

The echocardiography has a significant role in the diagnosis and follow-up of patients with acquired PV stenosis.¹⁵ TEE can be utilized for in-stent or in-vein restenosis intervention for such patients.¹⁶ However, post AF ablation induced PV stenosis without any intervention of stenting or angioplasty, CT or MRI should be preferred.⁸ De Piccoli et al. compared TEE and CT for follow up post AF ablation and observed CT was able to visualize more PVs than TEE; further the authors concluded that TEE provided additional functional data regarding the PV stenosis significance.¹⁷

As goes the sensible saying by Packer et al. "The best way to manage PV stenosis is to avoid it." It remains unclear, which is the best and most cost-effective way of detecting PV stenosis after ablation. However, on the basis of their experience, a staged approach starting with TEE and adding standard CT scanning if TEE gives insufficient results is proposed. Virtually every patient tolerated TEE first time, which was a prerequisite before PV ablation. However, not every PV could be assessed by peak Doppler flow velocity especially left inferior PV (in about 33% of the patients studied). In addition, TEE was repeated in only 71% and 48% of patients during follow-up at 3 and 6 months respectively, usually because patients were unwilling to repeat this test just for routine screening. Consequently, data set of serial measurements was too small to draw any firm conclusions. Peak Doppler flow measurements of usually >1 m/s in stenosed PVs was observed.¹⁸

If an interventional procedure is planned, 3 dimensional reconstruction using acquired images gives edge to CT and MRI. The most common modality used for PV stenosis evaluation before and after ablation is CT. For CT to be used for assessing PV stenosis, a reading cardiologist or a radiologist should have an understanding of the anatomical details and the training required to diagnose.⁸

In the 21st century, with perfection of 3-dimensional mapping, CT and their integration can aid the treating electrophysiologists for better delivery of radiofrequency lesions and improving the safety

profile of ablation procedures.¹⁹

Utmost, the highest care particularly in asymptomatic patients, when a high index of suspicion may not be present. CT tends to overestimate the PV stenosis. Pulmonary artery wedge angiography is a reliable option.²⁰ Moreover, PV stenosis may be misdiagnosed in some patients. Yamaji et al. highlighted 50% overdiagnosis of PV stenosis at the level of the descending aorta/left aortic arch. The authors further concluded that to assess PV pseudostenosis especially left inferior PV, a prone position (rather than supine) should be used.

The main advantage of CT over MRI is the quicker acquisition of images and the lower cost. Considering that MRI avoids radiation exposure, it should especially be considered for patients with long duration persistent AF who may need reinterventions.^{2,5}

Tintore et al. used a semiautomatic measurement with contrast-enhanced MRI of PV cross-sectional areas to not only accurately assess, but also quantify the degree of proximal PV stenosis.²¹

Ventilation-perfusion scans can reveal the perfusion defects of the affected lung segments in cases of severe stenosis and thus are extremely useful in showing the functional status.^{7,22} Perfusion values are less likely to be conclusive in patients with bilateral PV stenosis as the measured percent flow to each segment is, in turn, dependent on the flow to other segments.²⁰

There are several studies concluding that the use of intracardiac echo can lead to avoidance of such complications.^{5,8}

Other Techniques

Recognizing the risk of PV stenosis, the next evolution in the treatment of AF was to perform wide area circumferential ablation (WACA), in which the encircling point-by-point PV lesions were not performed at the ostia but at 1-2 cm away from the ostia of the PVs. This approach reduces the incidence of PV stenosis, but increases the risk of leaving gaps in the ablation lesions of a PV leading to arrhythmias. Figure 1 summarizes the intra-procedural parameters

