MEDDOCS Open Access Publisher

ISSN: 2639-4383

Annals of Cardiology and Vascular Medicine

Open Access | Research Article

Prescription of Guideline-Indicated Antibiotic Prophylaxis for Infective Endocarditis among Patients at High Risk

Anna Parbøl Engelund; Eva Havers-Borgersen; Lauge Østergaard; Lars Køber; Emil L Fosbøl

Department of Cardiology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark.

***Corresponding Author(s): Anna Parbøl Engelund**

Department of Cardiology, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark.

Tel: 0045-51-36-34-52;

Email: annaengelund11@gmail.com

Received: Jan 25, 2023

Accepted: Feb 23, 2023

Published Online: Jan 28, 2023

Journal: Annals of Cardiology and Vascular Medicine

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Infectious endocarditis; Cardiothoracic surgery; Grafts; Infection; Prophylactic antibiotic.

Abstract

Introduction: Clinical treatment guidelines recommend Antibiotic Prophylaxis (AP) in order to prevent Infective Endocarditis (IE) before invasive dental procedures to high-risk patients including those with prior infective endocarditis or a prosthetic heart valve. We assessed adherence to these recommendations.

Methods: In this retrospective study using discharge diagnoses codes, we randomly selected 232 patients with indications for antibiotic prophylaxis (132 discharged after infective endocarditis and 100 patients after heart valve replacement). Manual examination of medical records was performed to assess AP prescription within 3 months after discharge. Patient characteristics according to the prescription of AP were examined and compared.

Results: Among 232 patients at high risk of IE, 63 (48%) patients discharged after IE and 56 (56%) patients discharged after heart valve replacement were prescribed AP. Furthermore, we found 70% of those receiving AP in the heart valve surgery group were older than 70 years of age, indicating increasing age as a positive predictor for being prescribed antibiotic prophylaxis. Also, 98% of the patients treated with Transcatheter Aortic Valve Implantation (TAVI) compared with 25% of the patients undergoing surgical treatment received AP, indicating TAVI was associated with a higher likelihood of being prescribed antibiotic prophylaxis.

Conclusions: Our results indicate that for selected groups at high risk of developing infective endocarditis (i.e., patients undergoing heart valve replacement and patients with prior IE), underprescribing of antibiotic prophylaxis exists despite the current recommendations and strategies for reducing this problem are warranted.

Cite this article: Engelund AP, Havers-Borgersen E, Østergaard L, Køber L, Fosbøl EL. Prescription of Guideline-Indicated Antibiotic Prophylaxis for Infective Endocarditis among Patients at High Risk. Ann Cardiol Vasc Med. 2023; 6(1): 1069.

Introduction

Infective Endocarditis (IE) is a rare but potentially life-threatening condition due to an infection of the lining of the heart chambers [1]. It is associated with high mortality and morbidity [2,3]. Clinical treatment guidelines recommend antibiotic prophylaxis for those at high risk of infective endocarditis undergoing invasive dental procedures [4-6]. This relies on the idea that these procedures have increased rates of transient bacteremia that have been related to IE and patients with certain conditions such as prior IE or prosthetic valves are at increased risk of infection.

Antibiotic Prophylaxis (AP) preventing IE has been a controversial topic in recent decades. Initially, the prophylactic policy was generous, but since 2009 European guidelines on antibiotic prophylaxis for IE in patients undergoing invasive dental procedures were restricted to patients considered at high risk (patients with prior IE, prosthetic heart valve, or certain congenital heart diseases). Although recent studies have questioned the effectiveness of antibacterial prophylaxis[7-9] antibiotic prophylaxis persists as the standard of care in many parts of the world. Yet, data questioning the effectiveness of AP may also have influenced clinicians prescribing patterns and we lack current knowledge on clinical practice patterns.

To address whether the recommendations are being followed, we conducted a retrospective study among patients with prior IE and patients undergoing heart valve replacement by analyzing the percentage of these patients discharged with a prescription of antibacterial prophylaxis.

