

Infective Endocarditis: Clinical Features in Young and Elderly Patients

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The elderly constitute an increasing percentage of patients with infective endocarditis. The disease manifestations and outcomes in 53 episodes of endocarditis in patients over the age of 60 were reviewed and compared with 55 episodes of endocarditis in patients less than 40 years of age and 46 episodes of endocarditis in patients aged 40 to 60. The percentage of cases caused by staphylococci and streptococci were roughly equal in all groups. Enterococci, *Streptococcus bovis*, and coagulase-negative staphylococci were more common in the elderly. In the elderly, invasive vascular procedures were the most common source of infection. Endocarditis acquired nosocomially accounted for 23 percent of all episodes in older patients. The elderly reported fewer symptoms and showed a diminished febrile response. Errors in diagnosis were noted in 68 percent of elderly patients, and a delay in initiating appropriate therapy was more common in this age group. The mortality rate was significantly higher in the elderly (45.3 percent) than in the middle-aged (32.6 percent) and young (9.1 percent). Endocarditis in elderly patients is often nosocomially acquired, is difficult to diagnose, and is associated with a higher mortality than noted in younger patients.

Infective endocarditis appears to be increasing among the elderly [1-3]. Prior to the 1940s, less than 10 percent of cases were described in patients over 60 years of age [1]. Reviews of patients treated in the 1940s and 1950s showed that about 20 percent of cases of endocarditis were in patients over age 60 [4,5], and this percentage increased in the 1960s and 1970s [6-8]. Watanakunakorn et al [7] noted that 42 percent of the cases of *Staphylococcus aureus* endocarditis were in patients over 60 years of age, and another recent study found that 55 percent of the cases of endocarditis diagnosed from 1970 to 1977 in a hospital serving as a primary care and referral hospital occurred in those over age 60 [8]. Venezio et al [9], in a study from a community hospital, noted that 43 percent of all cases of endocarditis seen in the 1970s were in patients over the age of 70 [9].

Previous studies have pointed out special problems in the diagnosis of endocarditis in the older age group [10, 11]. The clinical presentation may be atypical and many of the classic findings may not be present. Other studies emphasize the fact that mortality in the elderly is much greater than in younger age groups [7, 12, 13]. However, to date, no study of endocarditis has systematically compared elderly patients and younger patients with regard to symptoms, signs, clinical course, and outcome. This study, using strict case criteria for the definition of endocarditis, as set forth by von Reyn et al [8] and Pelletier and Petersdorf [6], reviews endocarditis in adult patients in three different age groups in order to determine the effects of age on clinical presentation, course of the infection, and outcome.

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PATIENTS AND METHODS

Charts of patients discharged with a diagnosis of infective endocarditis from January 1976 to December 1985 were reviewed. A review was also conducted on charts of patients listed in the records of the Infectious Diseases Division as having possible infective endocarditis. Three hospitals were included: University Hospital, an 800-bed tertiary care referral hospital; the Ann Arbor Veterans Administration Medical Center, a 300-bed veterans facility; and St. Luke's Hospital, a 610-bed community hospital. Criteria for inclusion were based on those set forth by von Reyn et al [8]. Only definite or probable episodes and only those in which the chart was available for review were included in the final analysis of data. Only bacterial endocarditis was studied. Cases in which fungi were identified as the causative microorganism were excluded.

Definite episodes were proved by histology at surgery or necropsy to have an endocardial vegetation. There were 22 episodes proved at necropsy and 67 proved at the time of a cardiac surgery procedure, in which charts were available for review. Of a total of 89 definite episodes, 46 were from University Hospital, 33 were from St. Luke's Hospital, and 10 were from the Veterans Administration Hospital.

Probable episodes were proved by criteria other than necropsy or operation. To be included in this category, patients had to have either: (1) a minimum of two blood cultures performed with growth of the same microorganism in all cultures if two or three sets of blood cultures were obtained or more than 70 percent of cultures positive if four or more sets were done *and* a new or changing murmur or known underlying valvular heart disease with the presence of vascular/embolic phenomena (splinter hemorrhages, Roth's spots, Janeway lesions, Osler's nodes, or petechiae) or (2) intermittently positive blood cultures (less than 70 percent positive) with fever, a new regurgitant murmur, and the presence of vascular/embolic phenomena. Of 65 cases in which charts were available for review, there were 40 episodes with persistently positive blood cultures and new or changing murmurs and 22 episodes with persistently positive blood cultures, valvular disease, and vascular/embolic phenomena. There were three episodes in which the patient met criterion two listed previously. Of these 65 probable episodes, 37 were at University Hospital, 15 were at St. Luke's Hospital, and 13 were at the Veterans Hospital.

