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Appraising the safety and efficacy profile of left atrial appendage closure in 2016 and the future clinical perspectives. Results of the EAPCI LAAC survey

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KEYWORDS

- bleeding prevention
- cardioembolic stroke prevention
- left atrial appendage closure

Abstract

Aims: The aim of this study was to determine the opinion of the scientific community regarding percutaneous left atrial appendage closure (LAAC). The main focus of the survey was on concerns and expectations regarding the safety and efficacy profile of LAAC in clinical practice and on current and future clinical perspectives.

Methods and results: A voluntary web-based survey was distributed by the European Association of Percutaneous Coronary Interventions (EAPCI) to all individuals registered on the EuroIntervention mailing list (n=21,800). A total of 724 physicians responded to the survey, of whom 31.8% had first operator experience with LAAC. Exclusive use of the Amulet (34.4%) or WATCHMAN (30.3%) was similar, but the former was the most frequently used device in Europe. The majority of respondents (59.3%) deemed LAAC to be as effective as, but safer than oral anticoagulants (OAC) in reducing stroke risk. Periprocedural complications (40.3%) and cost (28.8%) were the major concerns. Most practitioners did not consider novel oral anticoagulants (NOACs) to be a deterrent for performing LAAC procedures. Moreover, a history of serious haemorrhage was not deemed necessary to justify LAAC for 59.8% of physicians.

Conclusions: The results of this survey reveal a high level of confidence in percutaneous LAAC amongst surveyed interventional cardiologists, with the majority believing it to be as effective as OAC in terms of stroke prevention and safer in terms of bleeding risk.

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Introduction

Atrial fibrillation (AF) is a major health issue due to its growing prevalence and potentially devastating complications, the most important of these being cardioembolic stroke[1]. The absence of atrial systole in the presence of AF results in stasis of blood in the left atrium, and, in particular, the tubular left atrial appendage (LAA). This structure, which is a remnant of the embryonic left atrium, has trabeculated walls which, in the absence of sinus rhythm, further increase the risk of thrombus formation. Over the past few decades, vitamin K antagonists (VKA) have been regarded as the treatment of choice for stroke prevention in AF patients, despite the considerable associated bleeding risk[2]. More recently, novel oral anticoagulants (NOACs) with more predictable pharmacokinetic and pharmacodynamic profiles have been approved for the prevention of thromboembolic events in patients with AF. The superior safety and non-inferior efficacy profiles of these agents compared with VKAs have been proven in randomised trials[3-5], and their use in clinical practice is growing. Despite this, some patients have an unacceptable bleeding risk to justify oral anticoagulation (OAC) and remain at considerable risk of thromboembolism.

The role of the LAA in systemic thromboembolism in AF patients is well established[6,7]. This has led to the development of surgical and, more recently, percutaneous strategies for effective amputatation or obliteration of the LAA to prevent stroke. There are a number of commercially available percutaneous transcatheter LAA closure (LAAC) devices, with WATCHMAN™ (Boston Scientific, Marlborough, MA, USA) and AMPLATZER™ Amulet™ (St. Jude Medical, St. Paul, MN, USA) accounting for the majority of devices used worldwide. Both of these devices received CE mark approval in Europe and have been granted a class IIb indication with level of evidence B for percutaneous LAAC in patients at high stroke risk and contraindications to long-term OAC in European guidelines[8].

The safety and efficacy of the WATCHMAN device were tested in two randomised trials, namely the WATCHMAN Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation (PROTECT AF) trial[9] and the Prospective Randomized Evaluation of the WATCHMAN LAA Closure Device In Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy (PREVAIL) trial[10]. Following these pivotal trials, the WATCHMAN device was granted approval by the Food and Drug Administration (FDA) for use in the United States of America with limited labelling: "patients that are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2- VASc scores and are recommended for anticoagulation therapy"; "are deemed by their physicians to be suitable for warfarin"; and "have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin"[11]. The Amulet device is not currently FDA-approved. Despite a lack of randomised clinical trial data, however, it is widely used in some jurisdictions – particularly in Europe – facilitating publication of registry data[12-14].

The aim of the current study was to determine the opinions of the scientific community regarding percutaneous LAAC. In particular, the study aimed to determine operators' experience with the procedure, their concerns regarding the risk/benefit profile of LAAC, and their opinions on current and future clinical perspectives.

Methods

This was a voluntary web-based survey undertaken by the European Association of Percutaneous Coronary Interventions (EAPCI). The survey was conducted using a free web-based survey tool (SurveyMonkey, Palo Alto, CA, USA) and comprised multiple-choice questions, including the possibility of adding further comments if desired. It was not mandatory to reply to the entire survey. The sample population comprised the mailing list of EuroIntervention – the official journal of the EAPCI. Overall, a total of 21,800 individuals were invited to participate. The invitation to participate in the survey was sent on 18 January 2016, and a reminder was issued on 8 February 2016. The data are reported as percentages and compared using the chi-square test. A two-sided p-value <0.05 was considered significant. The results were stratified by age (i.e., <40 vs. 40 to 50 vs. >50 years), jurisdiction of practice (i.e., European vs. non-European), experience with LAAC (procedural experience as first operator versus no prior direct procedural involvement), level of interventional cardiology experience (i.e., interventional cardiologist with more than 10 vs. 5 to 10 vs. <5 years of experience vs. non-interventional cardiologist). All analyses were performed with STATA, version 13.0 (StataCorp LP, College Station, TX, USA).

Results

CHARACTERISTICS OF RESPONDENTS

Of the 21,800 invitations sent, a total of 724 (3.3%) recipients responded to the survey. Among these, 604 (83%) provided personal and professional information with respect to age, medical qualification and country of practice **(Online Table 1)**. Participation in the survey was global, with the majority of respondents being European (54.3%) or Asian (22.7%). Leading contributing countries were Italy and Germany, with 55 responders each. The median age of respondents was 46 years. Most of the participants were interventional cardiologists at various stages of their career, with the majority (49%) having >10 years of experience, followed by non-interventional cardiologists and cardiologists in training (8.4% and 4.6%, respectively). A small proportion – accounting for 7.1% of respondents – categorised their profession as "other". Characteristics of respondents are detailed in **Table 1**, **Online Figure 1**, and **Online Figure 2**.

Q1. Do you have experience in percutaneous LAAC?

The majority of responders replied yes to this question, with 31.7% having performed LAAC as first operator and 27.8% working in centres offering percutaneous LAAC; 40.5% of participants declared no experience with LAAC **(Figure 1, Online Table 2)**. Procedural expertise varied across age groups, with 22.2% of first

Table 1. Characteristics of respondents.

Age group		
Answered: 601, Skipped: 123	Percentage	Response count
<40 years	27.65%	167
≥40 years ≤50	37.25%	225
>50 years	34.60%	209
Country		
Answered: 604, Skipped: 120	Percentage	Response count
Europe	54.30%	328
Asia	22.68%	137
North America	8.28%	50
South America	7.28%	44
Africa	5.46%	33
Oceania	1.82%	11
Antarctica	0.17%	1
Q10. Please select the professional figure, which describes you at best		
Answered: 604, Skipped: 120	Percentage	Response count
Interventional cardiologist with more than 10 years of experience	49.01%	296
Interventional cardiologist with more than 5 years of experience	16.89%	102
Interventional cardiologist with less than 5 years of experience	13.91%	84
Non-interventional cardiologist	8.44%	51
Cardiologist in training	4.64%	28
Others	7.12%	43

operators younger than 40 years compared with 40.7% among more senior (>50 years old) responders (p<0.0001).

Twice as many European, as compared to non-European, respondents declared having first operator LAAC procedural experience (44.8% vs. 22.1%, p<0.0001), and non-European participants more frequently reported working in centres where LAAC is not an established treatment option (European vs. non-European: 24.4% vs. 52.9%, p<0.0001) **(Figure 2, Online Figure 3)**.

