Positive predictive value of infective endocarditis in the Danish National Patient Registry: a validation study

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Abstract

The positive predictive value of an infective endocarditis diagnosis is approximately 80% in the Danish National Patient Registry. However, since infective endocarditis is a heterogeneous disease implying long-term intravenous treatment, we hypothesiszed that the positive predictive value varies by length of hospital stay. A total of 100 patients with first-time infective endocarditis in the Danish National Patient Registry were identified from January 2010 – December 2012 at the University hospital of Aarhus and regional hospitals of Herning and Randers. Medical records were reviewed. We calculated the positive predictive value according to admission length, and separately for patients with a cardiac implantable electronic device and a prosthetic heart valve using the Wilson score method. Among the 92 medical records available for review, the majority of the patients had admission length ⩾2 weeks. The positive predictive value increased with length of admission. In patients with admission length <2 weeks the positive predictive value was 65% while it was 90% for admission length ⩾2 weeks. The positive predictive value was 81% for patients with a cardiac implantable electronic device and 87% for patients with a prosthetic valve. The positive predictive value of the infective endocarditis diagnosis in the Danish National Patient Registry is high for patients with admission length ⩾2 weeks. Using this algorithm, the Danish National Patient Registry provides a valid source for identifying infective endocarditis for research.

Introduction

Infective endocarditis (IE) is a complex disease with a high mortality and morbidity [1]. Hospital administrative registries are cornerstones in epidemiological studies of IE [2, 3]. Many administrative healthcare registries are based on discharge diagnoses coded according to the *International Classification of diseases, Tenth revision* (ICD-10) [2, 4]. Data from such registries are essential tools in increasing the epidemiological knowledge of IE. Nationwide registries have not only proved valuable in observational studies but also in registry-supported randomised controlled clinical trials. Moreover, the use of nationwide registries to examine preventive strategies of IE has been debated in scientific communities [5, 6]. A prerequisite is, however, that the IE diagnosis in the administrative registries is reliable.

A recent validation study of the cardiovascular diagnoses in the Danish National Patient Registry (DNPR) found a positive predictive value (PPV) of 82% for IE [7]. However, because the IE population is heterogeneous and the minimum period of in-hospital intravenous antibiotic treatment in Denmark is 2 weeks [8], the PPV may be lower in patients with shorter hospital stays. We, therefore, examined the PPV of IE according to the length of hospital stay.

Methods

The Danish National Health Service provides free universal tax-supported health care. Denmark is a homogenous country, divided into five regions, all with similar demographic and socioeconomic characteristics [9]. We identified patients from the Central Denmark Region, specifically from the Aarhus University Hospital and from two regional hospitals (Herning and Randers) in the period from 1 January 2010 to 31 December 2012. The DNPR and its research potential have been described in details previously [2].

The current study is a post-hoc analysis of a previous validation study [7]. In brief, we identified a random sample of 100 patients diagnosed with first-time primary or secondary diagnoses of IE in the DNPR. IE was identified by the following ICD-10 codes: DI33.x, DI38.x and DI39.8. We excluded outpatients in this post-hoc analysis.
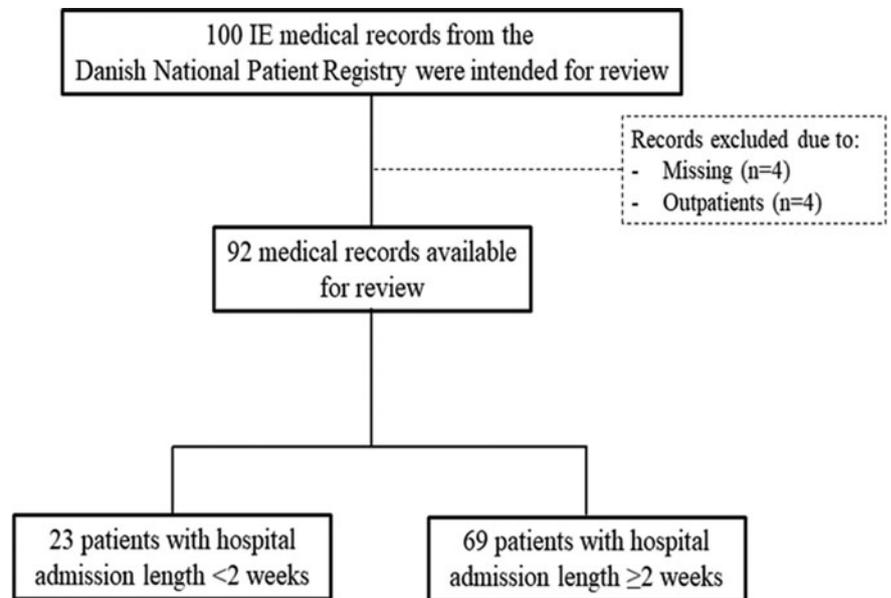
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Fig. 1. Flow chart of the study cohort selection process.

