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Clinical outcomes of patients undergoing percutaneous left atrial appendage occlusion in general anaesthesia or conscious sedation: data from the prospective global Amplatzer Amulet Occluder Observational Study

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ABSTRACT

Objective To evaluate the safety and efficacy of percutaneous left atrial appendage occlusion (LAAO) using conscious sedation (CS).

Background Several percutaneous structural heart disease interventions are safely and efficiently performed using CS instead of general anaesthesia (GA). This concept has not been evaluated in a large multicenter cohort of patients undergoing LAAO.

Methods Patients from the prospective, global Amplatzer Amulet Occluder Observational Study were divided into two groups (GA vs CS). Baseline information, periprocedural and postprocedural efficacy and complications, as well as outcomes through 7 days post implant were compared.

Results Patients undergoing transesophageal-guided implants were categorised by GA (n=607, 64%) or CS (n=342, 36%) usage. Mean age was 75 years in both groups. LAAO technical success was achieved in 99% of both groups. The procedure duration (GA: 35±22 min vs CS: 27±19 min, p<0.001), total amount of contrast medium (GA: 105±81 mL vs CS: 86±66 mL, p<0.001) and fluoroscopic time (GA: 13±9 min vs CS: 12±13 min, p<0.001) were less in CS cases. Procedure-related or device-related serious adverse events during the first 7 days were numerically higher in the CS group (GA: 4.9% vs CS: 7.6%, p=0.114). Peridevice residual flow was absent or ≤5 mm 1–3 months after the procedure in 99.7% of the GA and in 100% of the CS group (p=1.000).

Conclusions In a large global study, LAAO with the Amplatzer Amulet occluder is safe and feasible using CS. Procedure duration and total amount of contrast were less with CS than GA cases.

Trial registration number NCT02447081; Results.

Strength and limitations of this study

- This is the first study comparing percutaneous left atrial appendage occlusion under general anaesthesia and conscious sedation from a real-world, prospective, global, multicenter, non-randomised observational study.
- All serious adverse events were reviewed by an independent clinical events committee which adjudicated relatedness to the implant procedure and device.
- Participating centres were required to undergo a standardised site qualification process to ensure that only well-experienced centres and interventionalists with clinical trial expertise were selected for this study.
- Some potential landmark parameters such as time on the intensive care unit, time on ventilation or use of inotropes were not captured in the study.
- The exact type of sedation used was not collected in the study.

INTRODUCTION

With an overall estimated number of 33.5 million individuals, atrial fibrillation (AF) is the most common, clinically significant cardiac arrhythmia worldwide and prevalence increases with age.[1] The global burden of disease is high and AF represents a major cause of morbidity, mortality and healthcare expenditure.[2 3] Thromboembolic stroke may be one of the fatal complications and oral anticoagulation has been the mainstay therapy for decades to mitigate stroke risk. However, in poor candidates for long-term anticoagulation (ie, high bleeding risk, poor drug tolerance or adherence), non-pharmacological stroke prevention with percutaneous left atrial appendage occlusion (LAAO) may be a considerable treatment option.[4 5] As LAAO is an integral

part of catheter-based interventions for structural heart disease, the field is evolving to further develop and refine the implant procedure, including the mode of peri-interventional patient care. The anaesthesiologic method during LAAO has not yet been a particular research interest. Centres performing LAAO under conscious sedation (CS) report positive results,[6] although complications such as pneumonia and patient discomfort can exist with the transesophageal echocardiography (TEE) probe in place without technical protection against aspiration. No data on a direct comparison of general anaesthesia (GA) versus CS in patients undergoing LAAO exist. It is already known that several structural interventions are safe and feasible in CS.[7–9] Avoiding GA may be associated with a lower cardiopulmonary risk and may contribute to a shorter hospital length of stay.[10–12] On the other hand, CS without true aspiration protection, and a potentially agitated patient jeopardising the procedure, could provoke adverse events and may limit procedural success. The aim of this study is to evaluate safety and efficacy of LAAO using CS within a subanalysis of the prospective, global Amplatzer Amulet Occluder Observational Study.

