





Clinical practice and implementation of guidelines for the prevention, diagnosis and management of cardiac implantable electronic device infections

Traykov, Vassil; Bongiorni, Maria Grazia; Boriani, Giuseppe; Burri, Haran; Costa, Roberto; Dagres, Nikolaos; Deharo, Jean-Claude; Epstein, Laurence M.; Erba, Paola Anna; Snygg-Martin, Ulrika Published in:

Europace

DOI: 10.1093/europace/euz137

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version Publisher's PDF, also known as Version of record

Publication date: 2019

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Traykov, V., Bongiorni, M. G., Boriani, G., Burri, H., Costa, R., Dagres, N., Deharo, J-C., Epstein, L. M., Erba, P. A., Snygg-Martin, U., Nielsen, J. C., Poole, J. E., Saghy, L., Starck, C., Strathmore, N., & Blomstrom-Lundqvist, C. (2019). Clinical practice and implementation of guidelines for the prevention, diagnosis and management of cardiac implantable electronic device infections; results of a worldwide survey under the auspices of the European Heart Rhythm Association. Europace, 21(8), 1270-1279. https://doi.org/10.1093/europace/euz137

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverneamendment.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.



EUROPACE (2019) 21, 1270–1279 European Society doi:10.1093/europace/euz137

Clinical practice and implementation of guidelines for the prevention, diagnosis and management of cardiac implantable electronic device infections: results of a worldwide survey under the auspices of the European Heart Rhythm Association

Vassil Traykov ()^{1*}, Maria Grazia Bongiorni², Giuseppe Boriani³, Haran Burri ()⁴, Roberto Costa () (LAHRS representative)⁵, Nikolaos Dagres ()⁶, Jean-Claude Deharo ()⁷, Laurence M. Epstein (HRS representative)⁸, Paola Anna Erba ()⁹, Ulrika Snygg-Martin (ESCMID representative)¹⁰, Jens Cosedis Nielsen¹¹, Jeanne E. Poole () (HRS representative)¹², Laszlo Saghy¹³, Christoph Starck () (EACTS representative)¹⁴, Neil Strathmore (APHRS representative)¹⁵, and Carina Blomström-Lundqvist¹⁶

¹Department of Invasive Electrophysiology and Cardiac Pacing, Acibadem City Clinic Tokuda Hospital, Sofia, Bulgaria; ²Cardiology and Arrhythmology Division, CardioThoracic and Vascular Department, University Hospital of Pisa, Pisa, Italy; ³Cardiology Division, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Policlinico di Modena, Modena, Italy; ⁴Department of Cardiology, University Hospital of Geneva, Geneva, Switzerland; ⁵Department of Cardiovascular Surgery, Heart Institute (InCor) of the University of São Paulo, São Paulo, Brazil; ⁶Department of Electrophysiology, Heart Center Leipzig at the University of Leipzig, Leipzig, Germany; ⁷Department of Cardiology, Aix Marseille Université, CHU la Timone, Marseille, France; ⁸System Director, Electrophysiology, Northwell Health, Hofstra/Northwell School of Medicine, Manhasset, NY, USA; ⁹Department of Translational Research and New Technology in Medicine, University of Infectious Diseases, Institute of Biomedicine, ⁸ Molecular Imaging, University of Gothenburg, Gothenburg, Sweden; ¹¹Department of Cardiology, Aarhus University of Szeged, Juegary; ¹⁴Department of Cardiology, Seattle, WA, USA; ¹³Electrophysiology Division, 2nd Department of Medicine and Cardiology Centre, University of Szeged, Szeged, Hungary; ¹⁴Department of Cardiology, Seattle, WA, USA; ¹³Electrophysiology Division, 2nd Department of Medicine and Cardiology, Royal Melbourne Hospital, Parkville, Australia; and ¹⁶Department of Medical Science and Cardiology, Uppsala University, Uppsala, Sweden

Received 7 January 2019; editorial decision 16 April 2019; accepted 17 April 2019; online publish-ahead-of-print 17 June 2019

| Aims | Cardiac implantable electronic device (CIED) infection rates are increasing. Worldwide compliance and disparities to published guidelines for the prevention, diagnosis and management of these conditions are not well elucidated. The purpose of this survey, therefore, was to clarify these issues through an inquiry to arrhythmia-related associations and societies worldwide. |
|------------------------|--|
| Methods and results | A questionnaire comprising 15 questions related to CIED infections was distributed among members of seven ar- rhythmia societies worldwide. A total of 234 centres in 62 countries reported implantation rates of which 159 (68.0%) performed more than 200 device implantations per year and 14 (6.0%) performed fewer than 50 implanta- tions per year. The reported rates of CIED infections for 2017 were $\leq 2\%$ in 78.7% of the centres, while the infec- tion rates exceeded 5% in 7.8% of the centres. Preventive measures for CIED infection differed from published rec- ommendations and varied among different regions mainly in terms of pocket irrigation and administering post- operative antimicrobial therapy the use of which was reported by 39.9% and 44% of the respondents, respectively. Antibacterial envelopes were used by 37.7% of the respondents in selected circumstances. In terms of pocket |