Table 1. Positive predictive value of infective endocarditis in the Danish National Patient Registry

	N (%)	Confirmed diagnoses/all available records	PPV, % (95% CI)[a]
Total, IE inpatients	92 (100)	77/92	84 (75–90)
Admission length, weeks			
<2 weeks	23 (25)	15/23	65 (45–81)
≥2 weeks	69 (75)	62/69	90 (81–95)
2–<4 weeks	17 (18)	15/17	88 (66–97)
4–<6 weeks	14 (15)	13/14	93 (69–99)
≥6 weeks	38 (41)	34/38	89 (76–96)
Examination during admission			
TEE	63 (69)	52/63	83 (71–90)
No TEE	29 (31)	25/29	86 (69–95)
PET/CT	4 (4)	3/4	75 (30–95)
No PET/CT	88 (96)	74/88	84 (75–90)
Cardiac conditions before admission			
Prosthetic heart valve	15 (16)	13/15	87 (62–96)
No prosthetic heart valve	77 (84)	64/77	83 (73–90)
CIED	21 (23)	17/21	81 (60–92)
No CIED	71 (77)	60/71	85 (74–91)

PPV, positive predictive value; CI, confidence interval; IE, infective endocarditis; TEE, transesophageal echocardiography; PET/CT, positron emission tomography/computed tomography; CIED, cardiac implantable electronic device; IQR, interquartile range.
[a]Calculated using Wilson score method.

A medical record review was considered as the reference standard against which the ICD-10 codes were validated. Three physicians reviewed discharge summaries from the medical records and if the diagnosis of IE was not clear from the discharge summary, the full medical record was reviewed. If the reviewing physician was uncertain if the diagnosis was consistent with the medical record, an independent physician reviewed the medical record so that consensus could be reached. This decision was based on clinical findings (e.g. fever, malaise, vascular and immunologic phenomena) and paraclinical criteria (positive blood culture and positive echocardiography). Hence, the Duke criteria were inherent to the validation process, albeit not strictly followed [7].

We retrieved information on the type of admission (primary or secondary diagnoses) and admission length that was calculated as the total number of days admitted to hospital for IE including the admission and discharge dates. We accounted for transfer between departments, as IE patients discharged from one department still were considered to be hospitalised for IE if they were admitted to another department for IE within <24 h. We ascertained information from the DNPR on whether transesophageal echocardiography (TEE, procedure code: UXUC81) or positron emission tomography/computed tomography (PET/CT) scan (procedure codes: WDIPSFAXX, WDLPSFAXX and WDTCPXYXX) were performed during admission. However, the recordings themselves were not accessible. In addition, information on implantation of a prosthetic heart valve (procedure codes: KFKD, KFMD, KFGE and KFJF) or a cardiac implantable electronic device (procedure codes: BFCA0 and BFCB0) at any time before the IE admission was obtained.

Statistical analyses

The PPV and 95% confidence interval were computed using the Wilson score method [10]. First, we stratified by admission lengths <2 and ≥2 weeks. Admission lengths ≥2 weeks were also separated into 2 to <4 weeks, ≥4 to <6 weeks and ≥6 weeks. Third, we repeated the PPV calculation in patients who had a TEE or a PET/CT scan conducted during admission and in patients with a previous prosthetic valve or a cardiac implantable electronic device.

Ethical approval

The study was approved by the Danish Data Protection Agency (record number: 1-16-02-1-08) and the Chairs of participating departments as part of quality insurance.

Results

Of the 100 medical records, 92 were available for review (see study flowchart in the Fig.1). In 84 of patients (91%), IE was the primary diagnosis. The median admission length was 31 days (25 and 75 percentiles: 13–45 days). The Table 1 shows characteristics of the included patients. The majority of the patients had an admission length of ⩾2 weeks. The PPV was 65% for admission lengths <2 weeks and 90% for admission lengths ⩾2 weeks. The PPV was consistently high when stratifying by submission lengths ⩾2 weeks: 88% for 2 to <4 weeks, 93% for 4 to <6 weeks and 89% for ⩾6 weeks. No overall differences in the PPVs were observed between patients with or without a prosthetic heart valve or a cardiac implantable electronic device.

Discussion

Our study had three findings. First, the PPV of IE in the DNPR was higher for patients with an admission length ⩾2 weeks compared with patients with an admission length <2 weeks. Second, the PPV did not differ in patients undergoing TEE or PET/CT. Third, the PPV was similar for patients with and without a prosthetic heart valve or a cardiac implantable electronic device.

