Comparative efficacy and safety profile of high-power short duration with low power long duration radiofrequency ablation in atrial fibrillation: An updated systematic review and meta-analysis

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Abstract

Background: High power short duration (HPSD) radiofrequency ablation was expected to be more effective and safer than low power long duration (LPLD) in treating atrial fibrillation (AF). Given the limited data, the findings were controversial. This meta-analysis evaluated whether HPSD's clinical effects outweigh LPLD's. **Methods:** A systematic search of PubMed, EMBASE, and Google Scholar databases identified studies comparing HPSD to LPLD ablation. All the analyses used the random-effects model. **Results:** This analysis included 21 studies with a total of 4169 patients. Pooled analyses revealed that HPSD was associated with a lower recurrence of atrial tachyarrhythmias (ATAs) at one year (RR: 0.62; 95% CI: 0.50 to 0.78, p: 0.00001, I^2: 0%). Furthermore, the HPSD approach reduced the risk of AF recurrence (RR: 0.64; 95% CI: 0.40 to 1.01, p: 0.06, I^2: 86%), The HPSD approach was associated with a lower risk of esophageal thermal injury (ETI) (RR: 0.78; 95% CI: 0.58 to 1.04, p: 0.09, I^2: 73%;). The HPSD strategy increased first-pass pulmonary vein isolation (FPI) and decreased acute pulmonary vein re-connection (PVR) both of which were predominantly manifested in bilateral and left pulmonary veins (PVs). HPSD demonstrated a reduction in procedural time, ablation number for pulmonary vein isolation (PVI), and fluoroscopy time. **Conclusion:** The HPSD method reduces ETI, PV reconnection, and recurrent AF. The HPSD approach also reduced procedural time, PVI ablation number, fluoroscopy time, and post-ablation AF relapse in one year, improving patient outcomes and safety.

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Abstract

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Methods: A systematic search of PubMed, EMBASE, and Google Scholar databases identified studies comparing HPSD to LPLD ablation. All the analyses used the random-effects model.

Results: This analysis included 21 studies with a total of 4169 patients. Pooled analyses revealed that HPSD was associated with a lower recurrence of atrial tachyarrhythmias (ATAs) at one year (RR: 0.62; 95% CI: 0.50 to 0.78, p: 0.00001, I^2: 0%). Furthermore, the HPSD approach reduced the risk of AF recurrence (RR: 0.64; 95% CI: 0.40 to 1.01, p: 0.06, I^2: 86%), The HPSD approach was associated with a lower risk of esophageal thermal injury (ETI) (RR: 0.78; 95% CI: 0.58 to 1.04, p: 0.09, I^2: 73%;). The HPSD strategy increased first-pass pulmonary vein isolation (FPI) and decreased acute pulmonary vein re-connection (PVR) both of which were predominantly manifested in bilateral and left pulmonary veins (PVs). HPSD demonstrated a reduction in procedural time, ablation number for pulmonary vein isolation (PVI), and fluoroscopy time.

Conclusion: The HPSD method reduces ETI, PV reconnection, and recurrent AF. The HPSD approach also reduced procedural time, PVI ablation number, fluoroscopy time, and post-ablation AF relapse in one year, improving patient outcomes and safety.

Keywords: High power short duration, HPSD, Low power long duration, LPLD, atrial fibrillation, radiofrequency ablation, meta-analysis.

Highlights:

- HPSD approach is associated with a decreased risk of recurrence of atrial tachyarrhythmias
- Treatment with HPSD approach is associated with a decreased risk of esophageal thermal injury.
- HPSD approach is associated with increased first pass pulmonary vein isolation.
- On the other hand, HPSD approach reduces the procedure time, ablation time, ablation number, fluoroscopy time and the risk of acute pulmonary vein reconnection.

Introduction:

Atrial fibrillation (AF) is the most prevalent continuous dysrhythmia in clinical settings, with a preponderance of over 33 million individuals worldwide. [1] The frequency and prevalence of atrial fibrillation are rising worldwide. According to the Framingham Heart Study (FHS), the prevalence of atrial fibrillation (AF) has tripled over the past five decades. [2] In 2016, the Global Burden of Disease program estimated that approximately 46.3 million people globally were affected by atrial fibrillation. AF is strongly correlated with a higher risk of death. Patients rarely perish from the arrhythmia itself but rather from the myriad of coexisting diseases and conditions that often worsen it. [2]Patients with AF are treated to reduce stroke risk, improve symptoms, and control rate or rhythm. Catheter ablation has become the most widely accepted ablation technique in cardiology. It has been shown to reduce symptoms and regulate heart rate and rhythm effectively. Although Catheter ablation is a relatively secure process with limited periprocedural adverse effects, several relevant factors must be considered when recognizing patients with comparatively lesser success rates or relatively high postoperative complications, including concurrent heart problems, obesity, sleep problems, left atrial size, age at diagnosis and vulnerability. Comparing AF catheter ablation manifestations from 2016 to 2018 was determined using the 2014 American Heart Association and American College of Cardiology. Class I indications for this procedure included symptomatic paroxysmal AF unresponsive to at least one potential therapeutic drug, class IIA indications for persistent AF unresponsive to at least one antiarrhythmic drug, and class IIB indications for persistent AF.[3] In the 2019-centered revision, catheter ablation for symptomatic atrial fibrillation (AF) and cardiac failure with a lower ejection fraction was incorporated into class IIB to lessen heart failure hospital stays and mortality. This modification does not impact the category of guidelines for any patient populations included in the current analysis; however, cases meeting this implication may not be adequately portrayed in the sample population.[3]

Myocardial thickness varies in different parts of the left atrium (LA), making it a frame of considerable complexity. Impactful pulmonary vein isolation necessitates a comprehensive insight into the adjacent tissue that might be harmed by extreme radiofrequency (RF) power application to be achieved safely. [4] The thick ridge between the left atrium and upper left pulmonary veins complicates ablation due to the variable thickness of the atrial surface. For PV isolation, it is recommended to use radiofrequency ablation over a large area.[5] Radiofrequency (RF) energy is conveyed as low-power, long-duration (LPLD) lesions steered by factors such as the force–time integral (FTI); however, the ideal ablation specifications to accomplish resilient, long-term pulmonary vein isolation (PVI) in a relatively secure manner remain to be ascertained.[4,5] HPSD lesions are gaining in popularity due to the resistive combustion of extracardiac frameworks; this technique may minimize procedure and fluoroscopy durations, as well as the risk of adverse effects.[6] Conductive heating dominates the low-power, long-duration RF ablation. Compared to conventional ablation, HPSD ablation produces a broader domain of specific resistive heating of parenchyma with a more rapid temperature deterioration. This skyrockets resistance to conductive tissue heating and irreversibly damages the impedance endocardial zone. Many centers use catheters to isolate PVs and create extra-PV lesion configurations. Each site receives 20-40 W for 20-40 seconds at a contact force (CF) of 10-20 g. HPSD ablation is appealing due to lengthy procedure times and rising PV reconnection rates. HPSD ablation is defined arbitrarily as 40 to 90 W for less than 15 seconds per lesion. [7]

In the past several Randomized control trials (RCTs) have been done to compare the efficacy and safety of the high-power short duration (HPSD) approach with Low power long duration (LPLD). However, the majority of studies produced transient and inconsistent results due to short-term follow-up results and a need for more recently available studies (RCTs and observational studies). In this meta-analysis, we report findings after analyzing the available literature on this topic. Based on an extensive literature search, we conclude that this is the most recent updated meta-analysis assessing the safety and efficacy profile of conventional LPLD with the newly adopted HPSD technique for PVI.

Methodology:

This meta-analysis adheres to the Preferred Reporting Items for Systematic Review and Meta-analysis guidelines[8,9].

Data sources and search strategy

The databases of PubMed, OVID, the Cochrane Library, and Elsevier's ScienceDirect were thoroughly and without language restrictions electronically searched for clinical studies (updated in January 2023). To retrieve literature, straightforward keyword and medical subject heading (MeSH) term combinations (such as "high power short duration," "atrial fibrillation," "catheter ablation," "radiofrequency ablation," etc.) were used. Information about the search methodology is provided in Supplementary Table 1. The PICO (population, intervention, comparison, and outcome) approach was modified. The population of interest included patients with AF (paroxysmal AF [PAF] and persistent AF [PeAF]). Pulmonary vein isolation (additional lesions) was performed in the treatment of atrial fibrillation using RFCA (radiofrequency catheter ablation). The ablation energy was compared: high power, short duration vs. low power, long duration. Three researchers (MK, SK, and SuK) independently reviewed the titles and abstracts of potentially eligible studies.

Inclusion and exclusion criteria

Inclusion criteria:

(1) A randomized controlled trial (RCT), a cohort study, a case-control study, and a cross-sectional study are all examples of research methods. (2) The HPSD approach (>40 W) was used in the isolation of PVs. (3) Baseline data balance. (4) A comparative study.

Exclusion criteria:

(1) Nonclinical studies. (2) No controls. (3) Conference abstracts, case reports, case series studies, editorials, and review articles. (4) Sample size < 20. (5) Equivocal study results. (6) Full text unavailable.

Data extraction and definitions:

The data from each study, including the author's name, year of publication, country, study population, demographic data of participants, ablation procedure strategies, and clinical outcomes, were extracted to a specific data collection form. The primary outcomes were atrial tachyarrhythmias (ATAs) and AF, atrial tachycardia/atrial flutter (AT/AFL) recurrence post-blanking (two- or three-months post-ablation depending on the studies included), and major complications. The latter included esophageal thermal injury (ETI) and catheter ablation (CA)-related heart complications such as cardiac tamponade, among others. Secondary outcomes included first-pass pulmonary vein isolation (FPI) and acute pulmonary vein reconnection (PVR), procedural time, pulmonary vein isolation (PVI) ablation number, radiofrequency (RF) time and fluoroscopy time.

ATAs recurrence: Symptomatic or asymptomatic ATAs lasting more than 30 s after the blanking period post-ablation. ETI: The esophageal collateral thermal injury brought on by ablation. Endoscopy and/or MRI late gadolinium enhancement were used to evaluate the morphology of the abnormal esophageal inner exhibition. The esophageal temperature monitor's abnormal temperature rise was also considered. First-pass PVI: The first-pass radiofrequency delivery PVI achievement rate. Adenosine test and/or waiting time are used to measure the rate of pulmonary vein electrical reconnection following the first-pass ablation in acute PVR. Procedure time: the time between the beginning of anesthesia and the removal of all sheaths. The number of PVI ablation sites that will be used during the procedure. Fluoroscopy time: The total amount of time spent using a fluoroscope during the procedure.

Quality of included studies:

Quality assessment of all the included RCTs and observational studies was done by using the Cochrane risk of bias tool[9] Newcastle-Ottawa scale[10] (Supplementary Appendix, Table 2 and Figure 1).