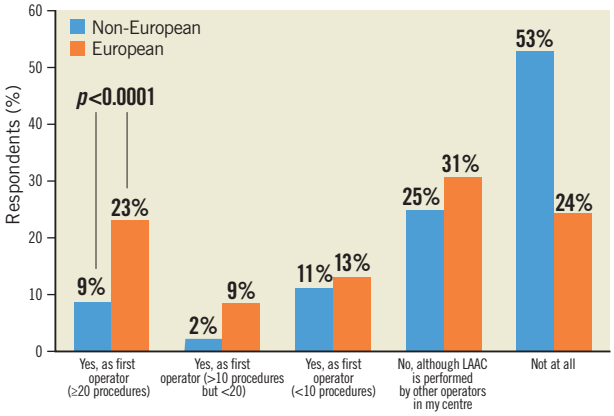

Figure 2. *Question 1 stratified by region.*

Q2. Which LAA occluder device do you or does your centre have experience with?

This question surveyed personal or centre-specific experience with different LAAC devices: in particular, respondents had to choose among WATCHMAN, Amulet, both or other devices (using a free text field). Overall experience with Amulet and WATCHMAN was similar at 34.4% and 30.3%, respectively. Approximately one third of respondents declared having experience with both devices. Among the small proportion of those who chose "other devices" (3.8%), the most frequently indicated choice was the AMPLATZER Cardiac Plug (St. Jude Medical), i.e., the first-generation AMPLATZER™ LAAC device **(Figure 3, Online Table 1)**. Not surprisingly, device penetration varied across countries, with the use of Amulet (resulting by combining declared experience with Amulet device only or "both") comprising 22.8% for non-European respondents versus 56.7% among European respondents (p<0.0001).

Q3. Based on your personal experience, do you think that the safety/efficacy profile of LAA occluders may differ in practice?

The majority of respondents selected the "I do not know" answer (39.1%), followed by those who considered the two available

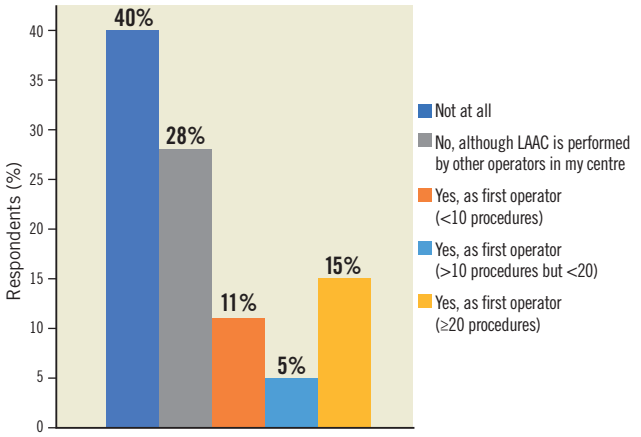

Figure 1. *Question 1: Do you have experience in percutaneous left atrial appendage closure (LAAC)?*

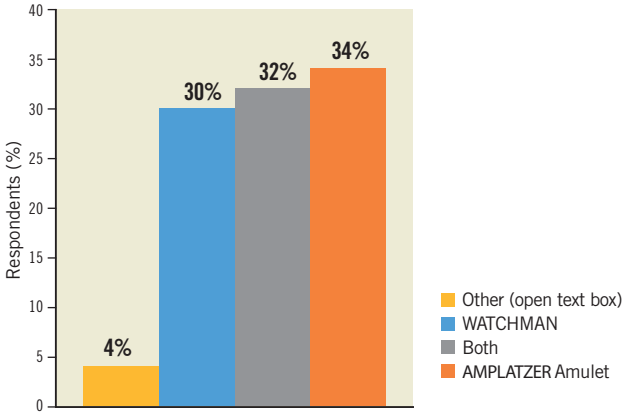

Figure 3. *Question 2: Which LAA occluder device do you or does your centre have experience with?*

devices equivalent (27.3%). Approximately 18% and 15% of participants stated a preference for WATCHMAN or Amulet, respectively **(Figure 4, Online Table 1)**. There was a significant relationship (p<0.0001) between perceived device superiority and prior procedural experience in that WATCHMAN and Amulet were considered superior by those operators disclosing selective prior experience with the WATCHMAN and Amulet device, respectively **(Figure 5)**. European respondents were more likely than their non-European colleagues to judge the clinical performance of these two devices as equivalent (European vs. non-European: 62.7% vs. 37.3%, p=0.008). There was no detectable age effect for this answer.

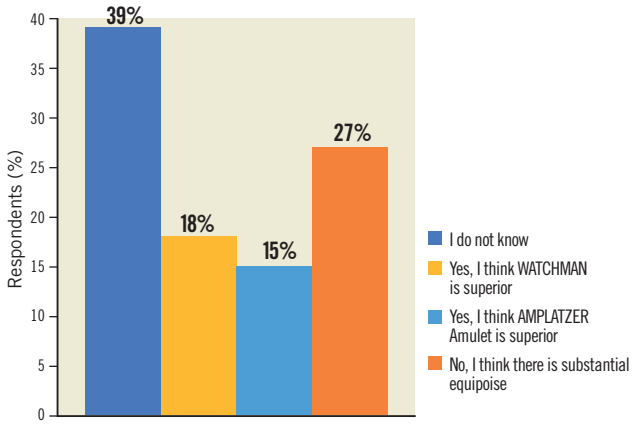

Figure 4. *Question 3: Based on your personal experience, do you think that the safety/efficacy profile of LAA occluders may differ in practice?*

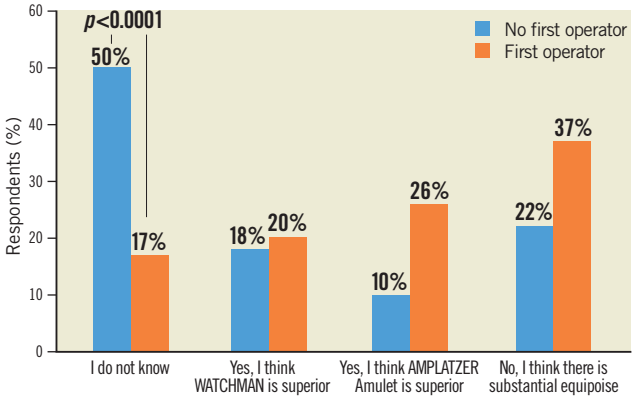

Figure 5. *Question 3: stratified by experience as operator.*

Q4. Do you think that the evidence supporting LAAC is:

Many responders regarded evidence in support of LAAC as "Good" (46.2%) or at least "Average" (40.1%), and 11.8% of responders considered it "Scarce" **(Figure 6, Online Table 1)**. Prior first operator LAAC experience affected the answers to this question, leading to higher satisfaction rates in favour of available evidence ("Good" choice in 57.3% vs. 40.6% of responses, p<0.0001)

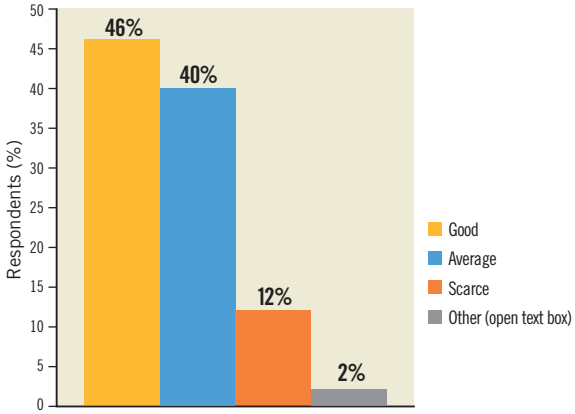

Figure 6. *Question 4: Do you think that the evidence supporting LAAC is:*

(Figure 7). On the other hand, no prior direct first operator experience was more frequently associated with the "Scarce" choice (no first operator vs. first operator: 14.1% vs. 7.3%, p=0.011). There were no differences among age groups or countries.

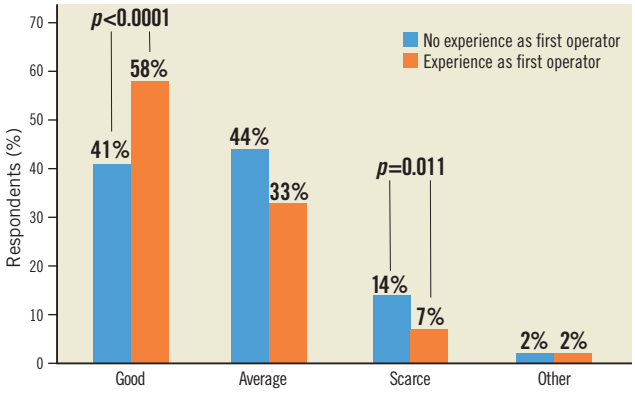

Figure 7. *Question 4 stratified by experience as operator.*

Q5. LAAC has been so far compared to vitamin K antagonists. Do you think that the availability of NOACs should further restrict LAAC?

