

Hospital-Acquired Infective Endocarditis: Should the Definition be Broadened?

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Hospital-acquired infective endocarditis (IE) is a growing health-care problem. Hospital-acquired IE, according to the commonly used definition, is IE manifesting ≥ 72 h after admission to the hospital or within several weeks after a hospital-based invasive procedure. To assess the validity of this definition, we evaluated 87 episodes of IE, with special attention to recent hospitalizations. The incidence rate of IE in the 6-month period after discharge from the hospital was 27 cases per 100,000 person-years, compared with 1.1 cases per 100,000 person-years in a population with no recent hospitalizations. Furthermore, episodes of IE manifesting during this 6-month period were notable for a high proportion of typically hospital-acquired pathogens (26% vs. 0%; $P = .001$) and a low proportion of viridans streptococci (0% vs. 36%; $P < .001$), compared with community-acquired episodes that did not involve recent hospitalization. We conclude that characteristics of hospital-acquired IE extend to episodes arising within 6 months after discharge from the hospital and suggest that the definition of hospital-acquired IE be broadened to include these episodes.

Hospital-acquired infective endocarditis (IE) constitutes 9%–29% of all cases of IE [1–5] and has increased in frequency in recent years owing to greater use of invasive procedures in hospitals [2, 6, 7]. Hospital-acquired IE has been defined as either IE with onset of symptoms ≥ 72 h after hospitalization or IE occurring from 4 to 8 weeks after discharge from the hospital if an invasive procedure was performed during hospitalization [1, 2, 4, 5]. However, in recent years, we have noted the occurrence of IE involving pathogens that are typically nosocomial in patients whose cases did not meet the above definition. These patients had been discharged from the hospital >8 weeks before the onset of symptoms, suggesting that the incubation period for hospital-acquired IE may be substantially longer than was previously suspected. The aim of the present study

was to reassess the definition of hospital-acquired IE, with particular emphasis on the relevance of recent hospitalization.

PATIENTS AND METHODS

Clinical data collection. The Tel Aviv Sourasky Medical Center is a 1150-bed tertiary care teaching hospital located in central Tel Aviv and serving a population of $\sim 700,000$. As part of ongoing prospective surveillance of positive blood culture results among adults, all cases of culture positive IE (defined below) diagnosed during a 4-year period (1995–1998) were included in this study.

For each episode of IE, data were collected by a member of the infectious diseases team who interviewed the patient and the attending physician and reviewed any relevant medical documentation [8]. Data from the most recent hospitalization, including data on comorbidities, events during hospitalization, and invasive procedures performed, were collected by review of the patient medical records.

Bacteriological methods. Blood culture specimens were inoculated into BacT/Alert bottles (Organon

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Teknika). Isolate identification and susceptibility testing were performed using standard bacteriological methods and an automated system (MicroScan; Baxter Healthcare). Single blood cultures growing diphtheroids, *Bacillus* species, or coagulase-negative *Staphylococcus* species (CoNS) were excluded as contaminants, and several other isolates were excluded on an individual basis [8].

Case definitions. IE was defined as definite or possible according to the modified Duke criteria [9]. Hospital-acquired IE, in accordance with the traditional definition, was defined as IE with onset ≥ 72 h after admission or IE acquired in association with a significant invasive procedure performed during a recent hospitalization ≤ 8 weeks before the onset of symptoms [2, 4, 5]. Significant invasive procedures were defined as procedures known to be associated with bacteremia or bloodstream infection, and they included dental procedures [10], urogenital procedures (e.g., cystoscopy or bladder catheterization) [2, 4, 5, 10], gastrointestinal procedures (e.g., endoscopy or esophageal dilatation) [4, 5, 10], cardiac surgery [4, 5], intravascular catheterization [1, 2, 4, 5], and surgical incision through mucous membranes or infected skin [4, 5].