Data Analysis:

Statistical analysis was done only for comparative studies using Review Manager version 5.4.1 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014, Denmark). This meta-analysis presents a pooled effect of relative risks (RRs) for dichotomous outcomes and weighted mean differences (WMDs) for continuous outcomes calculated using the generic-inverse variance with a random-effects model. All p-values less than 0.05 were deemed statistically significant. The results of pooled analyses were displayed through forest plots. Funnel plots for all primary outcomes were visualized to assess publication bias. Heterogeneity was evaluated using Higgin's I^2 test, which corresponded to low (< 25%), moderate (25–75%), and high (> 75%) heterogeneity [11]. A sensitivity analysis was performed to assess the influence of the individual studies on the overall results by omitting one study at a time when substantial heterogeneity (I^2>75%) was present. A p-value of <0.05 was considered significant for all analyses.

Results:

The literature review initially yielded 1050 articles. After removing duplicates and screening studies based on their titles and abstracts, a total of twenty-one [12-32] studies, including both retrospective and prospective studies, were found. Comparative studies comprised the entirety of those included in this meta-analysis. The PRISMA diagram illustrates a comprehensive search strategy (Figure 1). This collection of articles spans the years 2018 through 2022. High power was defined as >40 W, and the extracted data were separated into high power group (HP) and low power group (LP).

Characteristics of patients:

There were a total of 4169 participants (2285 in the HP group and 1884 in the LP group), with mean ages ranging from 58.2 ± 10.0 to 69.0 ± 11.8 and follow-up duration ranging from 2 to 3 years. 2,803 males (66.8%) and 1366 females (32.7%) were included and 2258 patients (54.16%) with paroxysmal AF and 1911 patients (45.8%) with persistent AF were included, respectively. Age, gender, CHA2DS2-VASc, the diameter of the left atrium, hypertension, diabetes mellitus, and other relative characteristics were comparable between the two groups. CF sensing irrigated catheters (ThermoCool SmartTouch NaviStar, ThermoCool SurroundFlow NaviStar [Biosense Webster], and TactiCath Quartz [St. Jude Medical]) were used in all 21 studies. In one study, irrigated catheters that did not have CF sensors (Thermocool SFTM, Biosens-Webster, and FlexAbilityTM, Abbott) were used[19] (LP group). The Drag lesion technique and continuous point-by-point focal radiofrequency technique were used in 13 and 4 studies, respectively. Another two studies[14,15] did not mention the ablation strategy, while two studies [17,19] used both techniques. Every patient underwent the CPVI procedure protocol. In nine studies, additional linear ablations (box isolation, SV isolation, CI isolation, MI isolation, and roofline isolation) as well as or not matrix modification (LVZ or CFAE ablation or complex fractionated atrial electrogram ablation) were carried out. 6 and 8 studies, respectively, mentioned the AADs being discontinued for five half-lives prior to the procedure and being maintained post-ablation. Tables 1 and 2 detail the baseline characteristics of the patients.

Quality assessment and publication bias:

The New Castle-Ottawa scale, a tool used to assess study quality, discovered a low likelihood of bias in observational studies (Supplementary Table 2). Using the Cochrane method of assessing RCTs, we discovered trials of medium to high quality (Supplementary Figure 1). The results were unaffected by publication bias, as demonstrated by the funnel plots (Supplementary Figure 2).

Primary efficacy outcomes:

In a pooled analysis, seven studies found that the HP approach was associated with a lower recurrence of atrial tachyarrhythmias (ATAs) at 1-year follow-up (RR: 0.62; 95% CI: 0.50 to 0.78, p: 0.00001; I^2: 0% Figure 2). In contrast, there was no statistically significant difference in the rate of ATA relapse after a 6-month follow-up (RR: 0.79; 95% CI: 0.46 to 1.36, p 0.39; I^2: 13% Figure 2). Eight studies indicated a lower AF recurrence in the HP group in the subgroup analysis (RR: 0.64; 95% CI: 0.40 to 1.01, p: 0.06, I^2: 86%; Figure 3), while six studies indicated similar atrial tachycardia/atrial flutter (AT/AFL) recurrence in both groups (RR: 0.98; 95% CI: 0.56 to 1.71, p: 0.94, I^2: 23%; Figure 3). Due to the high heterogeneity in AF recurrence, a leave-one-out analysis was performed, which revealed that excluding the study by Hansom et al [27]reduced the in-study heterogeneity and made the results statistically significant (RR: 0.57; 95% CI: 0.40 to 0.80, p: 0.001, I2: 50%).

Primary safety outcomes:

The pooled analysis of seven studies that included ETI found that the HP approach was linked to a lower risk of ETI (RR: 0.78; 95% CI: 0.58 to 1.04, p: 0.09; I^2: 73% Figure 4). When included studies were gradually eliminated because of high heterogeneity, it became clear that leaving out Kaneshiro et al.[17] reduced heterogeneity and improved the significance of the findings (RR: 0.70; 95% CI: 0.61 to 0.81; p: 0.00001; I^2: 5%). The HP approach was linked to a lower risk of other complications, such as pericardial tamponade, atrial-esophageal fistula, stroke, phrenic nerve injury, etc., according to eight studies that reported these issues (RR: 0.66; 95% CI: 0.29 to 1.50, p: 0.32; I^2: 0% Figure 4).

Secondary outcomes:

A higher overall rate of FPI was discovered to be linked to the HP group (RR: 1.19; 95% CI: 1.08 to 1.30, p 0.0003, I^2: 85%; Figure 5). Bilateral PVs had a significantly higher FPI rate (RR: 1.57; 95% CI: 1.19 to 2.09, p 0.002, I^2: 95%; Figure 5). High in-study heterogeneity prompted, leave one-out analysis, which demonstrated that results were unaffected by any particular study. There was a significant decrease in acute PVR by the HP approach (RR: 0.57; 95% CI: 0.45 to 0.73, p .00001, I^2: 52%; Figure 6), which was primarily represented in the left PVs subgroup (RR: 0.57; 95% CI: 0.43 to 0.76, p: 0.0001, $I^{2:}$ 0%; Figure 6) and bilateral PVs subgroup (RR: 0.52; 95% CI: 0.37 to 0.75, p: 0.0004, I^2: 69%; Figure 6). The HPSD strategy significantly reduced procedural time (WMD: -35.58; 95% CI: -46.16 to -25.01, p: .00001, I^2: 95%; Figure 7), and sensitivity analysis was performed to determine the cause of high heterogeneity, which revealed that results were not affected by any single study. Total fluoroscopy time was significantly lower in the HP group (WMD: -3.16 95% CI: -4.64 to –1.68, p <.00001, I^2: 96%; Figure 8) particularly when PVI alone was done

(WMD: -3.06; 95% CI: -4.73 to –1.39, p <.00001, I^2: 96%; Figure 8) rather than when additional strategies were used along with PVI (WMD: -3.12; 95% CI: -6.63 to 0.40, p: 0.08, I^2: 96%; Figure 8). Treatment with the HPSD approach is associated with significantly decreased ablation time (WMD: -19.19; 95% CI: -24.83 to –13.55, p <.00001, I^2: 97%; Figure 9), ablation number for PVI (WMD: -7.00; 95% CI: -9.74 to –4.25, p <.00001, I^2: 41%; Figure 10), ablation index (WMD: -30.17; 95% CI: -54.86 to –5.48, p: 0.02, I^2: 98%; Figure 11) and total RF time (WMD: -20.78; 95% CI: -26.46 to –15.10, p <.00001, I^2: 98%; Figure 12). However, there is no significant difference in impedance decrease among the two groups (WMD: 0.22; 95% CI: -1.42 to 1.87, p:0.79, I^2: 96%; Figure 13). Due to the high heterogeneity of these outcomes, leave one out sensitivity analysis was performed for each outcome which showed no single study affected these results.

Discussion

The prevalence of AF is rising, notably in developed countries, as the population ages and the strain of cardiovascular disease rises·[33] Finding that AF is often caused by ectopy inside the pulmonary veins prompted the introduction of pulmonary vein isolation as an extensively used therapy, and circumferential pulmonary vein isolation has become essential to the overwhelming majority of AF ablation practices.[33] Ablation involves the passage of Radiofrequency (RF) energy current through parenchyma, resistively heating and necrotizing the tissue layer in proximity to the catheter tip. The majority of the ablation lesion is formed by heat transfer from resistive heating deeper in the tissue. The RF power generation augments the depth of resistive and conductive heating substantially. [33,34] HPSD ablation definitions currently range from 50 W to 90 W for durations ranging from 2 to 20 seconds. For apparent patient safety purposes, the bulk of human experimentations to date have employed a peak energy of 50 W. The HPSD technique for AF catheter ablation is more proficient than the LPLD approach due to the reduced procedure, fluoroscopy, and ablation times. Compared to LPLD, the HPSD strategy lowers the risk of esophageal thermal injury (ETI) and has higher first-pass PVI. Furthermore, after a single radiofrequency catheter ablation (RFCA) procedure, the HPSD ablation technique effectively reduces the likelihood of PV reconnection and recurrent AF. [33,35] The possibility of the HPSD technique to increase first-pass PVI and reduce PV restoration and recurrent AF has been due to the HPSD method's ability to generate a lesion with a broader area, greater uniformity, and greater consistency.[35]

Main findings:

In this systematic review and meta-analysis, we included twenty-one studies comprising 4169 participants to compare the efficacy and safety profile of HPSD with the LPLD approach. Our findings suggested that the HPSD ablation technique is associated with a drop-in risk of recurrent atrial tachyarrhythmias and a drop in AF recurrence at 1-year follow-up. However, the Six-month follow-up showed no statistically-significant variation in ATA relapse rates. In addition, the AT/AFL recurrence rate did not differ between the two groups, which is a significant departure from the findings of previous meta-analyses. [5]

From a safety standpoint, our meta-analysis demonstrated that implementing radiofrequency ablation for atrial fibrillation (AF) using the HPSD strategy may decrease the likelihood of ETI. In percentage terms, however, this result was more significant than previous meta-analyses. [5,35] The HP approach was also associated with a reduced risk of complications such as pericardial tamponade, atrial-esophageal fistula, stroke, and phrenic nerve injury. The HPSD approach increased first-pass pulmonary vein isolation (FPI) and decreased acute pulmonary vein re-isolation (PVR) rate. In contrast to previous research, however, these findings did not demonstrate a reduction of more than half. Therefore, these variations in outcomes question previous studies' methodologies. The HPSD technique was strongly correlated with superior procedural characteristics, including reduced procedure time, ablation multitude for PVI, and fluoroscopy duration, thereby enhancing the efficacy of AF ablation. The results manifested a variety of heterogeneities, which were most evident in the retrospective cohort studies. Numerous studies contributed significantly to the high heterogeneity, necessitating a leave-one-out sensitivity analysis for each outcome. [17,27] We speculate that this resulted from the operator's freedom of choice regarding the size of the isolation circle around the PVs, the power setting, the contact force, the determination of the ablation endpoints, the inclusion of ablation, and so on. Furthermore, the left atrium's anatomy differed depending on the participants' races.

