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# Infectious complications following major heart surgery from the day of the surgery to hospital discharge

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## Abstract

**Background** At some point in their lives, many people will require major heart surgery (MHS). Patients are generally older adults with various risk factors for infection. However, the incidence of infection after MHS is poorly known, as reported infection data are frequently biased due to different factors like the surgical procedure, postoperative timing, and infectious syndromes or etiologic agents, among others. In addition, most patient data are retrospectively obtained.

**Purpose and methods** Data were prospectively collected regarding the incidence of all nosocomial infections produced from the time of surgery to hospital discharge in a cohort of 800 adults consecutively undergoing a MHS procedure.

**Results** During postoperative hospitalization, 124 of the 800 participants developed one or more infections (15.5%): during their ICU stay in 68 patients (54.8%), during their stay on the general ward post ICU in 50 (40.3%), and during their stay in both wards in 6 (4.8%). The most common infections were pneumonia (related or not to mechanical ventilation), surgical site and bloodstream. As etiological agents, 193 pathogens were isolated: mostly Gram-negative bacilli (54.4%), followed by Gram-positive bacteria (30%), viruses (4.6%) and fungi (1.5%). In our cohort, all-cause mortality was recorded in 33 participants (4.1%) and 9 infection-related deaths (1.1%) were produced. Among subjects who developed infections, overall mortality was 13.7% and in those who did not, this was only 2.3%.

**Conclusion** Infection following MHS remains frequent and severe. Our data suggest that hospital-acquired infection studies should consider episodes of infection in all populations during their entire hospital stay and not only those related to specific clinical syndromes or acquired while the patient is in intensive care.

**Keywords** Major heart surgery, Postoperative infections, Surgical site infections, Pneumonia, Ventilator associated pneumonia, Bloodstream infections, Mortality, Nosocomial infections

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## Background

A high number of patients undergoes one or more major heart surgery (MHS) procedures annually (29,319 procedures in 2021 in Spain). Patients are usually older persons with numerous risk factors for acquiring an infection. The overall infection risk has been calculated as 5.9 to 20% of all patients undergoing MHS [1, 2]. However, many of the data reported are biased for several reasons including the reporting of only one particular type of infection such as surgical site infection [3–6], ventilator-associated pneumonia [7–9] or catheter-related bloodstream infection [10]. Other reports focus on the causative agents such infections produced by *S. aureus* or *Mycobacterium chimer*a [11–13]. In other studies, the selective factor is the surgical procedure itself including infections following revascularization surgery or valve surgery [14]. Moreover, many infection studies seem to consider only the early post-operative period, when the patient is in a post-surgical ICU. In effect, infections occurring in the postoperative period when the patient has left the ICU have been less studied and are not usually compared with those occurring in the ICU.

In 2006, we reported the results of a hospital-acquired infection study performed in several European MHS-ICUs via a questionnaire sent to 17 hospitals. Overall, this retrospective study revealed that 9.9% of operated patients developed one or more nosocomial infections during their ICU stay along with an associated median mortality of 4.7% [1].

The aim of the present study was to determine the incidence, type, etiology and prognosis of infections produced in a cohort of adults undergoing MHS based on data prospectively collected from the day of surgery to hospital discharge. Our main objective was to better estimate the actual risk of infection and the type of infections produced during the entire period of hospitalization after MHS.

## Material and methods

### Hospital setting and patients

Our institution is a tertiary care hospital with approximately 1300 beds and around 50,000 admissions/year. More than 500 MHS procedures are performed annually in adults at the Dept. of Cardiovascular Surgery, a large referral unit.

### Study design

This was a prospective observational cohort study of adult patients undergoing MHS at our center over the inclusive period October 10, 2019 to December 17, 2021.

### Primary endpoint

The primary endpoint was the incidence of postoperative infections acquired before hospital discharge after MHS.

### Secondary endpoints

As secondary endpoints, we established the incidences of different types of infection, causative microorganisms, risk factors for infection, and infection-related mortality.

### Follow-up

Physicians from the Depts. of Anesthesia and Infectious Diseases monitored patients daily to check for the presence of infection. Our infection control team is multidisciplinary including physicians and nurses from the ICU, microbiologists, infectious disease specialists, and health care workers from the Dept. of Preventive Medicine. In adult patients undergoing MHS, data are regularly and prospectively collected into a database. Patient follow up at the center was no less than 4 months after MHS.

### Microbiological samples

All microorganisms were identified using standard methods, and antimicrobial susceptibility was tested according to Clinical and Laboratory Standards Institute recommendations.

All patients were tested for the presence of SARS-CoV 2 prior to surgery even if they were asymptomatic, and also after surgery to exclude cases of nosocomial acquisition. All respiratory specimens from symptomatic patients were tested for SARS-CoV 2.

