fluid removal, it establishes the fact that optimal diuretic dosing as advocated by the authors, is still a better initial approach in diuretic responsive patients of decompensated heart failure with persistent fluid overload.

The result of this trial should not undermine the utility of ultrafiltration which still remains important treatment strategy for diuretic unresponsive patients, rather sub serve for conducting future studies with aim of finding adequate ultrafiltration rates that may produce better results.

REFERENCES

1. Bart Bradley A, Goldsmith Steven R, Lee Kerry L, et al. Ultrafiltration in decompensated heart failure with cardiorenal syndrome. *N Engl J Med*. 2012;367:2296–2304.
2. Costanzo MR, Guglin ME, Saltzberg MT, et al. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. *J Am Coll Cardiol*. 2007;49:675–683.

Contributed by
Gurpreet Singh Wander*
Gaurav Mohan
Naved Aslam
Dayanand Medical College & Hospital Unit Hero DMC Heart Institute, Ludhiana, India

*Corresponding author.
E-mail address: drgswander@yahoo.com (G.S. Wander)

Vivek Y. Reddy, Shephal K. Doshi, Horst Sievert, Maurice Buchbinder, Petr Neuzil, Kenneth Huber, Jonathan L. Halperin, David Holmes, on behalf of the PROTECT AF Investigator, Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation 2.3-year follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection In Patients With Atrial Fibrillation) trial. Circulation 2013;127:720–729.

Background: The multicenter PROTECT AF study (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) was conducted to determine whether percutaneous left atrial appendage closure with a filter device (Watchman) was noninferior to warfarin for stroke prevention in atrial fibrillation.

Methods and results: Patients ($n = 707$) with nonvalvular atrial fibrillation and at least 1 risk factor (age >75 years, hypertension, heart failure, diabetes, or prior stroke/transient ischemic attack) were randomized to either the Watchman device ($n = 463$) or continued warfarin ($n = 244$) in a 2:1 ratio. After device implantation, warfarin was continued for ≈45 days, followed by clopidogrel for 4.5 months and lifelong aspirin. Study discontinuation rates were 15.3% (71/463) and 22.5% (55/244) for the Watchman and warfarin groups, respectively. The time in therapeutic range for the warfarin group was 66%. The composite primary efficacy endpoint included stroke, systemic embolism, and cardiovascular death, and the primary analysis was by intention to treat. After 1588 patient-years of follow-up (mean 2.3 ± 1.1 years), the primary efficacy event rates were 3.0% and 4.3% (percent per 100 patient-years) in the Watchman and warfarin groups, respectively (relative risk, 0.71; 95% confidence interval, 0.44%–1.30% per year), which met the criteria for noninferiority (probability of noninferiority >0.999). There were more primary safety events in the Watchman group (5.5% per year; 95% confidence interval, 4.2%–7.1% per year) than in the control group (3.6% per year; 95% confidence interval, 2.2%–5.3% per year; relative risk, 1.53; 95% confidence interval, 0.95–2.70).

Conclusions: The "local" strategy of left atrial appendage closure is noninferior to "systemic" anticoagulation with warfarin. PROTECT AF has, for the first time, implicated the left atrial appendage in the pathogenesis of stroke in atrial fibrillation.

1. Perspective

Balancing the benefits incurred by preventing stroke and systemic embolism versus risks of major bleed has been the cornerstone of developing effective anticoagulation strategies in atrial fibrillation (AF). Recently approved oral anticoagulants when compared to warfarin showed reduction in incidence of stroke/embolism by 20–34%, ICH by 50–70%. However, rate of major bleed has remained same with Dabigatran and Rivaroxaban, and only Apixaban showing 30% reduction in such events.[1] The data from these trials highlight an important fact, that an anticoagulant will always predispose an individual to risk of bleeding and fatal hemorrhagic strokes no matter how good it is. The recently published 2.3-year follow-up of the PROTECT AF[2] trial which looked at the strategy of occluding the left atrial appendage (LAA), is very important as it marks the first attempt of devising ways of preventing thromboembolic events without subjecting individuals to excessive bleeding risk. In this unblinded, multicenter study, 707 patients of nonvalvular AF (CHADS2 score of ≥1) were randomized to either the Watchman device ($n = 463$) or warfarin ($n = 244$) in a 2:1 ratio. Patients in device arm received warfarin for minimum of 45 days (more as guided by TEE), dual antiplatelet for 4.5 months thereafter and followed by lifelong aspirin. Eighty seven percent of patients receiving the device were able to discontinue warfarin at day 45 with number increasing to 95% by year-end.

The efficacy as assessed by composite of any stroke, cardiovascular or unexplained death, or systemic embolism was similar in both groups (3%/year in the device vs. 4.3%/year in the controls) proving noninferiority.

Excessive bleeding and procedure related events occurred more frequently in the device (5.5%) than in the control arm (3.6%). While the incidence decreased over time in device group it accrued in controls (post-procedure: 2.5%/year versus 4.3%/year). Similarly, on long term follow-up lower rate of major bleeding in device group (RR 0.35) were observed. The results indicate that after successful deployment, the device proved to be superior to well controlled systemic anticoagulation.

