Contemporary Clinical Profile and Outcome of Prosthetic Valve Endocarditis

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See also Patient Page.
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Context Prosthetic valve endocarditis (PVE) is associated with significant mortality and morbidity. The contemporary clinical profile and outcome of PVE are not well defined.

Objectives To describe the prevalence, clinical characteristics, and outcome of PVE, with attention to health care–associated infection, and to determine prognostic factors associated with in-hospital mortality.

Design, Setting, and Participants Prospective, observational cohort study conducted at 61 medical centers in 28 countries, including 556 patients with definite PVE as defined by Duke University diagnostic criteria who were enrolled in the International Collaboration on Endocarditis-Prospective Cohort Study from June 2000 to August 2005.

Main Outcome Measure In-hospital mortality.

Results Definite PVE was present in 556 (20.1%) of 2670 patients with infective endocarditis. Staphylococcus aureus was the most common causative organism (128 patients [23.0%]), followed by coagulase-negative staphylococci (94 patients [16.9%]). Health care–associated PVE was present in 203 (36.5%) of the overall cohort. Seventy-one percent of health care–associated PVE occurred within the first year of valve implantation, and the majority of cases were diagnosed after the early (60-day) period. Surgery was performed in 272 (48.9%) patients during the index hospitalization. In-hospital death occurred in 127 (22.8%) patients and was predicted by older age, health care–associated infection, and to determine prognostic factors associated with in-hospital mortality.

Conclusions Prosthetic valve endocarditis accounts for a high percentage of all cases of infective endocarditis in many regions of the world. Staphylococcus aureus is now the leading cause of PVE. Health care–associated infection significantly influences the clinical characteristics and outcome of PVE. Complications of PVE strongly predict in-hospital mortality, which remains high despite prompt diagnosis and the frequent use of surgical intervention.
vances in its diagnosis and treatment, PVE is associated with substantial morbidity and mortality. Prosthetic valve endocarditis has been estimated to occur at a rate of 0.3% to 1% per patient-year and to account for 1% to 5% of all cases of infective endocarditis (IE).\textsuperscript{9-12} Recent studies of predominantly native valve infective endocarditis (NVIE) have found an increased rate of Staphylococcus aureus infection, with an association between health care contact and this causative organism.\textsuperscript{13-15} However, the contemporary clinical profile and outcome of PVE have not been evaluated in large, prospective studies. Much of the current understanding of PVE has been based on studies limited by small sample size, retrospective design, or single-center experiences, and many of these investigations antedated the routine use of echocardiography in the diagnosis of IE and the contemporary and validated Duke diagnostic criteria for IE.\textsuperscript{16,17}

We hypothesized that the contemporary profile of PVE may be significantly influenced by health care–associated infection. The objectives of this study were (1) to prospectively describe the prevalence, clinical characteristics, and outcome of PVE, with attention to health care–associated infection; and (2) to determine prognostic factors associated with in-hospital mortality. To accomplish these goals, we analyzed data from the International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS), a large, prospective, contemporary, multinational registry of endocarditis.

**METHODS**

**International Collaboration on Endocarditis-Prospective Cohort Study**

Data from the International Collaboration on Endocarditis (ICE) were used for this study. The background and inclusion criteria of this prospective, multicenter, international registry of IE have been reported previously.\textsuperscript{14,15,18} Between June 2000 and August 2005, 3250 patients from 61 centers in 28 countries were enrolled. The ICE-PCS database is maintained at the Duke Clinical Research Institute, which is the coordinating center for ICE studies. Informed consent (oral or written) was obtained from all patients according to local institutional review boards or ethics committee guidelines at all sites. Geographic regions participating in ICE-PCS that enrolled patients with definite PVE included the following: United States (10 sites), South America (7 sites), Northern/Central Europe (14 sites), Southern Europe/Middle East/South Africa (11 sites), and Australia/New Zealand/Asia (11 sites).

**Patient Selection and Data Collection**

Patients were identified prospectively using site-specific procedures to ensure consecutive enrollment.\textsuperscript{15,18} Patients were enrolled in ICE-PCS if they met criteria for possible or definite IE based on modified Duke criteria.\textsuperscript{19} Only patients with definite IE were included in the current study. To preserve the assumption of independence of observations, only the first episode of IE recorded for an individual patient was used in the analysis.

The method of data collection for ICE-PCS has been previously reported.\textsuperscript{14} Briefly, a standard case report form was used at all sites to collect data. This case report form included 275 variables and was developed by ICE according to standard definitions.\textsuperscript{18} Data were collected during the index hospitalization and were then entered at the coordinating center or by site investigators using an Internet-based data entry system.