Twenty-two further cases were classified as *possible* by von Reyn's [8] criteria but were not included in this analysis. These patients were believed to have endocarditis by the physicians caring for them. However, not enough objective data was available on the chart or necropsy was not performed to enable inclusion in this study.

Where appropriate, data were analyzed using the chi-square test.

RESULTS

Patient Characteristics. There were a total of 154 episodes in 144 patients. The number of episodes in each age group was similar; there were 55 episodes in 52 patients under 40 years of age (36 percent of episodes), 46 episodes in 43 patients 40 to 60 years of age (30

TABLE I Episodes of Endocarditis

	Total Number	Number of Episodes by Age Group (percent)		
		<40	40-60	>60
University Hospital	84	44 (80.0)	21 (45.7)	19 (35.9)
Veterans Hospital	23	3 (5.4)	14 (30.4)	6 (11.3)
St. Luke's Hospital	47	8 (14.6)	11 (23.9)	28 (52.8)
Total episodes	154	55	46	53

TABLE II Microbiology of Infective Endocarditis

	Number of Organisms by Age Group (percent)		
	<40 (n = 55)	40-60 (n = 46)	>60 (n = 53)
Streptococci	24 (43.6)	19 (41.3)	24 (45.3)
Viridans streptococci	16	11	13
Group D enterococci	2	6	7
Group D non-enterococci	1	0	4
Pneumococci	3	0	0
Others (Groups A, B, G)	2	2	1
Staphylococci	23 (41.8)	23 (50.0)	23 (43.4)
Coagulase positive	21	19	15
Coagulase negative	2	4	8
Gram-negative bacilli	7 (12.8)	2 (4.3)	3 (5.7)
Hemophilus	2	1	1
Pseudomonas	5	0	1
Escherichia	0	1	1
Diphtheroids (JK bacillus)	0	1 (2.2)	0
Culture negative (confirmed by pathology)	1 (1.8)	1 (2.2)	2 (3.8)

percent of episodes), and 53 episodes in 49 patients over 60 (34 percent of episodes). Most of the elderly patients were seen at the community hospital and most of the young patients were from the University Hospital (Table I). The middle-aged patients were seen just as frequently at all three institutions. Six patients had two episodes of endocarditis and two additional patients each had three episodes of endocarditis; none of these episodes were a relapse from the original episode. There was a predominance of men; 66 percent of patients over age 60 were men, 76 percent of those aged 40 to 60 were men, and 65 percent of patients under 40 were men.

Microbiology. Staphylococci and streptococci were the organisms isolated most frequently in all age groups (Table II). Overall, 44.2 percent of all episodes of endocarditis were caused by streptococci, and 44.8 percent were caused by staphylococci. Coagulase-positive *S. aureus* was the single most common pathogen; the percentage of *S. aureus* manifesting resistance to methicillin was 0 percent in the over-60 age group, 10.5 percent in those 40 to 60, and 23.8 percent in those less than 40 years of

TABLE III Source of Infection in 154 Episodes of Infective Endocarditis

	Number of Episodes by Age Group (percent)		
	<40	40-60	>60
	(n = 55)	(n = 46)	(n = 53)
Intravenous drug use	28 (50.9)	7 (15.2)	0
Dental procedures	3 (5.4)	7 (15.2)	7 (13.2)
Invasive vascular procedures/intravenous lines	3 (5.4)	1 (2.2)	9 (17.0)
Skin lesions	3 (5.4)	6 (13.0)	6 (11.3)
Urinary tract procedures	0	4 (8.7)	3 (5.7)
Bowel/anorectal lesions	1 (1.8)	1 (2.2)	5 (9.4)
Other (endometrium, bone, lungs)	4 (7.2)	1 (2.2)	0
Unknown	13 (23.6)	19 (41.3)	23 (43.3)

TABLE IV Pre-Existing Endocardial Disease in 154 Episodes of Infective Endocarditis*

	Number of Episodes by Age Group (percent)		
	<40	40-60	>60
	(n = 55)	(n = 46)	(n = 53)
Rheumatic valvular disease	4 (7.3)	7 (15.2)	4 (7.5)
Bicuspid aortic valve	3 (5.4)	2 (4.3)	1 (1.9)
Calcific aortic stenosis	0	0	1 (1.9)
Mitral valve prolapse	5 (9.1)	5 (10.9)	4 (7.6)
Prosthetic device (valve, pacemaker)	5 (9.1)	9 (19.6)	14 (26.4)
Prior endocarditis	4 (7.3)	1 (2.2)	1 (1.9)
Pre-existing murmur, etiology unknown	2 (3.6)	2 (4.3)	5 (9.4)
Other endocardial lesions (thrombus, aneurysm)	0	0	2 (3.8)
None	32 (58.1)	20 (43.5)	21 (39.6)

* Only the primary underlying endocardial abnormality is listed for each episode. Episodes in patients with prosthetic valves are listed under "prosthetic device" regardless of the preceding condition affecting the native valve.

