Systematic Review
Effect of Continuous Positive Airway Pressure after Pulmonary Vein Isolation in Obstructive Sleep Apnea Patients with Atrial Fibrillation: A Systematic Review and Meta-Analysis

Angkawipa Trongtorsak 1, Omar Khalil 2, Hussein Krayem 2, Mathurin Suwanwalaikorn 3, Kimberly R. Ding 4, Natchaya Polpichai 5, Ronpichai Chokesuwattanaskul 6 and Narut Prasitlumkum 7,*

1 Cardiovascular Medicine, Virginia Commonwealth University, Richmond, VA 23230, USA; angkawipa.trongtorsak@vcuhealth.org
2 Internal Medicine, Virginia Commonwealth University, Richmond, VA 23230, USA; omar.khalil@vcuhealth.org (O.K.); hussein.krayem@vcuhealth.org (H.K.)
3 Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand; mintmathurin@docchula.com
4 Department of Internal Medicine, Harbor-UCLA, Torrance, CA 90502, USA; kding247@gmail.com
5 Internal Medicine, Weiss Hospital, Chicago, IL 60640, USA; natchaya.giift@gmail.com
6 Cardiovascular Medicine, Chulalongkorn University, Bangkok 10330, Thailand; drronpichaic@gmail.com
7 Cardiovascular Medicine, Mayo Clinic, Rochester, MN 55905, USA
* Correspondence: prasitlumkum.narut@mayo.edu

Abstract: Background: Obstructive sleep apnea (OSA) was associated with atrial fibrillation (AF) as well as the recurrence of AF after rhythm control strategy. However, the data on continuous positive airway pressure (CPAP) and recurrent AF after catheter ablation with pulmonary vein isolation (PVI) remain unclear. We conducted this systematic review and meta-analysis to evaluate the effect of CPAP treatment in OSA patients after atrial fibrillation ablation.

Methods: We searched MEDLINE and Embase databases from inception to September 2023 to identify studies that assess the effect of CPAP in OSA patients on the recurrence of AF after PVI. Data from each study were combined using the random effects model.

Results: Eight studies (one randomized controlled trial and seven cohort studies) with 1487 OSA patients (660 in the CPAP group and 827 in the control group) were included. The use of CPAP in OSA patients was associated with significantly lower AF recurrence after PVI (odds ratio (OR) = 0.36, 95% confidence interval (CI) 0.25–0.53, \( p < 0.001 \)). The results of sensitivity analysis remain the same as the main analysis.

Conclusions: Our meta-analysis demonstrated that CPAP treatment was associated with lower rates of AF recurrence after PVI.

Keywords: atrial fibrillation; OSA; CPAP; pulmonary vein isolation

1. Introduction

Obstructive sleep apnea (OSA) is one of the most common sleep breathing disorders. OSA has been found to be associated with an increased risk of cardiovascular conditions including atrial fibrillation (AF). The meta-analysis by Moula et al. showed that the incidence of AF is 88% higher in OSA compared to those without OSA [1]. The pathophysiology of OSA and AF is complex and multifactorial. One hypothesis is that local hypoxia promotes oxidative stress and inflammatory processes, leading to atrial remodeling and fibrosis [2–4]. Autonomic dysfunction is also thought to play roles in developing AF in OSA. High parasympathetic activities during apneic episodes followed by an increase in sympathetic activities immediately after the apneic events can lead to atrial remodeling and promote arrhythmogenesis [5,6].

OSA has been found to be a predictor of AF recurrence after catheter ablation [7]. There have been efforts to explore the impact of treating OSA with continuous positive airway pressure (CPAP) on the burden of AF. However, the data on CPAP and recurrent AF after catheter ablation with pulmonary vein isolation (PVI) remain unclear. Given the paucity...
of research on this specific topic, the aim of this systematic review and meta-analysis is to further investigate and summarize the effect of CPAP treatment in OSA patients after AF ablation and its risk of recurrence depending on CPAP use.

2. Materials and Methods

2.1. Search Strategy

Two investigators (AT and MS) independently performed a systematic search of the MEDLINE and Embase databases from inception to September 2023 using a search strategy including the terms “obstructive sleep apnea”, “continuous positive airway pressure”, “atrial fibrillation ablation”, and “pulmonary vein isolation”, as described in Supplementary Material. We hand-searched the bibliographies of selected studies and meta-analyses to identify further eligible studies. Only full articles in English were included.

2.2. Selection Criteria

Eligible studies for this systematic review and meta-analysis were matched cohort studies or randomized controlled trials (RCTs) that assess the effect of CPAP in OSA patients on the recurrence of AF after PVI. Relative risk, odds ratio, hazard ratio with 95% confidence intervals (CI), or sufficient raw data to calculate effect size must be provided.