**Definitions**

Definitions of the variables included in the ICE-PCS case report form have been previously reported.\textsuperscript{19} Intravascular access devices" were defined as an arterial venous fistula or an indwelling vascular catheter. A “long-term indwelling central venous catheter” was defined as a tunneled, cuffed catheter, or a subcutaneous port catheter. An “intravascular access device” was presumed to be a possible source of IE if it was present at the onset of IE symptoms. “Persistant bacteremia” was defined as previously reported.\textsuperscript{10,17} An “intracardiac abscess” was defined as a thickened area or mass with a heterogeneous echogenic or echolucent appearance by echocardiography, or the presence of pus by direct visualization at the time of surgery.\textsuperscript{19}

“Early PVE” was defined as the diagnosis of PVE within 60 days of prosthetic valve implantation.\textsuperscript{20-22} Health care–associated infection in PVE was categorized as either “nosocomial” or “non-nosocomial health care–associated infection.”\textsuperscript{23} “Nosocomial infection” was defined as PVE developing in a patient hospitalized for more than 48 hours before the onset of signs or symptoms consistent with IE. “Non-nosocomial health care–associated infection” was defined as IE diagnosed within 48 hours of admission in an outpatient with extensive health care contact as reflected by any of the following criteria: (1) received intravenous therapy, wound care, or specialized nursing care at home within the 30 days prior to the onset of PVE; (2) attended a hospital or hemodialysis clinic or received intravenous chemotherapy within the 30 days before the onset of PVE; (3) was hospitalized in an acute care hospital for 2 or more days in the 90 days before the onset of PVE; or (4) resided in a nursing home or long-term care facility.\textsuperscript{23}

**Statistical Analysis**

Continuous variables were presented as medians with 25th and 75th percentiles. Categorical variables were presented as frequencies and percentages of the specified group. Univariable comparisons of clinical characteristics were made with the Wilcoxon rank-sum test or the $\chi^2$ test as appropriate. Within the PVE group, analyses were performed to evaluate the nature of early PVE compared with late PVE and, more broadly, health care–associated PVE in comparison to community-acquired PVE. Regional differences in PVE were assessed by dividing the participating sites in ICE-PCS based on their geographic region while integrating regions with...
few PVE cases (eg, Africa) with other proximal regions (Southern Europe and Middle East).

An exploratory multivariable generalized estimating equation model was created to determine variables independently associated with in-hospital mortality in PVE. Final parameter estimates were converted to odds ratios with corresponding 95% confidence intervals. To avoid overfitting the data, 15 clinically relevant variables were considered for the final generalized estimating equation model using backward selection. Multicollinearity was assessed by examination of the estimated parameter correlation matrix and no significant collinearity was found. Clinically relevant interactions were investigated and none were found to be significant. Missing values were imputed to the most frequent category for categorical variables and to the median for continuous variables. Plots of each variable considered for the final regression model against the outcome of interest were created to identify excessively influential observations and none were found. The fit of the final regression model to the data was evaluated by the Hosmer-Lemeshow test,23 which partitions the observations into 10 equal-sized groups according to their predicted probabilities and compares the observed and expected mortality across the partitions.

Mortality rates for S aureus and health care–associated PVE were evaluated by plotting the survival distribution derived from Kaplan-Meier estimates, and differences in survival were assessed by the log-rank test. Event (or censoring) times for all patients were measured from the day of initial admission for PVE (time 0). For all tests, statistical significance was determined at the .05 level. All statistical analyses were performed using SAS software version 8.2 (SAS Institute, Cary, NC).

RESULTS

Prosthetic valve endocarditis was diagnosed in 556 (20.1%) of 2670 patients with definite IE. Among patients with PVE, a prosthetic aortic valve was present in 384 patients (69.1%), prosthetic mitral valve or ring in 280 patients (50.4%), prosthetic tricuspid valve or ring in 52 patients (9.4%), and prosthetic pulmonic valve in 31 patients (5.6%). Of the overall PVE cohort, 127 (22.8%) patients died during hospital admission for PVE.