TABLE V Other Pre-Existing Diseases in 154 Episodes of Infective Endocarditis

	Number of Episodes by Age Group* (percent)		
	<40	40-60	>60
	(n = 55)	(n = 46)	(n = 53)
Diabetes mellitus	0	6 (13.0)	8 (15.0)
Coronary artery disease	0	3 (6.5)	10 (18.8)
Chronic pulmonary disease	0	4 (8.6)	11 (20.7)
Chronic renal insufficiency	0	3 (6.5)	7 (13.2)
Malignancy	1 (1.8)	1 (2.1)	3 (5.6)
Alcohol abuse	1 (1.8)	5 (10.8)	3 (5.6)

* Some patients had more than one pre-existing disease.

age, reflecting the high incidence of methicillin-resistant staphylococcal infections in Detroit area drug abusers. Although no age-related differences were noted when staphylococci or streptococci were considered as a whole, certain specific organisms in these genera, namely group D enterococci, group D non-enterococci (all of which were *Streptococcus bovis*), and coagulase-negative staphylococci, were more common in the middle-aged and elderly patients. Four of the five *S. bovis* isolates were in those over 60 years of age. In contrast, all three pneumococcal and five of six *Pseudomonas* isolates were in patients less than 40 years of age. Three cases were positive by histology at necropsy (two of which had gram-positive cocci noted on Gram's stain), but had no pre-mortem cultures of blood performed. One patient had histologically proved culture-negative endocarditis at surgery, with vegetations showing gram-positive cocci. No episodes of polymicrobial endocarditis were noted.

Source of Infection. A probable source of infection was noted in 64 percent of all episodes of endocarditis (Table III). The most common sources in the elderly were invasive vascular procedures (17.0 percent), dental work within the preceding two months (13.2 percent), skin lesions (11.3 percent), and bowel or anorectal sources (9.4 percent). In the patients 40 to 60 years of age, the most common sources for infection were dental work (15.2 percent), intravenous drug abuse (15.2 percent), skin lesions (13 percent), and urinary tract procedures (8.7 percent). Overwhelmingly, the most common source in patients under age 40 was intravenous drug abuse (50.9 percent), whereas urinary tract or vascular procedures and skin or other infections were much less common. More than 40 percent of both middle-aged and elderly patient groups had no identifiable source of infection. The source was unknown in only 23.6 percent of episodes in patients under 40 years of age.

The organisms causing endocarditis varied with the source of infection. *S. aureus* and coagulase-negative staphylococci predominated in endocarditis traced to invasive vascular or skin sources, whereas viridans streptococci were most common in patients who had prior dental work. Enterococci were found most often in those with urinary tract sources, and *S. bovis* was noted primarily in those with pre-existing bowel lesions.

Pre-Existing Endocardial Disease. As shown in Table IV, most patients did not have known predisposing valvular disease prior to the development of endocarditis. This was especially striking in young adults, of whom 58.1 percent had no known underlying endocardial disease. Data shown in Table IV refer to the primary endocardial condition associated with each episode. In all groups, but especially in the elderly, prosthetic valves (or a pacemaker in one patient) were the most common underlying cardiac abnormality. Rheumatic valvular disease was common only in the 40- to 60-year-old group. In the

young, valvular damage due to prior endocarditis was as common as rheumatic valvular disease. In all age groups, nearly 10 percent of patients had evidence of mitral valve prolapse on echocardiogram; these patients all had mitral valve endocarditis.

Other Pre-Existing Diseases. Underlying chronic diseases, as expected, were common in the elderly and uncommon in the young (Table V). Diabetes mellitus, chronic pulmonary disease, and chronic renal insufficiency were noted most often. In no patient with renal insufficiency could the development of endocarditis be ascribed to prior infections related to hemodialysis or peritoneal dialysis.

Symptoms and Signs. The mean estimated duration of symptoms prior to hospitalization in 34 of 53 patients over the age of 60, in whom the data were available, was 30.1 ± 5.6 days. Estimated duration of symptoms was recorded in 40 of 46 patients aged 40 to 60; the mean was 37.4 ± 5.5 days. For those 31 patients less than 40 years old, in whom the data were available, the duration of symptoms was 35.1 ± 6.9 days. The estimated mean duration of symptoms for all patients with *S. aureus* endocarditis was 10 days shorter than that noted for endocarditis due to other bacteria.

