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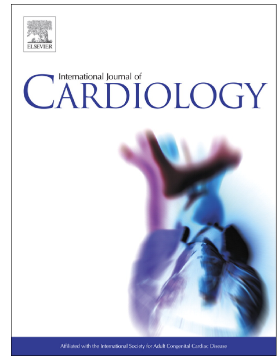
Effect of the type of surgical indication on mortality in patients with infective endocarditis who are rejected for surgical intervention



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Antonio Ramos-Martínez: aramos220@gmail.com. Unidad de Enfermedades Infecciosas. Servicio de Medicina Interna. Universitario Puerta de Hierro. Majadahonda. Madrid.

Jorge Calderón-Parra: jorge050390@gmail.com. Servicio de Medicina Interna. Hospital Universitario Puerta de Hierro. Majadahonda. Madrid.

José Mª Miró Meda: jmmiro@clinic.ub.es. Servicio de Enfermedades Infecciosas, Hospital Clinic-IDIBAPS. Universidad de Barcelona, Barcelona.

Patricia Muñoz García: pmuñoz@micro.hggm.es. Servicio de Microbiología Clínica y Enfermedades Infecciosas, Hospital General Universitario Gregorio Marañón, Madrid. Instituto de Investigación Sanitaria Gregorio Marañón. CIBER Enfermedades Respiratorias-CIBERES (CB06/06/0058). Facultad de Medicina, Universidad Complutense de Madrid.

Hugo Rodríguez Abella: rhugorodriguez@yahoo.es. Servicio de Cirugía Cardiaca, Hospital General Universitario Gregorio Marañón, Madrid.

Maricela Valerio Minero: mavami_valerio@yahoo.com.mx. Servicio de Microbiología Clínica y Enfermedades Infecciosas, Hospital General Universitario Gregorio Marañón, Madrid. Instituto de Investigación Sanitaria Gregorio Marañón.

Arístides de Alarcón González: aa2406ge@yahoo.es. Clinical Unit of Infectious Diseases, Microbiology and Preventive Medicine Infectious Diseases Research Group. Institute of Biomedicine of Seville (IBIS), University of Seville/CSIC/University Virgen del Rocío and Virgen Macarena. Seville.

Rafael Luque Márquez: rluque@luque.jazztel.es. Clinical Unit of Infectious Diseases, Microbiology and Preventive Medicine Infectious Diseases Research Group. Institute of Biomedicine of Seville (IBIS), University of Seville/CSIC/University Virgen del Rocío and Virgen Macarena. Seville.

Juan Ambrosioni: ambrosioni@clinic.ub.es. Servicio de Enfermedades Infecciosas, Hospital Clinic-IDIBAPS. Universidad de Barcelona, Barcelona.

Mª Carmen Fariñas Álvarez: mcfarinas@humv.es. Infectious Diseases Unit. Hospital Universitario Marqués de Valdecilla. University of Cantabria, Santander.

Miguel Ángel Goenaga Sánchez: goenagasanchez@gmail.com. Servicio de Enfermedades Infecciosas. Hospital Universitario Donosti. San Sebastián.

José Antonio Oteo Revuelta: jaoteo@riojasalud.es. Servicio de Enfermedades Infecciosas, Hospital San Pedro. Centro de Investigación Biomédica de La Rioja (CIBIR)

Francisco Javier Martínez Marcos: fcojmtz@telefonica.net. Unidad de Gestión Clínica de Enfermedades Infecciosas. Complejo Hospitalario Universitario de Huelva. Huelva.

David Vinuesa García: vinudav@yahoo.es. Servicio de Medicina Interna y Enfermedades Infecciosas. Hospital Clínico San Cecilio. Granada.

Fernando Domínguez: fdominguezrodriguez@gmail.com. Servicio de Cardiología. Hospital Universitario Puerta de Hierro. Majadahonda. Madrid.

On behalf of the Spanish Collaboration on Endocarditis – Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España (GAMES) (see Appendix)

Author for correspondence:
Antonio Ramos. Internal Medicine Department. Hospital Universitario Puerta de Hierro-Majadahonda. C/ Maestro Rodrigo 2. Majadahonda. Madrid. 28222. Spain. Tel: +34 638 211 120. Fax +34 91191 6807. Email: aramos220@gmail.com

Abstract

Aim: To evaluate the effect of the type of surgical indication on mortality in infective endocarditis (IE) patients who are rejected for surgery.

Methods and results: From January 2008 to December 2016, 2714 patients with definite left-sided IE were attended in the participating hospitals. One thousand six hundred and fifty-three patients (60.9%) presented surgical indications. Five hundred and thirty-eight patients (32.5%) presented surgical indications but received medical treatment alone. The indications for surgery in these patients were uncontrolled infection (366 patients, 68 %), heart failure (168 patients, 31.3%) and prevention of embolism (148 patients, 27.6%). One hundred and thirty patients (24.2%) presented more than one indication. The mortality during hospital admission was 60% (323 patients). The in-hospital mortality of patients whose indication for surgery was heart failure, uncontrolled infection or risk of embolism was 75.6%, 61.4% and 54.7%, respectively ($p<0.001$). Surgical indications due to heart failure (OR: 3.24; CI 95%: 1.99-5.9) or uncontrolled infection (OR: 1.83; CI 95%: 1.04-3.18) were independently associated with a fatal outcome during hospital admission. Mortality during the first year was 75.4%. The mortality during the first year in patients whose indication for surgery was heart failure, uncontrolled infection or risk of embolism was 85.9%, 76.7% and 72.7%, respectively ($p=0.016$). Surgical indication due to heart failure (OR: 3.03; CI 95%: 1.53-5.98) were independently associated with fatal outcome during the first year.

Conclusions. The type of surgical indication is associated with mortality in IE patients who are rejected for surgical intervention.

Keywords: Endocarditis; Mortality, Heart Failure, Embolism, Bacteremia

Introduction

Infective endocarditis (IE) is a major health problem characterized by increasing incidence and high mortality [1]. Despite improvements in medical and surgical treatment, patient prognosis as a whole has not substantially changed which could be related to increases in patient age and hospital-acquired cases [2].

