Brief report

Infective Endocarditis in Octogenarian Patients

Daniel López-Wolf, a Isidre Vilacosta, b, * José A. San Román, c Cristina Fernández, d Cristina Sarriá, e Javier López, f Ana Revilla, f and Rocio Manchado d

a Servicio de Medicina Interna, Hospital Universitario Clínico San Carlos, Madrid, Spain
b Instituto Cardiovascular, Hospital Universitario Clínico San Carlos, Madrid, Spain
c Instituto de Ciencias del Corazón, Hospital Clínico Universitario, Valladolid, Spain
d Servicio de Medicina Preventiva, Hospital Universitario Clínico San Carlos, Madrid, Spain
e Instituto Cardiovascular, Hospital Universitario Clínico San Carlos, Madrid, Spain
f Servicio de Medicina Interna, Hospital La Princesa, Madrid, Spain

ARTICLE INFO

Article history:
Received 27 May 2010
Accepted 31 May 2010
Available online 15 March 2011

Keywords:
Endocarditis
Aging
Echocardiography
Prognosis
Mortality

ABSTRACT

Our aims were to investigate the clinical features and prognosis of endocarditis in octogenarian patients (aged > 79 years) and in comparison with those in younger elderly patients (aged 65-79 years) and young patients (aged < 65 years). Octogenarian subjects more frequently were male and had a community-acquired infection, mitral valve disease, and chronic anemia. Their clinical course was more insidious and benign: they presented less often with fever or new heart murmurs. When heart failure was present, it tended to be less severe. The most frequently isolated microorganisms were streptococci. The detection rate for vegetation on transesophageal echocardiography was lower in octogenarians. Octogenarians had shorter periods of hospitalization, needed surgery less frequently, and had lower mortality. Mortality in those undergoing surgery was not higher in elderly patients. Age was not an independent predictor of in-hospital mortality.

Endocarditis infecciosa en pacientes octogenarios

RESUMEN

Nuestro objetivo es valorar las manifestaciones clínicas y pronóstico de la endocarditis en pacientes octogenarios (edad > 79 años) comparándolos con ancianos de menor edad (65-79 años) y pacientes jóvenes (edad < 65 años). Los octogenarios fueron con mayor frecuencia varones, con infección adquirida en la comunidad, afecición mitral y anemia crónica. Su cuadro clínico fue más insidioso y benigno y tuvieron con menor frecuencia fiebre y nuevos soplos. En los casos de insuficiencia cardiaca, esta tendió a ser de menor gravedad. Los estreptococos fueron los microorganismos más frecuentemente aislados. La tasa de detección de vegetaciones mediante ecocardiografía transesofágica fue menor entre octogenarios. Los octogenarios tuvieron una estancia hospitalaria más corta, necesitaron cirugía con menos frecuencia y su mortalidad fue menor. La mortalidad en pacientes operados no fue mayor en los ancianos. La edad no fue factor predictor independiente de mortalidad intrahospitalaria.

INTRODUCTION

One of the most remarkable changes in the epidemiology of infective endocarditis (IE) in developed countries over the last decades is the increasing proportion of elderly patients with this disease. The aim of this large prospective study was to define the current clinical presentation, predisposing risk factors, microbiological agents, echocardiographic findings, and clinical outcome of octogenarian patients (80 years or older) with IE as compared with younger persons.

METHODS

We prospectively recruited all episodes of possible or definitive IE diagnosed consecutively at four tertiary centers between 1996 and 2006, according to the Duke criteria (until 2000) or the modified Duke criteria (2001-2006). All episodes (n = 618; 582 patients; 401 men; mean age 57 ± 16 years, range: 12-93) were classified in 3 groups according to the patients age for comparative analysis: group I: < 65 years, n = 350 episodes (56.6%), 247 male; group II: 65-79 years, n = 234 episodes (37.9%), 134 male; and group III (octogenarians): ≥ 79 years, n = 34 episodes (5.5%), 20 male.

All patients underwent transthoracic (TEE) echocardiography. The morphology of vegetations was analyzed by TEE. Surgery in the active phase was performed when any of the following occurred: heart failure unresponsive to
medical treatment, septic shock, persistent signs of infection, fungal endocarditis, and recurrent systemic embolism despite appropriate antibiotic therapy.