Symptoms on admission to the hospital are shown in Table VI. The elderly were less likely to report fever and chills than were the young and middle-aged patients. Anorexia and weight loss were more common in the middle-aged and elderly groups. All symptoms were more prominent in the under-40 age group; chest pain, headache, dyspnea, arthralgias, and myalgias were each reported in more than 30 percent of patients in this group.

The physical signs noted on admission are shown in Table VII. For those with fever (temperature greater than 100°F or 37.8°C), average initial temperature was 101.1°F (38.4°C) for patients over 60, 102°F (38.9°C) for patients 40 to 60 years of age, and 102.3°F (39.1°C) for patients under 40. The elderly were less often tachycardic and more often hypotensive on admission to hospital. Vascular/embolic phenomena were noted in less than 15 percent of all episodes in all age groups. Confusion, noted in a quarter of the elderly patients, was less common in the younger patients. Fewer patients over age 60 had new or changing murmurs when compared with the other age groups.

For each age group, development of symptoms and signs later in the course of the infection was noted. Patients under the age of 40 were more often noted to have new cardiac murmurs (24 percent). An increase in chest pain and dyspnea in patients under the age of 40 paralleled the greater incidence of right-sided endocarditis in the younger age group. In those over age 60, the predominant developments were neurologic events. Most patients who were afebrile on admission manifested a fever later in the course of their illness. However, in seven

TABLE VI Presenting Symptoms in 154 Episodes of Infective Endocarditis

	Number of Episodes (percent)*		
	<40 (n = 55)	40-60 (n = 46)	>60 (n = 53)
Non-specific symptoms			
Fever	51 (92.7)	40 (86.9)	38 (71.7)
Chills	49 (89.1)	36 (78.3)	30 (56.6)
Anorexia	24 (43.6)	25 (54.3)	31 (58.5)
Weight loss	17 (30.9)	15 (32.6)	19 (35.8)
Specific symptoms			
Dyspnea	19 (34.5)	9 (19.5)	15 (28.3)
Chest pain	18 (32.7)	4 (8.6)	9 (16.9)
Headache	22 (40.0)	6 (13.0)	7 (13.2)
Nausea/vomiting	12 (21.8)	9 (19.5)	8 (15.0)
Abdominal pain	6 (10.9)	5 (10.8)	3 (5.6)
Arthralgias/myalgias	17 (30.9)	15 (32.6)	11 (20.7)

* Number of episodes in which symptom was reported by age group.

TABLE VII Presenting Signs in 154 Episodes of Infective Endocarditis

	Number of Episodes (percent)*		
	<40 (n = 55)	40-60 (n = 46)	>60 (n = 53)
Non-specific signs			
Fever (> 100°F)	48 (87.3)	37 (80.4)	43 (81.1)
Tachycardia	29 (52.7)	15 (32.6)	5 (9.4)
Hypotension	4 (7.3)	3 (6.5)	9 (17.0)
Vascular/embolic phenomena			
Splinter hemorrhages	6 (10.9)	2 (4.3)	6 (11.3)
Petechiae (skin, conjunctiva)	8 (14.5)	5 (10.9)	5 (9.4)
Osler's, Janeway lesions	8 (14.5)	3 (6.5)	6 (11.3)
Roth's spots	0	3 (6.5)	2 (3.8)
Central nervous system findings			
Confusion	8 (14.5)	8 (17.4)	14 (26.4)
Focal signs	10 (18.2)	6 (13.0)	7 (13.2)
Seizures	1 (1.8)	2 (4.3)	1 (1.9)
Murmur (new or changing)	29 (52.7)	23 (50.0)	20 (36.4)
Splenomegaly	8 (14.5)	10 (21.7)	9 (17.0)
Acute arthritis	6 (10.9)	4 (8.7)	5 (9.4)

* Number of episodes with specific sign noted by age group.

definite episodes of endocarditis, fever never developed; four of these seven were in patients over 60 years of age. Temperature greater than 103°F (39.4°C) developed in 9.4 percent of patients over age 60, 17.3 percent of patients aged 40 to 60, and 23.6 percent of patients under 40 years of age.

Incorrect Initial Diagnosis. Errors in diagnosis, defined as no mention of endocarditis by any physician on admission to the hospital, occurred frequently in all age groups but were much more common in the elderly (p < 0.001,

TABLE VIII Initial Diagnoses in 154 Episodes of Infective Endocarditis

	Number of Episodes by Age Group (percent)		
	<40	40-60	>60
	(n = 55)	(n = 46)	(n = 53)
Endocarditis	42 (76.4)	28 (60.9)	17 (32.1)
Incorrect diagnosis	13 (23.6)	18 (39.1)	36 (67.9)
Other infection	4	5	7
Non-infectious	9	13	29

Incorrect initial diagnosis was significantly associated with increasing age (chi square = 21.05, p <0.001).