Although antibiotic treatment remains the mainstay of IE therapy, around half of the patients should undergo surgery, principally due to heart failure, uncontrolled infection or prevention of embolism [1,3,4]. Despite the benefits of surgical treatment being firmly established in cases with a clear indication, surgery is not performed in a high percentage and an unfavorable prognosis ensues [5].

It should be noted that the potential differences in mortality in patients with surgical indications but who are not subsequently submitted to the same have not been sufficiently studied. Although the great negative impact that congestive heart failure has on prognosis in IE patients who do not undergo surgery has been firmly established, this effect may not be so marked when the surgical indication is to prevent episodes of embolism [6]. According to certain studies, early cardiac surgery may reduce mortality in patients with large vegetations or cardio-embolic strokes [4]. On the other hand, a recent meta-analysis, which studied IE patients with complications due to ischemic stroke, showed no benefit in 1-year survival in patients who underwent early surgery [7]. In addition, certain current guidelines present some discrepancies with respect to surgical indications for preventing embolism [4]. Because of the above-mentioned findings, we proposed to analyze whether the type of surgical indication had an influence on mortality in IE patients who did not undergo surgical treatment.

Patients and Methods

From January 2008 to December 2016, 3,524 consecutive patients with definite or possible IE, according to the modified Duke criteria [8], were prospectively included in the "Spanish Collaboration on Endocarditis - Grupo de Apoyo al Manejo de la Endocarditis infecciosa en España (GAMES)" registry maintained by 27 Spanish hospitals. Right-sided IE cases and patients with cardiac device infection were excluded from this study unless there was concomitant left-side infection. Multidisciplinary teams completed standardized case report forms with IE episode and follow-up data that included clinical, microbiological and echocardiographic sections [9,10]. The study was approved by regional and local ethics committees and all patients gave their informed consent. Patients were included if they presented a surgical indication during the admission that endocarditis was diagnosed and the surgical team or the patient rejected surgery.

Definitions

Active IE was defined as endocarditis with at least one of the following: positive blood cultures, fever, leukocytosis, raised inflammation markers or current antibiotic treatment [10]. Microbiological diagnoses were determined by blood, valve culture and/or molecular techniques [10]. Transthoracic (TTE) and transesophageal echocardiography (TEE) were performed on patients with clinical or microbiological suspicion of IE according to European guidelines [4]. The same protocol was implemented for the diagnosis of valve dysfunction and intracardiac complications: abscess, vegetation, pseudoaneurysm and fistula [11]. We considered hospital-acquired IE as either IE manifesting >48 hours after admission to the hospital or IE acquired in association with a significant invasive procedure performed within 6 months prior to diagnosis. The EuroScore and LogEuroScore were used to assess surgical risk [12]. All the necessary variables were collected to calculate the Charlson Comorbidity Index [13]. For better interpretation of the results, surgical indications were grouped according to the criteria and definitions of the European Guidelines (4). Consequently, the surgical indications were: 1) Heart failure manifested as Grade NYHA IV or III accompanied by valve regurgitation or severe stenosis or dehiscence of the prosthesis, 2) Prevention of embolism was considered when patients presented recurrent embolism and with a vegetation >10mm, vegetation >10mm together with regurgitation or severe aortic or mitral stenosis or had a vegetation >30mm, and 3) Uncontrolled infection was defined as the presence of pseudoaneurysm, abscess, fistula or vegetation that clearly grew in one week with respect to the same type of TTE or TEE, new heart block of any degree during the episode of endocarditis, persistent bacteremia (≥7 days despite an appropriate antibiotic regimen), fever persistent for more than 7 days, or aggressive bacillus: fungal, multiresistant organisms (e.g. prosthetic valve infection by methicillin-resistant *S. aureus* or vancomycin-resistant enterococci) as well as endocarditis caused by any type of non-HACEK gram-negative bacteria [4]. The timing of surgical intervention was defined as the median number of days between hospital admission and surgery.

Hospital mortality was defined as death, regardless of cause, that occurred during the hospital admission in which cardiac surgery was indicated. The Cockcroft-Gault equation was used to calculate creatinine clearance [14]. Pre-episode renal insufficiency was defined as plasma creatinine over 1.4 mg/dl. New or worsening renal insufficiency during the IE episode was defined as exacerbation of baseline creatinine clearance or plasma creatinine by at least 25% or creatinine levels over 1.4 mg/dl when a previous analysis had been normal. Endocarditis recurrence was defined as a new episode of endocarditis during the first year following diagnosis.

Patients

Data from patients with IE were analyzed, which included clinical manifestations at IE presentation, the pathogens identified, therapy used as well as morbidity and mortality during hospitalization and during the first year after hospitalization. Indications for surgery were evaluated by a multidisciplinary team taking into account, not only the immediate surgical risk, but also the chances of long-term survival. Patients not initially considered for surgery that subsequently presented surgical indications were included in the "surgical group" in the same way as those who were candidates for surgery at hospital admission. No data was collected regarding the number of days that patients spent in the hospital prior to the surgical indication being established. The reasons for not undergoing surgery were assessed throughout the hospitalization period, in some cases, these reasons were apparent on admission, but in others they arose during the period of hospitalization, and even up to the moment that the surgery was programmed. Follow-up information was obtained via programmed medical reviews, by telephone or through written or electronic correspondence with each patient or their primary-care physician. Patients were treated according to European endocarditis guidelines [4].

