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NEW RESEARCH PAPER

STRUCTURAL

Impact of Computational Modeling on Transcatheter Left Atrial Appendage Closure Efficiency and Outcomes

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ABSTRACT

BACKGROUND When performing transcatheter left atrial appendage (LAA) closure, peridevice leaks and device-related thrombus (DRT) have been associated with worse clinical outcomes—hence, their risk should be mitigated.

OBJECTIVES The authors sought to assess whether use of preprocedural computational modeling impacts procedural efficiency and outcomes of transcatheter LAA closure.

METHODS The PREDICT-LAA trial (NCT04180605) is a prospective, multicenter, randomized trial in which 200 patients were 1:1 randomized to standard planning vs cardiac computed tomography (CT) simulation-based planning of LAA closure with Amplatzer Amulet. The artificial intelligence-enabled CT-based anatomical analyses and computer simulations were provided by FEops (Belgium).

RESULTS All patients had a preprocedural cardiac CT, 197 patients underwent LAA closure, and 181 of these patients had a postprocedural CT scan (standard, n = 91; CT + simulation, n = 90). The composite primary endpoint, defined as contrast leakage distal of the Amulet lobe and/or presence of DRT, was observed in 41.8% in the standard group vs 28.9% in the CT + simulation group (relative risk [RR]: 0.69; 95% CI: 0.46-1.04; $P = 0.08$). Complete LAA closure with no residual leak and no disc retraction into the LAA was observed in 44.0% vs 61.1%, respectively (RR: 1.44; 95% CI: 1.05-1.98; $P = 0.03$). In addition, use of computer simulations resulted in improved procedural efficiency with use of fewer Amulet devices (103 vs 118; $P < 0.001$) and fewer device repositionings (104 vs 195; $P < 0.001$) in the CT + simulation group.

CONCLUSIONS The PREDICT-LAA trial demonstrates the possible added value of artificial intelligence-enabled, CT-based computational modeling when planning for transcatheter LAA closure, leading to improved procedural efficiency and a trend toward better procedural outcomes. (J Am Coll Cardiol Intv 2023;16:655-666) © 2023 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AI = artificial intelligence

CT = computed tomography

DRT = device-related thrombus

LAA = left atrial appendage

NVAF = nonvalvular atrial fibrillation

TEE = transesophageal echocardiography

Transcatheter left atrial appendage (LAA) closure is an accepted treatment strategy to prevent stroke in patients with nonvalvular atrial fibrillation (NVAF) and contraindication(s) to oral anticoagulant therapy.[1-5] The ongoing CATALYST and CHAMPION-AF randomized controlled trials seek to elevate transcatheter LAA closure to a first-line preventive therapy for all patients with NVAF and an increased stroke risk.

In order to obtain a successful transcatheter LAA closure, adequate closure device size selection as well as an optimal implant position should be strived for. Different cardiac imaging modalities can be used to assess the LAA morphology and dimensions, with transesophageal echocardiography (TEE) and cardiac computed tomography (CT) providing the possibility for 3-dimensional evaluation of the LAA and its surrounding structures.[6-8] Although an increasing number of studies have shown that cardiac CT can help to achieve a more detailed LAA evaluation, prediction of the actual landing zone of the LAA closure device remains difficult with any of the current cardiac imaging techniques.[9]

Patient-specific computational modeling has the potential to provide insight into the interaction between the device and the patient's anatomy, which may result in a more accurate and personalized selection of the LAA closure device size and implant position.[10] FEops HEARTguide simulation technology transforms cardiac images into digital twins, virtual copies of the heart or its substructures. By combining digital twins with artificial intelligence (AI)-enabled anatomical analyses and computer simulations, data-driven insights can be generated, aiming to improve procedural efficiency and outcomes. In a prior study, the cardiac CT-based computational model developed by FEops was validated based on real-life transcatheter LAA closure procedures and postprocedural cardiac CT imaging, showing the accurate prediction of LAA closure device deformation, wall apposition, and risk for peri-device leak.[10]

The aim of this prospective, multicenter, randomized PREDICT-LAA trial was to investigate the hypothesis that preprocedural planning using FEops HEARTguide, providing simulations of different Amulet closure device (Abbott) sizes and implant positions in a patient-specific LAA anatomy, would result in improved procedural efficiency, safety, and outcomes.