### Definitions

The definitions of infections were based on the criteria issued by the CDC, particularly the definitions of hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), bacteremia, catheter-related bloodstream infection (CR-BSI), surgical site infection, mediastinitis and urinary tract infection (UTI) [15–18].

### Preventive measures

All patients scheduled for an MHS procedure were routinely examined to determine their nasal *Staphylococcus aureus* carrier status by PCR testing and/or culture on traditional media. Colonized patients were decontaminated with nasal mupirocin. Daily hygiene was performed with chlorhexidine impregnated wipes.

The bundle of measures for prevention of pneumonia included aspiration of subglottic secretions using a TaperGuard Evac endotracheal tube (Mallinckrodt,

St Louis, Mo), with cuff pressure maintained at 20 to 30 mmHg, continuous monitoring with the patient in a semirecumbent position (30°–45°), and oral hygiene with chlorhexidine. Patients who remained under mechanical ventilation (MV) for more than 48 h were systematically subjected to selective digestive decontamination (SDD) without the contribution of systemic antibiotics. Was systematically applied to patients who remained under mechanical ventilation (MV) for more than 48 hours [19].

Catheter care included the following: daily recording of the need for catheter use, daily monitoring of the insertion site, skin disinfection with 2% alcoholic chlorhexidine, connector disinfection with 70% alcohol wipes before use, replacement of gauze/transparent/chlorhexidine dressing according to international guidelines, and use of split-septum closed connectors (CLAVE, ICU Medical, Inc., San Clemente, CA, USA) and replacement of continuous infusion systems every 7 days (except for parenteral nutrition every 24 h and propofol every 12 h).

Further information recorded daily was the need for a catheter. Patients were catheterized using lose drainage systems with the drainage bag always placed below the level of the bladder. Hygiene and care measures on the urethral meatus were performed daily. Patients started wearing a sternum support vest 24 h after surgery when possible [20, 21]. Antibiotic prophylaxis for surgery consisted of 2 g of cefazolin administered before surgery and every 8 h thereafter for a total of three doses (if allergic to cefazolin 1 g of vancomycin was given before surgery and two further doses every 12 h thereafter).

### Statistical analysis

Qualitative variables are provided with their frequency distributions. Quantitative variables are given as the mean and standard deviation (SD), and median and interquartile range (IQR) if their distribution was skewed. Continuous variables were compared using the *t* test for normally distributed variables, or median test for non-normally distributed variables. Categorical variables were compared using the chi-square or Fisher's exact test.

Variables included in the multivariate logistic analysis were those emerging as significant in the analysis and/or those considered clinically relevant [22].

Following the multivariate analysis, a risk score model was constructed to identify participants at a higher risk for intra-hospital infection. This model was subjected to ROC curve analysis and a cutoff value searched for to determine the accuracy and optimal threshold of high-risk patients for infection. Next, we calculated sensitivity, specificity, positive and negative predictive values, and likelihood ratios for different scores. The risk of infection according to the onset time of the first episode

of nosocomial infection was assessed through Kaplan-Meier analysis.

All statistical tests were performed using the software packages SPSS 21.0 and Epidat 2.1. Significance was set at  $p < 0.05$ .

## Results

### Study population

Participants were 800 subjects consecutively undergoing MHS who gave their written informed consent to participate. After enrolment, participants were prospectively followed until hospital discharge. Median participant age was 64 years (IQR 56–73.7); 68.3% were men (Table 1).

Patient comorbidities (Table 1) were classified using the modified Charlson method, yielding a mean index of 1.56 (SD 1.70). Diabetes mellitus was the most frequent underlying disease affecting 24.9% of the cohort, followed by congestive heart failure (22.6%), previous ischemic heart disease (13.5%) and COPD (13.1%). Surgical risk scores for the cohort were (medians): EuroScore=6 (IQR 3.09–8), RISK Euroscore=5.04 (IQR 2.54–10.71) and Euroscore 2=1.58 (IQR 0.90–3.12).

### Types of surgery

Of all the MHS interventions conducted, 49.1% were heart valve surgery, 30.7% were coronary artery bypass grafting (CABG) procedures and the remaining 6.1% were other types of surgeries or mixed surgeries (valve and heart). Median extracorporeal circulation time was 127 min (range 90–167).

In this cohort, 6.5% (52/800) required one or more re-interventions and 55.4% (444/800) of those operated on required a blood transfusion during the first 24 h.

### Hospital stay

The median length of hospital stay (Table 1) was 15 days for overall stay (IQR 10–25) and 4 days (IQR 3–6) for postoperative ICU stay (IQR 8–18). In our cohort, 12.6% required more than 48 h of mechanical ventilation.