Statistical analysis

Quantitative variables were reported as median and interquartile range (IQR), qualitative variables were reported as numbers and percentages. Continuous variables were compared using Student's t-test, and categorical variables were compared using the chi-square test or Fisher's exact test when appropriate. Adjusted odds ratios (ORs) were computed using logistic regression analysis. The variables related to patient prognoses could have been present at the time of hospital admittance or could have developed during the period of hospitalization. Stepwise logistic regression analysis was performed which mandatorily included surgical indication (heart failure, uncontrolled infection and prevention of embolism). For inclusion in the multivariate analysis, variables had to return a p value <0.1 and to also be considered clinically relevant. In order to avoid confounding variables, those that were very closely associated with death, such as septic shock, or consisted of a group of variables that were not strictly related to the pathogenesis or prognosis of endocarditis, were excluded from the analysis. It was considered appropriate to introduce one variable or factor for every 10 events in the multivariate analysis. Cox regression models for first-year survival according to surgical indication are shown in Figure 1 – 2. All statistical analyses were performed using SPSS software version 18 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 2,714 patients with definite left-sided infectious endocarditis were identified during the study period. One thousand six hundred and fifty three patients (60.9%) presented surgical indications. Among them, one thousand one hundred and fifteen (67.5%) underwent surgery during hospital admission. On the contrary, 538 patients (32.5%) presented surgical indication but received medical treatment alone. The indications for surgery in these patients were; uncontrolled infection (366 patients, 68 %), heart failure (168 patients 31.3%) and prevention of embolism (148 patients 27.6%, Table 1). One hundred and thirty patients (24.2%) presented more than one indication. The median time (and interquartile range) from hospital admission to surgery was 17 days (6 – 37 days). These values were 14 days (6 – 32 days) when the indication was heart failure, 23 days (9 – 44 days) in patients with uncontrolled infection, and 11 days (4 – 29 days) in patients with a high risk of embolism ($p<0.001$ for the comparison between the three groups). Patients who did not undergo surgery more frequently presented advanced age, comorbidity, hospital acquisition, prosthetic endocarditis, staphylococcal infection, central nervous system (CNS) vascular events and septic shock (Table 1). The reasons for not undergoing surgery were; hemodynamic instability (112 patients, 20.8%), neurological complications (110 patients, 20.4%), notable surgical difficulty (67 patients, 12.4 %), other medical causes (113 patients, 21%), patient refusal (76 patients, 14.1%) and death before surgery (60 patients, 11.2%).

In-hospital mortality was 60% (323 patients). The in-hospital mortality in patients whose indications for surgery were heart failure, uncontrolled infection or risk of embolism, was 75.6%, 61.4% and 54.7%, respectively ($p<0.001$, Table 2). The cause of death during admission was heart failure in 178 patients (55.1%), infection in 98 patients (30.3%), CNS events in 46 patients (14.2%) and other causes in 20 patients (6.7%). Nineteen patients (5.9%) presented more than one cause. In total, 359 patients died during the first year (75.4%). The first-year mortality in patients whose indication for surgery were heart failure, uncontrolled infection or risk of embolism, was 85.9%, 76.7, 72.7%, respectively ($p=0.016$). The clinical characteristics and the evolution of patients related to mortality one year after diagnosis are shown in Table 3. A Cox regression model for one-year-survival according to surgical indication and treatment received is shown in Figures 1-5. Thirty-six patients died during the first year (after hospital discharge). Of these, 18 patients (50%) died due to heart failure, 3 patients (8.3%) due to CNS events and 2 patients (5.6%) due to infection. Seven patients (19.4%) presented other causes and in 6 patients (15.4%) the cause was unknown.

Age >70 years, diabetes, neoplasia, previous renal insufficiency, age-adjusted Charlson index, hospital-acquired endocarditis, IE due to *S. aureus,* IE due to *Streptococcus* spp., renal function impairment and indication for surgery were included in the multivariate analysis (Table 2). Diabetes (OR: 1.88; CI 95%: 1.19-2.97), neoplasia (OR: 1.77; CI 95%: 1.02-3.07), renal function impairment (OR: 2.69; CI 95%: 1.77-4.07), IE due to *S. aureus* (OR: 1.61; CI 95%: 1.01-2.57), surgical indication due to heart failure (OR: 3.24; CI 95%: 1.99-5.9) and surgical indication due to uncontrolled infection (OR: 1.83; CI 95%: 1.04-3.18) were independently associated with a fatal outcome during hospital admission.

Age >70 years, neoplasia, previous renal insufficiency, age-adjusted Charlson index, hospital-acquired endocarditis, IE due to *S. aureus,* renal function impairment and surgery indication were included in the multivariate analysis (Table 3). Renal function impairment (OR: 2.35; CI 95%: 1.43-3.87) and surgical indication due to heart failure (OR: 3.03; CI 95%: 1.53-5.98) were independently associated with a fatal outcome during the first year following diagnosis.

Discussion

This study analyzed the influence of the type of surgical indication on mortality in IE patients who did not undergo surgery despite such an intervention being indicated. The main result was that prevention of embolism, as the main reason for surgery, was less strongly associated with in-hospital mortality than heart failure or uncontrolled infection.

Better knowledge concerning the indication and optimal timing of surgery, which is recommended in around 40%-60% of cases, has led to improved patient survival [5]. Despite this, the interaction between surgical indication, clinical severity, technical complexity of the surgery and the predictable prognosis is still a very complicated issue that can finally determine whether or not the patient receives surgical treatment [2,3 ,15,16].

It should be noted that surgery is not performed in 20%-40% of cases and is associated with notable adverse prognoses [5,15,16]. This may be related to underuse of scoring systems specifically designed for IE patients [19,17,18], lack of agreement between the attending team's decision and current guidelines [16] or, more commonly, presumed high surgical risk as observed in other series [2,5,15]. To mitigate this problem, the surgical team should attempt to make decisions about treatment before IE complications prevent the patient from being considered suitable for surgical treatment [19].

In this study, mortality in patients in whom surgery was indicated but not performed was 60% during hospitalization and 75% during the first year, which is considerable but similar to other reported series [5,15]. The differences in mortality between patients who do or do not undergo surgery are attributable, not only to conservative treatment, but also to patient characteristics that may differ significantly between the two groups. As in other studies, advanced age, underlying comorbidities, immunosuppression, prosthetic valve endocarditis, CNS vascular events and septic shock were more commonly presented by patients who were denied surgical treatment [20]. One task that remains pending is to improve the selection of patients who present some risk factors for a poor prognosis but in whom surgery could still improve their vital prognosis [3,15].

In our series there was a marked difference in patients' median age in relation to undergoing or not undergoing surgery (Table 1). It should be highlighted that although patients aged >65 years usually present noteworthy comorbidity and have a poor overall outcome, age alone should not preclude surgery [3,15,21,22]. Since surgical treatment is associated with a reasonably good outcome in these patients [3,15,22], suitable scoring systems should be used when considering comorbidities and other geriatric features for prognosis evaluation prior to performing cardiac surgery [15,23].