METHODS

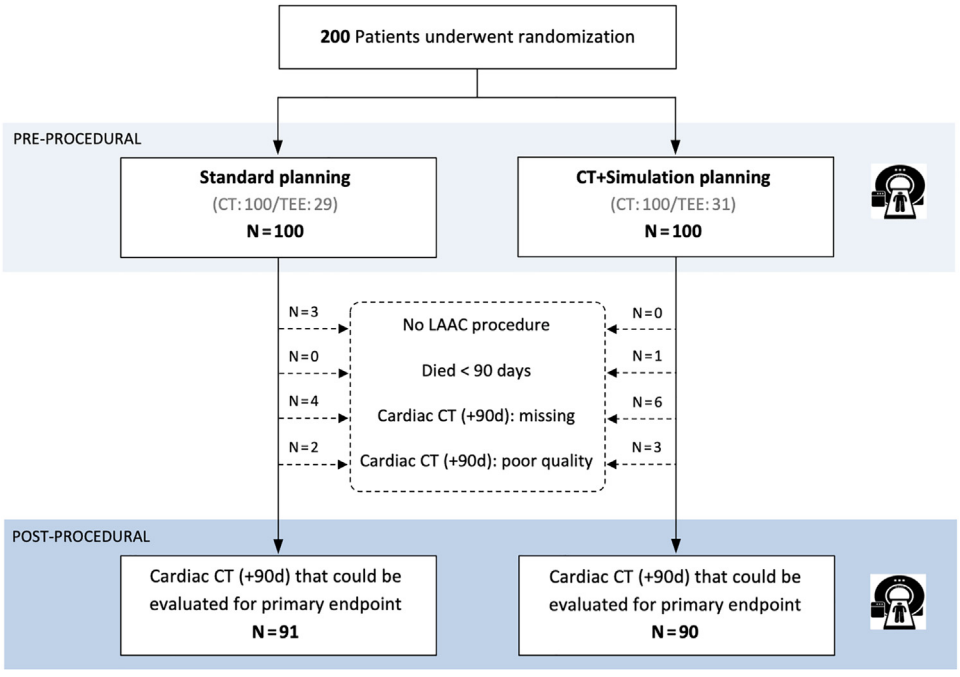
STUDY DESIGN. The PREDICT-LAA trial (NCT04180605) was designed as an investigator-initiated, prospective, multicenter, randomized, open-label clinical trial.[11] The study was executed under the academic leadership of investigators at Rigshospitalet (Denmark; Clinical Study Sponsor) and Institut Cardiovasculaire Paris Sud (France). The protocol was approved by the ethics committees and corresponding health authorities for all participating sites, and the trial was conducted in compliance with the Declaration of Helsinki. The study was economically supported by Abbott (United States) and FEops NV (Belgium) to cover study costs. Neither Abbott nor FEops NV had any role in the data analysis or reporting of the study results.

PATIENT SELECTION AND RANDOMIZATION. Patients with NVAF referred to and deemed eligible for transcatheter LAA closure with an Amplatzer Amulet device could be considered for inclusion in the trial (Supplemental Table 1). Exclusion criteria were a reduced renal function (glomerular filtration rate <30 mL/min/1.73 m^2), iodine contrast allergy, or any other condition that prohibited cardiac CT imaging. In total, 200 patients were 1:1 randomized to standard planning vs CT simulation-based planning of transcatheter LAA closure (**Figure 1**). The randomization was stratified per site. All patients were enrolled in the period 2020 to 2022.

TREATMENT. For patients randomized to standard planning, the preprocedural planning and LAA closure procedure were performed as per routine standard practice of the site. For patients randomized to the CT computational simulation arm, the procedure was performed according to the participating site's routine practice; however, the procedure was only performed after careful review of the CT-based FEops HEARTguide simulations—these contained a range of device implant options in terms of device size and position for each individual patient (**Figure 2**).

The transcatheter LAA closure procedure was performed as per routine practice of the site using general anesthesia, conscious sedation, or local anesthesia and by guidance of intraprocedural TEE or intracardiac echocardiographic imaging. All patients received a patient-tapered postprocedural antithrombotic medical regimen at the discretion of the treating physician.

FIGURE 1 **Population and Cardiac CT Scans**



Shown are the numbers of cardiac computed tomography (CT) scans that were available and of sufficient image quality to evaluate the primary endpoint in each treatment group in the intention-to-treat population. Reasons for missing the control CT scan at 90 days were logistic constraints, renal dysfunction, and patient preference. LAAC = left atrial appendage closure; TEE = transesophageal echocardiography.

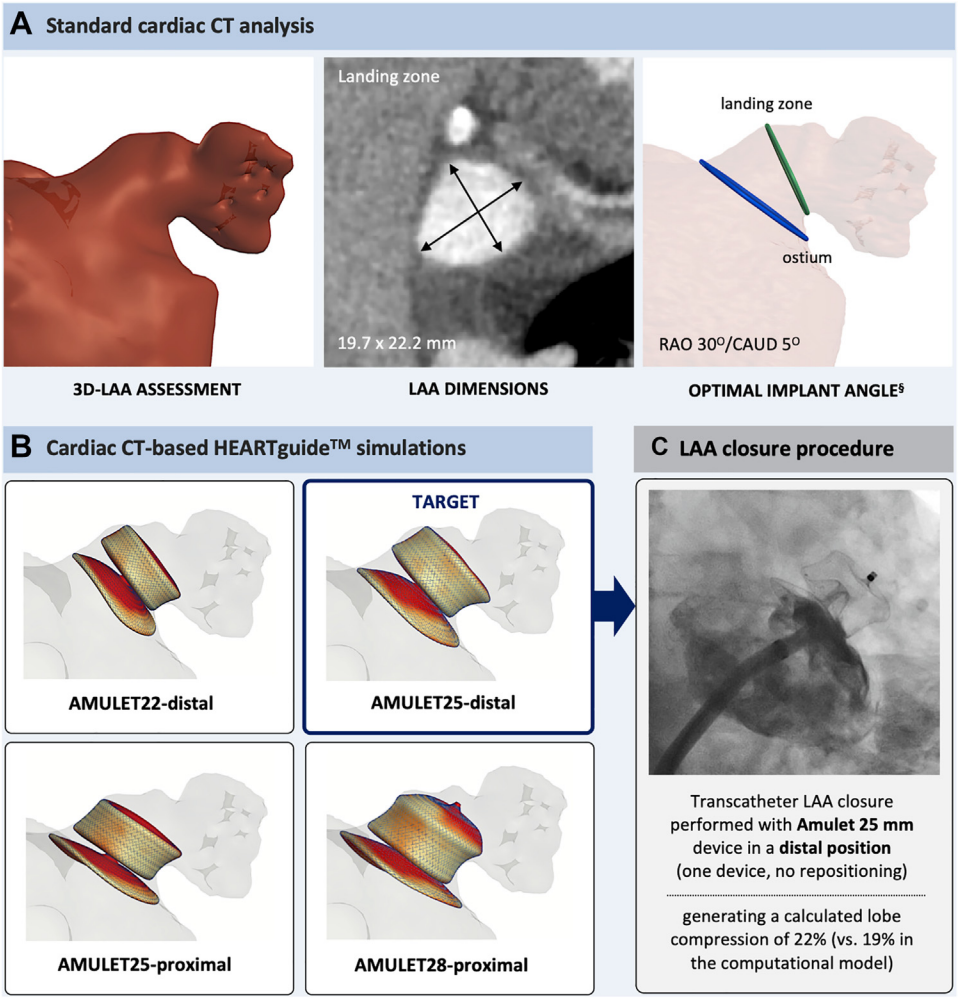
POSTPROCEDURAL CARDIAC CT IMAGING. All patients enrolled in the PREDICT-LAA trial were planned for a postprocedural cardiac CT scan at 90 ± 30 days after LAA closure to check for device position, completeness of LAA closure, and device-related thrombus (DRT). The same protocol as for the preprocedural CT scan was used (electrocardiogram gated, contrast enhanced, and slice thickness ≤1.0 mm).[12] Detailed information on the cardiac CT protocol and technical requirements can be found in the Supplemental Appendix. The CT CoreLab evaluation was performed at Rigshospitalet (Denmark) under supervision of K.F.K. The CT CoreLab evaluations were performed on anonymized cardiac CT scans and blinded from all study data and the randomization codes.