The comparison of qualitative variables between all 3 age groups was performed using the likelihood ratio test. We also compared groups II and III separately with the $\chi^2$ test and Fishers exact test when appropriate. Multivariable logistic regression analysis was performed to determine independent predictors of need for cardiac surgery and in-hospital death regardless of its cause. Variables included in the model were those with $P$ values <.05 in the univariable analysis and others selected a priori due to their clinical relevance. For all tests, a $P$ value <.05 was considered statistically significant.

RESULTS

The epidemiologic features, the localization of IE, the presence of previous heart disease, the comorbidity, and the portal of entry of the infection are summarized in Table 1. The proportion of community-acquired episodes of IE was higher in group III. Among predisposing heart conditions, degenerative valvular heart disease was more frequent in octogenarians, while the presence of a prosthetic valve was more common in group II. Most clinical features and laboratory findings were similar between the 3 groups (Table 1). There were no differences in the span of time between onset of symptoms and admission. Nonetheless, longer periods of time (>3 months) were more common in octogenarians than in group II (23.5% vs 11.4% of patients, $P < .07$). Elderly patients presented with fever less frequently. The presence of a new heart murmur was less frequent in octogenarians. No statistically significant differences between groups were found in the frequency of heart failure. Nonetheless, New York Heart Association (NYHA) classes III-IV were less common in octogenarians, while NYHA class I had a tendency to be more frequent in this oldest group.

The most frequently isolated pathogens (40.6%) were Staphylococci (Table 1). The proportion of Streptococcus bovis was higher in groups II and III than in group I ($P < .01$), whereas Staphylococcus aureus was more common in young patients. Staphylococci were more frequent in nosocomial IE episodes than in community-acquired IE cases (51.5% vs 34.5%; $P < .001$). Streptococci predominated in community-acquired episodes (27.5% vs 11.5%; $P < .001$).

Echocardiographic data are displayed in Table 2. In all groups, TEE was superior to TTE in the vegetation detection rate. The likelihood of TTE to detect vegetations was higher in group I than in the elderly groups (II-III), whereas that of TEE was lower in octogenarians than in the other 2 groups. Vegetations and abscesses were less frequent in octogenarians than in the other patients.

Clinical complications of IE and in-hospital outcome are shown in Table 2. Octogenarians underwent surgery less frequently than the other groups. In-hospital mortality was higher in patients from group II; mortality in octogenarians had a tendency to be lower than in patients from group II. No statistical differences were found between groups concerning the cause of death. In-hospital mortality after cardiac surgery was similar in all groups.

The multivariable analysis disclosed young age, pacemaker infection, prosthetic valve infection, periannular complications, and left heart failure as factors independently associated with the need for surgery. The variables associated with mortality were septic shock, left heart failure, leukocyte count, and renal failure. According to the analysis, age was not an independent predictor of mortality.

DISCUSSION

It is evident that the elderly in industrialized countries are at special risk for IE. This study is one of the largest published prospective series on IE in elderly patients (≥65 years) and the only series specifically dealing with a group of very old patients, the octogenarians.

In accordance with previous studies, males predominated over females. This was also true in octogenarians, an age group where there is usually a greater proportion of women than men. Octogenarians showed a paradoxical decrease of nosocomial infections compared to patients from group II. This might be partially explained by the lower frequency of prosthetic valves found in octogenarians and perhaps to a tendency to perform less invasive procedures in the late elderly. In many series, prosthetic valve endocarditis is more frequent in the elderly. In our study, prosthetic IE predominated in group II and all prosthetic valvular infections in octogenarians were on biologic prosthetic valves. In these very old patients the most frequently involved type of valve was the native mitral valve and the most common predisposing heart condition was degenerative valvular disease. Very old patients usually have thickened and calcified valve leaflets and mitral annulus calcification that may serve as a nidus for bacteria during transient bacteremias. A urinary presumed portal of entry was more frequent in octogenarians, whereas an intestinal portal of entry was more common in group II. The increasing rate of urinary and intestinal procedures, and the high incidence of colonic disease in these populations could explain the results.

Endocarditis had a more insidious and benign course in octogenarians. As observed in other series, fever occurred less frequently in the elderly groups (II-III). In octogenarian patients, the time from onset of symptoms to diagnosis tended to be longer and the appearance of a new heart murmur was less common. Both the absence of fever and of a new cardiac murmur might contribute to a longer delay until the diagnosis of IE is made in this group. In addition, heart failure in octogenarians, when present, had a tendency to be less severe and there was only 1 case of septic shock in this group. All of these particular clinical features might be explained by the less virulent microbiological profile (streptococci), and the lower frequency of prosthetic valve infections seen in octogenarians.

