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Impact of preprocedural computed tomography on left atrial appendage closure success: a post-hoc analysis of Swiss Apero trial

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Structured Abstract

Background. The benefit ~~related to the use~~ of preprocedural cardiac computed tomography angiography (CCTA) ~~on top of~~ ~~combined with~~ ~~periprocedural echocardiography~~ to plan percutaneous left atrial appendage (LAA) closure (LAAC) procedures is still unclear.

Objectives. We sought to evaluate the impact of preprocedural CCTA on LAAC procedural success.

Methods. In the investigator-initiated Swiss Apero trial, patients undergoing echocardiography guided LAAC were randomly assigned to receive Amulet or Watchman 2.5/FLX across 8 European centers. According to the study protocol ongoing at the moment of procedure, first operators had (CCTA unblinded group) or did not have (CCTA blinded group) access to pre-procedural CCTA images. In this post-hoc analysis, we compared blinded versus unblinded procedures in terms of procedural success defined as complete LAA occlusion as evaluated at end of LAAC (short-term) or at 45-day follow-up (long-term) without procedural related complications.

Results. Among 219 LAAC preceded by CCTA, 92 (42.1%) and 127 (57.9%) were assigned to the CCTA unblinded and blinded group, respectively. After adjusting for confounders, operator unblinding to pre-procedural CCTA ~~remained~~ was associated to a higher rate of short-term procedural success (93.5% vs. 81.1%; p= 0.009; adjusted Odds Ratio [adjOR]: 2.76; 95% Confidence Interval [CI]: 1.05-7.29; p=0.040) and long-term procedural success (83.7% vs. 72.4%; p= 0.050; adjOR:2.12; 95%CI: 1.03-4.35; p=0.041).

Conclusions. ~~In a prospective multicentre cohort of~~ patients having clinically indicated, echocardiography guided, LAAC, ~~unblinding of first operators to~~ pre-procedural CCTA imaging was independently associated to higher rate of both short and long-term procedural success. Further prospective, randomized, controlled, studies are needed to better evaluate the impact of pre-procedural CCTA on clinical outcomes.

Keywords: left atrial appendage closure, cardiac computed tomography angiography, procedural success, procedural safety

Condensed Abstract

In a post-hoc analysis of SwissApero trial we compared left atrial appendage (LAA) closure procedures performed by unblinded versus blinded operators to preprocedural obtained cardiac computed tomography angiography (CCTA) images. After adjusting for potential confounders, a higher rate of both short (93.5% vs. 81.1%; p= 0.009; adjusted Odds Ratio [adjOR]: 2.76; 95% Confidence Interval [CI]: 1.05-7.29; p=0.040) and long-term (83.7% vs. 72.4%; p= 0.050; adjOR: 2.12; 95%CI: 1.03-4.35; p=0.041) procedural success were observed in the CCTA unblinded group.

Abbreviations List

ACP Amplatzer Cardiac Plug

AF Atrial fibrillation

CEC Clinical Events Committee

CCTA Cardiac computed tomography angiography

DRT Device Related Thrombus

LA Left Atrium

LAA Left atrial appendage

LAAC Left atrial appendage closure

OAC Oral anticoagulation

PDL Peridevice leak

RCT Randomized clinical trial

TEE Transesophageal echocardiography

Left atrial appendage (LAA) closure (LAAC) has been established in clinical practice as a valid therapeutic strategy for stroke prevention in patients with atrial fibrillation (AF) and contraindication to oral anticoagulation (1).

Percutaneous LAAC, consisting of the implantation of a vascular device at the LAA ostium, aims at achieving a complete LAA exclusion without procedural complications. This technique has significantly evolved over the last decade showing a progressive improvement in terms of both degree of LAA closure and procedural safety (2,3). Increased operator expertise, the iteration of LAAC technique and devices, or the introduction of imaging in the planning and guidance of procedure may have contributed to improve procedural success (4).

Pre/peri-procedural transesophageal echocardiography (TEE) is the most common imaging method in clinical practice to guide LAAC and its use was recently associated to higher procedural safety and efficacy as compared to the fluoroscopic only guided LAAC (5). Preprocedural cardiac computed tomography angiography (CCTA), combined with peri-procedural TEE, is increasingly performed in clinical practice since it allows to prematurely and non-invasively exclude LAA thrombus and to confirm feasibility of percutaneous LAAC (6). In the latest expert consensus statement on catheter-based LAAC, either TEE or CCTA prior to LAAC procedure was recommended in order to exclude LAA thrombus and assess LAA morphology (4). However, no evidence is available whether preprocedural CCTA performance improves procedural outcomes.

We sought to investigate in a multicenter prospectively collected cohort of clinically indicated LAAC whether the routine use of preprocedural CCTA for planning LAAC improves procedural success as compared to echocardiography guidance alone.

Methods

Study design and population

The Swiss Apero trial (NCT03399851) was a European multi-center randomized clinical trial (RCT), including 221 patients with AF submitted to a clinically indicated LAAC, aimed at assessing the superiority of Amulet as compared to Watchman/FLX in terms of composite of justified crossover to a nonrandomized device during LAAC procedure or residual LAA patency as evaluated by 45-day CCTA (7,8). The study rationale and design have been previously reported (7). In brief, patients with non-valvular AF and clinical indication for LAAC were eligible if were 18 years or older, capable to provide written informed consent, with CHA2DS2-VAScscore ≥ 2 and either HAS-BLED score ≥3 or presence of high bleeding risk features as defined by Munich consensus document (9). Key exclusion criteria included presence of LAA thrombus or LAA morphology not suitable for both study devices as evaluated by TEE, creatinine clearance of <30 ml/min and enrolment in another cardiovascular device or investigational drug trial. Detailed inclusion and exclusion criteria are shown in the **Supplementary appendix**.

When the study was designed, pre-procedural CCTA was not standard of care in clinical practice and procedures were typically planned by using TEE alone (10). As a consequence, the first study protocol version required that the first operators were blinded to pre-procedural CCTA images. In 2020, after the publication of the consensus statement on LAAC including CCTA as potential imaging method in procedure planning (4), the study protocol was amended and first operators were able to plan LAAC procedures by using pre-procedural CCTA images in addition to TEE. This provided a unique opportunity to assess the impact of pre-procedural CCTA on top of echocardiography guidance in a multicentre cohort of clinically indicated LAAC procedures. Based on first operators with versus without access to pre-procedural CCTA images, LAACs were classified as CCTA unblinded or blinded (**Figure**

1). The Ethics Committee (EC) of each participating site approved the study protocol and the relative amendment and all patients provided written informed consent.