The large majority (66.8%) of respondents thought that the growth of LAAC is and will not be restricted by the availability of NOACs **(Figure 8, Online Table 1)**. This answer was consistent with replies obtained for previous questions: responders who deemed quality of evidence for LAAC "Good" or those with prior first operator experience were confident that NOACs should and will not restrict indications for LAAC ("Good" vs. "No good" in Q4: 80% vs. 55.5%, p<0.0001; first operator vs. no first operator: 75.3% vs. 62.6%, p<0.0001).

Q6. Do you think that LAAC should be restricted only to patients with previous serious or life-threatening bleeding?

Almost 60% of participants responded that LAAC is a reasonable treatment option also in patients without history of severe bleeding

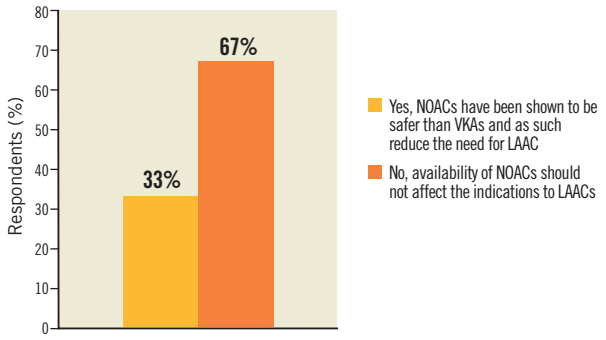

Figure 8. *Question 5: LAAC has been so far compared to vitamin K antagonists. Do you think that the availability of non-vitamin K oral anticoagulants (NOACs) should further restrict LAAC?*

as long as they are deemed at high bleeding risk **(Figure 9, Online Table 1)**. Those with prior first operator experience and those who judged NOACs' availability of no concern regarding current or future indications for LAAC were more likely to answer LAAC as bleeding primary prevention treatment option (first operator vs. no first operator: 67.1% vs. 53%, p=0.002; "No, …" vs. "Yes, …" in Q5: 70.5% vs. 38.2%, p<0.0001).

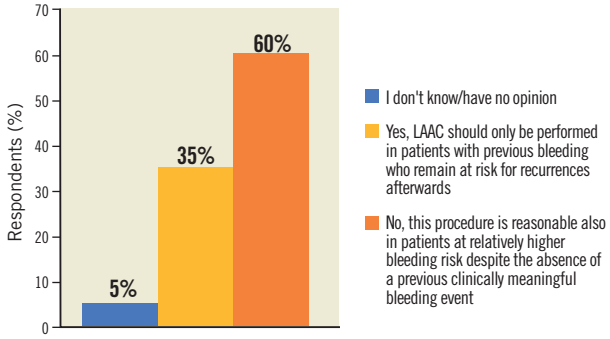

Figure 9. *Question 6: Do you think that LAAC should be restricted only to patients with previous serious or life-threatening bleeding?*

Q7. In your opinion, percutaneous LAAC compared to OAC is:

The majority of respondents (59.4%) stated that LAAC is "as effective as OAC in preventing stroke and safer due to lower bleeding risks". The other participants were almost equally divided among those who thought that LAAC is "less effective in preventing stroke but safer due to bleeding reduction" (19.5%), and those who considered LAAC "as effective as OAC in preventing stroke but with high periprocedural events rate" **(Figure 10, Figure 11, Online Table 1)**.

Q8. What worries you most about LAAC devices?

Respondents were most concerned about procedural complications of LAAC (40.3%), followed by device cost (28.8%) **(Figure 12, Online Table 1)**. Those who considered available evidence around LAAC "Scarce" in Q4 were more prone to believe that LAAC has limited efficacy in stroke prevention ("Limited efficacy in

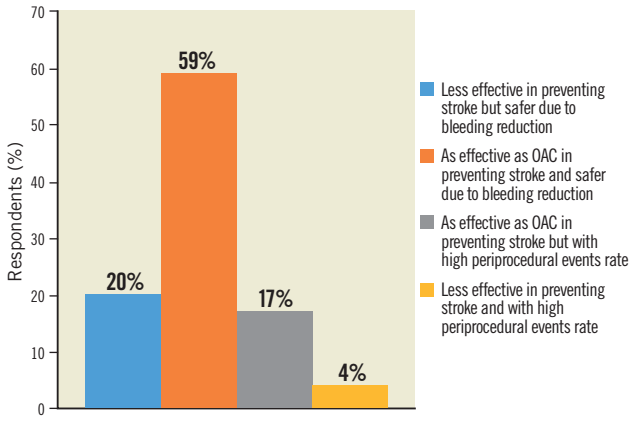

Figure 10. *Question 7: In your opinion, percutaneous LAAC compared to OAC is:*

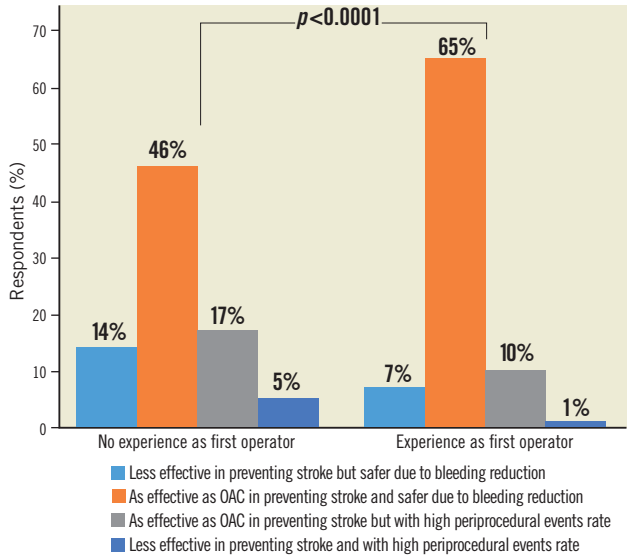

Figure 11. *Question 7 stratified by experience as operator.*

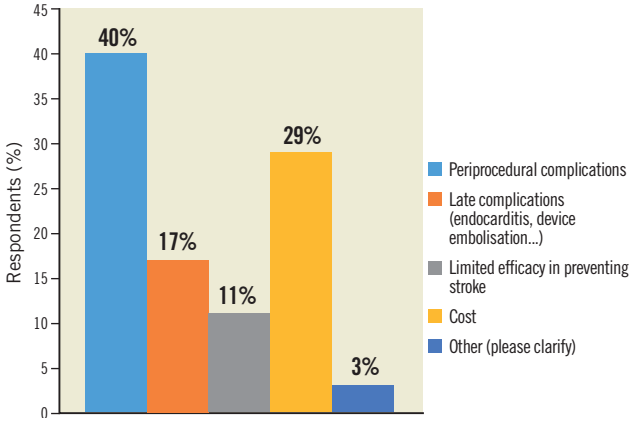

Figure 12. *Question 8: What worries you more about left atrial appendage closure devices?*

preventing stroke" vs. no "Limited efficacy in preventing stroke" in Q4: 24.7% vs. 8.7%, p<0.0001). Operators were more frequently worried about procedural complications than non-operators (47.4% vs. 36.6%, p=0.009). Finally, a greater number of non-European respondents indicated "Cost" of devices as a major issue compared with European respondents (40.2% vs. 19.2%, p<0.0001).

Q9. Do you think a short course of OAC is needed early after LAAC?

The majority of participants (55.4%) believed that there is a rationale for OAC to prevent thrombosis after the procedure prior to endothelialisation of the implanted device **(Figure 13, Online Table 1)**. However, operators who declared direct experience with LAAC procedure (any device) more frequently responded that OAC early after LAAC was not needed. This remained consistent when stratified according to the device used (operators vs. non-operators: any device 31.5% vs. 10.2%, p<0.0001; WATCHMAN: 22.6% vs. 9%, p=0.044; Amulet: 34% vs. 25%, p=0.279; both devices: 37.7% vs. 4%, p<0.0001). Moreover, in the subgroup of first-operator respondents, those with prior selective experience with WATCHMAN answered more frequently "Yes, to ensure proper endothelialisation of the implanted device" compared to physicians selectively experienced with Amulet (56.6% vs. 17.6%, p<0.0001).