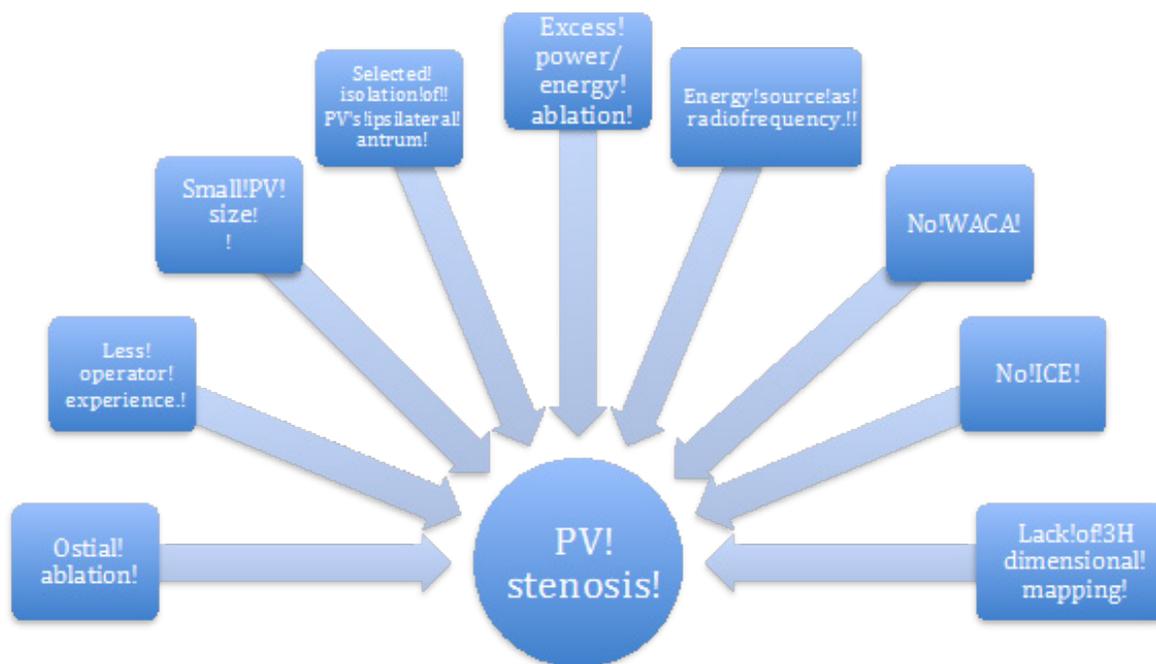


Figure 1: Intra procedural factors during catheter ablation associated with the development of pulmonary vein (PV) stenosis.

WACA; wide area catheter ablation, ICE; intra-cardiac echocardiography

during catheter ablation attributing to PV stenosis.²³

Maeda et al. observed that the strategy of the local extensive encircling pulmonary vein isolation (EPPVI) is effective for preventing complications of severe PV stenosis. The strategy helps to determine the optimal ablation site and endpoint of the ablation procedure occurrence of stenosis using multidetector computed tomography (MDCT). Asymptomatic and mild PV stenosis was seen in 15 of 700 PVs (2.1% of patients) who underwent significant narrowing after 12 months of follow up.²⁴

Role of Energy Sources

Cryoballoon (Arctic Front[®], Medtronic, Minneapolis, MN, USA) ablation has been developed to provide a safe alternative for PV isolation. Compared to radiofrequency catheter ablation, the cryoballoon ablation causes lesser damage at histological level leading to PV shrinkage in preclinical assessment. Cryo ablation of a PV leading to its stenosis has been reported neither in animals²⁵⁻²⁸ nor in humans²⁹⁻³² except STOP-AF trial where 7 (3.1%) of the 228 cryoablated patients (10 PVs) developed stenosis that included 5 left inferior PVs, 4 left superior PVs, and 1 right inferior PV. Five patients were asymptomatic. The sixth patient became asymptomatic at the end of 1 year and the last patient refused further interventions.³³ There was another case report of asymptomatic PV stenosis after cryoballoon ablation affecting left superior PV.³⁴