METHODS

Patients with non-valvular AF included in the real-world, prospective, global, multicentre, non-randomised Amplatzer Amulet Observational Study (NCT02447081) were analysed. The clinical investigation plan can be found in the supplement (online supplemental file 1). Participating centres were required to undergo a standardised site qualification process to ensure that only well-experienced centres and interventionalists with clinical trial expertise were selected for this study. Depending on the anaesthetic method used during LAAO, participants were classified either into a GA or CS group. Only patients undergoing TEE-guided implants are included in this analysis, those undergoing intracardiac echocardiography (ICE) guided implants were excluded. Baseline information, periprocedural and postprocedural events and outcomes over 7 days follow-up were compared. A flow chart (figure 1) provides an overview of patient stratification. Specific technical details regarding the LAAO procedure have been previously published.[13] All patients were treated with an Amplatzer Amulet occluder, and mode of anaesthesia was at the discretion of the implanting physician and thus not randomised. While the exact reason(s) for using CS or GA was not collected as part of the study, it is anticipated the decision was based on already established local best practice recommendations, physician experience and training, reimbursement and patient characteristics. The Amulet Observational Study followed subjects through 2 years, but this analysis focuses on the implant procedure and follow-up through 7 days. The objective was to report procedural success (technical success and the absence of major adverse events during hospitalisation. Major adverse events include death, stroke, embolism, pericardial or other major bleeding complications requiring intervention, device embolisation and major vascular complications), procedure duration (defined as the duration from the first delivery system in to the removal of the dilator/delivery system), the amount of contrast medium used, and total length of in-hospital stay. Additionally, the occurrence of procedure/device related events, major bleeding (Bleeding Academic Research Consortium type 3 or greater) and the cumulative incidence of a stroke or transient ischaemic attack at 7 days, as previously defined by the study protocol[14 15], were evaluated. All serious adverse events (SAEs) were reviewed by

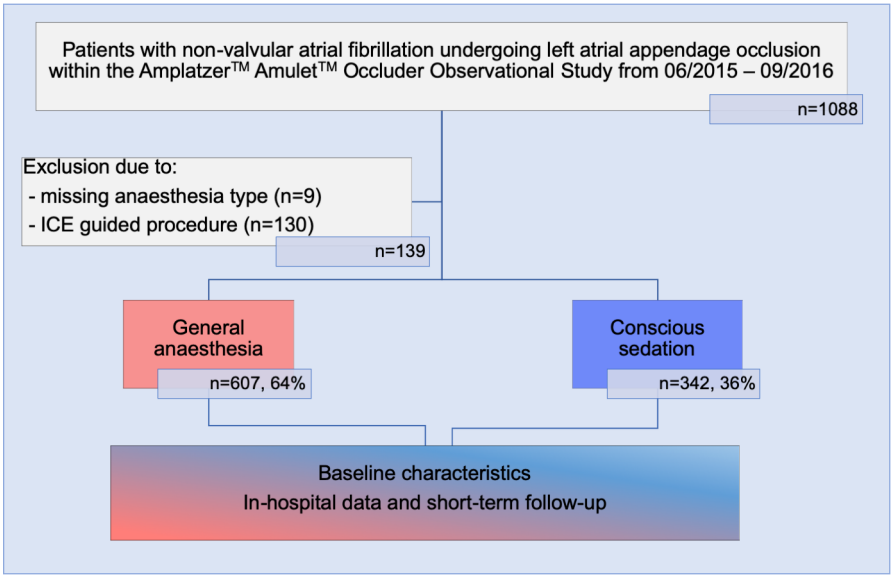

Figure 1 Patient selection process and study design. Of 949 subjects undergoing transesophageal echocardiography-guided implant attempt in the Amulet Observational Study, those managed with general anaesthesia (n=607, 64%) or conscious sedation (n=342, 36%) were analysed in regards of baseline characteristics, in-hospital data and 7-day follow-up. ICE, intracardiac echocardiography.

Table 1 Baseline characteristics

	General anaesthesia (n=607)	Conscious sedation (n=342)	P value	Difference (95% CI)
Age (years)	75±8	75±9	0.670	−6.0E−05 (−1.0 to 1.0)
Male gender	67%	63%	0.227	
Atrial fibrillation at time of implant	60%	57%	0.450	
Hypertension	81%	92%	<0.001	
Congestive heart failure	17%	19%	0.477	
Previous stroke	28%	21%	0.016	
Previous transient ischaemic attack	12%	7%	0.026	
Previous major bleed	75%	65%	0.001	
Previous percutaneous coronary intervention or coronary artery bypass grafting	26%	28%	0.400	
Peripheral vascular disease (peripheral artery or venous disease)	14%	20%	0.014	
CHA_2DS_2-VASc score	4.2±1.5	4.1±1.6	0.487	6.9E−06 (−5.3E−05 to 7.3E−05)
HAS-BLED score	3.3±1.1	3.4±1.2	0.068	−4.9E−05 (−2.3E−05 to 7.8E−05)
Contraindication to oral anticoagulation	84%	80%	0.075	
Absolute contraindication	6%	8%		
Relative contraindication	36%	26%		
Known bleeding risk	42%	46%		
Chicken wing left atrial appendage morphology	39%	51%	<0.001	

The column 'Difference (95%)'" is defined by an estimator for the difference of the location parameter and the non-parametric CI.

an independent clinical events committee which adjudicated relatedness to the implant procedure and device. A subanalysis of the anaesthetic method of choice was performed in regards of the operator experience and by country where TEE-guided implants occurred in the Amulet Observational Study.

