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Cohort profile

The ESC-EORP EURO-ENDO (European Infective Endocarditis) registry

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*A complete list of the EURO-ENDO Investigators is provided in the Appendix 1

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Abstract

Aims: The European Society of cardiology (ESC) EURObservational Research Programme (EORP) European Endocarditis (EURO-ENDO) registry aims to study the care and outcomes of patients diagnosed with infective endocarditis and compare findings with recommendations from the 2015 ESC Clinical Practice Guidelines for the management of infective endocarditis and data from the 2001 Euro Heart Survey.

Methods and results: Patients (n=3116) aged over 18 years with a diagnosis of infective endocarditis based on the ESC 2015 infective endocarditis diagnostic criteria were prospectively identified between January 1st, 2016 and March 31st, 2018. Individual patient data were collected across 156 centres and 40 countries. The primary end-point is all-cause mortality in hospital and at 1-year. Secondary end-points are 1-year morbidity (all-cause hospitalisation, any cardiac surgery and infective endocarditis relapse), the clinical, epidemiological, microbiological, and therapeutic characteristics of patients, the number and timing of non-invasive imaging techniques, and adherence to recommendations as stated in the 2015 ESC Clinical Practice Guidelines for the management of infective endocarditis.

Conclusion: EURO-ENDO is an international registry of care and outcomes of patients hospitalised with infective endocarditis which will provide insights into the contemporary profile and management of patients with this challenging disease.

Key words: infective endocarditis, registry, valve disease

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Introduction

Infective endocarditis (IE) is a lethal disease associated with not only high risk of death, but high rates of morbidity and healthcare expenditure (1-6). Despite improvements in diagnostic and therapeutic strategies, the incidence and severity of the disease remain unchanged – largely driven by the evolving epidemiological profile of patients as well as an increasing number with prosthetic or device related IE (7).

In addition to temporal changes in patient characteristics (1, 7) over time, changes in key health service factors have occurred with potential impact on IE care and outcomes. These include the development of new diagnostic and therapeutic strategies for the management of IE (2), publication of the 2015 European Society of Cardiology (ESC) Clinical Practice Guidelines on the management of IE (8), the increasing recognition of the importance of the IE Team, and the availability of multi-modality imaging (8). Notably, it remains uncertain whether recommendations for the use of early surgery in patients with complicated IE have been widely adopted and whether this is associated with better or worse clinical outcomes. Equally, there are limited international data regarding adherence to (and impact of) changing recommendations for IE antibiotic prophylaxis.

Given that the last major international survey of IE (the ESC Euro Heart Survey Programme dedicated to valvular heart disease) was performed in 2001 (9) with no comprehensive surveys since then, there is a compelling need to undertake a contemporary international investigation of the care and outcomes of IE. We therefore designed and implemented the ESC EORP European Endocarditis (EURO-ENDO) international registry (10).

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Aim of EURO-ENDO

The aim of the EURO-ENDO registry is to undertake an international observational study to allow an up-to-date investigation of the care and outcomes of patients with IE. The primary objective of EURO-ENDO is to evaluate the outcome of patients diagnosed with Infective Endocarditis. The secondary objectives are to assess the current clinical, epidemiological, microbiological, therapeutic, and prognostic characteristics of IE in Europe, to assess the current practices of imaging in IE in Europe and in affiliated countries, to assess the degree of implementation of the ESC guidelines in practice, and to compare these current data with those obtained in the Euro Heart Survey. The wide geospatial coverage of EURO-ENDO will allow regional investigation of the management and outcomes of patients hospitalised with IE.

Quality of care interventions

By means of an electronic case record form, individual patient data were collected across 430 unique data fields, including patient characteristics, clinical, biological, and microbiological data, the use of imaging procedures (and their results), antibiotic treatment and surgical interventions. Diagnostic methods for IE, antibiotic treatment, indications for and the use of surgery, and the frequency and type of patient follow-up were not pre-specified by the study protocol.