STUDY ENDPOINTS. The PREDICT-LAA trial was designed and powered to detect a difference in postprocedural imaging endpoints comparing two different planning strategies. The predefined composite primary endpoint of the PREDICT-LAA trial was assessed at postprocedural cardiac CT scans and was defined as incomplete LAA closure with residual contrast leakage into the LAA distal of the Amulet lobe (grade 3-4) and/or presence of a DRT. DRT was defined as high-grade hypoattenuated thickening on the device, as previously described by Korsholm et al.[13]

Secondary endpoints encompassed the component endpoints of the primary endpoint, the achievement of complete LAA closure (defined as no leak into the LAA with full coverage of all LAA trabeculations and no disc retraction into the LAA), procedural efficiency (number of LAA closure devices used, number of device repositionings, total procedure time, radiation time, contrast medium used), procedural safety (procedure-related complications), and clinical endpoints concerning thromboembolic events, major bleeding, and/or mortality.

STATISTICAL ANALYSIS. In the sample size calculation for the PREDICT-LAA trial, we assumed that the primary endpoint would occur in 30% of patients in the standard group. It was estimated that 200 patients would be required to demonstrate a projected

FIGURE 2 Cardiac CT Analysis in View of Transcatheter LAA Closure



(A) Standard computed tomography (CT) analysis that encompasses the assessment of the left atrial appendage (LAA) morphology, number of lobes and orientation, LAA dimensions, and calculated optimal implant angle in which the LAA ostium and landing zone can be visualized with minimal or no parallax. This could be performed with any CT analysis software and was not standardized between sites. **(B)** Patient-specific cardiac CT–based computer simulations of different Amulet device sizes and implant positions, as generated by FEops HEARTguide. **(C)** The final procedure, matching the targeted preprocedural computational model. §The optimal implant angle could not be calculated by all participating sites in the standard arm, depending on the used CT analysis software package. 3D = 3-dimensional; CAUD = caudal; RAO = right anterior oblique.

65% reduction in the proportion of patients with a primary endpoint in the CT+simulation group, with a loss to follow-up of 15%.

All study endpoints were evaluated in intention-to-treat analyses, as predefined. Unadjusted 95% CIs for the differences in proportions between the 2 treatment arms are reported[14]; these unadjusted intervals cannot be used to infer effects. The relative risk (RR), 95% CI, and the number needed to treat were calculated using the Altman methodology. The Fisher exact probability test and Student's *t* test were used to compare categorical variables (proportions) and continuous variables between both groups, respectively. Statistical analyses were performed with SPSS v.24 (IBM Corporation), and statistical significance was assumed for $P < 0.05$.

RESULTS

STUDY POPULATION. Among the 200 patients enrolled, 100 were assigned to standard preprocedural planning and 100 to CT+simulation planning.

For all 200 patients, there was a preprocedural cardiac CT scan available. Two cardiac CT scans (2%) in the CT+simulation arm were of too poor quality to generate HEARTguide simulations. Complementary LAA assessment by TEE was available for 29 and 31 patients in the standard and CT+simulation groups, respectively.

Three patients did not undergo LAA closure due to infection or critical renal dysfunction. **Figure 1** depicts the number of postprocedural cardiac CT scans that were available and of sufficient image quality to assess the primary endpoint (leak into the LAA and DRT) in both intention-to-treat groups (n = 181 in the overall population). The patient characteristics of the PREDICT-LAA trial population were well balanced in the 2 treatment arms (**Table 1**). The used pre- and postprocedural antithrombotic therapies are reported in Supplemental Table 2.