There is a case report of left superior PV stenosis after using pulmonary vein ablation catheter (PVAC), Medtronic Inc. Limiting the total number and/or the number of 2:1 modus applications, avoiding ablations too close to the PV ostium, and improved imaging modalities to delineate the PV ostia are potential ways to minimize the risk of PV stenosis using PVAC.³⁵ So, far there have been no clinical reports of PV stenosis with limited use of laser balloon.^{36,37}

Classification of PV Stenosis

As stated in the consensus statement on catheter and surgical ablation of AF guidelines; according to the percentage reduction of the luminal diameter, the severity of PV stenosis is generally defined as mild (<50%), moderate (50–70%), or severe (>70%).³⁸ The amount of reduction in luminal diameter of PV is not related

to clinical symptoms. The patients with mild and moderate stenosis can be asymptomatic. Respiratory symptoms for example coughing, hemoptysis and dyspnea are associated with severe stenosis of single or multiple PVs.³⁹ In contrast, even patients with severe PV stenosis or even complete occlusion can be asymptomatic too.^{2,5,40,41}

Maastricht Experience

Currently cryoablation is commonly used for paroxysmal AF at Maastricht university medical center. Since January 2009, cryoballoon has been used for more than 450 patients who have been mostly paroxysmal and some persistent type of AF. Hybrid ablation combining simultaneous thoracoscopic surgical bipolar radiofrequency devices (Atricure, West Chester, OH, USA) and transvenous catheter AF ablation is preferred for failed previously ablated paroxysmal AF (and dilated left atrium), persistent AF, and long standing persistent AF patients.^{42,43} Due to simultaneous use of videoscope during hybrid procedure PV fibrosis secondary to previous catheter ablation may also be visualized.⁴⁴

At our center, irrigated tip radiofrequency catheters are used for endocardial touchups for re-do cases of AF recurrence. The power settings are limited as per the targeted area for ablation e.g. for posterior wall > 25 watt and ablation deeper in PV is deliberately avoided.⁴⁵ Recently past more than 2 year, irrigated tip radiofrequency catheters with contact force sensors (SmartTouch[™], Biosense Webster Inc.) are being used. So far, we have never identified any symptomatic PV stenosis secondary to these AF ablation procedures yet.⁴⁶

We have also performed a limited amount of PV isolation using laser balloon CardioFocus, Inc., Marlborough, Massachusetts) for 96 PVs (24 patients) with follow up data of 15 months and yet to see any symptomatic PV stenosis case.⁴⁷ Several symptomatic patients whose PV isolation was done at other center were referred here, but were managed medically without any need for any interventions. (Figure 2a and 2b)

Management of PV Stenosis

There is limited literature on post procedural PV stenosis management secondary to catheter ablation of AF, in which the

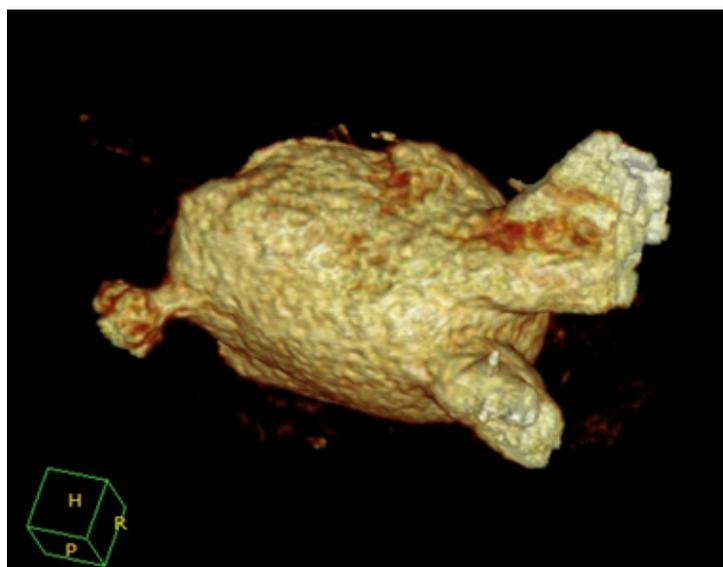


Figure 2A and 2B:

High-resolution computerized tomography scans of a patient with complete occlusion of left superior pulmonary vein secondary to previous radiofrequency catheter ablation.
a) Axial view b) 3-dimensional reconstruction

follow up is organized and according to standards of ESC or AHA.

