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Editorial

Nuanced Interpretation of Administrative Data: The Case of Hospitalization for Infective Endocarditis in Adults With Tetralogy of Fallot

Alexander R. Opotowsky, MD, MMSc,[a,b] Sarah S. Pickard, MD, MPH,[a] and Gary D. Webb, MD[c]

[a] Department of Cardiology, Boston Children's Hospital, Boston, Massachusetts, USA

[b] Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA

[c] Department of Medicine, Toronto General Hospital, Toronto, Ontario, Canada

See article by Egbe et al., pages 721–726 of this issue.

> *It has long been known that bacterial endocarditis is especially common on valves and in localities in the heart the seat of chronic change or of congenital malformation.*
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> —William S. Thayer[1]
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> *Bacterial or Infective Endocarditis, The Gibson Lectures for 1930*

Infective endocarditis (IE) was a feared complication of congenital heart disease (CHD) long before repair was feasible.[1,2] Surgical advances in the second half of the 20th century fundamentally transformed CHD care from a spectator sport into a full-contact sport, with dramatic improvements in patient survival and functional capacity. In parallel, there have been exceptional developments in treatment for bacterial infections. Despite this progress, IE remains a major cause of morbidity and mortality in the burgeoning, aging CHD population.[3-5]

The steady status of IE as a scourge on CHD patients, however, belies substantial changes in the epidemiology and clinical management of IE, even beyond the development and expansion of antimicrobial therapy. First, there has been a shift in causal bacterial species from *Streptococcus* to more aggressive *Staphylococcus* species.[6-8] Second, systemic host characteristics have changed. The aging CHD population brings with it a greater burden of medical comorbidities,[9] some of which are associated with immunosuppression. The epidemic of injection drug use has additionally affected IE epidemiology.[10] Better dental hygiene presumably has also had an effect.[11] Third, IE in unrepaired CHD is often associated with congenitally dysmorphic valves or jet lesions from intracardiac shunts; the nidus of risk in repaired CHD is increasingly related to prosthetic materials, especially prosthetic valves.[5] This issue has become only more acute with the development of percutaneous valve replacement.[12]

The article by Egbe and colleagues in the present issue of the *Canadian Journal of Cardiology*, entitled "Trends and outcomes of infective endocarditis in adults with tetralogy of Fallot: a review of the national inpatient sample database,"[13] provides a timely perspective into the epidemiology of IE hospitalization among adults with tetralogy of Fallot (TOF). The authors aimed to describe trends in the incidence of IE-related admissions for adults with TOF in the United States between 2000 and 2014. They contrasted characteristics of these IE-related TOF hospitalizations with hospitalizations without IE. To address these objectives, the authors used the National Inpatient Sample (NIS), a nationally representative administrative discharge database of United States nonfederal acute care hospitals. The large size and population-based design are key advantages of this data set. The NIS has, however, several major limitations. Information is only available for a single hospitalization and is limited to administrative codes without the capacity to identify noncoded chronic comorbidities, medication use, or clinical testing. More fundamentally, the NIS is representative of all hospitalizations in the United States rather than all people or all patients or all hospitalized patients.

Within this context, the study showed that the prevalence of an administrative diagnostic code for IE among hospitalizations for adults with TOF increased significantly, from 1.9% in 2000-2004 to 2.4% in 2010-2014. TOF patients hospitalized with IE were more likely than TOF patients hospitalized without IE to be male, younger, black, cared for at an urban hospital, and have implanted prosthetic material (eg, previous valve replacement, pacemaker, or defibrillator). In-hospital mortality was 6% in those admitted with IE. Notably, a high proportion of patients with IE were transferred to another acute-care hospital (20.5% vs 4.7% for non-IE TOF hospitalizations). The use of home health care services at discharge was 2.5-fold higher, and the rate of

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Corresponding author: Dr Alexander R. Opotowsky, Boston Children's Hospital, Brigham and Women's Hospital, Harvard Medical School, 300 Longwood Ave, Boston, Massachusetts 02115, USA. Tel.: +1-617-355-6508; fax: +1-617-739-8632.

E-mail: alexander.opotowsky@cardio.chboston.org

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discharge against medical advice was > 5-fold higher in IE hospitalizations compared with non-IE hospitalizations. These important findings emphasize the challenge of caring for IE in the current era and highlight the substantial resources these patients require even after discharge.