Procedural planning

All eligible patients who signed the informed consent underwent a pre-procedural CCTA. The CCTA protocol has previously been described in detail (7). Briefly, a 64- to 320-detector scanner was used, with a multiphasic acquisition in arterial and venous phase. A prospective high pitch flash mode or broad coverage single shot/step and shoot ECG-gated CT acquisition technique typically at 70% of R-R interval or a retrospectively ECG-gated CT acquisition at 30% to 70% of R-R interval was used. Images were reconstructed using iterative reconstruction or filtered back projection at a 0.75-mm slice width, 0.5-mm slice increment. First operators of LAAC procedures performed in the context of first study protocol version could not have access to pre-procedural CCTA images, and were only informed about presence of LAA thrombus and LAA suitability to both devices. After study protocol amendment, first operators were allowed to plan the procedures by using pre-procedural CCTA images and so with the possibility to plan trans septal puncture, to size the LAAC device and to better assess LAA morphology, its position within LA, its relationship with adjacent structures and to choose the angiographic views during the device implantation (**Figure 2**). Participating centres without local expertise in LAA CCTA, were supported by imaging experts representative of the Sponsor in assessing CCTA images and size the device. After confirming by TEE both absence of LAA thrombus and LAA suitability to both devices, patients were randomly assigned in a 1:1 ratio to receive Amulet or Watchman/FLX device.

LAAC procedures and follow-up

Both CCTA blinded and unblinded LAACs were performed by using an identical technic. All procedures were guided by both echocardiography and fluoroscopy and performed under conscious sedation or general anaesthesia. Unfractionated heparin was administered before or right after transseptal puncture at discretion of operators and activated clotting time was not routinely assessed. A device-specific delivery sheath was advanced over a stiff 0.035″ guidewire into the left atrium (LA). LA Pressure was measured and, if <12 mmHg, corrected accordingly. LAA Angiography was performed showing the LAA usually in more projections. The device dimension was selected according to the Instructions for Use of device and based on the available imaging methods: fluoroscopy and echocardiography in CCTA blinded group and pre-procedural CCTA on top of both previous ones in the CCTA unblinded group. Assessment of LAA angiography in at least two views and of TEE images in all the four LAA views (0-120 degree) was recommended. Maximal LAA ostium (for Watchman/FLX) and landing zone (for Amulet) were considered for sizing the devices. Assessment of preprocedural CCTA images was performed by 3D multiplanar reconstruction using the end-systolic phase series and the device sizing was performed considering both maximal and mean ostium/landing zone. All data related to LAAC procedures were collected including duration, dose of contrast medium, radiation exposure, number of implantation attempts or of transseptal punctures. Further LAA angiographies and TEE evaluations were performed just before and after the device release in order to confirm the correct device position and shape and LAA ostium sealing. Finally, a sustained tug test was performed before releasing the device in order to confirm optimal device stability. After device implantation, the recommended antithrombotic regimen consisted of acetylsalicylic acid and clopidogrel or OAC for three months followed by ASA alone until 12 months after LAAC. However, post-implantation drug regimen was left at discretion of the treating physician according to both bleeding and stroke risk. A transthoracic echocardiography was routinely performed before discharge in order to exclude clinically relevant pericardial effusion and to

confirm correct position of the device in the LAA. At 45 days after procedure, patients underwent an on-site clinical visit with both CCTA and TEE.

Endpoint definitions and sensitivity analysis

The study specified two composite endpoints. The short-term procedural success was defined as the completeness of LAA occlusion as evaluated by TEE and/or fluoroscopy at the end of procedure in absence of major procedure related complications including death, cerebrovascular event, systemic embolism, major bleeding (BARC 3-5), clinically relevant pericardial effusion, device embolization, or acute kidney injury occurring within 7 days or thereafter if deemed procedure-related by the multidisciplinary Clinical Events Committee (CEC). The long-term procedural success was defined as the completeness of LAA occlusion as evaluated by TEE at 45 days after LAAC in absence of major procedural related complications. Definitions of each components of the study endpoints are described in the **Supplementary Appendix**(7). The above endpoints were then assessed in a sensitivity analysis including only patients randomized to Amulet where the operator attempted at least once the implantation of randomized device and comparing blinded vs unblinded procedures.

Statistical analysis

Continuous variables are expressed as mean ± SD or median as appropriate, and categorical variables as a percentage. Variables and study endpoints were compared using Student t tests, test Mann-Whitney or Chi-Square test as appropriate. Predictors of the endpoints were determined by univariate and multivariate logistic regression analyses; variables associated to the endpoint of interest with a P-value of ≤ 0.10 at univariate analysis were retained in the multivariable regression models. Estimates of the odds ratios (OR) and 95% confidence

intervals (CI) for each variable are presented. A statistical significance threshold of 0.05 was accepted for hypothesis testing. Statistical tests were performed using Stata (Stata Statistical Software: College Station, TX:Stata Corp LP).

Funding

SwissApero Trial was partially supported by a research grant from Abbott. The funding company was not involved in the study processes, including site selection and management, and data collection and analysis.

Results

Baseline Characteristics

Between June 2018 and May 2021, 423 patients undergoing LAAC at 8 European centres were screened to be included into the SwissApero trial. Of them, 221 were randomized and so enrolled in the trial. Two patients were then excluded from the current analysis since they did not perform any preprocedural CCTA. The remaining 219 patients were divided into two groups according to the study protocol version ongoing at the moment of LAAC: 127 (57.9%) procedures were performed with operators blinded to the preprocedural CCTA findings (CCTA blinded group) and the subsequent 92 procedures (42.1%) were performed with preprocedural CCTA findings available to the operator (CCTA unblinded group) (**Figure 1**). The baseline characteristics were balanced between groups (**Table 1**) with the exception for arterial hypertension (87.0% vs. 74.8%, p=0.028) that was significantly higher in the CCTA unblinded group. The mean age was 76.9 years, and majority (70.6%) were men. The mean CHA2DS2-VASc score was 4.3 ± 1.4 and the mean HASBLED score 3.1 ± 0.9. The most common clinical indication to LAAC was history of relevant bleeding, reported in almost

90% of patients, majority of which were either intracranial (32.6%) or gastrointestinal (35.3%).