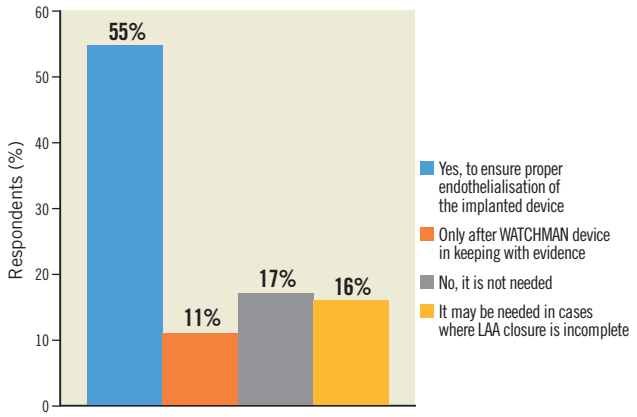

Figure 13. *Question 9: Do you think a short course of oral anticoagulants is needed early on after LAAC?*

Interpretation of the survey results

This survey confirms confidence in percutaneous LAAC, with more than seven out of ten respondents belonging to the interventional cardiology community thinking that the availability of NOACs should not limit the use of LAAC devices, despite a lack of randomised data comparing these two strategies of stroke prevention. Moreover, the majority of respondents declared that LAAC is as effective as OAC in preventing stroke and safer due to reduced bleeding risk (59.4%). Only a very small proportion of practitioners (4.3%) evaluated the safety/efficacy profile of these devices negatively ("less effective - compared to OAC - and with higher periprocedural events rate").

Along the same lines, a large proportion of participants (86%) considered the scientific evidence for LAAC to be at least "average", of whom 46% considered it "Good". Although two randomised trials have confirmed the safety and efficacy of the WATCHMAN device[9,10], only observational data exist for the Amulet device at present. While many respondents expressed uncertainty regarding the comparative effectiveness of Amulet versus WATCHMAN, one in three believed that the data supporting the use of WATCHMAN may be safely applied to the Amulet device.

The surveyed community expressed concerns regarding the occurrence of periprocedural complications (40% of respondents). The cost of the device was also raised as a potential limitation to wider use of this treatment modality, particularly outside European countries, with four out of ten in this group underlining this issue.

Finally, the community appeared uncertain regarding the need for a short course of OAC after LAAC.

It may be considered surprising that the large majority of respondents believed the availability of NOAC not to be a restriction to the future growth of LAAC procedures, despite established evidence on the improved safety/efficacy profile of NOAC compared to VKA. Likewise, Amulet utilisation was found to be high, in particular in Europe, where it was the most used device, although Amulet itself has not yet been validated in randomised clinical trials. Conversely, the concerns of physicians on periprocedural complications were expected.

Limitations

This survey has important limitations, which should be carefully weighed when interpreting the results. First, only a small percentage of invited practitioners took part in it. Therefore, the results are not necessarily representative of the opinion of the broader community. However, a low participation rate is a common limitation of surveys in general, in particular when the population targeted is that of professionals at an advanced career stage. Second, there is probably a selection bias towards respondents positively predisposed to the use of LAAC devices. Third, the respondents from European countries were more often first operators than those from non-European countries. Thus, the two sets of participants were somewhat different.

Conclusions

Despite concerns regarding the potential for periprocedural complications and increased device cost, the surveyed interventional cardiology community was predominantly in favour of LAAC as an effective and safer alternative to OAC for stroke prevention in patients with atrial fibrillation at high bleeding risk, regardless of a prior bleeding history. There was no consensus as to whether a short course of OAC is necessary after LAAC implantation nor regarding the comparative effectiveness of the two currently most used LAA occluders in practice.

Impact on daily practice

The balance between bleeding and ischaemic risk, especially in an aged and frail population, remains an unmet clinical need. Ischaemic stroke is a serious and disabling disease and it has a major impact on survival as well as on public health and costs. Similarly, bleeding events have a negative prognostic impact on mortality, morbidity and quality of life. LAAC has emerged as a viable and potentially growing treatment option in patients with atrial fibrillation at high bleeding risk. The need for risk mitigation processes regarding procedural complications and costs were the most frequently raised concerns. Lack of randomised data in support of the Amulet device or lack of comparative effectiveness data versus NOAC does not seem to undermine the value of LAAC in practice in the opinion of the respondents.

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Conflict of interest statement

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Supplementary data

Online Table 1. Survey results.
Online Table 2. List of respondents.
Online Figure 1. Region of work.
Online Figure 2. Country of work.
Online Figure 3. Question 1 stratified by professional figure.

Supplementary data

Online Table 1. List of respondents.

Name	Institution	Country
Abelson M.	Vergelegen Medi Clinic, Somerset West	South Africa
Abushokka R.	National Heart Institute	Egypt
Acevedo P.	Instituto Cardiologia Corrientes	Argentina
Acquaviva T.	U.O. Cardiochirurgia Policlinico, Bari	Italy
Adamo M.	Catheterization Laboratory, Spedali Civili, Brescia	Italy
Agarwal S.	KMC Manipal	India
Akesbi A.	CHU Bichat	France
Akin I.	University Hospital Mannheim	Germany
Alarbash M.	Madinah Cardiac Centre	Saudi Arabia
Albiero R.	Istituto Clinico San Rocco - Ome (BS)	Italy
Aldoori J.	Sulymaniah Heart Centre	Iraq
Alkinani T.	Nassiriya Heart Center	Iraq
Alli O.	University of Alabama, Birmingham	USA
Andò G.	University of Messina	Italy
Andrada B.	Monza Hospital	Romania
Angel J.	Centro Cardiovascular Sant Jordi, Barcelona	Spain
Antoniucci D.	Cardiology Department, Careggi Hospital, Florence	Italy
Arafa S.E.O.	Heart Hospital, Hamad Medical Corporation	Qatar
Arnous S.	University Hospital, Limerick	Ireland
Arroyo C.C.	Instituto de Terapia Endovascular de Mexico	Mexico
Ashikaga T.	Tokyo Medical and Dental University	Japan
Atef S.	TMGH/cardiac center	Yemen
Attar N.	Scunthorpe General Hospital	United Kingdom
Aubry P.	Bichat Hospital	France
Ayala F.J.	University of Chile, Clinical Hospital	Chile
Bailey S.R.	UTHSCSA	USA
Bakhshaliyev N.	Central Customs Hospital	Azerbaijan
Balbay Y.	TYIH	Turkey
Ballarino M.A.	Hospital Privado Universitario de Cordoba	Argentina
Banerjee P.	–	India
Baños A.	Hospital General de Culiacan	Mexico
Barrera E.	Hospital de Clínicas Buenos Aires	Argentina
Beckmann J.	CardioVascular Institute, North Colorado Medical Center	USA
Bergmann M.W.	Cardiologicum, Hamburg	Germany
Berti S.	Heart Hospital Fondazione G. Monasterio	Italy
Bett N.	Prince Charles Hospital	Australia
Bhat S.	Narayana Multispeciality Hospital, Whitefield, Bangalore	India
Bimlendu K.	BNH Jamshedpur	India
Binder R.K.	University Heart Center, University Hospital Zurich	Switzerland
Block M.	Klinik Augustinum München	Germany
Boersma L.V.	St. Antonius Hospital Nieuwegein	The Netherlands
Bolao I.G.	University of Navarra	Spain
Boldt L.H.	Charite – Universitätsmedizin, Berlin	Germany
Bonnet J.L.	Department of Interventional Cardiology, University Hospital Timone, Marseilles	France
Bun S.S.	Princess Grace Hospital, Monaco	Monaco
Buysschaert I.	ASZ Aalst	Belgium
Calenici E.	Institute of Cardiology	Moldova
Calle G.	Hospital Puerta del Mar (Cadiz)	Spain
Campante Teles R.	Hospital de Santa Cruz, CHLO	Portugal
Caprotta F.	Hospital Santa Clara de Asis	Argentina
Caramori P.	Hospital Sao Lucas, PUCRS	Brazil
Carsten W.I.	Dept. of Cardiology, Evangelical Hosp. Bielefeld	Germany
Cavalcante R.	Heart Institute (InCor), University of Sao Paulo Medical School	Brazil
Cavazza C.	S.S. Antonio e Biagio	Italy
Chamié F.	Hospital Federal Dos Servidores Do Estado	Brazil
Chan J.L.K.	Queen Elizabeth Hospital	Hong Kong
Chang C.	Chang Gung Memorial Hospital, Linkou	Taiwan
Charaf A.	–	Greece
Chaudhry N.	Aga Khan Hospital, Mombasa	Kenya
Chauhan H.K.C.	Dept. of Cardiology, Fortis Hospital Mohali	India
Chen M.	West China Hospital, Sichuan University	China
Choo W.S.	KPJ Seremban Hospital	Malaysia
Choon Chern A.K.	National Heart Institute (IJN)	Malaysia
Chudinov G.	Rostov State Medical University	Russian Federation
Chutani S.	Mount Sinai BL Hospital Center, New York, NY	USA
Clemente A.	G. Monasterio Foundation	Italy
Congnam P.	Hue Medical University Hospital	Vietnam
Correa Bastidas R.C.	Centro Médico de Caracas	Venezuela
Crean P.	St James's Hospital, Dublin	Ireland
Cresti A.	Department of Cardiology, Misericordia Hospital, Grosseto	Italy
Crowley J.	University Hospital Galway	Ireland
Dallan L.V.	InCor - HCFMUSP	Brazil
Damonte A.	Instituto Cardiovascular de Rosario	Argentina
Daneault B.	CIUSS Estrie CHUS	Canada
De Backer O.	Rigshospitalet	Denmark
De Leo A.	Cardiology Division, Cardiovascular Dpt., Treviso Hospital	Italy
De Oliveira E.I.	Hospital Santa Maria, Lisbon	Portugal
Demin V.	Orenburg Regional Clinical Hospital	Russian Federation
Depukat R.	University Hospital Krakow	Poland