Setting: University and non-university hospitals of any volume of activity within and beyond Europe were invited to join EURO-ENDO on a voluntary basis. All 57 ESC–member countries were invited to participate in EURO-ENDO, with centres within the countries being selected by a National Coordinator from the country. Participating centres were categorised by the European Association of Cardiovascular Imaging as either high level IE centres: high volume of treated patients (≥ 20 patients per year) with expertise in IE diagnosis,

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management, imaging and surgical therapy or low volume centres (< 20 patients per year) without surgical capabilities, as self-reported by the participating centres.

Population and consent: From January 1st, 2016 to March 31st, 2018, centers were asked to include consecutive patients aged greater than 18 years over a 1-year follow-up period with a diagnosis of definite IE (or possible IE, considered and treated as IE) based on the ESC 2015 infective endocarditis diagnostic criteria (8). Since all centres were asked to include patients during a 1-year period and to obtain 1-year follow-up for all these patients, the total duration of participation of each centre was 2 years, with end of follow-up of the study on March 31st, 2019. All participants received detailed written information concerning the study and provided signed informed consent. In total, 3116 index cases of IE from 156 centres across 40 countries were collected over the study period (Figures 1 and 2).

Patient identification: Potential participants were identified from echocardiographic laboratories and hospitals treating patients with IE and given a unique study number.

Start points: Any patient aged over 18 years and hospitalised between January 1st, 2016 to March 31st, 2018 with definite IE (or possible IE, considered and treated as IE) based on ESC 2015 diagnostic criteria.

Baseline and follow-up data: Baseline data included demographic data (site of inclusion, , age), patient history (previous IE, at-risk situation or procedure, history of cardiovascular and non-cardiac disease), clinical data (weight, height, date and timing of first signs and symptoms, temperature), previous cardiac or non-cardiac invasive intervention within the last 6 months (colonoscopy, dental procedure, urogenital or gastrointestinal intervention), biological and

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microbiological data (sedimentation rate, C-reactive protein, creatinine, haemoglobin, white blood cells, platelet count, blood cultures, serology), echocardiographic data (vegetation, abscess, valvular and perivalvular lesions, valve regurgitation or stenosis), other imaging techniques (CT scan, PET-CT, cerebral or cardiac MRI), treatment before admission and during hospitalization (including antibiotic therapy and all other treatments), complications under therapy (embolic event, infectious and haemodynamic complications, theoretical indications for surgery, in-hospital mortality), interventional treatments (valve surgery), and 1-year complications (any hospitalisation, recurrence of IE and 1-year all-cause mortality)

Data capture and storage: Participant identifiable data were used to track subsequent clinical care and outcomes, with the identifiable data only residing on local centre computers. These data were then pseudonymised by means of a unique patient study code before electronic transmission via the ESC-EORP Data Entry System Security using SSL (Secure Sockets Layer) network encryption to a dedicated secure server (Microsoft SQL Server 2012 Database server) at the central data warehouse (The European Heart House, France). Data Collection Officers and local investigators at participating centres had access to electronic case report forms through secure login on the EORP website. Individual login names and passwords were distributed by the EORP team to the participating centres.

Data quality Data quality was monitored by the ESC EORP EURO-ENDO administrative team. This included edit checks (for missing data, date chronology, numeric value ranges) and a Data Validation Plan listing all the checks carried out to ensure data consistency and adherence to the protocol, including missing data, consistency of the chronology in the dates and between the data of the different visits of the study (cross checks), and the numeric values entered are included in the predefined ranges

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Endpoints and linkages to other data: The primary end-points are in-hospital and 1-year mortality. Secondary end-points are 1-year morbidity (any hospitalisation, any cardiac surgery, IE recurrence), clinical, epidemiological, microbiological and therapeutic characteristics, number and timing of non-invasive imaging techniques, and implementation of the 2015 ESC Clinical Practice Guidelines for the management of IE. In-patient data are collected from hospital medical records, and 1 year follow up data collected by contact with the participants via telephone calls and / or scheduled outpatient clinic appointments.