Procedural characteristics

Procedural characteristics are summarized in **Table 2**. CCTA Unblinded procedures were associated with a significantly higher use of general anaesthesia during the procedure (52.2% vs. 31.5%; p=0.003), implantation of Watchman FLX device (52.2% vs. 31%; p<0.001) as this became available only during the course of the study and single antiplatelet therapy (SAPT) regimen prescribed at discharge (29.7% vs. 13.6%, p=0.029) as compared to CCTA blinded procedures. During CCTA blinded procedures a significantly higher amount of contrast medium (54.2 ± 30.4 vs. 66.8 ± 50.9; p = 0.038) and radiation dose (2237.0 [450.0; 4748.0] vs. 3306.0 [1465.5; 6545.0], p=0.030) were administered during the procedures. Furthermore, a significantly higher percentage of CCTA blinded procedures were performed under sinus rhythm (40.2% vs. 55.1%; p=0.040).

Short-term procedural success

Short term procedural success occurred in 86 (93.5%) patients in the CCTA unblinded group and in 103 (81.1%) patients in the CCTA blinded group (Risk Ratio [RR]: 2.90; 95%[CI]: [1.23-6.80]; p=0.009) (**Table 3**). Peri-device leak (PDL) detected at end of procedure trended lower in CCTA unblinded group (4.3% vs. 11.0%; RR: 0.39; 95%CI: [0.13-1.16]; p=0.076). The composite of major procedure related complications occurred in 2 (2.2%) patients in the CCTA unblinded group and in 11 (8.7%) patients in the CCTA blinded group (RR: 3.98; 95%CI: [0.90-17.55]; p=0.045) (**Table 3**) with a difference driven by major bleedings that trended higher in the CCTA blinded group (1.1% vs. 6.3%; RR: 5.80; 95%CI: [0.74-45.54];

p=0.055). There was no procedure related death in the CCTA unblinded group, whereas 2 procedural deaths occurred in the CCTA blinded group. The only two procedural strokes and the only two device embolizations occurred in the CCTA blinded group. Among baseline characteristics, unblinding of operator to preprocedural CCTA images remained an independent predictor of the short-term procedural success (adjusted odds ratio [AdjOD]: 2.76; 95%CI: 1.05-7.29; p=0.040) (**Table 4**).

Long-term procedural success

The long-term procedural success occurred in 77(83.7%) patients in the CCTA unblinded group and in 92 (72.4%) patients in the CCTA blinded group (RR: 1.16; 95%CI: [1.00-1.33]; p=0.050) (**Table 3**).

At 45 days after procedure, TEE was performed in 84.2% of patients (85.9% vs. 81.1%; p=0.864). The rates of PDL at TEE (16.9% vs. 23.3%; RR: 95%CI: [0.72 (0.43-1.40)]; p=0.353) did not significantly differ between the two groups. At multivariable analysis, unblinding of operator to preprocedural CCTA remained independently associated with a two-fold greater odds of long-term procedural success (adjOR: 2.12; CI: 1.03 – 4.35; p=0.041).

Sensitivity analysis

The sensitivity analysis was performed in 108 of the 111 patients randomized to Amulet since in two patients Amulet was not available at the time point of implantation and in one CCTA unblinded procedure CCTA was not performed before LAAC. As a consequence 63 Amulet CCTA blinded procedures were compared with 45 CCTA Amulet unblinded procedures. Baseline and procedural characteristics are summarized in the **Supplementary Appendix (Supplemental Table 5-6).** CCTA unblinded procedures were performed in a higher risk

population (median CHA2DS2Vasc Score 4.6 ± 1.4 vs. 3.9 ± 1.3; p=0.005; history of cerebrovascular event 53.3% vs. 30.2%; p=0.018). However, both short (93.3% vs. 81%; RR: 1.15; 95%CI: 1.00-1.33; p=0.067) and long-term (88.9% vs. 74.6%; RR: 1.19; 95%CI: 1.00-1.42; p=0.064) procedural success trended higher in CCTA unblinded procedures driven by a lower rate of major procedural complications (2.2% vs. 14.3%; RR:; 95%CI: [0.30 (0.07-1.34)]; p=0.089) **(Supplemental Table 7).** At uni-multivariate analysis, a stable trend toward a relationship between unblinding of operator to preprocedural CCTA images and long-term procedural success was shown (OR: 2.72; 95%CI: [0.92-8.09]; p=0.071; AdjOR: 2.85; 95%CI:[0.90-9.04]; p=0.075) (**Supplemental Table 8-9**).

Discussion

Randomized clinical trials and large multicentre observation studies so far conducted on LAAC showed over the last decade a progressive increase of procedural success despite the higher risk population treated. This observation might be explained at least in part by several factors as the increased operator expertise (11), the introduction of new devices (12,13) or procedure iteration including the introduction of CCTA in LAAC planning (4,6,10). Until 2015, vast majority of LAAC procedures included in large multicentre studies were guided by echocardiography and fluoroscopy (2,14,15). Subsequently, evidence related to the benefit of performing pre-procedural CCTA started to accrue (**Table 4**) with the consequent inclusion of CCTA among the imaging methods recommended to plan LAAC procedure (4,6). However, no evidence exists that pre-procedural CCTA in addition to echocardiography and fluoroscopy guidance improves clinical outcomes following LAAC.

The main findings of our study can be summarized as follows (**Central Illustration**):

1) In a prospective multicentre cohort of clinically indicated echocardiography guided LAAC, CCTA unblinding was associated with higher rate of procedure success at the end of procedure and at 45 days, driven by a lower rate of procedural complications. After adjustment for all confounders, CCTA unblinding remained independently associated with a higher rate of both short and long-term procedural success;
2) Availability of pre-procedural CCTA images for planning procedure was associated with a lower amount of both contrast medium and radiation dose during the procedure.