Online Table 1. List of respondents. (cont'd)

Name	Institution	Country
Dhar G.	Sparrow Health Care	USA
Dhirender S.	Medanta Hospital	India
Dolgov S.	Orenburg Regional Clinical Hospital	Russian Federation
Domaradzki W.	American Heart of Poland	Poland
Drewla P.	Medical University of Gdansk	Poland
Drieghe B.	University Hospital Gent	Belgium
Ebelt H.	Catholic Hospital, Erfurt	Germany
Eftychiou C.	Cardiology Department of Nicosia General Hospital	Cyprus
El Garhy M.	Zentralklinik Bad Berka	Germany
El Meguid K.R.A.	Benisuef University Hospital	Egypt
El-Salam Al-Ethawi A.	Ibn Al-Bittar Center for Cardiac Surgery	Iraq
Elias A.	401 GMHA	Greece
Elizaga J.	Gregorio Marañón Hospital	Spain
Eungyu L.	Naeun Hospital	South Korea
Fedele L.	Ospedale Civile di Legnano	Italy
Fernández G.B.	CHUVI- Hospital Alvaro Cunqueiro	Spain
Fernández G.B.	Complejo Hospitalario Universitario de Vigo	Spain
Ferreira P.C.	Santa Maria University Hospital, CHLN, Lisbon	Portugal
Festari I.P.	Universitas Baiturrahmah	Indonesia
Fischetti D.	Ospedale V. Fazzi, Lecce	Italy
Foley D.P.	Beaumont University Hospital, Dublin	Ireland
Fontes-Carvalho R.	Cardiology Department, Centro Hospitalar Gaia	Portugal
Frambach P.	INCCI	Luxembourg
Freixa X.	Hospital Clinic of Barcelona	Spain
Fridrich V.	National Institute of Cardiovascular Diseases, Bratislava	Slovakia
Fuks V.	Hospital Federal dos Servidores do Estado	Brazil
Funes R.	Instituto Nacional del Torax	Honduras
Gama V.	Gaia Hospital	Portugal
Garot P.	Institut Cardiovasculaire Paris Sud, Massy	France
Gaspardone A.	U.O.C. di Cardiologia Ospedale S. Eugenio Rome	Italy
Gerke R.	Bethesda KH Wuppertal	Germany
Ghione M.	Ospedale San Paolo, Savona	Italy
Gholoobi A.	Mashhad University of Medical Sciences	Iran
Ghonim A.	MCC	Egypt
Giacchi G.	Hospital Clinic, Barcelona	Spain
Giunio L.	University Hospital Split	Croatia
Gloekler S.	Bern University Hospital	Switzerland
Goktekin O.	Bezmialem Vakif University Hospital	Turkey
Goldberg S.L.	Kalispell Regional Medical Center	USA
Gomez Jaume A.	Hospital Univ Son Espases	Spain
Gómez-Anaya I.A.	Centro Medico Nacional 20 de Noviembre, I.S.S.S.T.E.	Mexico
Gori T.	University Medical Center Mainz	Germany
Greco F.	AO SS Annunziata Cosenza	Italy
Guerios E.	Hospital Pilar - Curitiba	Brazil
Gunalingam B.	St Vincents Hospital, Sydney	Australia
Gurbanna B.	Tripoli Medical Centre	Libya
Haager P.K.	Department of Cardiology, Kantonsspital St. Gallen	Switzerland
Hagikura A.	Fukuyama Cardiovascular Hospital	Japan
Halabi M.	Helios Klinik Köthen	Germany
Haritha P.N.S.	Ramesh Hospitals	India
Heggunje P.S.	Columbia Asia Hospital Yeshwanthpur	India
Hellig F.	Sunninghill Hospital	South Africa
Herrera G.M.	Unidad de Hemodinamia, Hospital Vargas de Caracas	Venezuela
Heshmat H.	Kasr Al-Ainy Hospital, Assalam International Hospital	Egypt
Heyrich G.	St Mary Medical Center, Langhorne, PA	USA
Holy E.W.	Heart Center Segeberger Kliniken	Germany
Hornung M.	CardioVascular Center, Frankfurt	Germany
Hossain A.S.	Cardiac Centre, Bahrain Defence Force Hospital	Bahrain
Hsueh S.	Kaohsiung Chang Gung Memorial Hospital	Taiwan
Htun Y.	No. 1 Military Hospital, Meik-hti-lar	Myanmar
Ibarra M.	Hospital Zambrano Helliön	Mexico
Ilic I.	Clinical Hospital Center Zemun, Belgrade	Serbia
Iñiguez A.	Hospital Alvaro Cunqueiro (Vigo)	Spain
Iorga V.	Emergency County Hospital Ploiesti	Romania
Jahangir M.	Department of Cardiology, Hospital Pulau Pinang	Malaysia
Jasmina K.T.	Kbc B Kosa	Serbia
Jensen U.	South General Hospital, Stockholm	Sweden
Juan Q.G.	TEC Salud	Mexico
Jubeh R.	Shaare Zedek Medical Center	Israel
Kannaiyan A.	Frontier Lifeline Hospital Chennai	India
Karaly Y.M.	Dubai Hospital	United Arab Emirates
Karen A.	Republican Medical Center of NKR	Armenia
Kawarada O.	National Cerebral and Cardiovascular Center	Japan
Ketteler T.	HELIOS Klinikum Aue	Germany
Khanna A.	Max Hospital, Vaishali, Ghaziabad	India
Kharlamov A.N.	De Haar Research Foundation, Rotterdam	The Netherlands
Kim J.	Asan Medical Center	South Korea
Kim J.S.	Yonsei University	South Korea
Kiviniemi T.	Turku University Hospital	Finland
Kleanthous Papaxenopoulou H.	–	Cyprus
Kluck B.	Lehigh Valley Health Network	USA
Kofflard M.J.M.	Albert Schweitzer Hospital	The Netherlands
Kónyi A.	Heart Institute, University of Pécs	Hungary
Kose N.	Mugla Yucelen Hospital	Turkey
Koskinas K.C.	Bern University Hospital	Switzerland

Online Table 1. List of respondents. (cont'd)