To define a high-risk postdischarge period, we first stratified all non-hospital-acquired cases according to the interval between the most recent hospital discharge and the onset of IE symptoms. Our initial finding, presented in figure 1, was that all cases of non-hospital-acquired IE involving pathogens that are typically nosocomial (i.e., enteric gram-negative bacilli

(EGNB), methicillin-resistant *Staphylococcus aureus* (MRSA), and CoNS) aggregated within the 6-month period following hospital discharge. In addition, there was an increased incidence of IE due to *Enterococcus* species (also a common cause of hospital-acquired infection [2, 11–13]) within the same time period. Therefore, we defined recently hospitalized patients as those discharged from the hospital ≤ 6 months before the onset of IE symptoms.

Microbiological and clinical features of IE were thus compared among the following 3 patient groups: (1) the hospital-acquired IE group, consisting of patients whose cases met the traditional definition of hospital-acquired IE; the recently hospitalized group, consisting of patients with IE who were discharged from the hospital ≤ 6 months before the onset of symptoms and did not meet criteria for inclusion in the hospital-acquired IE group; and the true community-acquired IE group, consisting of patients who were not hospitalized during the 6 months preceding the onset of IE symptoms. Prosthetic valve endocarditis (PVE) was defined as either “early” or “late” according to whether it occurred ≤ 60 days or >60 days after valve surgery, respectively [14].

Statistical analysis. Comparisons among patient groups were performed using χ^2 analysis or Fisher’s exact test, as applicable, for categorical variables and Student’s *t* test for continuous variables. Comparison of different patient populations with respect to the distribution of bacterial isolates was performed using the Kruskal-Wallis test. Because our hospital is

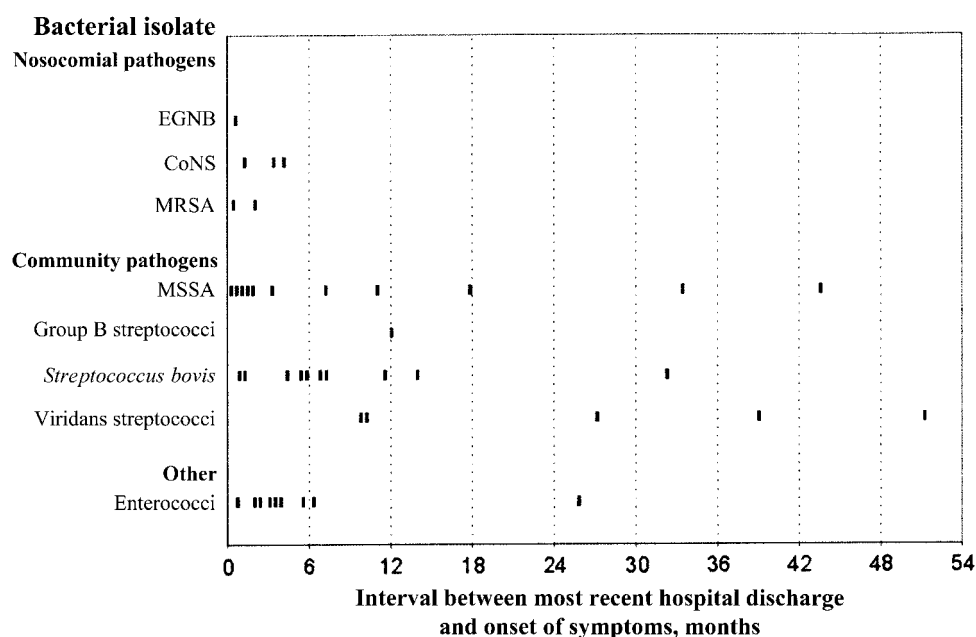


Figure 1. Stratification of infective endocarditis (IE) episodes in patients hospitalized within the previous 5 years, according to bacterial isolate and interval between the most recent hospital discharge and onset of symptoms. Data are shown for 42 isolates; 1 case of IE due to *Listeria monocytogenes* is not shown. CoNS, coagulase-negative staphylococci; EGNB, enteric gram-negative bacilli; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*.

