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Impact of pulmonary hypertension in patients undergoing atrial fibrillation ablation: A nationwide study

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1. Introduction

Pulmonary hypertension (PH) is a chronic pulmonary vascular disorder that can be caused by a variety of pathophysiological states. Five groups of PH sharing similar hemodynamics, and management were identified: 1) pulmonary arterial hypertension (Group 1); 2) PH due to left heart disease (Group 2); 3) PH due to chronic lung disease (Group 3); 4) chronic thromboembolic PH (Group 4); and 5) miscellaneous mechanisms (Group 5) [1]. Physiologically, PH is defined as mean pulmonary artery pressure (mPAP) ≥ 25 mm Hg at rest or >30 mm Hg with exercise. Clinically, PH leads to right heart ventricular failure and cardiac death [2,3]. Group 2 PH is found commonly and is reported in >60% of heart failure patients [4].

Patients with chronic left heart failure often have other atrial arrhythmias. Atrial fibrillation (AF) is commonly encountered in >3 million people in the United States [5]. Heart failure patients are 5 to 10 times more likely to develop AF than healthy patients [6,7]. AF portends a worse long-term prognosis attributable to the loss of atrial kick, loss of atrioventricular synchrony, and the increased risk of stroke [8,9]. Similarly, the prevalence of Group 2 PH related AF is as high as 57%, and 23% in other forms of PH [10].

The cornerstone of surgical treatment of AF has been AF ablation. Haussaiguarre et al. first reported that AF initiates in the posterior wall of the left atrium near the ostium of pulmonary veins [11]. AF ablation is achieved either radio-frequency (electrocautery) or cryoablation. To date, limited data are available regarding the impact of PH on patients undergoing AF ablation. Therefore, we have demonstrated the effect of PH in patients getting AF ablation in this National Inpatient Sample (NIS) analysis.

2. Methods

We have conducted a retrospective cohort study using the most recent 2016 NIS database, which is collected by the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project (HCUP). It is the largest all-payer inpatient publicly available database in the United States. It consists of 20% of all hospital discharges of all non-federal hospitals. The ICD-10 codes were used for the diagnosis of PH and AF ablation. We include the patients age ≥ 18 yrs. with a history of PH undergone AF ablation during hospitalization. Primary outcomes of interest were mortality. Secondary outcomes of interest included acute kidney injury (AKI), length of stay (LOS) and cost of care. Continuous variables were reported as mean (standard deviation) and categorical variables were expressed as frequencies (percentages). Multiple imputation was used to exclude the missing values. Multivariate logistic regression was used for adjustment of potential confounders including age, gender, race, socioeconomic status, diabetes (DM), hypertension (HTN), smoking, alcohol use, chronic kidney disease (CKD), obstructive sleep apnea(OSA), obesity, dyslipidemia, congestive heart failure(CHF) Charlson Comorbidity Index, hospital location, hospital region, teaching status, and hospital size. STATA 15.0/IC has been used for analysis. Institutional Review Board (IRB) of Mount Sinai St Luke's Roosevelt exempt this study from IRB approval as it is publicly available database containing de identified patient's information.

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3. Results

Among 152,385 patients with a history of AF ablation, 1855 were found to have PH (group A). Patients without PH were in group B. Mean age of the patients in group A was 67.7 years (56.7 to 78.6 years), and that of group B was 65.5 years (65 to 66 years). 85.7% of patients in group A were female; on the other hand, 39.6% of patients in the other group were female (p-value < 0.05). The proportion of patients with HTN (14% vs. 49%), smoking (14% vs. 27.8%), dyslipidemia (14% vs. 46%), CKD (14% vs. 20%), and CHF (30.3% vs. 14.3%) were higher in group B in comparison to group A but without any statistical significance. There was a significant difference in the percentage of obese patients (57% vs. 20%; p-value 0.01) between these two groups. There was statistically non-significant more number of OSA patients in group A in comparison to group B (42.86% vs. 16.8%). The length of stay (p-value 0.233) and cost of care (p-value 0.30) were higher in the group of patients with PH but failed to show any statistical significance. We have demonstrated a significant increase in acute kidney injury (AKI) [Odds Ratio (OR): 8.50 (1.35–54), p: 0.023] after multivariate analysis in patients having AF ablation with PH compared to the patients undergoing AF ablation without PH. The total number of deaths was 380 (Table 1).

4. Discussion

AF affects 2% of the population in the United States (US) with increased stroke risk associated with additional cardiac comorbidities [12]. The burden of AF is expected to rise by three-fold as the general US population gets older [13]. While some pharmacological therapies such as beta blockers and cardioversion offer mortality benefit, interventional therapies, such as AF ablation, offer alternative treatment options. AF ablation has an essential impact on the patient's lives as it helps them be free from long-standing medications. AF ablation is typically achieved via pulmonary vein isolation and the success rate is reported to be between 50 and 75%. Usually, higher success rates are noted in patients with paroxysmal AF compared to persistent AF [14–16]. Sparse data are available about the impact of pre-existing PH in patients undergoing such a procedure.