Although the identification of specific prognostic factors in patients with IE has been the subject of extensive study, none have focused on patients who are not considered suitable for surgical treatment [9,17,18]. The present study is, to our knowledge, the first to specifically analyze differences in mortality according to the indication for surgery in patients who are not submitted to surgery.

Congestive heart failure, mainly due to valve insufficiency, is the most important predictor of in-hospital and long-term mortality [24]. In a propensity-matched study, patients with moderate-to-severe congestive heart failure showed the greatest reduction in mortality with surgery [14% vs 51%] [25]. Our study demonstrated that patients who did not undergo surgery when heart failure was the indication presented a significantly higher short- and long-term mortality. Hence, as far as possible, it is necessary to avoid delaying the recognition of heart failure so as to prevent the development of subsequent serious hemodynamic compromise [19].

Uncontrolled infection was the main surgical indication, which was a definite difference in comparison with other similar studies [3,5,16,25]. This result could be related to the high percentage of prosthetic-valve IE compared to other series [3,16]. One previous study observed that the most common indications for surgery in prosthetic-valve IE were, in descending order, uncontrolled infection [56%], embolization risk [30%] and heart failure [19%] [26]. In addition, in contrast to other studies, a high proportion of IE cases were due to *S. aureus* [29.8%] [5,15] that, in addition, underwent surgery less than expected despite the fact that intervention usually improves the prognosis [25, 45]. Satisfactory identification of patients with IE due to *S. aureus* who do not show a response to antibiotic treatment could help prevent the development of a septic state, which was the main reason for these patients not undergoing surgery [15,28].

Although systemic embolic events may arise at any moment during the clinical evolution of the infection, most vascular complications occur before admission or within the first two weeks of antibiotic treatment [29,30]. This means that surgical treatment to prevent embolism should be carried out early. However, a decisive study compared early surgery with conventional treatment in patients with IE and large vegetations and did not demonstrate any significant reduction in mortality [as an isolated variable] [31]. The lower mortality in cases not undergoing surgery when the indication was embolic risk may be related to the type and location of eventual vascular phenomena, such as silent CNS embolism, that would not trigger fatal complications [32].

Our study also illustrates that the "prevention of embolism" indication is not as relevant as heart failure [and uncontrolled infection] for predicting mortality in patients who are refused surgical treatment. This should not mean that the intervention should not be performed in patients who meet the criteria for embolism prevention included in clinical guidelines; on the contrary, it only suggests that the better short- and long-term prognosis, compared to other surgical indications of conservative treatment in these patients, should be taken into account when a decision not to intervene is under consideration by the surgical team and/or the patient.

Some limitations of this study should be noted. Since current European guidelines criteria were followed, very different patients were grouped within the same category. Thus, with respect to uncontrolled infection, cases of persistent bacteremia were included in the same group as those with local progression of the infection [i.e. perivalvular abscess or pseudoaneurysm]. Similarly, the severity of patients with a vegetation greater than 10 mm and severe valvular insufficiency could mainly be due to the later development of heart failure than to the risk of embolism [the category in which they were finally included]. Moreover, the high proportion of patients with more than one surgical indication limits the power of the study to determine the effects of this variable on patient prognosis. Another limitation is that data concerning the number of patients who developed surgical indications during hospitalization, which were not present on admission, was not collected. In addition, most of the institutions participating in the GAMES registry are tertiary university hospitals that receive a substantial number of patients referred from other centers [most of which do not have facilities for cardiac surgery], which could represent a selection bias. Similarly, a possible cluster effect cannot be ruled out. However, we do not believe that the heterogeneity between centers is sufficient to have a significant influence on our results.

In summary, our study demonstrates that the type of surgical indication should be taken into consideration when appraising the prognosis in IE patient who are rejected for surgical intervention.