Methods

Study design and data sources

A quality improvement study with a systematic chart review was performed in 232 randomly allocated patients, of whom 132 were hospitalized for IE and 100 underwent elective heart valve replacement. Data were retrospectively collected from medical charts. Information on the following variables was collected: diagnosis, type of heart valve surgery, prescription fills, and clinical data such as age, gender, and medical history.

Study population

IE population

We identified 646 patients hospitalized at the department of Cardiology, University Hospital of Copenhagen, Rigshospitalet, due to IE between January 1, 2015 and January 1, 2019. Patients were identified from the hospital database using the International Classification of Diseases (ICD) 10 code for IE: I33 (acute and sub-acute endocarditis), I38 (endocarditis, valve unspecified), and I398 (endocarditis unspecified). These codes have been validated previously with a high positive predictive value over 90% [10].

From this population, we randomly selected 150 disease courses where antibiotic prophylaxis status was registered. The study sample was shown to be similar to the overall cohort **(Supplemental table 1)**. Patients were excluded if they were discharged with lifelong antibiotics or died during hospital admission. When a patient had more than one event with IE, we categorized the patient according to the last event and excluded the first. This led to the exclusion of 18 cases and a study sample of 132 patients ready for analyses.

Heart valve replacement population

From May 2016 to April 2021, 3593 heart valve replacements were performed at the department of Thoracic Surgery, University Hospital of Copenhagen, Rigshospitalet. Patients were identified from the hospital database by the Nordic Operation Classification system (NOCS): mitral valve replacement (KFKD), aortic valve replacement (KFMD), pulmonary valve replacement (KFJF), tricuspid valve replacement (KFGE). Retrospectively collected data were obtained from the patient chart, which contained data on sex, age, prescription of AP, and surgical procedures.

We excluded patients if they were diagnosed with IE before undergoing surgery, had a congenital heart defect, was discharged with lifelong antibiotics, emigrated, or died before discharge from the hospital. From this population, 100 patients were randomly selected, by choosing the first on our list of patients, which was sorted by the patient's birthday, by the day of month. Restricted data collection was due to limited permission.

The sample was shown to be similar to the overall cohort **(Supplementary table 1)**.

Supplementary table 1: Comparison between population and sample characteristics.

		Patients with prior IE				Patients undergoing valve surgery			
		Population		Sample		Population		Sample	
Sex	Man	464	72%	101	77%	2228	66%	73	73%
	Woman	182	28%	31	23%	1128	34%	27	27%
	Total	646	100%	132	100%	3356	100%	100	100%
Age	14-54	136	25%	35	27%	335	10%	9	9%
	55-69	179	32%	41	31%	864	26%	36	36%
	>70	230	43%	56	43%	2157	64%	55	55%
	Total	536*	100%	132	100%	3356	100%	100	100%

*Missing data from 110 patients about date of diagnosis

Outcome of interest

Register of Medicinal Products Statistics (RMPS) contains information on all prescription-drugs dispensed in any pharmacy in Denmark since 1994[11]. Tracking data on prescriptions over time on an individual-level is made possible by a unique personal registration number (CPR-number), assigned to all residents at birth or upon immigration. This individual number is included in all national registers [12].

The method of tracking AP prescribed by physicians consisted of examining RMPS for whether the patients were discharged with or without a prescription for antibiotic prophylaxis. Patients who were prescribed prophylaxis at follow-up visit within 3 months of discharge were included.

Statistics

The results are based on descriptive statistics. We analyzed the proportion of patients who were discharged with antibiotic prophylaxis based on sex, age, and type of surgery in the group undergoing heart valve replacement and based on sex and age in the group of IE patients.

Results

Table 1 depicts baseline characteristics for patients with prior IE and patients undergoing valve surgery. We randomly identified a study sample for our analyses and as shown in supplemental Table 1 there was no overall differences in sex and age between those patients included in the study sample and those there were not.