Table VIII). Sixty-eight percent of patients over age 60, but only 39 percent of patients aged 40 to 60, and 24 percent of patients under age 40, were believed initially to have a disease other than endocarditis. In the elderly, stroke, heart failure, syncope, ataxia, and fever of unknown origin were common misdiagnoses. In more than 50 percent of elderly patients, the initial diagnosis was a non-infectious disease or fever of unknown origin. An initial error in diagnosis was made in 11 of the 16 elderly patients who ultimately died.

Echocardiograms. Review of echocardiographic results for the 126 episodes in patients with native valve endocarditis revealed similar proportions of mitral valve prolapse in each age group (Table IV). The percentage of patients with native valve endocarditis who had echocardiograms performed was 88 percent in those less than 40 years, 62.2 percent in those 40 to 60 years of age, and 82.1 percent in those over age 60. The percentage of echocardiograms showing vegetations was 56.8 percent in those less than 40 years, 47.8 percent in those 40 to 60 years of age, and 43.7 percent in those over age 60. Elderly patients were more likely to have an echocardiogram read as normal and then have documented endocarditis at surgery or necropsy.

Laboratory Data. In 95.5 percent of elderly patients, 90.4 percent of those aged 40 to 60, and 78.0 percent of those less than age 40, results of the first three sets of blood cultures obtained were 100 percent positive. In the young age group, the intermittently positive cultures were found in intravenous drug abusers and those with Hemophilus endocarditis. Prior oral antibiotic use was not proved but was suspected in most of those with drug abuse.

Few differences were noted among the different age groups for other laboratory data. An initial hematocrit value under 40 percent was found in 68 percent of patients over age 60, 61 percent of patients between 40 and 60, and 84 percent of patients less than age 40. The initial leukocyte count ranged from 3,000/ μ l to 29,000/ μ l, with no significant differences noted among the three age groups. A white blood cell count exceeding 12,000/ μ l was noted in 54.3 percent of patients over age 60, 42.7 percent of patients aged 40 to 60, and 34.5 percent

of patients under the age of 40. Data on the Westergren erythrocyte sedimentation rate were available in only 69 patients. The range was from 7 to 120 mm/hour. Normal sedimentation rates were noted in five patients, three of whom were over 60 years of age and one in whom fever never developed. Hematuria was present in 23 percent of patients over the age of 60, 21 percent of patients aged 40 to 60, and 20 percent of patients under age 40.

Valvular Involvement. Overall, the aortic valve was infected most frequently, but in the elderly the mitral valve was involved most often (Table IX). Tricuspid involvement was seen mostly in the young; almost all were intravenous drug abusers. The three right-sided cases in the over-60 age group were related to central venous catheters. Multiple valves were infected in 11 patients, with one middle aged woman having aortic, mitral, and tricuspid valves infected. One elderly patient had an infected mural atrial thrombus and another had an infected ventricular aneurysm.

Prosthetic Valve Endocarditis. Twenty-eight episodes of infective endocarditis occurred in patients with prosthetic valves; fourteen (50 percent) of these were in patients over 60 years of age. Twenty-five of the 28 episodes occurred more than two months after surgery. Coagulase-negative staphylococci (10 episodes) and enterococci (six episodes) predominated. The frequency of symptoms in patients with prosthetic valve endocarditis was similar to that noted in patients with native valve endocarditis with the exception of fever and tachycardia. Fever was present on admission to the hospital in 75 percent of those with prosthetic valve endocarditis compared with 82.4 percent in those with native valve endocarditis, and tachycardia was present in only 17.8 percent of those with prostheses compared with 31.8 percent in those without.

Treatment. An improper antimicrobial regimen was defined as use of a drug with no activity against the organism isolated, inadequate antibiotic dosage for at least two days, or no antibiotic for at least seven days. Such improper regimens, either before or after diagnosis of endocarditis, were noted in 30 percent of patients over age 60, 33 percent of patients aged 40 to 60, and 11 percent of patients under age 40. In the course of treatment, 72

TABLE IX Valvular Involvement in 154 Episodes of Infective Endocarditis*

	Number of Episodes (percent)†		
	<40	40-60	>60
	(n = 55)	(n = 46)	(n = 53)
Aortic	25 (45.4)	28 (60.9)	23 (43.4)
Mitral	15 (27.3)	17 (37.0)	29 (54.7)
Tricuspid	16 (29.1)	6 (13.0)	2 (3.8)
Pulmonic	1 (1.8)	0	1 (1.9)
Other endocardial	0	0	2 (3.8)

* Several patients had more than one valve involved.