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APPENDIX

Members of GAMES: Hospital Costa del Sol, (Marbella): Fernando Fernández Sánchez, Mariam Noureddine, Gabriel Rosas, Javier de la Torre Lima; **Hospital Universitario de Cruces**, (Bilbao): José Aramendi, María José Blanco, Roberto Blanco, María Victoria Boado, Marta Campaña Lázaro, Alejandro Crespo, Josune Goikoetxea, José Ramón Iruretagoyena, Josu Irurzun Zuazabal, Leire López-Soria, Miguel Montejo, Javier Nieto, David Rodrigo, David Rodríguez, Regino Rodríguez, Yolanda Vitoria, Roberto Voces; **Hospital Universitario Virgen de la Victoria**, (Málaga): Mª Victoria García López, Radka Ivanova Georgieva, Guillermo Ojeda, Isabel Rodríguez Bailón, Josefa Ruiz Morales; **Hospital Universitario Donostia-Policlínica Gipuzkoa**, (San Sebastián): Ana María Cuende, Tomás Echeverría, Ana Fuerte, Eduardo Gaminde, Miguel Ángel Goenaga, Pedro Idígoras, José Antonio Iribarren, Alberto Izaguirre Yarza, Xabier Kortajarena Urkola, Carlos Reviejo; **Hospital General Universitario de Alicante**, (Alicante): Rafael Carrasco, Vicente Climent, Patricio Llamas, Esperanza Merino, Joaquín Plazas, Sergio Reus; **Complejo Hospitalario Universitario A Coruña**, (A Coruña): Nemesio Álvarez, José María Bravo-Ferrer, Laura Castelo, José Cuenca, Pedro Llinares, Enrique Miguez Rey, María Rodríguez Mayo, Efrén Sánchez, Dolores Sousa Regueiro; **Complejo Hospitalario Universitario de Huelva**, (Huelva): Francisco Javier Martínez; **Hospital Universitario de Canarias**, (Canarias): Mª del Mar Alonso, Beatriz Castro, Dácil García Rosado, Mª del Carmen Durán, Mª Antonia Miguel Gómez, Juan Lacalzada, Ibrahim Nassar; **Hospital Regional Universitario de Málaga**, (Málaga): Antonio Plata Ciezar, José Mª Reguera Iglesias; **Hospital Universitario Central Asturias**, (Oviedo): Víctor Asensi Álvarez, Carlos Costas, Jesús de la Hera, Jonnathan Fernández Suárez, Lisardo Iglesias Fraile, Víctor León Arguero, José López Menéndez, Pilar Mencia Bajo, Carlos Morales, Alfonso Moreno Torrico, Carmen Palomo, Begoña Paya Martínez, Ángeles Rodríguez Esteban, Raquel Rodríguez García, Mauricio Telenti Asensio; **Hospital Clínic-IDIBAPS, Universidad de Barcelona**, (Barcelona): Manuel Almela, Juan Ambrosioni, Manuel Azqueta, Mercè Brunet, Marta Bodro, Ramón Cartañá, Carlos Falces, Guillermina Fita, David Fuster, Cristina García de la Mària, Marta Hernández-Meneses, Jaume Llopis Pérez, Francesc Marco, José M. Miró, Asunción Moreno, David Nicolás, Salvador Ninot, Eduardo Quintana, Carlos Paré, Daniel Pereda, Juan M. Pericás, José L. Pomar, José Ramírez, Irene Rovira, Elena Sandoval, Marta Sitges, Dolors Soy, Adrián Téllez, José M. Tolosana, Bárbara Vidal, Jordi Vila; **Hospital General Universitario Gregorio Marañón**, (Madrid): Iván Adán, Javier Bermejo, Emilio Bouza, Daniel Celemín, Gregorio Cuerpo Caballero, Antonia Delgado Montero, Ana Fernández Cruz, Ana García Mansilla, Mª Eugenia García Leoni, Víctor González Ramallo, Martha Kestler Hernández, Amaia Mari Hualde, Mercedes Marín, Manuel Martínez-Sellés, Mª Cruz Menárguez, Patricia Muñoz, Cristina Rincón, Hugo Rodríguez-Abella, Marta Rodríguez-Créixems, Blanca Pinilla, Ángel Pinto, Maricela Valerio, Pilar Vázquez, Eduardo Verde Moreno; **Hospital Universitario La Paz**, (Madrid): Isabel Antorrena, Belén Loeches, Alejandro Martín Quirós, Mar Moreno, Ulises Ramírez, Verónica Rial Bastón, María Romero, Araceli Saldaña; **Hospital Universitario Marqués de Valdecilla**, (Santander): Jesús Agüero Balbín, Carlos Armiñanzas Castillo, Ana Arnaiz, Francisco Arnaiz de las Revillas, Manuel Cobo Belaustegui, María Carmen Fariñas, Concepción Fariñas-Álvarez, Rubén Gómez Izquierdo, Iván García, Claudia González Rico, Manuel Gutiérrez-Cuadra, José Gutiérrez Díez, Marcos Pajarón, José Antonio Parra, Ramón Teira, Jesús Zarauza; **Hospital Universitario Puerta de Hierro**, (Madrid): Fernando Domínguez, Pablo García Pavía, Jesús González, Beatriz Orden, Antonio Ramos; **Hospital Universitario Ramón y Cajal**, (Madrid): Tomasa Centella, José Manuel Hermida, José Luis Moya, Pilar Martín-Dávila, Enrique Navas, Enrique Oliva, Alejandro del Río, Soledad Ruiz; **Hospital Universitario Virgen de las Nieves**, (Granada): Carmen Hidalgo Tenorio; **Hospital Universitario Virgen Macarena**, (Sevilla): Manuel Almendro Delia, Omar Araji, José Miguel Barquero, Román Calvo Jambrina, Marina de Cueto, Juan Gálvez Acebal, Irene Méndez, Isabel Morales, Luis Eduardo López-Cortés; **Hospital Universitario Virgen del Rocío**, (Sevilla): Arístides de Alarcón, Emilio García, Juan Luis Haro, José Antonio Lepe, Francisco López, Rafael Luque; **Hospital San Pedro**, (Logroño): Luis Javier Alonso, Pedro Azcárate, José Manuel Azcona Gutiérrez, José Ramón Blanco, Antonio Cabrera Villegas, Lara García-Álvarez, José Antonio Oteo, Mercedes Sanz; **Hospital de la Santa Creu i Sant Pau**, (Barcelona): Natividad de Benito, Mercé Gurguí, Cristina Pacho, Roser Pericas, Guillem Pons; **Complejo Hospitalario Universitario de Santiago de Compostela**, (A Coruña): M. Álvarez, A. L. Fernández, Amparo Martínez, A. Prieto, Benito Regueiro, E. Tijeira, Marino Vega; **Hospital Santiago Apóstol**, (Vitoria): Andrés Canut Blasco, José Cordo Mollar, Juan Carlos Gainzarain Arana, Oscar García Uriarte, Alejandro Martín López, Zuriñe Ortiz de Zárate, José Antonio Urturi Matos; **Hospital SAS Línea de la Concepción**, (Cádiz): García-Domínguez Gloria, Sánchez-Porto Antonio; **Hospital Clínico Universitario Virgen de la Arrixaca** (Murcia): José Mª Arribas Leal, Elisa García Vázquez, Alicia Hernández Torres, Ana Blázquez, Gonzalo de la Morena Valenzuela; **Hospital de Txagorritxu**, (Vitoria): Ángel Alonso, Javier Aramburu, Felicitas Elena Calvo, Anai Moreno Rodríguez, Paola Tarabini-Castellani; **Hospital Virgen de la Salud,** (Toledo): Eva Heredero Gálvez, Carolina Maicas Bellido, José Largo Pau, Mª Antonia Sepúlveda, Pilar Toledano Sierra, Sadaf Zafar Iqbal-Mirza; **Hospital Rafael Méndez,** (Lorca-Murcia):, Eva Cascales Alcolea, Ivan Keituqwa Yañez, Ana Peláez Ballesta; **Hospital Universitario San Cecilio** (Granada): Eduardo Moreno Escobar, Alejandro Peña Monje, Valme Sánchez Cabrera, David Vinuesa García; **Hospital Son Llátzer** (Palma de