Name	Institution	Country
Kounis N.G.	Western Greece Highest Institute of Education and Technology	Greece
Kovarnik T.	Charles University Hospital, Prague	Czech Republic
Kubica J.	Dept. of Cardiology, CM Nicolaus Copernicus University, Bydgoszcz	Poland
Kumar Chaurasia A.	Hungarian Institute of Cardiology	Hungary
Kumar Das R.	NICVD	Bangladesh
Lalaguna L.M.A.	HUP La Fe de Valencia	Spain
Lange M.	Heart Center Osnabrueck-Bad Rothenfelde, Marienhospital Osnabrueck	Germany
Lanzer P.	Health Care Center Bitterfeld-Wolfen	Germany
Lawand S.	Dallah Hospital	Saudi Arabia
Lazzari M.E.A.	Emodinamica Diagnostica E Interventistica, Ospedale S. Luca, Lucca	Italy
Legrand V.	CHU de Liège	Belgium
Leiva-Pons J.L.	Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí	Mexico
Lempereur M.	University Hospital Liège, Liège	Belgium
Leoncini M.	Sanremo Cath Lab - Cardiology Unit	Italy
Lesiak M.	Ist Department of Cardiology, University Hospital, Poznan	Poland
Lim H.E.	Korea University Guro Hospital	South Korea
Lopez-Cuellar J.	American British Cowdray Hospital, Mexico City	Mexico
Lubis H.A.P.	Cardiology and Vascular Medicine of North Sumatera University	Indonesia
Luha O.	Universitätsklinikum Graz	Austria
Luna E.	ISSSTE	Mexico
Lurina A.	Pauls Stradins Clinical University Hospital	Latvia
Magdy A.	National Heart Institute, Cairo	Egypt
Mahesh N.K.	BHDC	India
Maisuradze D.	Aversi Clinic, Tbilisi	Georgia
Malik A.	BLK Hospital Delhi	India
Malviya A.	North Eastern Indira Gandhi Regional Institute of Health & Medical Science, Shillong	India
Malynovsky Y.	MI RMCCVD ZRC	Ukraine
Mansur M.	Ibn Sina Specialized Hospital	Bangladesh
Marchetti G.	Hospital Ferreyra, Necochea	Argentina
Marín F.	Hospital Universitario Virgen de la Arrixaca, Murcia	Spain
Marques J.S.	CHUC- Hospitais da Universidade de Coimbra	Portugal
Materne P.	Liège CHU	Belgium
Matsis P.P.	Wellington Hospital	New Zealand
Mattesini A.	Cardiology unit, Moriggia-Pelascini Hospital, Gravedona (CO)	Italy
Mazen S.A.	Speciality Hospital	Jordan
Meerkin D.	Shaare Zedek Medical Center, Jerusalem	Israel
Meier B.	Cardiology, University Hospital of Bern	Switzerland
Meucci F.	Azienda Ospedaliero Universitaria Careggi Firenze	Italy
Mezzapelle G.	Giovanni Paolo II Hospital, Sciacca	Italy
Milei J.	Instituto de Investigaciones Cardiológicas, University of Buenos Aires	Argentina
Minden H.H.	Oberhavel Kliniken Hennigsdorf	Germany
Mironova O.	Russian Cardiology Research and Production Complex	Russian Federation
Mohammadzadeh F.	Lavasani Hospital Tehran	Iran
Morice M.C.	Generale de Sante Hopital Prive Jacques Cartier, Massy	France
Moya Loor L.	INCORP Salud	Argentina
Mrabet K.	NMC Specialty Hospital, Dubai	United Arab Emirates
Muniz A.	UMAE 34, IMSS	Mexico
Musa Y.	National Cardiothoracic Centre, Khartoum	Sudan
Nabais S.	Salisbury NHS Foundation Trust	United Kingdom
Nagesh H.E.	Manipal Hospital, Bengaluru	India
Nakao F.	Yamaguchi Grand Medical Center	Japan
Narayanan S.	Little Flower Hospital & Research Institute	India
Natarajan R.	Kims, Trivandrum, Kerala	India
Naung Tun H.	MBBS	Myanmar
Nguyen Q.N.	Vietnam National Heart Institute	Vietnam
Nicosia A.	Cardiology - ASP 7 - Ragusa	Italy
Nikas D.	Ioannina University Hospital	Greece
Nikitpoulos A.	Interbalkan Medical Center, Thessaloniki	Greece
Nofrerias E.F.	H. Universitari Germans Trias i Pujol	Spain
Nora A.	University Mustapha Hospital	Algeria
Northridge D.B.	Royal Infirmary of Edinburgh	United Kingdom
Ochoa V.	Instituto Nacional de Cardiologia Ignacio Chávez, Mexico City	Mexico
Oels M.	Sana Klinikum Remscheid	Germany
Oepangat E.	Siloam Hospitals Lippo Village, Tangerang	Indonesia
Oktay Ergene A.	Dokuz Eylul University Izmir	Turkey
Oreglia J.A.	Sacco Hospital, Milan	Italy
Ottervanger J.P.	Isala, Zwolle	The Netherlands
Paiva L.	Coimbra University Hospital Centre	Portugal
Palazuelos J.	Hospital Universitario Central de la Defensa Gómez Ulla	Spain
Panduranga P.	National Heart Center, Oman	Pakistan
Panico C.	Istituto Clinico Humanitas	Italy
Pantaleo P.	ICLAS - GVM Care and Research, Rapallo (GE)	Italy
Pavlovic N.	University Hospital Centre "Sestre Milosrdnice", Zagreb	Croatia
Pedra C.A.C.	Instituto Dante Pazzanese de Cardiologia	Brazil
Peruga J.Z.	Invasive Cardiology Department Chair and Department of Cardiology Medical University in Łódz Bieganski Hospital	Poland
Pescoller F.	Ospedale Regionale San Maurizio	Italy
Pillai N.	Medical Center of Plano	USA

Online Table 1. List of respondents. (cont'd)