† Number of episodes involving each valve by age group.

patients required a change in antibiotic therapy because of complications, such as rash, renal toxicity (creatinine increase greater than 1 mg/dl), or leukopenia. Such changes due to complications affected 34 percent of patients over age 60, 22 percent of patients aged 40 to 60, and 16 percent of patients under age 40.

Cardiac surgery was performed in 15 patients over age 60 (28 percent), 22 patients aged 40 to 60 (48 percent), and 33 patients under age 40 (60 percent). Native valves were replaced in 53 patients and removed (tricuspid valve) in four patients. One patient had removal of a vegetation and another had repair of an infected ventricular aneurysm. Eleven patients had infected prosthetic valves replaced. Other surgical procedures, such as embolectomy, splenectomy, or clipping of mycotic aneurysms, were done in four patients over age 60, four patients aged 40 to 60, and five patients under 40 years of age.

Complications. The number of complications by age group is shown in **Table X**. Major neurologic complications were more common in patients over age 60, whereas pulmonary emboli or abscesses were more common in patients under age 40, reflecting tricuspid valve disease. Several complications, including arrhythmias and gastrointestinal bleeding, occurred equally in all age groups. Major limb emboli were equally frequent in middle-aged and elderly patients; all required surgery to remove emboli from the femoral artery. Two patients in the under-40 age group required enucleation for *Streptococcus pneumoniae* endophthalmitis.

Mortality. Deaths from endocarditis were defined as those related to refractory sepsis, emboli, cardiac decompensation, or cardiac operative deaths. Deaths from all causes were highest in patients over the age of 60; 45.3 percent of elderly patients died compared with 32.2 percent of the middle-aged and 9.1 percent of the young ($p < 0.001$) (**Table XI**). When intravenous drug abusers were omitted from the analysis, overall mortality for patients over age 60 was 45.3 percent, for patients aged 40 to 60 it was 33.0 percent, and for patients under age 40 it was 12.5 percent ($p < 0.001$). Among patients with prosthetic

TABLE XI Outcome in 154 Episodes of Infective Endocarditis

	Number of Episodes by Age Group (percent)		
	<40 (n = 55)	40-60 (n = 46)	>60 (n = 53)
Deaths:	5 (9.1)	15 (32.6)	24 (45.3)
Due to endocarditis	5 (9.1)	13 (28.2)	16 (30.2)
Due to other causes	0	2 (4.3)	8 (15.0)
Permanent disability:	6 (10.9)	2 (4.3)	7 (13.2)
Requiring long-term care	3 (5.4)	1 (2.2)	4 (7.5)
Functional at home	3 (5.4)	1 (2.2)	3 (5.6)

Mortality was significantly associated with increasing age (chi-square = 18.17, $p < 0.001$).

valve endocarditis, mortality was high in both middle-aged (44.4 percent) and elderly (35.7 percent) patients. When patients with prosthetic valve endocarditis were omitted from the analysis, overall mortality for patients over age 60 was 47.5 percent, for those 40 to 60 years, 30.5 percent, and for patients under age 40, 8.0 percent ($p < 0.001$). Permanent disability and a need for long-term care were also more common outcomes in patients over age 60, occurring in 13.2 percent of patients in this age group. Either permanent disability or death directly due to endocarditis occurred in 43.4 percent of patients over age 60, 32.6 percent of those aged 40 to 60, and 20 percent of patients less than age 40.

COMMENTS

Several important changes in infective endocarditis have occurred in the last 40 years [2]. One is the rising number of elderly patients with this infection [2,8,11]. The percentage of elderly patients in a given series depends, in part, on the population served by the reporting medical center. The majority of our elderly patients came from a large community hospital, which had both primary and referral populations. The elderly accounted for 60 percent of all cases of endocarditis seen at that hospital. Other recent studies from large hospitals serving as both a primary care and tertiary referral hospital have noted more than 50 percent of their cases of endocarditis to be in patients over age 60 [8,9]. One study of endocarditis in the 1970s in a community hospital reported 43 percent of all patients to be over age 70 [9].

The University Hospital, primarily a tertiary care referral center, contributed 80 percent of the young patients to this series. This reflects the large number of intravenous drug abusers in southeastern Michigan, many of whom were referred to the University Hospital for surgical procedures when they had severe complications of endocarditis. Overall, 34 percent of all of our patients for whom charts were available and who had definite or probable endocarditis were over age 60, roughly the percentage reported in other reviews in the last 20 years [2].

