

High Power Short Duration and Low Power Long Duration in Atrial Fibrillation Ablation: A Meta-Analysis

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August 28, 2020

Abstract

Background: Multiple strategies have advocacy for power titration and catheter movement during atrial fibrillation (AF) ablation. Comparative favoring evidence regarding the efficacy, logistics, and safety of a higher power, shorter duration (HPSD) ablation strategy compared to a lower power, longer duration (LPLD) ablation strategy is insubstantial. We performed a meta-analysis to compare arrhythmia-free survival, procedure times, and complication rates between the two strategies. Methods: We searched MEDLINE, EMBASE and Cochrane Library from inception to April 2020. We included studies comparing patients underwent HPSD and LPLD strategies for AF ablation and reporting either of the following outcomes: freedom from atrial tachyarrhythmia (AT) including AF and atrial flutter, procedure time, or periprocedural complications. We combined data using the random-effects model to calculate odds ratio (OR) and weight mean difference (WMD) with 95% confidence interval (CI). Results: Nine studies from 2006-2020 involving 2,282 patients were included (1,369 patients underwent HPSD strategy and 853 patients underwent LPLD strategy). HPSD strategy was not associated with an increased freedom from AT at 12-month follow-up (OR= 1.41, 95%CI:0.90-2.21). There was a significant reduction in the HPSD group for total procedure (WMD=49.60, 95%CI:29.76-69.44) and ablation (WMD=17.92, 95%CI:13.63-22.22) times, but not for fluoroscopy time (WMD=1.15, 95%CI:-0.67-2.97). HPSD was not associated with a reduction in esophageal ulcer/atrioesophageal fistula (OR=0.35, 95%CI:0.12-1.06) or pericardial effusion/cardiac tamponade rates (OR=0.96, 95%CI:0.24-3.79). Conclusions: When compared to a LPLD strategy, HPSD strategy does not improve recurrent AT nor reduce periprocedural complication risks. However, a HPSD strategy can significantly reduce total procedure and ablation times.

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Running head: High power short duration for atrial fibrillation ablation

Keywords: atrial fibrillation ablation, high power, low power

Acknowledgement: None

Financial support: None

Conflict of Interest : All authors declare no conflict of interest

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Word count: 2,857

References: 45

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Background: Multiple strategies have advocacy for power titration and catheter movement during atrial fibrillation (AF) ablation. Comparative favoring evidence regarding the efficacy, logistics, and safety of a higher power, shorter duration (HPSD) ablation strategy compared to a lower power, longer duration (LPLD) ablation strategy is insubstantial. We performed a meta-analysis to compare arrhythmia-free survival, procedure times, and complication rates between the two strategies.

Methods: We searched MEDLINE, EMBASE and Cochrane Library from inception to April 2020. We included studies comparing patients underwent HPSD and LPLD strategies for AF ablation and reporting either of the following outcomes: freedom from atrial tachyarrhythmia (AT) including AF and atrial flutter, procedure time, or periprocedural complications. We combined data using the random-effects model to calculate odds ratio (OR) and weight mean difference (WMD) with 95% confidence interval (CI).

Results: Nine studies from 2006-2020 involving 2,282 patients were included (1,369 patients underwent HPSD strategy and 853 patients underwent LPLD strategy). HPSD strategy was not associated with an increased freedom from AT at 12-month follow-up (OR= 1.41, 95%CI:0.90-2.21). There was a significant reduction in the HPSD group for total procedure (WMD=49.60, 95%CI:29.76-69.44) and ablation (WMD=17.92, 95%CI:13.63-22.22) times, but not for fluoroscopy time (WMD=1.15, 95%CI:-0.67-2.97). HPSD was not

associated with a reduction in esophageal ulcer/atrioesophageal fistula (OR=0.35, 95%CI:0.12-1.06) or pericardial effusion/cardiac tamponade rates (OR=0.96, 95%CI:0.24-3.79).