### Infections postsurgery and timing

Of the 800 patients who underwent MHS, 124 (15.5%) had one or more hospital-acquired infections during their hospital stay: 68 (54.8%) had one or more infections during their stay in the ICU (54.8%), 50 during their stay on the ward post ICU (40.3%), and 6 (4.8%) had infections in both wards.

### Types of infection

Table 2 shows the episodes of infection recorded and their etiology.

There were 29 episodes of mechanical ventilation-associated pneumonia (affecting 27 patients) leading to

**Table 1** Patient characteristics

| Patients   | Total N = 800         | WITH INFECTION N = 124 | WITHOUT INFECTION N = 676 | p       |
|--|-----------------------|------------------------|---------------------------|---------|
| Median age in years (IQR)                        | 64.0 (56.00–73.75)    | 64.0 (58.0–73.0)       | 64.0 (56.0–74.0)          | 0.893   |
| <b>Sex (%)</b>                                   |                       |                        |                           | 0.970   |
| Male   | 546 (68.3)            | 87 (70.1)              | 459 (67.8)                |         |
| Female   | 254 (31.8)            | 37 (29.8)              | 217 (32.1)                |         |
| Obesity (body mass index > 30) (%)               | 181 (22.62)           | 35 (28.22)             | 146 (21.59)               | 0.128   |
| <b>Underlying conditions (%)</b>                 |                       |                        |                           |         |
| Myocardial infarction                            | 108 (13.5)            | 20 (16.1)              | 89 (13.1)                 | 0.393   |
| Congestive heart failure                         | 181 (22.6)            | 53 (42.7)              | 128 (18.9)                | < 0.001 |
| Central nervous system disease                   | 94 (11.8)             | 19 (15.3)              | 75 (11.0)                 | 0.175   |
| Chronic obstructive pulmonary disease            | 105 (13.1)            | 24 (19.3)              | 81 (11.9)                 | 0.030   |
| Renal dysfunction                                | 54 (6.8)              | 20 (16.1)              | 34 (5.0)                  | < 0.001 |
| Diabetes mellitus                                | 199 (24.9)            | 45 (36.2)              | 154 (22.7)                | 0.002   |
| Peptic ulcer disease                             | 60 (7.5)              | 11 (8.8)               | 49 (7.2)                  | 0.577   |
| Peripheral vascular disease                      | 59 (7.4)              | 13 (10.4)              | 46 (6.8)                  | 0.188   |
| Tumor  | 73 (9.1)              | 12 (9.6)               | 61 (9.0)                  | 0.865   |
| <b>Positive asal Samples, n = 195</b>            |                       |                        |                           | 1.000   |
| Nasal-MSSA                                       | 187 (23.3)            | 29 (23.3)              | 158 (23.3)                |         |
| Nasal MRSA                                       | 8 (1.0)               | 1 (0.8)                | 7 (1.0)                   |         |
| <b>Urgent surgery (%)</b>                        | 18 (2.25)             | 7 (5.64)               | 11 (1.62)                 | 0.013   |
| Apache, mean (SD)                                | 7.49 (3.04)           | 8.7 (2.9)              | 7.2 (3.0)                 | < 0.001 |
| Charlson, mean (SD)                              | 1.56 (1.70)           | 2.4 (1.9)              | 1.4 (1.6)                 | < 0.001 |
| EuroScore, median (IQR)                          | 6.0 (3.09–8.00)       | 7.0 (5.0–9.0)          | 6.0 (3.0–8.0)             | < 0.001 |
| Risk, EuroScore, median (IQR)                    | 5.04 (2.54–10.71)     | 7.5 (3.5–15.9)         | 4.7 (2.4–9.3)             | 0.001   |
| EuroScore II, median (IQR)                       | 1.58 (0.90–3.12)      | 2.7 (1.2–7.4)          | 1.5 (0.8–2.8)             | < 0.001 |
| <b>Type of surgery (%)</b>                       |                       |                        |                           |         |
| Valve replacement                                | 393 (49.1)            | 63 (50.8)              | 330 (48.8)                | 0.697   |
| CABG   | 246 (30.7)            | 37 (29.8)              | 209 (30.9)                | 0.916   |
| Mixed (valve and CABG)                           | 49 (6.1)              | 10 (8.0)               | 39 (5.7)                  | 0.409   |
| Aortic no valve + Aortic and valve               | 39 (4.8)              | 4 (3.2)                | 35 (5.1)                  | 0.496   |
| Congenital                                       | 27 (3.3)              | 1 (0.8)                | 26 (3.8)                  | 0.104   |
| Other  | 46 (5.7)              | 8 (6.4)                | 38 (5.6)                  | 0.677   |
| <b>Surgical data</b>                             |                       |                        |                           |         |
| Median (IQR) CPBT (min)                          | 127.00 (90.00–167.00) | 135.0 (91.0–186.0)     | 125.0 (90.0–166.0)        | 0.055   |
| Median (IQR) aortic cross-clamp time (min)       | 84.00 (58.00–112.00)  | 89.0 (56.0–124.0)      | 83.0 (58.7–110.0)         | 0.568   |
| <b>Re-intervention (%)</b>                       | 52 (6.5)              | 17 (13.7)              | 35 (5.1)                  | 0.001   |
| <b>Transfusion (%)</b>                           | 444 (55.5)            | 91 (73.4)              | 353 (52.2)                | < 0.001 |
| <b>Packing (%)</b>                               | 30 (3.8)              | 17 (13.7)              | 13 (1.9)                  | < 0.001 |
| Median length of hospital stay in days (IQR)     | 15.0 (10.0–24.0)      | 32.0 (23.2–51.2)       | 14.0 (10.0–20.0)          | < 0.001 |
| Median length of ICU stay in days (IQR)          | 4.0 (3.0–6.0)         | 7.5 (5.0–16.0)         | 4.0 (2.0–6.0)             | < 0.001 |
| Median length of preoperative stay in days (IQR) | 2.0 (1.0–7.0)         | 4.0 (1.0–13.0)         | 1.5 (1.0–6.0)             | 0.001   |
| Days of MV, mean (IQR)                           | 2.6 (10.4)            | 9.7 (25.2)             | 1.3 (1.3)                 | < 0.001 |
| Patients with MV > 48 h (%)                      | 101 (12.6)            | 51 (41.1)              | 50 (7.4)                  | < 0.001 |
| Reintubation (%)                                 | 38 (4.7)              | 24 (19.3)              | 14 (2.0)                  | < 0.001 |
| DDD, mean (SD)                                   | 16.3 (31.0)           | 21.9 (37.8)            | 7.9 (14.1)                | 0.001   |
| Mortality (%)                                    | 33 (4.1)              | 17 (13.7)              | 16 (2.3)                  | < 0.001 |