Vegetation detection rate by TTE was higher in group I than in the other groups. The usually worse transthoracic window commonly seen in elderly patients may justify this result. Our study confirms that the sensitivity of TEE in detecting vegetative lesions is superior to that of TTE, also in the elderly. Nonetheless, the sensitivity of TEE in the detection of vegetations was lower in group III. TEE has a key role in the evaluation of patients with prosthetic valve endocarditis and in the detection of periannular complications, and neither of these conditions was frequently present in octogenarians. In addition, valve fibrosis and calcification is very frequent in octogenarians, and in some cases differentiating vegetations from degenerative valvular lesions can be a difficult task, even by TEE. Thus, the decreased sensitivity of TTE in the elderly (groups II-III) could be considered mainly a “chest” problem, whereas the decreased sensitivity of TEE in octogenarians is rather a “valve” problem. Finally, patients from group I had a higher frequency of moderate to severe valvular regurgitation. Not surprisingly, the frequency of severe heart failure (NYHA classes III-IV) was more common in the young.

Among octogenarians, the length of hospitalization was shorter and the need for surgery was lower. Even though they were operated less frequently, mortality rate was not higher. In fact, the most important finding of this large series is that age was not a predictor of in-hospital mortality according to multivariable
analysis. Some investigators have observed that age was associated with higher mortality rates, whereas others have not been able to show that age, per se, is a prognostic factor. These contradictory results might be explained by the small number of elderly patients included in many studies, the use of different definitions of elderly, and the fact that TEE was not systematically performed in all series. The present study lacks these limitations. Surgery in elderly patients (groups II-III) appears as an adequate alternative to medical treatment. Mortality in operated patients was not higher in the older age groups. In fact, mortality in

Table 1
Epidemiologic Features, Infective Endocarditis Localization, Underlying Cardiac Disease, Comorbidity, Portal of Entry, Clinical Presentation, In-Hospital Laboratory Findings, and Microbiology

<table>
<thead>
<tr>
<th>Valid cases No.</th>
<th>All episodes</th>
<th>Group I (&lt;65 y) (n = 350)</th>
<th>Group II (65-79 y) (n = 234)</th>
<th>Group III (&gt;79 y) (n = 34)</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
</table>

