What Lies Beneath Left Atrial Appendage Occlusion Know Your Enemy

Bernhard Meier, MD

In this issue of Circulation: Cardiovascular Interventions, a Polish institution carefully analyzed ≈100 patients undergoing left atrial appendage (LAA) occlusion with serial transesophageal echocardiographies or computer tomographies at 1.5 (early), 3 to 6 (late), and 12 (very late) months with particular focus on device-related thrombus (DRT) and peridevice leak (PDL).¹ The patients were treated without oral anticoagulation but with dual antiplatelet therapy for 1 to 6 months at the discretion of the operators. DRT was diagnosed in 7%. The distribution of DRTs to the 3 control intervals was quite even: 2% early, 2% late, and 3% very late. Of these 7 DRTs, 4 resolved by adding low-molecular weight heparin to the antiplatelet treatment and 3 persisted in spite of treatment adjustment. One of the patients with DRT had a stroke which was fatal. None of the patients without DRT had an embolic event during the 1-year follow-up.

See Article by Pracon et al

The 2 most common devices, the Amplatzer and the Watchman occluders, were used for about half of the cases each. Deep implantation was found to be the most significant predictor for DRT. The distance of the most proximal part of the device to the tip of the pulmonary ridge, the structure separating the LAA from the left upper pulmonary vein, was used for the definition of deep implantation. For the Amplatzer device, a 2-component structure consisting of an anchoring lobe and a covering disc according to the pacifier principle² any position not covering the peak of the pulmonary ridge was considered deep intubation. This resulted in 3 out of 4 Amplatzer patients meeting that definition. For the Watchman device, consisting of a single jellyfish-like plug, the definition was more lenient and only 1 out of 3 patients met it. Deep implantation has been identified as a problem for DRT with the Amplatzer device before, but a definition was used that makes more sense.^{3,4} The venous ridge encompasses only a small part of the circumference of the os of the LAA. Hence, opposing the Amplatzer disc to it may lift the disc off the wall of the left atrium where the venous ridge rises. This engenders leaks underneath the disk. The importance of them is unknown.

(Circ Cardiovasc Interv. 2018;11:e006360.

DOI: 10.1161/CIRCINTERVENTIONS.118.006360.) © 2018 American Heart Association, Inc.

Circ Cardiovasc Interv is available at

http://circinterventions.ahajournals.org

The importance of PDL, defined as flow past the lobe of the Amplatzer device or the Watchman device into the fundus of the LAA, was scrutinized for a relationship with dual antiplatelet therapy by the authors. They found none. This confirms earlier studies.⁵⁻⁹ It had even been suggested that repositioning a device to decrease the risk of PDL may not be justified because this maneuver may increase the risk for pericardial bleeding.⁷

An important lesson of the article is that not only Amplatzer devices but also Watchman devices can be used safely with a post-treatment of only antiplatelet agents. This has been the rule for Amplatzer devices from the start.¹⁰⁻¹² For the Watchman device, 6 weeks of oral anticoagulation is still standard, although literature on a simplified treatment with antiplatelet only is accruing.13,14 It might be questioned whether the 3 doses of low-molecular weight heparin given to the patients described in this study immediately after implantation laid a more favorable ground for thrombus-free further evolution compared with a therapy completely based on antiplatelets as it is usually adopted after Amplatzer implantation. Reports using no heparin or oral anticoagulation after implantation and even stopping platelet inhibitors completely after a few months in patients with no other indications for it showed during follow-up either more or less than the 7% DRTs observed in this study. They used exclusively transesophageal echocardiography for follow-up examination and the definition of thrombus varied. It was 4%8 to 5%3 in studies with Amplatzer devices using varying treatment regimens. Other reports used more sensitive definitions of DRT and came up with 16%11 or even 18%.15 Notwithstanding, worrisome DRT is most certainly going to happen but in a single digit percentage, irrespective of the anticoagulation treatment applied. Clinical events associated with DRT found on routine examinations are invariably low ($\leq 1\%$). So, not only PDLs but also most DRTs represent more a cosmetic than a clinical problem.

Nonetheless, we must have a common language defining PDL and DRT. The Amplatzer device has 2 kinds of leaks, a leak just reaching the space between lobe and disc and a leak reaching the fundus of the LAA. The Watchman device can only have the latter. The pacifier principle with Amplatzer devices is meant to decrease PDLs and has been shown to be effective in that respect if only leaks are counted that reach the fundus of the LAA. Such PDL rates were 5% for Amplatzer devices and 15% for Watchman devices in this study.¹ Again, there is probably no clinical meaning to that.