Conclusions: When compared to a LPLD strategy, HPSD strategy does not improve recurrent AT nor reduce periprocedural complication risks. However, a HPSD strategy can significantly reduce total procedure and ablation times.

Condensed abstract

We performed a meta-analysis to compare arrhythmia-free survival, procedure times, and complication rates between the two strategies. Data from each study were combined using the random-effects model. Nine studies from 2006 to 2020 were included. HPSD strategy does not improve recurrent AT at 12-month (OR= 1.41, 95%CI:0.90-2.21) nor reduce periprocedural complication risks including esophageal ulcer/atrioesophageal fistula (OR=0.35, 95%CI:0.12-1.06) or pericardial effusion/cardiac tamponade rates (OR=0.96, 95%CI:0.24-3.79). However, a HPSD strategy can significantly reduce total procedure (WMD=49.60, 95%CI:29.76-69.44) and ablation times (WMD=17.92, 95%CI:13.63-22.22)

1. Introduction

Evidence has shown that catheter ablation is an effective treatment option for symptomatic, drug-refractory atrial fibrillation (AF) and significantly improves quality of life compared to medical therapies alone [1, 2]. The principle aim of AF ablation is to achieve circumferential pulmonary vein isolation (PVI), which electrically separates the pulmonary vein (PV) from the left atrium (LA) at the level of PV ostia/antrum. Although AF ablation is considered relatively safe, the procedure still carries risks of complications that can be significant such as esophageal-related injuries including atrioesophageal fistula, esophageal ulcer, and esophageal dysmotility [3, 4]. Other complications include pericardial effusion or cardiac tamponade, cerebrovascular accident, PV stenosis, and phrenic nerve palsy [5]. Many of these complications can be attributed, in part, to excessive energy delivery during ablation.

To ensure efficacy and safety of PVI, several factors must be considered: (1) transmuralty of lesions to achieve conduction block, (2) necrosis of tissue and scar formation to sustain the conduction block, and (3) absence of excessive cardiac injury from a perforating steam pop or laceration as well as significant extracardiac collateral damage. These procedural and tissue factors can be modified by optimizing radiofrequency energy delivery through parameters such as power, duration and extent of contact, local thermal heating (resistive and conductive), electrode diameter of the radiofrequency catheter, and lesion size [6-10]. In current practice, power and duration are often selected for modification between two broad ablation strategies, high power, shorter duration (HPSD) and lower power, longer duration (LPLD). The conventional LPLD of 10 to 35 W (most commonly 25-35 W) for a duration of 10 to 30 s, is the more commonly used strategy [11, 12]. Recently, it has been suggested that another approach of HPSD ([?]40 W, duration of less than 10 s) can be used to lower the time spent per lesion, and since heat transfer in tissues is time dependent, reduces deep tissue heating and collateral injury [9, 13]. Results from experimental studies have reported that HPSD ablation approaches produce larger lesion diameters compared to LPLD that may augment lesion contiguity while still resulting in a sufficient lesion depth to ensure transmuralty [10, 13, 14].

Despite multiple observational studies comparing the two ablation techniques on arrhythmia-related outcomes and complication rates, results are contradictory and inconclusive [10, 15-22]. Thus, we performed a systematic review and meta-analysis to evaluate and compare arrhythmia-free survival, procedure times, and complications rates between the HPSD and LPLD strategies.

2. Methods

2.1 Search strategy

Two investigators (CT and CK) independently searched for published studies indexed in PubMed, EMBASE and Cochrane library databases from inception to April 2020 using the search terms including: “atrial fibrillation”, “ablation”, and “high power” as described in supplementary file 1. Only articles in English

were included. An additional manual search for potential additional pertinent studies was performed using the references from retrieved articles.