Statistical analysis

Descriptive statistics summarised baseline and procedural characteristics. T-tests or the Wilcoxon rank-sum test, as appropriate, were used to identify differences in continuous variables between CS and GA groups. Fischer's exact test was used to identify differences in categorical variables between groups, including the proportion of patients with adverse events through 7 days. Logistic regression to adjust for baseline covariates was not preferred due to the low event counts among the short-term outcomes (death, ischaemic stroke, significant peridevice flow). As there were 28 subjects with major bleeding events ≤7 days, we performed the analysis accordingly. The treatment effect is not significantly different between the two anaesthesia groups even after adjusting for the baseline covariates (online supplemental file 2). Therefore, unadjusted results were kept for analysis.

SAS V.9.4 (SAS Institute) was used for analysis and STATA/SE V.16.0 (StataCorp) and Prism V.8 (GraphPad Software, San Diego, California) for graphing.

Patient and public involvement statement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Baseline characteristics

Of 1088 subjects undergoing an implant attempt in the Amulet Observational Study, 130 were excluded because of ICE guidance and 9 did not have an anaesthesia type reported and were also excluded. Remaining patients were categorised by GA (n=607, 64%) or CS (n=342, 36%) usage and enrolled from 57 different clinical centres. Mean age of the study population was 75 years in both groups, and most of the patients were men (GA: 67% vs CS: 63%, p=0.227). The mean CHA_2DS_2Vasc score in the GA group was 4.2±1.5 and 4.1±1.6 in the CS group (p=0.487). Previous major bleeding events (GA: 75% vs CS: 65%, p=0.001) and stroke (GA: 28% vs CS: 21%,

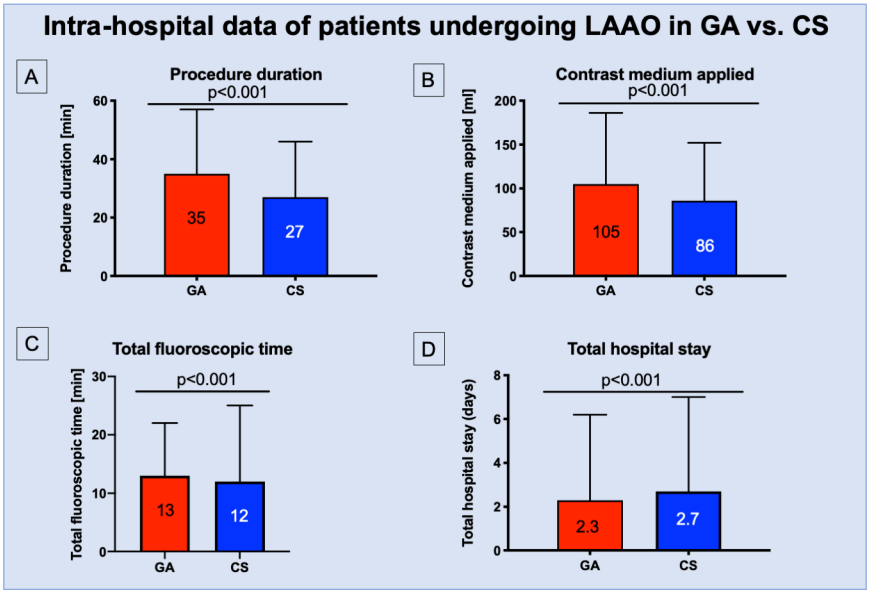

Figure 2 Intrahospital outcome of patients undergoing left atrial appendage occlusion (LAAO) in general anaesthesia (GA) versus conscious sedation (CS). (A) The procedure duration—defined as the duration from the first delivery system in to the removal of the dilator/delivery system—(GA: 35 min±22 vs CS: 27 min±19, p<0.001), (B) the total amount of contrast medium used (GA: 105 mL±81 vs CS: 86 min±66, p<0.001) and (C) the total fluoroscopy time (GA: 13 min±9 vs CS: 12 min±13, p<0.001) differed between groups. (D) The total length of stay was shorter in the GA group (GA: 2.3 days±3.9 vs CS: 2.7 days±4.3, p<0.001).

p=0.016) occurred more frequently in the GA group. Further baseline characteristics are presented in table 1.

