-low temperature cryoablation catheter for patients with atrial fibrillation. J Cardiovasc Electrophysiol. 2022;33(7):1371-1379.

- **45**. Popa MA, Bourier F, Lengauer S, Krafft H, Bahlke F, Förschner LV, et al. Safety profile and long-term efficacy of very high-power short-duration (60–70 W) catheter ablation for atrial fibrillation: Results of a large comparative analysis. Europace. 2022.
- 46. Martínez-Montesinos L, Rivera-Caravaca JM, Agewall S, Soler E, Lip GY, Marín F, et al. Polypharmacy and adverse events in atrial fibrillation: Main cause or reflection of multimorbidity? Biomed Pharmacother. 2023;158:114064.
- 47. Szegedi N, Széplaki G, Herczeg S, Tahin T, Salló Z, Nagy VK, et al. Repeat procedure is a new independent predictor of complications of atrial fibrillation ablation. Europace. 2019;21(5):732-737.
- 48. Behrendt CA, Thomalla G, Rimmele DL, Petersen EL, Twerenbold R, Debus ES, et al. Prevalence of peripheral arterial disease, abdominal aortic aneurysm, and risk factors in the Hamburg City Health Study: A Cross-Sectional Analysis. Eur J Vasc Endovasc Surg. 2023.
- 49. Xue S, Qiu X, Wei M, Kong Q, Dong J, Wang Q, et al. Changing trends and factors influencing anticoagulant use in patients with acute ischemic stroke and NVAF at discharge in the NOACs era. J Stroke Cerebrovasc Dis. 2023;32(2):106905.
- Cheng X, Hu Q, Gao L, Liu J, Qin S, Zhang D. Sex-related differences in catheter ablation of atrial fibrillation: A systematic review and metaanalysis. Europace. 2019;21(10):1509-1518.
- 51. Liu H, Lin M, Han W, Ge J, Maduray K, Zhong J. The risk factors of thrombus formation and the effect of catheter ablation on repetitive thrombus formation in patients with atrial fibrillation: A single center retrospective study in China. BMC Cardiovasc Disord. 2023;23(1):1-2.
- 52. Huo S, Wang Q, Jiang Y, Shi W, Luo P, Guo J, et al. Efficiency and safety of high-power ablation guided by Lesion size index: An *ex vivo* porcine heart study. Pacing Clin Electrophysiol. 2023.