### Epidemiologic features and IE localization

#### Male sex
618 401 (64.9) 247 (70.6) 134 (57.3) 20 (58.8) .009 .86

#### Community origin
611 403 (66) 239 (69.5) 136 (58.4) 28 (82.4) .002 .007

#### Native valves
618 364 (58.9) 230 (65.7) 115 (49.5) 19 (55.9) <.001 .46

#### Mitral
618 141 (22.8) 72 (20.6) 57 (24.4) 12 (35.3) .13 .17

#### Aortic
618 117 (18.9) 70 (20.0) 44 (18.8) 3 (8.8) .23 .15

#### Mitro-aortic
618 58 (9.4) 40 (11.4) 14 (6.0) 4 (11.8) .07 .26

#### Right valves
618 48 (7.8) 48 (13.7) 0 (0) 0 (0) <.001 -.01

#### Prosthetic valves
618 186 (30.1) 86 (24.6) 92 (39.3) 8 (23.5) <.001 .09

#### Mitral
618 84 (13.6) 37 (10.6) 43 (18.4) 4 (11.8) .03 .34

#### Aortic
618 71 (11.5) 32 (9.1) 36 (15.4) 3 (8.8) .07 .44

#### Mitro-aortic
618 31 (5.0) 17 (4.9) 13 (5.6) 1 (2.9) .77 .99

#### Bioprosthetic
618 35 (18.8) 6 (7.0) 21 (22.8) 8 (100) <.001 <.001

#### Mechanical
618 151 (81.2) 80 (93) 71 (77.2) 0 (0) <.001 <.001

### Predisposing cardiac conditions

#### Rheumatic valve disease
614 51 (8.3) 27 (7.8) 22 (9.4) 2 (5.9) .67 .48

#### Prosthetic valve
614 217 (35.3) 104 (30.0) 103 (44.2) 10 (29.4) <.002 .10

#### Degenerative valve
614 52 (8.5) 13 (3.7) 29 (12.4) 10 (29.4) .67 .48

#### Congenital heart defect
614 31 (5.0) 10 (2.9) 21 (9.1) 0 (0) <.001 <.001

#### None
614 176 (28.7) 129 (37.2) 45 (19.3) 2 (5.9) <.001 .06

### Comorbidity

#### Chronic anaemia
614 100 (16.3) 47 (13.5) 43 (18.4) 2 (5.9) <.001 .55

#### Diabetes
614 111 (18.1) 38 (11.0) 65 (27.8) 22 (64.7) <.001 .10

#### COPD
613 44 (7.2) 16 (4.6) 25 (10.7) 3 (9.1) .03 .78

#### Chronic renal failure
613 54 (8.8) 23 (6.6) 28 (12.0) 3 (9.1) .09 .62

#### Chronic renal failure
613 44 (7.2) 16 (4.6) 25 (10.7) 3 (9.1) .03 .78

#### Community origin
611 403 (66) 239 (65.7) 136 (58.4) 28 (82.4) <.001 .007

### Portal of entry

#### Unknown
617 270 (43.8) 153 (43.8) 99 (42.3) 18 (52.9) .51 .24

#### Dental
617 47 (7.6) 29 (8.3) 18 (7.7) 7 (20.6) .07 .44

#### Intestinal
617 18 (2.9) 11 (3.2) 7 (3.0) 4 (11.8) <.001 .60

#### Urinary
617 25 (4.1) 9 (2.6) 15 (6.3) 3 (8.8) .08 .48

#### Local infection
617 58 (9.4) 31 (8.9) 25 (10.7) 2 (5.9) .57 .35

### Clinical manifestations up to the moment of admission

#### Fever and malaise
615 523 (85.0) 307 (88.2) 189 (80.8) 27 (81.8) .04 .89

#### Constitutional syndrome
615 228 (37.1) 128 (36.9) 87 (37.2) 23 (68.8) <.001 .91

#### New murmur
616 308 (50.0) 202 (57.9) 98 (42.1) 3 (9.1) <.001 .46

#### Heart failure
616 227 (36.9) 124 (35.5) 93 (39.9) 10 (29.4) <.001 .26

#### NYHA Class I
598 311 (52.0) 176 (52.4) 113 (49.6) 22 (64.7) <.001 .10

#### NYHA Class II
598 114 (19.1) 67 (19.9) 41 (18.0) 6 (17.6) <.001 .96

#### NYHA Class III and IV
598 173 (28.9) 93 (27.7) 74 (32.5) 6 (17.6) <.001 .94

#### Chest X-Ray signs of LHF
612 195 (31.9) 107 (30.7) 82 (35.5) 6 (18.2) <.001 .10

#### Pulmonary embolism
616 42 (6.8) 17 (5.0) 25 (10.7) 2 (5.9) <.001 <.001

#### Abdominal pain
617 73 (11.8) 52 (15.3) 19 (8.1) 5 (14.7) <.001 .04

#### Septic shock
617 35 (5.7) 22 (6.3) 13 (5.6) 0 (0) <.001 .06

#### Sepsis
613 63 (10.3) 43 (12.4) 17 (7.3) 3 (8.8) .12 .76

#### Renal failure
617 89 (14.4) 43 (12.3) 42 (17.9) 4 (11.8) .16 .37

#### Haemorrhagic stroke
613 19 (3.1) 17 (4.9) 2 (9.0) 0 (0) <.001 .46

#### Ischaemic stroke
613 62 (10.1) 37 (10.7) 22 (9.4) 3 (8.8) .85 .91

### In-hospital laboratory findings

#### Leukocytosis >10.000/μL
568 384 (67.6) 212 (67.7) 156 (69.6) 16 (51.6) .15 .05

#### Hemoglobin <12 g/dL
606 509 (84.0) 284 (83.0) 197 (85.7) 28 (82.4) .68 .61

#### C-reactive protein >5 mg/L
82 56 (68.3) 24 (70.6) 24 (66.7) 4 (11.8) <.001 .99

#### ESR >20 mm/h
393 373 (94.9) 215 (95.1) 136 (95.8) 22 (88.0) .15 .16

#### Serum creatinine >2 mg/dL
520 339 (65.2) 84 (31.1) 91 (41.7) 6 (18.8) .006 .01

#### RF >20 IU/mL
129 77 (59.7) 39 (57.4) 34 (69.4) 4 (33.3) .06 .02
nonoperated patients was higher in group II. Surgical treatment has been associated with good prognosis in other series. Previous series with restrictive use of surgery in the aged led to a higher mortality in this group, at the expense of nonoperated patients. Potential limitations: this is an observational study; a referral bias in the inclusion of patients could be present; underdiagnosis of IE in octogenarian patients could possibly exist; due to the low number of patients in group III, some conclusions about IE in this age group may not be definitive.