In-hospital outcomes

Technical success (implantation of the Amplatzer Amulet occluder) was 99% (940 of 949 patients) in both groups. Seven implant attempts were unsuccessful due to LAA anatomy not accommodating an Amplatzer Amulet occluder. One procedure was terminated due to the X-ray system malfunction and occurrence of a thrombus on the sheath. The final unsuccessful implant was due to unknown reasons. There were no major differences in baseline characteristics between patients with and without successful implants. Chicken wing morphology was more often preset in the CS group (GA: 39% vs CS: 51%, p<0.001). Of the nine subjects with unsuccessful implant attempts six were under GA and three were under CS.

The procedure duration (GA: 35 min±22 vs CS: 27 min±19, p<0.001, figure 2A), and the total amount of contrast medium used (GA: 105 mL±81 vs CS: 86 mL±66, p<0.001, figure 2B) differed between groups. Early (≤1 day) procedure-related or device-related SAEs (GA: 4.1% vs CS: 4.4%, p=0.867) were evenly distributed, with pericardial effusion/tamponade as the most common complication (GA: 1.2% vs CS: 1.2%, p=1.000). No episode of aspiration pneumonia or pulmonary complication was noted in the CS group. In the GA group, one (0.16%) patient experienced and early ischaemic stroke and three patients (0.87%) in the CS group, respectively. One (0.29%) of those was attributed to air embolism. The total length of stay was shorter in the GA group (GA: 2.3 days±3.9 vs CS: 2.7 days±4.3, p<0.001, figure 2C). Further in-hospital data and SAEs during the first 7 days after the index procedure are displayed in table 2.

Choice of anaesthetic method by operator experience and regional preference

Implanters were analysed according to their volume of TEE-guided procedures performed during the Amulet Observational Study: lowest volume (n=24 operators, 1–3 implants each), moderate volume (n=41 operators, 4–18 implants each) and highest volume (n=21 operators, 19–42 implants each). The preferred anaesthesiologic method tended to be CS in operators with the highest volume (CS: 39%) as compared with operators with low (CS: 28%) or moderate (CS: 33%) volume of Amulet occluder implants performed in the study.

In Germany, 75% of all enrolled subjects undergoing TEE-guided implant were managed with CS, contributing to the most subjects in the entire CS group (n=279, 81.6%). Switzerland performed all TEE cases using CS, although only six cases. Thirty-four (34) of Spain's 99 implants, and 11 of Hong Kong's 41 implants, were performed using CS. As shown in figure 3 and in table 3, many countries exclusively managed patients with GA.

7-Day follow-up

The mortality rates were similar (GA: 0.3% vs CS: 0.3%, p=1.000, figure 4A). An ischaemic stroke occurred in 0.2% of GA, and in 0.9% of CS patients (p=0.136, figure 4B) and major bleeding events occurred in 2.3% of the GA group and in 4.1% of the CS group (p=0.160, figure 4C). Overall, the procedure-related or device-related SAEs tended to be higher in the CS group (GA: 4.9% vs CS:

Table 2 In-hospital data

	General anaesthesia (n=607)	Conscious sedation (n=342)	P value	Difference (95% CI)
Procedure duration (min)	35±22	27±19	<0.001	8.0 (5.0 to 10.0)
Total heparin (units)	7751±3991	7297±2399	0.329	
Maximum activated clotting time (s)	306±107	268±88	<0.001	
Total contrast (mL)	105±81	86±66	<0.001	15.0 (10.0 to 20.0)
Total fluoroscopic time (min)	13±9	12±13	<0.001	2.0 (1.4 to 3.0)
Technical success	99%	99%	1.000	
Procedural success	96%	94%	0.080	
Peridevice residual flow				
<3 mm	99.7%	98.2%	0.091	
≤5 mm	100%	100%	1.000	
Procedure-related/device-related SAE≤1 day	4.1%	4.4%	0.867	
-Pericardial effusion/tamponade	1.2%	1.2%	1.000	
-Delirium/confusion	0.2%	0%	1.000	
-Pneumoniae	0%	0.0%	1.000	
-Device embolisation	0.2%	0.3%	1.000	
Procedure-related/device-related SAE ≤7 days	4.9%	7.6%	0.114	
Acute pulmonary oedema	0.2%	0%		
Acute renal failure	0%	0.30%		
Air embolus	0%	0.30%		
Anemias	0%	0.90%		
Aphasia	0%	0.30%		
Atrioventricular block	0.2%	0%		
Bleeding	0.2%	0%		
Cardiac decompensation	0%	0.30%		
Cardiac perforation	0.2%	0%		
Chronic obstructive pulmonary disease	0%	0.3%		
Chronic subdural haematoma	0%	0.3%		
Decompensated heart failure	0%	0.3%		
Device embolisation	0.2%	0.3%		
Epistaxis	0.2%	0%		
Fall	0.2%	0%		
Fever	0.2%	0%		
Gastrointestinal bleeding	0.2%	0.60%		
Haematoma	0%	0.3%		
Haematuria	0%	0.3%		
Haemoperitoneum	0.2%	0%		
Hypotension	0.2%	0%		
Ischaemic stroke	0.2%	0.3%		
Pacemaker lead dislodgement	0%	0.3%		
Pericardial effusion	0.3%	1.2%		
Pericardial tamponade	0.8%	1.2%		
Pulmonary oedema	0.2%	0%		
Pulmonary embolism	0.2%	0%		

