Infective endocarditis in patients with cancer: a consequence of invasive procedures or a harbinger of neoplasm? A prospective, multicenter cohort

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Abstract
The aim of the study was to draw a comparison between the characteristics of infective endocarditis (IE) in patients with cancer and those of IE in noncancer patients. Patients with IE, according to the modified Duke criteria, were prospectively included in the GAMES registry between January 2008 and February 2014 in 30 hospitals. Patients with active cancer were compared with noncancer patients.

During the study period, 161 episodes of IE fulfilled the inclusion criteria. We studied 2 populations: patients whose cancer was diagnosed before IE (73.9%) and those whose cancer and IE were diagnosed simultaneously (26.1%). The latter more frequently had community-acquired IE (67.5% vs 26.4%, P < .01), severe sepsis (28.6% vs 11.1%, P = .013), and IE caused by gastrointestinal streptococci (42.9% vs 16.8%, P < .01). However, catheter source (7.1% vs 29.4%, P = .003), invasive procedures (26.2% vs 44.5%, P = .044), and immunosuppressants (9.5% vs 35.6%, P = .002) were less frequent.

When compared with noncancer patients, patients with cancer were more often male (75.2% vs 67.7%, P = .049), with a higher comorbidity index (7 vs 4). In addition, IE was more often nosocomial (49.7% vs 29%) and originated in catheters (23.6% vs 6.2%) (all P < .01). Prosthetic endocarditis (21.7% vs 30.3%, P = .022) and surgery when indicated (24.2% vs 46.5%, P < .01) were less common. In-hospital mortality (34.8% vs 25.8%, P = .012) and 1-year mortality (47.8% vs 30.9%, P < .01) were higher in cancer patients, although 30-day mortality was not (24.8% vs 19.3%, P = .087).

A significant proportion of cases of IE (5.6%) were recorded in cancer patients, mainly as a consequence of medical interventions. IE may be a harbinger of occult cancer, particularly that of gastrointestinal or urinary origin.

Abbreviations: GAMES = Grupos de Ayuda al Manejo de la Endocarditis (Spanish Collaboration on Endocarditis), ICE = International Collaboration on Endocarditis, IE = infective endocarditis, IQR = interquartile range, OR = odds ratio.

Keywords: cancer, infective endocarditis, neoplasm
1. Introduction

The importance of active cancer as an underlying disease in patients with infective endocarditis (IE) has not been specifically addressed, although neoplasms are common in patients with IE.\[1\]

The reciprocal and negative influence of cancer and IE on the management of both conditions is easy to envision but not frequently addressed. Potential higher mortality has been suggested in patients with cancer.\[2\] Some studies report an association between intra-abdominal cancer and endocarditis,\[3\] whereas others report a high incidence of nosocomial IE caused by staphylococci.\[4\] However, specific characteristics and prognostic factors have not been analyzed. Studies describing IE in patients with cancer or vice versa are subject to limitations; they analyze single-center cohorts,\[5\] do not draw comparisons with a population without cancer,\[6\] focus only on nonbacterial thrombotic endocarditis\[7\] or endocarditis associated with specific kinds of cancer,\[8\] and report the association in specific population subsets.\[9\]

Our objective was to describe the clinical characteristics and prognosis of IE in cancer patients in a large, multicenter cohort of patients with IE by comparing them with those of IE in noncancer patients. We assessed 2 populations: patients in whom cancer had been diagnosed before IE and patients in whom IE was diagnosed before cancer, thus pointing to cancer as a potential portal of entry for IE.

2. Materials and methods

2.1. Setting

In 2008, in association with the International Collaboration on Endocarditis (ICE),\[10\] a national cooperative endocarditis study group, Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España (GAMES [the Spanish Collaboration on Endocarditis]), was created in Spain with the objective of improving the care of IE patients and conducting research. GAMES is a prospective registry managed by a multicenter multidisciplinary group dedicated to improving the management of IE.\[11\]

2.2. Patients

Consecutive patients with IE were prospectively included in the GAMES registry between January 2008 and February 2014 in 30 Spanish hospitals. Multidisciplinary teams completed a standardized case report form. Patients were followed for 1 year. Patients with and without active cancer were compared.

