

RESEARCH ARTICLE



Changes in Clinical and Demographic Features of Infective Endocarditis Over Three Decades: A Tertiary Center Experience

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Background: Infective endocarditis (IE) continues to pose diagnostic and therapeutic challenges despite advances in healthcare. The epidemiology of IE has shifted globally, yet regional data from Türkiye remain limited.

Objective: To evaluate the changes in clinical and demographic characteristics of IE over three decades using data from a tertiary referral center.

Methods: This retrospective study analyzed 56 patients diagnosed with definite or probable IE between 2001-2010 and compared them with cohorts from 1978-1992 and 1992-2001. Diagnosis was based on modified Duke criteria. Clinical, microbiological, echocardiographic, and treatment outcomes were compared. Logistic regression identified predictors of in-hospital mortality.

Results: The mean age increased significantly across decades (from 32.3 to 51.7 years, p < 0.001). Rheumatic heart disease declined significantly, while prosthetic valve endocarditis and degenerative valve disease rose. Culture-negative cases decreased, whereas enterococcal and coagulase-negative staphylococcal infections increased. Surgery was performed in 46.4% of recent cases. Female gender, S3 or rales on auscultation, and mobile vegetations predicted higher mortality. Early surgery was protective.

Conclusion: Over the last 30 years, IE in Türkiye has evolved from a rheumatic to a prosthetic and device-related disease, paralleling trends in developed countries. Diagnostic and surgical advances have changed management, but mortality remains high, emphasizing the need for early intervention and standardized treatment protocols.

Keywords: Infective endocarditis; Prosthetic valve; Echocardiography; Mortality.

1. INTRODUCTION

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Infective endocarditis (IE) is a life-threatening infection of the endocardial surface of the heart, typidemographic indices [2-4].

cally involving the valves. Contrary to earlier beliefs, it is not a rare condition. In developed countries, its incidence ranges from 3 to 10 per 100,000 population annually [1]. Although the global burden of rheumatic heart disease has declined, the incidence of IE has risen, particularly in countries with higher socio-

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This trend is largely attributed to an increase in predisposing conditions such as prosthetic heart valves, degenerative valvular disease, and nosocomial infections related to hemodialysis, invasive procedures, and intracardiac devices [5,6]. Additionally, intravenous drug use and advancements in diagnostic modalities like transesophageal echocardiography (TEE) have contributed to the observed increase [7].

IE can affect both native and prosthetic valves, accounting for approximately 50% and 10% of cases, respectively [8]. Aortic valve involvement is more common than mitral valve involvement [9]. Recent studies indicate a shift in microbiological etiology, with a rising prevalence of Staphylococcus aureus and coagulase-negative staphylococci [10,11]. Despite therapeutic improvements, short-term mortality remains high, ranging between 10-24% [12-14]. Surgical intervention is required in nearly half of all IE cases [15].

Most of the existing data on infective endocarditis (IE) originate from large-scale studies conducted in Europe and North America [16-19], where healthcare infrastructure, diagnostic capabilities, and patient demographics differ significantly from those in many developing or transitional healthcare systems. As a result, the epidemiological and clinical patterns observed in high-income settings may not be fully generalizable to other regions. In Türkiye, published data on IE are sparse, often limited to single-center reports with short observation periods, and rarely offer comprehensive temporal comparisons. Moreover, previous studies have not adequately assessed how the evolving patterns in Türkiye relate to trends in neighboring countries or reflect the broader shift in IE seen globally—such as the decline in rheumatic heart disease and the rise of prosthetic valve and device-related infections. To address these gaps, we aimed to evaluate the longitudinal changes in clinical, demographic, microbiological, and echocardiographic features of IE over a 30-year period at a high-volume tertiary referral center. Specifically, we compared patients hospitalized with IE between 2001-2010 with two historical cohorts from the same institution (1978-1992 and 1992-2001), providing one of the most comprehensive longitudinal analyses of IE in the region to date.

