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Brief report

Infective Endocarditis in Octogenarian Patients

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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.

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Endocarditis infecciosa en pacientes octogenarios

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RESUMEN

Nuestro objetivo es valorar las manifestaciones clínicas y el 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, afección 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.

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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.[1] 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 (TTE) and transesophageal (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

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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 χ^2 test and Fisher's 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.[2-5] 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.[6]

Endocarditis had a more insidious and benign course in octogenarians. As observed in other series,[2,3] 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.[3] 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,[2,4-6] whereas others have not been able to show that age, *per se*, is a prognostic factor.[3,7] These contradictory results might be explained by the small number of elderly patients included in many studies,[2-4] 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

		No. (%)					
	Valid cases No.	All episodes	Group I (<65 y) (n = 350)	Group II (65-79 y) (n = 234)	Group III (>79 y) (n = 34)	P^a	P^b
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	-
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
Pacemaker	618	49 (7.9)	19 (5.4)	26 (11.1)	4 (11.8)	.03	.99
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)	<.001	.02
Congenital heart defect	614	31 (5.0)	30 (8.6)	1 (.4)	0 (0)	<.001	.60
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)	10 (30.3)	.04	.11
Diabetes	614	111 (18.1)	38 (11.0)	65 (27.8)	8 (24.2)	<.001	.67
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
Cancer	613	39 (6.4)	15 (4.3)	23 (9.8)	1 (3.0)	.02	.15
Immunodepression	613	78 (12.7)	56 (16.2)	18 (7.7)	4 (12.1)	.008	.41
Drug abuse	618	61 (9.9)	60 (17.1)	1 (.4)	0 (0)	<.001	.60
HIV	618	43 (7.0)	41 (11.7)	2 (.9)	0 (0)	<.001	.46
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)	15 (6.4)	3 (8.8)	.67	.61
Intestinal	617	18 (2.9)	6 (1.7)	11 (4.7)	1 (2.9)	.12	.63
Urinary	617	25 (4.1)	9 (2.6)	13 (5.6)	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)	13 (38.2)	.99	.91
New murmur	616	308 (50.0)	202 (57.9)	98 (42.1)	8 (23.5)	<.001	.04
Heart failure	616	227 (36.9)	124 (35.5)	93 (39.9)	10 (29.4)	.36	.24
NYHA Class I	598	311 (52.0)	176 (52.4)	113 (49.6)	22 (64.7)	.25	.10
NYHA Class II	598	114 (19.1)	67 (19.9)	41 (18.0)	6 (17.6)	.83	.96
NYHA Class III and IV	598	173 (28.9)	93 (27.7)	74 (32.5)	6 (17.6)	.14	.08
Chest X-Ray *signs of LHF*	612	195 (31.9)	107 (30.7)	82 (35.5)	6 (18.2)	.15	.10
Pulmonary embolism	616	42 (6.8)	37 (10.6)	3 (1.3)	2 (5.9)	<.001	.26
Abdominal pain	617	73 (11.8)	52 (14.9)	19 (8.1)	2 (5.9)	.02	.64
Septic shock	617	35 (5.7)	22 (6.3)	13 (5.6)	0 (0)	.12	.06
Splenomegaly	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)	.004	.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)	8 (66.7)	.93	.99
ESR > 20 mm/h	393	373 (94.9)	215 (95.1)	136 (95.8)	22 (88.0)	.35	.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

Table 1 (*continued*)

	Valid cases No.	No. (%) All episodes	Group I (<65 y) (n = 350)	Group II (65-79 y) (n = 234)	Group III (>79 y) (n = 34)	P[a]	P[b]
Microbiology							
Streptococcus viridans	618	79 (12.8)	49 (14.0)	26 (11.1)	4 (11.8)	.58	.91
Streptococcus bovis	618	21 (3.4)	6 (1.7)	11 (4.7)	4 (11.8)	.01	.13
Other streptococci	618	35 (5.7)	22 (6.3)	9 (3.8)	4 (11.8)	.16	.08
Enterococci	618	44 (7.1)	15 (4.3)	27 (11.5)	2 (5.9)	.004	.29
Staphylococcus aureus	618	114 (23.3)	104 (29.7)	36 (15.4)	4 (1.8)	<.001	.58
Coagulase-negative staphylococci	618	107 (17.3)	45 (12.9)	55 (23.5)	7 (20.6)	.004	.71
Gram negative bacilli	618	28 (4.5)	13 (3.7)	14 (6.0)	1 (2.9)	.40	.44
Anaerobic	618	9 (1.5)	5 (1.4)	4 (1.7)	0 (0)	.58	.30
Polymicrobial	618	41 (6.6)	23 (6.6)	18 (7.7)	0 (0)	.08	.02
Fungi	618	7 (1.1)	5 (1.4)	2 (.9)	0 (0)	.55	.46
Negative	618	78 (12.6)	51 (14.6)	23 (9.8)	4 (11.8)	.23	.73