* Corresponding author. Tel: +359 2 4034606; fax: +359 2 8155205. E-mail address: vtraykov@yahoo.com

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2019. For permissions, please email: journals.permissions@oup.com.

| | infection management, 62% of the respondents applied complete system removal as an initial step. Diagnostic pocket needle aspiration and pocket surgical debridement were reported by 15.8% and 11.8% of centres, respectively. |
|------------|--|
| Conclusion | Clinical practices for prevention and management of CIED do not fully comply with current recommendations and demonstrate considerable regional disparities. Further education and programmes for improved implementation of guidelines are mandatory. |
| Keywords | Cardiac implantable electronic device infection • Prevention • Guidelines • Cardiac resynchronization therapy • Implantable cardioverter-defibrillator • EHRA survey |

What's new?

- Significant global and regional variations still exist in the prevention, diagnosis and management of patients with cardiac implantable electronic device infections.
- Existing guidelines and recommendations are not adequately implemented worldwide.

Introduction

The rate of cardiac implantable electronic device (CIED) infection continues to rise and is out of proportion to the increasing rate of device implantation.^{1,2} Possible causes are: increasing patient longevity with resultant generator changes; increasing comorbidities; increasing implantation rates of complex devices—implantable cardioverter-defibrillators (ICDs), cardiac resynchronization therapy pacemakers/ defibrillators (CRT-P/Ds); in higher risk patients.

The impact of CIED infections on patients and society is significant. It includes patient suffering, need for complex surgical interventions with complete lead extraction, prolonged hospitalization and increased mortality, all leading to high costs with substantial impact on the healthcare systems.^{3,4} Scientific medical organizations in Europe and in the United States have published recommendations on the prevention and management of CIED infections.^{5–10} Given the impact of CIED infections on health care resources and patient morbidity/mortality, global and regional adherence to these guidelines is of paramount importance. This survey aimed to analyse practices applied worldwide for prevention, diagnosis and treatment of CIED infections, and current adherence to published guidelines and recommendations.

Methods

An internet-based physician-centered survey, comprising 15 questions concerning common clinical settings and scenarios related to CIED infection prevention and handling was distributed among members of six medical societies worldwide (Supplementary material online). The survey was sent to the European Heart Rhythm Association (EHRA), the European Association for Cardiothoracic Surgery (EACTS), the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythms Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), and the Brazilian Association of Cardiac Pacing (ABEC), which in turn were responsible for further

distribution of the questionnaire among their members. Surveyed physicians represented the practice at their centres therefore data received may be extrapolated for a larger pool of implanting physicians. The survey was active from 1 May 2018 until mid-June 2018. Results are presented as numbers and percentages for each answered option. The χ^2 criterion was used to compare categorical variables, while continuous data were analysed using Mann–Whitney U test or Kruskal–Wallis test as appropriate.

Results

A total of 380 responses to at least one of the questions were received from 62 countries (*Figure 1*, Supplementary material online, *Table S1*), of which 182 (47.8%) came from Europe and Central Asia, 104 (27.4%) from Latin America and the Caribbean, 45 (11.8%) from North America, 39 (10.2%) from the Asia-Pacific Region, 9 (2.4%) from the Middle East and North Africa, and 1 (0.3%) from elsewhere in Africa. Of these, 218 (57.4%) were replies from university hospitals, 98 (25.7%) from private hospitals, and the remaining 64 (16.8%) from non-university public hospitals. More than half of the responding physicians (54.1%, 131 of 242) providing information on their specialty were cardiologists, while 32.2% (78/242) were thoracic or cardiovascular surgeons. The median number of replies for each of the questions on the survey questionnaire was 175 (46.1%).