2. MATERIAL AND METHOD

This is a retrospective study of 56 patients with infective endocarditis (IE) who were hospitalized between 2001 and 2010 at the Istanbul University Cardiology Institute (Department of Cardiology) and Cerrahpaşa Medical Faculty (Departments of Infectious Diseases and Internal Medicine). Of these, 38 patients were from the Cardiology Institute and 18 from Cerrahpaşa. Patients were retrospectively identified from the transesophageal echocardiography (TEE) database and hospital records. All patients underwent TEE as part of their diagnostic workup, ensuring consistency in case selection.

A total of 52 patients met the criteria for a definite diagnosis and 4 for a probable diagnosis, according to the modified Duke criteria [1]. All TEE examinations were performed by trained cardiologists in accordance with the guidelines of the American Society of Echocardiography [2]. TEE was routinely available throughout the study period, and all patients in this cohort were evaluated with TEE, which enhanced diagnostic sensitivity and uniformity.

The following parameters were recorded for each patient: age, gender, presenting symptoms, duration of symptoms, predisposing conditions, presumed route of entry of the infectious agent, physical examination findings, inflammatory and biochemical markers, microbiological and echocardiographic findings, treatments (including surgical interventions), complications, and in-hospital outcomes. After discharge, patients were contacted to determine their long-term prognosis, and deaths were documented.

The data from this cohort (2001-2010) were compared with two previous patient groups diagnosed at the same institution: one from 1978-1992 (n = 88), and the other from 1992-2001 (n = 66). In both cohorts, diagnosis was also made using the modified Duke criteria [1]. These earlier cohorts were extracted from two previously published studies from the same institution and were also based on retrospective review. Data availability and record completeness were consistent across the three time periods. Microbiological diagnostic methods, including the number of blood cultures and collection protocols, followed institutional standards and remained stable over time, although minor improvements in culture techniques may have occurred. This supports the observed reduction in culture-negative cases as a genuine trend rather than a methodological artifact.

Ethical approval for this study was obtained from the Ethics Committee of the Istanbul University Cardiology Institute (Decision No: B.30.2.İST.0.51.00.00-23, dated 01.02.2011), based on a submission regarding the medical specialty thesis titled "What has changed in the clinical and demographic characteristics of infective endocarditis patients in the last three decades?" This retrospective study was conducted in accordance with the ethical standards of the institutional ethics committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Statistical analysis was performed using SPSS for Windows version 27. The Mann-Whitney U test was used for comparison of continuous variables, and the Chi-square test was applied for categorical data. A logistic regression analysis was conducted to identify independent predictors of in-hospital mortality. A two-sided p-value <0.05 was considered statistically significant [3].

3. RESULTS

A total of 56 patients with infective endocarditis (IE) were identified between 2001 and 2010. The mean age was 51.7 ± 16.5 years, significantly higher than in the previous cohorts (32.3 ± 11.6 in 1978-1992 and 34.4 ± 15.2 in 1992-2001; p < 0.001, Table 1). The proportion of female patients rose to 46.4%, though this increase was not statistically significant (p = 0.26, Table 1). Among predisposing factors, the presence of a prosthetic valve was the most frequent (42.8%), followed by rheumatic heart disease (17.8%) and congenital heart disease (12.5%). There was a statistically significant decrease in rheumatic heart disease over time (p = 0.04), while prosthetic valve endocarditis showed a rising trend but did not reach significance (p = 0.07). Degenerative valve disease emerged as a new predisposing factor in the latest cohort (p = 0.01, Table 1).

In terms of portal of entry, no source was identified in 58.9% of cases. Among the identifiable sources, other systemic infections (14.2%), dental procedures (10.7%), therapeutic invasive interventions (8.0%), diagnostic procedures (7.1%), and intracardiac devices (7.1%) were reported. Compared to earlier decades, significant increases were observed in diagnostic procedures and device-related cases (p=0.01 for both), while the proportion of patients with no identified entry site decreased significantly (p=0.005, Table 1).

Fever (91.1%) and heart murmur (96.4%) remained the most common clinical features. Laboratory evaluations revealed elevated CRP in 96.4%, leukocytosis in 75% (p=0.01), anemia in 53.6%, and elevated ESR in 76.7%. Chest radiography showed an increased cardiothoracic index (CTI > 0.5) in 42.8% of patients, which had decreased significantly compared to previous decades (p=0.01, Table 1).

