

Pulmonary vein stenosis

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INTRODUCTION

Radiofrequency catheter ablation (RFCA) to treat atrial fibrillation (AF) was introduced into clinical medicine in 1987. Initially ablation was performed inside the pulmonary veins (PV), but this caused pulmonary vein stenosis (PVS) in some patients. The technique was then modified to move the ablation lines to the ostium of the veins and then eventually outside the ostium using a circumferential configuration. Symptoms of pulmonary venous stenosis and/or occlusion secondary to catheter ablation can develop anytime between several weeks to several months after the procedure; the presentation is not specific and is similar to other more common pulmonary and cardiac diseases.^{1,2,3,4} Consequently, post-procedural monitoring of symptoms and a high clinical suspicion are necessary to make this diagnosis. We provide a brief review of this complication.

MECHANISM OF INJURY

In experimental animal studies, energy application results in membrane abnormalities leading to cardiomyocyte death, intimal thickening, organizing thrombus, endovascular contraction of the media, deposition of extracellular matrix, and proliferation of the elastic lamina.⁵ The development of PVS depends on the amount of energy applied. Histologic examination of pulmonary veno-occlusive disease in patients following RFCA shows markedly thickened vein walls

due to cardiomyocyte death followed by myofibroblast proliferation, resulting in luminal sclerosis of the post-capillary veins and recurrent alveolar hemorrhage. Not only are the large pulmonary veins obstructed, but the small pulmonary veins within the lung and the intrapulmonary arteries exposed to high pressures in the distal pulmonary bed are narrowed.⁶

PRESENTATION AND DIAGNOSIS

Pulmonary vein stenosis is classified as mild when luminal narrowing is 20-50%, moderate when 50–69%, and severe when more than 70%.^{7,8} The severity of symptoms is associated with the degree of stenosis.^{7,9} Patients may present with progressive dyspnea, chest pain, cough, or hemoptysis. Some patients remain asymptomatic with single-vessel stenosis, even with a complete occlusion, or with mild to moderate stenosis of more than one vessel.^{1,7} In these cases, recognition of this complication may be delayed or unrecognized.

The lack of a specific presentation or unique characteristics of PVS makes it very difficult to diagnose.^{7,10,11} Not only is the clinical picture challenging, but the plain chest x-ray, CT radiography, and V/Q scans can be misleading and suggest other diagnoses, such as pneumonia, pulmonary embolism, tuberculosis, and lung cancer. Plain chest and CT radiography show mainly consolidations and/or pleural effusions.^{1,7} V/Q scans may reveal mismatch defects, similar to pulmonary emboli.^{1,7,12} Pulmonary vein stenosis can be accurately diagnosed with multislice spiral chest CT angiography (MCTA), magnetic resonance perfusion imaging, and catheter venography. In 2004, Burgstahler and his colleagues studied the utility and diagnostic accuracy of MCTA in the detection of PVS and compared it to conventional angiogra-

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phy.¹³ Thirty-three patients were retrospectively evaluated with MCTA scans within 1 day to 380 days after RFCA. These studies were compared to conventional angiography which was performed routinely before and after the RF ablation. Pulmonary vein stenosis was detected by conventional angiography in 26 of 73 targeted pulmonary veins (36%); two had severe obstruction (>50%),¹⁴ had intermediate obstruction (20-50%), and 10 had mild obstruction (<20%). Using MCTA, PVS was found in 13 of 73 (17%; one severe, six intermediate, and six mild). The authors concluded that MCTA can identify PVS in some but not all patients. However, the severity of stenosis seems to be underestimated, and not all lesions could be accurately detected.¹³

OUTCOMES

Saad, *et al.* reported outcomes in 608 patients undergoing RFCA for AF.⁷ These patients had spiral CT angiography before and at 3, 6, and 12 months after the procedure. Ninety-five patients (15.6%) had PV stenosis post RFCA; 21 had severe stenosis, 27 had moderate stenosis, and 47 had mild stenosis. Patients with severe stenosis had dyspnea (11 patients), cough (8), chest pain (6), hemoptysis (5), and no symptoms (8). All patients with severe stenosis had V/Q mismatch on V/Q scans. Patients with symptoms had more than one vein involved. Balloon angioplasty was done in 17 of the 21 patients with severe stenosis, including 10 with stent placement. One patient had pulmonary hypertension which resolved after stent placement. Symptom improvement occurred in 10 patients. However, eight developed restenosis, and four required a second intervention. Progression of stenosis occurred in 22 patients (8.8%) of 249 with serial scans; regression occurred in 26 patients (10.4%).

Yamaguchi and his co-workers reported a prospective observational study with 238 patients who had paroxysmal AF (PAF) undergoing radiofrequency hot balloon catheter ablation between 2006 and 2009 to evaluate the effectiveness and safety of

this procedure.³ Follow-up continued for 75 months (2009-2014). Enhanced 3-dimensional computed tomography (CT) was used to evaluate the targeted PV diameter before and at 3, 6, and 12 months following the procedure in all patients. Four patients (1.7%) developed asymptomatic significant PV stenosis (>70% reduction in PV diameter). These four patients were monitored for five years and did not require interventions.³ This report did not include the number of the mild and moderate PVS cases.