TABLE X Complications in 154 Episodes of Infective Endocarditis

	Number of Episodes by Age Group (percent)		
	<40 (n = 55)	40-60 (n = 46)	>60 (n = 53)
Major neurologic event	12 (21.8)	13 (28.3)	18 (33.9)
Arrhythmia	9 (16.3)	10 (21.7)	12 (22.6)
Myocardial infarction	0	0	2(3.7)
Glomerulonephritis	4 (7.2)	4 (8.7)	1 (1.8)
Pulmonary embolus	15 (27.2)	2 (4.3)	3 (5.6)
Major limb embolus	1 (1.8)	2 (4.3)	2 (3.7)
Major gastrointestinal bleed	3 (5.4)	2 (4.3)	3 (5.6)

Our series differs from most others in that as many cases were due to staphylococci as streptococci. The trend toward increasing numbers of patients with staphylococcal endocarditis has been evident over the last 40 years [2]. The organisms causing endocarditis were remarkably similar in all three age groups. This was surprising since we thought there would be more staphylococci in the young, predominantly drug-abusing population, and more streptococci in the middle-aged and elderly groups. Although the overall percentages of staphylococci and streptococci were quite similar in the three age groups, there were several striking trends noted in the elderly patients with endocarditis.

In the elderly, *S. aureus* was the predominant pathogen and in most patients could be traced to an infected intravenous catheter or a skin lesion. This contrasted with the young patients, in whom almost all *S. aureus* endocarditis was directly attributable to drug abuse and in whom many of the organisms were methicillin resistant. In many regards, our middle-aged and elderly patients mirrored staphylococcal endocarditis as described by Watanakunakorn et al [7], who found a predominance of older patients with a nosocomial or skin source in their large series of patients with staphylococcal endocarditis.

The 14 cases (9 percent) of endocarditis caused by coagulase-negative staphylococci reflect the rising incidence of serious infection with this organism in recent years [14]. The fact that most of these patients were elderly is due, in part, to the increasing numbers of middle-aged to elderly patients undergoing valve replacement. However, four patients had coagulase-negative staphylococcal endocarditis on native valves; two were elderly and two were middle-aged. The patients had previously abnormal valves including probable mitral valve prolapse in two, as described by Baddour et al [15].

As expected, enterococcal endocarditis was primarily noted in middle-aged and elderly men, a trend commented upon previously [16,17]. Many of these patients had had procedures or prior infection of the urinary tract. Very few cases were seen in young women with genitourinary sources, a common event in the 1940s and 1950s [18]. Enterococcal infection, often nosocomially acquired, has become a prominent problem in hospitalized patients [19] and most likely enterococci will continue to be a major pathogen in the elderly with endocarditis.

S. bovis was seen almost solely in the elderly, all of whom had carcinoma of the colon or polyps with marked atypia. The association of *S. bovis* bacteremia and underlying disease of the gastrointestinal tract, especially adenocarcinoma of the colon, has been noted frequently since the mid-1970s [20,21].

In this series, only one patient had true culture-negative endocarditis; three others were diagnosed at necropsy only because they had no pre-mortem cultures of blood performed. Culture-negative endocarditis has been seen

with relative rarity in recent years and has not consistently been noted in any specific age group [8].

An important finding in this study was the number of elderly patients with endocarditis acquired as a nosocomial infection. This amounted to 23 percent of the episodes of endocarditis in those over age 60. This is a trend noted in other recent series as well [8,22]. Most of these patients had staphylococcal endocarditis related to infected intravenous catheters. Tricuspid endocarditis and, in one instance, an infected right atrial mural thrombus were seen in patients with subclavian catheters in place. More commonly, the source was a peripheral intravenous catheter, and left-sided endocarditis ensued, as noted in other series [7,22]. Several cases of nosocomial endocarditis were associated with prior urinary tract procedures or vascular invasive procedures, such as arteriography or pacemaker placement.

The fact that the most common cardiac abnormality predisposing to endocarditis in our patients was the presence of a valvular prosthesis and that most of the patients with prosthetic valve endocarditis were elderly illustrates the changing epidemiology of endocarditis in the last few decades [2]. Rheumatic heart disease was uncommon, as noted by others in recent years [23]. There were roughly equal numbers of patients with mitral valve prolapse in each age group. Other investigators have recently reported this as a major underlying lesion predisposing to endocarditis [23,24] and have commented on its common occurrence in older men [25].