2.2 Inclusion criteria

The inclusion criteria were as follows

- (1) Cohort study, case-control study, cross-sectional study, or randomized controlled trial (RCT) conducted in patients with AF undergoing PVI, using or comparing HPSD strategy and LPLD strategy
- (2) Studies must use an irrigated catheter with the following for each ablation strategy; LPLD : Power [?] 35 W, duration > 10 s in any ablation, HPSD: Power [?]40 W, duration [?] 10 s in every ablation or less than LPLD group
- (3) Studies must report either recurrence rates of atrial tachyarrhythmias (AT) including AF and atrial flutter, procedural times, or complications rates following the index ablation. Effect size or sufficient raw data to calculate the effect size must be provided

2.3 Quality of included studies

The Newcastle-Ottawa quality assessment scale (NOS) was used. The Newcastle-Ottawa Scale uses a star system (0 to 9) to evaluate included studies on 3 domains: recruitment and selection of the participants, similarity and comparability between the groups, and ascertainment of the outcome of interest among cohort and case-control studies [23]. Higher scores represent higher study quality. Cochrane Collaboration tool for assessing risk of bias was used to evaluate the quality of each randomized controlled trial by assigning a score (high, low, or unclear) for each individual element from five domains (selection, performance, attrition, reporting, and other) [24].

2.4 Data extraction

A standardized data collection form was used to obtain the following data from each study including name of the first author, year of publication, country of origin, study population, inclusion and exclusion criteria, demographic data of participants, ablation procedure details

To ensure accuracy, this data extraction process was independently performed by all investigators. Any data discrepancy was also resolved by referring back to the original articles.

2.5 Statistical analysis

We performed meta-analysis of included studies using a random-effects model and the generic inverse-variance method of Der Simonian and Laird [25]. We extracted from these studies the freedom from AT rate and complications rate. The heterogeneity of effect size estimates was firstly assessed using forest plots to detect non-overlapping confidence interval (CI), and then was calculated using the Q statistic and I^2 statistic. For the Q statistic, substantial heterogeneity was defined as $p < 0.10$. The I^2 statistic ranges in value from 0 to 100% ($I^2 < 25\%$, low heterogeneity; $I^2 = 25\% - 50\%$, moderate heterogeneity; and $I^2 > 50\%$, substantial heterogeneity). A sensitivity analysis was performed to assess the influence of the individual studies on the overall results by omitting one study at a time. Publication bias was assessed using funnel plot and Egger's regression tests [26] ($p < 0.05$ was considered significant). All statistical tests were performed using the STATA 14.1 software (College Station, TX).

3. Results

3.1 Search result

Our search strategy yielded 282 potentially relevant articles (132 articles from PubMed, 110 articles from EMBASE, 46 articles from Cochrane Library) as shown in Figure 1. After the exclusion of 157 duplicated articles, 125 articles underwent title and abstract review. Further 86 articles were excluded as topics were irrelevant or conducted in animals, leaving a total of 39 articles for a full-length article review. At this stage, further 30 articles were excluded as they did not meet inclusion criteria or did not have comparable outcome

of interests between the two ablation strategies. No additional articles were added through manual search. Thus, a total of 9 articles met all eligibility criteria and were included in the data analysis [10, 15-22].

3.2 Description of included studies

Nine studies from 2006 to 2020 involving 2,282 patients were included (1,369 patients underwent HPSD strategy and 853 patients underwent LPLD strategy) [10, 15-22]. There were 6 in the prospective cohort and 3 in the retrospective cohort. Power used in the HSPD groups ranged from 40-70 W. Other study characteristics of the included studies are shown in table 1.

3.3 Quality assessment of included studies

The Newcastle–Ottawa scales (NOS) of the included studies are described in supplementary file 2. We did not use the Cochrane Collaboration tool for assessing risk of bias as there were no RCT designs included.

3.2 Meta-analysis results

3.2.1 Freedom from atrial tachyarrhythmia

The outcome of AT recurrence was available in 8 studies. We found that a HPSD strategy was not associated with an increased freedom from AT at 12-months follow-up compared to a LPLD strategy (OR= 1.41, 95%CI:0.90-2.21, $I^2=65.2\%$, p-value=0.13). A forest plot of this analysis is shown in figure 2.