IQR interquartile range, SD standard deviation, CABG coronary artery by-pass grafting, CPBT cardiopulmonary by-pass time, MV mechanical ventilation

**Table 2** Microorganisms causing nosocomial infection

| Microorganisms                          | Bacteremia<br>12 patients<br>(13 episodes) | CR-BSI 4<br>patients | VAP 27 patients<br>29 episodes (1<br>polimicrobial) | Tracheobronchitis<br>18 patients 21<br>episodes (2<br>polimicrobial) | Pneumonia not<br>associated with<br>MV 25 patients<br>26 episodes (2<br>polimicrobians) | Surgical Wound<br>37 patients<br>39 episodes<br>Superficial<br>Surgical Wound<br>24 patients 25<br>episodes (4<br>policrobians) | Mediastinitis<br>13 patients 14<br>episodes (2<br>policrobians) | Urinary Tract<br>Infection 30<br>patients 31<br>episodes (2<br>polimicrobians) | Invasive<br>aspergillosis | CDI (11<br>patients) | Covid-19 | Total      |
|---|--|----------------------|---|--|---|---|---|--|---------------------------|----------------------|----------|------------|
| <b>Gram positive</b>                    |  |                      |   |  |   |   |   |  |                           |                      |          | <b>47</b>  |
| <i>S.epidermidis/</i><br>CoNS           |  | 3                    |   |  |   | 15  | 9   |  |                           |                      |          | 27         |
| <i>Staphylococcus</i><br><i>aureus</i>  |  |                      | 2   | 1  |   | 3   | 2   |  |                           |                      |          | 8          |
| <i>Enterococcus</i><br>species          | 2  |                      |   | 1  |   | 1   |   | 2  |                           |                      |          | 6          |
| <i>Corynebacterium</i><br>spp           |  |                      |   |  |   | 1   | 1   |  |                           |                      |          | 2          |
| Others                                  | 1  |                      |   |  |   | 1   | 2   |  |                           |                      |          | 4          |
| <b>Gram negative</b>                    |  |                      |   |  |   |   |   |  |                           |                      |          | <b>105</b> |
| <i>Serratia marc-</i><br><i>escens</i>  | 3  |                      | 7   | 8  | 2   | 2   |   | 3  |                           |                      |          | 25         |
| <i>Klebsiella</i> spp.                  |  |                      |   | 2  | 3   |   |   | 7  |                           |                      |          | 12         |
| <i>Pseudomonas</i><br><i>aeruginosa</i> | 1  |                      | 4   | 1  | 1   | 3   |   | 6  |                           |                      |          | 16         |
| <i>Proteus mirabilis</i>                | 2  |                      | 2   |  | 1   |   | 1   | 9  |                           |                      |          | 15         |
| <i>Enterobacter</i><br>species          | 1  |                      | 2   | 1  | 2   |   |   | 3  |                           |                      |          | 9          |
| <i>Escherichia coli</i>                 | 3  |                      | 5   |  | 2   | 2   | 1   | 2  |                           |                      |          | 15         |
| <i>H.influenzae</i>                     |  |                      | 1   | 2  | 4   |   |   |  |                           |                      |          | 7          |
| Others                                  |  |                      | 3   | 3  |   |   |   |  |                           |                      |          | 6          |
| <b>Fungi</b>                            |  |                      |   |  |   |   |   |  |                           |                      |          | <b>3</b>   |
| <i>Candida</i> spp                      |  | 1                    |   |  |   |   |   |  |                           |                      |          | 1          |
| <i>Aspergillus</i>                      |  |                      |   |  |   |   |   |  | 2                         |                      |          | 2          |
| <b>Virus</b>                            |  |                      |   |  |   |   |   |  |                           |                      |          | <b>9</b>   |
| Covid-19                                |  |                      |   |  | 3   |   |   |  |                           |                      | 4        | 7          |
| Influenza A                             |  |                      |   |  | 2   |   |   |  |                           |                      |          | 2          |
| <b>C.difficile</b>                      |  |                      |   |  |   |   |   |  |                           | 11                   |          | <b>11</b>  |
| <b>No microorgan-</b><br><b>isms</b>    |  |                      | 5   | 4  | 8   | 1   |   |  |                           |                      |          | <b>18</b>  |
| <b>TOTAL</b>                            |  |                      |   |  |   |   |   |  |                           |                      |          | <b>193</b> |