Continued

Table 2 Continued

	General anaesthesia (n=607)	Conscious sedation (n=342)	P value	Difference (95% CI)
Pleural effusion	0%	0.6%		
Pneumonia	0%	0.3%		
Respiratory failure	0%	0.3%		
Shock	0.2%	0%		
Seizure/convulsions/epilepsy	0%	0%		
TEE-related event	0.2%	0%		
Thrombus on device	0.2%	0.3%		
Urinary retention	0.2%	0.3%		
Vascular access site AV fistula	0.2%	0.3%		
Vascular access site bleeding	0.3%	0.3%		
Vascular access site haematoma	0.5%	0.3%		
Vascular access site pseudoaneurysm	0%	0.6%		
Length of stay (days)	2.3±3.9	2.7±4.3	<0.001	−2.6E−06 (−4.8E−05, −3.6E−05)

The column 'Difference (95%)' is defined by an estimator for the difference of the location parameter and the non-parametric CI.
SAE, serious adverse event.

7.6%, p=0.114). Peridevice residual flow ≤5 mm was in 99.7% of the GA patients and in 100% of CS patients (p=1.000, figure 4D).

DISCUSSION

Over recent years, percutaneous LAAO became of growing importance in the field of non-pharmacological stroke prevention, especially in patients with AF not fit for long-term anticoagulation therapy. This current analysis of the Amplatzer Amulet Observational Study shows that:

1. Percutaneous LAAO using CS has non-inferior periprocedural and 7-day outcomes as compared with LAAO under GA;
2. The use of CS was associated with a shorter procedure duration and less contrast medium used.

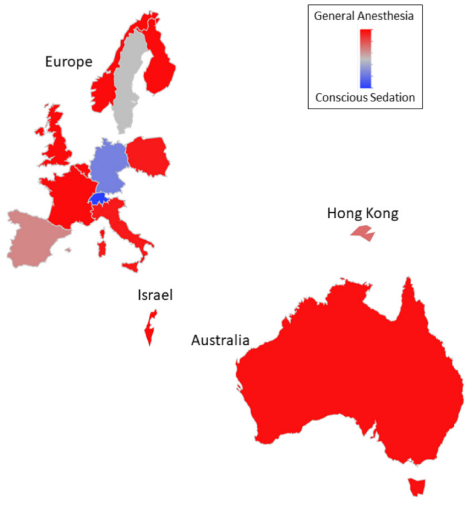

Figure 3 Heat map of anaesthetic method in the Amplatzer Amulet Occluder Observational Study. Countries performing transoesophageal echocardiography-guided implants in the Amplatzer Amulet Observational Study are color-coded based on their anaesthesiologic method of choice: shades of blue represent countries where conscious sedation is the method of choice, whereas shades of red stand for countries where general anaesthesia is most often used during left atrial appendage occlusion procedure.

Safety and efficacy of structural heart disease interventions in CS

In the growing field of percutaneous structural heart disease interventions, the ability to perform procedures using CS is increasingly important.[7 16] On the one hand, this might be attributed to a budget-restricted healthcare system, where time-effectiveness and cost-effectiveness[17–20] play an increasing role. On the other hand, CS may benefit patients with a less invasive procedure and a potential early recovery. Regarding LAAO, only one small study[6] with 11 patients explicitly examined the role of CS and found it to be feasible and safe. Irrespective of the anaesthesiologic method of choice, patients participating in the Amplatzer Amulet Observational Study experienced high procedural technical success and low complication rates as compared with similar studies and registries.[21]

An often-stated drawback of CS is the perceived inability to adequately react to procedural complication. Major complications of the LAAO procedure may include cardiac complications (ie, cardiac tamponade or pericardial effusion), vascular complications or stroke, which can be managed without the need for GA in almost all cases. The procedure-related or device-related SAEs tended to be higher in the CS group. The detailed