Name	Institution	Country
Pizzetti G.	San Raffaele Hospital IRCCS	Italy
Portela A.	Hospital São Marcos - APCC	Brazil
Predescu L.M.	Carol Davila University of Medicine and Pharmacy	Romania
Predescu L.M.	Cc Iliescu Emergency Institute for Cardiovascular Diseases	Romania
Prog R.	Sana Krankenhaus Benrath	Germany
Protopopov A.	Krasnoyarsk State Regional Hospital	Russian Federation
Przewlocki T.	Institute of Cardiology, Collegium Medicum in Jagiellonian University, Cracow	Poland
Pyun W.B.	Ewha Womans University	South Korea
Qarawani D.	Baruch Padea Center, Bar Ilan University	Israel
Qasem M.	PSCCQ	Saudi Arabia
Quizhpe R.	Hospital José Carrasco Arteaga	Ecuador
Ragy H.	Cardiocath Medical	Egypt
Rahman T.	National Institute of Cardiovascular Diseases	Bangladesh
Ramallal R.	Complejo Hospitalario de Navarra	Spain
Ranc S.	Centre Hospitalier Saint Joseph Saint Luc, Lyon	France
Rapacciuolo A.	Federico II University of Naples	Italy
Rasul H.	Doctor Hospital Lahore	Pakistan
Ratib K.	University Hospital North Midlands	United Kingdom
Reyes C.	Clinica Nogales	Colombia
Roccario E.S.	St Peter's Health Partners	USA
Rodríguez D.F.	Nuestra Señora de La Candelaria University Hospital	Spain
Rodríguez de Leiras Otero S.	Hospital Universitario Virgen Macarena, Sevilla	Spain
Roemer A.	St. Josefs-Hospital Wiesbaden	Germany
Romanek R.	10 Military Clinical Hospital Bydgoszcz	Poland
Romeo F.	Hospital Italiano de Buenos Aires	Argentina
Rotter A.	Klinik Dr Schindlbeck Herrsching	Germany
Rubboli A.	Ospedale Maggiore, Bologna	Italy
Rudzitis A.	P. Stradins Clinical University Hospital	Latvia
Ruiz-Garcia J.	Hospital Universitario de Torrejón, Madrid	Spain
Sabate M.	Hospital Clinic-Barcelona	Spain
Saboe A.	Department of Cardiology and Vascular Medicine, Universitas Padjadjaran, Bandung	Indonesia
Sadowski M.	The Jan Kochanowski University, Kielce	Poland
Said A.	Cardiovascular Hospital, Ain Shams University	Egypt
Saka M.	Erbil Cardiac Center	Iraq
Sakr S.	Mansoura University Hospital	Egypt
Salari M.	Rajayi Hospital	Iran
Sammut M.A.	Mater Dei Hospital	Malta
Santos L.	Centro Hospitalar Gaia, Porto	Portugal
Sanz-Ruiz R.	Cardiology Dept, Hospital Gregorio Marañón, Madrid	Spain
Schmidt B.	Cardioangiologisches Centrum Bethanien, Frankfurt/Main	Germany
Schmitz T.	Contilia Heart & Vascular Center Essen	Germany
Schneider F.	Southcoast Hospitals Group	USA
Scholtz W.	Herz- und Diabeteszentrum NRW, Bad Oeynhausen	Germany
Schuchlenz H.W.	Department für Kardiologie LKH Graz West	Austria
Segev A.	Chaim Sheba Medical Center	Israel
Semmelweis E.R.	Univ. Clinics Giessen & Marburg GmbH	Germany
Seneviratne DN.H.G.	NHSL Sri Lanka	Sri Lanka
Sesana M.	ASST Desenzano Del Garda	Italy
Sharma R.K.	NRS Medical College, Kolkata	India
Sharp J.	Sydney Adventist Hospital	Australia
Shbayek M.H.	National Heart Institute	Egypt
Shishkevich A.	VMA	Russian Federation
Shuker M.K.	–	Iraq
Silveira J.B.	CHP – HSA, Porto	Portugal
Silvestry F.E.	Hospital of the University of Pennsylvania	USA
Simovic S.	Clinic for Cardiology, Clinical Center Kragujevac	Serbia
Siqueira M.J.	Hospital Unimed Missoes	Brazil
Slhessarenko J.	Amecor	Brazil
Smith D.H.	Sussex Cardiac Centre, Brighton and Sussex University Hospitals	United Kingdom
Smoljan I.	KBC Rijeka	Croatia
Sohail A.	Madinah Cardiac Center	Saudi Arabia
Soliman-Hamad M.A.	Catharina Hospital, Eindhoven	The Netherlands
Solioz G.	Clinica De Los Virreyes	Argentina
Sorokhtey L.	Ivano-Frankivsk Central City Hospital	Ukraine
Sotirios P.	Konstantopoulio General Hospital, Athens	Greece
Sreenivas C.G.	Vijaya Heart Foundation Chennai	India
Srikanth K.	NICS	India
Srinivas B.	NIMS	India
Štásek J.	University Hospital Hradec Králové, Charles University	Czech Republic
Stellbrink C.	Klinikum Bielefeld	Germany
Sukiennik A.	Department of Cardiology, University Hospital No 1, Collegium Medicum UMK Bydgoszcz	Poland
Swaans M.	St. Antonius Hospital, Nieuwegein	The Netherlands
Sykora J.	Privatklinik Mariahilf, Klagenfurt	Austria
Taha N.	Minia University Cardiology Department	Egypt
Tarhbalouti R.	Centre Cardiologique du Sud, Agadir	Morocco
Tatarczuk A.	American Heart of Poland Polanica Zdr	Poland
Ternacle J.	Henri Mondor Hospital, Creteil	France
Tesic M.	Clinical Center of Serbia	Serbia
Thai Giang P.	Heart Institute	Vietnam
Theodoropoulos K.C.	King's College Hospital, London	United Kingdom

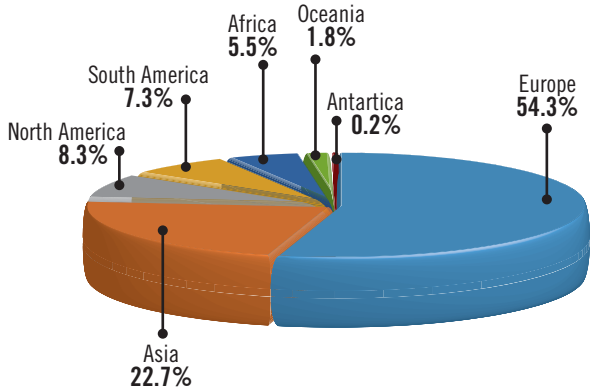
Online Table 1. List of respondents. (cont'd)

Name	Institution	Country
Tigen K.	Marmara University School of Medicine Department of Cardiology	Turkey
Tiwari B.	–	India
Todorov S.	Faculty of Medical Sciences	Macedonia
Tomai F.	European Hospital of Rome	Italy
Tondo C.	Cardiac Arrhythmia Research Centre, Centro Cardiologico Monzino, IRCCS, University of Milan	Italy
Torres Bosco A.	Hospital Universitario de Alava	Spain
Torresani E.M.	Sanatorio Modelo Quilmes	Argentina
Toth G.G.	University Heart Survey Graz	Austria
Toutouzas K.	First Department of Cardiology, Athens Medical School	Greece
Trbuši M.	Sisters of Charity University Hospital Centre	Croatia
Trujillo P.	Cvvu. Hospital de Clinicas	Uruguay
Tsui K.L.	Pamela Youde Nethersole Eastern Hospital	Hong Kong
Tsujita K.	Kumamoto University	Japan
Tulepbergenov G.K.	City Cardio Center of Almaty	Kazakhstan
Tzikas A.	AHEPA University Hospital	Greece
Unger P.	CHU Saint-Pierre, Brussels	Belgium
Uretsky B.F.	University of Arkansas for Medical Sciences	USA
Vallecillo A.	Hospital Regional Salamanca Pemex	Mexico
Valsecchi O.	ASST Papa Giovanni XXIII, Bergamo	Italy
Vaquerizo B.	Hospital del Mar, Barcelona	Spain
Vásquez S.	Instituto del Corazón de Bucaramanga	Colombia
Vatwani A.	Kalyani Hospital	India
Vermeersch P.	ZNA Middelheim	Belgium
Verna E.	Ospedale di Circolo & Fondazione Macchi Varese	Italy
Vicedomini G.	Policlinico San Donato, Milan	Italy
Vidal-Perez R.	Hospital Universitario Lucus Augusti	Spain
Vinicius Melo F.	Unimed Recife	Brazil
Vojacek J.F.	Dept Cardiovascular Medicine I, Charles University Prague, University Hospital Hradec Kralove	Czech Republic
Vokac D.	UKC Maribor, Dep. of Cardiology	Slovenia
Volkov D.	Cardiosurgery Center	Russian Federation
Vranckx P.	Jessa Ziekenhuis Hasselt	Belgium
Vucic R.	Clinical Center Kragujevac	Serbia
Wisthon M.V.	Hospital José Carrasco Arteaga	Ecuador
Xuereb R.G.	Mater Dei Hospital	Malta
Yakubu P.D.	Barau Dikko Teaching Hospital (Kaduna State University), Kaduna	Nigeria
Yan-Biao Liao	West China Hospital of Sichuan University	China
Yeni H.	Johanniter Krankenhaus Duisburg-Rheinhausen	Germany
Yoann B.	CHR Citadelle, Liège	Belgium
Youssef A.	Suez Canal University Hospital	Egypt
Zahran M.	Ain Shams University	Egypt
Zbigniew K.	Silesian Center for Heart Diseases	Poland
Zein K.	Luxor International Hospital	Egypt
Zelimir A.	Dedinje Cardiovascular Institute	Serbia
Zeus T.	University Hospital Düsseldorf	Germany
Zoelfakar Soliman T.S.	Madina National Hospital	Saudi Arabia