3.2.3 Procedure time

Outcomes regarding total procedure, ablation, and fluoroscopy times were available in 6, 4, and 5 of the studies, respectively. There was a significant reduction in the total procedure [weighted mean difference (WMD)=49.60, 95%CI:29.76-69.44, $I^2=95.2\%$, p-value<0.001] and ablation times (WMD=17.92, 95%CI:13.63-22.22), $I^2=89.2\%$, p-value<0.001) in the HPSD strategy group. The fluoroscopy times were not significantly different between the two groups (WMD=1.15, 95%CI:-0.67-2.97, $I^2=82.5\%$, p-value=0.21). A forest plot demonstrating the WMD for the total procedure, ablation, and fluoroscopy times are shown in figure 3, 4, and 5, respectively.

3.2.4 Periprocedural complications

Outcomes regarding esophageal ulcer/arterioesophageal fistula and pericardial effusion/cardiac tamponade rates were available in 3 and 3 studies, respectively. There were no significant differences in any periprocedural complications between the two groups (p-value>0.05 for all). There were insufficient data to perform additional analysis for other complications including stroke or transient ischemic attack, phrenic nerve injury and PV stenosis. A forest plot of the analysis is shown in figures 6A and 6B, respectively.

3.3 Publication bias

We aimed to investigate potential publication bias via the funnel plot and Egger’s test. However, as we only had up to 9 studies in the main analysis (figure 2), the number was insufficient to reject the assumption of no funnel plot asymmetry. Thus, we did not perform a funnel plot or Egger’s test [27, 28].

4. Discussion

The main findings from our study are: 1) There was no significant difference in 1-year freedom from AT between patients who underwent HPSD ablation and those who underwent LPLD ablation, 2) HPSD ablation significantly reduced total procedure and ablation times, without lowering fluoroscopy time, and 3) Periprocedural complications, including atrial-esophageal fistula or ulcer formation and pericardial effusion or tamponade are similar between the two strategies.

Our meta-analysis is the first meta-analysis to assess the outcomes among patients with AF who underwent HPSD ablations, comparing it to the more conventional LPLD ablation. Theoretically, HPSD strategy could be superior to LPLD ablation for several reasons. Firstly, HPSD ablations shorten the radiofrequency application time, decreasing catheter motion and collateral damage to adjacent structure near left atrium [14].

Additionally, development of tissue edema is less with HPSD [17] and therefore the risk of pulmonary vein reconnection may be lower [29, 30]. HPSD ablation may also help achieve complete encirclement of the PVs by creating contiguous lesions that are larger in diameter with sufficient lesion depth compared to standard ablation lesions [9]. A study by Bourier et al. demonstrated that minimum lesion depth achieved by HPSD was 3.1 mm [9], while the mean atrial wall thickness is 1.5-2 mm [31, 32]. Therefore, lesion transmuralities can be consistently produced by the HPSD ablation. Despite these theoretical advantages with HPSD, when applied clinically and in this meta-analysis evaluation, there were no measurable advantages for efficacy or safety when compared to LPSD. This finding is not overly surprising as among the 8 studies that reported 1-year freedom from AT, 6 of 8 studies did not demonstrate a statistically significant difference in outcomes when comparing the two ablation strategies [10, 15, 16, 19, 21, 22].

There are unresolved questions when considering these different power-based approaches to AF ablation. For example, the definition of what constitutes a HPSD ablation is evolving and as a consequence may influence the likelihood of achieving a successful and safe ablation. There is variance in both the advocated power to use as well as the dwell time required. In our analysis, most of the included studies used a power setting of 40-50 W for 5-15 s. The study by Kottmaier et al. was the only included study that used a significantly higher power of 70W for 5-7 s, and was also one of the two studies that demonstrated significantly higher atrial arrhythmia recurrences with LPLD (32.3% vs 14.2%, OR=2.73, 95%CI:1.39-5.36, p=0.003) at 12-month follow-up [17]. The second study that demonstrated the benefit of HPSD was performed by Matiello et al. This study demonstrated a significantly higher AT recurrent with LPLD at 12 months (55% vs 35%, OR=2.20, 95%CI:1.03-4.7, p=0.041) where patients underwent higher power ablation with 40 W (vs 30 W in lower power ablation group)[18].