Patients with IE

After exclusion criteria were applied, 132 patients hospitalized for IE were included in this study of whom 63 (48%) had AP prescribed.

101 (77%) were men, and 31 (23%) were women **(Table 1)**. Overall, median age among patients with IE was 67 (IQR 53-75). The baseline characteristics were comparable between the group of patients **(Table 1 and Figure 2)**.

Patients undergoing heart valve surgery

A total of 100 patients undergoing heart valve replacement surgery were included, of whom 73 (73%) were men and 27 (27%) were women (Table 1). Overall, median age among patients undergoing heart valve replacement was 72 years (IQR 64-79 years).

We identified that 56% of the patients had received AP, whilst 44% had not **(Table 1)**. The corresponding median age in these two groups was found to be 76 (IQR 68-80) and 65 (IQR 61-73) **(Table 1)**. This difference indicates that age could be a contributing factor regarding weather patients receive AP or not.

Figure 1 depicts the percentages of patients receiving AP. We found that 98% (N=43) of the patients treated with Transcatheter Aortic Valve Implantation (TAVI) were prescribed AP and 25% (N=13) of patients undergoing surgical valve replacement **(Figure 1)**. **Figure 2** shows the distribution of patients by age group and procedure, stratified by whether they receive a prescription of AP or not. Overall, we found a difference by increasing age and type of surgery.

Table 1: Baseline characteristics among patients with prior IE and patients undergoing valve surgery. Separated by whether they receive a prescription of antibiotic prophylaxis or not.

		Patients with IE	Patients undergoing valve surgery		
		AP prescribed (N=63 (48%))	No AP prescribed (N=69 (52%))	AP prescribed (N=56 (56%))	No AP prescribed (N=44 (44%))
Sex	Man	76%	77%	75%	70%
	Woman	24%	23%	25%	30%
Age (years)	14-54	27%	26%	9%	9%
	55-69	32%	30%	21%	55%
	>70	41%	44%	70%	36%
	Median	67	67	76	65
	IQR	21	21	12	12
Comorbidity	Renal disease	13%	22%	11%	2%
	Diabetes	24%	25%	23%	23%
	Liver disease	3%	4%	4%	0%
	COPD	14%	12%	14%	5%
	Earlier diagnosed cancer	11%	10%	13%	5%
	Active cancer	6%	14%	9%	5%
	Cerebral hemorrhage and/or cerebral infarction	14%	14%	14%	7%
	Heart failure	8%	10%	7%	2%
	Native heart disease	13%	7%	NA	NA
	Pacemaker/ICD/CRT	14%	32%	11%	5%
	HIV	2%	4%	0%	0%
Dentist visit within 3 months before hospitalization	Yes	8%	7%	NA	NA
	No	92%	93%		
Medication within 3 months before hospitalization	Antithrombotic drugs	51%	52%	71%	52%
	Immunosuppressant drugs	8%	13%	13%	0%

Alcohol use	Nondrinker	24%	23%	26%	27%
	<7 drinks pr week	67%	62%	40%	46%
	>7 drinks pr week	9%	15%	34%	27%
Cigarette smoking	Active	17%	24%	12%	18%
	Previous	51%	37%	59%	36%
	Never	32%	34%	29%	46%
Intraveneous drug abuse	Yes	3%	7%	0%	0%
	No	97%	93%	100%	100%
Surgical procedure	Biological SAVR	**NA**	**NA**	14%	64%
	Biological SMVR			0%	7%
	Biological STVR			0%	2%
	Mechanical SMVR/SAVR			9%	25%
	TAVI			77%	2%

SAVR: Surgical Aortic Valve Replacement; **SMVR;** Surgical Mitral Valve Replacement; **STVR:** Surgical tricuspid Valve Replacement; **TAVI:** Transcatheter Aortic Valve Implantation.