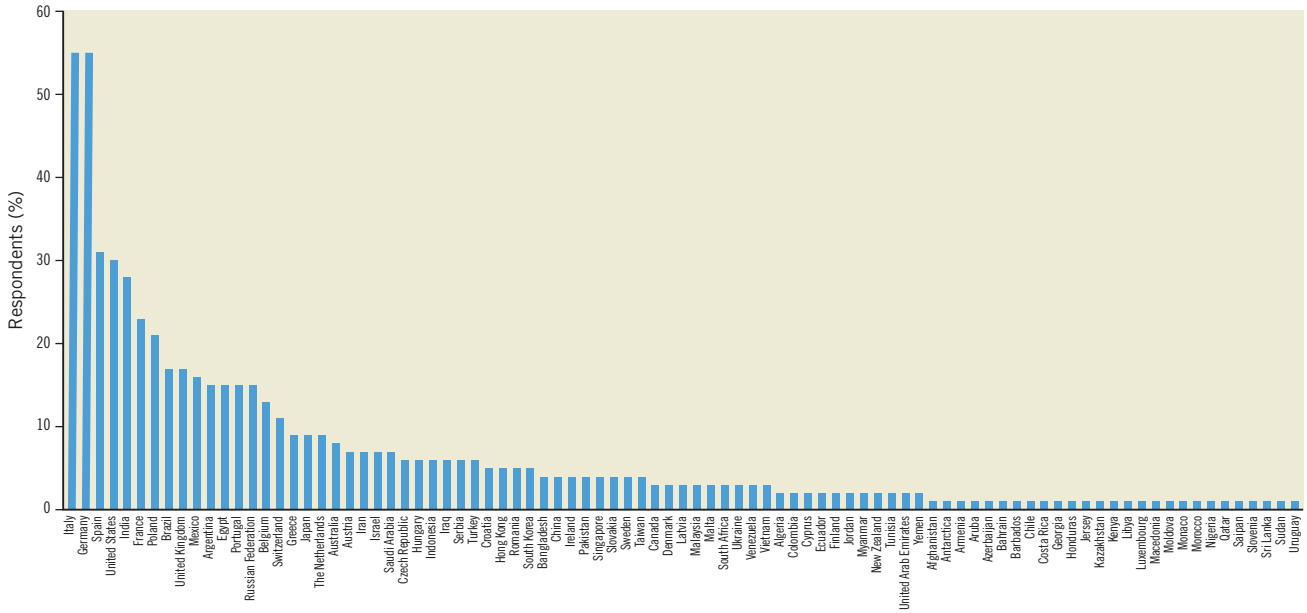
Online Table 2. Survey results.

Q1. Do you have experience in percutaneous left atrial appendage closure (LAAC)?		
Answered: 724, Skipped: 0	Percentage	Response count
Yes, as first operator (≥20 procedures)	15.19%	110
Yes, as first operator (>10 procedures but less than 20)	5.39%	39
Yes, as first operator (<10 procedures)	11.19%	81
No, although LAAC is performed by other operators in my centre	27.76%	201
Not at all	40.47%	293
Q2. Which LAA occluder device do you or does your centre have experience with?		
Answered: 422, Skipped: 302	Percentage	Response count
WATCHMAN	30.33%	128
AMPLATZER Amulet	34.36%	145
Both	31.52%	133
Other (open text box)	3.79%	16
Q3. Based on your personal experience, do you think that the safety/efficacy profile of LAA occluders may differ in practice?		
Answered: 693, Skipped: 31	Percentage	Response count
Yes, I think WATCHMAN is superior	18.33%	127
Yes, I think AMPLATZER Amulet is superior	15.30%	106
No, I think there is substantial equipoise	27.27%	189
I do not know	39.11%	271
Q4. Do you think that the evidence supporting LAAC is:		
Answered: 660, Skipped: 64	Percentage	Response count
Good	46.21%	305
Average	40.15%	265
Scarce	11.82%	78
Other (open text box)	1.82%	12
Q5. LAAC has been so far compared to vitamin K antagonists. Do you think that the availability of novel oral anticoagulants (NOACs) should further restrict LAAC?		
Answered: 660, Skipped: 88	Percentage	Response count
Yes, NOACs have been shown to be safer than VKAs and as such reduce the need for LAAC	33.18%	219
No, availability of NOACs should not affect the indications to LAACs	66.82%	441
Q6. Do you think that LAAC should be restricted only to patients with previous serious or life-threatening bleeding?		
Answered: 636, Skipped: 88	Percentage	Response count
Yes, LAAC should only be performed in patients with previous bleeding who remain at risk for recurrences afterwards	35.06%	223
No, this procedure is reasonable also in patients at relatively higher bleeding risk despite the absence of a previous clinically meaningful bleeding event	59.75%	380
I don't know/have no opinion	5.19%	33

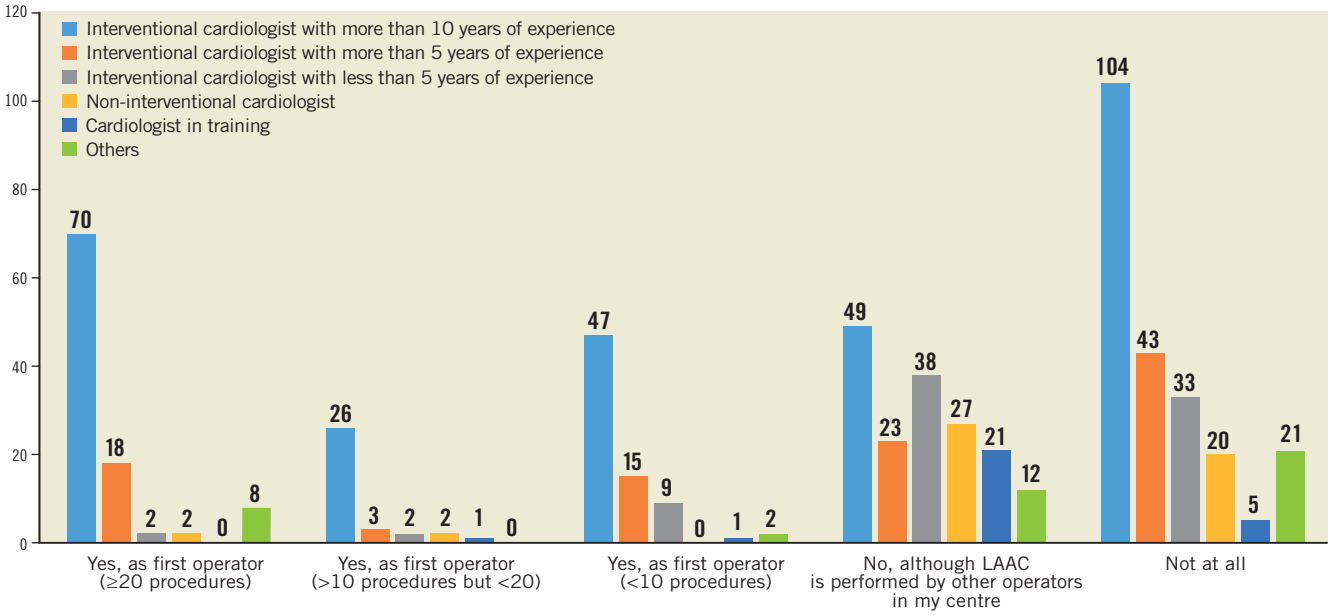
Q7. In your opinion, percutaneous LAAC compared to OAC is:		
Answered: 636, Skipped: 88	Percentage	Response count
Less effective in preventing stroke but safer due to bleeding reduction	19.50%	124
As effective as OAC in preventing stroke and safer due to bleeding reduction	59.43%	378
As effective as OAC in preventing stroke but with high periprocedural events rate	16.82%	107
Less effective in preventing stroke and with high periprocedural events rate	4.25%	27
Q8. What worries you more about left atrial appendage closure devices?		
Answered: 625, Skipped: 99	Percentage	Response count
Periprocedural complications	40.32%	252
Late complications (endocarditis, device embolisation…)	16.96%	106
Limited efficacy in preventing stroke	10.56%	66
Cost	28.80%	180
Other (please clarify)	3.36%	21
Q9. Do you think a short course of oral anticoagulants is needed early on after LAAC?		
Answered: 625, Skipped 99	Percentage	Response count
Yes, to ensure proper endothelialisation of the implanted device	55.36%	346
Only after WATCHMAN device in keeping with evidence	11.04%	69
No, it is not needed	17.44%	109
It may be needed in cases where LAA closure is incomplete	16.16%	101
Q10. Please select the professional figure, which describes you at best		
Answered: 604, Skipped: 120	Percentage	Response count
Interventional cardiologist with more than 10 years of experience	49.01%	296
Interventional cardiologist with more than 5 years of experience	16.89%	102
Interventional cardiologist with less than 5 years of experience	13.91%	84
Non-interventional cardiologist	8.44%	51
Cardiologist in training	4.64%	28
Others	7.12%	43



Online Figure 1. *Region of work.*



Online Figure 2. *Country of work.*



Online Figure 3. *Question 1 stratified by professional figure.*