CDI Clostridioides difficile infection

an incidence density of 13.5 episodes/1000 days of ventilation. There were also 21 episodes of tracheobronchitis during mechanical ventilation (26.2/1000 admissions). In addition, 26 episodes of pneumonia not related to mechanical ventilation (32.5/1000 admissions) were diagnosed, and these episodes occurred mostly outside the ICU. Superficial wound infection was observed in 24 patients (25 episodes). There were 14 episodes (13 patients) classified as mediastinitis (1.75%). We recorded 13 episodes of bloodstream infection, 4 related to endovascular catheters (0.5/1000 admissions), none of which were classified as postsurgical endocarditis. There were also 31 (30 patients) episodes of urinary tract infection (38.75/1000 admissions) recorded.

Eleven episodes of hospital-acquired infection (1.4%) were attributed to *Clostridioides difficile* infection (CDI).

Further infections recorded were: 1 episode of cholangitis, 2 of invasive pulmonary aspergillosis (2 patients) and 7 patients had a hospital-acquired mild COVID infection (4 with pneumonia and 3 without pneumonia).

#### Causative microorganisms

Of all infections occurring in the postoperative period after heart surgery (191 episodes, 193 microorganisms identified), 18 could not be etiologically identified. The remaining episodes (Table 2) were mainly caused by Gram-negative bacilli (105–54.4%) and Gram-positive bacteria (47–24.3%). Cytomegalovirus (CMV) reactivation occurred in 25 patients (3.1%), but as the virus was not hospital-acquired, these cases are not included in the table.

#### *S. aureus* nasal carrier status

Of the whole cohort, 195 patients were identified as nasal carriers of *S. aureus* and the remaining 605 (75.6%) returned a negative nasal PCR result for *S. aureus* on admission. *Staphylococcus aureus* infection rates in patients who were nasal carriers and non-carriers of this bacterium were respectively 3/195 (1.5%) and 5/605 (0.8%;  $p=0.411$ ).

#### Risk factors for infection

Table 1 compares the characteristics of participants with and without postoperative nosocomial infections. Those with one or more hospital-acquired infections had more frequent heart failure, renal dysfunction, a higher APACHE score and a higher Charlson's comorbidity index. These patients received more transfusions and required sternal packing more frequently. In our univariate analysis, it emerged that infected patients spent more days on mechanical ventilation, required reintubation on more occasions, consumed more defined daily doses of antibiotics, and their ICU and hospital stays were longer.