Vegetations were observed on echocardiography in 91.1% of patients. The aortic and mitral valves were equally involved (37.5% each), with additional cases showing dual-valve involvement (10.7%) or tricuspid valve involvement (5.3%). Pulmonary valve vegetations, noted in prior cohorts, were absent in this decade, indicating a statistically significant trend across periods (p=0.01, Table 2). Other echocardiographic findings included abscesses (12.5% aortic, 3.5% mitral), prosthetic valve dehiscence (7.1% aortic, 14.2% mitral, and 1.7% tricuspid), new valvular regurgitation, pericardial effusion (5 cases), and one case of vegetation on a ventricular septal defect (Table 2).

Microbiological analysis revealed a marked reduction in culture-negative cases to 8.9% (p<0.001, Table 2). Meanwhile, infections due to *Enterococcus* spp. (19.6%, p=0.04) and coagulase-negative staphylococci (19.6%, p=0.03) increased significantly. *Staphylococcus aureus* accounted for 17.8% of cases and *Streptococcus viridans* re-emerged after being absent in the prior decade (Table 2).

Complications were common. Heart failure occurred in 19.6% of patients, followed by embolic events (17.8%), hemorrhagic stroke (7.1%), acute renal failure (5.3%), and mycotic aneurysm (3.5%). Mortality was 45% in patients with heart failure, 50% in those with embolic complications, and 25% among those with stroke. Overall, in-hospital mortality was 17.8%, which did not differ significantly from earlier cohorts (p=0.50, Table 1).

Surgical treatment was performed in 26 patients (46.4%). Indications included congestive heart failure (42.3%), uncontrolled infection (26.9%), and prosthetic valve endocarditis (7.6%), the latter showing a

statistically significant decrease compared to previous decades (p=0.007, Table 3). Among surgical cases, 38.4% had staphylococcal infections, 23.1% had streptococcal infections, 19.3% had enterococcal infections, and 7% were culture-negative. Surgical mortality was 19% (Table 3).

Binary logistic regression identified female gender (OR: 2.8, 95% CI: 2.48-4.1, p=0.02), the presence of S3 or rales on auscultation (OR: 5.2, 95% CI: 4.81-6.2, p=0.011), and mobile vegetation (OR: 1.8, 95% CI: 1.49-2.30, p=0.035) as significant predictors of in-hospital mortality. Conversely, early surgical intervention was associated with a significant reduction in mortality (OR: 0.007, 95% CI: 0.0-0.954, p=0.048, Table 4).

Table 1. Clinical and Biochemical Findings of the Patients.

Parameter	1978-1992 (n=88)	1992-2001 (n=66)	2001-2010 (n=56)	p-value
AGE (years)	32.3 ± 11.6	34.4 ± 15.2	51.7 ± 16.5	< 0.001
Female (%)	40.9	36.3	46.4	0.26
Male (%)	59.1	63.7	53.6	0.26
Rheumatic heart disease	65.9%	48.5%	17.8%	0.04
Prosthetic valve	14.7%	27.3%	42.8%	0.07
Mitral valve prolapsus	3.4%	3.0%	1.7%	0.51
Congenital heart disease	9.1%	13.6%	12.5%	0.91
Degenerative valvular disease	-	-	8.9%	0.01
No predisposing factor	5.7%	7.5%	12.5%	0.36
Prosthetic valve endo- carditis	14.7%	27.2%	42.8%	0.07
Dental procedures	22.7%	4.5%	10.7%	0.19
Diagnostic invasive intervention	3.4%	-	7.1%	0.01
Therapeutic invasive intervention	28.4%	9.1%	8.0%	0.97
Other system infections	2.3%	4.5%	14.2%	0.06
No entry site found	32.9%	81.8%	58.9%	0.005
Intracardiac device	2.3%	-	7.1%	0.01
Fever (>38°C)	87.5%	83.3%	91.1%	0.20
Cardiac murmur	89.8%	90.9%	96.4%	0.86
Increased ESR	95.4%	74.2%	76.7%	0.73
Increased CRP	84.1%	69.6%	96.4%	0.20
Leukocytosis	40.9%	46.9%	75%	0.01
Anemia	65.9%	68.2%	53.6%	0.23
CTI >0.5	86.4%	63.6%	42.8%	0.01
In-hospital mortality	22%	22%	17.8%	0.50

Note: HD: Heart Disease; VD: Valvular Disease; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; CTI: Cardiothoracic Index; IE: Infective Endocarditis.

