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Regional variations in baseline characteristics of cardiac rhythm device recipients: The PANORAMA observational cohort study ☆

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ABSTRACT

Background: The PANORAMA study was designed to collect concurrent data on subjects from different worldwide regions implanted with CRM devices.
Methods: In this prospective, multi-center study, we analyzed baseline data on 8586 subjects implanted with CRM devices with no additional selection criteria (66% pacemaker (IPG), 16% implantable cardiac defibrillators (ICD), 17% cardiac resynchronization therapy (CRT) and <1% Internal Loop Recorder) from 156 hospitals across 6 geographical regions between 2005 and 2011.
Results: Regardless of the device implanted, subjects from the Middle East and India often had more diabetes than other regions. Eastern and Western Europe had higher rates of atrial fibrillation reported, and men were more likely to smoke than women (46% vs 11%, $p < 0.001$). Within the CRT cohort there was significant variation in the proportion of males receiving a device, ranging from 55% in India to 83% in Eastern Europe.
Conclusions: We provide comprehensive descriptive data on patients receiving CRM devices from a range of geographies that are not typically reported in literature. We found significant variations in clinical characteristics and implant practices. Long term follow-up data will help evaluate if these variations require adjustments to outcome expectations.

1. Introduction

Device therapies for treating cardiac rhythm disorders include pacemakers (IPG) and implantable cardiac defibrillators (ICD), both with and without cardiac resynchronization therapy (CRT). Randomized trials have established the effectiveness of device therapies for cardiac rhythm and disease management [1–5]. These trials have played an important role in establishing guidelines for the application of these therapies.

Translating evidence from randomized trials into global clinical practice guidelines involves extrapolating results from a study cohort to the population of interest in the guideline. However it is not a priori certain that study results from a specific patient population in a specific region can be extrapolated to a less well-defined patient population or to other geographies. Regional variations in disease incidence [6–8], patient demographics and comorbidities [9], genetics [10], healthcare systems and reimbursement conditions [11], cultural attitudes to

Abbreviations: ICD, implantable cardioverter-defibrillator; IPG, implantable pulse generator; CRT, cardiac resynchronization therapy; CRM, cardiac rhythm management; AV, atrio-ventricular; DFT, defibrillation threshold testing.

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disease and implant practices exist which affect the choice of therapy and may influence the expected therapy outcomes [12]. Risk factors can be considered and treated differently across geographies [13] and approaches to diagnostic testing can also differ. Understanding the patients, the practice patterns and the healthcare settings of a geography are important for setting expectations and interpreting patient outcomes.

While randomized trials are indispensable in understanding the benefit of therapies in strictly controlled settings, observational studies are designed to assess the relevance and credibility of clinical trial outcomes in real-life settings [14]. Our current understanding of the real world application of cardiac rhythm management (CRM) therapies comes largely from registries conducted in North America and Europe [15,16]. To date there is little evidence available to shed light on regional differences in practice patterns, particularly to understand demographics, comorbidities and treatment patterns in emerging geographies.

This is the first report of the world wide PANORAMA study, a long term, multi-center, prospective, non-randomized observational study. The primary purpose of the study was to construct a computerized database of national profiles and epidemiological data on patients wearing Medtronic implantable pacemakers, cardioverter defibrillators (both with and without cardiac resynchronization therapy), and implantable loop recorders. The study was conducted in 34 countries across 6 geographical regions. Minimal selection criteria ensured that the study population included elderly patients, patients with comorbidities and patients presenting for a replacement device in an effort to ensure that participants were representative of patients receiving therapy for cardiac rhythm disorders. The objective of this analysis is to describe the patients and implant procedures and to provide information on clinical characteristics in regions previously underrepresented.

2. Methods

2.1. Study population

Consenting patients included those who were implanted (either de novo device or replacement) with a Medtronic market-released CRM device (IPG or ICD with or without CRT capability); no other selection criteria were applied. The protocol specified that enrollment should take place within 30 days of the planned/performed implant procedure.

PANORAMA (ClinicalTrials.gov Identifier: NCT00382525) was designed and conducted in compliance with the local ethical considerations and according to the principles outlined in the 'World Medical Association Declaration of Helsinki' (October 2000) and the laws and regulations in the countries in which the study was conducted. The study was submitted to locally appointed ethics committees and informed consent was obtained from the subjects (or their guardians).