**Table 3** Multivariate analysis of risk factors for nosocomial infection in patients who underwent MHS

| Variables                             | <i>p</i>         | OR (95%CI)       |
|---------------------------------------|------------------|------------------|
| Chronic obstructive pulmonary disease | 0.133            | 1.56 (0.87–2.80) |
| Congestive heart failure              | <b>0.008</b>     | 1.88 (1.18–3.02) |
| Renal dysfunction                     | <b>0.028</b>     | 2.13 (1.08–4.20) |
| Diabetes                              | 0.581            | 1.14 (0.70–1.86) |
| Preoperative length of stay > 3 days  | <b>0.063</b>     | 1.51 (0.97–2.35) |
| Transfusion                           | 0.205            | 1.37 (0.84–2.24) |
| Emergency surgery                     | 0.704            | 1.26 (0.38–4.18) |
| Inotropic support after surgery       | 0.414            | 1.55 (0.54–4.50) |
| Mechanical ventilation > 48 hours     | <b>&lt;0.001</b> | 4.19 (2.40–7.33) |
| Re-intubation                         | <b>0.009</b>     | 3.08 (1.32–7.15) |
| Re-intervention                       | 0.943            | 1.03 (0.48–2.20) |

**Table 4** Logistic regression model coefficients converted to calculate a simplified score

| Variables                            | <i>p</i>         | OR (95%CI)       | Score |
|--------------------------------------|------------------|------------------|-------|
| Congestive heart failure             | <b>&lt;0.001</b> | 2.09 (1.33–3.30) | 1     |
| Renal dysfunction                    | <b>0.001</b>     | 2.27 (1.15–4.45) | 1     |
| Preoperative length of stay > 3 days | <b>0.040</b>     | 1.56 (1.02–2.40) | 1     |
| Mechanical ventilation > 48 hours    | <b>&lt;0.001</b> | 4.84 (2.84–8.25) | 3     |
| Re-intubation                        | <b>0.005</b>     | 3.29 (1.44–7.51) | 2     |

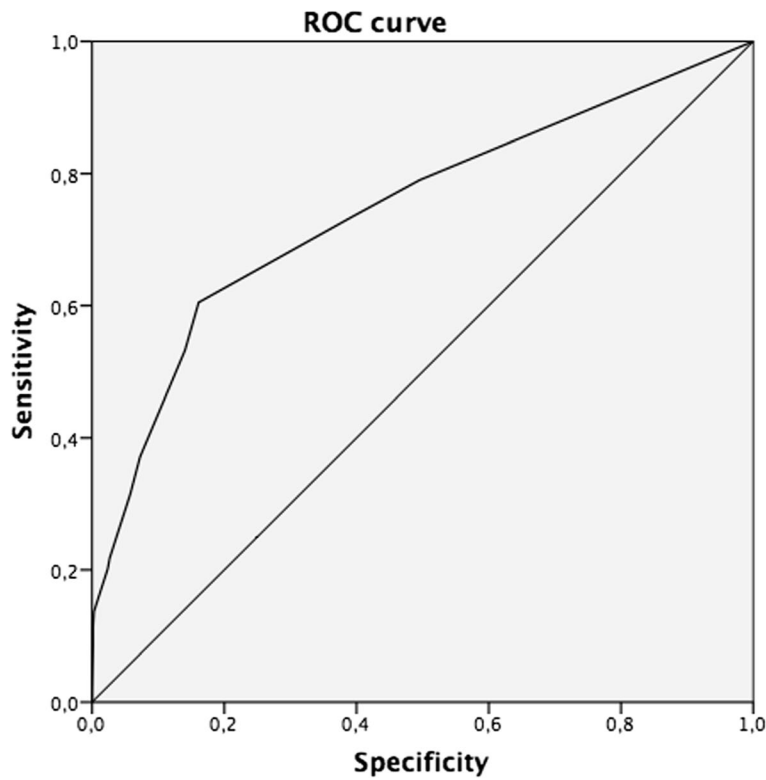
Multivariate analysis identified several independent variables associated with hospital-acquired infection: congestive heart failure, renal dysfunction, preoperative hospital stay > 3 days, mechanical ventilation > 48 h and reintubation (Table 3).

Table 4 shows the logistic regression model of coefficients converted into a simplified score. One of our ROC curves (Fig. 1) yielded a specific value of 7 as the cutoff with an AUC = 0.745 (CI 95%).

Our Kaplan-Meier assessment of infection risk according to timing of the first episode of hospital-acquired infection is depicted in Fig. 2.