These differences were accentuated in historic cohort studies because of measurement errors and lost data. On the other hand, both primary and secondary outcome data were more consistently distributed across prospective studies.

Lesion variations and complications:

Prior research on humans has examined ablations with greater power and shorter duration. None of the research findings was large enough to investigate the emergence of rare complications such as gastroesophageal fistulas or pulmonary stenosis. Nilsson et al.[36] evaluated by comparing ablations performed with 30 W for 120 seconds to those performed with 45 W for 20 seconds. In both groups, the long-term outcomes and consequences were identical. In the group that underwent the higher power, shorter-duration ablation, isolation time, mean fluoroscopy time, radiation dose, and total RF application time were all reduced· [36] In previous studies, the minimum power used was 50 W for 5 s, which produced a mean depth of 2.3 mm. Since all lesions were transmural, the only limitation was tissue thickness. If the tissue is thicker, the lesion may also be thicker. Studies that have tried to deliver 50 W continuously have often had to reduce the power because of hyperechogenic tissue changes observed on ICE, a sharp interim impedance drop, or a lack of transmural lesions in relatively thick cardiac muscle (mitral annulus and the septal side of the right superior PV). In the in vitro model, 40 W/5 s was insufficient to produce a 2 mm cut-off point. In vivo ablations utilized 50–80 W. All configurations for in vivo ablation achieved transmurality·[13,37] In vitro, Fatima Ali-study Ahmed's indicated that a higher power setting (50 W/5s) produced a larger lesion with a maximum width of 7.2 versus 5.7 mm and a depth of 2.9 versus 2.1 mm within the identical radiofrequency period and irrigation stream (2 ml/min).[38] According to Bhaskaran's study, the lesion thickness at 80 W/5s (6.5 mm) and 70 W/5s (5.9 mm) was greater than at 40 W/30s (5.2 mm) when the contact force was 10 g. In vitro, the depth was comparable (80/5, 70/5, 40/30 s: 2.9, 2.6, 2.7 mm).[37] Additionally, catheter stability is a significant factor in lesion structure. Longer-duration power implementations may result in breached catheter contact consistency. Lesion features ascertained in ex vivo static tissue preparations do not precisely reflect the spectrum of movement observed in a beating heart, where there is greater variance among lesions and relatively small lesion dimensions, especially when compared to ablation in a fixed muscle formation. [33] An atrial-esophageal fistula following left atrial ablation is exceedingly uncommon and frequently fatal. The esophagus is positioned 2 mm from the posterior wall of the left atrium and is vulnerable to damage from lesion depth changes. Even though the study group had a few more health problems, the left atrial volumes were bigger based on the volume index, and the esophagus was closer to the center of the left atrial wall; HPSD and LPLD severity patterns were the same· [33,34,37,38]

Our meta-analysis has numerous advantages: (1) As a result of the inclusion of six additional studies, the sample group of our meta-analysis is more significant than that of past meta-analyses, lending credibility to our study results. (2) Using diverse plots and tests, including the funnel plot, Egger's test, and Begg's test, publication biases were determined and revealed to be nonexistent. (3) A sensitivity analysis was conducted to assess the effect of non - homogenous studies on the pooled estimate. (4) Furthermore, we compared our meta-analysis to those conducted by Min Xu et al. in the past. The fifteen studies comprising [5] were predominantly retrospective studies and RCTs. Our meta-analysis entailed a plethora of prospective studies that may have addressed biases inherent to retrospective studies.

Even though this analysis produced sufficient statistical evidence, it is essential to note its limitations. (1) Variations in research design, intervention strategies, and patient characteristics such as BMI, age, sample sizes, ethnic background, and trial attributes may have caused clinical heterogeneity. (2) Second, the follow-up durations of the majority of studies were variable, with some studies reporting longer durations. When evaluating such techniques, longer-term follow-ups are more valuable. (3) Several studies employed varying power levels (35W, 45W, 50W, 60W, and 70W) at various weeks, which may have introduced ambiguity.

Conclusion:

Based on the results of this systematic review and meta-analysis, we conclude that the HPSD method reduces the likelihood of ETI, improves first-pass PVI, and reduces the risk of PV reconnection and recurrent AF.

The HPSD technique was strongly correlated with decreased procedural time, ablation number for PVI, fluoroscopy time, and post-ablation AF relapse in one-year follow-up, thereby improving clinical outcomes with enhanced safety.

Declarations of interest

None

Disclosures

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in the article.

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None

Author's contributions

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References:

1. Parameswaran R, Al-Kaisey AM, Kalman JM. Catheter ablation for atrial fibrillation: current indications and evolving technologies. Nat Rev Cardiol. 2021 Mar;18(3):210-225. doi: 10.1038/s41569-020-00451-x. Epub 2020 Oct 13. PMID: 33051613.

2. Kornej J, Börschel CS, Benjamin EJ, Schnabel RB. Epidemiology of Atrial Fibrillation in the 21st Century: Novel Methods and New Insights. Circ Res. 2020 Jun 19;127(1):4-20. doi: 10.1161/CIRCRESAHA.120.316340. Epub 2020 Jun 18. PMID: 32716709; PMCID: PMC7577553.

3. Loring Z, Holmes DN, Matsouaka RA, Curtis AB, Day JD, Desai N, Ellenbogen KA, Feld GK, Fonarow GC, Frankel DS, Hurwitz JL, Knight BP, Joglar JA, Russo AM, Sidhu MS, Turakhia MP, Lewis WR, Piccini JP. Procedural Patterns and Safety of Atrial Fibrillation Ablation: Findings From Get With The Guidelines-Atrial Fibrillation. Circ Arrhythm Electrophysiol. 2020 Sep;13(9):e007944. doi: 10.1161/CIRCEP.119.007944. Epub 2020 Jul 23. PMID: 32703018; PMCID: PMC7502261.

4. Knotts RJ, Barbhaiya CR. High-power, short-duration ablation for atrial fibrillation: Pros and cons. Prog Cardiovasc Dis. 2021 May-Jun;66:86-91. doi: 10.1016/j.pcad.2021.06.005. PMID: 34332664.

5. Xu M, Yang Y, Zhang D, Jiang W. Meta-analysis of high power short duration in atrial fibrillation ablation - a superior efficient ablation strategy. Acta Cardiol. 2022 Feb;77(1):14-32. doi: 10.1080/00015385.2021.1939512. Epub 2021 Jul 5. PMID: 34218737.

6. Chen CC, Lee PT, Van Ba V, Chuang CM, Lin YJ, Lo LW, Hu YF, Chung FP, Lin CY, Chang TY, Vicera JJ, Huang TC, Liu CM, Wu CI, Lugtu IC, Jain A, Chang SL, Chen SA. Comparison of lesion characteristics between conventional and high-power short-duration ablation using contact force-sensing catheter in patients with paroxysmal atrial fibrillation. BMC Cardiovasc Disord. 2021 Aug 9;21(1):387. doi: 10.1186/s12872-021-02196-y. PMID: 34372779; PMCID: PMC8353766.

7. Naniwadekar A, Dukkipati SR. High-power short-duration ablation of atrial fibrillation: A contemporary review. Pacing Clin Electrophysiol. 2021 Mar;44(3):528-540. doi: 10.1111/pace.14167. Epub 2021 Jan 31. PMID: 33438279.

8. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, Ioannidis JP, Straus S, Thorlund K, Jansen JP, Mulrow C, Catalá-López F, Gøtzsche PC, Dickersin K, Boutron I, Altman DG, Moher D. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med. 2015 Jun 2;162(11):777-84. doi: 10.7326/M14-2385. PMID: 26030634.

9. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomized trials. BMJ. 2011 Oct 18;343:d5928. doi: 10.1136/bmj.d5928. PMID: 22008217; PMCID: PMC3196245.

10. Wells GA, Shea B, O'Connell DA, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (Accessed Jan 15, 2023)

11. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003 Sep 6;327(7414):557-60. doi: 10.1136/bmj.327.7414.557. PMID: 12958120; PMCID: PMC192859.

12. Vassallo F, Meigre LL, Serpa E, Cunha C, Simoes A Jr, Carloni H, Amaral D, Meira K, Pezzin F. Changes and impacts in early recurrences after atrial fibrillation ablation in contact force era: comparison of high-power short-duration with conventional technique-FIRST experience data. J Interv Card Electrophysiol. 2021 Nov;62(2):363-371. doi: 10.1007/s10840-020-00911-x. Epub 2020 Nov 5. PMID: 33151444.

13. Yavin HD, Leshem E, Shapira-Daniels A, Sroubek J, Barkagan M, Haffajee CI, Cooper JM, Anter E. Impact of High-Power Short-Duration Radiofrequency Ablation on Long-Term Lesion Durability for Atrial Fibrillation Ablation. JACC Clin Electrophysiol. 2020 Aug;6(8):973-985. doi: 10.1016/j.jacep.2020.04.023. PMID: 32819533.

14. Yazaki K, Ejima K, Kanai M, Kataoka S, Higuchi S, Yagishita D, Shoda M, Hagiwara N. Impedance drop predicts acute electrical reconnection of the pulmonary vein-left atrium after pulmonary vein isolation using short-duration high-power exposure. J Interv Card Electrophysiol. 2020 Dec;59(3):575-584. doi: 10.1007/s10840-019-00691-z. Epub 2020 Jan 4. PMID: 31902084.

15. Shin DG, Ahn J, Han SJ, Lim HE. Efficacy of high-power and short-duration ablation in patients with atrial fibrillation: a prospective randomized controlled trial. Europace. 2020 Oct 1;22(10):1495-1501. doi: 10.1093/europace/euaa144. PMID: 32810203.

16. Kottmaier M, Popa M, Bourier F, Reents T, Cifuentes J, Semmler V, Telishevska M, Otgonbayar U, Koch-Büttner K, Lennerz C, Bartkowiak M, Kornmayer M, Rousseva E, Brkic A, Grebmer C, Kolb C, Hessling G, Deisenhofer I. Safety and outcome of very high-power short-duration ablation using 70 W for pulmonary vein isolation in patients with paroxysmal atrial fibrillation. Europace. 2020 Mar 1;22(3):388-393. doi: 10.1093/europace/euz342. PMID: 31872249.

17. Kaneshiro T, Kamioka M, Hijioka N, Yamada S, Yokokawa T, Misaka T, Hikichi T, Yoshihisa A, Takeishi Y. Characteristics of Esophageal Injury in Ablation of Atrial Fibrillation Using a High-Power Short-Duration Setting. Circ Arrhythm Electrophysiol. 2020 Oct;13(10):e008602. doi: 10.1161/CIRCEP.120.008602. Epub 2020 Sep 11. PMID: 32915644.

18. Ejima K, Higuchi S, Yazaki K, Kataoka S, Yagishita D, Kanai M, Shoda M, Hagiwara N. Comparison of high-power and conventional-power radiofrequency energy deliveries in pulmonary vein isolation using unipolar signal modification as a local endpoint. J Cardiovasc Electrophysiol. 2020 Jul;31(7):1702-1708. doi: 10.1111/jce.14532. Epub 2020 May 15. PMID: 32378266; PMCID: PMC7383605.