There must be a clinical meaning to undulating DRTs although that has not been specifically examined to date. The Figure depicts various types of DRTs and points out the ones that represent a clinical hazard and should entrain reinforced anticoagulation, if at all possible.

The informative article shows that the 2 market leader devices for LAA occlusion have a similarly low potential for

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Cardiovascular Department, University Hospital of Bern, Switzerland.

Correspondence to Bernhard Meier, MD, Cardiovascular Department, University Hospital of Bern, 3010 Bern, Switzerland. E-mail bernhard. meier@insel.ch

DOI: 10.1161/CIRCINTERVENTIONS.118.006360

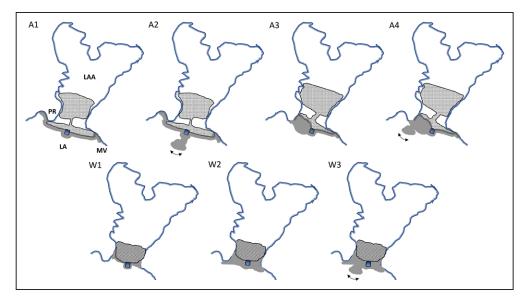


Figure. Classification of different types of thrombus on left atrial appendage (LAA) occluders. A1: Normal endocardialization of an Amplatzer occluder; A2: undulating thrombus attached to the central screw of an Amplatzer occluder; A3: tissue filling of a dead space between the disc of an Amplatzer occluder and the left atrium (LA); A4: tissue filling and undulating thrombus on an Amplatzer occluder; W1: normal endocardialization of a Watchman occluder; W2: tissue filling of the dead space between the device and the LA of a somewhat more deeply implanted Watchman occluder; and W3: tissue filling and on undulating thrombus on a Watchman occluder. Only the situations in A2, A4, and W3 require further or intensified anticoagulation as they seem to represent a clinical hazard. MV indicates mitral valve; and PR, pulmonary ridge.

clinically relevant DRT. It showed a $3 \times$ larger but still clinically insignificant risk for PDL in the case of the Watchman device. DRTs can usually be treated safely with a simple antiplatelet regimen which usually consists of dual antiplatelet therapy for at least 1 month (a single antiplatelet agent may suffice, but this was never examined). This is important as the most common indication for LAA occlusion is poor or no tolerance for oral anticoagulation and every day the patient can spend without oral anticoagulation is a blessing.

Major banes of LAA occlusion remain the relative intricacy of implantation with a shallow learning curve and the risk of acute complications such as pericardial bleeding and device embolization. Periprocedural ischemic events can almost completely be avoided with proper technique and preimplantation imaging excluding mobile thrombi on the way. Follow-up clinical problems are fortunately extremely rare, and this constitutes the major advantage of LAA occlusion over continued oral anticoagulation with unrelenting and even increasing risk for bleeding over time.

Transesophageal echocardiography or computer tomography imaging on the lookout of silent DRT may be justified at least once but only the dangerous types (Figure) should be reacted to. PDL does not need to be looked for or if found to be reacted on. Exceptions are those already appearing as uncovered lobes at the end of the implantation procedure.

Disclosures

Dr Meier was supported by speakers' bureau of Abbott.

References

 Pracon R, Bangalore S, Dzielinska Z, Konka M, Kepka C, Kruk M, Kaczmarska-Dyrda E, Petryka-Mazurkiewicz J, Bujak S, Solecki M, Pskit A, Dabrowska A, Sieradzki B, Plonski A, Ruzyllo W, Witkowski A, Demkow M. Device thrombosis after percutaneous left atrial appendage occlusion is related to patient and procedural characteristics but not to duration of post implantation dual antiplatelet therapy. *Circ Cardiovasc Interv*. 2018;11:e005997. doi: 10.1161/ CIRCINTERVENTIONS.117.005997.