Implantation volumes and prevalence of cardiac implantable electronic device infections

A total of 159 of the 234 (67.9%) responders providing data on volumes of device implants, had implantation volumes above 200 devices for 2017. Low volumes, defined as fewer than 50 devices annually, were reported by 14 of 234 (6.0%) of the responding centres. Complex devices (ICD, CRT-P/D) were implanted in 225 centres, of which 140 centres (62.2%) had an implantation rate exceeding 50 devices for 2017, while 85 centres (37.7%) had an implantation rate of fewer than 50 devices for 2017. Self-reported infection rates for 2017 were provided by 234 centres. The overall rate of CIED infections in the survey was as follows: 44.8% of the centres reported infection rates of \leq 0.5%, 16.5% were in the range >0.5 to 1%, 17.4% were in the range >1 to 2%, 13.5% were in the range of >2% to 5%, and 7.8% reported an infection rate of >5%. There was no difference in the infection rates in centres with <50 implantations per year (median 4.65%, 25th/75th percentile = 0.00/8.33%) vs. those



with 50–200 implantations (median 0.99%, 25th/75th percentile = 0.00/2.39%) and those with >200 implantations (median 0.90, 25th/75th percentile = 0.45/1.82%), P = non significant (NS). A detailed description of the infection rates in different types of procedures is shown in *Figure 2* and in Supplementary material online, *Table S2*.

Prevention of cardiac implantable electronic device infections

A total of 154 of 184 respondents (83.7%) reported that during CIED implantation the implant procedural room met regional/national operating room standards for sterility and equipment as used for general surgical procedures. As a preventive measure, 135 of 184 responding centres (73.4%) applied regulations to limit the number of people in the operating room. Preprocedural nasal swab culture was infrequent and only used in 41/180 centres (22.8%).

Preoperative antimicrobial prophylaxis was used in 178 of 192 (92.7%) of the responding centres. The antimicrobial was administered intravenously 30–60 min before the procedure in 62.8% and at the start of the procedure in another 29.8% of the centres. The most commonly administered antimicrobial prophylaxis was intravenous (i.v.) cefazolin which was used in 149 of 187 centres (79.7%), while vancomycin i.v., oxacillin/flucloxacillin i.v., and teicoplanin i.v. were less frequently used. The regional distribution of the type of antimicrobial for the prevention of surgical site infection is shown in *Table 1*. There were no significant disparities in preoperative antimicrobial prophylaxis in different regions apart from a trend for higher vancomycin use in the Asia-Pacific region.

Preprocedural skin antisepsis was achieved with alcoholic chlorhexidine in 80/187 centres (42.8%), followed by aqueous povidone-iodine in 20.9%. Aqueous chlorhexidine and alcoholic povidone-iodine were less commonly used; in 15.5% and 15.0%,

respectively. The practices of skin antisepsis show significant regional differences as demonstrated in Figure 3. Hair removal was carried out by clippers in 121/181 (66.9%) of the responding centres. During implantation, iodinated incise drapes were used for skin preparation in 81 of 178 centres (45.5%), most commonly in North America (93.8% of the centres), and least commonly in Latin America and Caribbean (16.9%). Centres reporting using them had significantly higher median implantation rates: 498.5 (25th/75th percentile =194.8/688.3) vs. 215.5 (25th/75th percentile = 102.0/448.3), P = 0.004. Pocket irrigation with antimicrobials or antiseptics was used by 73 of 183 responding centres during implantation (39.9%). There were wide and significant regional differences in this practice as shown in Figure 4. Overall, pocket irrigation was reported more frequently by higher-volume centres: median 426.0 (25th/75th percentile = 143.5/ 737.0) implantations in centres applying this practice vs. 252.0 (25th/ 75th percentile = 102.8/512.3) implantations in those not using it, P = 0.021. Antibacterial envelopes were infrequently utilized, and only 69 of 183 responders (37.7%) reported using them. Antibacterial envelopes were most commonly used in patients considered at high risk of CIED infection (42 of 183 responses, 22.9%) and both during device replacements and in high-risk patients as reported by 24 respondents (13.1%). Fourteen of 16 North American centres (87.5%) used antibacterial envelopes in the two above-mentioned situations, while the survey results show that they were not used at all in the Middle East/North Africa. Centres reporting using antibacterial envelopes showed significantly higher implantation rates: median 598.0 (25th/75th percentile = 102.8/512.3) vs. 240.5 (25th/75th percentile = 124.5/473.3) implantations per year, P = 0.01. Antibacterial envelopes were used by 47 out of 97 (48.5%) responding university centres vs. 23/86 (26.7%) of the responding non-university centres, P=0.002. Prolonged post-



Figure 2 Reported rates of device infections in different types of procedures. CRT, cardiac resynchronization therapy; ICD, implantable cardioverter-defibrillator.