the principal health care facility for a defined urban population, we used the number of patients discharged as the denominator for incidence rate calculations among recently hospitalized patients, assuming that discharged patients were not subsequently hospitalized elsewhere. Incidence rates of IE with specific pathogens were expressed as cases per 100,000 person-years and were compared among the different patient populations using Fisher's exact test for rate ratio. Logistic regression analysis was used to calculate the effect of various patient characteristics on mortality. A *P* value of $<.05$ was considered to be significant. All statistical tests were 2-sided.

RESULTS

During the 4-year study period, there were 3719 documented bacteremic episodes. After clinical and microbiological investigation, 87 of these episodes in 84 patients met the modified Duke criteria for IE (60 cases were classified as definite IE, and 27 were classified as possible IE). Sixty-four cases (74%) were native valve endocarditis (NVE), 22 (25%) were PVE, and 2 were cardiac pacemaker infections, including 1 case in which both a pacemaker and a native valve were involved.

Fifteen episodes of IE (17%) were classified as hospital-acquired according to the traditional definition. Of 72 episodes of non-hospital-acquired IE, 41 (with 43 pathogens isolated) occurred in patients who had been hospitalized within the previous 5 years (figure 1). Of these 41 episodes, 23 occurred within 6 months after discharge from the hospital; patients who experienced these episodes constituted the recently hospitalized group. Twenty-one of these 23 episodes occurred following discharge from a medical service, and 2 occurred following discharge from a surgical service. Patients who experienced the remaining 49 episodes constituted the true community-acquired IE group.

There were 171,503 hospital discharges during the study period. The overall incidence of IE (expressed in cases per 100,000 person-years) was 27 among persons discharged from the hospital within the previous 6 months, 2.3 among persons discharged from hospital >6 months previously, and 1.1 among persons not hospitalized during the previous 5 years. Therefore, the incidence of IE in the 6-month period after hospital discharge was 25-fold greater than the incidence in a population with no recent hospitalization (95% CI, 13.8–43.2; $P < .001$).

Distribution of bacterial isolates among the 3 patient groups. A total of 90 bacterial isolates were obtained from 87 IE episodes. The frequency of each bacterial species, including typically nosocomial pathogens such as MRSA, EGNB, and CoNS, was similar in the hospital-acquired IE group and the recently hospitalized group. In contrast, in the recently hospitalized group, there was a significantly higher frequency of CoNS endocarditis and a lower frequency of IE caused by

viridans streptococci, compared with the true community-acquired IE group (table 1 and figure 2).

Because MRSA, CoNS, and EGNB are strongly associated with hospital-acquired infection [12], these isolates were analyzed in aggregate as well as individually. These nosocomial pathogens accounted for 47% of isolates in the hospital-acquired IE group and 26% of isolates in the recently hospitalized group ($P = .20$). In contrast, there were no cases of IE involving pathogens that are typically nosocomial in the true community-acquired IE group ($P = .001$) (table 1 and figure 2). The incidence rates for IE involving nosocomial pathogens were 41, 7, and 0 cases per 100,000 person-years, in the hospital-acquired IE, recently hospitalized, and true community-acquired IE groups, respectively.

There was a notable aggregation of IE due to *Enterococcus* species among patients discharged from the hospital within the previous 6 months (figure 1). Incidence rates for enterococcal endocarditis were 23.5 cases per 100,000 person-years among hospitalized patients, 8.2 cases per 100,000 person-years among patients discharged <6 months previously ($P = .10$), and 0.3 cases per 100,000 patients years among patients with no recent hospitalization ($P < .001$). Nevertheless, *Enterococcus* species were second only to viridans streptococci as a cause of IE in the true community-acquired IE group, accounting for 20% of episodes in this group (table 1).