TABLE 1 Baseline Characteristics in the Intention-to-Treat Study Population

	Standard Planning	CT+Simulation Planning
Clinical characteristics		
Age, y	76.0 ± 8.1	77.6 ± 7.1
Male	75/100 (75.0)	64/100 (64.0)
Arterial hypertension	83/100 (83.0)	80/100 (80.0)
Diabetes mellitus	24/100 (24.0)	23/100 (23.0)
Coronary artery disease[a]	32/100 (32.0)	26/100 (26.0)
Atrial fibrillation		
Paroxysmal	50/100 (50.0)	54/100 (54.0)
Persistent/permanent	50/100 (50.0)	46/100 (46.0)
Permanent pacemaker	8 (8.0)	12/100 (12.0)
Left ventricular ejection fraction <45%	11/100 (11.0)	8/100 (8.0)
Prior stroke[b]	51/100 (51.0)	50/100 (50.0)
Peripheral artery disease	15/100 (15.0)	17/100 (17.0)
Glomerular filtration rate <45 mL/min/1.73 m^2	12/100 (12.0)	13/100 (13.0)
CHADS-VASc score	4.2 ± 1.4	4.5 ± 1.2
HAS-BLED score	3.2 ± 1.0	3.4 ± 0.9
Antithrombotic treatment		
None	33/100 (33.0)	35/100 (35.0)
Antiplatelet therapy[c]	17/100 (17.0)	17/100 (17.0)
Anticoagulant therapy[d]	45/100 (45.0)	43/100 (43.0)
Anticoagulant + antiplatelet therapy	5/100 (5.0)	5/100 (5.0)
Preprocedural CT characteristics		
Angulated LAA morphology	43/100 (43.0)	44/100 (44.0)
Single-lobe LAA	68/100 (68.0)	70/100 (70.0)
LAA ostium (mean diameter), mm	26.8 ± 5.6	26.0 ± 4.2
LAA landing zone (mean diameter), mm	21.3 ± 4.2	21.4 ± 5.5
LAA free from thrombus	99/100 (99.0)	99/100 (99.0)
Procedural characteristics		
Anesthesia		
General anesthesia	39/97 (40.0)	44/100 (44.0)
Local anesthesia/conscious sedation	58/97 (60.0)	56/100 (56.0)
Intraprocedural echo imaging		
Transesophageal echocardiography	49/97 (50.0)	55/100 (55.0)
Intracardiac echocardiography	48/97 (50.0)	45/100 (45.0)

Values are mean ± SD or n/N (%). [a]Defined as prior myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting. [b]Ischemic or/and hemorrhagic stroke. [c]Either single or dual antiplatelet therapy. [d]Direct oral anticoagulant therapy, vitamin K antagonist, or low-molecular-weight heparin.

CT = computed tomography; LAA = left atrial appendage.

CARDIAC CT ENDPOINTS. The primary endpoint of residual leak into the LAA grade 3 to 4 and/or DRT was observed in 38 (41.8%) patients randomized to standard planning vs 26 (28.9%) patients randomized to CT+simulation planning (between-group difference: -12.90%; 95% CI: -26.10% to +1.10%; RR: 0.69; 95% CI: 0.46 to 1.04; $P = 0.08$) (**Table 2**).

As the main secondary endpoint, complete LAA closure without residual leak or disc retraction into the LAA was noted in 40 (44.0%) patients in the standard arm vs 55 (61.1%) patients in the CT+simulation arm (between-group difference: +17.1%; 95% CI: +2.6% to +31%; $P = 0.03$); this corresponds to a relative benefit of 1.44 (95% CI: 1.05 to 1.98) and an estimated number needed to treat of 6 patients in order to obtain one more patient with complete LAA closure (**Table 2, Figure 3**).

Consistent results were observed for retraction of the Amulet disc into the LAA and the risk for DRT, which were both lower in the CT+simulation arm as compared with the standard arm, reaching a statistically significant difference for the risk of disc retraction into the LAA (RR: 0.42; 95% CI: 0.18 to 0.96; $P = 0.04$) when using cardiac CT-based computational modeling.

PROCEDURAL EFFICIENCY AND SAFETY. The number of LAA closure procedures in which 2 or more LAA closure devices of different size were attempted to be implanted were 16 (16.5%) and 3 (3.0%) in the standard vs CT+simulation groups, respectively (between-group difference: -13.50%; 95% CI: -22.40% to -0.05%; $P < 0.01$). In total, 115 closure devices were used in the Standard group to achieve 94 (96.9%) successful device implantations vs 103 closure devices used in the CT+simulation group to accomplish 100 (100%) successful implantations (**Table 2**). In the standard group, 3 procedures were not successful due to device retrieval without final LAA closure in 2 cases and 1 device embolization.

The number of LAA closure device repositionings was significantly higher in the Standard arm as compared with the CT+simulation arm ($P = 0.02$). In accordance, total procedure time, radiation time and contrast medium used were also higher in the standard arm (**Table 2**, Supplemental Table 3).

A procedure-related complication—predefined by device embolization, pericardial effusion requiring intervention, and/or procedure-related stroke or