#### Prognosis

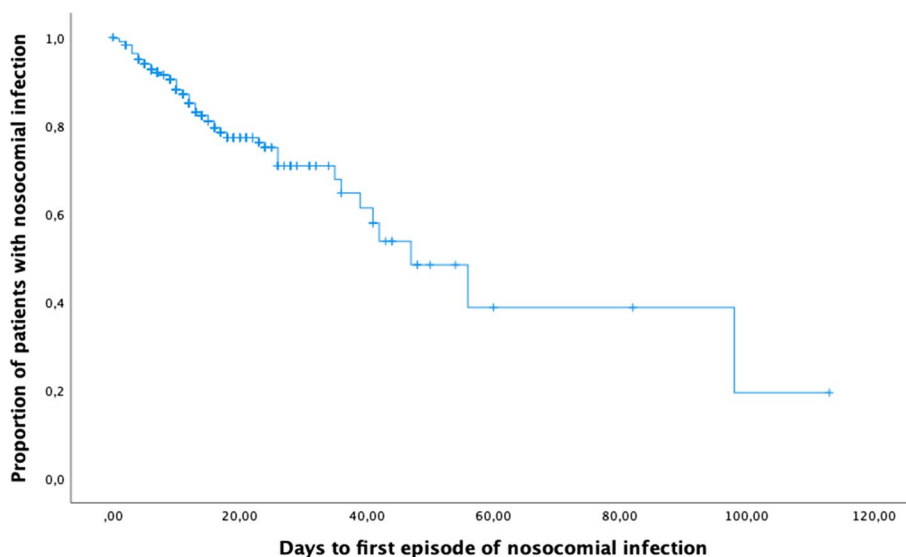
Overall mortality in all 800 surgical patients was 33 (4.1%). Of these, 27 (81.8%) patients died during ICU stay and the remaining 6 (18.2%) patients during their postoperative stay in general wards after ICU discharge. Of these 33 deaths, 9 (27.2%) were primarily due to infection. Overall mortality was higher (13.7%) in patients who developed infections than in those who did not (2.3%).



| cut-off point |   | Sensitivity (CI95%)     | Specificity (CI95%)     | PPV(CI95%)              | NPV(CI95%)              | Youden      | p_ex |
|---------------|---|-------------------------|-------------------------|-------------------------|-------------------------|-------------|------|
| >= 0.000      | 1 | 79.0 (70.8-85.8)        | 50.4 (46.6-54.3)        | 22.6 (18.8-26.9)        | 92.9 (89.8-95.3)        | 29.5        |      |
| >= 0.000      | 2 | 62.1 (52.9-70.7)        | 83.7 (80.7-86.4)        | 41.2 (34.0-48.6)        | 92.3 (89.9-94.3)        | 45.8        |      |
| >= 0.000      | 3 | 43.5 (34.7-52.7)        | 91.1 (88.7-93.2)        | 47.4 (37.9-56.9)        | 89.8 (87.3-92.0)        | 34.7        |      |
| >= 0.000      | 4 | 34.7 (26.4-43.7)        | 93.9 (91.9-95.6)        | 51.2 (40.0-62.3)        | 88.7 (86.1-90.9)        | 28.6        |      |
| >= 0.000      | 5 | <b>25.8 (18.4-34.4)</b> | <b>97.2 (95.6-98.3)</b> | <b>62.7 (48.1-75.9)</b> | <b>87.7 (85.1-90.0)</b> | <b>23.0</b> |      |
| >= 0.000      | 6 | 15.3 ( 9.5-22.9)        | 99.0 (97.9-99.6)        | 73.1 (52.2-88.4)        | 86.4 (83.8-88.8)        | 14.3        |      |
| >= 0.000      | 7 | 9.7 ( 5.1-16.3)         | 99.9 (99.2-100.0)       | 92.3 (64.0-99.8)        | 85.8 (83.1-88.1)        | 9.5         |      |
| >= 0.024      | 8 | 1.6 ( 0.2- 5.7)         | 100.0 (99.5-100.0)      | 100.0 (15.8-100)        | 84.7 (82.0-87.1)        | 1.6         |      |

PPV: positive predictive value; PNV: negative predictive value

Fig. 1 ROC curve analysis and a cutoff value searched for to determine the accuracy and optimal threshold of high-risk patients for infection



**Fig. 2** Kaplan-Meier analysis of the risk of infection according to the onset time of the first episode of nosocomial infection

## Discussion

Our work shows that when all infections recorded after heart surgery up until hospital discharge are considered, figures are higher at 15.5% than those commonly reported in the literature. It also reveals that MHS continues to give rise to a high incidence of infection and a not insignificant mortality rate. This study also identifies a need for global figures that offer a real perspective of the risk of infection.

Following MHS, infection risk estimates are often biased as different reports usually consider only certain factors such as a given period of postoperative stay, type of surgery, type of infection or even certain groups of causative microorganisms. For instance, the reported incidence of surgical wound infection ranges from 2.6 to 5.5% and is higher in heart transplant recipients [5, 23–25].