Patients were enrolled from 6 geographies: Latin America (Argentina, Bahamas, Brazil, Colombia, Dominican Republic, Ecuador, Mexico, Puerto Rico, Uruguay, Venezuela, and Virgin Islands), Western Europe (Austria, Belgium, Denmark, Spain, Germany, Greece, Luxemburg, Netherlands, and United Kingdom), Eastern Europe (Belarus, Czech Republic, Latvia, Lithuania, Poland, Romania, Russian Federation, Serbia, Slovakia, and Turkey), Middle East (Kuwait and Saudi Arabia), South Africa and India.

2.2. Study design

Patients were assessed at study entry and during follow-up visits for at least 1 year after implant. Patients were followed according to the standard follow-up visit scheme of the participating centers, and did not require any procedures beyond regular practice. All treatment decisions were at the discretion of the treating physician. PANORAMA was designed to enroll 10,000 patients.

2.3. Data collection and measures

Clinical data were collected by the investigators using an electronic case report form designed specifically for the study, and stored in a centralized database. The data collected at baseline included demographics and clinical characteristics, medical history, and cardiovascular pharmacological therapy. At implant, data were collected on the implantation procedure and techniques, adverse experiences and device programming.

The IPG cohort includes patients implanted with a single or dual chamber pacemaker. Indications were defined as: AV block (any form of atrioventricular conduction disorder), sinus node disease (any form of atrial based bradyarrhythmia) or other (neither of the previous two). The ICD cohort includes patients implanted with a single or dual chamber ICD. Indications were defined as: secondary prevention (survivor of prior sustained ventricular tachyarrhythmia) or primary prevention (risk factors for sudden cardiac arrest without prior episode). The CRT cohort includes patients implanted with a CRT-D or a CRT-P.

2.4. Statistics

Data are reported as mean $\pm$ standard deviation (SD), median (interquartile range (IQR)) or as n (percentage). For continuous variables, comparisons across the regional groups were made using analysis of variance (ANOVA) with pairwise comparisons performed using Tukey's studentized range test. For categorical variables a chi-square test was used. All statistical analyses were performed using SAS software version 9.3 (SAS Institute). P values less than 0.05 were considered statistically significant. Stratification of the analysis was specified a priori by region, pathology, indication, and device type.

3. Results

A total of 10,064 subjects were enrolled in the PANORAMA study between 2005 and 2011. From the total study population 1478 patients were excluded from the database due to the lack of evidence of a signed Patient Informed Consent or Patient Data Release Form (1428), or because the same patient was, by mistake, created twice in the electronic database (50). This analysis includes data of the remaining 8586 subjects, all implanted with a CRM device, and enrolled by 156 centers across 34 countries. Two thirds of the study population was implanted with an IPG, 16% with ICD, 17% with CRT, and 1% were implanted with an implantable loop recorder or missing information about the device type. One third of the subjects were enrolled from Eastern Europe (EE), 17% from Western Europe (WE), 17% from South Africa (SA), 17% from the Middle East (ME), 13% from Latin America (LA) and 7% from India (IN) (Table 1).

Regardless of the type of device implanted, several cardiovascular risk factor patterns were noted to be similar. In particular, subjects from the Middle East had substantially more diabetes present than other regions (47% vs 20% EE, 19% LA, 15% SA, 25% WE, 33% IN, $p < 0.001$ for ME vs all); subjects from India were significantly lighter in weight (66 $\pm$ 13 kg vs 81 $\pm$ 16 EE, 71 $\pm$ 15 LA, 82 $\pm$ 20 SA, 79 $\pm$ 16 WE, 76 $\pm$ 19 ME, $p < 0.001$ for IN vs all) and in all regions men were more likely to smoke than females (46% vs 11%, $p < 0.001$).

There were also distinct differences in the amount of atrial fibrillation reported across the regions with Eastern and Western Europe reporting more atrial fibrillation than other regions (42% EE and 36% WE vs 15% LA, 15% ME, 26% SA, 9% IN, $p < 0.001$ for EE vs all and $p < 0.05$ for WE vs all).

The use of general anesthesia for all types of device implants was higher in Latin America than in other regions (26% vs 2% EE, 1% IN, 2% ME, 12% SA, 14% WE, $p < 0.001$ for LA vs all).

In the IPG cohort 46% were female and 41% were aged over or equal to 75 years of age. Table 2 reports the baseline and initial treatment characteristics of patients who received IPG therapy stratified by region.