When elderly patients were compared with younger patients, a major difference noted was that the elderly reported fewer symptoms. Only 71.7 percent of the elderly reported fever, although 81.1 percent actually were febrile on admission. Others have noted the frequency with which the elderly do not perceive the presence of fever [11]. Although the percentage of patients who were febrile on admission was similar in all three age groups, the height of the febrile response was diminished in the elderly, when they were compared with the young patients; in very few elderly patients did temperatures as high as 103°F develop. Poor febrile responses in elderly patients with endocarditis has been noted by other investigators, with some reporting that 40 to 50 percent of elderly patients with endocarditis were afebrile on admission to hospital [12,13,26,27]. In those studies in which comment was made, most elderly patients eventually became febrile during the course of hospitalization; no previous studies have commented on the lessened height of the febrile response noted in the elderly as seen in this study.

Confusion as a presenting sign was common in elderly patients in this series, as well as in others [12,26]. When confusion, focal neurologic signs, and seizures were considered together, however, about one third of all patients in each group had neurologic signs at the time of admis-

sion. Central nervous system involvement during the course of endocarditis has been noted frequently, beginning with descriptions by Osler [28] and continuing in very recent series [29–31]. Major cerebral emboli are among the most devastating neurologic complications of endocarditis and were found more frequently during the course of the infection in our elderly patients than in the young patients.

New murmurs or changing murmurs were heard less frequently in the elderly with endocarditis, a finding commented upon frequently by others caring for older patients with endocarditis [26,27]. Frequently, murmurs in the elderly have been thought to be insignificant and, thus, did not increase the suspicion of the physician as to the possibility of endocarditis [27].

Errors in diagnosis were significantly more frequent in the elderly, occurring in two thirds of the 53 patients over age 60. The more vague complaints (anorexia, fatigue, weakness) expressed by the elderly, coupled with confusion commonly seen at admission, probably contributed to the frequent diagnosis of diseases such as fever of unknown origin, stroke, heart failure, and syncope in these patients. Errors in diagnosis were common in other series of elderly patients with endocarditis as well [5,11–13]. The diagnosis of endocarditis in the young patients was undoubtedly aided by the history of intravenous drug abuse. In our patients, as well as those described by others, the inability to make the diagnosis of endocarditis led to the use of improper antibiotics or no antibiotic therapy and may have contributed to the death of the patients in the older age group [5,11–13].

Elderly patients had more mitral valve infection than did younger patients. This distribution is similar to that seen by others [4,8,11,26], but is at variance with other series that showed a predominance of aortic valve infection in the elderly [32]. One wonders whether pre-existing mitral valve prolapse was not present in even more of our elderly patients, given the large number of cases with mitral valve infection. The greater frequency of misleading echocardiographic results in the older age group may have resulted in an underestimation of pre-existing mitral valve prolapse in patients over age 60. Calcified mitral annulus fibrosus is another underlying mitral valve lesion seen in the elderly population, which predisposes to endocarditis, but which was not noted in our patients [33].

Mortality was significantly greater for the elderly than the younger patients in this study. This remained significant even if patients with underlying drug abuse or pros-

thetic valves were omitted from the analysis. Forty-five percent of the patients over age 60 died, 30 percent as a direct result of endocarditis and the remaining 15 percent from other underlying diseases or from diseases acquired while being treated for endocarditis. Mortality rates for elderly patients have been very similar or even higher in most series. Habte-Gabr et al [11], Robbins et al [13], and Anderson and Staffurth [4] all noted mortality rates from 43 to 45 percent, whereas Cummings et al [5] and Applefeld and Hornick [12] recorded mortality rates over 70 percent in their elderly patients with endocarditis. The mortality rate has generally decreased in the last several decades, but still is much higher for the elderly than the younger population. Permanent disability and the subsequent need for long-term care were more frequent in elderly patients who survived the acute episode, when compared with the younger patients.

Increased chronologic age alone probably is not responsible for the differences observed in mortality. One reason for increased mortality in the elderly may be the number of underlying diseases present in this age group; thus, a serious infection, such as endocarditis, might be the final insult leading to death from existing heart failure or chronic renal insufficiency. Another important point concerns frequent errors in diagnosis in the elderly; these errors probably contributed to a higher mortality rate in this group, as noted by others, as well [5,11]. It is possible that the higher proportion of left-sided and prosthetic valve endocarditis in the elderly contributed significantly to the higher mortality rate in this group. Differences in virulence of pathogens probably weighed more against the younger patients, who had a greater incidence of *S. aureus* endocarditis.

This study shows that elderly patients constitute a large proportion of patients with infective endocarditis. Elderly patients often have more non-specific symptoms than do younger patients, and thus are more frequently the victims of confusion in diagnosis and errors in antibiotic choice. They are more likely to have a nosocomial source of infection. The risk of infective endocarditis in elderly patients will increase if current trends continue toward increased hospitalization and the use of invasive procedures in an aging population.

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