 Table I
 Regional differences in preoperative intravenous antimicrobial regimens used to prevent surgical site infection

| Type of antimicrobial | Total | Asia/Pacific | Europe/Central Asia | Latin America/ Caribbean | Middle East/North Africa | North America |
|--------------------------|------------|--------------|------------------------|-----------------------------|-----------------------------|------------------|
| Cefazolin | 149 (79.7) | 14 (82.4) | 59 (74.7) | 58 (81.7) | 4 (100) | 14 (87.5) |
| Oxacillin/Flucloxacillin | 6 (3.2) | 0 (0) | 6 (7.6) | 0 (0) | 0 (0) | 0 (0) |
| Vancomycin | 11 (2.9) | 2 (11.8) | 3 (3.8) | 5 (4.8) | 0 (0) | 1 (6.2) |
| Teicoplanin | 4 (1.1) | 0 (0) | 4 (5.1) | 0 (0) | 0 (0) | 0 (0) |
| Other | 17 (4.5) | 1 (5.9) | 7 (8.9) | 8 (11.3) | 0 (0) | 1 (6.2) |
| Number of responses | 187 | 17 | 79 | 71 | 4 | 16 |

Figures represent number of responses and percentages in brackets.

operative antimicrobial prophylaxis (oral or i.v.) of varying duration was administered by 84 of the 191 responding centres (44.0%).

Diagnosis and management of cardiac implantable electronic device infections Pocket infection

In cases of suspected pocket infection, defined as swelling, erythema, and tenderness of the skin overlying the device without signs of systemic involvement, there were several alternatives available to respondents. One hundred sixteen of 187 (62.0%) of the centres responded that in the absence of contraindications to removal or high-risk factors, patients would be hospitalized for complete system removal, while 22 out of 187 centres (11.8%) responded that patients would be admitted for a procedure involving surgical pocket debridement in an attempt to salvage the system. Needle aspiration of the pocket for culture and treatment based on microbiology results was applied in 29 of the centres (15.8%), and these centres had significantly lower median implantation rates than the rest of the centres; 157 (25th/75th percentile = 170.8/678.3) vs. 398.5 (25th/75th percentile = 91.5/324.0) implantations, P < 0.005. In 25 of 187 (13.4%) responses there was no





specific action taken in case of suspected pocket infection apart from waiting until the next regular device visit and/or asking the patient to notify the centre if symptoms or signs worsened. There were 17 responses (9.3%) stating that 18-fluorodeoxyglucose positron emission tomography computerized tomography ([¹⁸F]FDG-PET/CT) would be used and 9 (4.9%) reported that they would refer the patient to another centre for further management. There were significant regional disparities in the management of patients with suspected pocket infections as shown in *Table 2*.

When asked about the pocket management strategy in case of CIED infection necessitating complete system removal, the responses were as follows: pocket irrigation with antiseptics/antimicrobials was reported by 112 of 159 (70.4%) centres responding to this entry, wound drainage by 106 centres (66.7%), and complete capsulectomy by 127 of 167 centres (76.0%). Following complete system removal, interrupted/mattress sutures were used for wound closure by 108 of 174 responding centres (62.1%). Negative-pressure wound therapy was infrequently used—by 43 of 153 centres who responded to this entry (28.5%).

Perioperative antimicrobial therapy during complete system removal was administered by most of the responding centres—161 out of 174 (92.5%) and was initiated at least 48 h before the procedure by 90 of the 156 responding centres (57.7%). Less frequently perioperative antimicrobial treatment was started immediately before the procedure (27 centres, 17.3%) or at least two to four weeks before the procedure, depending on clinical status of the patient and the type of infection, as reported by 39 centres (25%).

Suspected cardiac implantable electronic device infection with systemic involvement

The survey asked physicians about their approach to CIED infection with systemic involvement. *Figure 5* shows the diagnostic tests applied by physicians in this setting.

The survey also asked specific questions regarding the evaluation of the patient's infectious status after CIED removal. The majority of the responders (140 of 175 centres, 80.0%) reported that infection evaluation was mainly based on complete blood count or C-reactive protein (131, 74.9%). Additionally, two sets of blood cultures were obtained in 104 (59.3%) of the centres, and 82 (46.9%) of the 175 centres reported using the results from post-procedural transthoracic echocardiography. Less commonly used were erythrocyte sedimentation rate, reported by 59 (33.7%); procalcitonin, reported by 47 (26.9%), and transoesophageal echocardiography, reported by 63 (36.0%) of the 175 centres. Other imaging techniques were occasionally used, including pulmonary scintigraphy in 3 (1.7%) and [¹⁸F]FDG-PETCT in 5 (2.9%) of the responses. Scintigraphy with radiolabelled leucocytes was never selected in any of the 175 responses. In 14 centres (8.0%) no specific strategy to assess response to therapy was applied. Regional differences were observed in the use of biomarkers



Figure 4 Intraoperative pocket irrigation with antimicrobials or antiseptics in different regions. There was a significant (P = 0.002) difference in this practice among different regions. Number of replies is presented in brackets below each region on the x-axis.