Table 2. Echocardiographic and Microbiologic Findings of the Patients.

Parameter	1978-1992 (n=88)	1992-2001 (n=66)	2001-2010 (n=56)	p-value
Vegetation localization	63.6%	81.8%	91.1%	0.34
Aortic valve	29.5%	33.3%	37.5%	0.49
Mitral valve	23.8%	25.7%	37.5%	0.16
Mitral and Aortic valve	6.8%	13.6%	10.7%	0.76
Tricuspid valve	3.4%	7.6%	5.3%	0.62
Pulmonary valve	-	4.5%	-	0.01
Streptococcus Viridans	12.5%	1.5%	12.5%	0.01
α Hemolytic streptococ- cus	4.5%	1.5%	7.1%	0.11
β Hemolytic streptococ- cus	3.4%	9.1%	1.7%	0.08
Staphylococcus Aureus	13.6%	12.1%	17.8%	0.37
Coagulase Neg. Staphy- lococcus	2.3%	3.0%	19.6%	0.03
Staphylococcus Epi- dermidis	14.7%	12.1%	3.6%	0.08
Enterococcus	-	7.6%	19.6%	0.04
HACEK	-	1.5%	3.6%	0.46
Brucella	1.1%	1.5%	3.6%	0.46
Candida	-	1.5%	-	0.35
Gram Negative Bacilli	1.1%	1.5%	1.7%	0.90
Diphtheroid	-	-	1.7%	0.35
Culture negative	46.6%	46.9%	8.9%	< 0.001

Note: HACEK: Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella, Kingella; CONS: Coagulase-Negative Staphylococcus; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; IE: Infective Endocarditis.

Table 3. Information of the Patients Who Underwent Surgery.

Parameter	1978-1992 (n=88)	1992-2001 (n=66)	2001-2010 (n=56)	p-value
Surgery (n,%)	20 (22.7%)	42 (63.6%)	26 (46.4%)	0.057
Congestive heart failure	7 (35%)	15 (35.7%)	11 (42.3%)	0.09
Prosthetic valve endo- carditis	5 (25%)	9 (21.4%)	2 (7.6%)	0.007
Uncontrolled infection	4 (20%)	7 (16.6%)	7 (26.9%)	0.24
Recurrent emboli	3 (15%)	4 (9.5%)	2 (7.7%)	0.41
Other	1 (5%)	7 (16.6%)	4 (15.4%)	0.27

Note: CHF: Congestive Heart Failure; IE: Infective Endocarditis; OR: Odds Ratio; CI: Confidence Interval.

Table 4. Predictors of In-Hospital Mortality (2001-2010).

Parameter	OR (95% CI)	p-value
Age	1.163 (0.971-1.393)	0.10
Female gender	2.8 (2.48-4.1)	0.02
Prosthetic valve	0.84 (0.435-2.300)	0.097
History of acute rheumatic fever	1.016 (0.030-1.35)	0.993
S3 or rales on auscultation	5.2 (4.81-6.2)	0.011
Streptococcus	1.2 (0.032-1.7)	0.276
Staphylococcus	0.22 (0.001-0.44)	0.572
Enterococcus	1.2 (0.032-1.7)	0.252
Mobile vegetation	1.8 (1.488-2.300)	0.035
Vegetation < 10mm	0.93 (0.78-1.4)	0.99
Vegetation 10-15 mm	0.87 (0.04-1.5)	0.99
Vegetation > 15mm	0.94 (0.72-1.67)	0.99
Surgery	0.007 (0.0-0.954)	0.048
Duration of symptoms	0.967 (0.911-1.027)	0.275

Note: OR: Odds Ratio; CI: Confidence Interval; IE: Infective Endocarditis; S3: Third Heart Sound.

4. DISCUSSION

This study analyzed patients diagnosed with infective endocarditis (IE) between 2001 and 2010, comparing their clinical characteristics and outcomes with data from previous decades. The findings reveal a notable increase in patient age and a higher frequency of prosthetic valve endocarditis in recent years.