2.3. Definitions

We defined active cancer as hematological neoplasm or solid tumors diagnosed ≤5 years before IE or any cancer managed with active cancer therapy at admission for IE. In the case of nonadvanced cancer, only those diagnosed ≤6 months before IE were considered active.\[12\] Cancer was stratified according to the stage of the disease at diagnosis of IE. Stage was considered advanced when the tumor was locally advanced or metastatic (solid tumors), or when the patient had received reinduction therapy, or a recurrence had been diagnosed (hematological cancer). We analyzed 2 subsets: patients with a diagnosis of cancer before the diagnosis of IE (established cancer) and patients in whom cancer was diagnosed simultaneously with IE (same admission) or subsequently (newly discovered cancer).

IE was defined according to the modified Duke criteria.\[13\]

Site of acquisition of IE was defined following ICE recommendations.\[14\]

In brief, community-acquired IE was defined as IE diagnosed within the first 48 hours of admission in a patient who did not fulfill the criteria for nosocomial or health care-associated infection. Nosocomial IE was defined as IE in a patient who had been hospitalized for ≥48 hours before the onset of signs or symptoms consistent with IE. Health care-associated IE was diagnosed within 48 hours of admission of an outpatient with any of the following criteria: intravenous therapy, wound care, or specialized nursing care at home within the 30 days before the onset of IE; attendance at a hospital or hemodialysis clinic or receipt of intravenous chemotherapy within the 30 days before the onset of IE; hospitalization in an acute care hospital for ≥2 days during the 90 days before the onset of IE; or residence in a nursing home or long-term care facility.

The source of endocarditis was considered to be the alleged source when the same microorganism was isolated in blood cultures and the potential source (e.g., catheter), when there was a clinical source compatible with the microorganism (e.g., Enterococcus and evidence of urinary infection in a patient with a permanent urinary catheter) and/or when an invasive intervention was performed before the diagnosis of IE that could be temporally and microbiologically related to the etiology of the endocarditis.

An implantable cardiac device was defined as a permanent pacemaker and/or cardioverter-defibrillator.

Prosthetic valve IE was defined as an endovascular infection affecting a prosthetic valve or reconstructed native heart valve, irrespective of whether the prosthesis was a mechanical prosthesis and/or bioprosthetic xenograft (stented or unstented) and/or repaired native valve with implantation of an annular ring.

The EuroSCORE was used to assess operative risk in heart surgery.\[15\] We used the age-adjusted Charlson comorbidity index to categorize comorbidities.\[16\]

All patients were evaluated by cardiac surgeons following international indications to determine the need for surgery.\[17\] The final decision on surgery was made in agreement with the multidisciplinary endocarditis team at each center, including the oncologist.

Both in-hospital mortality (overall mortality rate during the hospital stay) and 30-day mortality (considered likely related to the infection) were analyzed. Long-term mortality was defined as mortality at 1 year.

2.4. Data analysis

Patients with active cancer at admission for IE were analyzed and compared with the rest of the patients in the database.

Among patients with cancer, those with a previous diagnosis of cancer were compared with those who had a simultaneous diagnosis of IE and cancer (same month).

Quantitative variables were expressed as mean and standard deviation or as median and interquartile range (IQR), as appropriate; qualitative variables were expressed as frequency and percentage. Continuous variables were compared using the t test, and categorical variables were compared using the χ² test or Fisher exact test when the χ² test was not appropriate. Adjusted odds ratios (ORs) were computed using logistic regression analysis. Stepwise logistic regression analysis was performed including variables with a P < .1 in the univariate analysis. All
statistical analyses were performed using PASW Statistics for Windows, version 18.0 (SPSS Inc, Chicago, IL).

2.5. Ethics
The study and the common case report form were approved by the local and national institutional review boards and ethics committees (E.C. 18/07).

3. Results
3.1. Incidence and etiology of IE in cancer patients
During the 6-year study period, 161 cases in 160 patients from 30 Spanish hospitals fulfilled the inclusion criteria (5.6% of all cases of IE diagnosed during the same period-2888 episodes of endocarditis). The characteristics of patients with and without cancer are summarized in Table 1.

The etiology of IE in cancer patients is shown in Figure 1. A significant association was found between colon cancer and streptococcal etiology (32.7% vs 18.3%, \( P = .048 \)). We failed to find any further association between other etiologies and other kinds of cancer.

Of note, an etiological diagnosis for IE was not attained in 14 cases (8.7%); therefore, it was not possible to exclude any further association between other etiologies and other kinds of cancer.