Table 2 Regional differences in the management of suspected CIED pocket infection without systemic involvement

| Action taken | Total | Asia/Pacific | Europe/Central Asia | Latin America/ Caribbean | Middle East/North Africa | North America |
|---|-----------|--------------|------------------------|-----------------------------|-----------------------------|------------------|
| No action, wait until next regular visit | 25 (13.7) | 3 (17.6) | 12 (16.2) | 10 (13.9) | 0 (0) | 0 (0) |
| Needle aspiration and therapy based on microbiology* | 29 (16) | 6 (35.3) | 4 (5.4) | 17 (23.6) | 1 (25) | 1 (6.2) |
| [¹⁸ F]FDG-PET/CT | 17 (9.3) | 1 (5.9) | 10 (13.5) | 6 (8.3) | 0 (0) | 0 (0) |
| Debridement with system left in place [#] | 22 (12) | 4 (23.5) | 8 (10.8) | 8 (11.1) | 2 (50) | 0 (0) |
| Complete system removal ^{&} | 116 (62) | 7 (41.2) | 51 (68.9) | 42 (58.3) | 2 (50) | 14 (87.5) |
| Refer to another centre | 9 (4.8) | 2 (11.8) | 6 (8.1) | 0 (0) | 0 (0) | 1 (6.2) |

Figures represent number of responses with percentages in brackets. The total percentages exceed 100% because several options could be chosen. *P = 0.004, #P = 0.042, *P = 0.046 for all regions.

to assess response to therapy. Significant differences were found for the use of C-reactive protein (P < 0.005), procalcitonin (P = 0.001), and erythrocyte sedimentation rate (P = 0.032) among different regions of the world. Indeed, the use of C-reactive protein was more common in Middle Eastern/North African (4/4, 100%) compared with North American centres, where only 4 out of 15 (26.7%) were using this biomarker. Procalcitonin was more commonly used in Europe/Central Asia than in North America (43.1% of centres vs. 0%) and erythrocyte sedimentation rate was utilized by 15 of the 72 European/Central Asian centres (20.8%) vs. two out of four centres (50%) in the Middle East/North Africa.

Adherence to guidelines

Physicians were asked to determine the indications for complete system removal in the setting of common clinical situations such as valvular or lead endocarditis, sepsis, pocket abscess, device erosion, skin adherence, bacteraemia, or superficial incisional infection. There was considerable deviation from published guidelines as shown in *Table 3*.



Figure 5 Laboratory tests (A) and imaging modalities (B) used to diagnose CIED infection with systemic involvement. All results are presented in percent. Total percentage for each test/modality may exceed 100% because most respondents provided more than one option. There were significant differences in the use of CRP (P < 0.005), ESR (P = 0.006), and PCT (P < 0.005) among different regions. CBC, complete blood count; CIED, cardiac implantable electronic device; CRP, C-reactive protein, ESR, erythrocyte sedimentation rate; [¹⁸F]FDG-PET/CT, 18-fluorodeoxyglucose positron emission tomography; PCT, procalcitonin.

| | Yes (%) | No (%) | Do not know (%) |
|---|----------------|--------|-----------------|
| Valvular or lead endocarditis, or sepsis (<i>n</i> = 174) | 98.3 | 1.7 | 0 |
| Pocket abscess, device erosion or chronic draining sinus ($n = 174$) | 98.9 | 0.6 | 0.6 |
| Signs of skin adherence ($n = 167$) | 32.9 | 54.5 | 12.6 |
| Valvular endocarditis without definitive involvement of the lead(s) ($n = 170$) | 75.9 | 15.3 | 8.8 |
| Occult Gram-positive bacteraemia (not contaminant) (<i>n</i> = 163) | 55.2 | 26.4 | 18.4 |
| Occult Gram-negative bacteraemia ($n = 166$) | 34.3 | 45.2 | 20.5 |
| Incisional infection without involvement of the device and/or leads ($n = 169$) | 21.3 | 69.8 | 8.9 |

| I able 3 Responses to university cumical scenarios regarding indications for complete naroware remo | Table 3 | Responses to different clinical | l scenarios regarding | g indications for com | plete hardware remova |
|--|---------|--|-----------------------|-----------------------|-----------------------|
|--|---------|--|-----------------------|-----------------------|-----------------------|

The number of responses is presented in brackets next to each entry.