Table 1 shows the clinical characteristics of individuals with PVE in comparison to NVIE. Patients with PVE were significantly older, less likely to use injection drugs, and more likely to have health care–associated infection and intracardiac abscess. In-hospital mortality was significantly higher among PVE cases despite similar rates of complications and surgical intervention. Although patients with PVE had a higher rate of coagulase-negative staphylococcal infection (16.9%) and a lower rate of S aureus infection (23.0%) than patients with NVIE (8.3% and 32.9%, respectively; P<.001 for both), S aureus was the most common cause of PVE (Table 2). For 384 patients for whom time from valve implantation was available, the microbiology of early and late PVE are also shown. During the index hospitalization, surgical therapy was used in 272 (48.9%) patients with PVE and 879 (46.4%) patients with NVIE (P=.30).

A comparison of PVE across geographic regions is shown in Table 3. Direct correlations were found between the percentages of PVE due to staphylococcal species (either S aureus or coagulase-negative staphylococcus as causative microorganism) and percentages of PVE cases (r=0.713, P<.001) as well as health care–associated PVE (r=0.623, P<.001). Patients in the United States were significantly more likely to have nosocomial health care–associated PVE, an intravascular device source of infec-

**Table 1. Comparison of Patients With Prosthetic Valve Endocarditis (PVE) and Native Valve Infective Endocarditis (NVIE) in the International Collaboration on Endocarditis-Prospective Cohort Study**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PVE (n = 556)</th>
<th>NVIE (n = 1995)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>65.0 (49.9-74.3)</td>
<td>56.3 (41.1-69.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male</td>
<td>363 (65.3)</td>
<td>1299 (68.6)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Hemodialysis dependent</td>
<td>25 (4.5)</td>
<td>173 (9.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>100 (18.0)</td>
<td>292 (15.4)</td>
<td>&lt;.13</td>
</tr>
<tr>
<td>Current injection drug use</td>
<td>10 (1.8)</td>
<td>235 (12.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Chronic immunosuppressive therapy</td>
<td>24 (4.3)</td>
<td>127 (6.7)</td>
<td>.05</td>
</tr>
<tr>
<td>Cancer</td>
<td>32 (5.8)</td>
<td>169 (8.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Other chronic illness</td>
<td>246 (44.2)</td>
<td>916 (48.3)</td>
<td>.12</td>
</tr>
<tr>
<td>Previous endocarditis</td>
<td>112 (20.1)</td>
<td>91 (4.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Health care–associated infection</td>
<td>203 (36.5)</td>
<td>587 (31.0)</td>
<td>.01</td>
</tr>
<tr>
<td>Transesophageal echocardiography</td>
<td>467 (84.0)</td>
<td>1290 (68.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Time from admission to transesophageal echocardiography, mean (range), d</td>
<td>2.0 (0-6.0)</td>
<td>3.0 (0-7.0)</td>
<td>.13</td>
</tr>
</tbody>
</table>

**Echocardiographic findings**

- Vegetation: 406 (73.0) vs 1703 (89.9); <.001
- New regurgitation: 257 (46.2) vs 1346 (71.0); <.001
- Abscess: 165 (29.7) vs 222 (11.7); <.001

**Complications and outcome**

- Heart failure: 183 (32.9) vs 616 (32.5); .90
- Stroke: 101 (18.2) vs 322 (17.0); .56
- Other systemic embolization: 83 (14.9) vs 468 (24.7); <.001
- Surgery during admission: 272 (48.9) vs 879 (46.4); .30
- Persistent bacteremia: 49 (8.8) vs 166 (8.8); .92
- Duration of hospitalization, mean (range), d: 33 (19-49) vs 29 (16-44); <.001
- In-hospital death: 127 (22.8) vs 310 (16.4); <.001

*Data are presented as number and percentage unless otherwise indicated.*
tion, hemodialysis treatment, \textit{S. aureus} infection, and higher rates of complicated PVE (P < .005 for all comparisons). In-hospital mortality rates were not statistically different across the various regions.

Health care–associated PVE was reported in 36.5% (203/556) of the overall cohort. Of these patients with health care–associated PVE, 141 (69.5%) were classified as having nosocomial infection and 62 (30.5%) were classified as having non-nosocomial health care–associated infection. An intravascular device source of infection was presumed in 42.9% of health care–associated infections. Health care–associated PVE was characterized by high rates of \textit{S. aureus} (34.0%, including methicillin-resistant \textit{S. aureus} in 13.3%) and coagulase-negative staphylococci infection (25.6%) and low rates of enterococcal (9.4%) and viridans streptococcal (4.9%) infections. The in-hospital mortality rate of health care–associated PVE was 30.5% (62/203), including 31.9% (45/141) of patients with nosocomial PVE who died and 27.4% (17/62) of patients with non-nosocomial health care–associated infection who died (P = .52).