Mallorca): María Arrizabalaga Asenjo, Carmen Cifuentes Luna, Juana Núñez Morcillo, Mª Cruz Pérez Seco, Aroa Villoslada Gelabert; **Hospital Universitario Miguel Servet** (Zaragoza): Carmen Aured Guallar, Nuria Fernández Abad, Pilar García Mangas, Marta Matamala Adell, Mª Pilar Palacián Ruiz, Juan Carlos Porres; **Hospital General Universitario Santa Lucía** (Cartagena): Begoña Alcaraz Vidal, Nazaret Cobos Trigueros, María Jesús Del Amor Espín, José Antonio Giner Caro, Roberto Jiménez Sánchez, Amaya Jimeno Almazán, Alejandro Ortín Freire, Monserrat Viqueira González; **Hospital Universitario Son Espases** (Palma de Mallorca): Pere Pericás Ramis, Mª Ángels Ribas Blanco, Enrique Ruiz de Gopegui Bordes, Laura Vidal Bonet; **Complejo Hospitalario Universitario de Albacete** (Albacete): Mª Carmen Bellón Munera, Elena Escribano Garaizabal, Antonia Tercero Martínez, Juan Carlos Segura Luque.

Table 1. Characteristics of IE patients and surgical indication related to treatment during admission

	Medical treatment (n=538)	Medical and surgical treatment (n=1115)	P
Age (years)	74 (63 - 79)	65 (54 - 73)	<0.001
Male gender	301 (55.9)	743 (66.6)	<0.001
Hospital-acquired	201 (37.3)	277 (24.8)	<0.001
Comorbidity			
Diabetes mellitus	170 (31.5)	271 (24.3)	0.002
Renal insufficiency [1]	185 (34.4)	229 (20.5)	<0.001
Implantable cardiac device	77 (14.3)	68 (6.1)	<0.001
Age-adjusted Charlson Comorbidity Index (points)	6 (4 - 7)	4 (2 - 5)	<0.001
Microbiology			
Coagulase-negative staphylococci	160 (29.7)	161 (14.4)	<0.001
S. aureus	107 (19.9)	104 (9.3)	<0.001
Streptococcus spp	89 (16.5)	319 (28.6)	<0.001
Enterococcus spp	81 (15.1)	150 (13.5)	0.379
Affected valve			
Native	332 (61.7)	723 (64.8)	0.214
Prosthetic	230 (42.8)	398 (35.7)	0.006
Aortic	310 (57.6)	762 (68.3)	<0.001
Mitral	314 (58.4)	520 (46.6)	<0.001
Clinical complications			
Septic shock	127 (23.6)	135 (12.1)	<0.001
Persistent bacteremia	104 (19.3)	119 (10.6)	<0.001
CNS vascular events	166 (30.8)	223 (20.0)	<0.001
Non-neurologic embolisms	121 (22.4)	232 (20.8)	0.472
Heart failure	336 (62.4)	664 (59.5)	0.281
Renal function impairment	238 (44.6)	470 (42.3)	0.393
Intracardiac complications			
Perivalvular abscess	140 (26.0)	336 (30.1)	0.094
Pseudoaneurysm	41 (7.6)	119 (10.6)	0.060
Intracardiac fistula	25 (4.6)	56 (5.0)	0.833
Surgery indication	132 (55.0)	40 (42.6)	0.041
Heart failure	168 (31.2)	466 (41.8)	<0.001
Uncontrolled infection	366 (68.0)	602 (54.0)	0.153
Prevention of embolism	148 (27.5)	345 (30.9)	<0.001
In-hospital mortality	366 (68.0)	290 (26.0)	<0.001
One-year mortality [2]	359 (75.4)	333 (33.7)	<0.001

CNS: central nervous system. Quantitative variables are reported with median and interquartile range. [1] Renal insufficiency was defined as plasma creatinine over 1.4 mg/dl. No follow-up information was available for 190 (calculated) patients [2]

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Table 2. Clinical characteristics of IE patients who did not undergo surgery related to in-hospital mortality.

	Survivors (n=215)	Non-survivors (n=323)	OR (CI 95%)	P
Age (years)	72 (63 - 79)	75 (64 - 80)		0.199
Male gender	127 (59.0)	174 (53.8)		0.270
Hospital-acquired	70 (32.5)	131 (40.5)		0.073
Comorbidity				
Diabetes mellitus	53 (24.7)	117 (36.6)	1.88 (1.19-2.97)	0.006
Renal insufficiency [1]	60 (27.9)	125 (38.7)		0.010
Chronic liver disease	32 (15.3)	58 (18.4)		0.357
Neoplasia	32 (15.0)	67 (20.9)	1.77 (1.02-3.07)	0.041
Immunosuppressive therapy	15 (7.0)	27 (8.4)		0.540
Implantable cardiac device	25 (11.6)	52 (16.1)		0.143
Age-adjusted Charlson Comorbidity Index (points)	5 (4 - 7)	6 (4 - 8)		0.003
Microbiology				
Coagulase-negative staphylococci	43 (20.0)	64 (19.8)		0.958
S. aureus	48 (22.3)	112 (34.7)	1.61 (1.01-2.57)	0.046
Streptococcus spp	48 (22.3)	41 (12.7)		0.003
Enterococcus spp	38 (17.7)	43 (13.3)		0.166
Affected valve				
Native	130 (60.5)	202 (62.5)		0.628
Prosthetic	96 (44.7)	134 (41.5)		0.467
Aortic	117 (54.4)	193 (59.8)		0.220
Mitral	130 (60.5)	184 (57.0)		0.420
Clinical complications				
Septic shock	22 (10.2)	105 (32.5)		<0.01
Persistent bacteremia	35 (16.5)	69 (22.0)		0.118
CNS vascular events	62 (28.8)	104 (33.0)		0.308
Non-neurologic embolisms	46 (21.5)	75 (24.0)		0.496
Heart failure	73 (43.9)	243 (76.2)		<0.01
Renal function impairment	60 (28.0)	178 (55.6)	2.69 (1.77-4.07)	<0.001
Intracardiac complications				
Perivalvular abscess	55 (25.6)	85 (26.3)		0.953
Pseudoaneurysm	18 (8.4)	23 (7.1)		0.726
Intracardiac fistula	12 (5.6)	13 (4.0)		0.683
Surgery indication [2]				
Heart failure	41 (19.1)	127 (39.3)	3.24 (1.99-5.9)	<0.001
Uncontrolled infection	141 (65.6)	225 (69.7)	1.83 (1.04-3.18)	0.037
Prevention of embolism	67 (31.2)	81 (25.1)	1.34 (0,78.2,31)	0.122

CNS: central nervous system. Quantitative variables are reported with median and interquartile range. [1] Renal insufficiency was defined as plasma creatinine over 1.4 mg/dl. [2] One hundred and thirty patients (24.1%) presented more than one indication.