19. Castrejón-Castrejón S, Martínez Cossiani M, Ortega Molina M, Escobar C, Froilán Torres C, Gonzalo Bada N, Díaz de la Torre M, Suárez Parga JM, López Sendón JL, Merino JL. Feasibility and safety of pulmonary vein isolation by high-power short-duration radiofrequency application: short-term results of the POWER-FAST PILOT study. J Interv Card Electrophysiol. 2020 Jan;57(1):57-65. doi: 10.1007/s10840-019-00645-5. Epub 2019 Nov 12. PMID: 31713704.

20. Bunch TJ, May HT, Bair TL, Crandall BG, Cutler MJ, Mallender C, Weiss JP, Osborn JS, Day JD. Long-term outcomes after low power, slower movement versus high power, faster movement irrigated-tip catheter ablation for atrial fibrillation. Heart Rhythm. 2020 Feb;17(2):184-189. doi: 10.1016/j.hrthm.2019.08.001. Epub 2019 Aug 6. PMID: 31398477.

21. Vassallo F, Cunha C, Serpa E, Meigre LL, Carloni H, Simoes A Jr, Hespanhol D, Lovatto CV, Batista W Jr,, Serpa R. Comparison of high-power short-duration (HPSD) ablation of atrial fibrillation using a contact force-sensing catheter and conventional technique: Initial results. J Cardiovasc Electrophysiol. 2019 Oct;30(10):1877-1883. doi: 10.1111/jce.14110. Epub 2019 Aug 22. PMID: 31397522.

22. Pambrun T, Durand C, Constantin M, Masse A, Marra C, Meillet V, Haïssaguerre M, Jaïs P, Bortone A. High-Power (40-50 W) Radiofrequency Ablation Guided by Unipolar Signal Modification for Pulmonary Vein Isolation: Experimental Findings and Clinical Results. Circ Arrhythm Electrophysiol. 2019 Jun;12(6):e007304. doi: 10.1161/CIRCEP.119.007304. Epub 2019 Jun 5. PMID: 31164003.

23. Okamatsu H, Koyama J, Sakai Y, Negishi K, Hayashi K, Tsurugi T, Tanaka Y, Nakao K, Sakamoto T, Okumura K. High-power application is associated with shorter procedure time and higher rate of first-pass pulmonary vein isolation in ablation index-guided atrial fibrillation ablation. J Cardiovasc Electrophysiol. 2019 Dec;30(12):2751-2758. doi: 10.1111/jce.14223. Epub 2019 Oct 21. PMID: 31600006.

24. Berte B, Hilfiker G, Russi I, Moccetti F, Cuculi F, Toggweiler S, Ruschitzka F, Kobza R. Pulmonary vein isolation using a higher power shorter duration CLOSE protocol with a surround flow ablation catheter. J Cardiovasc Electrophysiol. 2019 Nov;30(11):2199-2204. doi: 10.1111/jce.14122. Epub 2019 Sep 2. PMID: 31424123.

25. Baher A, Kheirkhahan M, Rechenmacher SJ, Marashly Q, Kholmovski EG, Siebermair J, Acharya M, Aljuaid M, Morris AK, Kaur G, Han FT, Wilson BD, Steinberg BA, Marrouche NF, Chelu MG. High-Power Radiofrequency Catheter Ablation of Atrial Fibrillation: Using Late Gadolinium Enhancement Magnetic Resonance Imaging as a Novel Index of Esophageal Injury. JACC Clin Electrophysiol. 2018 Dec;4(12):1583-1594. doi: 10.1016/j.jacep.2018.07.017. Epub 2018 Sep 26. PMID: 30573123.

26. Wielandts JY, Kyriakopoulou M, Almorad A, Hilfiker G, Strisciuglio T, Phlips T, El Haddad M, Lycke M, Unger P, Le Polain de Waroux JB, Vandekerckhove Y, Tavernier R, Duytschaever M, Knecht S. Prospective Randomized Evaluation of High Power During CLOSE-Guided Pulmonary Vein Isolation: The POWER-AF Study. Circ Arrhythm Electrophysiol. 2021 Jan;14(1):e009112. doi: 10.1161/CIRCEP.120.009112. Epub 2020 Dec 10. PMID: 33300809.

27. Hansom SP, Alqarawi W, Birnie DH, Golian M, Nery PB, Redpath CJ, Klein A, Green MS, Davis DR, Sheppard-Perkins E, Ramirez FD, Nair GM, Sadek MM. High-power, short-duration atrial fibrillation ablation compared with a conventional approach: Outcomes and reconnection patterns. J Cardiovasc

Electrophysiol. 2021 May;32(5):1219-1228. doi: 10.1111/jce.14989. Epub 2021 Mar 29. PMID: 33751694.

28. Sousa PA, Puga L, Barra S, Adão L, Primo J, Khoueiry Z, Lebreiro A, Fonseca P, Pereira M, Lagrange P, d'Avila A, Oliveiros B, Elvas L, Gonçalves L. High-power short-duration versus low-power long-duration ablation guided by the ablation index. Int J Cardiol. 2023 Jan 1;370:209-214. doi: 10.1016/j.ijcard.2022.10.013. Epub 2022 Oct 10. PMID: 36228764.

29. Salló Z, Perge P, Balogi B, Orbán G, Piros K, Herczeg S, Nagy KV, Osztheimer I, Ábrahám P, Merkely B, Gellér L, Szegedi N. Impact of High-Power and Very High-Power Short-Duration Radiofrequency Ablation on Procedure Characteristics and First-Pass Isolation During Pulmonary Vein Isolation. Front Cardiovasc Med. 2022 Jul 7;9:935705. doi: 10.3389/fcvm.2022.935705. PMID: 35872909; PMCID: PMC9300971.

30. Chieng D, Segan L, Sugumar H, Al-Kaisey A, Hawson J, Moore BM, Nam MCY, Voskoboinik A, Prabhu S, Ling LH, Ng JF, Brown G, Lee G, Morton J, Debinski H, Kalman JM, Kistler PM. Higher power short duration vs. lower power longer duration posterior wall ablation for atrial fibrillation and oesophageal injury outcomes: a prospective multi-centre randomized controlled study (Hi-Lo HEAT trial). Europace. 2022 Oct 28:euac190. doi: 10.1093/europace/euac190. Epub ahead of print. PMID: 36305561.

31. Cheng C, Xu B, Sheng J, Huang Z, He F, Gao F, Wang X. Procedural Efficiency, Efficacy, and Safety of High-Power, Short-Duration Radiofrequency Ablation Delivered by STSF Catheter for Paroxysmal Atrial Fibrillation. Evid Based Complement Alternat Med. 2022 Aug 8;2022:6009275. doi: 10.1155/2022/6009275. PMID: 35979002; PMCID: PMC9377865.

32. Vassallo F, Meigre LL, Cunha C, Serpa E, Simoes A Jr, Lovatto C, Gasparini D, Corcino L, Schmidt A. Comparison of outcomes with low-power long duration versus high-power short duration of ablation: the role of the acute change in sinus rhythm after the ablation as a predictor of long-term success. Heart Vessels. 2022 Oct;37(10):1749-1756. doi: 10.1007/s00380-022-02066-3. Epub 2022 Apr 16. PMID: 35430635.

33. Kotadia ID, Williams SE, O'Neill M. High-power, Short-duration Radiofrequency Ablation for the Treatment of AF. Arrhythm Electrophysiol Rev. 2020 Feb 12;8(4):265-272. doi: 10.15420/aer.2019.09. PMID: 32685157; PMCID: PMC7358956.

34. Rozen G, Ptaszek LM, Zilberman I, Douglas V, Heist EK, Beeckler C, Altmann A, Ruskin JN, Govari A, Mansour M. Safety and efficacy of delivering high-power short-duration radiofrequency ablation lesions utilizing a novel temperature sensing technology. Europace. 2018 Nov 1;20(FI_3):f444-f450. doi: 10.1093/europace/euy031. PMID: 29579196.

35. Waranugraha Y, Rizal A, Firdaus AJ, Sihotang FA, Akbar AR, Lestari DD, Firdaus M, Nurudinulloh AI. The superiority of high-power short-duration radiofrequency catheter ablation strategy for atrial fibrillation treatment: A systematic review and meta-analysis study. J Arrhythm. 2021 Jul 2;37(4):975-989. doi: 10.1002/joa3.12590. PMID: 34386124; PMCID: PMC8339091.

36. Nilsson B, Chen X, Pehrson S, Svendsen JH. The effectiveness of a high output/short duration radiofrequency current application technique in segmental pulmonary vein isolation for atrial fibrillation. Europace. 2006 Nov;8(11):962-5. doi: 10.1093/europace/eul100. PMID: 17043070.

37. Bhaskaran A, Chik W, Pouliopoulos J, Nalliah C, Qian P, Barry T, Nadri F, Samanta R, Tran Y, Thomas S, Kovoor P, Thiagalingam A. Five seconds of 50-60 W radio frequency atrial ablations were transmural and safe: an in vitro mechanistic assessment and force-controlled in vivo validation. Europace. 2017 May 1;19(5):874-880. doi: 10.1093/europace/euw077. PMID: 27207815.

38. Ali-Ahmed F, Goyal V, Patel M, Orelaru F, Haines DE, Wong WS. High-power, low-flow, short-ablation duration-the key to avoid collateral injury? J Interv Card Electrophysiol. 2019 Jun;55(1):9-16. doi: 10.1007/s10840-018-0473-5. Epub 2018 Oct 30. PMID: 30377925.

Legends to figures:

Figure 1: Prisma flow chart

Figure 2: Forest plot of recurrence of atrial tachyarrhythmias (ATAs); RR: relative risk, CI; Confidence interval

Figure 3: Forest plot showing subgroup analysis of recurrence of atrial fibrillation (AF) and atrial tachycardia/atrial flutter (AT/AFL); RR: relative risk, CI; Confidence interval

Figure 4: Forest plot of major complications showing subgroup analysis of esophageal thermal injury (ETI) and other complications;RR: relative risk, CI; Confidence interval

Figure 5: Forest plot showing the rate of First pass Pulmonary vein isolation (FPI) ; RR: relative risk, CI; Confidence interval

Figure 6: Forest plot showing the risk of acute Pulmonary vein reconnection (PVR) and subgroup analysis of left, right, and bilateral PVR; RR: relative risk, CI; Confidence interval

Figure 7: Forest plot showing total procedure time; WMD: weighted mean difference, SD: Standard deviation, CI; Confidence interval.

Figure 8: Forest plot of total fluoroscopy time; WMD: weighted mean difference, SD: Standard deviation, CI; Confidence interval.

Figure 9: Forest plot of ablation time; WMD: weighted mean difference, SD: Standard deviation, CI; Confidence interval.

Figure 10: Forest plot of ablation number for PVI; WMD: weighted mean difference, SD: Standard deviation, CI; Confidence interval.