We believe that one of the biggest limitations of this study is the relatively small number of patients enrolled as compared to other studies involving new oral anticoagulants. Drawing indirect conclusions seems inappropriate even

though the authors of above study have found favorable comparison between the device and new anticoagulants in terms of follow-up, patient characteristics and time in therapeutic range. Also, the study is not powered enough to answer questions in specific subgroups (e.g. patients with prior history of TIA/stroke).

We believe that further studies with large number and long term follow-up will clarify whether use of such devices can be generalized. If approved, this therapy will not only revolutionize the management of AF (by minimizing issues like major bleed, drug interruption for surgical procedures and compliance) but also design studies targeting patients deemed in eligible to oral anticoagulation.

REFERENCES

1. Tan Ru San, Mark Yan Yee Chan, Teo Wee Siong, et al. Stroke prevention in atrial fibrillation: understanding the new oral anticoagulants dabigatran, rivaroxaban, and apixaban. *Thrombosis* 2012. http://dx.doi.org/10.1155/2012/108983.
2. Vivek Y. Reddy, Shephal K. Doshi, Horst Sievert, et al. Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3 year follow-up of the PROTECT AF trial. http://dx.doi.org/10.1161/CIRCULATIONAHA.112.114389.

Contributed by
Gaurav Mohan
Naved Aslam
Gurpreet Singh Wander*
Dayanand Medical College & Hospital Unit, Hero DMC Heart Institute, India

*Corresponding author.
E-mail address: drgswander@yahoo.com (G.S. Wander)

Hiroki Mizoguchi, Aiko Ogawa, Mitsuru Munemasa, Hiroshi Mikouchi, Hiroshi Ito, Hiromi Matsubara, Refined balloon pulmonary angioplasty for inoperable patients with chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv 2012;5:748–755.

Background: Although balloon pulmonary angioplasty (BPA) for inoperable patients with chronic thromboembolic pulmonary hypertension was first reported over a decade ago, its clinical application has been restricted because of limited efficacy and complications. We have refined the procedure of BPA to maximize its clinical efficacy.

Methods and results: Sixty-eight consecutive patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH) underwent BPA. We evaluated pulmonary artery diameters and determined the appropriate balloon size by using intravascular ultrasound. We performed BPA in a staged fashion over multiple, separate procedures to maximize efficacy and reduce the risk of reperfusion pulmonary injury. A total of 4 (2–8) sessions were performed in each patient, and the number of vessels dilated per session was 3 (1–14). The World Health Organization functional class improved from 3 to 2 ($p < 0.01$), and mean pulmonary arterial pressure was decreased from 45.4 ± 9.6 to 24.0 ± 6.4 mm Hg ($p < 0.01$). One patient died because of right heart failure 28 days after BPA. During follow-up for 2.2 ± 1.4 years after the final BPA, another patient died of pneumonia, and the remaining 66 patients are alive. In 57 patients who underwent right heart catheterization at follow-up, improvement of mean pulmonary arterial pressure was maintained (24.0 ± 5.8 mmHg at 1.0 ± 0.9 years). Forty-one patients (60%) developed reperfusion pulmonary injury after BPA, but mechanical ventilation was required in only 4 patients.

Conclusions: Our refined BPA procedure improves clinical status and hemodynamics of inoperable patients with chronic thromboembolic pulmonary hypertension, with a low mortality. A refined BPA procedure could be considered as a therapeutic approach for patients with inoperable chronic thromboembolic pulmonary hypertension.

1. Perspective

Pulmonary endarterectomy is the only potentially curative treatment for CTEPH. However, nearly one-third patients of CTEPH are not fit for this procedure because of various reasons. Although vasodilator therapy such as epoprostenol has been tried in such cases, they have very limited efficacy in terms of functional class or hemodynamics. Considering the high mortality of such patients when untreated an alternative therapeutic option is required. It is in this context that BPA can play some role.

BPA for a patient with CTEPH was first reported in 1988. In 2001, Feinstein et al reported improvement in hemodynamics in 18 inoperable cases of CTEPH. However, even after more than 20 years after the first report of BPA, it is still not widely accepted as a therapeutic option for inoperable patients with CTEPH because of the following reasons: 1) insufficient improvement in hemodynamics after BPA, 2) inaccurate estimate of balloon size based only on angiographic findings thereby leading to pulmonary artery rupture and 3) high incidence of pulmonary reperfusion injury and pulmonary edema.

The present study has tried to overcome these limitations by **refining** BPA by use of the following measures: 1) use of IVUS to provide more accurate estimates of the diameters of target pulmonary arteries, thereby preventing rupture of pulmonary arteries to a great extent, 2) BPA done in a staged fashion over multiple procedures to reduce the risk of pulmonary reperfusion injury while still achieving an effective therapeutic result. Also, in this study, a soft-tipped 6F guiding catheter, a thinner 0.014-inch wire and a low profile balloon were used, which potentiated the opening of completely obstructed lesions with a lower risk of perforation. All these armamentarium are commercially available and this procedure can be performed in any catheterization laboratory. After determination of the vessel diameter with IVUS, initial dilatation was done with a 2 mm balloon and the diameter of the balloon was gradually increased to a maximum size of not more than 90% of the original vessel diameter. This avoided rupture and dissection of the pulmonary artery. The procedure was repeated in multiple sessions until a sufficient amount of stenosis were dissolved. The more segments