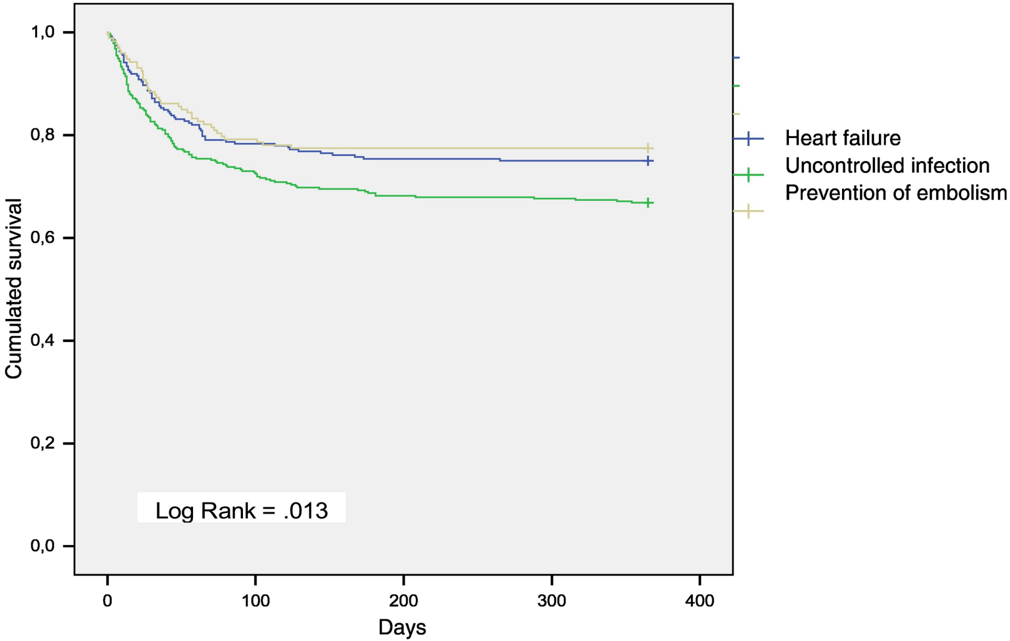
Table 3. Clinical characteristics patients presenting with IE refused for surgery according to one-year mortality

	Survivors (n=117)	Non-survivors (n=359)	OR (CI 95%)	P
Age (years)	70 (59 - 78)	75 (64 - 80)		0.011
Male gender	74 (63.2)	197 (54.8)		0.138
Hospital-acquired	33 (28.2)	143 (39.8)		0.031
Comorbidity				
Diabetes mellitus	27 (23.1)	128 (36.0)		0.010
Renal insufficiency [1]	25 (21.4)	141 (39.3)		<0.001
Chronic liver disease	13 (11.1)	67 (18.6)		0.079
Neoplasia	14 (11.9)	77 (21.4)		0.033
Immunosuppressive therapy	11 (9.4)	28 (7.8)		0.454
Implantable cardiac device	11 (9.4)	56 (15.6)		0.092
Age-adjusted Charlson Comorbidity Index (points)	5 (3 - 6)	6 (4 - 8)		<0.001
EuroScore	25 (10 - 48)	54 (29 - 71)		<0.001
Microbiology				
Coagulase-negative staphylococci	21 (17.9)	73 (20.3)		0.573
S. aureus	26 (22.2)	122 (34.0)		0.017
Streptococcus spp	22 (18.8)	49 (13.6)		0.174
Enterococcus spp	23 (19.7)	46 (12.8)		0.093
Affected valve				
Native	75 (64.1)	226 (63.0)		0.823
Prosthetic	51 (43.6)	147 (40.9)		0.615
Aortic	63 (53.8)	212 (59.1)		0.322
Mitral	78 (66.7)	202 (56.3)		0.047
Vegetation size (mm)	10 (7 – 15)	12 (7 – 17)		0.614
Clinical complications				
Septic shock	14 (12.0)	106 (29.5)		<0.001
Persistent bacteremia	20 (17.4)	77 (22.1)		0.285
CNS vascular events	34 (29.0)	114 (31.7)		0.665
Non-neurologic embolisms	26 (22.2)	84 (23.3)		0.892
Heart failure	49 (42.2)	262 (73.8)		<0.001
Renal function impairment	32 (27.4)	192 (53.9)	2.35 (1.43-3.87)	<0.001
Intracardiac complications				
Perivalvular abscess	26 (22.2)	93 (25.9)		0.511
Pseudoaneurysm	8 (6.8)	28 (7.8)		0.570
Intracardiac fistula	6 (5.1)	14 (3.9)		0.616
Surgery indication [3]				
Heart failure	22 (18.8)	134 (37.3)	3.03 (1.53-5.98)	<0.001
Uncontrolled infection	75 (64.1)	247 (68.8)	1.9 (0.96-3.77)	0.345
Prevention of embolism	36 (30.8)	96 (26.7)	1.77 (0.9-3.46)	0.398

CNS: central nervous system. Quantitative variables are reported with median and interquartile range. [1] In-hospital mortality. [2] Renal insufficiency was defined as plasma creatinine over 1.4 mg/dl.. [3] One hundred twenty patients (22.4%) presented than one indication. In 62 patients follow-up information was not available