The general consensus is that patients with symptomatic severe PV stenosis should be treated with PV angioplasty with or without stenting.^{2,5} For a single PV with severe stenosis but an asymptomatic case, there is no uniform opinion on whether or not intervention is warranted. However, the available evidence suggests that an early intervention in such patients translates to clinical benefit. Di Biase et al. also concluded single vessel PV occlusion is frequently asymptomatic if there is no ipsilateral PV stenosis.

In the last decade, several studies have demonstrated that PV angioplasty and stenting are feasible and successful for a majority of patients, resulting in symptomatic improvement.^{20,32,48-51} However, their follow up revealed the susceptibility of such patients to high rates of in-segment or in-stent restenosis.⁸ Polytetrafluoroethylene covered stents have been used for congenital and acquired PV stenosis. Balloon expandable covered stents have better success rates in comparison to bare expandable stents for PV stenosis intervention.⁵²⁻⁵⁵ An isolated report of 2 cases successfully treated with endovascular conventional stenting and adjuvant oral Sirolimus provides an interesting point of view on this issue.⁵⁶ De Potter et al. showed implantation of drug eluting stents (DES) for PV stenosis with an excellent stent patency rate during follow up of 12 ± 14 months. They further claimed that for monitoring stent patency, TEE Doppler measurements provide a viable way.⁵⁷ Jariwala et al. who used bifurcation DESs also confirmed such an approach for PV stenosis post AF ablation. The patient neither had any instant restenosis confirmed by CT angiography after 12 months nor any arrhythmia or hemoptysis at 24 month follow up. Notably, during the 12 months following the angioplasty patient was taking Clopidogrel 75 mg/day, AAS 75 mg/day, and warfarin. Clopidogrel and warfarin were stopped after almost 1 year.⁵⁸

Dragulescu et al. reported Paclitaxel to be particularly appropriate as it is highly lipophilic and hydrophobic and may increase vascular absorption in surrounding tissue.^{56,59} Neointimal proliferation can lead to narrowing of the orifice or distal branches of the PV.⁶⁰ For PV in-stent stenosis, cutting balloon angioplasty appears to improve the intermediate results of repeat angioplasty compared with standard angioplasty.⁶¹ Furukawa et al. implanted 3 bare metal stents and 3

Sirolimus-eluting stents (SESs) in pigs. The neointimal thickness, calculated using injury score after 8 weeks, was lesser in the SES group compared with the other group.⁶²

There are several surgical procedures to treat the PV stenosis, for example, reimplantation of the PV with direct anastomosis,⁶³ excision of the stenosis,⁶⁴ patchplasty,⁶⁴ and finally a sutureless technique.^{65,66} The sutureless technique has been used successfully to treat PV stenosis secondary to catheter ablation of an adult patient.⁶⁷ Especially for redo cases after failure of conventional patchplasty, this technique effectively prevents reactive hyperplasia of the intima over the left atrium and the PV junction.

If a “wait and watch policy” strategy is employed, regular follow up is a must. The treating physician needs to reinvestigate even the slightest sign of symptoms. For PV stenosis patients, an “earlier the better” approach seem more realistic. Late intervention, even if associated with good restoration of venous patency, is not associated with significant improvement in affected lung-segments perfusion.