Clinical presentation was unspecific, although the diagnostic criteria were less often definite than in noncancer patients (73.9% vs 80.6%, \( P = .04 \)). Prosthetic IE was less frequent in patients with cancer (21.7% vs 30.3%, \( P = .02 \). Interestingly, 4 cases had mural IE (among 16 cases of nonvalvular IE).

Candida and polymicrobial IE were significantly more frequent among cancer patients (4.3% vs 1.6%, \( P = .009 \); and 5% vs 1.7%, \( P = .003 \), respectively) (Fig. 2). Persistent bacteremia was more common in cancer patients (16.9% vs 10.9%, \( P = .009 \)).

Surgery, although indicated, was performed less often in cancer patients (24.2% vs 46.5%, \( P = .01 \). The reasons for not performing surgery were death before surgery (18.4%), poor prognosis after surgery (7.9%), poor prognosis of underlying disease (53.3%), hemodynamic instability (5.3%), and cirrhosis, stroke, or patient/surgeon refusal (2.6% each). The reasons for not operating were unknown in 2 cases.

There were no differences in 30-day mortality (24.8% vs 19.3%, \( P = .09 \), although in-hospital mortality was higher in cancer patients (34.8% vs 25.8%, \( P = .01 \). One-year mortality was significantly higher in cancer patients (47.8% vs 30.9%, \( P = .01 \) (Fig. 3).

The multivariate analysis (Table 4) confirmed that IE in cancer patients more often affected men, with a higher age-adjusted comorbidity index, and was more often hospital-acquired and originated in catheters. Prosthetic valve endocarditis was less frequent, and cancer patients underwent surgery significantly less frequently when surgery was indicated.

3.2. Characteristics of IE according to the time of cancer diagnosis
The underlying neoplasm was hematological in 19.4% and a solid tumor in 80.6% (Fig. 2). The most common malignant neoplasm was colon cancer (33.5%), followed by prostate cancer (9.7%), lymphoma (8.4%), and urothelial tumors (8.4%).

We identified 2 different populations: patients with a cancer diagnosis before IE (established cancer) (119, 73.9%) and patients in whom IE was diagnosed simultaneously with cancer (same admission) or subsequently (newly discovered cancer) (42, 26.1%).

In patients with established cancer, the median time from cancer to IE was 257 days (IQR 67–809). Cancer was at an advanced stage in 56.1%. At diagnosis of IE, only 1 patient was neutropenic, although 42 (25.6%) had recently received chemotherapy.

Patients with established and newly discovered cancer were compared (Table 3). Cases where endocarditis was a harbinger of cancer were more likely to be community-acquired, were less frequently treated with immunosuppressors, presented with severe sepsis, and were caused by gastrointestinal streptococci. On the contrary, catheter source and invasive procedures before the IE episode were less frequent. There were no differences in surgical management or outcome.

3.3. Comparison between patients with and without cancer
When we compared patients with and without cancer (Table 1), cancer patients were more often male (75.2% vs 67.7%, \( P = .049 \) and significantly older (median age 70 [IQR 63–77] vs 68 [IQR 56–77], \( P = .02 \) and had a higher age-adjusted Charlson comorbidity index (mean 7 vs 4, \( P < .01 \). IE was more often nosocomial in cancer patients (48.7% vs 29.9%, \( P = .01 \). In 23.6% of cases, a central venous catheter was purportedly the source of IE compared with only 6.2% in noncancer patients (\( P = .01 \). Genitourinary or intestinal sources of endocarditis were also significantly more frequent in cancer patients.

4. Discussion
Our study shows that a significant proportion of IE patients (5.6%) have underlying active cancer and that IE may be a harbinger or a consequence of cancer. Endocarditis behaves differently in cancer patients, although risk factors for 30-day
### Table 1

Characteristics of infective endocarditis in patients with and without cancer.