Table 3 Analysis of the anaesthesiologic method by country and site

Country	Number of sites	Number of subjects	Number of patients in GA	Number of patients in CS	%GA	%CS
Belgium	2	17	17	0	100	0
Finland	3	55	55	0	100	0
France	5	59	59	0	100	0
Israel	1	1	1	0	100	0
Norway	1	3	3	0	100	0
The Netherlands	1	1	1	0	100	0
United Kingdom	4	59	59	0	100	0
Australia	4	69	68	1	99	1
Poland	2	26	25	1	96	4
Italy	7	129	124	5	96	4
Hong Kong	2	41	30	11	73	27
Spain	7	99	65	34	66	34
Sweden	2	10	5	5	50	50
Germany	15	374	95	279	25	75
Switzerland	1	6	0	6	0	100

CS, conscious sedation; GA, general anaesthesia.

listing in table 2 shows that singular SAEs occur only in very small numbers in both groups and do not lead to a remarkable difference in clinical outcomes. However, the numerically higher number of procedure/device-related SAE in the CS group might be attributed to the predominantly more complex LAA anatomy (chicken wing morphology GA: 39% vs CS: 51%, p<0.001). LAAO is feasible and safe in all typical LAA morphologies,[22] but chicken wing morphology can constitute a special challenge for the implanting team, especially when an anterior orientation[23] or early and severe bands[24] are present. As our study could show, a very low rate of pulmonary complications was observed in the CS group and an early ischaemic stroke due to air embolism was noted in only one patient. Moreover, neurological impairment or pain, important signals of access site bleeding, can be detected

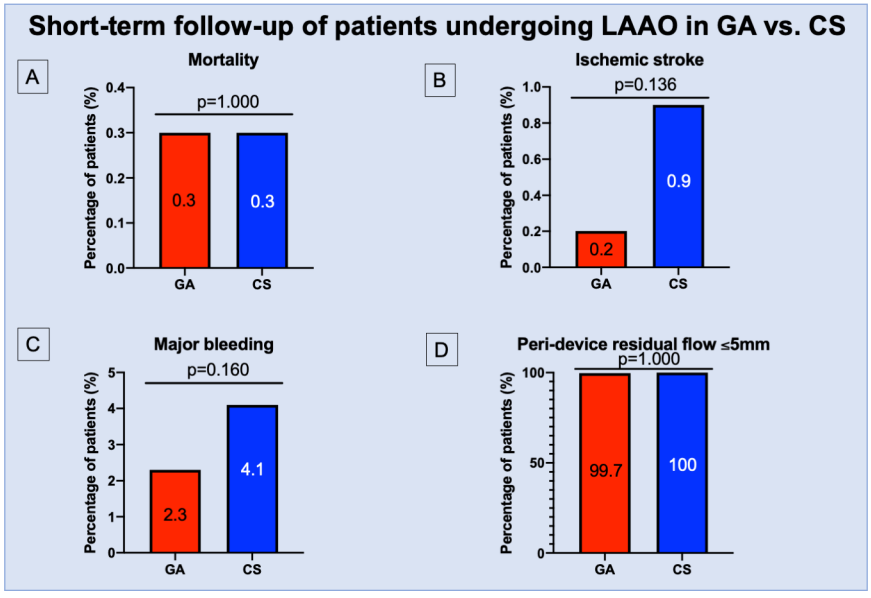

Figure 4 Short-term follow-up. (A) The overall mortality rate at 7 days did not differ (general anaesthesia (GA): 0.3% vs conscious sedation (CS): 0.3%, p=1.000). (B) An ischaemic stroke occurred in 0.2% of GA, and in 0.9% of CS patients (p=0.136) and (C) major bleeding events occurred numerically more often in the CS group (GA: 2.3% vs CS: 4.1%, p=0.160) 7 days post implant. (D) Peridevice residual flow ≤5 mm was evenly distributed (GA: 99.7% vs CS: 100%, p=1.000). LAAO, left atrial appendage occlusion.

earlier in CS patients. Additionally, CS should be sufficient for TEE tolerance and to suppress agitation potentially jeopardising the procedural success. A structured team training may help to give centres the opportunity to confidently switch from GA to CS for LAAO implants. Catheterisation laboratory nurses, the imaging cardiologist, if applicable the anaesthesiologist and of course the interventionalist should participate in this team training, since these individuals guide patients through LAAO. The aim is to achieve patient comfort and safety with a spontaneously breathing patient, who does not jeopardise the procedure by agitation or body movements. Several approaches to minimalise image guidance with micro-TEE or ICE[25–27] are new ideas to further increase patient comfort during the procedure. As our data show, very low rates of procedure-related events occurred in the GA and CS group with comparable results. The procedure duration was even shorter and less contrast medium applied which might also be related to an increased operator experience and potentially more frequent procedural preplanning with TOE or cardiac CT in the CS group. However, the total hospital length of stay favoured GA but with questionable clinical relevance as the mean difference was only 1/5 of a day.