Figure 11: Forest plot for ablation index; WMD: weighted mean difference, SD: Standard deviation, CI; Confidence interval.

Figure 12: Forest plot of total RF time; WMD: weighted mean difference, SD: Standard deviation, CI; Confidence interval.

Figure 13: Forest plot showing impedance decrease; WMD: weighted mean difference, SD: Standard deviation, CI; Confidence interval.

Table 1: Study and Procedure characteristics

Study	Study design	Total no. of patients	No. of patients	No. of patients	Mapping tools

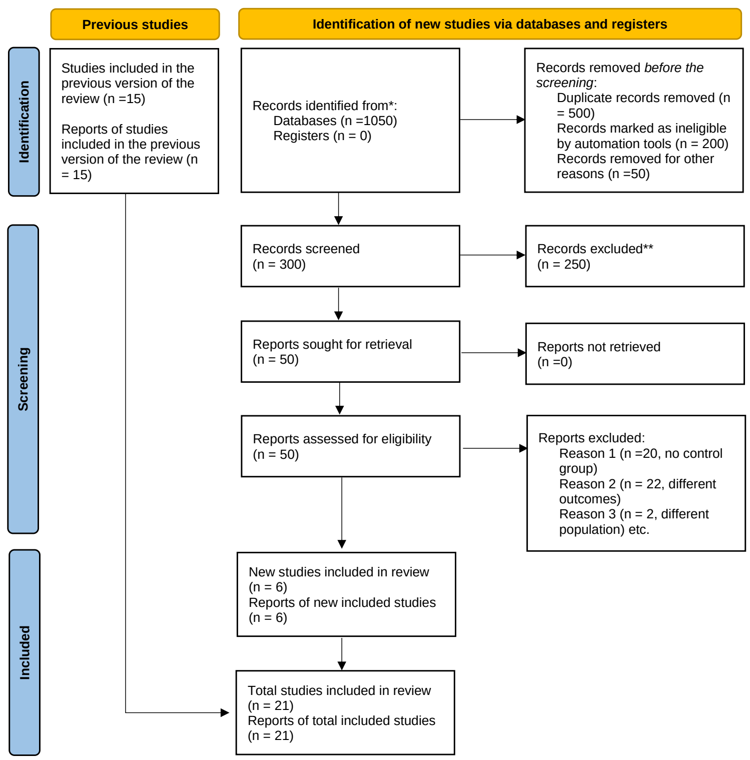
Table 2: Demographics and co-morbidities of patients

Study	Age (Mean± SD)	Age (Mean± SD)	Male No. (%)	Male No. (%)	LVEF (Mean± SD)	LVEF (Mean± SD)	CHA2DS2VASc	CHA2DS2VASc	LAD mm (Mean± SD)	LAD mm (Mean± SD)	BMI (Mean± SD)	BMI (Mean± SD)	Hypertension No. (%)	Hypertension No. (%)	D No (%
	HPSD	LPLD	HPSD	LPLD	HPSD	LPLD	HPSD	LPLD	HPSD	LPLD	HPSD	LPLD	HPSD	LPLD	HI
Vassallo (2020)	59.7	60.7	50 (70.4)	50 (68.4)	N/A	N/A	2.57± 5.92	2.22± 5.18	N/A	N/A	N/A	N/A	52 (73.2)	53 (72.6)	20 (2
Yavin (2020)	62.3± 5.2	64.8± 7.2	71 (63.3)	79 (70.5)	60.3± 6.1	57.8± 5.4	2.4± 1.3	2.6 ± 1.4	44.2± 4.7	47.1± 5.1	47.1± 5.1	27.6±3.9	70 (62.5)	76 (67.8)	11 (9
Yazaki (2020)	66± 11	61± 11	27 (84)	20 (63)	55± 7	56± 7	2	2	40± 13	41± 14	N/A	N/A	N/A	N/A	N/
Shin (2020)	58.5± 7.9	58.7± 11.1	39 (78)	33 (66)	55.7± 11.4	58.9± 8.3	1.6± 1.5	1.7± 1.6	39.9± 4.6	40.7± 6.5	23.8± 2.8	24.6± 2.7	24 (48)	22 (44)	8 (1

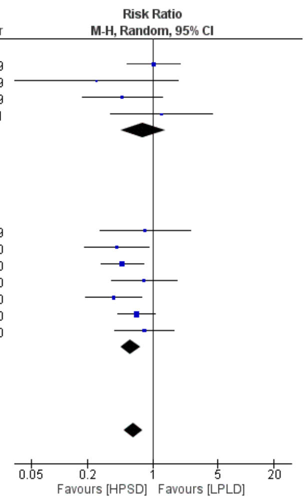
Study	Age (Mean± SD)	Age (Mean± SD)	Male No. (%)	Male No. (%)	LVEF (Mean± SD)	LVEF (Mean± SD)	CHA2DS2VASc	CHA2DS2VASc	LAD mm (Mean± SD)	LAD mm (Mean± SD)	BMI (Mean± SD)	BMI (Mean± SD)	Hypertension No. (%)	Hypertension No. (%)	D No. (%
Kottmaier (2020)	60.8± 13.9	60.8± 10.5	57 (58)	60 (60)	57± 5	55± 9	1.95	1.64	N/A	N/A	27.9± 4.0	28.0 ± 4.5	56 (57.7)	58 (58)	N/
Kaneshiro (2020)	63± 10	61± 10	77 (76.2)	138 (81.2)	N/A	N/A	N/A	N/A	40.8± 6.3	38.8± 6.5	24.9± 4.0	24.5±3.7	N/A	N/A	N/
Ejima (2020)	63± 11.3	66.7± 8.9	44 (73)	42 (70)	57.7± 3.9	57.4± 6.3	1.8± 1.4	2.2 ± 1.4	34.3± 10.3	36.1± 8.7	23.9± 2.8	23.8± 3.2	29 (48)	30 (50)	10 (1
Castrejon (2020)	61± 10	60± 10	32 (67)	28 (60)	57± 9	56± 11	N/A	N/A	N/m HP 40(85%), M/S HP 7 (15%)	N/m LP 36 (82%), M/S LP 8 (18%)	28± 4	29± 5	N/A	N/A	N/
Bunch 2020	67.1± 10.5	66.4± 12.2	253 (62.9)	262 (65.2)	54.6± 12.1	54.7± 12.8	N/A	N/A	N/A	N/A	30.8± 7.0	30.5± 6.8	358 (89.1)	348 (86.6)	12 (3
Vassallo (2019)	64± 10	61± 12	34 (83)	22 (64.7)	N/A	N/A	2± 1.6	2± 1.97	43.3± 6.3	41.9± 6.1	27	28	33 (80)	26 (64.3)	18 (4
Pambrun (2019)	65± 8.2	62.5± 10.6	35 (70)	30 (60)	61.7± 5.6	61.1± 4.4	N/A	N/A	N/A	N/A	N/A	N/A	14 (28)	12 (24)	3 (
Okamatsu (2019)	65± 10	68± 8	13 (65)	15 (75)	65± 8.1	64± 5.1	2± 1.48	2± 0.74	40± 6	39± 6	24± 2.2	24± 5.1	10 (50)	10 (50)	5 (2
Berte (2019)	62± 9	63± 9	50 (62)	67 (71)	58± 8	59± 11	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/
Baher (2018)	69± 11.8	68.3± 11.6	385 (67.1)	67 (59.3)	N/A	N/A	2.9± 1.7	2.5± 1.6	N/A	N/A	N/A	N/A	369 (64.2)	68 (60.1)	11 (1
Wieland (2021)	64± 11	61± 11	32 (67)	33 (69)	N/A	N/A	1± 2.22	1± 2.22	39± 7	40± 7	26.4± 4.2	26.8± 4.0	N/A	N/A	N/
Hansom (2021)	62± 9	62± 9	69 (65)	81 (76)	N/A	N/A	1.9	2	41± 0.7	41± 0.6	N/A	N/A	44 (41)	47 (44)	9 (
Sousa (2022)	61± 10.3	62± 14.8	44 (55)	53 (66)	60± 9.2	60± 3.7	2± 1.48	1± 0.74	40.9± 5.9	40.3± 4.7	27.3± 3.5	27.9± 4	47 (59)	53 (66)	7 (
Sallo (2022)	58± 8.14	60± 6.48	27 (54)	32 (60)	55± 5.9	60± 5.9	2± 1.48	2± 1.48	43± 5.9	44± 6.6	N/A	N/A	37 (74)	33 (62)	7 (1
Chieng (2022)	62.9 ± 8.2	59.7± 10	31 (77.2)	30 (68.1)	55.4± 13	54.6±11	2± 2	1.5 ± 1.5	N/A	N/A	29.2± 5.6	29.2± 4.8	25 (56.8)	14 (31.8)	3 (6
Cheng (2022)	58.9± 11.9	63.1± 9.9	27 (75)	20 (55.5)	63± 4.4	61.5± 4.07	1.69±1.4	2.31± 1.9	38.1± 6.4	38.0± 6.4	24.11 ± 2.9	25.3±3.2	20 (55.6)	18 (50)	6 (1
Vassallo (2022)	58.4± 14	52.9± 10.5	131 (71.8)	113 (71.5)	61± 9.2	63.2± 7.4	2.4± 5.92	2± 5.18	42.9± 5.1	40.6± 4.25	N/A	N/A	126 (69.2)	105 (66.4)	34 (1

Values are expressed as the (Mean± SD: Standard deviations) and no. (%) according to the original text

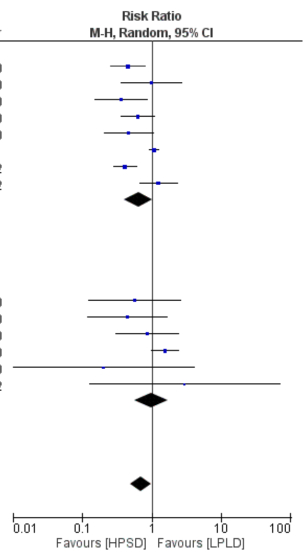
Abbreviations: SVC: superior vena cava, MIL: mitral isthmus line, RL: roof line, LVA: low voltage ablation, FAT: focal atrial tachycardia, LVEF: left ventricular ejection fraction, HF: heart failure, LAD: left atrial diameter, LAVI: left atrial volume index, TIA: transient ischemic attack, N/m: Normal/Mild, M/s: Moderate/severe, DM: Diabetes mellitus, SVC: superior vena cava, CTI: cavotricuspid isthmus, BMI: body mass index