Population analysis showed a significant difference in the distribution of types of pathogens between the hospital-acquired IE and community-acquired IE groups ($P = .03$). The distribution of types of pathogens in the recently hospitalized group was shown to be of an intermediate composition, but it more closely resembled that in the hospital-acquired IE group than that in the true community-acquired IE group.

Episodes of NVE were also analyzed separately from episodes of PVE (table 2). The same distribution of clinical isolates was evident, with nosocomial pathogens constituting 50%, 37%, and 0% of cases in the hospital-acquired IE, recently hospitalized, and community-acquired IE groups, respectively. The recently hospitalized group did not include any cases of PVE involving pathogens that are typically nosocomial. Therefore, the occurrence of IE involving nosocomial pathogens in the recently hospitalized group could not be ascribed to late procedure-related PVE.

Patient characteristics. There were no differences in sex and age distribution among the patient groups. The types of valves involved in the episodes of IE were also similar, except that early PVE occurred exclusively in the hospital-acquired group (table 3). Comparison of the hospital-acquired IE group with the recently hospitalized group with respect to demographic variables and comorbid conditions showed no significant differences. However, comorbid conditions were more common in the recently hospitalized group, compared with

Table 1. Frequencies of bacterial isolates among patients with infective endocarditis (IE), by patient group.

Isolate, by class and type	Patient group, no. (%) of isolates			P	
	Hospital-acquired IE (15 episodes)	Recently hospitalized (23 episodes)	True community-acquired IE (49 episodes)	Hospital-acquired IE vs. recently hospitalized	Recently hospitalized vs. community-acquired IE
Community-acquired					
Viridans streptococci	1 (7)	0 (0)	18 (36)	.3	<.001
<i>Streptococcus bovis</i>	1 (7)	5 (22)	9 (18)	.3	.7
Group B <i>Streptococcus</i>	0 (0)	0 (0)	1 (2)	1.0	1.0
<i>Actinobacillus</i> species	0 (0)	0 (0)	1 (2)	1.0	1.0
MSSA ^a	1 (7)	6 (26)	10 (20)	.2	.7
Nosocomial					
MRSA ^a	3 (20)	2 (9)	0 (0)	.3	.09
EGNB	2 (13)	1 (4)	0 (0)	.5	.3
CoNS	2 (13)	3 (13)	0 (0)	1.0	.03
Subtotal of nosocomial isolates	7 (47)	6 (26)	0 (0)	.2	.001
Other					
<i>Enterococcus</i> species	4 (27)	7 (30)	10 (20)	1.0	.3
<i>Listeria</i> species	1 (7)	1 (4)	0 (0)	1.0	.3
Diphtheroid	0 (0)	0 (0)	1 (2)	1.0	1.0
Total	15 (100)	25 (100)	50 (100)		

NOTE. For definition of patient groups, see Patients and Methods. CoNS, coagulase-negative staphylococci; EGNB, enteric gram-negative bacilli; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*. Percentages may not sum because of rounding.

^a For all MSSA and MRSA isolates combined, data, expressed as no. (%) of isolates, are as follows: hospital-acquired IE group, 4 (27); recently hospitalized group, 8 (35); true community-acquired IE group, 10 (20). For all MSSA and MRSA isolates combined, P values are as follows: hospital-acquired IE group vs. recently hospitalized group, P = .7; recently hospitalized group vs. community-acquired IE group, P = .2.

those in the true community-acquired IE group. Specifically, cardiovascular disease, heart failure, hypertension, and chronic obstructive lung disease each occurred more commonly among patients in the recently hospitalized group (table 3).

Associated invasive procedures. There were 29 IE episodes in which ≥ 1 preceding invasive procedure could be identified. Of the 15 patients included in the hospital-acquired IE group, 13 had undergone a previous invasive procedure; 4 developed IE during the same hospitalization, and 9 developed IE after discharge from the hospital (table 4). Median duration of the interval between the implicated procedure and the onset of symptoms was 36.5 days (range, 5–60 days).