The responses to the proposed clinical scenarios were not affected by the implantation volumes of different centres (P = NS).

Discussion

The purpose of this survey was to gain insights into disparities in global and regional practices in CIED infection prevention and management as well as compliance with published recommendations or guidelines. This knowledge could potentially be used to increase awareness of risk factors for CIED infections and improve implementation of the upcoming consensus recommendations and thereby possibly contribute to the reduction of this increasingly common device-related complication.

The survey represents a broad range of replies from centres of different volume and expertise: university hospitals, private hospitals, and non-university public hospitals. Based on the results, two primary observations were made: (i) guidelines and recommendations were commonly not adhered to in clinical practice, and (ii) there were significant regional variations in the diagnosis and management of CIED infections. Another important finding was that the implementation of guidelines on CIED infection prevention, diagnosis and management was insufficient, potentially leading to decisional strategies deviating from recommendations.

Preventive measures

Preoperative prophylactic antimicrobial treatment was administered in the majority of patients, most commonly cefazolin. This choice may have been related to previously published data^{9,11} or ease of administration but is not in accordance with recently published recommendations by the British working group.⁵ In contrast, the European guidelines advise the use of cefazolin as the first-line antimicrobial for prophylaxis during implantation. The timing of preoperative antimicrobial administration, i.e. within 1 h prior to implantation, was in compliance with recommendations in most of the centres.^{5,7} Antiseptic skin preparation with alcoholic chlorhexidine solution as recommended in guidelines, was used in less than half of the centres.⁵ Significant regional variations in the types of antiseptics used for skin preparation were also identified, such as the use of povidone-iodine solutions (especially aqueous solution) frequently reported by centres in the Asia/Pacific region, a practice which is contrary to the British recommendations⁵ and to a recent paper issued by the World Health Organization recommending alcohol-based antiseptic solutions for surgical skin antisepsis.¹² Prolonged post-operative antimicrobial prophylaxis was a widely used practice worldwide (44.0% of the centres) despite the lack of evidence of benefit.⁵ It should be emphasized that this practice is mentioned in some guidelines in the 24 to 36-h period following implantation, but this mention comes without a firm recommendation.⁷ The recent PADIT trial, results of which were not available prior to this survey, demonstrated no benefit to post-procedure antibiotic therapy and will undoubtedly inform future guidelines.¹³ Intraoperative pocket irrigation with an antiseptic or antimicrobial, although discouraged by available guidelines,⁵ was practiced by a considerable number of centres, particularly those in North America. Interestingly higher-volume centres tended to use this practice more often. A potential explanation for this observation might be the recently published data showing beneficial outcomes from pocket irrigation with antimicrobials but not with antiseptics.¹⁴

Antibacterial envelopes were not widely used and the observed regional and institutional differences in their use may be due to costs and lack of randomized trials showing their benefit. In terms of healthcare resource utilization antibacterial envelopes represent a cost-effective preventive measure at least in high-risk patients.¹⁵ Results from non-randomized retrospective and prospective trials point out the reduced incidence of CIED infections with the use of antibacterial envelopes.^{16,17} The results of a forthcoming large randomized trial evaluating the efficacy of antibacterial envelopes in patients with a high CIED infection risk undergoing procedures such as generator changes is expected to have a large impact on practices if the use of these envelopes is shown to be beneficial [World-wide Randomized Antibiotic Envelope Infection Prevention Trial (WRAP-IT), NCT02277990].

Management of infections

Surprisingly, in cases of pocket infection without systemic involvement, hospitalization and complete hardware removal (a Class I recommendation), was applied by under two-thirds of responding physicians. Worldwide practices differed considerably, with physicians from some regions reporting a high rate of pocket needle aspiration to obtain material for microbiological study or a practice of surgical debridement with the intention to leave the system in place. These practices were predominantly reported by centres in the Asia/ Pacific, Latin America/Caribbean, and Middle East/North Africa regions, and may potentially be explained by economic issues and limited access to referral centres performing lead extractions since the centres reporting pocket needle aspiration had lower implantation rates.