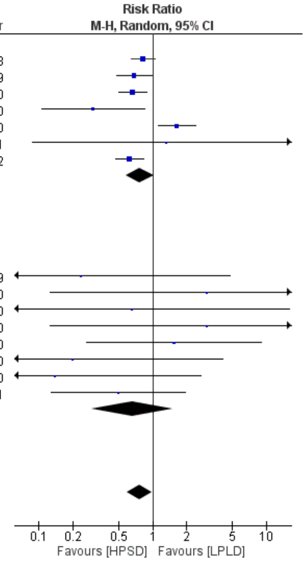
Study or Subgroup	HPSD Events	HPSD Total	LPLD Events	LPLD Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.5.1 6 months							
Berte et al (2019) [24]	14	80	16	94	11.5%	1.03 [0.54, 1.97]	2019
Okamatsu et al (2019) [23]	1	20	8	40	1.2%	0.25 [0.03, 1.86]	2019
Vassallo et al (2019) [21]	5	41	9	35	4.9%	0.47 [0.18, 1.28]	2019
Wielandts et al (2021) [26]	5	48	4	48	3.1%	1.25 [0.36, 4.37]	2021
Subtotal (95% CI)		**189**		**217**	**20.7%**	**0.79 [0.46, 1.36]**	
Total events	25		37				
Heterogeneity: Tau² = 0.04; Chi² = 3.44, df = 3 (P = 0.33); I² = 13%							
Test for overall effect: Z = 0.85 (P = 0.39)							
1.5.2 1 year							
Pambrun et al (2019) [22]	5	50	6	50	3.9%	0.83 [0.27, 2.55]	2019
Ejima et al (2020) [18]	7	60	17	60	7.6%	0.41 [0.18, 0.92]	2020
Kottmaier et al (2020) [16]	16	97	35	100	18.0%	0.47 [0.28, 0.79]	2020
Shin et al (2020) [15]	7	49	17	97	7.4%	0.82 [0.36, 1.83]	2020
Vassallo et al (2020) [12]	9	71	24	73	10.2%	0.39 [0.19, 0.77]	2020
Yavin et al (2020) [13]	23	112	34	112	23.1%	0.68 [0.43, 1.07]	2020
Yazaki et al (2020) [14]	9	32	11	32	9.1%	0.82 [0.39, 1.70]	2020
Subtotal (95% CI)		**471**		**524**	**79.3%**	**0.58 [0.45, 0.74]**	
Total events	76		144				
Heterogeneity: Tau² = 0.00; Chi² = 5.01, df = 6 (P = 0.54); I² = 0%							
Test for overall effect: Z = 4.28 (P < 0.0001)							
Total (95% CI)		**660**		**741**	**100.0%**	**0.62 [0.50, 0.78]**	
Total events	101		181				
Heterogeneity: Tau² = 0.00; Chi² = 9.86, df = 10 (P = 0.45); I² = 0%							
Test for overall effect: Z = 4.20 (P < 0.0001)							
Test for subgroup differences: Chi² = 0.99, df = 1 (P = 0.32), I² = 0%							



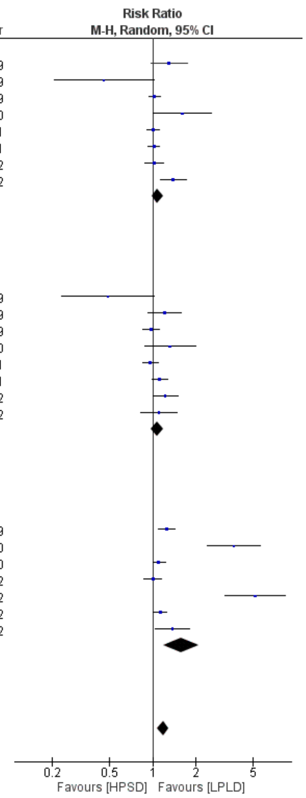
Study or Subgroup	HPSD Events	HPSD Total	LPLD Events	LPLD Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.6.1 AF recurrence							
Kottmaier et al (2020) [16]	14	97	32	100	9.6%	0.45 [0.26, 0.79]	2020
Shin et al (2020) [15]	5	49	10	97	6.1%	0.99 [0.36, 2.74]	2020
Vassallo et al (2020) [12]	6	71	17	73	7.1%	0.36 [0.15, 0.87]	2020
Yavin et al (2020) [13]	17	112	27	112	9.8%	0.63 [0.36, 1.09]	2020
Ejima et al (2020) [18]	7	60	15	60	7.5%	0.47 [0.20, 1.06]	2020
Hansom et al (2021) [27]	84	107	78	107	12.6%	1.08 [0.92, 1.25]	2021
Vassallo et al (2022) [32]	30	182	64	158	11.2%	0.41 [0.28, 0.59]	2022
Chieng et al (2022) [30]	15	44	12	44	9.0%	1.25 [0.66, 2.36]	2022
Subtotal (95% CI)		**722**		**751**	**73.0%**	**0.64 [0.40, 1.01]**	
Total events	178		255				
Heterogeneity: Tau² = 0.34; Chi² = 48.55, df = 7 (P < 0.00001); I² = 86%							
Test for overall effect: Z = 1.90 (P = 0.06)							
1.6.2 AFL/AT recurrence							
Shin et al (2020) [15]	2	49	7	97	3.7%	0.57 [0.12, 2.62]	2020
Vassallo et al (2020) [12]	3	71	7	73	4.5%	0.44 [0.12, 1.64]	2020
Yavin et al (2020) [13]	6	112	7	112	5.9%	0.86 [0.30, 2.47]	2020
Bunch et al (2020) [20]	45	402	29	402	10.7%	1.55 [0.99, 2.42]	2020
Ejima et al (2020) [18]	0	60	2	60	1.2%	0.20 [0.01, 4.08]	2020
Chieng et al (2022) [30]	1	44	0	44	1.1%	3.00 [0.13, 71.70]	2022
Subtotal (95% CI)		**738**		**788**	**27.0%**	**0.98 [0.56, 1.71]**	
Total events	57		52				
Heterogeneity: Tau² = 0.12; Chi² = 6.53, df = 5 (P = 0.26); I² = 23%							
Test for overall effect: Z = 0.07 (P = 0.94)							
Total (95% CI)		**1460**		**1539**	**100.0%**	**0.70 [0.50, 1.00]**	
Total events	235		307				
Heterogeneity: Tau² = 0.24; Chi² = 51.94, df = 13 (P < 0.00001); I² = 75%							
Test for overall effect: Z = 1.98 (P = 0.05)							
Test for subgroup differences: Chi² = 1.33, df = 1 (P = 0.25), I² = 24.7%							



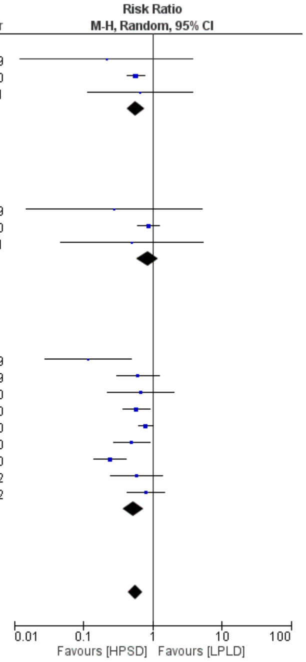
Study or Subgroup	HPSD Events	HPSD Total	LPLD Events	LPLD Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.13.1 ETI							
Baher et al(2018) [25]	202	574	48	113	19.0%	0.83 [0.65, 1.05]	2018
Vassallo et al (2019) [21]	21	41	26	35	15.8%	0.69 [0.48, 0.99]	2019
Vassallo et al (2020) [12]	34	71	52	73	17.9%	0.67 [0.51, 0.89]	2020
Castrejon et al (2020) [19]	4	48	13	47	4.7%	0.30 [0.11, 0.86]	2020
Kaneshiro et al (2020) [17]	37	101	38	170	15.2%	1.64 [1.12, 2.40]	2020
Wielandts et al (2021) [26]	1	19	1	25	0.8%	1.32 [0.09, 19.71]	2021
Vassallo et al (2022) [32]	52	182	72	158	17.8%	0.63 [0.47, 0.83]	2022
Subtotal (95% CI)		**1036**		**621**	**91.2%**	**0.78 [0.58, 1.04]**	
Total events	351		250				
Heterogeneity: Tau² = 0.09; Chi² = 22.03, df = 6 (P = 0.001); I² = 73%							
Test for overall effect: Z = 1.71 (P = 0.09)							
1.13.2 Other complications							
Berte et al (2019) [24]	0	80	2	94	0.7%	0.23 [0.01, 4.82]	2019
Ejima et al (2020) [18]	1	60	0	60	0.6%	3.00 [0.12, 72.20]	2020
Shin et al (2020) [15]	0	50	1	100	0.6%	0.66 [0.03, 15.92]	2020
Yazaki et al (2020) [14]	1	32	0	32	0.6%	3.00 [0.13, 71.00]	2020
Kottmaier et al (2020) [16]	3	97	2	100	1.9%	1.55 [0.26, 9.05]	2020
Yavin et al (2020) [13]	0	112	2	112	0.7%	0.20 [0.01, 4.12]	2020
Castrejon et al (2020) [19]	0	48	3	47	0.7%	0.14 [0.01, 2.64]	2020
Hansom et al (2021) [27]	3	107	6	107	3.0%	0.50 [0.13, 1.95]	2021
Subtotal (95% CI)		**586**		**652**	**8.8%**	**0.66 [0.29, 1.50]**	
Total events	8		16				
Heterogeneity: Tau² = 0.00; Chi² = 4.95, df = 7 (P = 0.67); I² = 0%							
Test for overall effect: Z = 1.00 (P = 0.32)							
Total (95% CI)		**1622**		**1273**	**100.0%**	**0.77 [0.60, 0.99]**	
Total events	359		266				
Heterogeneity: Tau² = 0.07; Chi² = 27.07, df = 14 (P = 0.02); I² = 48%							
Test for overall effect: Z = 2.05 (P = 0.04)							
Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%							