Of 23 IE episodes in the recently hospitalized group, 6 had been preceded by ≥ 1 invasive procedure in the 6 months before the onset of symptoms. Three of these 6 episodes were associated with a hospital-based procedure but did not meet traditional criteria for hospital-acquired IE because of a long interval (>8 weeks) between discharge from the hospital and onset of IE. Procedures were performed a median of 45 days (range, 7–175 days) before admission to the hospital (table 4).

Ten of 49 IE episodes in the community-acquired IE group were preceded by an invasive procedure that did not involve hospitalization, which was performed a median of 30 days

(range, 4–60 days) before admission. Six of these episodes were associated with dental procedures (table 4).

The most commonly isolated pathogens among cases of procedure-related IE were *Enterococcus* species, accounting for 11 of 29 episodes. Exploring the association between specific organisms and the type of procedure gave the following statistically significant results: enterococci were isolated in 7 (53.8%) of 13 episodes associated with urogenital or gastrointestinal procedures, compared with 14 (18.9%) of 74 episodes not associated with such procedures (OR 5.0; 95% CI, 1.2–20.7; P = .01). *S. aureus* was isolated in 7 (53.8%) of 13 episodes associated with skin incision or soft-tissue manipulation, compared with 15 (20.2%) of 74 episodes not associated with such procedures (OR 4.5; 95% CI, 1.1–18.9; P = .01). The corresponding values for MRSA were 4 (30.7%) of 13 episodes associated with skin or soft-tissue procedures, compared with 1 (1.3%) of 74 episodes not associated with such procedures (OR, 32.4; 95% CI, 2.6–1617.8; P = .001).

Clinical outcome. The overall in-hospital all-cause mortality rate was 24% (death occurred after 21 of 87 episodes). Mortality rate did not differ significantly between the hospital-acquired IE group (mortality rate, 20% [death occurred after 3 of 15 episodes]) and the recently hospitalized group (mor-

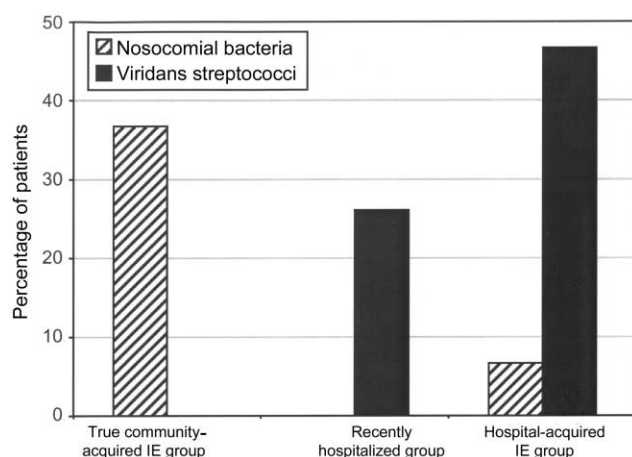


Figure 2. Percentage of patients in the hospital-acquired infective endocarditis (IE) group, recently hospitalized group, and true community-acquired IE group who were infected with nosocomial bacteria and/or viridans streptococci. For definition of the groups, see Patients and Methods. "Nosocomial bacteria" denotes the aggregate of coagulase-negative staphylococci, enteric gram-negative bacilli, and methicillin-resistant *Staphylococcus aureus*.

tality rate, 48% [death occurred after 11 of 23 episodes]) ($P = .10$). However, mortality rate was significantly greater in the recently hospitalized group (48%) than in the true community-acquired IE group (14% [7 of 49 patients]) (OR, 5.5; 95% CI, 1.5–20.3; $P = .004$).