To the best of our knowledge, only two studies have so far tested the impact of additional pre-procedural CCTA on top of TEE guidance on LAAC outcomes (16,17). Eng et al. randomized 24 consecutive clinically indicated LAACs with Watchman to performing procedure by using either only TEE images or the combination of CCTA and TEE data (16). The authors showed in this pilot study that procedures planned by both CCTA and TEE were free of procedural complications (composite of death, stroke, myocardial infarction and cardiac perforation were 0% in CCTA+TEE group and 8.3% in TEE only group; p=NS) and were more frequently successful in implanting the first used device (100% vs. 92%; p=NS) as compared to LAAC planned by TEE alone. However, the small sample precluded firm conclusions. Recently, So et al. showed in a single centre retrospective observation study including 485 consecutive clinically indicated LAACs with Watchman implantation that those planned by using an additional pre-procedural CCTA (67.6%) as compared to those only TEE guided were faster (median of 45.5 vs. 51.0 minutes; p=0.03), associated with a significantly higher successful device implantation rate (98.5% vs.94.9%; p=0.02) defined as lack of peridevice leak >5 mm at the end of procedure, and with a less frequent change of device size (5.6% vs 12.1%; p=0.01)(17). However, no significant difference in terms of procedural complications was observed between the two groups (2.1% versus 1.9%; p=0.87). This apparent inconsistency

may be explained by the lack of selection bias (operators did not have the option to decide whether or not to assess CCTA) and by the broader definition of procedural complications used in our study (including major bleedings and those events occurred even later 7 days after LAAC if deemed procedure related) leading to significant differences in our study as compared to the study of So et al.

Our findings suggest that preprocedural CCTA may improve LAAC success mostly by minimizing the rates of procedural complications. The underlying mechanism may include various aspects. Preprocedural CCTA may be used to plan the transseptal puncture, to size the device, to better assess LAA morphology (bends, proximal lobes, depth, internal septum, etc.), to better describe the position of LAA within the left atrium, and its relationship with adjacent structures and to better choose the angiographic views **(Figure 2**). As a consequence, we may expect in LAAC planned by additional CCTA a lower number of transseptal punctures, device implantation attempts, duration of procedures, contrast medium and radiation dose administered during the procedure. Indeed, we observed a significantly lower amount of radiation dose (1985.0 [150.0; 3473.1] vs. 3767.0 [1465.5; 6927.0]; p=0.008) and of contrast medium (54.2 ± 30.4 vs. 66.8 ± 50.9; p=0.038) administered in the CCTA unblinded group. Furthermore, complex procedures with >2 device implantation attempts were numerically more frequent in the CCTA blinded group (24.4% vs. 20.7%, p=0.356) and the only aborted LAAC procedure occurred in the CCTA blinded group. In our study the lower rate of procedure complications observed in unblinded procedures was mostly driven by a lower number of major bleedings (1.1% vs. 6.3%; p=0.055) and in particular of pericardial tamponade (1.1% vs. 2.4%; p=0.487). We cannot exclude that the higher percentage of patients under DAPT in the CCTA blinded group might have favoured this difference. However, we corrected the analyses based on multiple imbalances between groups, including antithrombotic therapy prescribed at discharge (**Table 4-5**). Furthermore, a

numerically higher rate of procedural major bleedings was observed in the CCTA blinded as compared to CCTA unblinded procedures within both SAPT (5.9% vs. 0.0%; p=0.386) and DAPT (5.1% vs. 0%; p=0.160) subgroups **(Supplemental Table 10).** We speculated that the longer duration of some blinded procedures and the supposed higher number of delivery sheath manipulation within the LA and LAA (not included among the collected recaptures) as consequence of a minor operator awareness of LA/LAA anatomy, leaded to prolongation of periprocedural anticoagulation, higher number of contrast medium injection and higher mechanical stress on the LA/LAA walls, with a consequent higher rate of both bleedings and pericardial effusion. In this respect, Berti et al. observed in a retrospective national study including 187 intracardiac echocardiography guided LAACs with implantation of ACP or Amulet devices that procedures preceded by CCTA as compared to those without CCTA were associated to a significantly lower rate of procedural pericardial tamponade (0.7% vs. 4.0%; p=0.047)(18).

Potential downsides of pre-procedural CCTA are contrast nephropathy, increased radiation dose and costs. In SwissApero trial, patients with severely reduced kidney function (Clearence of Creatinine <30ml/min) were excluded and no acute kidney injury procedure related (potential consequence of the pre-procedural CCTA as well) were observed (8). Furthermore, the additional dose of contrast medium administered during preprocedural CCTA (in SwissApero trial was approximately 70ml per CCTA) was partially counterbalanced by the reduced contrast medium dose given during LAAC procedure (54.2 ± 30.4 vs. 66.8 ± 50.9; p=0.038). The same occurred for radiation dose with 2.0-2.5 mSv administered during preprocedural CCTAs and a reduction of approximately 1.71 mSv (2237.0 [450.0; 4748.0] vs. 3306.0 [1465.5; 6545.0]; p=0.030) of radiation given during LAAC procedure.

Limitations

Our study has several important limitations. 1 The non-randomized nature of the study and the small population size don't allow us to draw any definitive conclusion. However, it should be noted as the design of this study unlike occurred in previous studies (**Table 4**) is not affected by similar selection bias since operators were allowed or not allowed to use pre-procedural CCTA images based only on the study protocol version ongoing at the time of procedure.

Some baseline and procedural characteristics as arterial hypertension, use of general anaesthesia, type of Watchman device implanted or post-LAAC drug regimen were not balanced between the two groups. However, the effect of unblinding CCTA on study endpoints observed at the univariate analysis remained stable at multivariate analysis including multiple imbalances between groups. Recent multicentre studies did not show any difference in terms of safety between Watchman 2.5 and Watchman FLX (12) and the uni-multivariate sensitivity analysis showed a stable trend toward an independent effect of unblinding operator to CCTA images on long-term procedural success (**Supplemental Table 8-9**).

Blinded procedures were generally performed earlier (June 2018 - October 2020) respect to the unblinded procedures (June 2020 – May 2021) so we cannot exclude that procedure iteration and increased operators expertise have played a role in reducing procedural complications over time. However, it should be noted that all participating operators were expert operators with more than 40 LAAC procedures performed as first operator before starting the trial. Finally, before participating to Swiss-Apero Trial, almost all participating operators routinely performed pre-procedural CCTA to plan their procedures; our data cannot be therefore generalized to those centres where pre-procedural CCTA is not standard of care.

Conclusion

In a prospective multicentre cohort of clinically indicated echocardiography guided LAAC, unblinding of first operators to pre-procedural CCTA images was independently associated with higher rate of procedural success at the end of procedure and at 45-day follow-up, driven by lower rate of procedural complications. Further studies are needed to better evaluate the impact of pre-procedural CCTA on clinical outcomes.