Prosthetic valve endocarditis associated with health care contact occurred at a median of 83.5 days (interquartile range, 39.5–543.0 days) from valve implantation, with 71% diagnosed within 1 year of prosthetic valve implantation. Health care–associated PVE occurred beyond the early period in 62.1% (87/140) of patients. In comparison to early PVE, health care–

### Table 2. Causative Organisms for Total Cohort, Early, and Late Prosthetic Valve Endocarditis (PVE)

<table>
<thead>
<tr>
<th>Causative Organism</th>
<th>Total, No. (%)</th>
<th>Early PVE, No. (%)</th>
<th>Late PVE, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Staphylococcus aureus}</td>
<td>128 (23.0)</td>
<td>19 (35.9)</td>
<td>61 (18.4)</td>
</tr>
<tr>
<td>Methicillin-sensitive \textit{S. aureus}</td>
<td>82 (14.7)</td>
<td>8 (15.1)</td>
<td>43 (13.0)</td>
</tr>
<tr>
<td>Methicillin-resistant \textit{S. aureus}</td>
<td>36 (6.5)</td>
<td>10 (18.9)</td>
<td>11 (3.3)</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>94 (16.9)</td>
<td>9 (17.0)</td>
<td>66 (19.9)</td>
</tr>
<tr>
<td>\textit{Enterococcus spp}</td>
<td>71 (12.8)</td>
<td>4 (7.5)</td>
<td>42 (12.7)</td>
</tr>
<tr>
<td>Viridans streptococci</td>
<td>67 (12.1)</td>
<td>1 (1.9)</td>
<td>34 (10.3)</td>
</tr>
<tr>
<td>Culture negative</td>
<td>62 (11.2)</td>
<td>9 (17.0)</td>
<td>41 (12.4)</td>
</tr>
<tr>
<td>\textit{Streptococcus bovis}</td>
<td>29 (5.2)</td>
<td>1 (1.9)</td>
<td>22 (6.7)</td>
</tr>
<tr>
<td>Fungal</td>
<td>23 (4.1)</td>
<td>5 (9.4)</td>
<td>11 (3.3)</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>10 (1.8)</td>
<td>0</td>
<td>6 (1.8)</td>
</tr>
<tr>
<td>\textit{HACEK} spp*</td>
<td>8 (1.4)</td>
<td>0</td>
<td>7 (2.1)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>7 (1.3)</td>
<td>1 (1.9)</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>\textit{Streptococcus agalactiae}</td>
<td>5 (0.9)</td>
<td>0</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>\textit{Propionibacterium acnes}</td>
<td>4 (0.7)</td>
<td>0</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>\textit{Propionibacterium NOS}</td>
<td>3 (0.5)</td>
<td>0</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>\textit{Pseudomonas aeruginosa}</td>
<td>3 (0.5)</td>
<td>1 (1.9)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>\textit{Streptococcus anginosus}</td>
<td>3 (0.5)</td>
<td>0</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>\textit{Streptococcus pneumoniae}</td>
<td>3 (0.5)</td>
<td>0</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>\textit{Listeria monocytogenes}</td>
<td>2 (0.4)</td>
<td>0</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>\textit{Micromonas micros}</td>
<td>2 (0.4)</td>
<td>0</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>\textit{Mycoplasma spp}</td>
<td>2 (0.4)</td>
<td>0</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>\textit{Serratia marcescens}</td>
<td>2 (0.4)</td>
<td>1 (1.9)</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Streptococcus galloyticus}</td>
<td>2 (0.4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Streptococcus group B}</td>
<td>2 (0.4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Streptococcus group C}</td>
<td>2 (0.4)</td>
<td>0</td>
<td>1 (0.3)</td>
</tr>
</tbody>
</table>

*Data are presented as number and percentage unless otherwise indicated. P values are results of \( \chi^2 \) analysis of each variable across all regions.

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associated with mortality. Mortality resource, and hemodialysis included, care–associated infection, was re-

When the composite variable, health

tics related to in-hospital mortality.