Univariate analysis revealed that infection with *S. aureus* was associated with increased mortality (OR, 5.5; 95% CI, 1.6–18.3; $P = .003$) and that infection with viridans streptococci was associated with reduced mortality (OR, 0.0; 95% CI, 0.0–0.54; $P = .005$). Logistic regression identified infection with *S. aureus* as the only variable independently predictive of mortality (OR, 3.6; 95% CI, 1.2–10.8; $P = .02$).

DISCUSSION

Hospital-acquired IE is characterized by a bacterial spectrum distinct from that of community-acquired IE. Viridans strep-

tococci, which are dominant pathogens in cases of community-acquired IE, are rare in the hospital setting. In comparison, MRSA, CoNS, and EGNB are typical of hospital-acquired disease [1, 2, 4, 5, 11, 12]. Infection with these pathogens seems to follow bacteremia incited by hospital-based procedures [2]. *Enterococcus* species are an important cause of bacteremia and IE in both the hospital and the community [2, 11–13, 15].

There is currently no clearly defined duration during which hospital-acquired bacterial IE may be expected to develop following hospital stay. The common definition of patients with hospital-acquired IE includes patients who underwent a hospital-based procedure during the 4–8 week period before onset of illness. This definition potentially neglects 2 groups of patients with hospital-acquired IE: patients who acquired a pathogen in the hospital without having undergone a hospital-based invasive procedure and patients whose illness has had an incubation period of >8 weeks. With regard to the first group, it is possible that seemingly trivial hospital events, such as the flushing of a peripheral intravenous catheter or the manipulation of an existing urinary catheter, could result in bacteremia involving nosocomial pathogens. As for the second group, patients may become colonized during hospitalization, thus setting the stage for bacteremia involving hospital-acquired pathogens to occur weeks or months after discharge from the hospital [16]. The incubation period for streptococcal endocarditis is rarely >2 weeks [17]. However, CoNS, which are important causes of hospital-acquired IE, produce illnesses with a significantly longer incubation period, which may be as protracted as 1 year [18]. For patients with drug addiction who presented with community-acquired *S. aureus* endocarditis, recent hospitalization was a risk factor for infection with MRSA [19]. Finally, IE due to fastidious microorganisms has been described as occurring as long as 6 months after an associated invasive procedure [20].

We found that patients recently discharged from the hospital are at increased risk of developing IE. The incidence of IE among patients discharged >6 months before onset of illness or not hospitalized within 5 years before the onset of illness

Table 2. Frequency among patients with native valve endocarditis or prosthetic valve endocarditis of bacterial isolates that are typically nosocomially acquired (MRSA, CoNS, and EGNB), by patient group.

Type of endocarditis	Proportion (%) of patients with pathogens isolated			<i>P</i>	
	Hospital-acquired IE group	Recently hospitalized group	True community-acquired IE group	Hospital-acquired IE vs. recently hospitalized	Recently hospitalized vs. community-acquired IE
Native valve	4/8 (50)	6/16 (37)	0/40 (0)	.6	<.001
Prosthetic valve	3/7 (43)	0/7 (0)	0/9 (0)	.1	1.0
All	7/15 (47)	6/23 (26)	0/49 (0)	.4	.001

NOTE. For definition of patient groups, see Patients and Methods. CoNS, coagulase-negative staphylococci; EGNB, enteric gram-negative bacilli; IE, infective endocarditis; MRSA, methicillin-resistant *Staphylococcus aureus*.

Table 3. Demographic characteristics and comorbid conditions among patients with infective endocarditis, by patient group.