COPD, chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; HIV, human immunodeficiency virus; IE, infective endocarditis; LHF, left heart failure; NYHA: New York Heart Association; RF: rheumatoid factor.
[a] *P* value of the test comparing the three age groups.
[b] *P* value of the test comparing groups II and III.

nonoperated patients was higher in group II. Surgical treatment has been associated with good prognosis in other series.[6] Previous series with restrictive use of surgery in the aged led to a higher mortality in this group, at the expense of nonoperated patients.[2,4]

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 2
Echocardiographic Findings and Pathologic Confirmation, in-Hospital Complications and Outcome

	Valid cases No.	No. (%) All episodes	Group I (<65 years) (n = 350)	Group II (65-79 years) (n = 234)	Group III (>79 years) (n = 34)	P[a]	P[b]
Valvular damage detected by echocardiography							
Vegetations detected by TTE or TEE	618	503 (81.4)	295 (84.3)	185 (79.1)	23 (67.6)	.04	.14
Vegetations detected by TTE	618	280 (45.3)	190 (54.3)	80 (34.2)	10 (29.4)	<.001	.58
Vegetations detected by TEE	618	459 (74.3)	263 (75.1)	180 (76.9)	16 (47.1)	.002	<.001
Abscess	618	131 (21.2)	76 (21.7)	54 (23.1)	1 (2.9)	.006	.007
Pseudoaneurysm	618	101 (16.3)	65 (18.6)	32 (13.7)	4 (11.8)	.22	.76
Fistula	618	31 (5.0)	22 (6.3)	9 (3.8)	0 (0)	.07	.12
Regurgitation (moderate or severe)	618	409 (66.2)	249 (71.1)	140 (59.8)	20 (58.8)	.01	.91
Vegetations length > 10mm	618	150 (24.3)	81 (23.1)	63 (26.9)	6 (17.6)	.37	.35
Vegetations length (mm)	405	139 ± 7.2	141 ± 7.1	137 ± 7.6	135 ± 5.7	.84	.99
Detection of vegetations by means of echocardiography in episodes with histological confirmation of endocardtis (echocardiographic sensitivity)							
Number of vegetations confirmed by pathologic findings		234 (37.9)	148 (42.3)	80 (34.2)	6 (17.6)	.10	[c]
Vegetations detected by TTE or TEE		223 (95.3)	141 (95.3)	77 (96.3)	5 (83.3)	[c]	[c]
Vegetations detected by TTE		130 (55.6)	91 (61.5)	37 (46.2)	2 (33.3)	[c]	[c]
Vegetations detected by TEE		208 (88.9)	132 (89.2)	72 (93.7)	4 (66.7)	[c]	[c]
In-hospital complications and outcome							
Mean hospital stay (days)	543	43 ± 28	41 ± 26	48 ± 30	35 ± 16	.003	.04
Embolism (all localizations)	618	145 (23.5)	91 (26)	50 (21.4)	4 (11.8)	.90	.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)	.31	.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 (30.2)	1 (16.7)	.40	.67
Mortality in non operated patients	282	89 (31.6)	37 (25.3)	46 (42.6)	6 (21.4)	.007	.04
P[d]		.14	.78	.05	.79		

CNS: central nervous system; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.
Express data in N (%) or mean ± standard deviation.
[a] *P* value of the test comparing the three age groups.
[b] *P* value of the test comparing groups II and III.
[c] Not calculated due to the small number of patients in group III.
[d] *P* value of the test comparing operated and non operated patients.

CONFLICTS OF INTEREST

None declared.

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