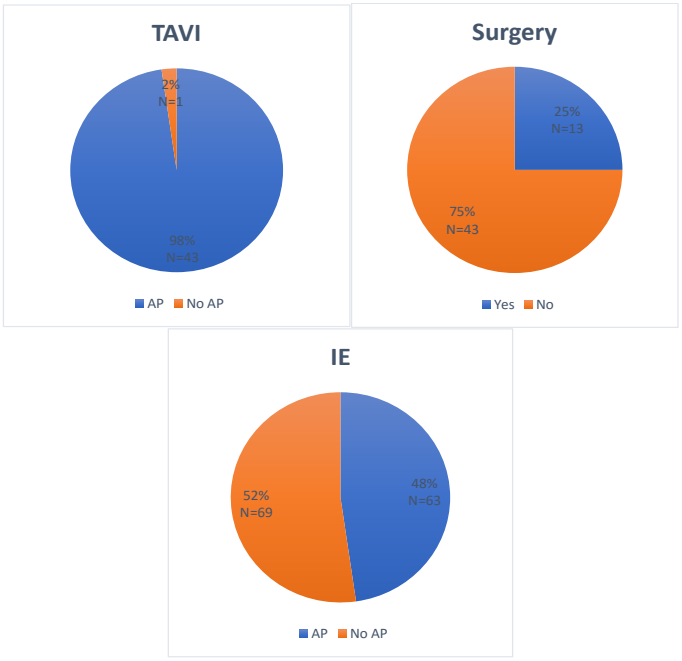

Figure 1: Percentages of total patients receiving antibacterial prophylaxis are depicted.

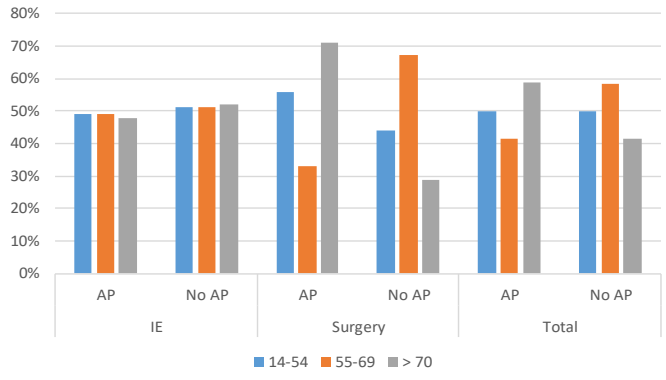

Figure 3: Distribution of patients with heart valve replacement and IE by age group. Separated by whether they receive a prescription of antibiotic prophylaxis or not. N(S) = 100; N(IE) = 132.

Discussion

This study examined the extent to which antibiotic prophylaxis was prescribed to high-risk patients in accordance with guidelines in a large tertiary center in Denmark. The main findings of this study were that 48 % of patients hospitalized due to IE were prescribed antibiotic prophylaxis within 3 months after discharge, while it concerned 56% of patients undergoing heart valve replacement. Furthermore, we found that patients undergoing heart valve replacement were more likely to be prescribed AP after TAVI as compared with surgical valve replacement.

Our findings are consistent with those of several other studies [13-15]. Researchers from a 2020 American study reported 36% of high-risk patients were covered by AP [13]. A large French cohort and case crossover study reported 50% [14]. These findings are also consistent with those of researchers investigating the impact of the 2007 changes in American Heart Association (AHA) recommendations [16-17]. These studies identified a 15-20% decline in AP prescribing for high-risk patients, for whom AP according AHA guidelines still are recommended [16-17].

Survey data suggest that interpretation of guidelines maybe contributing to our observations. A 2000 survey study by Seto et al. [15] found an evident underprescribing of AP. In this study, 66% of patients who met the criteria of the AHA guidelines for antibiotic prophylaxis (patients at moderate and high risk, existing guidelines in 2000) reported that their physicians recommended use of antibiotics preceding dental or other nonsterile procedures [15]. Additionally, 26% of the patients who had negligible risk were instructed to use antibiotic prophylaxis [15]. An essential difference between the survey by Seto et al. and our study is that the previous study was based on a patient's report of his or her physician's recommendation, whereas our study included screening for AP prescriptions in a hospital database.