2.3. Data Extraction and Quality Assessment Tool

Two authors (NP and HK) independently extracted the data from included studies, with disputes resolved by consensus following discussion with a third author (AT). Included studies were assessed using the Newcastle–Ottawa Scale (NOS) for quality assessment [8].

2.4. Outcomes

The primary outcome was the recurrence of AF after PVI in OSA using CPAP compared to those that did not use CPAP.

2.5. Statistical Analysis

This meta-analysis was performed using a random effects model. The hazard ratio (HR) was used to determine the difference in outcomes between the two groups. The Q-statistic and I² statistic were used to assess evidence of heterogeneity [9]. The I² statistic ranges in value from 0 to 100% (I² < 25%, low heterogeneity; I² = 25–50%, moderate heterogeneity; and I² ≥ 50%, substantial heterogeneity) [10]. Publication bias was assessed using a funnel plot, Begg’s test, and Egger’s test [11,12]. The p-value < 0.05 in publication bias tests was suggestive of publication bias. Sensitivity analysis was also performed to assess the influence of individual studies on the overall meta-analysis, as described by Patkopoulos et al. [9,13]. Sensitivity analysis was performed for each outcome by excluding one study at a time to assess the stability of the results of the meta-analysis. All analyses were conducted using Review Manager 5.1 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) and STATA software (version 14 STATA Corp, College Station, TX, USA).

3. Results

3.1. Literature Search

The initial literature search identified 1894 studies from MEDLINE and Embase databases. We excluded 505 studies due to duplication. A total of 1076 studies were excluded as they were not cohort studies, case-control studies, experimental trials, or RCTs or did not study the population of interest. This left 13 studies for full-text review. A total of 5 studies were further excluded due to reasons given in the PRISMA flow diagram in Figure 1. Therefore, 8 studies were included in this meta-analysis [14–21].
Figure 1. PRISMA flow diagram.

3.2. Description of Included Studies

A total of 8 studies were included in this meta-analysis. There was 1 RCT and 7 cohort studies. The final analysis included a total of 1487 patients (660 in the CPAP group and 827 in the control group). The baseline characteristics of the included studies are shown in Table 1.

Table 1. The baseline characteristics of the included studies [14–21].

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Total (CPAP/No CPAP)</th>
<th>Mean Age ± SD (Treatment/Control)</th>
<th>Male (%)</th>
<th>Mean BMI (kg/m²)</th>
<th>LA Size (cm²) or LA Dimension (mm)</th>
<th>LVEF (%)</th>
<th>Persistent AF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fein</td>
<td>2013</td>
<td>USA</td>
<td>62 (32/30)</td>
<td>56.8 ± 1.2/58.5 ± 1.4 (p = 0.27)</td>
<td>76.7/71.9</td>
<td>28.7 ± 0.45/29.58 ± 0.4 (p = 0.11)</td>
<td>54.5 mm/55.9 mm (p = 0.51)</td>
<td>60.2/59.5 (p = 0.96)</td>
<td>N/A</td>
</tr>
<tr>
<td>Hunt</td>
<td>2022</td>
<td>Norway</td>
<td>83 (37/46)</td>
<td>62 ± 8/62 ± 7 (p = 0.22)</td>
<td>76/80 (p = 0.63)</td>
<td>30.0 ± 3.9/29.9 ± 4.1 (p = 0.22)</td>
<td>25.2 cm² ± 4.0 / 24.5 cm² ± 4.9 (p = 0.88)</td>
<td>56.7/57.1 (p = 0.87)</td>
<td>N/A</td>
</tr>
<tr>
<td>Jongnarungsin</td>
<td>2008</td>
<td>USA</td>
<td>32 (18/14)</td>
<td>59 ± 7</td>
<td>81.25</td>
<td>36 ± 7</td>
<td>46 mm ± 7</td>
<td>51</td>
<td>28</td>
</tr>
<tr>
<td>Naruse</td>
<td>2013</td>
<td>Japan</td>
<td>116 (82/34)</td>
<td>N/A but no significant difference (p = 0.6)</td>
<td>N/A but no significant difference</td>
<td>25.3 ± 3.1/25.3 ± 3.6</td>
<td>41.6 ± 6.2 mm/41 mm ± 7.1 (p = 0.96)</td>
<td>N/A but no significant difference</td>
<td>N/A but no significant difference</td>
</tr>
<tr>
<td>Neilan</td>
<td>2013</td>
<td>USA</td>
<td>142 (71/71)</td>
<td>56 ± 9/57 ± 10 (p = 0.39)</td>
<td>32.7 ± 6/32.7 ± 5 (p = 0.02)</td>
<td>41 ± 6 mm/44 ± 6 mm (p = 0.002)</td>
<td>56/55 (p = 0.27)</td>
<td>55/73 (p = 0.04)</td>
<td></td>
</tr>
<tr>
<td>Patel</td>
<td>2010</td>
<td>USA</td>
<td>640 (315/325)</td>
<td>49 ± 8/53 ± 12 (p &lt; 0.001)</td>
<td>30 ± 3/31 ± 2 (p = 0.098)</td>
<td>40 ± 6 mm/50 ± 8 (p &lt; 0.001)</td>
<td>50/48 (p = 0.175)</td>
<td>52/67 (p &lt; 0.001)</td>
<td></td>
</tr>
<tr>
<td>Suzuki</td>
<td>2021</td>
<td>Japan</td>
<td>290 (43/247)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Zhou</td>
<td>2022</td>
<td>China</td>
<td>122 (62/60)</td>
<td>59.8 ± 13.4/62.3 ± 9.7 (p = 0.19)</td>
<td>72.6/76.7 (p = 0.23)</td>
<td>29.9 ± 0.56/30.5 ± 0.71 (p = 0.42)</td>
<td>45 ± 2.7 mm/44 ± 3.5 mm (p = 0.07)</td>
<td>52/30 (p = 0.35)</td>
<td>95.1/96.7 (p = 0.09)</td>
</tr>
</tbody>
</table>