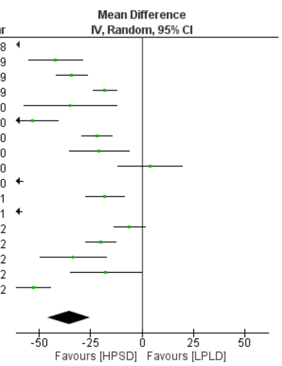
Study or Subgroup	HPSD Events	HPSD Total	LPLD Events	LPLD Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.3.1 Left PVs							
Okamatsu et al (2019) [23]	17	20	26	40	3.9%	1.31 [0.98, 1.75]	2019
Vassallo et al (2019) [21]	7	41	13	35	1.1%	0.46 [0.21, 1.02]	2019
Berte et al (2019) [24]	75	80	85	94	5.9%	1.04 [0.95, 1.13]	2019
Castrejon et al (2020) [19]	27	48	16	46	2.4%	1.62 [1.01, 2.58]	2020
Hansom et al (2021) [27]	94	107	93	107	5.8%	1.01 [0.91, 1.12]	2021
Wielandts et al (2021) [26]	46	48	45	48	5.9%	1.02 [0.93, 1.12]	2021
Chieng et al (2022) [30]	39	44	38	44	5.3%	1.03 [0.88, 1.20]	2022
sallo et al (2022) [29]	46	50	35	53	4.7%	1.39 [1.13, 1.72]	2022
Subtotal (95% CI)		**438**		**467**	**35.0%**	**1.09 [0.99, 1.20]**	
Total events	351		351				
Heterogeneity: Tau² = 0.01; Chi² = 18.79, df = 7 (P = 0.009); I² = 63%							
Test for overall effect: Z = 1.70 (P = 0.09)							
1.3.2 Right Pvs							
Vassallo et al (2019) [21]	8	41	14	35	1.3%	0.49 [0.23, 1.02]	2019
Okamatsu et al (2019) [23]	17	20	28	40	4.1%	1.21 [0.92, 1.60]	2019
Berte et al (2019) [24]	66	80	79	94	5.5%	0.98 [0.86, 1.12]	2019
Castrejon et al (2020) [19]	27	46	19	43	2.8%	1.33 [0.88, 2.01]	2020
Hansom et al (2021) [27]	87	107	90	107	5.6%	0.97 [0.86, 1.09]	2021
Wielandts et al (2021) [26]	46	48	41	48	5.5%	1.12 [0.98, 1.28]	2021
sallo et al (2022) [29]	44	50	38	53	4.9%	1.23 [1.01, 1.50]	2022
Chieng et al (2022) [30]	31	44	28	44	3.9%	1.11 [0.83, 1.49]	2022
Subtotal (95% CI)		**436**		**464**	**33.5%**	**1.07 [0.97, 1.18]**	
Total events	326		337				
Heterogeneity: Tau² = 0.01; Chi² = 12.69, df = 7 (P = 0.08); I² = 45%							
Test for overall effect: Z = 1.38 (P = 0.17)							
1.3.3 Bilateral PVs							
Pambrun et al (2019) [22]	92	100	73	100	5.5%	1.26 [1.10, 1.44]	2019
Vassallo et al (2020) [12]	61	71	17	73	2.7%	3.69 [2.41, 5.65]	2020
Yavin et al (2020) [13]	103	112	93	112	5.8%	1.11 [1.00, 1.22]	2020
Sousa et al (2022) [28]	73	91	75	94	5.4%	1.01 [0.87, 1.16]	2022
Vassallo et al (2022) [32]	118	152	14	94	2.3%	5.21 [3.19, 8.51]	2022
Cheng et al (2022) [31]	69	72	61	72	5.7%	1.13 [1.01, 1.26]	2022
sallo et al (2022) [29]	39	50	30	53	4.0%	1.38 [1.04, 1.82]	2022
Subtotal (95% CI)		**648**		**598**	**31.5%**	**1.57 [1.19, 2.09]**	
Total events	555		363				
Heterogeneity: Tau² = 0.13; Chi² = 123.87, df = 6 (P < 0.00001); I² = 95%							
Test for overall effect: Z = 3.14 (P = 0.002)							
Total (95% CI)		**1522**		**1529**	**100.0%**	**1.19 [1.08, 1.30]**	
Total events	1232		1051				
Heterogeneity: Tau² = 0.04; Chi² = 148.08, df = 22 (P < 0.00001); I² = 85%							
Test for overall effect: Z = 3.58 (P = 0.0003)							
Test for subgroup differences: Chi² = 6.47, df = 2 (P = 0.04), I² = 69.1%							



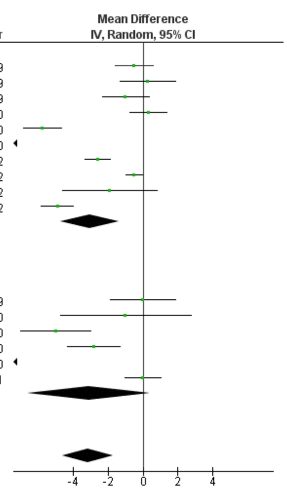
Study or Subgroup	HPSD Events	HPSD Total	LPLD Events	LPLD Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.12.1 Left PVR							
Okamatsu et al (2019) [23]	0	20	4	40	0.7%	0.22 [0.01, 3.84]	2019
Ejima et al (2020) [18]	28	60	49	60	13.8%	0.57 [0.43, 0.77]	2020
Wielandts et al (2021) [26]	2	48	3	48	1.7%	0.67 [0.12, 3.81]	2021
Subtotal (95% CI)		**128**		**148**	**16.2%**	**0.57 [0.43, 0.76]**	
Total events	30		56				
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 2 (P = 0.79); I² = 0%							
Test for overall effect: Z = 3.82 (P = 0.0001)							
1.12.2 Right PVR							
Okamatsu et al (2019) [23]	0	20	3	40	0.7%	0.28 [0.02, 5.15]	2019
Ejima et al (2020) [18]	27	60	31	60	12.3%	0.87 [0.60, 1.26]	2020
Wielandts et al (2021) [26]	1	48	2	48	1.0%	0.50 [0.05, 5.33]	2021
Subtotal (95% CI)		**128**		**148**	**14.0%**	**0.84 [0.59, 1.22]**	
Total events	28		36				
Heterogeneity: Tau² = 0.00; Chi² = 0.82, df = 2 (P = 0.66); I² = 0%							
Test for overall effect: Z = 0.91 (P = 0.36)							
1.12.3 Bilateral PVR							
Pambrun et al (2019) [22]	2	100	17	100	2.4%	0.12 [0.03, 0.50]	2019
Berte et al (2019) [24]	10	75	18	82	7.0%	0.61 [0.30, 1.23]	2019
Castrejon et al (2020) [19]	5	94	7	89	3.7%	0.68 [0.22, 2.05]	2020
Yazaki et al (2020) [14]	28	384	48	384	11.0%	0.58 [0.37, 0.91]	2020
Ejima et al (2020) [18]	37	60	47	60	14.8%	0.79 [0.62, 1.00]	2020
Yavin et al (2020) [13]	14	225	29	231	8.3%	0.50 [0.27, 0.91]	2020
Kottmaier et al (2020) [16]	13	97	55	100	9.4%	0.24 [0.14, 0.42]	2020
Sousa et al (2022) [28]	7	80	12	80	5.3%	0.58 [0.24, 1.41]	2022
Chieng et al (2022) [30]	12	44	15	44	7.9%	0.80 [0.42, 1.51]	2022
Subtotal (95% CI)		**1159**		**1170**	**69.8%**	**0.52 [0.37, 0.75]**	
Total events	128		248				
Heterogeneity: Tau² = 0.18; Chi² = 25.55, df = 8 (P = 0.001); I² = 69%							
Test for overall effect: Z = 3.53 (P = 0.0004)							
Total (95% CI)		**1415**		**1466**	**100.0%**	**0.57 [0.45, 0.73]**	
Total events	186		340				
Heterogeneity: Tau² = 0.09; Chi² = 29.35, df = 14 (P = 0.009); I² = 52%							
Test for overall effect: Z = 4.53 (P < 0.00001)							
Test for subgroup differences: Chi² = 3.95, df = 2 (P = 0.14), I² = 49.3%							



Study or Subgroup	HPSD Mean	HPSD SD	HPSD Total	LPLD Mean	LPLD SD	LPLD Total	Weight	Mean Difference IV, Random, 95% CI	Year
Baher et al(2018) [25]	149	65	574	251	101	113	5.3%	-102.00 [-121.37, -82.63]	2018
Vassallo et al (2019) [21]	106	23	41	148	33.6	35	5.9%	-42.00 [-55.17, -28.83]	2019
Pambrun et al (2019) [22]	73.1	18.2	50	107.4	21.2	50	6.2%	-34.30 [-42.04, -26.56]	2019
Berte et al (2019) [24]	82	18	80	100	22	94	6.3%	-18.00 [-23.94, -12.06]	2019
Yazaki et al (2020) [14]	115	32	32	150	57	32	5.0%	-35.00 [-57.65, -12.35]	2020
Shin et al (2020) [15]	108.7	23.1	50	161.9	37.9	50	5.9%	-53.20 [-65.50, -40.90]	2020
Kottmaier et al (2020) [16]	89.5	23.9	97	111.5	27.9	100	6.3%	-22.00 [-29.25, -14.75]	2020
Ejima et al (2020) [18]	119.3	28.1	60	140.1	51.2	60	5.7%	-20.80 [-35.58, -6.02]	2020
Castrejon et al (2020) [19]	124	31	48	120	45	47	5.7%	4.00 [-11.57, 19.57]	2020
Bunch et al (2020) [20]	104.3	63.6	402	170.8	59.2	402	6.2%	-66.50 [-74.99, -58.01]	2020
Wielandts et al (2021) [26]	85	21.96	48	103	25.18	48	6.1%	-18.00 [-27.45, -8.55]	2021
Hansom et al (2021) [27]	234.5	57.4	107	311	75	107	5.5%	-76.50 [-94.40, -58.60]	2021
sallo et al (2022) [29]	79	19.26	50	85	19.26	53	6.3%	-6.00 [-13.44, 1.44]	2022
Sousa et al (2022) [28]	80	18.51	80	100	28.15	80	6.3%	-20.00 [-27.38, -12.62]	2022
Cheng et al (2022) [31]	111.8	36.1	36	145.4	34.3	36	5.6%	-33.60 [-49.87, -17.33]	2022
Chieng et al (2022) [30]	133.3	37.6	44	150.9	45.8	44	5.5%	-17.60 [-35.11, -0.09]	2022
Vassallo et al (2022) [32]	92.4	31.3	182	145.3	45.7	158	6.2%	-52.90 [-61.35, -44.45]	2022
Total (95% CI)			**1981**			**1509**	**100.0%**	**-35.58 [-46.16, -25.01]**	
Heterogeneity: Tau² = 450.25; Chi² = 291.83, df = 16 (P < 0.00001); I² = 95%									
Test for overall effect: Z = 6.60 (P < 0.00001)									