Table 4. Relationship Between Prosthetic Valve Endocarditis Characteristics and In-Hospital Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>In-Hospital Mortality, No. (%)</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>277</td>
<td>42 (15.2)</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>65-75</td>
<td>151</td>
<td>38 (25.2)</td>
<td>1.71 (1.01-2.00)</td>
<td>1.82 (1.09-3.03)</td>
</tr>
<tr>
<td>&gt;75</td>
<td>128</td>
<td>47 (36.7)</td>
<td>3.10 (1.80-5.32)</td>
<td>3.73 (2.10-6.61)</td>
</tr>
<tr>
<td>Male</td>
<td>363</td>
<td>76 (20.9)</td>
<td>0.73 (0.47-1.12)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>100</td>
<td>28 (28.0)</td>
<td>1.40 (0.92-2.13)</td>
<td></td>
</tr>
<tr>
<td>Prior infective endocarditis</td>
<td>112</td>
<td>21 (18.8)</td>
<td>0.74 (0.49-1.12)</td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>25</td>
<td>10 (40.0)</td>
<td>2.31 (1.12-4.77)</td>
<td></td>
</tr>
<tr>
<td>Presumed intravascular device source</td>
<td>87</td>
<td>30 (34.5)</td>
<td>1.86 (1.03-3.38)</td>
<td></td>
</tr>
<tr>
<td>Health care–associated infection</td>
<td>203</td>
<td>62 (30.5)</td>
<td>1.83 (1.22-2.74)</td>
<td>1.62 (1.08-2.44)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>128</td>
<td>44 (34.4)</td>
<td>2.12 (1.25-3.60)</td>
<td>1.73 (1.01-2.95)</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>94</td>
<td>24 (25.5)</td>
<td>1.13 (0.81-1.58)</td>
<td></td>
</tr>
<tr>
<td>Mitral valve prosthesis</td>
<td>280</td>
<td>64 (22.9)</td>
<td>0.98 (0.70-1.38)</td>
<td></td>
</tr>
<tr>
<td>Time since valve implantation in 30-d intervals</td>
<td>1.00</td>
<td>1.00 (0.99-1.01)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent bacteremia</td>
<td>49</td>
<td>27 (55.1)</td>
<td>1.67 (1.07-2.27)</td>
<td>4.29 (1.99-9.22)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>183</td>
<td>60 (32.8)</td>
<td>2.29 (1.59-3.32)</td>
<td>2.33 (1.62-3.34)</td>
</tr>
<tr>
<td>Intracardiac abscess</td>
<td>144</td>
<td>47 (32.6)</td>
<td>2.10 (1.22-3.60)</td>
<td>1.86 (1.10-3.15)</td>
</tr>
<tr>
<td>Stroke</td>
<td>101</td>
<td>34 (33.7)</td>
<td>2.10 (1.25-3.53)</td>
<td>2.25 (1.25-4.03)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

COMMENT

Surgical treatment of valvular heart disease is an increasingly common cardiac intervention and as a result, the number of patients at risk of developing PVE is growing. In addition, changes in health care delivery may influence the epidemiology of PVE. The current study, representing the largest study of PVE to date, offers several important insights regarding this disease in the current era.

Prosthetic valve endocarditis accounted for over 20% of all IE cases in this prospective, multicenter, international registry, reflecting a considerably higher proportion of IE compared with earlier reports but similar to the findings of a recent 1-year survey of IE in France. An increased sensitivity of diagnostic modalities, including use of the Duke criteria for all cases and transesophageal echocardiography in 84% of cases, likely enhanced the detection of PVE.

Also, in contrast to previous estimates, we found that S aureus, rather than coagulase-negative staphylococcal infection, was the most common causative microorganism for PVE. In studies of predominantly NVIE, S aureus has been similarly found to be the most common cause of NVIE, and a strong association between an increase in S aureus IE and health care contact has been noted. However, few data regarding health care–associated PVE, aside from analyses of early PVE, have been reported and have generally been limited to small sample sizes and prospective, single-center experiences.

In 1993, an association between nosocomial bacteremia and new PVE in 18 patients was described. Although one third of new endocarditis cases were attributable to intravascular devices, the study was performed before routine diagnostic use of transesophageal echocardiography for evaluating staphylococcal bacteremia. More recently, among 50 cases of late-onset PVE at a single Spanish center, increases in staphylococcal infection and late, hospital-acquired PVE increased were observed.

A causal relationship between health care contact and PVE has been inferred and well described for PVE occurring within 60 days of valve implantation. Initial reports estimated that early PVE accounted for approximately 35% to 50% of all cases of PVE and noted its association with gram-positive microorganisms (particularly coagulase-negative staphylococci and S aureus) presumed to be nosocomial in origin. Early PVE accounted for only 14% of all PVE cases in the ICE-PCS cohort but continued to be associated with an extremely high mortality rate. This lower rate of early PVE was similar to other recent reports and may be related to a number of factors, including improvements in surgical techniques, hygiene, and infection control.