Despite advancements in diagnostics and therapeutics, IE continues to be associated with substantial morbidity and mortality. Over the years, the epidemiological profile of IE has evolved. Previous large series, such as those by Loupa et al. and Murdoch et al., reported mean patient ages of 54.4 and 57.9 years, respectively [22,23]. In our cohort, the mean age was 51.7 ± 16.5 years, which is consistent with the global trend toward older age at diagnosis. This trend has similarly been observed in Somali patients, as documented by Abdi et al., where older individuals with underlying comorbidities presented with severe IE [33]. This increase is likely due to a decline in rheumatic heart disease incidence and a concurrent rise in degenerative and congenital heart conditions, attributable to longer life expectancy [4]. Recent case reports from resource-limited settings further reflect this epidemiologic transition, where degenerative valve disease and healthcare-associated infections are increasingly prominent [36]. The decreasing prevalence of acute rheumatic fever, facilitated by effective antibiotic use, may also contribute to this shift [1,9].

Strikingly, the prevalence of prosthetic valve endocarditis in our study was 42%, which significantly exceeds the 20% typically reported in large series [14]. This discrepancy may reflect referral bias to our tertiary center and a higher proportion of post-surgical patients, many of whom had undergone procedures for rheumatic heart disease. Supporting this, 46% of patients in our series had a history of acute rheumatic fever. Furthermore, diagnostic invasive procedures and device-related IE are increasingly observed in our setting, mirroring international trends [25]. These trends are echoed in reports from Somalia, where coagulase-negative staphylococci (CoNS)-related IE has emerged in non-IV drug users and immunocompromised individuals, such as post-splenectomy patients [35].

These shifts may also be influenced by increased healthcare exposure, including catheter-based interventions, valve replacement surgeries, and broader use of intracardiac devices, which are known risk factors for IE in contemporary cohorts [26,27].

Transesophageal echocardiography (TEE) remains a cornerstone in IE diagnosis due to its high sensitivity (>90%) and ability to detect vegetations and complications [26]. In our study, vegetations were identified in 91.1% of patients. These were most commonly located on the aortic (37.5%) and mitral valves (37.5%), with 10.7% affecting both valves and 5.3% involving the tricuspid valve. These results are broadly consistent with findings by Murdoch et al. and Chu et al., although minor variations may be due to differences in population characteristics and imaging protocols [23,28]. A recent Somali case of right-sided IE caused by coagulase-negative staphylococci with pulmonary septic emboli in a non-IV drug user further exemplifies the evolving pathogenic role of CoNS even in native valves [34].

Microbiologically, the increasing prevalence of Enterococcus and coagulase-negative staphylococci is noteworthy. These shifts, alongside a reduction in culture-negative cases, likely reflect improved diagnostic capabilities and changing patient demographics. While Staphylococcus aureus remains the most prevalent organism in Europe and North America [29], case reports from Abdi et al. have highlighted similar microbial patterns in Somalia, with both Staphylococcus aureus and CoNS implicated in severe disease [33,34,35]. Enterococcus species are emerging pathogens in elderly patients, particularly those with prolonged hospital stays or genitourinary infections [30]. Among our enterococcal IE cases, patients had a mean age of 53 years, with a prosthetic valve involvement rate of 36%, surgical intervention in 54%, and a mortality rate of 27%. The significant decline in culture-negative IE aligns with trends reported in the literature [31].

The non-significant reduction in in-hospital mortality over time may reflect the increasing severity of presentations—such as prosthetic valve involvement—and delayed surgical intervention in some cases. Additionally, resource limitations and delays in referral may have contributed to unchanged mortality rates despite improvements in diagnostic and therapeutic tools [5,11].

Surgical intervention is increasingly favored due to improved outcomes, with surgery rates now approaching 50% in many series [32]. Indications include heart failure, uncontrolled infection, and recurrent emboli. In our cohort, surgery was performed in 46.4% of cases, with primary indications being congestive heart failure (42.3%), uncontrolled infection (26.9%), and recurrent embolism (7.7%). Notably, fewer surgeries were performed for prosthetic valve endocarditis compared to previous periods. Most surgically treated patients had staphylococcal infections.