Utilizing the large NIS sample of 152,385 patients in 2016, we showed the following significant findings: 1) a higher percentage of female patients were found in patients with PH undergoing AF ablation than in patients without PH undergoing the same procedure. 2) More obese patients were found in the PH group than the non-PH group. 3) After multivariate analysis, the odds of AKI were significantly higher in patients undergoing AF ablation with PH compared to the non-PH group; 4) the incidence of mortality was 0.25% in all patients undergoing AF ablation and 5) no significant differences were noted in length of stay or cost of care between PH and non-PH groups.

AF related cardiovascular morbidity and mortality is significantly higher in women [7]. Women with AF also tended to have a poor quality of life, poorer physical health, and functional status [17]. The RACE study also showed that women did worse with a rhythm control strategy [18]. Thus, catheter ablation of AF may be an effective modality of treatment for women, yet women are referred three-times less frequently for catheter ablations [19]. Typically, literature has shown that women undergoing AF ablation are an independent predictor of procedural or vascular complications such as cardiac tamponade [20]. However in our study, the national trend from the NIS database suggests that a higher percentage of women with PH are undergoing AF ablation. The following fact can explain this finding that as the catheter technology improves, experienced electrophysiologists can tackle a greater number of patients with co-morbidities such as obesity and PH including the female patients.

Similarly, obesity is another risk factor which is associated with worse outcomes in AF ablation driven by vascular complication [21,22]. Obesity increases the prevalence of AF, but paradoxically patients with AF and obesity have a better prognosis than thinner patients with AF [23]. This should not stop aggressive risk factor modification by weight loss for the management of patients with AF. Obese patients are more likely to develop PH from long-standing sleep apnea/obesity hypoventilation syndrome [23]. Interestingly, the percent of AF obese patients with PH undergoing ablation was also significantly higher in our study database.

The cardiorenal syndrome typically emphasizes the function of left ventricle leading to renal arterial under perfusion. But, the right ventricle (RV), the often "forgotten ventricle," which is also subject to dysfunction with chronic PH is an essential determinant of AKI and AKI-associated mortality [24,25]. The RV dysfunction affects the kidney by venous congestion, which as postulated to cause increased sodium retention, lowered urinary output and decreased glomerular filtration rate [26]. Chen et al. showed that in critically ill patients with isolated RV dysfunction and AKI there was an 8-fold increased risk of death [25]. Our study cohort findings of increased AKI in patients with PH are likely to be a consequence of RV failure than AF ablation. Other factors that can affect the kidney function are baseline volume status of the patients, duration of AF ablation procedure, the perceived assessment of volume status during the procedure by the electrophysiologist or anesthesiologist of the patients with ascites and lower extremity edema.

There was no significant difference in length of stay or cost of care between patients with PH and patients without PH. The mean duration of stay was 11-days in PH group compared to 5-days in the non-PH group. One possible explanation is AF ablation is often an elective procedure with a patient presenting in a compensated euvolemic state on optimized medical therapy.

Table 1
Baseline demographics, comorbidities and in-hospital outcomes in patients undergoing atrial fibrillation (AF) ablation (n = 152,385) with and without pulmonary hypertension (PH).

	With PH (n = 1855)	Without PH (n = 150,530)	Adjusted Odds Ratio (OR) or β coefficient (95% CI) (AF ablation with PH compared to AF ablation without PH)	p value
Mean age	67.7(56.7–78.6)	65.5 (65–66)		0.70
Female gender	85.7%	39.6%		0.01
Hypertension	14%	49%		0.06
Diabetes	28%	28%		0.98
Smoker	14%	27.8%		0.42
Dyslipidemia	14%	46%		0.08
Obesity	57%	20%		0.01
CKD	14%	20%		0.70
OSA	42.86%	16.8%		0.07
CHF	14.3%	30.3%		0.36
Length of stay	11(4–7.9)	5.3 (5–5.6)	5.8 (−3.7–15)	0.23
Cost of care	213,220	148,409	117,998	0.30
Acute kidney injury			OR: 8.5 (1.35–54)	0.02

Total deaths: 380.
CKD: chronic kidney disease, OSA: obstructive sleep apnea, CHF: congestive heart failure.

5. Limitations

Being a retrospective analysis using administrative database this study does have some limitations. NIS database does not code for the severity of PH, imaging details, and it is vulnerable to coding errors. We lack information on the prevalence of different WHO groups of PH and the mean duration of AF ablation procedure. The factors mentioned above that can affect the kidney function status were also not accounted for in our study. Despite accounting for some major confounders and performing multivariate analysis, we are likely missing information on some confounders, thus introducing a certain extent of bias. But the NIS database is representative of >95% of the US population and is a well-validated tool. The reaching implications of this study are to

recognize RV dysfunction, AKI, and PH as factors that may potentially influence the outcomes of AF ablation.

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