TABLE 2 Study Outcomes: Intention-to-Treat Analysis

	Standard Planning	CT+Simulation Planning	Difference (95% CI) (%)	Relative Risk (95% CI)	*P* Value
Procedural efficiency					
Use of ≥2 closure devices	16/97 (16.5)	3/100 (3.0)	-13.50 (-22.40 to -0.05)	0.18 (0.05-0.60)	<0.01[a]
Device repositioning >3 times	22/97 (22.7)	10/100 (10.0)	-12.70 (-23.00 to -2.30)	0.44 (0.22-0.88)	0.02[a]
Total procedure time, min	55.2 ± 24.7	45.1 ± 18.3	–	–	0.01[a]
Radiation time, min	17.6 ± 11.4	12.5 ± 6.8	–	–	<0.001[a]
Contrast medium used, mL	80 ± 65	59 ± 56	–	–	0.02[a]
Successful device implantation	94/97 (96.9)	100/100 (100)	+3.10 (-1.10 to +8.70)	–	–
Procedure-related complication[b]	2/97 (2.1)	0	-2.10 (-7.20 to +1.90)	–	–
Cardiac CT endpoints at 90 d					
Primary endpoint					
Leak grade 3-4 and/or DRT[c]	38/91 (41.8)	26/90 (28.9)	-12.90 (-26.10 to +1.10)	0.69 (0.46-1.04)	0.08
Secondary endpoints					
Leak grade 3-4 (distal of lobe)	34/91 (37.4)	25/90 (27.8)	-9.60 (-22.70 to +4.00)	0.74 (0.49-1.14)	0.20
Complete LAA closure	40/91 (44.0)	55/90 (61.1)	+17.10 (+2.60 to +31.00)	1.44 (1.05-1.98)	0.03[a]
Retraction of disc into LAA	17/91 (18.7)	7/90 (7.8)	-10.90 (-20.90 to -0.90)	0.42 (0.18-0.96)	0.04[a]
DRT[c]	5/91 (5.5)	1/90 (1.1)	-4.40 (-11.2 to +1.40)	0.20 (0.02-1.70)	0.21
Clinical endpoints at 90 d[d]					
Composite clinical endpoint	7/96 (7.3)	4/98 (4.1)	-3.20 (-10.60 to +3.80)	0.56 (0.17-1.85)	0.37
Major or life-threating bleeding	4/96 (4.2)	2/98 (2.0)	-2.20 (-8.40 to +3.60)	–	–
Thromboembolic event	4/96 (4.2)	1/98 (1.0)	-3.20 (-9.30 to +2.10)	–	–
Death	0	1/98 (1.0)	+1.00 (-2.90 to +5.60)	–	–

Values are n/N (%) or mean ± SD unless otherwise indicated. [a]$P < .05$. [b]Composite of device embolization, pericardial effusion requiring intervention, procedure-related stroke, and/or death. [c]As defined by Korsholm et al.[13] [d]Adjudicated according to the Valve Academic Research Consortium-3 definitions.

CT = computed tomography; DRT = device-related thrombus; other abbreviations as in Table 1.

death—was observed in 2 patients, both in the standard arm (ie, 1 device embolization [as described previously] requiring surgical intervention and 1 periprocedural stroke in a case that required 5 device repositionings).

CLINICAL ENDPOINTS. The number of patients in this study with a major or life-threating bleeding, thromboembolic event, or mortality at 90 days was <5 for each of these distinct clinical outcomes; this did not allow reliable statistical analysis (Table 2).

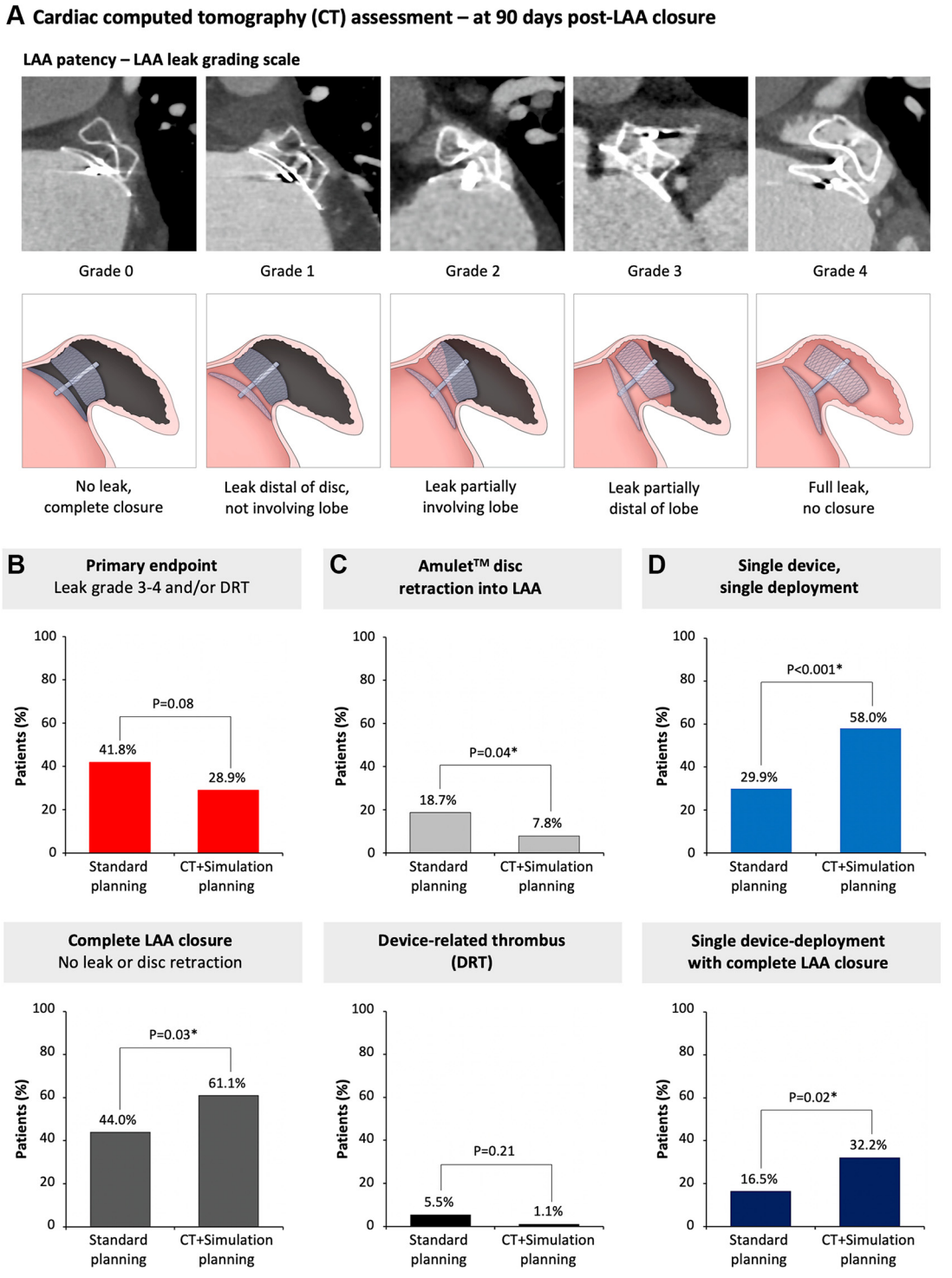
In both treatment groups, there was reported 1 patient with pericardial effusion requiring pericardiocentesis (classified as a major bleeding), and 1 other major bleeding was related to a surgical intervention to retrieve an embolized device in the standard arm. Five patients were noted to have had a thromboembolic event within the first 90 days after LAA closure (4 in the standard arm and 1 in the CT+simulation arm); possible association(s) with procedural or cardiac CT findings will be discussed in the Discussion. One patient died 81 days after LAA closure because of a noncardiovascular cause. A detailed description and analysis of every single clinical event can be found in Supplemental Table 4.