AF: atrial fibrillation; BMI: body mass index; cm²: square centimeter; mm: millimeter; CPAP: continuous positive airway pressure; LA: left atrial; LVEF: left ventricular ejection fraction; N/A: not available; SD: standard deviation.
3.3. Quality Assessment Tool

The NOS of the included studies are described in Supplementary Table S2.

3.4. Meta-Analysis Results

3.4.1. Meta-Analysis Results

AF recurrent rates after AF ablation with PVI were 32.3% and 43.9% in the CPAP group and the control group, respectively. The CPAP group had significantly lower AF recurrence after PVI (odds ratio (OR) = 0.36, 95% CI 0.25–0.53, p < 0.001, I² = 55%), as shown in Figure 2.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[()]</th>
<th>SE</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fein 2013</td>
<td>-1.4848</td>
<td>0.546</td>
<td>8.3%</td>
<td>0.23 (0.08, 0.66)</td>
<td></td>
</tr>
<tr>
<td>Hunt 2022</td>
<td>0</td>
<td>0.4426</td>
<td>10.9%</td>
<td>1.00 (0.42, 2.38)</td>
<td></td>
</tr>
<tr>
<td>Jongnarrangsin 2008</td>
<td>-0.9163</td>
<td>0.7565</td>
<td>5.1%</td>
<td>0.40 (0.09, 1.76)</td>
<td></td>
</tr>
<tr>
<td>Naruse 2013</td>
<td>-0.942</td>
<td>0.419</td>
<td>11.6%</td>
<td>0.39 (0.17, 0.89)</td>
<td></td>
</tr>
<tr>
<td>Neitan 2013</td>
<td>-1.4271</td>
<td>0.2069</td>
<td>20.3%</td>
<td>0.24 (0.16, 0.36)</td>
<td></td>
</tr>
<tr>
<td>Patel 2010</td>
<td>-0.8845</td>
<td>0.1634</td>
<td>22.3%</td>
<td>0.41 (0.30, 0.57)</td>
<td></td>
</tr>
<tr>
<td>Suzuki 2022</td>
<td>-0.3843</td>
<td>0.5061</td>
<td>9.2%</td>
<td>0.68 (0.25, 1.84)</td>
<td></td>
</tr>
<tr>
<td>Zhou 2022</td>
<td>-1.7492</td>
<td>0.399</td>
<td>12.3%</td>
<td>0.17 (0.08, 0.38)</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 100.0% 0.36 [0.25, 0.53]

Heterogeneity: Tau² = 0.14; Chi² = 15.51, df = 7 (P = 0.03); I² = 55%
Test for overall effect: Z = 5.35 (P < 0.000001)

Figure 2. Forest plot showing that use of CPAP was associated with favorably lower risk of AF recurrence from pooled meta-analyses of studies involving OSA patients who underwent AF ablation [14–21].

3.4.2. Sensitivity Analysis and Publication Bias

We conducted a sensitivity analysis for each outcome by excluding one study at a time to assess the stability of the results of the meta-analysis. None of the results were significantly altered, as the results were similar to those of the main meta-analysis, indicating that our results were robust, as shown in Supplemental Table S3.