In another study, the incidence of pneumonia after heart surgery was estimated at 3.5% of 7439 consecutive patients, including 120 (47%) cases of non-VAP episodes [26]. Eleven studies on ventilator associated pneumonia (VAP) after MHS included in a meta-analysis reported a figure of 21 episodes/1000 ventilator-days. Prevalence was 6.4% of all patients and 35.2% of patients who were on mechanical ventilation for more than 48 h [27]. According to more recent data, the incidence density was of 17.7 episodes per 1000 ventilator-days [28]. Our findings show that if infections are prospectively recorded without any bias, the incidence of infection after this “clean surgery” procedure remains high.

Numerically, infections occur almost as frequently in the postoperative ICU period as in the time spent in

general wards, although it is true that the severity and risk of death of the infections acquired are higher in the former [29, 30].

In our analysis of causative microorganisms and another study [31], Gram-negative bacteria emerged as predominant, representing 54% of all causes of infection. However, in a study focusing on local infectious complications of heart surgery the predominance of Gram-positive cocci was observed [32]. Fungal infections following MHS are much less common.

Our data indicate the continued need for *S. aureus* colonization screening in patients scheduled to undergo MHS.

It is well known that VAP, SSI and catheter-related bloodstream infections are major concerns following MHS [30, 33]. However, a more detailed look at our findings reveals that almost half of all post-MHS episodes of pneumonia cannot be ascribed to mechanical ventilation but rather they occur after extubation and transfer of the patients to a general ward. The numerous episodes of urinary tract infection detected in patients requiring bladder catheterization after surgery is also striking. The need for catheterization should be re-examined by means of a daily check list to reduce this risk factor.

We feel that comprehensive programs are needed in which the same team controlling infection in intensive care continues to follow these patients until they are discharged from hospital. These programs should target zero tolerance to these infections with education and other types of interventions.

The risk factors for infection in our patient subset were relatively well defined as in other studies and include



surgery duration, heart failure, need for continuous veno-venous hemofiltration, longer mechanical ventilation, reintubation and tracheostomy, and delayed closure of the sternal wound [2, 4, 30, 31]. The model constructed and a cutoff value could be used in future investigations to implement preventive measures.

As we have previously observed, a very clear marker of these infections was the need for whatever reason to remain in the ICU for more than 72 hours after surgery. It is clear that this subgroup of patients requires special attention and interventions to prevent and lower the incidence of these infections [1, 22, 34, 35]. We are not aware, however, of programs that have specifically managed to reduce mortality due to infections attributed to a lengthened ICU stay.

Our mortality differences between infected and uninfected patients (23% vs. 2%) resemble those reported in another Spanish study in which rates were 18% versus 5% respectively [30].

The economic burden of hospital-acquired infection is another factor to consider if only to raise awareness in hospital managers so that control measures are justified. In Japan, the cost of VAP alone has been estimated at £15,124 compared to £6295 for non-ventilator-associated pneumonia. Infected patients were reported by the authors of this last study to cost 5 times more, and hospital stay was lengthened  $9.3 \pm 2.6$  days [36].

The main limitation of our work was that it was a single-center study so its results may not be necessarily transferable to other institutions. Nevertheless, our main message remains that postoperative infection assessment after MHS should not discriminate between types of patients, types of infections, or times at which infection occurs. We should also mention that while our study period coincided with that of the COVID-19 pandemic, we found no difference in infection rates between the two periods.

## Conclusion

Most studies designed to analyze infections occurring after MHS fail to consider certain types of infection, types of patients, or times at which infection occurs. Accordingly, our study reveals a higher incidence of infections after MHS than generally reported in the literature. This information confirms that infections are still frequent and severe, and identifies an urgent need for standardized protocols so that infection rates can be effectively compared across different centers.

## Abbreviations

|     |                        |
|-----|------------------------|
| ICU | Intensive care unit    |
| MHS | Major heart surgery    |
| MV  | Mechanical ventilation |

|        |  |
|--------|--|
| VAP    | Ventilator-associated pneumonia                    |
| SDD    | Selective digestive decontamination                |
| SD     | Standard deviation                                 |
| HAP    | Hospital-acquired pneumonia                        |
| VAP    | Ventilator-associated pneumonia                    |
| CR-BSI | Bacteremia, catheter-related bloodstream infection |
| SSI    | Surgical site infection                            |
| MD     | Mediastinitis                                      |
| UTI    | Urinary tract infection                            |
| ROC    | Receiver Operating Characteristic                  |
| AUC    | Area under the curve                               |

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## Availability of data and materials

All data generated or analyzed during this study are included in this article.

## Declarations

### Ethics approval and consent to participate

The Ethics Committee of our institution (Hospital Gregorio Marañón) approved the study (code MICRO.HGUGM.2018–008) and all patients gave their written informed consent before inclusion. All procedures were performed in accordance with the relevant guidelines and regulations or in accordance with the principles of the Declaration of Helsinki.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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