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Readmission for Infective Endocarditis After Ischemic Stroke or Transient Ischemic Attack

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Abstract

Background and Purpose: Providers vary in their thresholds for obtaining blood cultures in patients with ischemic stroke or transient ischemic attack (TIA). We assessed the rate of missed diagnoses of infective endocarditis (IE) in patients discharged with stroke or TIA before blood culture results could have been available. **Methods:** Using administrative claims data, we performed a retrospective cohort study of all patients discharged from nonfederal California emergency departments or acute care hospitals from 2005 through 2011 with stroke (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] codes 433.x1, 434.x1, or 436 in any position) or TIA (*ICD-9-CM* code 435 in the primary diagnosis position). We excluded patients with a length of stay >2 days to focus on those discharged before conclusive blood culture results could have been available. Our outcome was hospitalization within 14 days with a new diagnosis of IE (*ICD-9-CM* codes 391.1 or 421.x in any position). **Results:** Among 173 966 eligible patients, 24 were subsequently hospitalized for IE—a readmission rate of 1.4 per 10 000 (95% confidence interval [CI], 0.8-1.9 per 10 000). Multiple logistic regression identified the following potential associations with readmission: prosthetic valve: odds ratio (OR), 15.8 (95% CI, 1.9-129.0); other valvular disease: OR, 1.5 (95% CI, 0.2-10.8); urinary tract infection: OR, 3.5 (95% CI, 1.0-12.3; $P = .05$). **Conclusions:** In patients with acute cerebral ischemia discharged before blood culture results could have been available, the rate of subsequent IE was negligible. These findings argue against the liberal use of blood cultures for the routine evaluation of stroke or TIA.

Keywords

infective endocarditis, stroke, transient ischemic attack, blood cultures

Introduction

Ischemic stroke is a major complication of infective endocarditis (IE), and its occurrence portends a poor prognosis.[1-3] Early identification of the underlying infection is critical, as appropriate antibiotic therapy significantly reduces the risk of further complications.[1-4] As a result, the recommended practice at some institutions is to obtain a transthoracic echocardiogram and blood cultures in all cases of stroke.[5]

Without evidence-based practice parameters, there is likely significant variation in provider thresholds for obtaining blood cultures in patients with stroke or transient ischemic attack (TIA). Given the potential impact that a diagnosis of IE would have on stroke management, diagnostic tests including blood cultures may be useful when appropriately selected and guided by the history and physical examination, that is, in the presence of fever, heart murmur, and leukocytosis.[5-8] Indiscriminate collection of blood cultures, on the other hand, may be of low yield considering the multitude of stroke etiologies more common than IE. To explore the potential utility of blood cultures in the evaluation of stroke or TIA, we assessed the rate of missed diagnoses of IE in patients diagnosed with stroke or TIA and discharged before conclusive blood culture results could have been available.

Materials and Methods

Design

To assess the rate of readmission for IE among patients discharged with a diagnosis of stroke or TIA, we performed

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a retrospective cohort study using administrative claims data from the California State Inpatient Database and State Emergency Department Database. The California Office of Statewide Healthcare Planning and Development collects data about all emergency department (ED) visits and hospital stays at nonfederal acute care hospitals in California. After quality checking, these data are provided in a deidentified format to the Agency for Healthcare Quality and Research for its Healthcare Cost and Utilization Project.[9] A unique record linkage number for each patient allows longitudinal tracking of ED encounters and hospitalizations.[10] As this publicly available database includes only deidentified data, our study was certified as exempt from review by our institutional review board.

Patients

Our cohort was comprised of consecutive patients discharged from 2005 to 2011 with a first recorded diagnosis of ischemic stroke or TIA. In accordance with an established and validated algorithm, stroke was defined as *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes 433.x1, 434.x1, or 436 in any diagnosis code position, in the absence of a primary discharge code for rehabilitation (V57) or any codes for subarachnoid hemorrhage (430), intracerebral hemorrhage (431), or trauma (800-804 and 850-854).[11] Transient ischemic attack was defined as *ICD-9-CM* code 435 in the primary diagnosis position with the same exclusions for rehabilitation, hemorrhage, or trauma. Patients with any diagnosis of IE before or at the time of their first stroke or TIA were excluded. To target patients discharged without conclusive blood culture results, only patients discharged directly from the ED or within 2 days of admission were included.