Current in-hospital mortality for IE remains between 15% and 20%, with one-year mortality nearing 40% [2,6]. Despite evolving disease profiles and therapeutic advances, our study did not find a significant reduction in in-hospital mortality over time. Multiple factors may contribute to persistent mortality, including microbial virulence, comorbidities, delays in diagnosis and treatment, and timing of surgery. A case from Somalia involving severe mitral regurgitation and markedly elevated troponin levels due to Staphylococcus aureus IE emphasized the prognostic utility of cardiac biomarkers in guiding urgent surgical decisions [33]. Conversely, early surgical intervention was associated with reduced mortality, highlighting the importance of timely surgical decision-making in eligible patients.

5. COMPARISON WITH INTERNATIONAL REGISTRIES AND MIDDLE-INCOME CONTEXTS

Our findings are broadly consistent with international registry data, including the EURO-ENDO registry and the International Collaboration on Endocarditis (ICE) cohort. These large-scale registries have shown a similar shift from rheumatic to prosthetic valve and device-associated endocarditis, with rising prevalence of staphylococcal and enterococcal infections [31,23].

Compared to high-income countries, middle-income nations like Türkiye are experiencing a dual burden: the persistence of rheumatic heart disease in older patients and rising healthcare-associated IE in those exposed to medical devices and invasive procedures. This pattern mirrors trends seen in countries with transitioning healthcare systems, including evidence from Brazil, Greece, and other low- to middle-income nations [9,12,24].

6. IMPACT OF HEALTHCARE SYSTEM EVOLUTION AND REGIONAL CASE SUPPORT

The changing IE landscape may also reflect broader improvements in the healthcare system, including widespread use of echocardiography (particularly TEE), greater access to ICU care, and more targeted antimicrobial therapy. These factors may contribute to earlier diagnosis, better pathogen identification, and improved management [20,26,32]. Although advancements such as improved TEE imaging quality [26], increased access to surgery [32], and better antimicrobial stewardship have enhanced management strategies, systemic limitations may still constrain outcomes in middle-income settings.

7. STRENGTHS AND LIMITATIONS

This study offers several notable strengths. It presents a rare longitudinal comparison of infective endocarditis (IE) cases across three decades within a tertiary referral center. By utilizing consistent diagnostic criteria (modified Duke criteria) and standardized data collection, the study provides a unique perspective on the evolving epidemiology, microbiological spectrum, and clinical management of IE in a large urban academic hospital. Furthermore, the inclusion of both native and prosthetic valve IE cases, and detailed surgical indications and outcomes, enhances the clinical relevance and depth of the analysis.

However, some limitations must be acknowledged. This is a retrospective, single-center study, which may introduce selection bias and limit generalizability. Differences in diagnostic tools, microbiological techniques, echocardiographic imaging, and clinical practices over the study period may have influenced data uniformity. The reliance on medical record documentation, particularly from earlier decades, may have led to incomplete or missing data, especially concerning antibiotic regimens and long-term outcomes. Additionally, the relatively small sample size in the 2001-2010 cohort may have limited the power of statistical analyses, particularly for identifying predictors of mortality. Lastly, the lack of external validation or prospective follow-up reduces the ability to draw firm causal inferences.

CONCLUSION

Infective endocarditis remains a serious condition with high mortality despite medical advances. Over the past 30 years, the patient profile in our country has shifted—rheumatic heart disease has declined, while prosthetic valve involvement and staphylococcal infections have increased. These changes reflect global trends and highlight the importance of timely diagnosis, early surgical intervention when indicated, and the need for standardized treatment protocols in specialized centers.

AI USE DISCLOSURE

During the preparation of this manuscript, ChatGPT (GPT-4, OpenAI, 2025) was used to assist in the revision of grammar, language clarity, reference formatting, and structuring of tables and figures. The content, analysis, and conclusions were entirely conceived, verified, and approved by the authors. The AI tool did not contribute to the originality or interpretation of the scientific data.

AUTHORS' CONTRIBUTIONS

The author confirms sole responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The author confirms that this article's content has no conflict of interest.

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