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Original article

Time trends in the aetiology of prosthetic joint infections: a multicentre cohort study☆

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ABSTRACT

It is important to know the spectrum of the microbial aetiology of prosthetic joint infections (PJIs) to guide empiric treatment and establish antimicrobial prophylaxis in joint replacements. There are no available data based on large contemporary patient cohorts. We sought to characterize the causative pathogens of PJIs and to evaluate trends in the microbial aetiology. We hypothesized that the frequency of antimicrobial-resistant organisms in PJIs has increased in the recent years. We performed a cohort study in 19 hospitals in Spain, from 2003 to 2012. For each 2-year period (2003–2004 to 2011–2012), the incidence of microorganisms causing PJIs and multidrug-resistant bacteria was assessed. Temporal trends over the study period were evaluated. We included 2524 consecutive adult patients with a diagnosis of PJI. A microbiological diagnosis was obtained for 2288 cases (90.6%). Staphylococci were the most common cause of infection (1492, 65.2%). However, a statistically significant rising linear trend was observed for the proportion of infections caused by Gram-negative bacilli, mainly due to the increase in the last 2-year period (25% in 2003–2004, 33.3% in 2011–2012; p 0.024 for trend). No particular species contributed disproportionally to this overall increase. The percentage of multidrug-resistant bacteria PJIs increased from 9.3% in 2003–2004 to 15.8% in 2011–2012 (p 0.008), mainly because of the significant

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rise in multidrug-resistant Gram-negative bacilli (from 5.3% in 2003–2004 to 8.2% in 2011–2012; p 0.032). The observed trends have important implications for the management of PJIs and prophylaxis in joint replacements. **N. Benito, CMI 2016;22:732.e1–732.e8**

Introduction

Prosthetic joint replacement is one of the most useful medical advances of recent decades and is increasingly performed worldwide. Although prosthetic joint infection (PJI) occurs in a small proportion of patients (1%–3%), it is a devastating complication and the absolute number of such infections is expected to rise in the coming years [1–4].

In clinical practice, knowledge of the microbiological spectrum of PJIs is of paramount importance. First, this information is essential for guiding empiric antibiotic therapy, particularly in early postoperative infections [5]. Patients who receive effective initial treatment before microbiological results are confirmed are less likely to experience treatment failure, according to a recent study [6]. Second, the surgical antimicrobial prophylaxis chosen for joint replacement should cover the most common pathogens causing surgical site infections [7].

Much of the current understanding of the microbial aetiology of PJIs comes from studies that are limited by small sample sizes [5,6,8–21], or describe single-centre experiences [5,10–18,20–22]. Few studies have systematically described the full microbiological spectrum of PJIs [10,16,18–20]. Most focus on a specific category of infection, mainly early [6,14,21] or late [12,17] infections, or on treatment using particular surgical strategies [5,15]. Most of these studies were carried out in the USA or the UK [5,9–13,15,16,20], and were performed more than a decade ago [5,8–18]. Recent studies suggest however that the microorganisms causing PJIs can change over time or vary in different geographical areas [23–25]. The threat of infections caused by multidrug-resistant organisms is increasing worldwide, yet little is known about their possible role in PJIs. There are no available data based on large contemporary patient cohorts to address these questions.

Our aim was to characterize the pathogens causing PJIs and to evaluate trends in microbial aetiology in a large cohort of patients from 2003 to 2012. We hypothesized that the frequency of antimicrobial-resistant organisms in PJIs has increased in recent years.

Methods

Setting, study design and patients

An ambidirectional observational study was performed in 19 hospitals in Spain, within the framework of the Spanish Network for Research in Infectious Diseases (REIPI) (www.reipi.org). The REIPI Group for the Study of Prosthetic Joint Infections is a multicentre collaborative research group of infectious disease specialists and microbiologists nationwide with long-term experience of managing orthopaedic infections.

Consecutive patients older than 16 years with PJIs diagnosed from 2003 to 2012 were included in the current study. Only episodes of infection diagnosed for the first time during the study period were included; reactivation of infection prior to this period was excluded.

Data collection

This cohort study was ambidirectional, with both prospective and retrospective data collection. First, data were obtained from the REIPI cohort, which prospectively enrolled consecutive patients with PJIs from 2003 to 2006. Characteristics of this cohort have been previously described [21,26]. Except for queries on critical variables, additional information was not requested for cases from the REIPI prospective cohort. Second, we also retrospectively collected data from patients who developed PJIs from 2007 through 2012 from the REIPI and other hospitals meeting the participation criteria. The participation criteria included: (1) centres with access to orthopaedic surgery, (2) identification procedures to ensure that all consecutive cases diagnosed at the centre were included and that ascertainment bias was minimized; (3) availability of and/or access to most of the requested data for resolving queries. A standard case report form specifically developed for this study was used to collect data at all sites. Most participating centres have electronic databases with prospectively collected information on patients with PJI; data were obtained from the databases and, when necessary, from the patient's medical records at each participating hospital. Completed case report forms were sent to the coordinating centre for data entry or were entered directly into the common electronic database by site investigators. The Hospital de la Santa Creu i Sant Pau (Barcelona, Spain) was the coordinating centre for the current study. The Institutional Review Board of the Hospital de la Santa Creu i Sant Pau approved the study before data collection. All case report forms were reviewed at the coordinating centre. The process of gathering data, reviewing the case report forms, and sending and resolving queries was carried out by the coordinating centre between January 2013 and December 2014.

Clinical data and definitions

We collected information on patient demographics and pre-existing conditions, arthroplasty characteristics, classification of the PJI and microbiological diagnosis. Definitions were established for all variables to ensure standardized data collection. For every patient, the following data were recorded: age and gender; comorbidities and immunosuppressive therapy; the American Society of Anesthesiologists (ASA) score for the patient before the surgical procedure closest to diagnosis of infection (usually the implant of the arthroplasty); previous exposure to antibiotics (≥7 days) or hospitalization in the previous 90 days (≥2 days); receipt of haemodialysis, intravenous therapy, wound care or specialized nursing care at home in the 30 days before the last surgical procedure or onset of haematogenous PJI; residence in a nursing home or long-term care facility. We collected the following information about the arthroplasty: the reason for and date of implantation, site, time from admission to implantation, primary or revision arthroplasty, cemented versus uncemented arthroplasty and use of antibiotics in bone cement. Date of diagnosis, classification of the PJI, type and number of cultured samples and their results were also recorded.