- Schmid M, Khattab AA, Gloekler S, Meier B. Future epidemic impact of atrial fibrillation and a new interventional strategy for stroke prophylaxis. *Future Cardiol.* 2011;7:219–226. doi: 10.2217/fca.10.122.
- Lempereur M, Aminian A, Freixa X, Gafoor S, Kefer J, Tzikas A, Legrand V, Saw J. Device-associated thrombus formation after left atrial appendage occlusion: a systematic review of events reported with the Watchman, the Amplatzer Cardiac Plug and the Amulet. *Catheter Cardiovasc Interv*. 2017;90:E111–E121. doi: 10.1002/ccd.26903.
- Korsholm K, Nielsen KM, Jensen JM, Jensen HK, Andersen G, Nielsen-Kudsk JE. Transcatheter left atrial appendage occlusion in patients with atrial fibrillation and a high bleeding risk using aspirin alone for postimplant antithrombotic therapy. *EuroIntervention*. 2017;12:2075–2082. doi: 10.4244/EIJ-D-16-00726.
- 5. Viles-Gonzalez JF, Kar S, Douglas P, Dukkipati S, Feldman T, Horton R, Holmes D, Reddy VY. The clinical impact of incomplete left atrial appendage closure with the Watchman Device in patients with atrial fibrillation: a PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) substudy. J Am Coll Cardiol. 2012;59:923–929. doi: 10.1016/j.jacc.2011.11.028.
- Freixa X, Tzikas A, Sobrino A, Chan J, Basmadjian AJ, Ibrahim R. Left atrial appendage closure with the Amplatzer[™] Cardiac Plug: impact of shape and device sizing on follow-up leaks. *Int J Cardiol*. 2013;168:1023– 1027. doi: 10.1016/j.ijcard.2012.10.031.
- Wolfrum M, Attinger-Toller A, Shakir S, Gloekler S, Seifert B, Moschovitis A, Khattab A, Maisano F, Meier B, Nietlispach F. Percutaneous left atrial appendage occlusion: effect of device positioning on outcome. *Catheter Cardiovasc Interv*. 2016;88:656–664. doi: 10.1002/ccd.26646.
- Saw J, Tzikas A, Shakir S, Gafoor S, Omran H, Nielsen-Kudsk JE, Kefer J, Aminian A, Berti S, Santoro G, Nietlispach F, Moschovitis A, Cruz-Gonzalez I, Stammen F, Tichelbäcker T, Freixa X, Ibrahim R, Schillinger W, Meier B, Sievert H, Gloekler S. Incidence and clinical impact of device-associated thrombus and peri-device leak following left atrial appendage closure with the Amplatzer Cardiac Plug. *JACC Cardiovasc Interv.* 2017;10:391–399. doi: 10.1016/j.jcin.2016.11.029.
- Raphael CE, Friedman PA, Saw J, Pislaru SV, Munger TM, Holmes DR Jr. Residual leaks following percutaneous left atrial appendage occlusion: assessment and management implications. *EuroIntervention*. 2017;13:1218–1225. doi: 10.4244/EIJ-D-17-00469.

- Meier B, Palacios I, Windecker S, Rotter M, Cao QL, Keane D, Ruiz CE, Hijazi ZM. Transcatheter left atrial appendage occlusion with Amplatzer devices to obviate anticoagulation in patients with atrial fibrillation. *Catheter Cardiovasc Interv*. 2003;60:417–422. doi: 10.1002/ccd.10660.
- Nietlispach F, Gloekler S, Krause R, Shakir S, Schmid M, Khattab AA, Wenaweser P, Windecker S, Meier B. Amplatzer left atrial appendage occlusion: single center 10-year experience. *Catheter Cardiovasc Interv*. 2013;82:283–289. doi: 10.1002/ccd.24872.
- 12. Tzikas A, Shakir S, Gafoor S, Omran H, Berti S, Santoro G, Kefer J, Landmesser U, Nielsen-Kudsk JE, Cruz-Gonzalez I, Sievert H, Tichelbäcker T, Kanagaratnam P, Nietlispach F, Aminian A, Kasch F, Freixa X, Danna P, Rezzaghi M, Vermeersch P, Stock F, Stolcova M, Costa M, Ibrahim R, Schillinger W, Meier B, Park JW. Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicentre experience with the AMPLATZER Cardiac Plug. *EuroIntervention*. 2016;11:1170–1179. doi: 10.4244/EIJY15M01_06.
- 13. Reddy VY, Möbius-Winkler S, Miller MA, Neuzil P, Schuler G, Wiebe J, Sick P, Sievert H. Left atrial appendage closure with the Watchman

device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology). *J Am Coll Cardiol.* 2013;61:2551–2556. doi: 10.1016/j.jacc.2013.03.035.

- Boersma LV, Schmidt B, Betts TR, Sievert H, Tamburino C, Teiger E, Pokushalov E, Kische S, Schmitz T, Stein KM, Bergmann MW; EWOLUTION investigators. Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry. *Eur Heart J*. 2016;37:2465–2474. doi: 10.1093/eurheartj/ehv730.
- Plicht B, Konorza TF, Kahlert P, Al-Rashid F, Kaelsch H, Jánosi RA, Buck T, Bachmann HS, Siffert W, Heusch G, Erbel R. Risk factors for thrombus formation on the Amplatzer Cardiac Plug after left atrial appendage occlusion. *JACC Cardiovasc Interv.* 2013;6:606–613. doi: 10.1016/j. jcin.2013.02.014.

KEY WORDS: Editorials ■ anticoagulation ■ antiplatelets ■ atrial appendage ■ heparin ■ pulmonary vein