These results generally agree with our previous beliefs about IE in TOF. For instance, we have good reasons to believe the rate of IE among adults with TOF has been rising over the past 2 decades. First, the incidence of IE has increased in the general population, along with several subsets, and most of the proposed underlying factors would be expected to apply to TOF.[7,8] These include aging of the population, the epidemic of injection drug use, and the growing prevalence of immunosuppression. It remains unclear whether recent changes in antibiotic prophylaxis recommendations have increased the risk of IE[7,14]; if the change in IE prophylaxis practice has affected incidence, the effect on TOF might be less prominent because high-risk patients (eg, those with a prosthetic valve) would still receive recommended prophylaxis. A second factor favouring an increasing incidence of IE in TOF is the progressive liberalization of accepted indications for pulmonary valve replacement (PVR) in TOF with pulmonary regurgitation.[15-18] Prosthetic valves are associated with higher risk for developing IE and worse outcomes when IE occurs.[19] Whatever the benefits of a proactive approach to PVR, placement of a prosthetic PVR earlier in life should be associated with a longer time at risk for complications of a prosthetic valve, presumably including higher cumulative lifetime risk of IE. Third, there has been a paradigm shift toward percutaneous PVR. Although percutaneous PVR is associated with excellent outcomes and less acute morbidity than surgical PVR, experience and emerging data suggest at least some types of percutaneous PVR are associated with a higher risk for IE than traditional surgically-implanted valves.[20-22]

Because of the expectation that IE is becoming more common in adults with TOF on the basis of existing evidence, readers might understandably infer that the current report provides clear support for this assertion. However, an increasing proportion of TOF hospitalizations including an administrative code indicating IE is present does not necessarily imply a rise in the incidence of IE in TOF (eg, cases per year per population at risk). The relationship between TOF hospitalizations and IE-related administrative codes can be confounded by changes in other factors: (1) the size of the population of adults with TOF at risk for hospitalization; (2) the number of TOF hospitalizations for other reasons; and (3) the likelihood that an administrative code for IE will be recorded in a given clinical context.

Without a doubt, the first 2 factors mentioned previously are in flux. The number of adults with TOF is increasing, and the reasons for hospitalization are changing because of evolving clinical understanding (eg, lower threshold for PVR) and changes in population characteristics (eg, aging), as has been seen in CHD overall.[23,24] Less obviously, the implications of an administrative code being present have probably also changed. We queried the same database used for the current analysis (National/ Nationwide Inpatient Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality) for all hospitalizations in patients ≥ 18 years old with the exclusion of those involving childbirth.[25] Between 2005 and 2014 the average number of diagnoses listed per each admission increased by 66%, from 7.1 to 11.8 (median, 7-11; Fig. 1). A similar shift has occurred in Medicare claims. This phenomenon has caused sophisticated models to unexpectedly overestimate the effectiveness of Medicare programs to prevent readmissions because the risk-adjustment models have assumed stable coding practices.[26] It is implausible that patient complexity increased 66% over 10 years. More credible reasons for code inflation include incentives to list more and more complex diagnoses for reimbursement, adoption of electronic medical records facilitating more comprehensive coding, and, most directly, a change in 2010 when the maximum number of diagnoses allowed increased from 15 to 25. Thus, no discharge included > 15 diagnoses before 2010. In 2010, 10.2% of discharges listed > 15 diagnoses; that figure had increased to 26.3% by 2014. One might reasonably argue this shift should have only a modest influence on the specific codes in question, because IE is a distinct and nonchronic diagnosis, and its presence would be of major importance to any hospitalization. However, IE diagnosis is often not straightforward. It is possible that IE is increasingly likely to be coded in cases of possible, but not definite, IE or for recurrent hospitalizations for long-term complications of previously treated endocarditis. For perspective, institutional databases identified 216 patients hospitalized at 66 Japanese centres between 1997 and 2001 with a diagnosis of IE; of these, 137 (63%) fulfilled the modified Duke criteria for definite endocarditis.[27]

Why does the distinction between the data reported and the actual incidence rate of IE in TOF matter? Clinicians and patients care about the absolute risk for IE, not the proportion of all hospitalizations that involve IE. It is difficult to understand the relevance of the latter concept to these primary "stakeholders." However, the current findings have real implications for administrators and policymakers.