PVS is a well recognized complication of radiofrequency energy application, but it remains a rare complication after cryo-ablation.^{12,14,15} Thomas and his colleagues reported a 45-year-old man who underwent a cryo-ablation for PAF.¹⁵ At a three month follow-up the patient was found to have asymptomatic left superior PVS, approximately 70% by pulmonary venography done as a pre-procedure evaluation prior to the next cryo-ablation for recurrent PAF.¹⁵ These authors suggested that mechanical pressure applied by the balloon catheter could contribute to myocardial injury. A prospective observational study with 24 patients with PAF following a cryothermal ablation of 46 pulmonary veins to evaluate for PVS with CTA showed no change of PV diameter of any veins at three months follow-up.¹⁶

TREATMENT

The long term progression and management of PVS are unclear and challenging.¹⁷ Yang, *et al.* and Di Biase, *et al.* have suggested that early intervention in severely symptomatic PVS improves clinical symptoms and the long-term outcomes.^{11,18} The main treatment modality for PVS usually involves balloon angioplasty and/or stent implantation.^{9,11,18} Holmes, *et al.* prefer balloon dilation as a primary intervention and stent placement in cases of restenosis.⁹ Packer and his coworkers reported 23 patients with severe stenosis in 34 pulmonary veins who underwent either dilation followed by stenting or stenting as the initial intervention. Significant PVS with or without symptoms was treated to prevent development of pulmonary hypertension, progression to total occlusion, and recur-

rent pneumonia. Fourteen (60%) had restenosis and required repeat stentings (total of 2-4 repeated stentings). Despite restenosis in some pulmonary veins all patients remained asymptomatic during follow-up at 7 ± 2 months after intervention.¹² Prieto, *et al.* reported that stent angioplasty was associated with a lower rate of restenosis (33% of stented veins vs. 72% balloon dilated veins) and that restenosis was less frequent with larger stents (>10mm).¹⁹ The recent use of drug-eluting stents, such as paclitaxel-eluting stents, has reduced the restenosis rate significantly.^{20,21} Important complications associated with angioplasty and stenting include pulmonary hemorrhage, PV tears requiring immediate surgery, and cerebral embolic events.²

CONCLUSIONS

Symptoms in patients with PVS secondary to AF ablation develop during variable time periods following the procedure. The condition is likely underdiagnosed due to lack of specific presentation with inconsistent follow up. Previous reports and available experience suggest that the occurrence and severity of symptoms are related both to the degree of luminal narrowing and to the number of pulmonary veins affected. Post-procedural observation and monitoring of the symptoms and diagnostic imaging modalities, including spiral CT scans or magnetic resonance imaging and magnetic resonance angiography, should detect this complication. Detecting PVS acutely with selective angiogram is relatively simple. However, identification of slowly progressing PVS in follow-up visits is challenging. Transesophageal echocardiography provides reliable, cost-effective, non-invasive follow-up in cases of moderate-severe PVS. Establishing accurate diagnosis of PVS is very difficult. Therefore, a careful review of the medical history and follow-up is needed in all the patients who have RFCA to recognize PVS in an early stage. Finally, the methods used for ablation are evolving and complication rates may be changing.

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REFERENCES

1. Lu HW, Wei P, Jiang S, Gu SY, Fan LC, Liang S, Ji X, Rajbanshi B, Xu JF. Pulmonary Vein Stenosis Complicating Radiofrequency Catheter Ablation: Five Case Reports and Literature Review. *Medicine* 2015 Aug; 94(34):e1346.
2. Qureshi AM, Prieto LR, Latson LA, *et al.* Transcatheter angioplasty for acquired pulmonary vein stenosis after radiofrequency ablation. *Circulation* 2003; 108:1336–1342.
3. Yamaguchi Y, Sohara H, Takeda H, Nakamura Y, Ihara M, Higuchi S, Satake S. Long-Term Results of Radiofrequency Hot Balloon Ablation in Patients with Paroxysmal Atrial Fibrillation: Safety and Rhythm Outcomes. *J Cardiovasc Electrophysiol* 2015 Sep 2. doi: 10.1111/jce.12820.
4. De Greef Y, Schwagten B, De Keulenaer G, Stockman D. Pulmonary vein stenosis after pulmonary vein ablation catheter-guided pulmonary vein isolation. *Heart Rhythm* 2010 Sep; 7(9):1306-8.
5. Taylor GW, Kay GN, Zheng X, Bishop S, Ideker RE. Pathological effects of extensive radiofrequency energy applications in the pulmonary veins in dogs. *Circulation* 2000; 101 (14):1736-1742.
6. Ernst S, Ouyang F, Goya M, Lober F, Schneider C, Hoffmann-Rhiem M, Schwarz S, Hornig K, Muller KM, Antz M, Kaukel E, Kugler C, Kuck KH. Total pulmonary vein occlusion as a consequence of catheter ablation for atrial fibrillation mimicking primary lung disease. *J Cardiovasc Electrophysiol* 2003; 14:366-370.
7. Saad EB, Rossillo A, Saad CP, Martin DO, Bhargava M, Erciyes D, Bash D, Williams-Andrews M, Beheiry S, Marrouche NF, Adams J, Pisanò E, Fanelli R, Potenza D, Raviele A, Bonso A,