To date, there is no consensus on the standardized power and duration settings for HPSD ablation strategy and the boundaries of high-power settings to consider are increasing. Despite many experimental studies that used a higher range of ablation power [13, 14, 33], very few in-human clinical trials of HPSD ablation have adopted ablation power of more than 50W. For example, the Clinical Study for Safety and Acute Performance Evaluation of the THERMOCOOL SMARTTOUCH® SF-5D System Used With Fast Ablation Mode in Treatment of Patients With Paroxysmal Atrial Fibrillation (QDOT-FAST) trial was one of the few prospective in-human trials, albeit single-armed, that used very high ablation power of 90W for 4 seconds delivered by a novel contact force-sensing catheter with optimized temperature control, which reported that up to 94.2% of the patients remained in sinus rhythm over short-term follow-up (3 months) [34]. These results showed promising efficacy of a very high-power ablation setting delivered over a short duration, and further studies will be required to ascertain the most optimal power and timing for a HPSD ablation to allow a more precise definition and approach.

In addition to improving HPSD duration and approach, there are other reasons to consider that may influence the lack of benefit compared to LPSD. First, Ücer et al. reported 32% of patients who underwent a HPSD ablation, developed acute PV reconnections, unmasked by adenosine provocation test shortly after ablation [35]. High recurrence rates may reflect edema, incomplete lesion sets, or lack of consistent transmuralities across a heterogeneous atrial substrate. There are also areas of increased LA wall thickness (e.g. the mitral isthmus, the vein of Marshall/ridge, or the left atrial appendage orifice) in which a standardized, HPSD approach may not be able to create a transmural lesion and would potentially require a lower power and/or longer duration to allow the creation of deeper lesions without tissue overheating. [9]. In a recent study in porcine model, when ablation index (AI) was used as a predefined target for different power settings, HPSD ablation was found to lead to a significantly smaller lesion volume [36]. Additionally, an observational study found that HPSD ablation was associated with a higher risk of atrial flutter, a potential surrogate for incomplete sets/lines [16].

Nonetheless, HPSD ablation may have other unique advantages outside of efficacy. Due to shorter procedure time, HPSD ablation limits the patient's exposure to left atrial dwell time, intravenous fluids and anesthesia [16] and also reduces catheter motion, resulting in improved stability of energy delivery [37]. In our meta-analysis, we found that HPSD ablation significantly decreased total procedural time and ablation time, which

are consistent across every included study that reported this outcome [13, 22, 34, 38]. Bunch et al. is the only group that found a significant reduction in fluoroscopy time, whereas the other 4 studies that reported this outcome did not.

HPSD may also augment safety by minimizing risk of deep tissue heating that can result in esophageal injury, amongst others, given the relative shift to primarily resistive heating [39]. A significant finding from our study is that HPSD ablation had comparable safety profiles to the LPLD ablation strategy. Specifically, there were no statistically significant differences in incidence of periprocedural complications including atrial-esophageal fistula or ulcer formation and pericardial effusion or cardiac tamponade between the two ablation strategies. These data have to be considered cautiously as the incidences of these complications are low and even in a meta-analysis the study is underpowered to detect difference. Unfortunately, there was not adequate reported data from our included studies to run analyses for other complications such as stroke or transient ischemic attack, phrenic nerve injury and pulmonary vein stenosis. These results are congruent with several previous experimental and clinical studies [13, 14, 20, 39, 40].