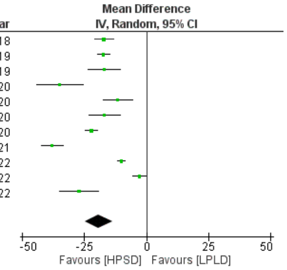


Study or Subgroup	HPSD Mean	HPSD SD	HPSD Total	LPLD Mean	LPLD SD	LPLD Total	Weight	Mean Difference IV, Random, 95% CI	Year
1.8.1 PVI									
Pambrun et al (2019) [22]	6	2.8	50	6.5	2.7	50	6.7%	-0.50 [-1.58, 0.58]	2019
Vassallo et al (2019) [21]	8.8	3.6	41	8.52	3.5	35	6.4%	0.28 [-1.32, 1.88]	2019
Berte et al (2019) [24]	6	4	80	7	5	94	6.6%	-1.00 [-2.34, 0.34]	2019
Kottmaier et al (2020) [16]	6.3	3.9	97	6	3.8	100	6.7%	0.30 [-0.78, 1.38]	2020
Vassallo et al (2020) [12]	7.6	1.29	71	13.37	4.54	73	6.7%	-5.77 [-6.85, -4.69]	2020
Castrejon et al (2020) [19]	8	3	48	30	16	47	4.1%	-22.00 [-26.65, -17.35]	2020
Sousa et al (2022) [28]	3.4	2.07	80	6	2.52	80	6.8%	-2.60 [-3.31, -1.89]	2022
Cheng et al (2022) [31]	4	1.3	36	4.5	0.7	36	6.9%	-0.50 [-0.98, -0.02]	2022
Chieng et al (2022) [30]	11.2	4.3	44	13.1	8.1	44	5.6%	-1.90 [-4.61, 0.81]	2022
Vassallo et al (2022) [32]	8.5	3.4	182	13.4	5.02	158	6.7%	-4.90 [-5.83, -3.97]	2022
Subtotal (95% CI)			**729**			**717**	**63.1%**	**-3.06 [-4.73, -1.39]**	
Heterogeneity: Tau² = 6.50; Chi² = 227.85, df = 9 (P < 0.00001); I² = 96%									
Test for overall effect: Z = 3.59 (P = 0.0003)									
1.8.2 PVI + additional ablation									
Okamatsu et al (2019) [23]	10	2.22	20	10	3.7	20	6.2%	0.00 [-1.89, 1.89]	2019
Yazaki et al (2020) [14]	12	9	32	13	6	32	4.8%	-1.00 [-4.75, 2.75]	2020
Bunch et al (2020) [20]	15	8.4	402	20	18.6	402	6.1%	-5.00 [-7.00, -3.00]	2020
Shin et al (2020) [15]	9.7	4.1	50	12.5	3.6	50	6.5%	-2.80 [-4.31, -1.29]	2020
Ejima et al (2020) [18]	0.4	1.14	60	10	5.18	60	6.5%	-9.60 [-10.94, -8.26]	2020
Wielandts et al (2021) [26]	5	2.2	48	5	2.96	48	6.7%	0.00 [-1.04, 1.04]	2021
Subtotal (95% CI)			**612**			**612**	**36.9%**	**-3.12 [-6.63, 0.40]**	
Heterogeneity: Tau² = 18.19; Chi² = 139.18, df = 5 (P < 0.00001); I² = 96%									
Test for overall effect: Z = 1.74 (P = 0.08)									
Total (95% CI)			**1341**			**1329**	**100.0%**	**-3.16 [-4.64, -1.68]**	
Heterogeneity: Tau² = 8.22; Chi² = 381.60, df = 15 (P < 0.00001); I² = 96%									
Test for overall effect: Z = 4.19 (P < 0.0001)									
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.98), I² = 0%									



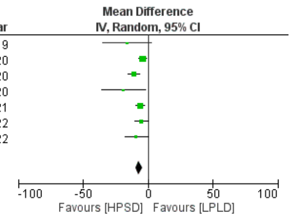
Study or Subgroup	HPSD Mean	HPSD SD	HPSD Total	LPLD Mean	LPLD SD	LPLD Total	Weight	Mean Difference IV, Random, 95% CI	Year
Baher et al(2018) [25]	37.9	13.9	574	55	19.2	113	9.5%	-17.10 [-20.82, -13.38]	2018
Pambrun et al (2019) [22]	13	2.9	50	30.3	8.8	50	9.7%	-17.30 [-19.87, -14.73]	2019
Okamatsu et al (2019) [23]	15.5	12.56	20	32.5	8.37	20	8.7%	-17.00 [-23.61, -10.39]	2019
Shin et al (2020) [15]	38.2	14.8	50	73.1	30.5	50	7.7%	-34.90 [-44.30, -25.50]	2020
Ejima et al (2020) [18]	25.9	11.4	60	37.5	20.1	60	8.9%	-11.60 [-17.45, -5.75]	2020
Vassallo et al (2020) [12]	96.54	17.76	71	113.55	20.74	73	8.8%	-17.01 [-23.31, -10.71]	2020
Yavin et al (2020) [13]	41.5	7.3	112	63.7	11.6	112	9.7%	-22.20 [-24.74, -19.66]	2020
Hansom et al (2021) [27]	27.2	8.4	107	65.3	21.5	107	9.3%	-38.10 [-42.47, -33.73]	2021
Sousa et al (2022) [28]	20	3.7	80	30	5.92	80	9.8%	-10.00 [-11.53, -8.47]	2022
sallo et al (2022) [29]	23.3	8.51	50	26.1	4.9	53	9.7%	-2.80 [-5.50, -0.10]	2022
Vassallo et al (2022) [32]	81.2	32.7	182	108.3	40.59	158	8.3%	-27.10 [-35.01, -19.19]	2022
Total (95% CI)			**1356**			**876**	**100.0%**	**-19.19 [-24.83, -13.55]**	

Heterogeneity: $Tau^2 = 83.91$; $Chi^2 = 288.82$, df = 10 (P < 0.00001); $I^2 = 97\%$
Test for overall effect: Z = 6.67 (P < 0.00001)



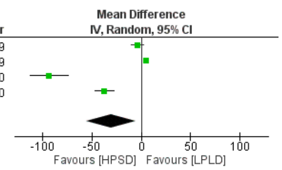
Study or Subgroup	HPSD Mean	HPSD SD	HPSD Total	LPLD Mean	LPLD SD	LPLD Total	Weight	Mean Difference IV, Random, 95% CI	Year
Okamatsu et al (2019) [23]	119	40.7	20	135	14.81	20	2.0%	-16.00 [-34.98, 2.98]	2019
Yavin et al (2020) [13]	87.2	12.1	112	91.2	10.3	112	27.6%	-4.00 [-6.94, -1.06]	2020
Shin et al (2020) [15]	83.6	8.9	50	94.6	13.7	50	19.3%	-11.00 [-15.53, -6.47]	2020
Castrejon et al (2020) [19]	88	17	48	107	57	47	2.5%	-19.00 [-35.99, -2.01]	2020
Wielandts et al (2021) [26]	54	7.4	48	60	8.88	48	25.7%	-6.00 [-9.27, -2.73]	2021
sallo et al (2022) [29]	56	15.5	50	61	12.6	53	15.5%	-5.00 [-10.47, 0.47]	2022
Chieng et al (2022) [30]	67	23.3	44	76	19.8	44	7.5%	-9.00 [-18.03, 0.03]	2022
Total (95% CI)			**372**			**374**	**100.0%**	**-7.00 [-9.74, -4.25]**	

Heterogeneity: $Tau^2 = 4.86$; $Chi^2 = 10.23$, df = 6 (P = 0.12); $I^2 = 41\%$
Test for overall effect: Z = 5.00 (P < 0.00001)



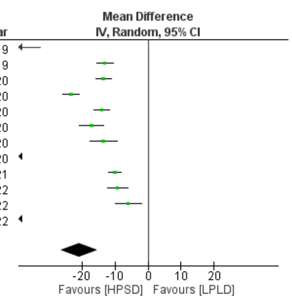
Study or Subgroup	HPSD Mean	HPSD SD	HPSD Total	LPLD Mean	LPLD SD	LPLD Total	Weight	Mean Difference IV, Random, 95% CI	Year
Berte et al (2019) [24]	550.9	18.84	80	554.8	22.83	94	25.8%	-3.90 [-10.09, 2.29]	2019
Okamatsu et al (2019) [23]	408	19.3	2333	403	23.74	2887	26.2%	5.00 [3.83, 6.17]	2019
Shin et al (2020) [15]	359.9	46.5	50	452.8	49.6	50	22.8%	-92.90 [-111.75, -74.05]	2020
Yazaki et al (2020) [14]	351	57	384	388	77	384	25.2%	-37.00 [-46.58, -27.42]	2020
Total (95% CI)			**2847**			**3415**	**100.0%**	**-30.17 [-54.86, -5.48]**	

Heterogeneity: $Tau^2 = 605.10$; $Chi^2 = 180.79$, df = 3 (P < 0.00001); $I^2 = 98\%$
Test for overall effect: Z = 2.39 (P = 0.02)



Study or Subgroup	HPSD Mean	HPSD SD	HPSD Total	LPLD Mean	LPLD SD	LPLD Total	Weight	Mean Difference IV, Random, 95% CI	Year
Vassallo et al (2019) [21]	31.8	11.3	41	76	33.3	35	6.5%	-44.20 [-55.76, -32.64]	2019
Berte et al (2019) [24]	23	5	80	36	11	94	8.7%	-13.00 [-15.48, -10.52]	2019
Yavin et al (2020) [13]	17.5	10.8	112	31	6.7	112	8.7%	-13.50 [-15.85, -11.15]	2020
Kottmaier et al (2020) [16]	12.4	3.4	97	35.6	12.1	100	8.7%	-23.20 [-25.67, -20.73]	2020
Yazaki et al (2020) [14]	10	3	32	24	6	32	8.7%	-14.00 [-16.32, -11.68]	2020
Ejima et al (2020) [18]	17.9	7.2	60	34.9	12.7	60	8.5%	-17.00 [-20.69, -13.31]	2020
Castrejon et al (2020) [19]	20.5	9.2	48	34	11	47	8.4%	-13.50 [-17.58, -9.42]	2020
Vassallo et al (2020) [12]	32.7	7.12	71	83.6	31	73	7.7%	-50.90 [-58.20, -43.60]	2020
Wielandts et al (2021) [26]	16	3	48	26	5.92	48	8.7%	-10.00 [-11.88, -8.12]	2021
Cheng et al (2022) [31]	32.1	7	36	41.3	6.2	36	8.6%	-9.20 [-12.25, -6.15]	2022
Chieng et al (2022) [30]	23.8	9.45	44	29.7	9.2	44	8.5%	-5.90 [-9.80, -2.00]	2022
Vassallo et al (2022) [32]	27.8	9.4	182	71.96	22.6	158	8.5%	-44.16 [-47.94, -40.38]	2022
Total (95% CI)			**851**			**839**	**100.0%**	**-20.78 [-26.46, -15.10]**	

Heterogeneity: $Tau^2 = 95.32$; $Chi^2 = 454.64$, df = 11 (P < 0.00001); $I^2 = 98\%$
Test for overall effect: Z = 7.17 (P < 0.00001)



Study or Subgroup	HPSD Mean	HPSD SD	HPSD Total	LPLD Mean	LPLD SD	LPLD Total	Weight	Mean Difference IV, Random, 95% CI	Year
Pambrun et al (2019) [22]	14.6	3	50	14.7	2.7	50	23.7%	-0.10 [-1.22, 1.02]	2019
Kottmaier et al (2020) [16]	10.8	1.5	97	12.4	1.9	100	26.0%	-1.60 [-2.08, -1.12]	2020
Yavin et al (2020) [13]	10.9	3.65	112	8.2	3.45	112	24.5%	2.70 [1.77, 3.63]	2020
Yazaki et al (2020) [14]	5.5	3.9	384	5.5	3.5	384	25.9%	0.00 [-0.52, 0.52]	2020
Total (95% CI)			**643**			**646**	**100.0%**	**0.22 [-1.42, 1.87]**	

Heterogeneity: $Tau^2 = 2.65$; $Chi^2 = 69.47$, df = 3 (P < 0.00001); $I^2 = 96\%$
Test for overall effect: Z = 0.26 (P = 0.79)