DISCUSSION

The PREDICT-LAA trial is the first randomized controlled trial investigating the possible added value of AI-enabled, CT-based computational modeling when planning for a cardiac device implantation. The main study findings were as follows: preprocedural availability and use of cardiac CT-based computer simulations resulted in improved procedural outcomes with a trend toward a lower LAA patency rate and a significantly higher rate of complete LAA closure. Furthermore, there was a significantly improved procedural efficiency with use of fewer Amulet devices and fewer device repositionings in cases prepared with FEops HEARTguide simulations (Central Illustration).

Transcatheter LAA closure is increasingly adopted as a stroke prevention strategy for patients with NVAF and increased stroke and bleeding risk. Although procedural safety outcomes with current-

FIGURE 3 **The PREDICT-LAA Trial Outcomes**



(A) The different degrees of LAA patency or LAA leak grading scale as determined on the 90-day post-LAA closure cardiac CT scans (grades 0-4). **(B)** Impact of CT simulations in terms of the primary endpoint and obtaining complete LAA closure. **(C)** Impact of CT simulation planning in terms of Amulet disc retraction into the LAA and the presence of device-related thrombus (DRT). **(D)** Impact of CT simulations on the possibility to occlude the LAA with a single device and single deployment, and with obtaining complete LAA closure. Abbreviations as in Figure 2.

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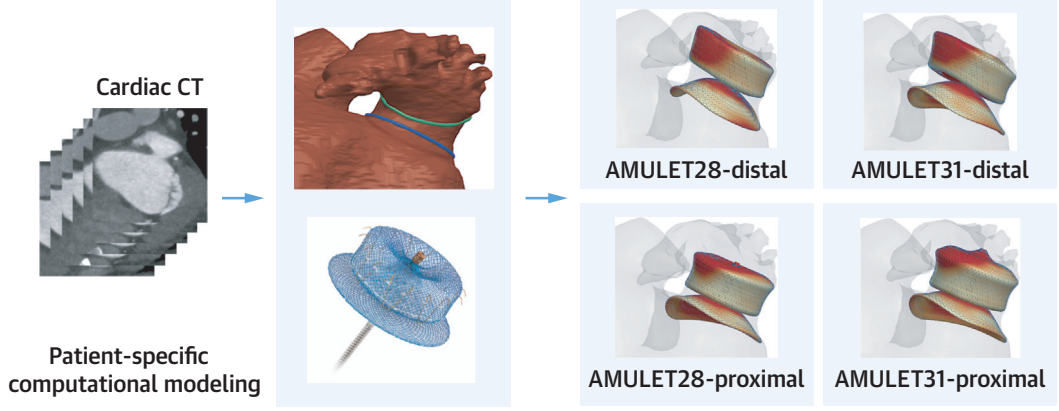
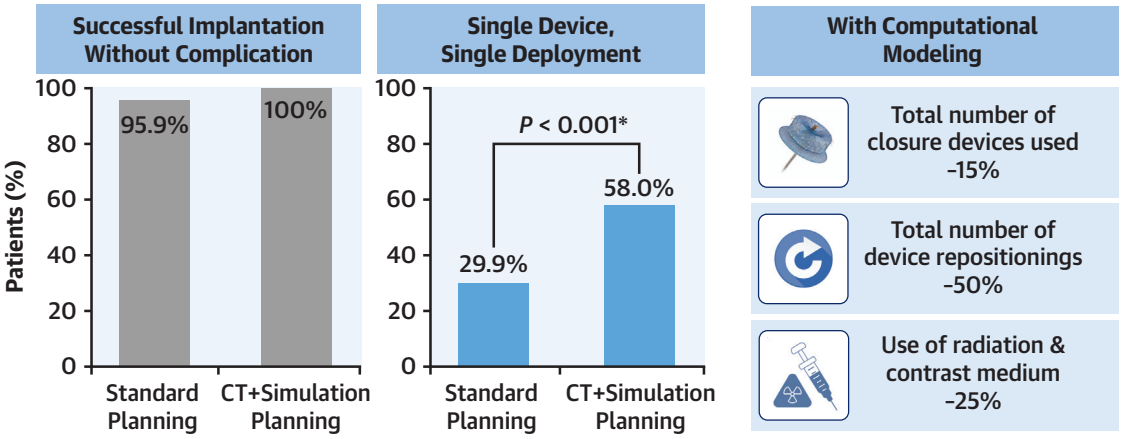
CENTRAL ILLUSTRATION Computational Modeling in LAA Closure Planning