Despite a promising safety profile, it is important to note that HPSD ablation has a narrow safety and efficacy window. Increasing ablation time with high power might lead to overheating resulting in creation of steam-pops, formation of thrombus, and excessive lesion depth, while inadequate ablation times can create non-transmural lesions, incomplete lesion sets, and pro-arrhythmia [41]. In a prospective clinical trial using ablation power of 90 W for 4 seconds, 1 of 52 patients developed an esophageal ulcer resulting in a hemorrhage [34]. As such, in addition to finding the most optimal ablation power, precise ablation duration is also critical to reduce the risks of complications. Methods to evaluate lesion formation in real-time is an area of interests. Magnetic resonance imaging (MRI) has been proposed as a tool to assess radiofrequency ablation lesions given its excellent myocardial scar or fibrosis visualization [42]. However, the use of real-time MRI to evaluate lesions is still in development and has yet to demonstrate clinical benefit [43-45].

5. Limitations

We acknowledge several limitations in our study. First there were significant variations in ablation power and duration between the included studies as we discussed. Each study also used different contact forces, types of catheters, target temperatures or ablation index, irrigation fluid delivery rate, all of which contributed to differences in lesion formation. Data extracted from the included studies were not adjusted for these variables. These factors, including operator experiences, likely contribute to the significant heterogeneity in the freedom from AT and procedural time (I2>50%). Second, all the studies included in our meta-analysis are non-randomized comparative studies. Further randomized controlled trials conducting head-to-head comparisons between the two ablation strategies will provide better evidence for the differences in outcomes. Third, we have a limited number of studies that reported comprehensive complication rates. Overall the event rates were low, and we further excluded several studies that reported no complications in both HPSD and LPLD group as they could not be statistically combined with other studies. As mentioned earlier, we did not have sufficient data to perform analysis for other complications such as stroke or transient ischemic attack, phrenic nerve injury and PV stenosis.

Acknowledgement

None

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Fig. 1: PRISMA flow diagram.

Fig. 2: Forest plot of the included studies comparing 12-month freedom from atrial tachyarrhythmia between high power, short duration strategy and low power, long duration strategy

Fig. 3: Forest plot of the included studies comparing total procedure time between high power, short duration strategy and low power, long duration strategy

Fig. 4: Forest plot of the included studies comparing ablation time between high power, short duration strategy and low power, long duration strategy

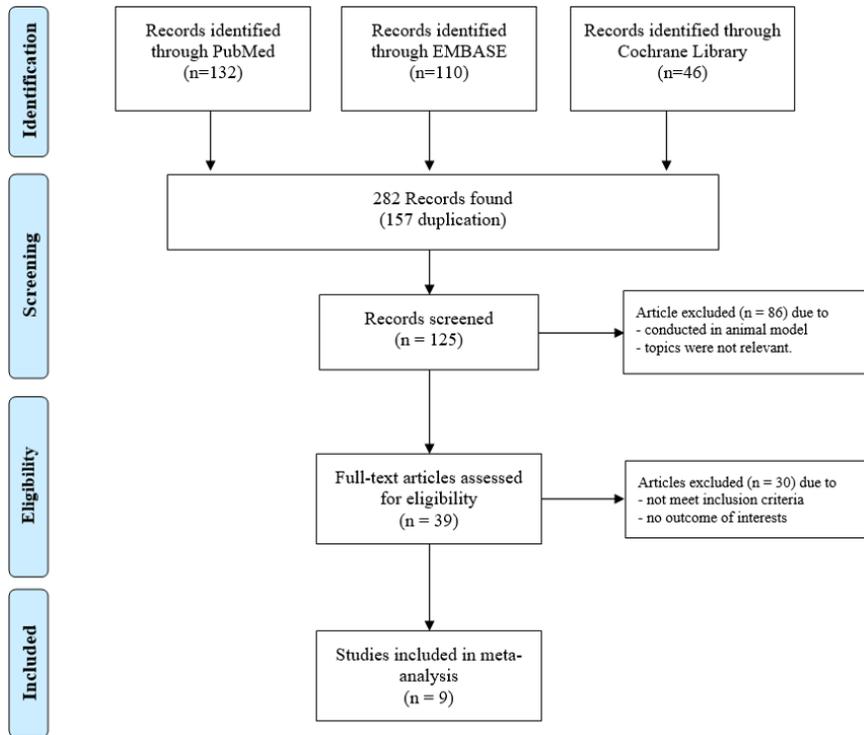
Fig. 5: Forest plot of the included studies comparing fluoroscopy time between high power, short duration strategy and low power, long duration strategy