Variable	Patient group			<i>P</i>	
	Hospital-acquired IE	Recently hospitalized	True community-acquired IE	Hospital-acquired IE vs. recently hospitalized	Recently hospitalized vs. community-acquired IE
Episodes of IE, no.	15	23	49		
Age in years, mean \pm SD	69 \pm 13	74 \pm 15	68 \pm 15		
Male sex	10 (67)	13 (57)	37 (76)	.7	.1
Comorbid condition					
Diabetes mellitus	5 (33)	5 (22)	7 (14)	.4	.5
Hypertension	4 (27)	11 (48)	6 (12)	.3	.002
Cardiovascular disease and heart failure	10 (67)	19 (83)	19 (39)	.4	.001
Malignancy	3 (20)	3 (13)	6 (12)	.6	1.0
Cerebrovascular disease	1 (7)	5 (22)	4 (8)	.3	.1
COPD or Asthma	1 (7)	3 (13)	0 (0)	1.0	.03
Cirrhosis	0 (0)	1 (4)	1 (2)	1.0	.5
Chronic renal insufficiency	2 (13)	6 (26)	4 (8)	.4	.06
Alcoholism	0 (0)	1 (4)	1 (2)	1.0	.5
IDU	0 (0)	1 (4)	0 (0)	1.0	.3
Known valvular disease	4 (27)	10 (43)	25 (51)	.3	.6
Site of infection					
Native valve	8 (53)	16 (70)	40 (82)	.4	.3
Mitral	4 (27)	8 (35)	26 (53)	.7	.2
Aortic	5 (33)	6 (26)	10 (20)	.7	.7
Tricuspid	0 (0)	2 (9)	5 (10)	.5	1.0
Unknown	1 (7)	1 (4)	6 (12)	1.0	.4
Prosthetic valve	6 (40)	7 (30)	9 (18)	.7	.3
Early	3 (20)	0 (0)	0 (0)	.05	1.0
Late	3 (20)	7 (30)	9 (18)	.7	.3
Pacemaker	1 (7)	1 (4)	0 (0)	1.0	.3
In-hospital mortality	3 (20)	11 (48)	7 (14)	.1	.004

NOTE. Data are no. (%) of patients, unless otherwise indicated. COPD, chronic obstructive pulmonary disease; IDU, injection drug use.

was 2.3 cases per 100,000 patient-years and 1.1 cases per 100,000 patient-years, respectively. This is similar to the incidence of community-acquired IE reported in previous studies [21, 22]. However, we found a strikingly higher incidence of IE (27 cases per 100,000 patient-years) in the first 6 months after hospital discharge. This translates into a mean incidence of IE within 6 months after hospital discharge of 1.5 cases per 10,000 hospital discharges.

Our observations on the bacterial spectrum of hospital-acquired IE are generally consistent with those of previous reports [1, 2, 4, 5]. However, our observation that the 6 months after hospital discharge were a period of susceptibility to IE involving hospital-acquired pathogens has not been previously reported in association with NVE. Although outbreaks of PVE involving pathogens acquired during surgery have been described in which the onset of illness occurred as much as 13 months after the procedure [23], there was no evidence of such an outbreak being involved in the PVE episodes in our study. Population

analysis could not demonstrate a difference in the distribution of bacterial isolates between the hospital-acquired IE group and the recently hospitalized group. Among patients whose cases were not included in the traditional definition of hospital-acquired IE, infection with typical nosocomial pathogens occurred exclusively within 6 months after hospital discharge. It is interesting to note that studies that have defined "recent hospitalization" as discharge within the previous 4 to 8 weeks have described hospital-acquired and community-acquired CoNS endocarditis as occurring with equal frequency [1, 2, 5], whereas we found that CoNS infection occurred exclusively in patients who were hospitalized or recently hospitalized. Of 3 patients in our study who developed CoNS endocarditis outside of the hospital, 2 were discharged >8 weeks before the onset of symptoms, and their cases would thus be considered community-acquired according to traditional criteria.

Other researchers have noted the poor prognosis of IE acquired in the hospital, with mortality rates of 40%–56% [1, 2,

Table 4. Association between invasive procedures and episodes of infective endocarditis (IE), by patient group.