Measurements

The primary outcome was a subsequent hospitalization within 14 days with any new diagnosis of IE (*ICD-9-CM* codes 391.1 or 421.x in any position). The 14-day interval was chosen to avoid patients who subsequently developed IE unrelated to the preceding stroke or TIA; a prior study suggests that for over 80% of cases where cerebral ischemia is the first manifestation of IE, the infectious etiology becomes apparent within 2 weeks of the initial manifestation, with a median interval of 8 days.[5]

To explore potential predictors of readmission for IE, we noted the following previously reported risk factors for IE: age, sex, race, insurance status, diabetes mellitus, HIV, drug abuse, prosthetic valve, other valvular disease, wound infection, urinary infection, and gastrointestinal infection.[12-18] All comorbidities were defined using the Healthcare Cost and Utilization Project's Clinical Classification Software categorization scheme.[9]

Table 1. Baseline Characteristics of Study Participants, Stratified by the Occurrence of Readmission for Infective Endocarditis.[a]

Characteristics	Infective Endocarditis (N = 24)	No Infective Endocarditis (N = 173 942)	*P* Value
Age, mean (SD), y	69.2 (14.1)	70.4 (14.2)	.66
Female	10 (41.7)	93 041 (53.5)	.31
Race/ethnicity			.46
White	17 (70.8)	110 962 (66.9)	
Black	4 (16.7)	12 938 (7.8)	
Hispanic	2 (8.3)	27 858 (16.8)	
Asian	1 (4.2)	10 890 (6.6)	
American Indian	0 (0)	149 (0.1)	
Other	0 (0)	3038 (1.8)	
Payment source			.99
Medicare	16 (66.7)	107 912 (62.1)	
Medicaid	1 (4.2)	10 844 (6.2)	
Private	7 (29.2)	44 354 (25.5)	
Self-pay	0 (0)	5771 (3.3)	
Other	0 (0)	5034 (2.9)	
Diabetes	4 (16.7)	47 471 (27.3)	.36
HIV infection	0 (0)	161 (0.1)	.99
Drug abuse	1 (4.2)	2077 (1.2)	.25
Valvular disease	7 (29.2)	9613 (5.5)	<.001
Valve prosthesis	6 (25.0)	2481 (1.4)	<.001
Urinary tract infection	3 (12.5)	8967 (5.2)	.12
Gastroenteritis	0 (0)	4 (0)	.99
Dental caries	0 (0)	21 (0.01)	.99
Wound infection	0 (0)	27 (0.02)	.99

Abbreviations: HIV, human immunodeficiency virus; SD, standard deviation.
[a]Data are presented as number (%) of participants unless otherwise specified.

Statistical Analysis

Standard descriptive statistics were used to report the rates of our outcome in the overall cohort and separately in the prespecified subgroup of patients discharged directly from the ED with a diagnosis of TIA. Multiple logistic regression was used to examine the association between the IE risk factors mentioned earlier and the primary outcome.

Results

Among 173 966 patients discharged with stroke or TIA, 24 were subsequently hospitalized for IE, equating to a readmission rate of 1.4 per 10 000 (95% confidence interval [CI], 0.8-1.9 per 10 000). Compared to patients without subsequent IE, those with IE readmission were more often male, more often black and less often Hispanic, less frequently had diabetes, and more often had valvular disease, valve prosthesis, and urinary tract infection (Table 1).

Subgroup analysis of 38 485 patients diagnosed with TIA and discharged directly home from the ED revealed a readmission rate of 0.8 per 10 000 (n = 3; 95% CI, 0-1.7 per 10 000).

To prevent overfitting, we included only age, sex, and the 3 comorbidities that appeared most strongly associated with IE in univariate analyses: prosthetic valves, other valvular

disease, and urinary tract infection. Multiple logistic regression identified the following potential associations with readmission for IE after discharge for stroke or TIA: prosthetic valve: odds ratio [OR], 15.8 (95% CI, 1.9-129.0); other valvular disease: OR, 1.5 (95% CI, 0.2-10.8); urinary tract infection: OR, 3.5 (95% CI, 1.0-12.3; $P = .05$).