The observed clinical practices for the management of CIED infections with systemic involvement were more consistent with current recommendations. Widely available tests such as biomarkers of inflammation, two sets of blood cultures, and transthoracic and/or transoesophageal echocardiography were the mainstay of diagnosis and assessment of therapy, as the majority of centres used these tests as routine examinations. Apart from some regional disparities in the use of laboratory tests, there were no significant inconsistencies in the use of these imaging techniques. [¹⁸F]FDG-PET/CT has emerged as a new imaging tool in the diagnosis of CIED infections with systemic involvement, consistent with the increasing use of multimodality imaging in this clinical setting, as supported by data from recent publications.^{18–20} Interestingly, according to our results this modality was not used in Middle Eastern/North African or North American centres. In cases of complete system removal due to infection perioperative antimicrobial therapy was initiated and maintained as recommended in the vast majority of patients.

There are several published international documents on the diagnosis and management of CIED infections.⁵⁻⁹ This survey included a question on indications for complete hardware removal in different clinical scenarios without a requirement to provide the exact class or level of evidence. The observed replies demonstrated very good adherence to guidelines for valvular or lead endocarditis and pocket infection, both of which are well-established indications for device system removal according to several published recommendations.^{5–9} Surprisingly, a considerable proportion of centres were hesitant to determine the best management strategy or would choose a conservative strategy for patients with signs of skin adherence over the device, although skin adherence is a well-known marker of pocket infection and a strong indication for complete system removal.^{8,9} Valvular endocarditis without definite lead involvement is another class I indication for complete system removal according to the most recent recommendations,⁶ although approximately a quarter of the responders to our survey reported that they would not consider complete system removal in such cases. Similarly, this survey showed that only slightly over half of respondents would deem occult Grampositive bacteraemia (not contaminant) an indication for complete system removal despite a strong recommendation for system removal in published guidelines.^{6,8} The disparate replies on how to manage patients with occult Gram-negative bacteraemia; however, probably reflect the lack of clear recommendations regarding this clinical situation.

While superficial incisional infections would be treated conservatively by most physicians as recommended by guidelines, some respondents would still consider complete system removal. The observed divergence of routines for the prevention and management of CIED infections in most of the presented clinical situations suggests that the strategies for implementation of guidelines need to be improved.

A publication by Bongiorni et al.²¹ on clinical practices in the management of CIED infections reported observations similar to those in the present study but included only highly experienced centres in Europe. The present survey reflected contemporary practices worldwide including regional differences in the management of CIED infections. The main limitation of this report was that replying to the survey was voluntary; thus, the exact reply rate cannot be reported, and there is no way to monitor or validate the data provided. Therefore, the results should be interpreted with caution.

Conclusion

This survey provided important information on the preventive, diagnostic and management strategies of CIED infections around the world. The results demonstrated significant regional differences in current practice, along with a lack of profound knowledge regarding central topics in CIED infection prevention and treatment and incomplete adherence to guideline recommendations. These findings support the need to increase awareness of the problem and promoting education about existing guidelines within this field as crucial measures for improving patient outcomes and reducing the costs linked to these harmful complications.

Supplementary material

Supplementary material is available at Europace online.

Acknowledgements

The distribution of the survey questionnaire was greatly supported by the representatives of the HRS (J. Poole and L. Epstein), the LAHRS (R. Costa), the APHRS (N. Strathmore), the EACTS (C. Starck), as well as by EHRA. We would like to thank V. Meyen and L. Tapp of the EHRA staff for their technical help with the preparation and distribution of the questionnaire.

Conflict of interest: N.D. declares receiving research grants from Abbott, Biotronik, Boston Scientific and Medtronic to the institution (Heart Center Leipzig) without personal financial benefits. G.B. reports receiving speaker fees of small amount from Biotronik, Boehringer Ingelheim, Boston Scientific and Medtronic. C.B-L. reports receiving honoraria from Bayer, Merck, Sharp & Dohme, Boehringer Ingelheim, Medtronic, Sanofi, Boston Scientific and Cardiome. The other authors have no relevant conflict of interest to declare.

References

- Kurtz SM, Ochoa JA, Lau E, Shkolnikov Y, Pavri BB, Frisch D et al. Implantation trends and patient profiles for pacemakers and implantable cardioverter defibrillators in the United States: 1993-2006. Pacing Clin Electrophysiol 2010;33:705–11.
- Raatikainen MJP, Arnar DO, Merkely B, Nielsen JC, Hindricks G, Heidbuchel H et al. A decade of information on the use of cardiac implantable electronic devices and interventional electrophysiological procedures in the European Society of Cardiology Countries: 2017 report from the European Heart Rhythm Association. Europace 2017;19:ii1–90.
- Reynolds MR, Cohen DJ, Kugelmass AD, Brown PP, Becker ER, Culler SD et al. The frequency and incremental cost of major complications among medicare beneficiaries receiving implantable cardioverter-defibrillators. J Am Coll Cardiol 2006;47:2493–7.
- Rizwan Sohail M, Henrikson CA, Jo Braid-Forbes M, Forbes KF, Lerner DJ. Increased long-term mortality in patients with cardiovascular implantable electronic device infections. *Pacing Clin Electrophysiol* 2015;**38**:231–9.
- 5. Sandoe JA, Barlow G, Chambers JB, Gammage M, Guleri A, Howard P et al. Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE). J Antimicrob Chemother 2015;**70**:325–59.

- Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul CI, Birgersdotter-Green UM, Carrillo R et al. 2017 HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. *Heart Rhythm* 2017; 14:e503–51.
- 7. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F et al. 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J 2015;36:3075–128.
- Wilkoff BL, Love CJ, Byrd CL, Bongiorni MG, Carrillo RG, Crossley GH 3rd et al. Transvenous lead extraction: heart Rhythm Society expert consensus on facilities, training, indications, and patient management: this document was endorsed by the American Heart Association (AHA). *Heart Rhythm* 2009;6:1085–104.
- Baddour LM, Epstein AE, Erickson CC, Knight BP, Levison ME, Lockhart PB et al. Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. *Circulation* 2010;**121**:458–77.
- Bongiorni MG, Burri H, Deharo JC, Starck C, Kennergren C, Saghy L et al.; ESC Scientific Document Group. 2018 EHRA expert consensus statement on lead extraction: recommendations on definitions, endpoints, research trial design, and data collection requirements for clinical scientific studies and registries: endorsed by APHRS/HRS/LAHRS. *Europace* 2018;20:1217.
- 11. de Oliveira JC, Martinelli M, Nishioka SA, Varejão T, Uipe D, Pedrosa AA et al. Efficacy of antibiotic prophylaxis before the implantation of pacemakers and cardioverter-defibrillators: results of a large, prospective, randomized, doubleblinded, placebo-controlled trial. *Circ Arrhythm Electrophysiol* 2009;**2**:29–34.
- Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis* 2016;16: e276–87.

- Krahn AD, Longtin Y, Philippon F, Birnie DH, Manlucu J, Angaran P et al. Prevention of arrhythmia device infection trial: the PADIT trial. J Am Coll Cardiol 2018;72:3098–109.
- Kang FG, Liu PJ, Liang LY, Lin YQ, Xie SL, He Y et al. Effect of pocket irrigation with antimicrobial on prevention of pacemaker pocket infection: a meta-analysis. BMC Cardiovasc Disord 2017;17:256.
- Kay G, Eby EL, Brown B, Lyon J, Eggington S, Kumar G et al. Cost-effectiveness of TYRX absorbable antibacterial envelope for prevention of cardiovascular implantable electronic device infection. J Med Econ 2018;21:294–300.
- Henrikson CA, Sohail MR, Acosta H, Johnson EE, Rosenthal L, Pachulski R et al. Antibacterial envelope is associated with low infection rates after implantable cardioverter-defibrillator and cardiac resynchronization therapy device replacement: results of the citadel and centurion studies. JACC Clin Electrophysiol 2017;3: 1158–67.
- Mittal S, Shaw RE, Michel K, Palekar R, Arshad A, Musat D et al. Cardiac implantable electronic device infections: incidence, risk factors, and the effect of the AigisRx antibacterial envelope. *Heart Rhythm* 2014;11:595–601.
- Mahmood M, Kendi AT, Farid S, Ajmal S, Johnson GB, Baddour LM et al. Role of (18)F-FDG PET/CT in the diagnosis of cardiovascular implantable electronic device infections: a meta-analysis. J Nucl Cardiol 2017;doi:10.1007/s12350-017-1063-0.
- Juneau D, Golfam M, Hazra S, Zuckier LS, Garas S, Redpath C et al. Positron emission tomography and single-photon emission computed tomography imaging in the diagnosis of cardiac implantable electronic device infection: a systematic review and meta-analysis. *Circ Cardiovasc Imaging* 2017;10:e005772.
- Sollini M, Berchiolli R, Delgado Bolton RC, Rossi A, Kirienko M, Boni R et al. The "3M" approach to cardiovascular infections: multimodality, multitracers, and multidisciplinary. Semin Nucl Med 2018;48:199–224.
- Bongiorni MG, Marinskis G, Lip GY, Svendsen JH, Dobreanu D, Blomstrom-Lundqvist C. How European centres diagnose, treat, and prevent CIED infections: results of an European Heart Rhythm Association survey. *Europace* 2012; 14:1666–9.