Operator experience and regional preferences determine the anaesthetic method of choice

Especially in the field of interventional cardiology, operator experience is often key to success and leads to improved risk-adjusted in hospital outcomes.[28] Data from the early WATCHMAN (Boston Scientific, Marlborough, Massachusetts, USA) experience suggest that this applies to LAAO, with improvements in procedural safety, corresponding with increased operator experience.[29] Increasing familiarity with the procedure might be associated with a less-invasive approach, thus switching from GA to CS. High-volume and thus more experienced implanters in the Amplatzer Amulet Occluder Observational Study tended to use a higher proportion of CS. Unfortunately, we do not have information on the implanters experience before participation in the study, which could have helped to clarify this important question. In addition to operator experience, regional preferences seem to have impact on the choice of anaesthetic strategy. However, institutional preferences could also play a role as no complete national LAAO cohorts are reported. In other structural heart disease interventions, like transcatheter aortic valve replacement, centres in Europe tend to choose CS over GA, whereas Northern America often relies on GA.[30] This might also apply to patients undergoing interventional LAAO. Here, selection of anaesthesia appears to be substantially influenced by operator's preference and national practice rather than patient characteristics.

Limitations

This is a prospective, multicentre-global trial with nearly 1000 participants in this subanalysis. However, it is not randomised and only one specific device for LAAO was used. The study was initially not powered to determine difference between patients undergoing the procedure in CS or GA. The exact type of sedation used and who managed the sedation (ie, operator or anesthesiologist) were not collected in the study. Some potential landmark parameters such as time on the intensive care unit, time on ventilation or use of inotropes were not captured in the study. Additionally, no cost data or quality of life indices were collected throughout the study period. Some factors confounding the impact of anaesthesia method may not have been accounted for. Analyses were not adjusted for centre due to the high number patients were enrolled from, for country as the anaesthesia method is generally constant within most countries, or for patient characteristics as most are unlikely to impact the results of this analysis using short follow-up focused on periprocedural outcomes.

CONCLUSION

Percutaneous LAAO in CS seems to be safe and periprocedural clinical results through 7 days may be comparable to those of GA. In this study, patients undergoing LAAO in CS have a shorter procedure duration and less contrast medium applied. However, the total length of hospital stay was longer as compared with GA patients but with questionable clinical relevance and likely some residual confounding given the differences between groups which cannot be sufficiently adjusted for.