Soto et al. indicated that in 2000, deviation from current guidelines was often caused by an unconcise formulation which resulted in misclassification of patients and thereby mistreatment [15]. Present guidelines have corrected past faults resulting in more applicable ones. Regardless of improved guidelines, the current study does not find any drastic improvement in treatment with AP.

Danish guidelines, as well as international guidelines, recommend routine use of antibiotic prophylaxis preceding dental procedures to prevent IE in patients with specific predisposing cardiac conditions, but this is not the case in the UK [18]. Concurrently, there is no conclusive evidence that dental treatment is directly related to the development of IE, nor that prophylactic antibiotic can prevent the development of the disease or not [7-9]. These conflicting opinions, the lack of data supporting the evidence of antibiotic prophylaxis, along with concerns about the risk of adverse drug reactions and selection of drug resistance, may have contributed to the low rates of AP prescribing seen in both the IE group and the heart valve group (excluding patients undergoing TAVI surgery) in our study.

The noticeable trend between type of surgery and AP shown in **Figure 1**, may be due to different factors. TAVI surgery was primarily performed in elderly patients. TAVI's lower invasiveness compared to Surgical Aortic Valve Replacement (SAVR) has made it the procedure of choice in high-risk patients. Aligned, an observational study from Danish nationwide data conducted by Butt et al. showed that patients undergoing TAVI were older and had higher perioperative risks than patients receiving SAVR [19]. Additionally, they showed that the incidence of IE following TAVI was not significantly different from the incidence following treatment with SAVR, matched on age [19]. However, the IE-associated mortality for patients who underwent TAVI has proven to be higher than in any other IE subgroup, around 47% [20].

Patients with prosthetic valves of any kind are considered as high-risk of IE. However, patients who received TAVI, may be considered as particularly vulnerable due to their high mortality in IE, and explain the difference between age groups, hence the types of surgery **(Figure 2)**. Another explanation for the notable difference, is that in Denmark TAVI patients are cared for post-procedure by cardiologists whereas surgical valve replacement patients are cared for by surgeons. This may influence the results if cardiologists have increased vigilance on prescribing AP.

Both IE and TAVI patients were treated and discharged from the cardiologic department. According to the guidelines both groups should receive AP. Nonetheless, only 48% of the IE patient was discharged with sufficient prophylactics. In contrast, 97% of TAVI patients received AP in accordance with the guidelines.

Looking into the IE group, we found no significant differences between the group that would receive AP and the one that did not.

The initial treatment of IE patients was often carried out by a specialist unit at Rigshospitalet. Afterwards, IE patients were moved to a less specialized ward at a local hospital for further observation and treatment. Once ready, patients were discharged from the local ward to their homes. One could hypothesize that due to less experience regarding IE the local wards would more often discharge patients without AP, which may explain the difference between TAVI patients and IE patients.

Limitations

The findings of this study have to be seen in the light of some limitations. First, our study was observational. Second, the number of included patients can influence the statistical power of this study. The data granularity was limited as this was an observational quality improvement study where data permissions are restricted. Third, in this study we assessed prescription patterns, which means that actual adherence and medication intake is assumed. Futhermore, because data were derived from a single tertiary center, extrapolation of these results should be done cautiously.

Conclusion

In conclusion, our results indicate that for patients with prior IE or a recent heart valve replacement, there is a significant level of underprescribing of antibiotic prophylaxis for invasive dental procedures despite the current recommendations. This applies to both patients with IE and patients undergoing heart valve surgery. For patients undergoing TAVI nearly 100% were prescribed AP; we should learn from this experience in order to improve quality of care.

Although data on the effectiveness of AP is conflicting, it is still worrisome that AP seems to be underprescribed—especially when considering the strong recommendations brought forward by current treatment guidelines.

Disclosures/Conflicts of Interest

Novo Nordisk Foundation, Independent research Grant for valvular heart disease.