Assessment of CT-Based Computational Modeling for Planning of Transcatheter LAA Closure

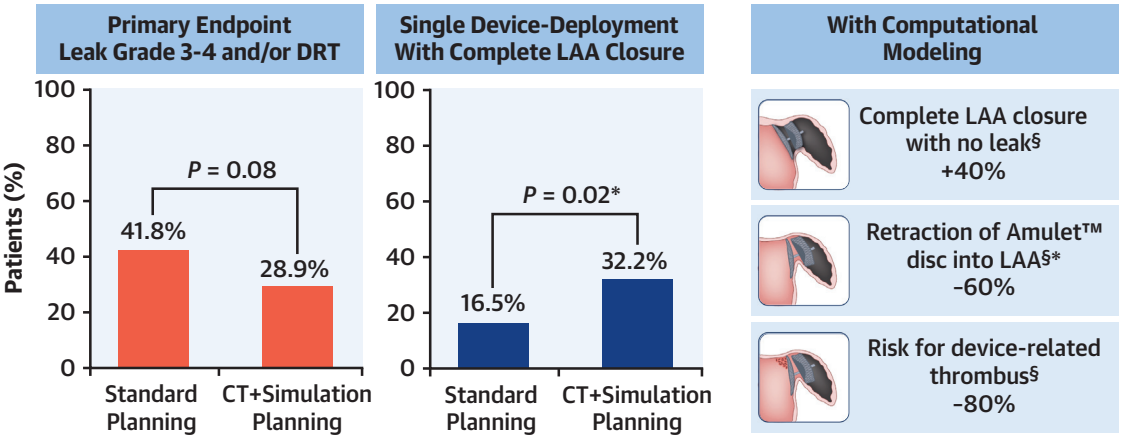
AI-Enabled Computational Modeling - FEops HEARTguide™



Procedural Efficiency



Procedural Outcomes (as Assessed by 90-Day Cardiac CT)



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generation LAA closure devices are already at a high level,[15,16] there is still much to gain in terms of optimizing procedural efficiency and efficacy. Previously, transcatheter LAA closure procedures have been classified as being successful in case the closure device could be implanted without device embolization, pericardial effusion, or major peridevice leak (>5 mm). However, recent studies have provided evidence that even minor peridevice leaks are associated with worse clinical outcomes.[17,18] Hence, complete LAA closure should be strived for in all cases. In addition, new insights have been reported on the incidence, characterization, and clinical impact of DRT, which may be a consequence of the LAA closure device implant position.[19-23]

Taking into consideration the high degree of variability in LAA morphologies and LAA dimensions between patients, use of advanced AI-enabled computational modeling technology may open up the possibility for more precision medicine in the field of transcatheter LAA closure. This was also the underlying hypothesis of the PREDICT-LAA randomized trial.

CARDIAC CT-LAA PATENCY. The primary endpoint to the PREDICT-LAA trial was predefined as incomplete LAA closure with residual contrast leakage into the LAA distal of the Amulet lobe and/or presence of a DRT as assessed at cardiac CT at 90 days; the rate was 41.8% in the standard arm vs 28.9% in the CT+simulation arm. Despite a relative risk reduction of 31% (RR: 0.69; 95% CI: 0.46 to 10.40), statistical significance was just not reached ($P = 0.08$). One of the main reasons for not reaching statistical significance can be found in the fact that a 65% reduction in the proportion of patients with a primary endpoint was projected in the PREDICT-LAA sample size calculation. A larger sample size would have been desirable and could have led to a statistically significant reduction in the primary endpoint in the CT+simulation arm.

Prior studies have shown that reported rates of peridevice leaks are dependent on the imaging modality used; rates are substantially higher on CT as compared with TEE.[26] In addition, residual LAA patency on cardiac CT cannot always be explained by side gap leaks but also intra-device leaks; in case of the Amulet, the latter has been suggested as the main mechanism for residual LAA patency.[27] In other words, assessment of leaks post-LAA closure can be complex. Retrospectively, the assessment for complete LAA closure could have been a more robust primary endpoint.

In the SWISS-APERO study,[27] residual LAA patency on CT was reported in 70% of cases following LAA closure with Amulet (ie, complete LAA closure was obtained in 30%). In the standard arm of the PREDICT-LAA trial, complete LAA closure was seen in 44% of cases. This higher rate of complete LAA closure as compared with the SWISS-APERO Amulet cohort can be explained by the 100% use of cardiac CT preprocedurally in the standard cohort of the PREDICT-LAA trial. With HEARTguide simulations available, the rate of complete LAA closure on cardiac CT could be further increased to 61% in the PREDICT-LAA simulation cohort (relative benefit 1.44; $P = 0.03$).

CARDIAC CT-DRT. Another important study endpoint was the presence of DRT, which can appear on the atrial surface of LAA occluders. Prior studies reported that: 1) DRT rates are low following LAA closure with Amulet; 2) DRTs are not rarely found on Amulet discs which are retracted into the LAA[19]; and 3) DRTs are not benign and associated with a higher risk of stroke and systemic embolism.[20] The findings in the PREDICT-LAA trial are in line with these reports with: 1) an overall DRT rate of 3.3% as seen on the 90-day cardiac CT scans; 2) 4 out of 6 DRTs were found on an Amulet disc, which was retracted into the LAA; and 3) one of the patients with a DRT at the time of the control cardiac CT scan also presented with a thromboembolic event.