| Variable (%) | No cancer (N=2727) | Cancer (N=161) | P |
|--------------|---------------------|----------------|---|
| Sex (male)   | 1842 (67.7)         | 121 (75.2)     | .049|
| Age (median, IQR) | 68 (56–77) | 70 (63–77) | .02 |
| Days of symptoms before diagnosis (median, IQR) | 20 (10–43) | 11 (9–21) | .01 |
| Underlying conditions | | | |
| Age-adjusted Charlson comorbidity score (mean, SD) | 4 (3–6) | 7 (5–8) | .01 |
| Chronic heart failure | 865 (32.6) | 28 (17.4) | .01 |
| Dyslipemia | 930 (34.3) | 42 (26.4) | .04 |
| Connective tissue disease | 85 (3.1) | 1 (0.6) | .07 |
| Immunosuppressive therapy | 131 (4.8) | 46 (28.8) | .01 |
| Patients with cardiac devices | 493 (18.1) | 20 (12.4) | .17 |
| Patients with previous valve surgery or prosthesis | 946 (34.8) | 44 (27.3) | .15 |
| Acquisition | | | |
| Community-acquired | 1610 (61.6) | 56 (37.6) | .01 |
| Hospital-acquired | 782 (29.9) | 73 (48.7) | .01 |
| Health care-related | 220 (8.4) | 21 (14.1) | .02 |
| Source of endocarditis | 1251 (45.9) | 108 (67.1) | .01 |
| Catheter | 169 (6.2) | 38 (23.6) | .01 |
| Odontogenic | 163 (6.0) | 5 (3.1) | .13 |
| Respiratory | 28 (1.0) | 4 (2.5) | .09 |
| Gastrointestinal | 170 (6.2) | 24 (14.9) | .01 |
| Skin and soft tissue | 182 (6.7) | 10 (6.2) | .82 |
| Diagnosis | | | |
| Definite | 2188 (80.6) | 119 (73.9) | .04 |
| Possible | 527 (19.4) | 42 (26.1) | .04 |
| Affected valve | | | |
| Aortic | 1331 (48.8) | 71 (44.1) | .25 |
| Mitral | 1170 (42.9) | 72 (44.7) | .65 |
| Tricuspid | 143 (5.2) | 10 (6.2) | .59 |
| Pulmonary | 43 (1.6) | 2 (1.2) | .54 |
| Prosthetic valve | 825 (30.3) | 35 (21.7) | .02 |
| Native valve | 1668 (61.2) | 106 (65.8) | .24 |
| Nonvalvular (pacemaker wire or other) | 379 (13.9) | 16 (9.9) | .16 |
| Etiology | | | |
| Coagulase negative staphylococci | 476 (17.5) | 26 (16.1) | .67 |
| Staphylococcus aureus | 606 (22.3) | 38 (23.6) | .68 |
| Enterococcus | 378 (13.9) | 23 (14.3) | .88 |
| Streptococcus | 694 (25.5) | 38 (23.6) | .60 |
| Gram-negative bacilli | 110 (4.0) | 5 (3.1) | .56 |
| Anaerobes | 30 (1.1) | 1 (0.6) | .57 |
| Candida | 43 (1.6) | 7 (4.3) | .009 |
| Other fungi | 10 (0.4) | 1 (0.6) | .61 |
| Other etiologies | 83 (3.0) | 0 (0) | .03 |
| Polymicrobial | 46 (1.7) | 8 (5) | .003 |
| Unknown | 251 (9.2) | 14 (8.7) | .83 |
| Outcome | | | |
| Embolisms | 943 (34.6) | 46 (28.6) | .15 |
| Intracardiac complication | 773 (28.5) | 46 (28.8) | .99 |
| Perforation or tear | 352 (12.9) | 17 (10.5) | .46 |
| Pseudaneurysm | 138 (5.0) | 6 (3.7) | .57 |
| Abscess | 384 (14.1) | 28 (17.4) | .29 |
| Intracardiac fistula | 69 (2.5) | 4 (2.4) | .82 |
| Heart failure | 1099 (40.6) | 50 (31.3) | .06 |
| New conduction abnormality | 226 (8.4) | 16 (10.0) | .41 |
| Severe sepsis | 420 (15.4) | 25 (15.3) | .94 |
| Septic shock | 312 (11.4) | 21 (13.0) | .47 |
| Persistent bacteremia | 295 (10.9) | 27 (16.9) | .009 |
| Surgery indicated | 1784 (66.0) | 78 (48.8) | .01 |
| Cardiovascular surgery | 1268 (46.5) | 39 (24.2) | .01 |
| 30-d mortality | 527 (19.3) | 40 (24.8) | .09 |
| In-hospital mortality | 703 (25.8) | 56 (34.8) | .01 |
| 1-year mortality | 844 (30.9) | 77 (47.8) | .01 |

IQR = interquartile range, SD = standard deviation.