The current study demonstrates that health care–associated PVE beyond the early period, representing the majority of health care–associated infection, significantly influences the epidemiology of PVE. In a previous investigation, Calderwood et al reported that the cumulative hazard of developing PVE was

CONTEMPORARY CLINICAL PROFILE AND OUTCOME OF PROSTHETIC VALVE ENDOCARDITIS

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highest within the initial 12 months after valve replacement surgery, influenced by an increased incidence of coagulase-negative staphylococcal infection from 2 to 12 months after valve implantation. Our results confirm that the first year after implantation is a vulnerable period for prosthetic valve infection with both 𝑆 𝑎𝑢𝑟𝑒𝑢𝑠 and coagulase-negative staphylococci. Possible explanations for the time course of health care-associated PVE include greater exposure to health care contact and lack of complete endothelialization of the prosthetic valve early after implantation.

Although PVE was diagnosed promptly and treated commonly with surgical intervention, the morbidity and in-hospital mortality rates were very high. *Staphylococcus aureus* and health care–associated PVE were found to be independently predictive of in-hospital mortality. These results confirm earlier studies that reported a significant association between *S aureus* infection and mortality in both native and prosthetic valve IE and adds prognostic significance to its high prevalence in this study. Prosthetic valve endocarditis occurring in association with health care contact may represent a composite of prognostic factors, such as virulence of causative organism and host factors (eg, end-stage renal disease or other conditions requiring intravascular catheter access) and emphasizes the need for preventive strategies, particularly those related to intravascular catheter access, to reduce this potential causative factor.

The strongest predictors of mortality were well-recognized complications of PVE: persistent bacteremia, heart failure, intracardiac abscesses, and stroke. Persistent bacteremia, as well as health care–associated infection, has been found to be independently associated with *S aureus* IE. These serious complications may be evident early in the course of the disease and are common indications for surgical intervention. Heart failure, one of the strongest predictors of in-hospital mortality in the current study, has been found to predict 6-month mortality in NVIE and may identify a subgroup of patients for whom cardiac surgery is associated with a significant survival benefit. Our previous study demonstrated that hospital survival rates were similar between complicated PVE treated with surgery and uncomplicated PVE after adjustment for those characteristics associated with surgical intervention, but additional studies are needed to define more clearly the role, timing, and effect of surgery in PVE.

Although the ICE-PCS study design was a large, prospective, multinational registry of definite IE cases, this investigation has certain limitations. This is an observational study involving centers with voluntary participation and thus, population sampling was not obtained, limiting any epidemiological inferences. Specifically, because this cohort only included patients with definite IE and not patients with normal prosthetic valves, we were unable to evaluate risk factors for developing PVE. The definition of nosocomial health care–associated infection, although previously validated as similar to nosocomial bloodstream infections with regard to source of infection, microbiology, antibiotic susceptibility, and prognosis, may be imprecise, particularly regarding recent hospitalization as the presumed source of infection. Because each geographic region was represented by a few centers, regional characterization was based only on those participating centers. Finally, the primary end point of mortality was assessed at hospital discharge, and thus, does not reflect PVE outcome at a specific time interval from diagnosis.

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Days Since Initial Hospitalization</th>
<th>Mortality, Proportion</th>
<th>Log-Rank</th>
<th>HR; 1.54 (95% CI, 1.07-2.21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Care–Associated Infection</td>
<td>199</td>
<td>183</td>
<td>147</td>
<td>114</td>
</tr>
<tr>
<td>Community-Acquired Infection</td>
<td>346</td>
<td>325</td>
<td>267</td>
<td>197</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio; CI, confidence interval; PVE, prosthetic valve endocarditis.
In conclusion, PVE accounts for a high percentage of all cases of IE in many regions of the world. Staphylo-
coccus aureus is now the leading cause of PVE. Health care–associated infec-
tion significantly influences the clinical characteristics and outcome of PVE.

Despite prompt diagnosis and the common use of surgical treatment in PVE,
morbidity and mortality remain high, emphasizing the need for further stud-
ies of preventive and therapeutic strategies for this serious disease.

Author Contributions: Dr Wang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Wang, Athan, Pappas, Fowler, Corey, Cabell

Acquisition of data: Athan, Fowler, Oloaia, Paré, Almirante, Muñoz, Rizzi, Naber, Logar, Taltevin, Iarussi, Selton-Sykes, Jones, Cabell

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REFERENCES


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