

Impact of Infectious Disease Consultation on Management and Clinical Outcomes of Infective Endocarditis: Results of an interrupted time series analysis

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Background

- Infective endocarditis is associated with significant morbidity and mortality, and successful management requires expertise in both cardiac surgery and infectious disease.
- Consultation with ID specialists is suggested by the American Heart Association and the European Society of Cardiology.
- However, the effects of ID consultation on IE clinical outcomes such as mortality, embolization rate, and unplanned cardiac surgery rate have not yet been fully evaluated.
- The aim of the present study was to evaluate the impact of ID consultation on the management and outcomes of IE.

Methods

- We conducted a single-center, retrospective cohort study from April 1998 to March 2019 at Kobe University Hospital in Kobe, Japan, an acute tertiary care hospital with 934 beds. The ID division in the hospital was established in April 2008 and began offering consultations for IE in May 2008.
- This study was an interrupted time series analysis of the clinical outcomes of patients with IE before (April 1998–April 2008) and after (May 2008–March 2019) the establishment.
- The primary outcome was clinical failure within 90 days, defined as a composite of all-cause mortality, unplanned cardiac surgery, new-onset embolic events, and relapse of bacteremia caused by the original pathogen. Secondary outcomes included continuous bacteremia longer than 7 days and inappropriate case management, which was retrospectively judged by four ID specialists.
- We corrected the monthly incidence of outcomes for changes in the number of IE cases, and compared the data before and after May 2008 using segmented regression analysis of ITS. We applied a Poisson regression model allowing for overdispersion to estimate changes in the level and trends of the outcomes. Model appropriateness was assessed by inspecting a residual plot. No adjustment for seasonality was conducted due to the disease characteristics. Autocorrelation was assessed by Durbin–Watson statistics, and by inspecting an autocorrelation plot and a partial autocorrelation plot.

Results

Variable	Pre	Post	P value
IE cases, n	59	179	
Demographics			
Age, y, mean (±SD)	58 (±14)	62 (±16)	0.04
Male sex, n (%)	36 (61%)	125 (70%)	0.2
Definite IE (modified Duke criteria), n (%)	55 (93%)	171 (96%)	0.49
Type of IE, n (%)			
Native valve IE	47 (80%)	149 (83%)	0.53
Prosthetic valve IE	12 (20%)	26 (15%)	0.29
Cardiac device IE	0 (0%)	4 (2%)	0.57
Heart valve affected, n (%)			
Mitral-valve endocarditis	25 (42%)	86 (48%)	0.45
Aortic-valve endocarditis	14 (24%)	36 (20%)	0.55
Tricuspid-valve endocarditis	3 (5%)	7 (4%)	0.71
Prosthetic mitral-valve endocarditis	6 (10%)	7 (4%)	0.09
Prosthetic aortic-valve endocarditis	6 (10%)	13 (7%)	0.58
Mitral-valve and aortic-valve endocarditis	5 (8%)	18 (10%)	0.72
Endocarditis in other locations	0 (0%)	11 (6%)	
Pathogen, n (%)			
Streptococcus	21 (36%)	67 (37%)	0.8
Staphylococcus aureus	17 (29%)	45 (25%)	0.58
Culture negative	13 (22%)	10 (6%)	<0.001
Enterococcus faecalis	2 (3%)	21 (12%)	0.06
Coagulase-negative staphylococci	3 (5%)	11 (6%)	1.0
Abiotrophia defectiva	0 (0%)	6 (3%)	0.34
Cardiobacterium hominis	0 (0%)	3 (2%)	1.0
Streptococcus pneumoniae	0 (0%)	2 (1%)	1.0
Candida	0 (0%)	3 (2%)	0.58
Others	3 (5%)	11 (6%)	
Perivalvular abscess or valvular perforation	13 (22%)	70 (39%)	0.02
Vegetation size > 10mm	33 (56%)	94 (54%)	0.65
Planned surgery, n (%)	38 (64%)	132 (74%)	0.17
ID consultation, n (%)	0 (0%)	178 (99%)	<0.001

Table 1. Comparison of the clinical characteristics of the patients between the pre-intervention and post-intervention periods