Highlights

- Clinical guidelines allow to group patients according to the surgical indication
- Many IE patients are not operated on despite presenting a clear surgical indication
- The type surgical indication may influence the mortality of these patients
- Prevention of embolism, as surgical indication, is associated with lower mortality
- Conversely, CHF is associated with higher short- and long-term mortality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Cumulated survival
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100
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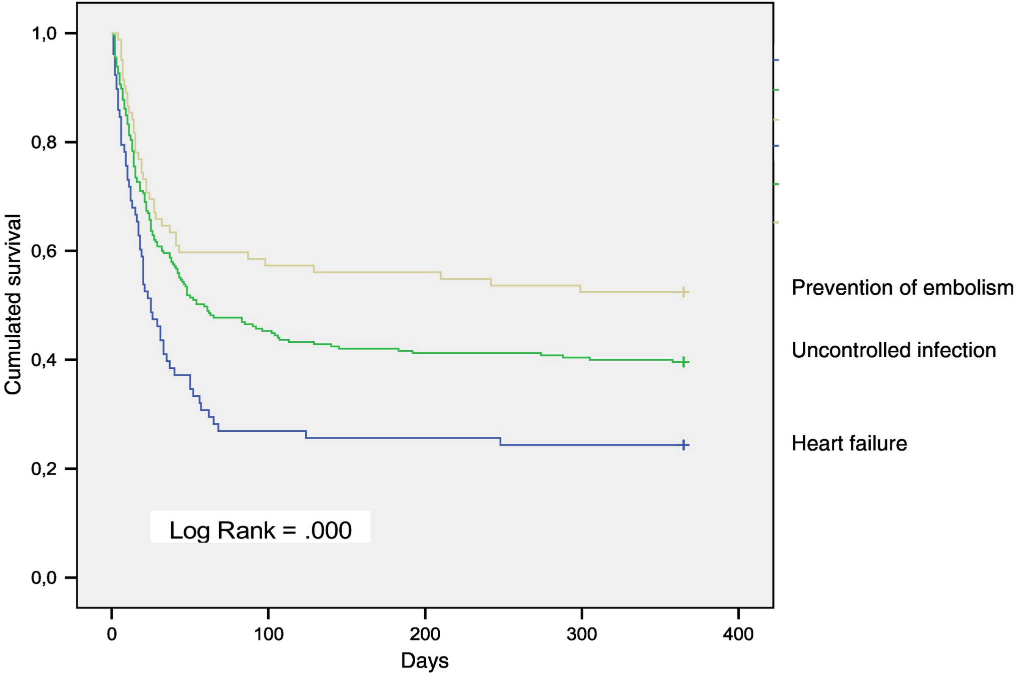
Days
Log Rank = .013
Heart failure
Uncontrolled infection
Prevention of embolism

Figure 1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Days
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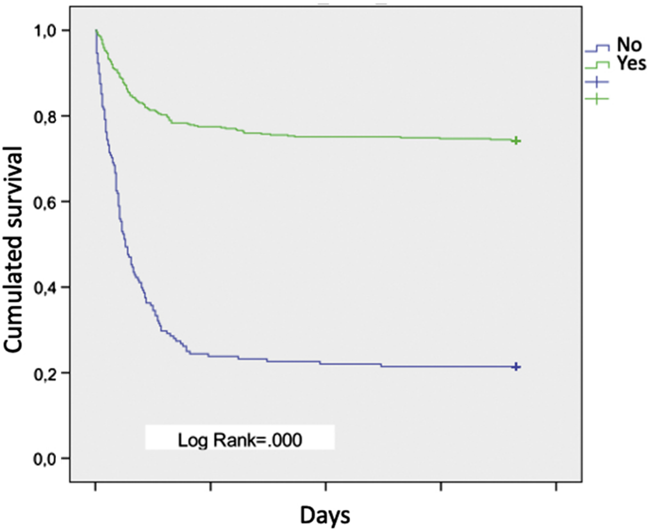
Prevention of embolism
Uncontrolled infection
Heart failure

Figure 2



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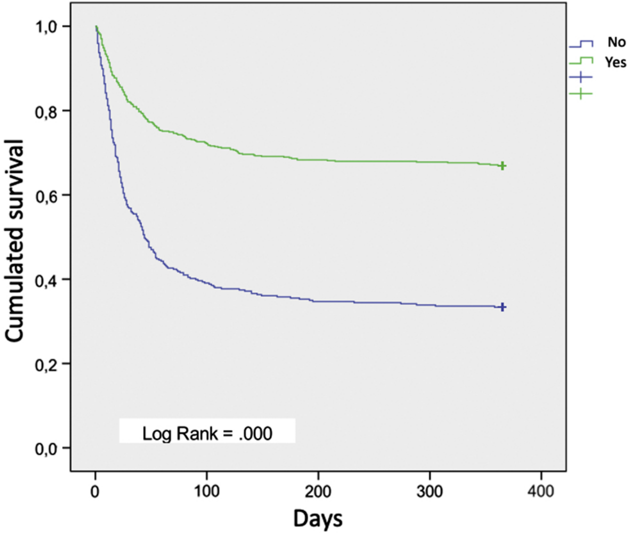

Cumulated survival
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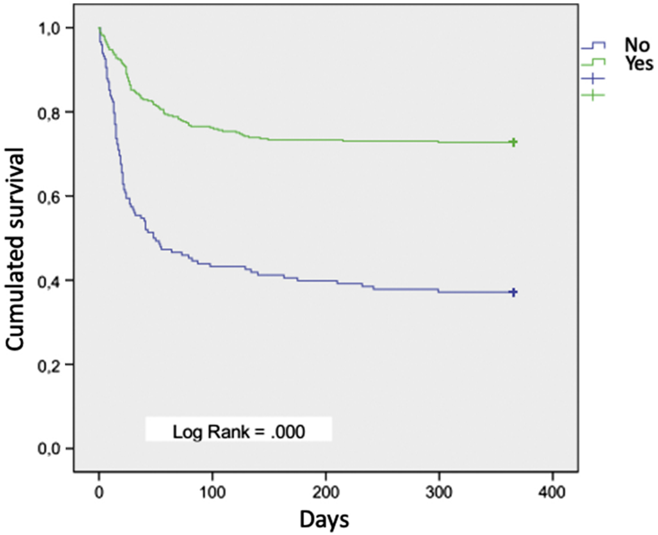
100
200
300
400
Days
No
Yes
Log Rank = .000

Figure 4



Cumulated survival
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Yes
Log Rank = .000
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300
400
Days

Figure 5