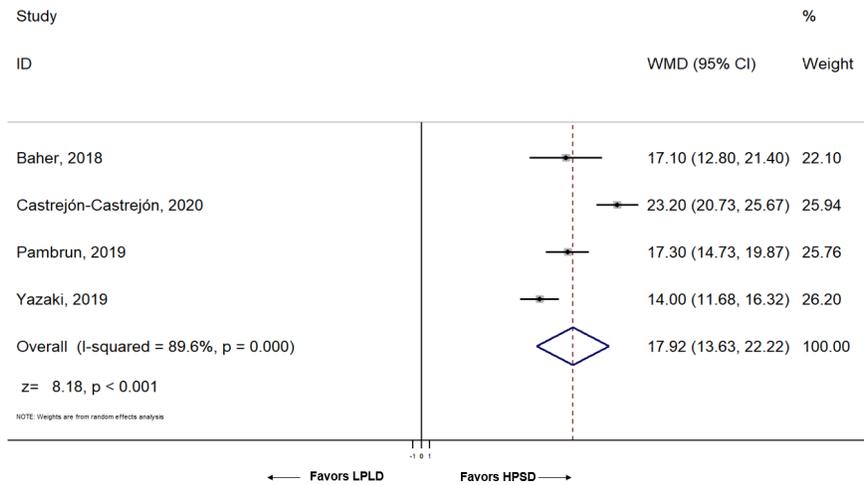
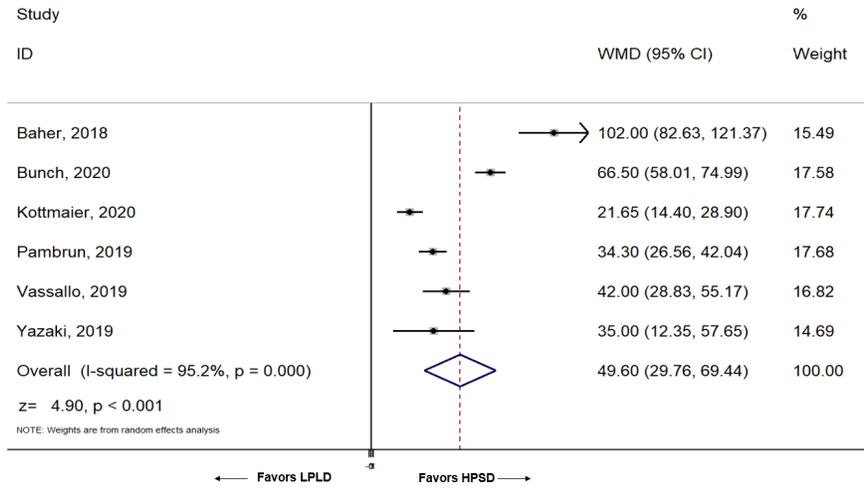
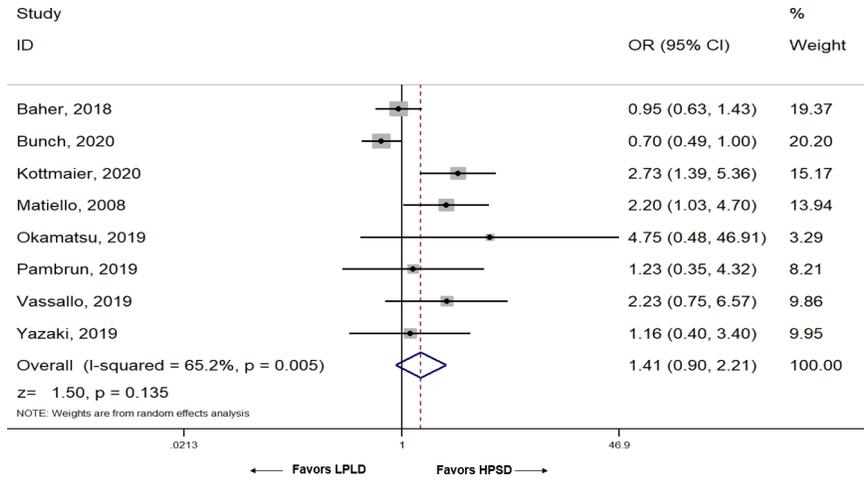
Fig. 6: Forest plot of the included studies comparing peri-procedure complications between high power, short duration strategy and low power, long duration strategy; 6A: Esophageal ulcer/arterioesophageal fistula, 6B: Pericardial effusion/cardiac tamponade