Conclusion:

To our knowledge, the ESC EORP EURO-ENDO registry is the most comprehensive and far reaching observational cohort of patients hospitalised with IE. The registry will describe the contemporary profile of patients admitted to hospital with IE, their investigations, treatment and clinical outcomes, and document how we care for patients with IE in the light of recommendations from the 2015 ESC Clinical Practice Guidelines for the management of IE. EURO-ENDO will, for example, offer insight into the implementation and impact of changing recommendations for the use of IE antibiotic prophylaxis. In addition, since EURO-ENDO registry finally includes patients from 4 continents countries, it represents a unique opportunity to compare the characteristics of IE across the world. Although it will unavoidably suffer the limitations of such a registry (voluntary nature, international reach, lack of a central/core laboratory to review echo images and microbiological samples), and given the paucity of randomized and large-scale observational data, the ESC EORP EURO-ENDO registry offers a unique opportunity to provide key information about the current care and outcomes of patients with IE across a wide range of countries.

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Conflict of Interest statement

G Habib, D. Popescu, R. Citro, B. Cosyns, E Donal, P Erba, C Gale, J Ternacle, P Lancellotti, B Prendergast, A Sadeghpour, A Sambola, S Furnaz, C Laroche, M Meshaal, P Tornos, M. Pazdernik declare no conflict of interest. Dr. Iung reports personal fees from Edwards Lifesciences, personal fees from Boehringer Ingelheim, personal fees from Novartis, outside the submitted work. Dr. Maggioni reports personal fees from Bayer, personal fees from Fresenius, personal fees from Novartis, outside the submitted work.

Accepted manuscript

References

1. Wang A, Athan E, Pappas PA, Fowler VG, Jr., Olaison L, Pare C, et al. Contemporary clinical profile and outcome of prosthetic valve endocarditis. JAMA 2007;297(12):1354-1361.

2. Habib G. Management of infective endocarditis. Heart 2006;92(1):124-130.

3. Heredia-Rodríguez M, Hernández A, Bustamante-Munguira J, Álvarez FJ, Eiros JM, Castrodeza J, et al. Evolution of the Incidence, Mortality, and Cost of Infective Endocarditis in Spain Between 1997 and 2014. J Gen Intern Med. 2018 Oct;33(10):1610-1613

4. Murdoch DR, Corey GR, Hoen B, Miro JM, Fowler VG, Jr., Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med 2009;169(5):463-473.

5. Chu VH, Cabell CH, Benjamin DK, Jr., Kuniholm EF, Fowler VG, Jr., Engemann J, et al. Early predictors of in-hospital death in infective endocarditis. Circulation 2004;109(14):1745-1749.

6. San Roman JA, Lopez J, Vilacosta I, Luaces M, Sarria C, Revilla A, et al. Prognostic stratification of patients with left-sided endocarditis determined at admission. Am J Med 2007;120(4):369-7.

7. Duval X, Delahaye F, Alla F, Tattevin P, Obadia JF, Le Moing V. Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications: three successive population-based surveys. J Am Coll Cardiol. 2012;59:1968-76

8. 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; 36:3075-3128

Accepted manuscript

9. Tornos P, Iung B, Permanyer-Miralda G, Baron G, Delahaye F, Gohlke-Barwolf C, et al. Infective endocarditis in Europe: lessons from the Euro heart survey. Heart 2005;91(5):571-575.

10. https://www.escardio.org/portal/site/Escardio/menuitem.c9f480f01a3ca18798f54de7202031ca/?vgnextoid=5c4407daabb2b410VgnVCM1000004e03a8c0RCRD&vgnextchannel=2f468124b9945510VgnVCM1000005303a8c0RCRD&vgnextfmt=default&vgnextlocale=EN)

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Figure legends:

Figure 1 Numbers of patients included in the ESC EORP EURO-ENDO registry according to participating country