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REFERENCES

1 Chugh SS, Havmoeller R, Narayanan K, *et al*. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. *Circulation* 2014;129:837–47.
2 Zimetbaum P. Atrial fibrillation. *Ann Intern Med* 2017;166:ITC33–48.
3 Freeman JV, Hutton DW, Barnes GD, *et al*. Cost-Effectiveness of percutaneous closure of the left atrial appendage in atrial fibrillation based on results from protect AF versus prevail. *Circ Arrhythm Electrophysiol* 2016;9.
4 , January CT, Wann LS, *et al*, Writing Group Members. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American heart association Task force on clinical practice guidelines and the heart rhythm Society. *Heart Rhythm* 2019;16:e66–93.
5 Kirchhof P, Benussi S, Kotecha D, *et al*. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;37:2893–962.
6 Chan N-Y, Lau C-L, Tsui P-T, *et al*. Experience of left atrial appendage closure performed under conscious sedation. *Asian Cardiovasc Thorac Ann* 2015;23:394–8.
7 Rassaf T, Balzer J, Zeus T, *et al*. Safety and efficacy of deep sedation as compared to general anaesthesia in percutaneous mitral valve repair using the MitraClip system. *Catheter Cardiovasc Interv* 2014;84:E38–42.
8 Eskandari M, Aldalati O, Dworakowski R, *et al*. Comparison of general anaesthesia and non-general anaesthesia approach in Transfemoral transcatheter aortic valve implantation. *Heart* 2018;104:1621–8.
9 Hyman MC, Vemulapalli S, Szeto WY, *et al*. Conscious sedation versus general anesthesia for transcatheter aortic valve replacement: insights from the National cardiovascular data registry Society of thoracic Surgeons/American College of cardiology transcatheter valve therapy registry. *Circulation* 2017;136:2132–40.
10 van Haperen M, Preckel B, Eberl S. Indications, contraindications, and safety aspects of procedural sedation. *Curr Opin Anaesthesiol* 2019;32:769–75.
11 Memtsoudis SG, Rasul R, Suzuki S, *et al*. Does the impact of the type of anesthesia on outcomes differ by patient age and comorbidity burden? *Reg Anesth Pain Med* 2014;39:112–9.
12 Ahmad M, Patel JN, Vipparthy SC, *et al*. Conscious sedation versus general anesthesia in transcatheter aortic valve replacement: a cost and outcome analysis. *Cureus* 2019;11:e4812.
13 Casu G, Gulizia MM, Molon G, *et al*. ANMCO/AIAC/SICI-GISE/SIC/SICCH consensus document: percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation patients: indications, patient selection, staff skills, organisation, and training. *Eur Heart J Suppl* 2017;19:D333–53.
14 Hildick-Smith D, Diener H-C, Schmidt B, *et al*. Rationale and design of a global registry to evaluate real-world clinical outcomes in patients with atrial fibrillation and high risk of stroke treated with left atrial appendage occlusion using the AMPLATZER amulet device-Perspective of available/ongoing registries of catheter-based LAA occlusion. *Catheter Cardiovasc Interv* 2018;91:540–7.
15 Landmesser U, Schmidt B, Nielsen-Kudsk JE, *et al*. Left atrial appendage occlusion with the AMPLATZER Amulet device: periprocedural and early clinical/echocardiographic data from a global prospective observational study. *EuroIntervention* 2017;13:867–76.
16 Greif M, Lange P, Näbauer M, *et al*. Transcutaneous aortic valve replacement with the Edwards SAPIEN XT and medtronic CoreValve prosthesis under fluoroscopic guidance and local anaesthesia only. *Heart* 2014;100:691–5.
17 Hong JC, Blankstein R, Shaw LJ, *et al*. Implications of Coronary Artery Calcium Testing for Treatment Decisions Among Statin Candidates According to the ACC/AHA Cholesterol Management Guidelines: A Cost-Effectiveness Analysis. *JACC Cardiovasc Imaging* 2017;10:938–52.
18 Cowper PA, Sheng S, Lopes RD, *et al*. Economic analysis of apixaban therapy for patients with atrial fibrillation from a US perspective: results from the ARISTOTLE randomized clinical trial. *JAMA Cardiol* 2017;2:525–34.
19 Arrieta A, Hong JC, Khera R, *et al*. Updated cost-effectiveness assessments of PCSK9 inhibitors from the perspectives of the health system and private payers: insights derived from the Fourier trial. *JAMA Cardiol* 2017;2:1369–74.
20 Reddy VY, Akehurst RL, Gavaghan MB, *et al*. Cost-Effectiveness of left atrial appendage closure for stroke reduction in atrial fibrillation: analysis of pooled, 5-year, long-term data. *J Am Heart Assoc* 2019;8:e011577.
21 Reddy VY, Sievert H, Halperin J, *et al*. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. *JAMA* 2014;312:1988–98.
22 Fastner C, Nienaber CA, Park J-W, *et al*. Impact of left atrial appendage morphology on indication and procedural outcome after interventional occlusion: results from the prospective multicentre German LAARGE registry. *EuroIntervention* 2018;14:151–7.
23 Murarka S, Lazkani M, Moualla S, *et al*. Left atrial anatomy and patient-related factors associated with adverse outcomes with the Watchman device-a real world experience. *J Interv Cardiol* 2017;30:163–9.
24 Freixa X, Tzikas A, Basmadjian A, *et al*. The chicken-wing morphology: an anatomical challenge for left atrial appendage occlusion. *J Interv Cardiol* 2013;26:509–14.

25 Barreiro-Perez M, Cruz-González I, Moreno-Samos JC, *et al*. Feasibility, Safety, and Utility of Microtransesophageal Echocardiography Guidance for Percutaneous LAAO Under Conscious Sedation. *JACC Cardiovasc Interv* 2019;12:1091–3.
26 Nijenhuis VJ, Alipour A, Wunderlich NC, *et al*. Feasibility of multiplane microtransoesophageal echocardiographic guidance in structural heart disease transcatheter interventions in adults. *Neth Heart J* 2017;25:669–74.
27 Basman C, Parmar YJ, Kronzon I. Intracardiac echocardiography for structural heart and electrophysiological interventions. *Curr Cardiol Rep* 2017;19:102.
28 Salemi A, Sedrakyan A, Mao J, *et al*. Individual Operator Experience and Outcomes in Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv* 2019;12:90–7.
29 Reddy VY, Holmes D, Doshi SK, *et al*. 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.
30 Dall'Ara G, Eltchaninoff H, Moat N, *et al*. Local and general anaesthesia do not influence outcome of Transfemoral aortic valve implantation. *Int J Cardiol* 2014;177:448–54.