<table>
<thead>
<tr>
<th>Table 1 (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valid cases No.</td>
</tr>
<tr>
<td>Microbiology</td>
</tr>
<tr>
<td>Streptococcus viridans</td>
</tr>
<tr>
<td>Streptococcus bovis</td>
</tr>
<tr>
<td>Other streptococci</td>
</tr>
<tr>
<td>Enterococci</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
</tr>
<tr>
<td>Gram negative bacilli</td>
</tr>
<tr>
<td>Anaerobic</td>
</tr>
<tr>
<td>Polymicrobial</td>
</tr>
<tr>
<td>Fungi</td>
</tr>
<tr>
<td>Negative</td>
</tr>
</tbody>
</table>

<p>| Table 2 |</p>
<table>
<thead>
<tr>
<th>Echocardiographic Findings and Pathologic Confirmation, In-Hospital Complications and Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
</tr>
<tr>
<td>Valid cases No.</td>
</tr>
<tr>
<td>Valvular damage detected by echocardiography</td>
</tr>
<tr>
<td>Vegetations detected by TTE or TEE</td>
</tr>
<tr>
<td>Vegetations detected by TTE</td>
</tr>
<tr>
<td>Vegetations detected by TEE</td>
</tr>
<tr>
<td>Abscess</td>
</tr>
<tr>
<td>Pseudoaneurysm</td>
</tr>
<tr>
<td>Fistula</td>
</tr>
<tr>
<td>Regurgitation (moderate or severe)</td>
</tr>
<tr>
<td>Vegetations length &gt;10mm</td>
</tr>
<tr>
<td>Vegetations length (mm)</td>
</tr>
</tbody>
</table>

| Detection of vegetations by means of echocardiography in episodes with histologic confirmation of endocarditis (echocardiographic sensitivity) |
| | | | | | |
| Number of vegetations confirmed by pathologic findings | 234 (37.9) | 148 (42.3) | 80 (34.2) | 6 (17.6) | .10 | .04 |
| Vegetations detected by TTE or TEE | 223 (95.3) | 141 (95.3) | 77 (96.3) | 5 (83.3) | .001 | .45 |
| Vegetations detected by TTE | 130 (55.6) | 91 (61.5) | 37 (46.2) | 2 (33.3) | .001 | .45 |
| Vegetations detected by TEE | 208 (88.9) | 132 (89.2) | 72 (93.7) | 4 (66.7) | .001 | .45 |

| In-hospital complications and outcome |
| Mean hospital stay (days) | 543 | 43 ± 28 | 41 ± 26 | 48 ± 30 | 57 ± 16 | .003 | .04 |
| Embolism (all localizations) | 543 | 145 (23.5) | 91 (26) | 50 (21.4) | 4 (11.8) | .001 | .19 |
| CNS embolism | 618 | 107 (17.3) | 66 (18.9) | 39 (16.7) | 2 (5.9) | .10 | .10 |
| Spleen embolism | 618 | 42 (6.8) | 26 (7.4) | 14 (6.0) | 2 (5.9) | .77 | .92 |
| Persistent infection | 352 | 80 (22.7) | 47 (20.8) | 32 (28.3) | 1 (7.7) | .11 | .08 |
| Septic shock | 290 | 30 (10.3) | 15 (8.0) | 14 (15.2) | 1 (9.1) | .10 | .40 |
| Heart failure | 618 | 99 (16) | 45 (12.9) | 47 (20.1) | 7 (20.6) | .05 | .95 |
| Renal failure | 618 | 153 (24.8) | 75 (21.4) | 70 (29.9) | 8 (23.5) | .07 | .44 |
| Surgery | 618 | 336 (54.4) | 204 (58.3) | 126 (53.8) | 6 (17.6) | <.001 | <.001 |
| Overall mortality | 618 | 177 (28.6) | 86 (24.6) | 84 (35.9) | 7 (20.6) | .07 | .08 |
| Mortality in operated patients | 336 | 88 (26.2) | 49 (24.0) | 38 (20.2) | 1 (16.7) | .40 | .67 |
| Mortality in non operated patients | 282 | 89 (31.6) | 37 (23.5) | 46 (24.2) | 5 (17.4) | .007 | .04 |

CNS: central nervous system; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography. Express data in N (%) or mean ± standard deviation.

* P value of the test comparing the three age groups.
* P value of the test comparing groups II and III.
* Not calculated due to the small number of patients in group III.
* P value of the test comparing operated and non operated patients.
CONFLICTS OF INTEREST

None declared.

REFERENCES