References

1. Habib G. Management of infective endocarditis. Heart. 2006; 92: 124-130.
2. Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG, et al. Clinical Presentation, Etiology and Outcome of Infective Endocarditis in the 21st Century. Arch Intern Med. 2009; 169: 463.
3. Cabell CH, Jollis JG, Peterson GE, Corey GR, Anderson DJ, et al. Changing Patient Characteristics and the Effect on Mortality in Endocarditis. Arch Intern Med. 2002; 162: 90-94.
4. Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis. Eur Heart J. 2009; 30: 2369-2413.
5. Wilson W, Taubert KA, Gewitz M, et al. Prevention of Infective Endocarditis. Circulation. 2007; 116: 1736-1754.
6. Moser C, Fosbøl EL, Rosenvinge F, Arildsen H, Helweg-Larsen J, et al. Behandlingsvejledning, Infektiøs endocarditis. 2022.
7. Thornhill MH, Dayer MJ, Forde JM, Corey GR, Chu VH, et al. Impact of the NICE guideline recommending cessation of antibiotic prophylaxis for prevention of infective endocarditis: before and after study. BMJ. 2011; 342: d2392.
8. Duval X, Delahaye F, Alla F, Tattevin P, Obadia JF, et al. Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications: Three successive population-based surveys. J Am Coll Cardiol. 2012; 59: 1968-1976.
9. Glenny AM, Oliver R, Roberts GJ, Hooper L, Worthington HV. Antibiotics for the prophylaxis of bacterial endocarditis in dentistry. Cochrane Database of Systematic Reviews. 2013; 4: CD003813.
10. Østergaard L, Adelborg K, Sundbøll J, Pedersen L, Fosbøl EL, et al. Positive predictive value of infective endocarditis in the Danish National Patient Registry: a validation study. Epidemiol Infect. 2018; 146: 1965-1967.
11. Wallach Kildemoes H, Toft Sørensen H, Hallas J. The Danish national prescription registry. Scand J Public Health. 2011; 39: 38-41.
12. Pedersen CB. The Danish civil registration system. Scand J Public Health. 2011; 39: 22-25.

13. Thornhill MH, Gibson TB, Durkin MJ, Dayer MJ, Lockhart PB, et al. Prescribing of antibiotic prophylaxis to prevent infective endocarditis. Journal of the American Dental Association. 2020; 151: 835-845.e31.

14. Tubiana S, Blotière P-O, Hoen B, Lesclous P, Millot S, et al. Dental procedures, antibiotic prophylaxis, and endocarditis among people with prosthetic heart valves: nationwide population based cohort and a case crossover study. BMJ. 2017; 358: 3776.

15. Seto TB, Kwiat D, Taira DA, Douglas PS, Manning WJ, et al. Physicians' Recommendations to Patients for Use of Antibiotic Prophylaxis to Prevent Endocarditis. JAMA. 2000; 284: 68-71.

16. Thornhill MH, Gibson TB, Cutler E, Dayer MJ, Chu VH, et al. Antibiotic Prophylaxis and Incidence of Endocarditis Before and After the 2007 AHA Recommendations. J Am Coll Cardiol. 2018; 72: 2443-2454.

17. DeSimone DC, el Rafei A, Challener DW, Carr AB, Kelly JA, et al. Effect of the American Heart Association 2007 Guidelines on the Practice of Dental Prophylaxis for the Prevention of Infective Endocarditis in Olmsted County, Minnesota. Mayo Clin Proc. 2017; 92: 881-889.

18. Prophylaxis against infective endocarditis: antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures. NICE, 2018.

19. Butt JH, Ihlemann N, de Backer O, Søndergaard L, Havers-Borgersen E, et al. Long-Term Risk of Infective Endocarditis After Transcatheter Aortic Valve Replacement. J Am Coll Cardiol. 2019; 73: 1646-1655.

20. Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H. Infective Endocarditis After Transcatheter Aortic Valve Implantation. Circulation 2015; 131: 1566-1574.