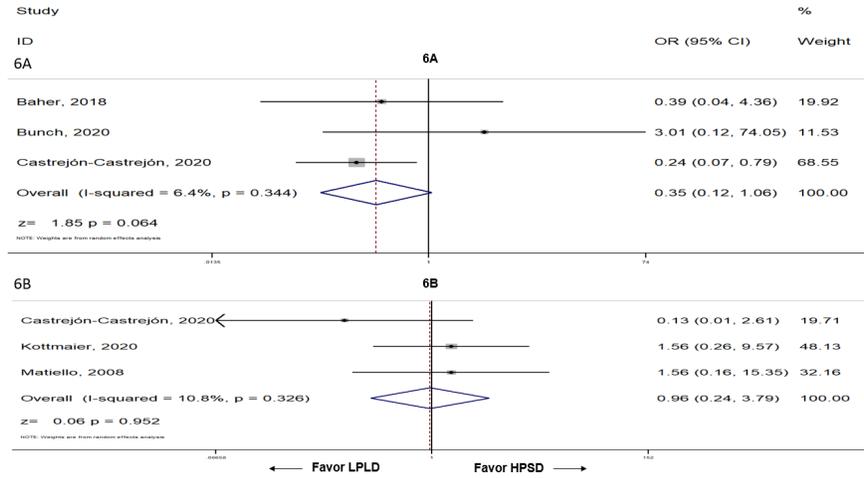
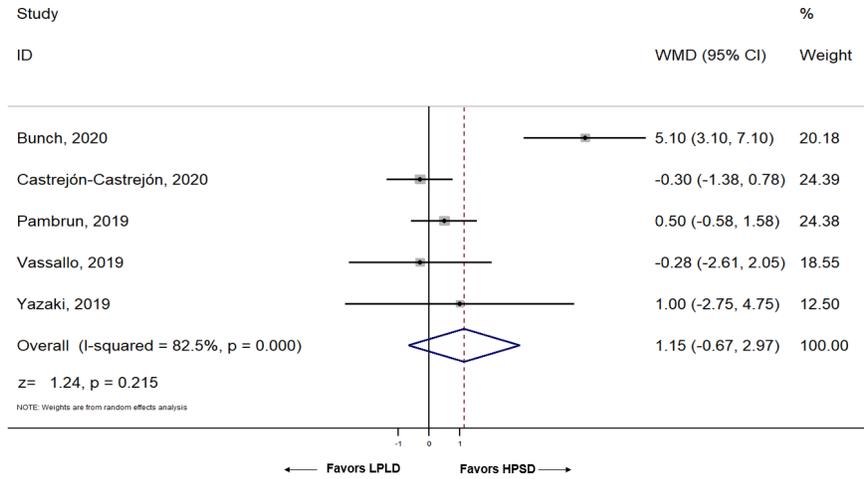
Supplementary material 1: Search term

Supplementary material 2: Newcastle-Ottawa scale of the included studies

Table 1: Study characteristics of included studies in the meta-analysis







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Table 1.revised.docx available at <https://authorea.com/users/315715/articles/477376-high-power-short-duration-and-low-power-long-duration-in-atrial-fibrillation-ablation-a-meta-analysis>