References

1. Hindricks G, Potpara T, Dagres N et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. European heart journal 2021;42:373-498.
2. Holmes DR, Reddy VY, Turi ZG et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet 2009;374:534-42.
3. Lakkireddy D, Thaler D, Ellis CR et al. Amplatzer Amulet Left Atrial Appendage Occluder Versus Watchman Device for Stroke Prophylaxis (Amulet Ide): A Randomized Controlled Trial. Circulation 2021.
4. Glikson M, Wolff R, Hindricks G et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion - an update. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 2020;15:1133-1180.
5. Galea R RL, Fuerholz M, Häner J, Siontis J, Brugger N, Moschovitis A, Heg D, Fischer U, Meier B, Windecker S, Valgimigli M. Impact of echocardiographic guidance on safety and efficacy of left atrial appendage closure: an observational study. JACC Cardiovascular interventions 2021;14:1815-1826.
6. Korsholm K, Berti S, Iriart X et al. Expert Recommendations on Cardiac Computed Tomography for Planning Transcatheter Left Atrial Appendage Occlusion. JACC Cardiovascular interventions 2020;13:277-292.
7. Galea R, De Marco F, Aminian A et al. Design and Rationale of the Swiss-Apero Randomized Clinical Trial: Comparison of Amplatzer Amulet vs Watchman Device in Patients Undergoing Left Atrial Appendage Closure. J Cardiovasc Transl Res 2021.
8. Galea R, De Marco F, Meneveau N et al. Amulet or Watchman Device for Percutaneous Left Atrial Appendage Closure: Primary Results of the SWISS-APERO Randomized Clinical Trial. Circulation 2021.
9. Tzikas A, Holmes DR, Jr., Gafoor S et al. Percutaneous left atrial appendage occlusion: the Munich consensus document on definitions, endpoints, and data collection requirements for clinical studies. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology 2017;19:4-15.
10. Meier B, Blaauw Y, Khattab AA et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology 2014;16:1397-416.
11. Reddy VY, Holmes D, Doshi SK, Neuzil P, Kar S. Safety of percutaneous left atrial appendage closure: results from the Watchman Left Atrial Appendage System for Embolic Protection in Patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation 2011;123:417-24.
12. Galea R, Mahmoudi K, Grani C et al. Watchman FLX vs. Watchman 2.5 in a Dual-Center Left Atrial Appendage Closure Cohort: the WATCH-DUAL study. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology 2022.
13. Gloekler S, Shakir S, Doblies J et al. Early results of first versus second generation Amplatzer occluders for left atrial appendage closure in patients with atrial fibrillation. Clinical research in cardiology : official journal of the German Cardiac Society 2015;104:656-65.

14. Boersma LV, Schmidt B, Betts TR et al. Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry. European heart journal 2016;37:2465-74.
15. Holmes DR, Jr., Kar S, Price MJ et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. Journal of the American College of Cardiology 2014;64:1-12.
16. Eng MH, Wang DD, Greenbaum AB et al. Prospective, randomized comparison of 3-dimensional computed tomography guidance versus TEE data for left atrial appendage occlusion (PRO3DLAAO). Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions 2018;92:401-407.
17. So CY, Kang G, Villablanca PA et al. Additive Value of Preprocedural Computed Tomography Planning Versus Stand-Alone Transesophageal Echocardiogram Guidance to Left Atrial Appendage Occlusion: Comparison of Real-World Practice. Journal of the American Heart Association 2021;10:e020615.
18. Berti S, Pastormerlo LE, Santoro G et al. Intracardiac Versus Transesophageal Echocardiographic Guidance for Left Atrial Appendage Occlusion: The LAAO Italian Multicenter Registry. JACC Cardiovascular interventions 2018;11:1086-1092.
19. Tondo C. Seize the day, ...s(e)ize the device: The emerging imaging modality to improve left atrial appendage device sizing. Journal of cardiovascular electrophysiology 2022.
20. Schmidt B, Betts TR, Sievert H et al. Incidence of pericardial effusion after left atrial appendage closure: The impact of underlying heart rhythm-Data from the EWOLUTION study. Journal of cardiovascular electrophysiology 2018;29:973-978.

FIGURES LEGEND

Figure 1. Flowchart. 423 Patients with a clinically indicated LAAC planned at one of participating centers were screened. Of them, 221 were randomized. Two patients who did not undergo preprocedural CCTA were excluded by our analysis. Of the remaining 219 LAAC procedures, 127 were performed in the context of the first study protocol version (and so blinding first operators to preprocedural CCTA) whereas the other 92 procedures were performed following the second study protocol version (and so unblinding first operators to preprocedural CCTA)

LAAC, Left Atrial Appendage Closure; CCTA, Cardiac Computed Tomography Angiography.

Figure 2. Advantages of LAAC Planning by using additional preprocedural CCTA on top of TEE guidance only. Preprocedural CCTA allows, as compared to the TEE guidance alone, to early detecting LAA thrombus and LAA morphologies not feasible for percutaneous closure. Furthermore, preprocedural CCTA can be used to size the LAAC device and to plan the transseptal puncture, but also to assess LAA morphology (bend, proximal side lobes, internal septa, etc.), its position within LA (with the effect of guiding the choice of the delivery sheath), the relationship with adjacent structures and to choose the angiographic views during the device implantation.

CCTA, Cardiac Computed Tomography Angiography; TEE, Transesophageal Echocardiography; LAA, Left Atrial Appendage; LAAC, Left Atrial Appendage Closure.

Central Illustration. Main findings of the study. In a cohort of 219 clinically indicated echocardiography guided LAAC, unblinding of first operators to pre-procedural CCTA images was independently associated to higher rate of procedural success at end of procedure and at 45-day follow-up.