Variable	No. of IE episodes associated with procedure indicated	Patient group ^a		
		Hospital-acquired IE ^b	Recently hospitalized	True community- acquired IE ^c
IE episodes				
Total no.	...	15	23	49
No. (%) procedure-related ^d	...	13 (87)	6 (26)	10 (20)
Type of procedure				
Urogenital	9	Enterococci (1), EGNB (1), <i>Listeria</i> species (1)	Inpatient: Enterococci (1), MRSA (1); outpatient: Enterococci (1), <i>S. bovis</i> (1)	Enterococci (2)
Gastrointestinal	4	...	Inpatient: <i>S. bovis</i> (1); outpatient: Enterococci (1), <i>S. bovis</i> (1)	Enterococci (1)
Dental	8	...	Outpatient: Enterococci (1), <i>S. bovis</i> (1)	Enterococci (2), <i>S. bovis</i> (2), Viridans streptococci (2)
Valve surgery	3	CoNS (1), Enterococci (1), <i>S. bovis</i> (1)
Pacemaker implantation	2	Enterococci (2)
CVC insertion	3	MSSA (1), MRSA (2)
PTA	2	MRSA (1), viridans streptococcus (1)
Soft-tissue excision	2	MSSA (2)
Orthopedic surgery	1	...	Inpatient: MRSA (1)	...

NOTE. Data are bacterial isolates (no. of episodes), unless otherwise indicated. CoNS, coagulase-negative staphylococci; CVC, central venous catheter; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*; PTA, percutaneous transluminal angioplasty (for peripheral arterial occlusion); *S. bovis*, *Streptococcus bovis*.

^a For a definition of the patient groups, see Patient and Methods.

^b For the hospital-acquired IE group, all procedures occurred in an inpatient setting.

^c For the true community-acquired IE group, all procedures occurred in an outpatient setting.

^d Some episodes of IE were preceded by >1 invasive procedure.

4, 5]. In our analysis, episodes of IE among recently hospitalized patients were associated with a mortality rate of 48%, which was significantly higher than the mortality rate in the true community-acquired IE group (14%). The adverse prognosis of hospital-acquired IE may be attributed to the bacterial species involved. Mortality in our study was associated with infection caused by *S. aureus*, whereas viridans streptococci portended a favorable prognosis. Multivariate analysis revealed that infection with *S. aureus* remained the only predictor of mortality (OR, 5.5) after adding patient age and preexisting medical conditions to the model.

Seventeen percent of all IE cases in our study (15 of 87) were cases of hospital-acquired IE, as defined by traditional criteria. Similar percentages (9%–29% of cases) have been found in previous studies [1–5]. If, however, we include episodes in the recently hospitalized group in the hospital-acquired IE category, as our results would suggest is appropriate, a figure of 43% (38 of 87 episodes) is obtained, which is substantially greater than previously reported. Thus, the extent of hospital-acquired IE may be underestimated by the currently used definitions.

There are evident limitations to this retrospective study. It is possible that, rather than being a cause of endocarditis, recent hospitalization is a marker for patients who are at increased risk for the disease. A case-control study might be better suited

to addressing this issue. From a clinical standpoint, however, our results can nonetheless serve as a useful guide to categorizing patients presenting with IE. In addition, in calculating incidence rates, we assumed that patients were not hospitalized at other hospitals, thus potentially underestimating the true incidence of IE in the study population.

Our findings suggest that hospitalization within the previous 6 months should be considered when evaluating patients with suspected IE. In particular, the high prevalence of MRSA and CoNS in this group (26% of all isolates) could justify the empirical use of vancomycin as part of the initial antimicrobial regimen, especially if MRSA carriage and infection are prevalent in the discharging medical institution. In addition, the alarmingly high mortality rate among recently hospitalized patients with IE mandates aggressive diagnostic investigation and treatment. For these practical considerations, we suggest that the traditional definition of hospital-acquired IE be modified to include all patients discharged from the hospital within 6 months before onset of symptoms.

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