Figure 2 Countries participating in the ESC EORP EURO-ENDO registry

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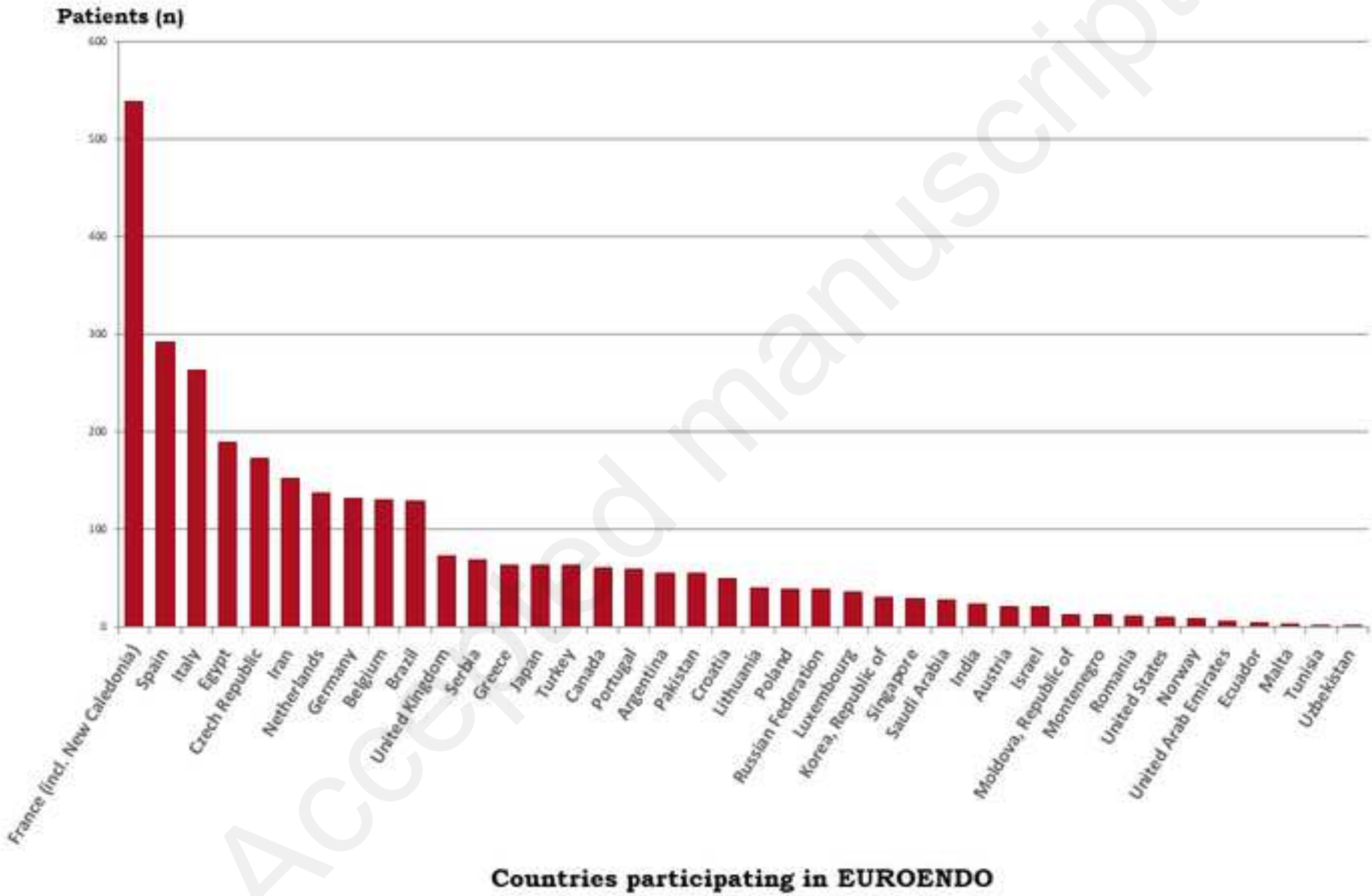
Countries participating in EURO-ENDO