Many of the same caveats apply to the inferences we can make from observed differences between those with and without IE in this database. Some seemingly protective factors rather indicate an increased risk for an alternative competing indication for admission and might only appear to be protective because they will be over-represented in the denominator of non-IE admissions. For example, atrial fibrillation was less common among those with IE (9.3% vs 15.6%). The lower rate of atrial fibrillation in the IE group could be due to other factors such as younger age; it could, however, be a consequence of patients admitted with a primary indication of atrial fibrillation rather than atrial fibrillation in the context of another diagnosis. A true protective effect, whereby IE causes a lower risk for atrial fibrillation compared with the average patient who does not have IE, however, seems unlikely. Likewise, patient characteristics might be associated with a higher risk for non-IE hospitalizations. Female sex is quite strongly associated with an increased risk of hospitalization for childbirth. Approximately one-fifth of all discharges for women in the United States are for childbirth, and, consequently, among hospitalizations for patients 15-44 years old, the discharge rate for women is much higher than for men (1248 vs 450 per 10,000 population, in 2007).[28] Surely, patients admitted for the indication of childbirth are unlikely to happen to also have IE. Therefore, including delivery hospitalizations in the denominator artifactually suggests a

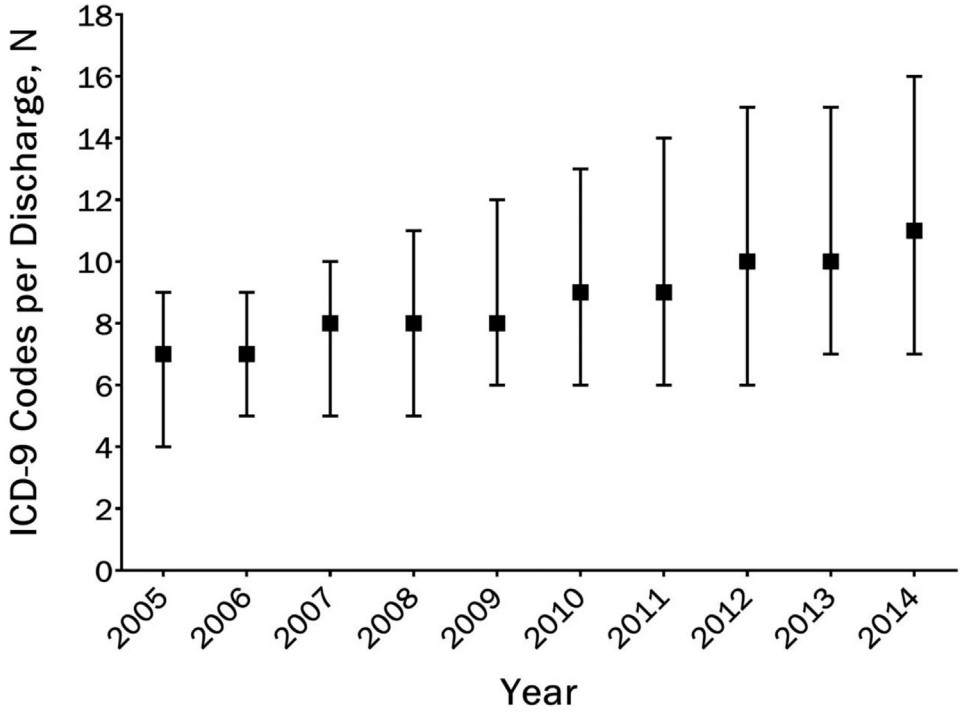

Figure 1. The median number of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9) diagnoses listed for each hospital discharge increased between 2005 and 2014, from 7 to 11. Error bars represent the 25th to 75th percentiles. These data are for patients at least 18 years old at the time of discharge and exclude any hospitalization including a diagnosis code suggestive of childbirth.

lower rate of IE in women than men. Although existing data suggest men with CHD do have a higher risk for IE,[3,5,20] the current analysis is likely to overestimate this effect.

In summary, IE is an increasingly common issue among hospitalized adults with TOF, although the current report, because of limitations intrinsic to study design, cannot provide definitive insight into whether the absolute risk for IE is changing or whether patient characteristics are associated with increased risk. The limitations of deidentified administrative data require cautious analysis and interpretation, for an array of reasons. Unexpected findings should, therefore, be viewed with caution and rarely should such analyses substantially disturb a well considered previous belief. The current study, taken in the context of other existing information, argues that adults with TOF are at markedly increased risk for IE compared with the general population. It also supports the idea that the risk of IE is increasing in TOF, and that patients with IE differ systematically from those admitted for other reasons. IE hospitalizations involve greater use of resources, and this burden extends beyond the time of discharge. More detailed study is warranted to understand the reason for these differences and improve our management of these patients.

Disclosures

The authors have no conflicts of interest to disclose.

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