*Statistically significant P values are highlighted (bold).
mortality (which we consider attributable mortality) are similar to those for the general population of patients with endocarditis.\(^7\) Long-term prognosis is related to the underlying disease.

Data on the prevalence of cancer among patients with IE are scarce in the literature, and it is generally not determined whether cancer is active or not when IE is diagnosed.\(^1\) In our series, we only included patients with active cancer, thus possibly accounting for the somewhat lower prevalence in the present study (5.6% vs 8% elsewhere\(^11\)).

We identified 2 different populations in cancer patients with IE: one with a previous diagnosis of cancer, in which IE is a consequence of cancer management, and another, in which IE is diagnosed after the diagnosis of cancer. There are opportunities both for early diagnosis of cancer and for prevention of endocarditis.

The association between colon cancer and IE is well known\(^3,6,17,18\); however, in our series, a high risk of IE was also present for lymphoma, prostate cancer, and genitourinary cancer. In many cases, IE occurs concurrently with, and even leads to, a diagnosis of cancer (42; 26% cases).\(^19\) The only association we were able to find between the etiology of IE and the underlying tumor was streptococcal endocarditis in patients with colon cancer. An association between \textit{Streptococcus bovis} (\textit{S. gallolyticus} subsp \textit{gallolyticus}) and colon cancer has been thoroughly described\(^18\) and several mechanisms have been proposed\(^17\). Although an association between other types of streptococcal endocarditis and colon cancer has been reported (Kestler et al, in press), this is not as strong as in the case of \textit{S. gallolyticus}. Some authors suggest that the risk of being diagnosed with cancer is higher in patients with IE than in those without IE, in particular during the first 3 months of follow-up, although this period can be as long as 4 years.\(^19,20\) This is an important issue for early diagnosis of cancer, particularly when made based on colonoscopy in patients with streptococcal endocarditis. The current European guidelines\(^15\) recommend ruling out cancer in cases of IE caused by \textit{S. bovis} (\textit{gallolyticus}). The increasing use of PET/CT in the extension study can help diagnose occult cancer in patients with IE.\(^7\)
Table 3

Characteristics of infective endocarditis according to when cancer was diagnosed.