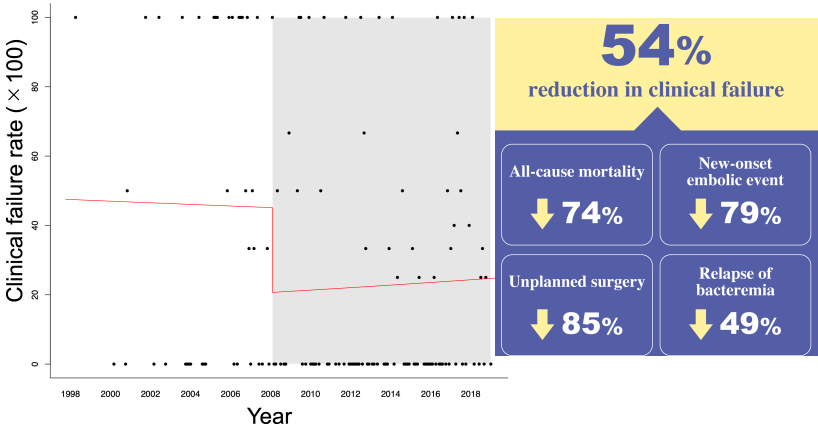


Figure. Segmented regression analysis for monthly rates of clinical failure. The red line indicates the estimates of the segmented regression model. The gray shading area indicates the post-intervention period.

Outcome	Change in Trend (p value, 95% CI)	Relative change at the intervention, % (p value, 95% CI)
Clinical failure	0.00 (p=0.80, -0.01 to 0.02)	-54% (p=0.054, -79% to 2%)
All-cause mortality	-0.01 (p=0.74, -0.06 to 0.03)	-74% (p=0.21, -97% to 110%)
New-onset embolic event	0.00 (p=0.96, -0.02 to 0.02)	-79% (p= 0.01 , -93% to -29%)
Unplanned cardiac surgery	0.01 (p=0.53, -0.02 to 0.04)	-85% (p=0.06, -98% to 4%)
Relapse of bacteremia	-0.06 (p= 0.047 , -0.12 to -0.01)	-49% (p=0.41, -90% to 160%)
Bacteremia longer than 7days	0.02 (p=0.31, -0.02 to 0.05)	-62% (p=0.37, -95% to 221%)
Inappropriate management	0.02 (p= 0.01 , 0.00 to 0.04)	-94% (p< 0.01 , -98% to -78%)
Inappropriate choice of antibiotics	0.00 (p=0.73, -0.02 to 0.03)	-95% (p< 0.01 , -99% to -70%)
Inappropriate treatment duration	0.04 (p= 0.048 , 0.00 to 0.09)	-97% (p=0.10, -100% to 100%)
Inappropriate submission of culture tests	0.03 (p= 0.01 , 0.01 to 0.06)	-60% (p=0.32, -94% to 145%)

Table 2. Results of primary and secondary outcomes between pre-intervention and post-intervention periods

Discussion

- This study revealed ID consultation reduced clinical failure in IE patients, though the difference was not statistically significant. Moreover, ID consultation significantly reduced inappropriate antibiotic management, new-onset embolic events, and bacteremia relapse.
- Previous studies have identified that ID consultation improves outcomes in various infectious diseases. However, these studies did not focus on IE. Our findings are more specific to IE and evaluated specific clinically important outcomes.
- The number of IE cases was larger in the post-intervention period than in the pre-intervention period, and more patients were diagnosed with CNE in the pre-intervention period than in the post-intervention period. Contrastingly, fastidious bacteria, including Bartonella species, nutritionally variant streptococci, and HACEK organisms were more frequently detected in the post-intervention period. This suggests that the establishment of an ID division contributed to the diagnosis of IE caused by fastidious organisms, and reduced the number of CNE cases by antimicrobial stewardship and proper diagnostic criteria.
- This study include several limitations. First, this was a single-center, retrospective study, conducted in a tertiary care hospital in Japan. Therefore, the results might not be applicable to patients in different settings, and further studies are needed to validate the results. Second unrecognized concurrent interventions other than establishment of the ID division could confound the observed associations. Third, few observations were available at each data point of the time series. ITS analysis is frequently used to evaluate the effectiveness of population-level health interventions, and the numbers of observations at each data point are usually larger than those of the present study.

Conclusions

This study suggests that ID consultation optimizes management and improves clinical outcomes in IE. However, further studies in other settings are needed to validate these findings.