The validity of the IE diagnosis was unknown in Danish registries until 2016 where the PPV overall was estimated to 82% [7]. Since the diagnosis of IE is highly complex especially among patients with a prosthetic heart valve or a cardiac implantable electronic device, further analyses were warranted [11]. We identified a high PPV for the IE diagnosis with admission length ⩾2 weeks, but also that restriction beyond 2 weeks of admission did not increase the PPV further. This is in line with clinical practice where IE is treated with intravenous antibiotics for 4–6 weeks in left-sided IE and 2 weeks in right-sided IE [8]. The full treatment period is carried out in hospital in Denmark. A forthcoming randomised clinical trial (Partial Oral Treatment of Endocarditis (POET), ClinicalTrials.gov identifier: NCT01375257) will clarify whether 2 weeks of intravenous antibiotics followed by oral antibiotics will be sufficient for treating IE. If national treatment guidelines will be changed followed by the results of POET, the PPV of the IE diagnosis may change with varying admission length.

The diagnosis of IE in patients with a prosthetic heart valve or a cardiac implantable electronic device may be challenging since echocardiography can be complicated by shadowing and artefacts in these patients and TEE is an option to overcome these issues. The finding that the PPV was similar for patients with and without a cardiac implantable electronic device and a prosthetic heart valve is important for all future studies in these high-risk populations with poor outcome and a mortality rate between 20 and 40% [8, 11].

Combining the IE diagnosis code with admission length ⩾2 weeks, our IE algorithm has almost the same high PPV as the diagnosis of myocardial infarction in the DNPR [12]. Further, the PPV of the IE algorithm seems higher than stroke, however lower than e.g. the diagnoses of atrial fibrillation and atrial flutter [13, 14].

Our study has limitations. First, the Duke criteria [8] were not assessed formally as part of the confirmation. Second, data collection was only made in one region of Denmark. However, due to the homogeneity of the country, these results are most likely generalisable to other parts of the country [9]. Further, our results may be transferable to other countries with similar healthcare structure. Third, our data synthesis is made from 2010 to 2012 and the accuracy of the IE algorithm before and after this period is not clarified in this study.

In conclusion, the IE diagnosis in the DNPR was reliable for patients with admission length ⩾2 weeks and also applied to patients with prosthetic heart valves or cardiac implantable electronic devices.

Conflict of interest

None.

References

1. **Delahaye F et al.** (2007) In-hospital mortality of infective endocarditis: prognostic factors and evolution over an 8-year period. *Scandinavian Journal of Infectious Diseases* **39**, 849–857.
2. **Schmidt M et al.** (2015) The Danish National Patient Registry: a review of content, data quality, and research potential. *Clinical Epidemiology* **7**, 449–490.
3. **Erichsen P, Gislason GH and Bruun NE** (2016) The increasing incidence of infective endocarditis in Denmark, 1994–2011. *European Journal of Internal Medicine* **35**, 95–99.
4. **Tan C et al.** (2016) Accuracy of administrative data for identification of patients with infective endocarditis. *International Journal of Cardiology* **224**, 162–164.
5. **Jolly SS et al.** (2015) Randomized trial of primary PCI with or without routine manual thrombectomy. *New England Journal of Medicine* **372**, 1389–1398.
6. **Programme | ISCVID Dublin 2017**. Available at http://iscviddublin2017.com/programme/ (Accessed 5 November 2017).
7. **Sundbøll J et al.** (2016) Positive predictive value of cardiovascular diagnoses in the Danish National Patient Registry: a validation study. *BMJ Open* **6**, e012832.
8. **Habib G et al.** (2015) 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC)Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *European Heart Journal* **36**, 3075–3128.
9. **Henriksen DP et al.** (2015) Comparison of the five danish regions regarding demographic characteristics, healthcare utilization, and medication use – a descriptive cross-sectional study. Dalal K, ed. *PLoS ONE* **10**, e0140197.
10. **Wilson EB** (1927) Probable inference, the law of succession, and statistical inference. *Journal of the American Statistical Association* **22**, 209.
11. **Habib G, Thuny F and Avierinos J-F** (2008) Prosthetic valve endocarditis: current approach and therapeutic options. *Progress in Cardiovascular Diseases* **50**, 274–281.
12. **Madsen M** (2003) The validity of the diagnosis of acute myocardial infarction in routine statistics. A comparison of mortality and hospital discharge data with the Danish MONICA registry. *Journal of Clinical Epidemiology* **56**, 124–130.
13. **Wildenschild C et al.** (2014) Registration of acute stroke: validity in the Danish Stroke Registry and the Danish National Registry of Patients. *Clinical Epidemiology* **6**, 27–36.
14. **Rix TA et al.** (2012) Validity of the diagnoses atrial fibrillation and atrial flutter in a Danish patient registry. *Scandinavian Cardiovascular Journal: SCJ* **46**, 149–153.