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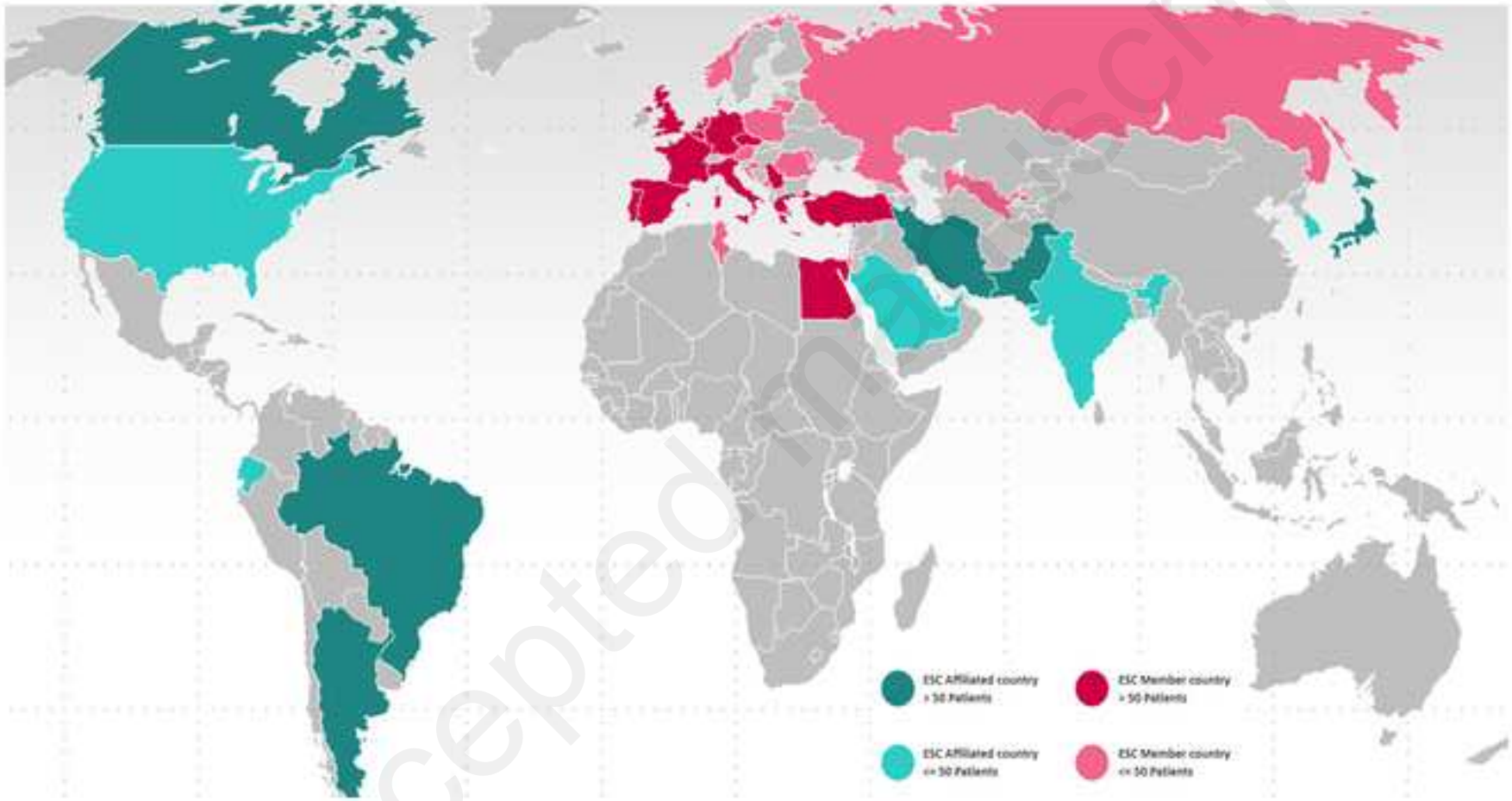
Map ESC members-nonmembers



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Appendix 1.

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