We aimed to assess publication bias using a funnel plot, Begg’s test, and Egger’s test. However, as we have only 8 studies, we have insufficient power to reject the assumption of no funnel plot asymmetry. Therefore, we did not perform a funnel plot, Begg’s test, or Egger’s test [22,23].

4. Discussion

In this meta-analysis, we determined the effect of CPAP in OSA with AF after AF ablation with PVI on the rates of AF recurrence. The pooled analysis of included 8 studies including 1487 patients with OSA undergoing AF ablation with PVI showed that patients with CPAP treatment were significantly associated with lower AF recurrence after PVI compared to those who were not on CPAP.

OSA has been well-known to be significantly associated with an increased risk of arrhythmias including AF. The pathophysiology of developing AF is multifactorial, including inflammation, autonomic dysfunction, and atrial remodeling [24–26]. Moreover, previous studies have reported that OSA patients had dramatically higher rates of AF recurrence after catheter ablation. The meta-analysis in 2014 by Li et al. revealed that patients with OSA had 31% greater risks of AF recurrence after catheter ablation compared to those without OSA undergoing ablation (p < 0.001) [27]. The updated meta-analysis by Congrete et al. in 2018 also demonstrated similar findings. The authors showed that the odds of AF recurrence after successful ablation in OSA were 1.7 (p < 0.001) [28].

CPAP remains a gold standard and first-choice treatment for OSA. The device increases the upper airway pressure and then allows OSA patients to maintain upper airway patency throughout their sleep [29]. CPAP reduces episodes of hypoxia in OSA patients at night,
resulting in a reduction in systemic inflammation, autonomic dysfunction, and atrial fibrosis. Studies reported that after the CPAP treatment, the inflammatory marker levels including C-reactive proteins, interleukin, and tumor necrosis factor were significantly reduced [30–32]. The study by Narkiewicz et al. showed that OSA patients with CPAP treatment at 1 year can experience decreased muscle sympathetic nerve activities [33]. These may explain why those with CPAP had lower rates of AF recurrence after PVI.

Our results were in concordance with previously published studies. The meta-analysis by Congrete et al. in 2018 including 5 studies found that treating with CPAP resulted in almost 0.3-fold reduction in AF recurrence after ablation [28]. We have included 3 more studies with bigger sample size, giving more power to the study. This finding supported that CPAP treatment can reduce rates of AF recurrence in OSA undergoing PVI. Even though the CPAP group had significantly lower rates of AF recurrence after PVI compared to the non-CPAP group, one-third of patients experienced AF recurrences. The exploration of factors that lead to recurrences of AF might help us to find solutions to help patients with OSA maintain sinus rhythm after PVI.

Our study is not without limitations. First, most of the studies included were observational studies. This carries a risk of potential biases due to the nature of their study design. Further studies with better baseline adjustment are needed to support our hypothesis. Second, our study was based on published studies, and due to the limited number of studies, we were unable to perform analysis to assess publication bias. However, we did perform sensitivity analysis, which showed similar findings to the main analysis.

5. Conclusions

Our study suggested that CPAP treatment on OSA patients might be effective for a reduction in AF recurrences in those who obtained AF ablation with PVI. However, further studies with better baseline adjustment are needed to support our findings.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ohbm5020009/s1, Table S1: search strategy; Table S2: the Newcastle-Ottawa Scale (NOS) for quality assessment; Table S3: Sensitivity analysis for AF recurrence after PVI.

Author Contributions: Conceptualization, A.T., N.P. (Narut Prasitlumkum) and R.C.; methodology, N.P. (Narut Prasitlumkum), R.C. and M.S.; software, N.P. (Narut Prasitlumkum) and R.C.; validation, A.T., O.K., N.P. (Narut Prasitlumkum) and R.C.; formal analysis, N.P. (Narut Prasitlumkum); investigation, A.T., O.K., H.K. and M.S.; resources, R.C. and N.P. (Narut Prasitlumkum); data curation, A.T., O.K., H.K., M.S., K.R.D. and N.P. (Natchaya Polpichai); writing—original draft preparation, A.T., O.K. and M.S.; writing—review and editing, A.T., N.P. (Narut Prasitlumkum) and R.C.; visualization, K.R.D., N.P. (Natchaya Polpichai) and M.S.; supervision, N.P. (Narut Prasitlumkum) and R.C.; project administration, N.P. (Narut Prasitlumkum) and R.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Ethical review and approval were waived for this study as this systematic review and meta-analysis was conducted using publicly available data.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data sharing will be available upon request to the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

References


**Disclaimer/Publisher’s Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.