| Variable (%) | Newly discovered cancer (N = 42) | Established cancer (N = 119) | P |
|--------------|----------------------------------|-----------------------------|---|
| Sex (male)   | 34 (81%)                         | 87 (73.1%)                  | .41|
| Age (median, IQR) | 69.5 (62.8–76.3)               | 70 (63–77)                  | .98|
| Underlying conditions |                                |                             |   |
| Age-adjusted Charlson comorbidity score (mean, SD) | 6 (4–8.25)                   | 7 (5–8)                     | .84|
| Chronic heart failure | 9 (21.4%)                    | 19 (16%)                    | .48|
| Dyslipemia | 14 (34.1%)                      | 28 (23.7%)                  | .42|
| Benign colonic pathology | 6 (17.6%)                    | 13 (14.6%)                  | .78|
| Immunosuppressive therapy | 4 (9.5%)                    | 42 (35.6%)                  | .002|
| Patients with cardiac devices | 6 (14.3%)                   | 14 (11.8%)                  | .79|
| Patients with previous valve surgery or prosthesis | 8 (19.0%)                    | 36 (30.3%)                  | .23|
| Acquisition |                                |                             |   |
| Community-acquired | 27 (67.5%)                  | 29 (26.4%)                  | <.001|
| Hospital-acquired | 11 (27.5%)                  | 62 (56.4%)                  | .003|
| Health care–related | 2 (5%)                      | 19 (17.3%)                  | .06|
| Source of endocarditis |                                |                             |   |
| Catheter | 3 (7.1%)                         | 35 (29.4%)                  | .003|
| Odontogenic | 2 (4.9%)                       | 3 (2.5%)                    | .60|
| Respiratory | 1 (2.4%)                       | 3 (2.5%)                    | >.99|
| Genitourinary | 2 (4.9%)                      | 15 (12.6%)                  | .24|
| Gastrointestinal | 11 (26.8%)                   | 13 (10.9%)                  | .02|
| Skin and soft tissue | 4 (9.8%)                      | 6 (5.1%)                    | .26|
| Invasive procedure | 11 (26.2%)                   | 53 (44.5%)                  | .04|
| Diagnosis |                                |                             |   |
| Definite | 28 (66.7%)                       | 91 (76.5%)                  | .23|
| Possible | 14 (33.3%)                       | 28 (23.5%)                  | .23|
| Affected valve |                                |                             |   |
| Aortic | 15 (35.7%)                       | 56 (47.1%)                  | .21|
| Mitral | 21 (50%)                         | 51 (42.9%)                  | .47|
| Tricuspid | 2 (4.8%)                       | 8 (6.7%)                    | >.99|
| Pulmonary | 1 (2.4%)                        | 1 (0.8%)                    | .46|
| Prosthetic valve | 5 (11.9%)                     | 30 (25.2%)                  | .08|
| Native valve | 31 (73.8%)                   | 75 (63.0%)                  | .26|
| Mitral or other |                                |                             |   |
| Neurovascular (pacemaker wire or other) | 6 (14.3%)                    | 14 (11.8%)                  | .79|
| Etiology |                                |                             |   |
| Coagulase negative staphylococci | 3 (7.1%)                      | 23 (19.3%)                  | .09|
| Staphylococcus aureus | 8 (19.0%)                     | 30 (25.2%)                  | .53|
| Enterococcus | 3 (7.1%)                       | 20 (16.8%)                  | .20|
| Streptococcus | 18 (42.9%)                     | 20 (16.8%)                  | .001|
| Gram-negative bacilli | 1 (2.4%)                      | 4 (3.4%)                    | >.99|
| Anaerobes | 1 (2.4%)                         | 0 (0%)                      | .26|
| Candida | 0 (0%)                           | 7 (5.9%)                    | .19|
| Other fungi | 0 (0%)                          | 1 (0.8%)                    | >.99|
| Polymicrobial | 2 (4.8%)                      | 6 (5%)                      | >.99|
| Unknown | 6 (14.3%)                        | 8 (6.7%)                    | .20|
| Outcome |                                |                             |   |
| Embolisms | 16 (38.1%)                      | 30 (25.2%)                  | .19|
| Intracardiac complication | 10 (21.7%)                    | 36 (30.5%)                  | .62|
| Perforation or tear | 5 (12.2%)                      | 12 (10.3%)                  | .79|
| Pseudoaneurysm | 1 (2.4%)                       | 5 (4.3%)                    | .73|
| Abscess | 4 (9.8%)                         | 24 (20.5%)                  | .24|
| Intracardiac fistula | 0 (0%)                         | 4 (3.4%)                    | .41|
| Heart failure | 15 (35.7%)                     | 35 (29.7%)                  | .56|
| New conduction abnormality | 4 (9.5%)                      | 12 (10.2%)                  | .65|
| Severe sepsis | 12 (28.6%)                     | 13 (11.1%)                  | .01|
| Septic shock | 9 (21.4%)                       | 12 (10.3%)                  | .10|
| Persistent bacteremia | 4 (9.5%)                       | 23 (19.5%)                  | .33|
| Surgery indicated | 22 (52.4%)                     | 56 (47.5%)                  | .64|
| EuroSCORE | 10 (7–12.5)                      | 11 (8–14)                   | .37|
| Cardiovascular surgery | 11 (26.2%)                     | 28 (23.5%)                  | .83|
| 30-d mortality | 9 (21.4%)                       | 31 (26.1%)                  | .68|
| In-hospital mortality | 12 (28.6%)                      | 44 (37%)                    | .35|
| 1-year mortality | 19 (45.2%)                      | 54 (45.4%)                  | >.99|

IQR = interquartile range, SD = standard deviation.
In other cases, endocarditis is diagnosed after cancer and application of its diagnostic and therapeutic measures. Previous cancer facilitates IE by means of associated thrombotic phenomena in cardiac valves that favor bacterial colonization or as a consequence of medical management (e.g., catheter-associated disease).

Nonbacterial thrombotic endocarditis is also found in cancer patients. Yusuf et al[4] reported a 42% frequency of culture-negative endocarditis in a retrospective series of consecutive cancer patients. Classically, embolisms are more frequent in nonbacterial thrombotic endocarditis, which occurs more frequently in patients with lung, pancreas, and gastric cancer and healthy valves.[21,22] In our series, it was not possible to reach a microbiological diagnosis in 8.7% of cases, and we cannot rule out the possibility that these cases involved nonbacterial thrombotic endocarditis. Consistent with this finding, patients with no known etiology had significantly more native valve endocarditis, more embolisms, and higher long-term mortality. It is important to bear in mind the possibility of noninfectious endocarditis, which needs different management strategies.[23]