Table 1. Baseline characteristics stratified by the first operator blinding to pre-procedural CCTA

	CCTA Unblinded group (92 pts)	***CCTA Blinded group (127 pts)***	**p value**
Age (yr), mean±SD	n = 92, 76.9 ± 7.7	n = 127, 76.8 ± 7.8	0.929
Male sex, no.(%)	n = 92, 65 (70.7%)	n = 127, 89 (70.1%)	1.000
BMI (kg/m²), mean±SD	n = 92, 27.0 ± 5.3	n = 127, 26.8 ± 4.6	0.715
Known Arterial hypertension, no.(%)	n = 92, 80 (87.0%)	n = 127, 95 (74.8%)	0.028
Diabetes mellitus, no.(%)	n = 92, 24 (26.1%)	n = 127, 34 (26.8%)	1.000
Renal failure *, no.(%)	n = 92, 3 (3.3%)	n = 127, 4 (3.1%)	1.000
CHA2DS2Vasc Score, median [IQR]	n = 92, 4.5 ± 1.4	n = 127, 4.2 ± 1.4	0.126
HASBLED Score, median [IQR]	n = 92, 3.1 ± 1.0	n = 127, 3.1 ± 0.9	0.978
Paroxysmal atrial fibrillation, no.(%)	n = 92, 46 (50.0%)	n = 127, 77 (60.6%)	0.130
History of cerebrovascular event, no. (%)	n = 92, 44 (47.8%)	n = 127, 43 (33.9%)	0.050
History of carotid artery disease†, no. (%)	n = 92, 6 (6.5%)	n = 127, 3 (2.4%)	0.171
History of coronary heart disease, no. (%)	n = 92, 26 (28.3%)	n = 127, 52 (40.9%)	0.063
Previous myocardial infarction, no.(%)	n = 92, 17 (18.5%)	n = 127, 31 (24.4%)	0.324
History of arterial embolism, no.(%)	n = 92, 2 (2.2%)	n = 127, 3 (2.4%)	1.000
History of congestive heart failure, no. (%)	n = 92, 17 (18.5%)	n = 127, 29 (22.8%)	0.503
EHRA Score III or IV, no. (%)	n = 92, 32 (34.8%)	n = 127, 34 (26.8%)	0.233
History of bleeding¶, no.(%)	n = 92, 84 (91.3%)	n = 127, 108 (85.0%)	0.212
History of intracranial bleeding, no.(%)	n = 92, 36 (39.1%)	n = 127, 36 (28.3%)	0.109
History of gastrointestinal bleeding, no.(%)	n = 92, 36 (39.1%)	n = 127, 40 (31.5%)	0.253
History of anticoagulant therapy failure ‡, no.(%)	n = 92, 6 (6.5%)	n = 127, 7 (5.5%)	0.779
Left ventricular function (%),median [IQR]	n = 89, 56.1 ± 11.6	n = 126, 54.4 ± 12.0	0.313

* Renal failure was defined if at least one of the following criteria was met: <30 eGFR mL/min per 1.73m2 (using the Modification of Diet in Renal Disease formula) and/or Creat > 200 mcmol/l and/or dialysis or history of kidney transplantation

† Carotid artery disease was defined as either presence of stenosis > 50% in at least one carotid artery or previous carotid treatment

‡History of anticoagulant therapy failure: Thromboembolic event or documented presence of LAA thrombus despite adequate anticoagulant therapy

¶History of bleeding was defined as history of any type of bleeding requiring medical attention.

CCTA, Cardiac Computed Tomography Angiography; SD, Standard Deviation; BMI, Body Mass Index; IQR, interquartile range; EHRA, European Heart Rhythm Association.

Table 2. Procedural characteristics stratified by the first operator blinding to pre-procedural CCTA

		CCTA Unblinded group (92 pts)	***CCTA Blinded group (127 pts)***	**p value**
Sinus rhythm during procedure, no. (%)		n = 92, 37 (40.2%)	n = 127, 70 (55.1%)	0.040
General anesthesia, no. (%)		n = 92, 48 (52.2%)	n = 127, 40 (31.5%)	0.003
Transseptal puncture repetition (n.>1), no. (%)		n = 92, 5 (5.4%)	n = 127, 6 (4.7%)	0.471
Distance between transseptal puncture and mitral plane (mm), mean ±SD		n = 65, 35.6 ± 8.9	n = 97, 33.6 ± 8.3	0.151
Number of device implantation attempts (>2), no. (%)		n = 92, 19 (20.7%)	n = 127, 31 (24.4%)	0.356
Amulet device implanted, no. (%)		n = 92, 44 (47.8%)	n = 127, 62 (49.2%)	<0.001
Watchman 2.5 device implanted, no. (%)		n = 92, 0 (0.0%)	n = 127, 25 (19.8%)	
Watchman FLX device implanted, no. (%)		n = 92, 48 (52.2%)	n = 127, 39 (31.0%)	
Procedure aborted, no. (%)		n = 92, 0 (0.0%)	n = 127, 1 (0.8%)	1.000
Implanted device size (mm), mean ±SD		n = 92, 25.4 ± 3.9	n = 127, 25.1 ± 4.3	0.563
Procedure time (min), mean ±SD		n = 92, 47.2 ± 25.4	n = 127, 42.8 ± 23.1	0.185
Amount of contrast medium (ml), mean ±SD		n = 88, 54.2 ± 30.4	n = 127, 66.8 ± 50.9	0.038
Radiation dose (cGy.cm2), median [IQR]		n = 87, 2237.0 (450.0; 4748.0)	n = 127, 3306.0 (1465.5; 6545.0)	0.030
Discharge antithrombotic therapy *	None, no. (%)	n = 91, 2 (2.2%)	n = 125, 3 (2.4%)	0.029
	Any SAPT, no. (%)	n = 91, 27 (29.7%)	n = 125, 17 (13.6%)	
	Any DAPT, no. (%)	n = 91, 56 (61.5%)	n = 125, 99 (79.2%)	
	Any OAC alone, no. (%)	n = 91, 3 (3.3%)	n = 125, 5 (4.0%)	
	Any SAPT + anticoagulant therapy, no. (%)	n = 91, 3 (3.3%)	n = 125, 1 (0.8%)	
	Any Triple Therapy†, no. (%)	n = 91, 2 (2.2%)	n = 125, 3 (2.4%)	

*No discharge therapy was reported in three patients due to intra-hospital death

† Triple therapy includes DAPT plus either an oral anticoagulant or low molecular weight heparin

CCTA, Cardiac Computed Tomography Angiography; SD, Standard Deviation; IQR, interquartile range; SAPT, Single antiplatelet therapy; DAPT, dual antiplatelet therapy; OAC, Oral Anticoagulant.