Although the risk of DRT after LAA closure is multifactorial, there is now convincing data indicating that coverage of the LAA ostium should be aimed for when implanting an Amulet LAA occluder; this is most likely also valid for other types of LAA occluders. Importantly, this more favorable Amulet implant position, with full coverage of the LAA ostium, was more often obtained in the CT+simulation arm as compared with the standard arm. In

CENTRAL ILLUSTRATION Continued

Use of artificial intelligence (AI)–enabled computational modeling **(top)** results in optimized procedural efficiency with use of fewer left atrial appendage (LAA) closure devices, device repositionings, and less radiation and contrast medium used per procedure **(middle)**, and improved procedural outcomes with a trend toward a lower incidence in the primary endpoint and a significantly higher rate of complete LAA closure without retraction of the Amulet disc into the LAA **(bottom)**. *Retraction of Amulet disc into LAA, defined as <90° angle between disc and LAA wall/coumadin ridge measured at the atrial side. §Based on the relative risk calculation. CT = computed tomography; DRT = device-related thrombus.

accordance, DRTs were more often noted in the standard arm (n = 5) as compared with the CT+simulation arm (n = 1).

PROCEDURAL EFFICIENCY. Based on the observation that Amulet devices had to be less frequently changed to another device size and/or less frequently repositioned in the CT+simulation arm, we can conclude that preprocedural availability of computational simulations results in improved procedural efficiency. In line with these findings, less radiation and contrast medium were used in the CT+simulation arm, also pointing to improved procedural efficiency. As a side note to these results, it is important to remark that a preprocedural CT scan was available in 100% of patients in the standard arm. Prior studies have reported that the use of cardiac CT is associated with improved device size selection accuracy as compared with the more traditional LAA sizing by TEE.[7,24,25] This study now demonstrates that use of computational modeling can lead to a further optimization of device size selection, with a correct selection in 97% of cases.

Ultimately, an LAA closure device was implanted in 100% of cases without any procedure-related complication in the CT+simulation arm. In contrast, 3 (3.1%) of 97 device implantations were not successful in the standard arm (2 cases without final device implantation, 1 device embolization). The overall rate of procedure-related complications further increased to 2.1% in the standard arm because of a minor stroke that became apparent 1 hour after LAA closure; this occurred in a case in which 5 device repositionings were undertaken.

THROMBOEMBOLIC EVENTS. In the overall study population, 5 patients presented with a stroke or systemic embolism within 90 days after LAA closure. One patient was immediately postprocedure following 5 device repositionings in the standard arm (as mentioned previously). Two other patients in the standard arm had a retracted Amulet disc into the LAA, with a detectable DRT at the time of the follow-up CT in 1 of the patients. In 2 more patients, 1 patient in each group, no apparent explanatory or procedure-related cause could be identified.

Taken together, the ideal scenario for transcatheter LAA closure is that the procedure can be successfully and uneventfully completed with a minimum of complexity—a so-called single-device, single-deployment implantation—and that it results in complete LAA closure at the level of the ostium without LAA patency. As shown in **Figure 3**, use of computational modeling strongly helped in obtaining these goals. A next step may be fusing the computer simulations intraprocedurally with the fluoroscopic and/or echocardiographic images; this will have to be validated in future studies.

In conclusion, the PREDICT-LAA trial is the first study to demonstrate that use of AI-enabled, CT-based computational modeling in the planning of a cardiac device implantation can result in optimized procedural efficiency, efficacy, and safety. This may result in not only an obvious clinical benefit, but also an economical benefit to health care providers and MedTech companies and may ultimately contribute to elevate and establish LAA closure as a true alternative, and possibly even superior therapy, to oral anticoagulation as stroke prevention for patients with NVAF.

STUDY LIMITATIONS. Limitations of the PREDICT-LAA trial include its limited sample size as well as its inability to adequately correlate imaging findings with clinical events. Also, there was no standardization of the preprocedural planning (CT and/or TEE analysis) between sites in the standard planning arm, and a third treatment group in which only traditional TEE imaging would be used is missing. The PREDICT-LAA trial was also not designed and powered to study and compare long-term outcomes in the two treatment arms. On the other hand, the study could enroll 200 patients in a relatively short study period, and this despite the COVID-19 pandemic. The dropout level for the follow-up CT imaging was also lower than projected in the study design, with only 10% of patients having no follow-up CT.

CONCLUSIONS

The PREDICT-LAA trial is the first-ever randomized controlled trial demonstrating the added value of AI-enabled, CT-based computational modeling when planning for transcatheter LAA closure, with markedly improved procedural efficiency and a trend toward better procedural outcomes. This new technology may also be expected to be studied and adopted in the preprocedural planning of other (cardiac) device implantations in the future.

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PERSPECTIVES

WHAT IS KNOWN? Transcatheter LAA closure is the preferred stroke prevention strategy for patients with nonvalvular atrial fibrillation, increased stroke risk, and contraindications for oral anticoagulant therapy. For patients who underwent LAA closure, peridevice leaks and DRT have been associated with worse clinical outcomes; hence, their risk should be kept to a minimum.

WHAT IS NEW? This prospective randomized clinical trial showed that use of patient-specific, cardiac CT–based computer simulations in the preprocedural planning of LAA closure results in improved procedural outcomes with a trend toward a lower LAA patency rate, a significantly higher rate of complete LAA closure and improved procedural efficiency.

WHAT IS NEXT? Future studies should address whether integration of computational models intraprocedurally by means of fusion imaging can further improve procedural efficiency and outcomes.

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KEY WORDS cardiac computed tomography, computational modeling, left atrial appendage closure, randomized controlled trial, simulations

APPENDIX For an expanded Methods section and supplemental tables, please see the online version of this paper.