Hospital and health care-related acquisition were significantly more frequent among patients with cancer, probably as a result of the use of invasive techniques and devices, such as catheters.[23] Long-term catheters are necessary in cancer patients, and although the risk of infection in totally implantable catheters is lower than in other catheters, these stay in place for longer periods of time and are eventually responsible for a considerable number of infections.[24] In a retrospective series of endocarditis in patients with cancer, 60% of those with culture-positive endocarditis had a central venous catheter.[4] In our series, the catheter was purportedly the source of endocarditis in 23.6%. Preventive measures have successfully prevented catheter-related bloodstream infections in other settings.[25] As suggested by Chu,[26] appropriate management of catheter-related bacteremia is essential for source control in endocarditis. Both prevention and management of catheter-related bacteremia are necessary to prevent the development of endocarditis in cancer patients. Programs specifically addressing long-term catheters are essential.

Interestingly, we found 4 cases of mural endocarditis (all right-sided). It is possible that chemotherapy administered through central venous catheters irritates the atrial wall and favors the development of atrial endocarditis. Other authors have described an association between thrombotic complications and catheter-related bloodstream infections in long-term catheters.[27] Nonvalvular endocarditis is characteristically associated with central catheters.[27–30]

Risk factors for 30-day mortality were similar to those of the general population and were all noncancer-related factors, whereas in-hospital mortality was also related to underlying disease and comorbidity. Cancer was a risk factor for 1-year mortality after IE, although not for short-term mortality, as previously reported by our group.[7]

Surgery is rarely offered because of concern over major postoperative complications and deterioration of an already compromised health status. Whether endocarditis affects cancer mortality[2,6] or does not affect it[3] remains a controversial issue.

In our series, there were no differences in postoperative mortality between patients with and without cancer who had undergone surgery. When evaluating a particular patient’s prognosis, we need to bear in mind that short-term prognosis is similar to that of any other patient with endocarditis, and in cases with a favorable cancer prognosis and no other comorbidity, intensive management and surgical therapy should be considered.

Our series may not represent the situation of IE in countries where levels of health care differ from those of Spain, which has a universal public health system.

| Variable | OR | 95% CI | \( P \) |
|----------|----|--------|-------|
| Sex (male) | 1.61 | 1.08–2.4 | .02 |
| Surgery | 0.454 | 0.301–0.694 | .01 |
| Noncultural infection | 1.75 | 1.21–2.53 | .03 |
| Age-adjusted Charlson comorbidity index >5 | 2.9 | 2.01–4.20 | .01 |
| Central catheter as a source | 3.28 | 2.10–5.13 | .01 |
| Prosthetic endocarditis | 0.608 | 0.398–0.930 | .02 |

\( CI = \) confidence interval, OR = odds ratio.

Table 4

| Variable | OR | 95% CI | \( P \) |
|----------|----|--------|-------|
| Staphylococcus aureus infection | 11.590 | 1.757–76.457 | .01 |
| New heart failure | 9.610 | 1.580–58.447 | .01 |
| Surgery | 0.143 | 0.021–0.982 | .048 |

\( CI = \) confidence interval, OR = odds ratio.

Table 5

| Variable | OR | 95% CI | \( P \) |
|----------|----|--------|-------|
| Staphylococcus aureus infection | 0.12 | 0.04–0.39 | <.001 |
| New heart failure | 4.885 | 2.226–10.718 | <.001 |
| Age-adjusted Charlson comorbidity index | 1.172 | 1.014–1.356 | .03 |

\( CI = \) confidence interval, OR = odds ratio.

Table 6

Figure 3. One-year survival in patients with and without cancer.
Surgery indicated and not performed 549 (20.1) 292 (52.9) .02
Surgery indicated and performed 1234 (45.3) 265 (21.5)
Surgery indicated and performed 1234 (45.3) 312 (25.2)
Missing 156 (5.7) 47 (30.3) 6 (10.7) 7 (8.0) 1 (100%)

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In conclusion, a significant proportion of cases of IE (5.6%) occur in cancer patients, mainly as a consequence of medical interventions in established cancers. IE should prompt a search for occult cancer, particularly in the gastrointestinal or urinary tract. Our results will facilitate informed clinical decisions in patients with IE and active cancer, thus enabling adequate preventive measures to be established.

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