Discussion

In a large cohort of patients discharged with stroke or TIA before conclusive blood culture results could have been available, we found that the readmission rate for IE was extremely low, occurring at a rate of 1.4 per 10 000. Readmission for IE was even rarer among the subgroup of patients diagnosed with TIA and discharged directly home from the ED. We found potential associations with readmission for IE after discharge for stroke or TIA in valve prosthesis, valvular disease, and urinary tract infection.

Multiple retrospective studies have shown that stroke is not uncommonly the first presenting sign of IE.[1,2,19] Few studies have evaluated the delay between diagnosis of stroke and subsequent diagnosis of IE. In a retrospective review of 34 patients diagnosed with stroke due to IE, 26 had stroke before the diagnosis of IE, and the mean delay before the diagnosis of IE was 8 days; diagnostic delay was no more than 4 days in 17 (50%) patients, and in 15 patients, IE was diagnosed within 2 days of stroke.[5] We were unable to find population-based studies evaluating the rate of subsequent diagnosis of IE after a diagnosis of stroke or population-based studies evaluating the utility of screening for IE by obtaining blood cultures in patients presenting with stroke or TIA. The results of our study suggest that among patients with stroke or TIA, there is a negligible rate of missed diagnoses of IE among those discharged without blood culture results.

Limitations of our study arise from the nature of administrative claims data. First, the study population was identified based on *ICD-9-CM* codes, which lacked important clinical information about signs and symptoms of IE. Therefore, it must be assumed that our findings only hold true for patients without obvious clinical signs of endocarditis, such as fever or other stigmata. To target patients without conclusive blood cultures, only patients discharged within 2 days of stroke or TIA were included. Patients with severe and multiple strokes caused by endocarditis would necessarily have stayed in the hospital for more than 2 days and thus were excluded from this study. However, we were primarily interested in making sure that current diagnostic practices were not leading to missed cases of IE on initial evaluation of stroke or TIA, and this is more likely to happen in less severely affected patients who do not fit the typical profile of endocarditis. Minor strokes and TIAs were specifically assessed because missing a diagnosis of endocarditis in these patients may have detrimental consequences. It should also be noted our study does not pertain to patients in whom clinicians suspect or diagnose endocarditis even in the absence of positive blood cultures or valve vegetations found on echocardiogram. Rather, our study simply points out that the prevalence of endocarditis is low in patients discharged without a presumed diagnosis of endocarditis and without positive blood cultures. It is possible that blood cultures were drawn for patients who were ultimately discharged before results became available. This would not be expected to affect our results as patients whose cultures returned positive within 14 days would presumably be called to return to the hospital for readmission.

Second, *ICD-9-CM* codes have variable sensitivities and specificities. Definite IE is a clinical diagnosis made based on the Duke Criteria,[20] and to our knowledge, there have been no prior studies validating *ICD-9-CM* code 391.1 or 421.x for a definite diagnosis of IE. This limitation would likely lead to an overestimation of the rate of readmission for IE, as 2 previous retrospective studies of patients with IE have found rates of definite diagnoses among all suspected IE cases to be 86% and 85%.[19,21] Third, readmission was interpreted in this study as a surrogate indicator of a missed diagnosis of underlying IE. There remains the possibility that the preceding stroke or TIA could be unrelated to the subsequent admission for IE. To minimize this possibility, we considered only those patients readmitted for IE within 2 weeks of their discharge for stroke or TIA. It is also possible that cases of readmission for IE were missed as there have been rare reports of delayed diagnosis of IE several weeks after stroke.[21,22] Additionally, it is possible that some patients could be readmitted to hospitals outside of California. This is likely a rare occurrence that would have minimal impact on our study results, especially because we took care to exclude non-California residents. Finally, our study lacked data from federal health care facilities. However, these hospitals only comprise 3.1% of the total facilities in California,[23] and it is unlikely that data from the subset of the population seen at federal hospitals would significantly change our study results.

Conclusion

We found a negligible rate of readmission for IE among patients with cerebral ischemia who were discharged before conclusive blood culture results could have been available. This suggests that the rate of IE in patients diagnosed with stroke or TIA and without clinical evidence of IE is negligible. On this basis, the liberal use of blood cultures in the routine evaluation of stroke or TIA appears to be unnecessary.

Declaration of Conflicting Interests

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