Table 3. Short and long-term procedural success endpoints

	CCTA Unblinded group (92 pts)	***CCTA Blinded group (127 pts)***	***Risk Ratio (95% CI)***	**p value**
TEE evaluation at the end of LAAC, no. (%)	n = 92, 92 (100%)	n = 127, 127 (100%)		/
LAA Angiography at the end of LAAC, no. (%)	n = 92, 74 (80.4%)	n = 127, 97 (76.4%)		0.513
45-day TEE follow-up, no. (%)	n = 92, 79 (85.9%)	n = 127, 103 (81.1%)		0.864
Procedural complications assessable, no. (%)	n = 92, 92 (100%)	n = 127, 126* (99.2%)		0.239
Short-term procedural success†, no. (%)	n = 92, 86 (93.5%)	n = 127, 103 (81.1%)	2.90 (1.23-6.80)	0.009
PDL detected at the end of procedure, no. (%)	n = 92, 4 (4.3%)	n = 127, 14 (11.0%)	0.39 (0.13-1.16)	0.076
Major procedure related complication‡, no. (%)	n = 92, 2 (2.2%)	n = 127, 11 (8.7%)	3.98 (0.90-17.55)	0.045
Death, no. (%)	n = 92, 0 (0.0%)	n = 127, 2 (1.6%)		0.227
Cerebrovascular event, no. (%)	n = 92, 0 (0.0%)	n = 127, 2 (1.6%)		0.227
Systemic or pulmonary embolism, no. (%)	n = 92, 1 (1.1%)	n = 127, 0 (0.0%)		0.239
Major bleeding (BARC 3-5), no. (%)	n = 92, 1 (1.1%)	n = 127, 8 (6.3%)	5.80 (0.74-45.54)	0.055
Any pericardial effusion (new onset)‡, no. (%)	n = 92, 12 (13.0%)	n = 127, 18 (14.2%)	1.09 (0.55-2.14)	0.810
-clinically relevant, no. (%)	n = 92, 1 (1.1%)	n = 127, 3 (2.4%)	2.17 (0.23-20.56)	0.487
Device embolization, no. (%)	n = 92, 0 (0.0%)	n = 127, 2 (1.6%)		0.227
Acute kidney injury, no. (%)	n = 92, 0 (0.0%)	n = 127, 0 (0.0%)		/
Long-term procedural success¶, no. (%)	n = 92, 77 (83.7%)	n = 127, 92 (72.4%)	1.16 (1.00-1.33)	0.050
Peridevice leak at 45-day TEE, no. (%)	n = 79, 13 (16.9%)	n = 103, 24 (23.3%)	0.72 (0.43-1.40)	0.353

*One patient withdrew consent at discharge after experience a major bleeding during the hospitalization

†Short-term procedural success was defined as the completeness of LAA occlusion as evaluated by TEE and/or fluoroscopy at the end of procedure in absence of major procedure related complications

‡Major procedure related complications include death, cerebrovascular event, systemic embolism, major bleeding (BARC 3-5), clinically relevant pericardial effusion, device embolization, or acute kidney injury occurring within 7 days or thereafter if deemed procedure-related

¶The long-term procedural success was defined as the completeness of LAA occlusion as evaluated by TEE at 45 days after LAAC in absence of major procedural related complications.

TEE, Transesophageal Echocardiography; LAAC, Left Atrial Appendage Closure; LAA, Left Atrial Appendage; PDL, Peridevice leak; BARC, Bleeding Academic Research Consortium; TEE, Transesophageal Echocardiography; CR, Coumadin Ridge.

Table 4. Baseline univariate and multivariate predictors of short-term procedural success

	Univariate		*Multivariate*	
	OR (95% CI)	***P value***	***Adjusted OR (95% CI)***	**P value**
Age	1.01 (0.96-1.06)	0.664		
Male sex	1.45 (0.65-3.24)	0.369		
Body mass index	1.01 (0.94-1.10)	0.737		
Known Arterial hypertension	1.25 (0.50-3.13)	0.634		
Diabetes Mellitus	1.21 (0.49-3.00)	0.674		
Renal failure*	1.00 (1.00-1.00)	/		
CHA2DS2Vasc Score	1.06 (0.80-1.39)	0.684		
HASBLED Score	0.95 (0.62-1.45)	0.824		
Persistent or chronic atrial fibrillation	1.64 (0.71-3.77)	0.245		
History of cerebrovascular event	1.64 (0.71-3.77)	0.245		
Hystory of carotid artery disease†	1.00 (1.00-1.00)			
History of coronary artery disease	0.50 (0.23-1.09)	0.080	0.63 (0.28-1.43)	0.273
Previous myocardial infarction	0.50 (0.22-1.16)	0.108		
History of arterial embolism	1.00 (1.00-1.00)	/		
Known History of Heart Failure	0.39 (0.17-0.90)	0.027	0.43 (0.18-1.03)	0.057
EHRA III or IV	1.49 (0.61-3.67)	0.384		
History of bleeding‡	2.00 (0.73-5.45)	0.176		
History of intracranial bleeding	2.15 (0.84-5.51)	0.113		
History of gastrointestinal bleeding	1.28 (0.56-2.96)	0.561		
History of anticoagulant therapy failure¶	0.85 (0.63-1.16)	0.313		
Ejection Fraction	1.01 (0.98-1.04)	0.512		
Unblinded Operator to CCTA	3.34 (1.31-8.54)	0.012	2.76 (1.05-7.29)	0.040
Randomized LAAC device Watchman	0.99 (0.46-2.14)	0.979		
Sinus rhythm during procedure	0.50 (0.23-1.12)	0.092	0.56 (0.24-1.29)	0.172
General anaesthesia	1.41 (0.62-3.17)	0.412		
Discharge antithrombotic therapy β	0.73 (0.38-1.42)	0.356		

* Renal failure was defined if at least one of the following criteria was met: <30 eGFR mL/min per 1.73m2 (using the Modification of Diet in Renal Disease formula) and/or Creat > 200 mcmol/l and/or dialysis or history of kidney transplantation

† Carotid artery disease was defined as either presence of stenosis > 50% in at least one carotid artery or previous carotid treatment

‡History of bleeding was defined as history of any type of bleeding requiring medical attention

¶History of anticoagulant therapy failure: Thromboembolic event or documented presence of LAA thrombus despite adequate anticoagulant therapy

β Simplified as linear effect (i.e. no APT and no OAC = 0 (reference), 1 = SAPT, 2 = DAPT, 3 = OAC, 4 = SAPT with OAC, 5 = DAPT with OAC)

OR, Odds Ratio; CI, Confidence Interval; EHRA, European Heart Rhythm Association; CCTA, Cardiac Computed Tomography Angiography; LAAC, Left Atrial Appendage Closure.