- Themistoclakis S, Brachmann J, Saliba WI, Schweikert RA, Natale A. Pulmonary vein stenosis after radiofrequency ablation of atrial fibrillation. Functional characterization, evolution, and influence of the ablation strategy. *Circulation* 2003; 108(25):3102-3107.
8. Baranowski B, Saliba W. Our approach to management of patients with pulmonary vein stenosis following AF ablation. *J Cardiovasc Electrophysiol* 2011; 22(3):364-367.
9. Holmes DR, Monahan KH, Packer D. Pulmonary vein stenosis complicating ablation for atrial fibrillation: clinical spectrum and interventional considerations. *JACC: Cardiovascular Interventions* 2009; 2(4):267-276.
10. De Greef Y, Tavernier R, Raeymaeckers S, et al. Prevalence, characteristics, and predictors of pulmonary vein narrowing after isolation using the primary vein ablation catheter. *Circ Arrhythm Electrophysiol* 2012; 5(1):52-60.
11. Di Biase L, Fahmy TS, Wazni OM, Bai R, Patel D, Lakkireddy D, Cummings JE, Schweikert RA, Burkhardt JD, Elayi CS, Kanj M, Popova L, Prasad S, Martin DO, Prieto L, Saliba W, Tchou P, Arruda M, Natale A. Pulmonary vein total occlusion following catheter ablation for atrial fibrillation. Clinical implications after long-term follow-up. *J Am Coll Cardiol* 2006; 48(12):2493-2499.
12. Packer DL, Keelan P, Munger TM, Breen JF, Asirvatham S, Peterson LA, Monahan KH, Hauser MF, Chandrasekaran K, Sinak LJ, Holmes DR Jr. Clinical presentation, investigation, and management of pulmonary vein stenosis complicating ablation for atrial fibrillation. *Circulation* 2005; 111: 546-554.
13. Burgstahler C, Trabold T, Kuettner A, Kopp AF, Mewis C, Kuehlkamp V, Claussen CD, Schroeder S. Visualization of pulmonary vein stenosis after radio frequency ablation using multi-slice computed tomography: initial clinical experience in 33 patients. *Int J Cardiol* 2005 Jul 10; 102(2):287-291.
14. Vogt J, Heintze J, Gutleben KJ, Muntean B, Horstkotte D, Nölker G. Long-term outcomes after cryoballoon pulmonary vein isolation: results from a prospective study in 605 patients. *J Am Coll Cardiol* 2013; 61:1707-12.
15. Thomas D, Katus HA, Voss F. Asymptomatic pulmonary vein stenosis after cryoballoon catheter ablation of paroxysmal atrial fibrillation. *J Electrocardiol* 2011 Jul-Aug; 44(4):473-6.
16. Maksimović R, Scholten MF, Cademartiri F, Jordaens LJ, Pattynama PM. Sixteen multidetector row computed tomography of pulmonary veins: 3-months' follow-up after treatment of paroxysmal atrial fibrillation with cryothermal ablation. *Eur Radiol* 2005 Jun; 15(6):1122-7.
17. Tsang VT, Tran PK. Pulmonary vein stenosis: Challenges ahead. *J Thorac Cardiovasc Surg* 2015; 150(4):776.
18. Yang J, Wang C, Du R, Yuan W, Liang Y. Pulmonary vein stenosis and occlusion after radiofrequency catheter ablation for atrial fibrillation. *Int J Cardiol*, 2013; 168(2):68-71.
19. Prieto LR, Schoenhagen P, Arruda MJ, Natale A, Worley SE. Comparison of stent versus balloon angioplasty for pulmonary vein stenosis complicating pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2008; 19(7):673-678.
20. Dragulescu A, Ghez O, Quilici J, et al. Paclitaxel drug-eluting stent placement for pulmonary vein stenosis as a bridge to heart-lung transplantation. *Pediatric Cardiol.*2009; 30:1169-1171.
21. Quinonez LG, Gauvreau K, Borisuk M, Ireland C, Marshall AM, Mayer JE, Jenkins KJ, Fynn-Thompson FE, Baird CW. Outcomes of surgery for young children with multivessel pulmonary vein stenosis. *J Thorac Cardiovasc Surg* 2015; 150(4):911-7.