Anticoagulation

This is another area that definitely needs attention due to lack of optimal anticoagulation strategy following PV intervention. Considering the high rate of restenosis in treated PV segments, oral anticoagulation should be continued, in an effort to avoid thrombotic occlusion of the vein. The delay or failure in recognizing PV stenosis may lead to interruption of the anticoagulation after the procedure in asymptomatic patients. This tends to affect the pulmonary perfusion and attenuates the risk of the developing respiratory infections, pulmonary hypertension, pulmonary infarction and even thrombotic occlusion of the PV.² If patients have no evidence of in-stent restenosis or AF recurrence after 12 months, patients with larger stents (9–10 mm) can be discontinued with warfarin and started on aspirin therapy henceforth.²⁰ Baranowski and Saliba et al. also advocate that the size of the stent used should be decisive in determining the duration of warfarin therapy. Due to the higher risk of occlusion in patients receiving smaller stents (<1 cm), warfarin is typically continued indefinitely. On the other hand, warfarin should be continued for at least a year for a patient receiving a larger stent (≥1 cm). They did not use Clopidogrel therapy routinely following a PV intervention.⁶⁸ Similarly, Prieto et al. continued prescribing

Table 1:

Major studies about pulmonary vein stenosis management secondary to atrial fibrillation ablation using interventions and their follow up.

Study (Year)	No. of patient (lesions)	Treatment modality	Follow up Duration(Months)	First procedure success rate (%)	Follow up using imaging modality
Qureshi et al. (2003)	19 (30)	Angioplasty and stenting)	11	53	Spiral CT,Echocardiogram, Perfusion scan
Saad et al. (2003)	17(NA)	Angioplasty and stenting	12	53	CT, Perfusion scan
Pu rrefellner et al (2004)	6 (7)	Angioplasty and stenting	7 ± 2	71	TEE, CT, MRI
Di biase et al (2006)	18(24)	Angioplasty and stenting	NA	54	CT, Perfusion scan
Bedogni F et al (2007)	6(5)	Angioplasty and stenting	17.1	100	CT, TEE
Prieto et al (2007)	9 (9)	Angioplasty and stenting	11.3 ± 8.7	87.5	CT, Perfusion scan
Bromberg-Marin et al. (2007)	2 (6)	oral Sirolimus, angioplasty, BMS	12	100	CT angiography
Packer et al. (2009)	23 (34)	Angioplasty and stenting	18 ± 12	43	CT, MRI
Neumann T et al (2009)	10(13)	Angioplasty and stenting	12	77	CT, MRI Perfusion scan
Furukawa et al. (pigs) (2010)	6(NA)	BMS, SESs	2	NA	Neointimal thickness by injury score
De Potter et al. (2011)	5(8)	Paclitaxel DES	12 ± 14	87.5	PV angiography, TEE.
Jariwala et al (2012)	1(2)	bifurcation DESs	12	100	CT angiography
J. Yan et al. (2013)	1 (3)	Angioplasty and stenting	9	100	TTE, CT

BMS = bare metal stent, CT = computed tomography, DES= drug eluting stent, MR = magnetic resonance, NA = not available, PV = pulmonary vein, SES = sirolimus eluting stent, TEE =transoesophageal echocardiography, TTE = transthoracic echocardiography

warfarin indefinitely for patients with small stents and/or diffusely hypoplastic veins.

Potter et al. initiated dual antiplatelet therapy with aspirin and clopidogrel for patients on an empirical basis giving due weightage to stents being placed in a low-flow system (PVs) and the lack of clinical data on venous DES thrombosis.^{56,57,69} This approach cannot be recommended as general practice and must be exercised with extreme caution.

Future Perspectives

Ever evolving techniques in AF ablation and increasing operator experience will reduce the incidence of PV stenosis in the future. Fool proof technology complemented by suitable techniques which can withstand the test of time to prevent PV stenosis are yet to be developed. Anticoagulation strategy in spite of its importance in preventing any reocclusion still has to become a standard guideline. There is a need for large randomized studies to demonstrate the reduced restenosis and safety of using stents (bare metal and or drug eluted) in the setting of PV stenosis, and also regarding the use of imaging modality for follow up of patients after intervention.

Conclusion:

Even though catheter ablation for symptomatic drug refractory AF is a safe technique, complications such as PV stenosis may still occur. With growing awareness of such complications and their improved management, its incidence should continue to decrease which is in the best interests of not only the patients and but physicians too. Ultimately, "Prevention is better than cure."

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