Table 5. Baseline univariate and multivariate predictors of long-term procedural success

	Univariate		*Multivariate*	
	OR (95% CI)	***P value***	***Adjusted OR (95% CI)***	**P value**
Age	1.00 (0.96-1.04)	0.904		
Male sex	0.90 (0.45-1.81)	0.767		
Body mass index	0.96 (0.90-1.02)	0.177		
Known Arterial hypertension	1.35 (0.64-2.88)	0.433		
Diabetes Mellitus	0.91 (0.45-1.83)	0.782		
Renal Failure*	1.80 (0.21-15.34)	0.589		
CHA2DS2Vasc Score	0.82 (0.65-1.03)	0.084	0.85 (0.67-1.09)	0.207
HASBLED Score	0.96 (0.68-1.35)	0.807		
Persistent or chronic atrial fibrillation	1.10 (0.57-2.10)	0.777		
History of cerebrovascular event	1.05 (0.52-2.12)	0.892		
History of carotid artery disease†	0.80 (0.42-1.51)	0.482		
Hystory of coronary artery disease	0.63 (0.33-1.20)	0.161		
Previous myocardial infarction	0.65 (0.31-1.33)	0.239		
History of arterial embolism	0.58 (0.14-2.39)	0.448		
Known History of Heart Failure	0.46 (0.22-0.94)	0.032	0.59 (0.25-1.39)	0.230
EHRA III or IV	0.50 (0.26-0.97)	0.039	0.55 (0.27-1.12)	0.098
History of bleeding‡	1.21 (0.48-3.06)	0.683		
History of intracranial bleeding	0.83 (0.43-1.62)	0.593		
History of gastrointestinal bleeding	0.83 (0.43-1.60)	0.577		
History of anticoagulant therapy failure¶	0.99 (0.26-3.73)	0.983		
Ejection fraction	1.02 (1.00-1.05)	0.084	1.01 (0.98-1.04)	0.570
Unblinded Operator to CCTA	1.95 (0.99-3.84)	0.052	2.12 (1.03-4.35)	0.041
Randomized LAAC device: Watchman	0.72 (0.38-1.36)	0.317		
Sinus rhythm during procedure	0.69 (0.37-1.30)	0.251		
General anaesthesia	0.73 (0.39-1.39)	0.340		
Discharge antithrombotic therapy β	0.91 (0.54-1.55)	0.733		

* Renal failure was defined if at least one of the following criteria was met: <30 eGFR mL/min per 1.73m2 (using the Modification of Diet in Renal Disease formula) and/or Creat > 200 mcmol/l and/or dialysis or history of kidney transplantation

† Carotid artery disease was defined as either presence of stenosis > 50% in at least one carotid artery or previous carotid treatment

‡ History of bleeding was defined as history of any type of bleeding requiring medical attention

¶ History of anticoagulant therapy failure: Thromboembolic event or documented presence of LAA thrombus despite adequate anticoagulant therapy

β Simplified as linear effect (i.e. no APT and no OAC = 0 (reference), 1 = SAPT, 2 = DAPT, 3 = OAC, 4 = SAPT with OAC, 5 = DAPT with OAC)

OR, Odds Ratio; CI, Confidence Interval; EHRA, European Heart Rhythm Association; CCTA, Cardiac Computed Tomography Angiography; LAAC, Left Atrial Appendage Closure.

Table 6 – Studies assessing the role of preprocedural CCTA in planning LAAC

First author, YOP*	Study design	Treatment arms		Patient (No)	LAAC Device	Clinical Endpoint definition	Results	Imaging Endpoint definition	Results
Clemente et al. 2015	Single Center OS	CCTA + Echo guidance (Single arm)		66	ACP	/		Agreement between the suggested and used device (CCTA vs. TEE)	32.4% vs. 5.9%; p=NA
Wang et al. 2016	Single Center OS	CCTA + TEE guidance (Single arm)		53	Watchman	Composite of pericardial effusions, cardiac ruptures, device embolizations or migrations	0%	Mean device implantation attempts	1.24
								Any peridevice leak	7.5%
Rajwany et al. 2017	Single Center OS	CCTA + TEE guidance (Single arm)		73	ACP, Watchman, WaveCrest Occluder	Composite of death, stroke, systemic embolism, new pericardial effusion, device embolization	0%	Peridevice leak≥5mm at TEE follow-up	0%
Eng et al. 2017	Single Center RCT	2D TEE + CCTA	2D TEE	24	Watchman	Composite of death, stroke, myocardial infarction and cardiac perforation	0% vs. 8.3%; p=NS	Successful Implantation of first device used	100% vs. 92%; p=NS
Chow et al. 2017	Single Center OS	CCTA	2D TEE	67	Amulet, Watchman /FLX	/		Mean difference between LAA sizing and final LAAC device size†	4.8 mm vs. 8.4mm; p= NA
Berti et al. 2018	Multi Center OS	CCTA +ICE	ICE	187	ACP, Amulet	Pericardial tamponade	0.7% vs. 4.0% p=0.047	Fluoroscopy time	22 ±9 vs. 30±18 min; p <0.001
								Use of a second device	2.9% vs. 8%; p=0.049
Korsholm et al. 2020	Single Center OS	CCTA+ TEE/ICE guidance (Single arm)		91	Watchman FLX	Composite of death, stroke, major bleeding, device embolization cardiac tamponade, vascular complications occurred within 7 days after LAAC	5.5%	Successful device implantation	99%
								PDL at 45-day TEE	3.3%
								PDL at 45-day CCTA	17%
So et al. 2021	Single Center OS	2D TEE + CCTA	2D TEE	485	Watchman	Composite of death, stroke, myocardial infarction, new pericardial effusion requiring intervention, device embolization and surgical conversion	2.1% vs. 1.9%; p=0.87	Successful device implantation without major PDL (>5 mm)	98.5% vs. 94.9%; p=0.02
Zhang et al. 2022	Single Center OS	CCTA	2D TEE	148	Watchman	/		Mean difference between LAA sizing and final LAAC device size	2.92 mm vs. 4.64 mm, p= NS
Dallan et al. 2022	Single Center OS	CCTA + ICE guidance (Single arm)		136	Watchman FLX	Composite of death, stroke, bleedings, device embolization pericardial effusion requiring intervention, vascular complications	2.9%	Successful device implantation	98.5%

*Studies with less than 20 patients were excluded

†Patients with residual leak at CCTA follow-up were excluded

YP, Year of Publication; OS, Observational Study; CCTA, Cardiac Computed Tomography Angiography; ACP, Amplatzer Cardiac Plug; PDL, Peridevice Leak; NA, Not Available;

RCT, Randomized Clinical Trial; TEE, Transesophageal Echocardiography; NS, Non significant.