Impact of postoperative antibiotics duration on prognosis in patients with infective endocarditis

Jinnam Kim[a,b], Jung Ho Kim[a,b], Hi Jae Lee [c], Se Ju Lee[a,b], Ki Hyun Lee[a,b], Changhyup Kim[a,b], Jung Ah Lee[a,b], Jin Young Ahn[a,b], Su Jin Jeong[a,b], Nam Su Ku[a,b], Seung Hyun Lee[c], Jun Yong Choi[a,b], Joon-Sup Yeom[a,b]

[a]Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)
[b]AIDS Research Institute, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)
[c]Department of Cardiovascular Surgery, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)

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INTRODUCTION

Infective endocarditis (IE) remains a major medical problem with high morbidity and mortality. Appropriate antibiotic treatment in patients with IE lowers the risk of embolism, recurrence, and long-term mortality. However, there are concerns about renal toxicity and an increase in the incidence of resistant strains due to long-term use of antibiotics. In this study, we compare the difference in overall mortality according to the duration of postoperative antibiotics therapy in patients with IE for each group.

METHODS

From 2005 to 2017, we retrospectively reviewed 416 patients with IE at a 2400-bed tertiary hospital in South Korea. A total of 239 IE patients who underwent valve surgery and appropriate antibiotics duration were enrolled. The primary endpoint was long-term overall mortality. The secondary endpoints were reoperation rate, recurrence rate, and postoperative complications, such as new-onset heart failure, paravalvular and embolic complications.

RESULTS

The median follow-up duration was 71 (interquartile range, 46–109) months. The duration of postoperative antibiotic therapy was less than 2 weeks in 67 patients (28.0%) and more than 2 weeks in 127 patients (72.0%). The median age was 53 years. The overall mortality was 13.0% (31/239). There were no statistical differences in overall mortality (13.4% vs. 12.8%, p=0.894), reoperation (6.0% vs. 4.1%, p=0.507), and recurrence (7.5% vs. 2.9%, p=0.148) between patients with postoperative antibiotic therapy for ≥2 weeks and less than 2 weeks. The duration of postoperative antibiotic therapy based on 2 weeks in the Kaplan-Meier curve was not associated with overall mortality (log-rank test, p=0.971).

CONCLUSION

In conclusion, there was no statistically significant difference in the overall mortality, recurrence, and reoperation rate according to the duration of postoperative antibiotic therapy. When surgery and recommended total antibiotics duration are properly performed according to guidelines, the effect of duration of postoperative antibiotic therapy on overall mortality, recurrence rate, and reoperation rate is reduced to a statistically insignificant extent.

Table 1. Baseline Characteristics of patients with infective endocarditis who underwent valve surgery

| | Total (n=234) | Postoperative antibiotics duration | | p value |
		≤2wks (n=62, 26.5%)	>2wks (n=172, 73.5%)	
Age (years)	53 (39-63)	53 (37-67)	53 (39-63)	0.853
Male sex	155 (66.2%)	40 (64.5%)	115 (66.9%)	0.738
Nosocomial infection	23 (9.8%)	3 (4.8%)	20 (11.6%)	0.124
Previous IE (infective endocarditis)	8 (3.4%)	2 (3.2%)	6 (3.5%)	0.999
Previous history of valves	92 (39.3%)	22 (35.5%)	70 (40.7%)	0.471
Prosthetic valve	27 (11.5%)	6 (9.7%)	21 (12.2%)	0.593
Previous valve surgery	36 (15.4%)	9 (14.5%)	27 (15.7%)	0.825
Cardiac devices	4 (1.7%)	0 (0.0%)	4 (2.3%)	0.576
Affected valve				
Aortic valve	112 (47.9%)	25 (40.3%)	87 (50.6%)	0.166
Mitral valve	154 (65.8%)	47 (74.8%)	107 (62.2%)	0.053
Tricuspid valve	12 (5.1%)	4 (6.5%)	8 (4.7%)	0.523
Pulmonary valve	6 (2.6%)	1 (1.6%)	5 (2.9%)	0.999
Multiple valves	46 (19.7%)	14 (22.6%)	32 (18.6%)	0.499
Other Comorbidities				
Diabetes mellitus	34 (14.5%)	7 (11.3%)	27 (15.7%)	0.399
Chronic heart failure	10 (4.3%)	2 (3.2%)	8 (4.7%)	0.999
End stage renal disease	5 (2.1%)	0 (0.0%)	5 (2.9%)	0.329
Liver disease	10 (4.3%)	0 (0.0%)	10 (5.8%)	0.066
Solid cancer	13 (5.6%)	3 (4.8%)	10 (5.8%)	0.999
Hematologic malignancy	2 (0.9%)	1 (1.6%)	1 (0.6%)	0.461
Connective tissue disease	7 (3.0%)	2 (3.2%)	5 (2.9%)	0.999
Immunosuppressive therapy	5 (2.1%)	1 (1.6%)	4 (2.3%)	0.999
Central venous access	7 (3.0%)	0 (0.0%)	7 (4.1%)	0.194
Charlson Comorbidity Index	1 (0-3)	1 (0-3)	1 (0-3)	0.171
EuroSCORE value	2.06 (1.53-2.86)	1.86 (1.53-2.84)	2.08 (1.53-2.87)	0.066
Clinical signs and symptoms (initial)				
Fever (≥ 38°C)	167 (71.4%)	44 (71.0%)	123 (71.5%)	0.935
LV dysfunction (EF<50%)	90 (38.5%)	19 (30.6%)	71 (41.3%)	0.140
Sepsis (including septic shock)	155 (66.2%)	40 (64.5%)	115 (66.9%)	0.738
CNS embolic complications	70 (29.9%)	19 (30.6%)	51 (29.7%)	0.883
Peripheral embolic complications	19 (8.1%)	5 (8.1%)	14 (8.1%)	0.985
Skin lesions	3 (1.3%)	1 (1.6%)	2 (1.2%)	0.999
Microbiology				
Coagulase negative staphylococci (CoNS)	18 (7.7%)	6 (9.7%)	12 (7.0%)	0.578
S.aureus (Staphylococcus aureus)	17 (7.3%)	4 (6.5%)	13 (7.6%)	0.999
MSSA	11 (4.7%)	3 (4.8%)	8 (4.7%)	0.999
MRSA	6 (2.6%)	1 (1.6%)	5 (2.9%)	0.999
Enterococcus species	17 (7.3%)	3 (4.8%)	14 (8.1%)	0.570
Streptococcus species	99 (42.3%)	27 (43.5%)	72 (41.9%)	0.818
HACEK	2 (0.9%)	1 (1.6%)	1 (0.6%)	0.461
Gram negative bacilli (except HACEK)	3 (1.3%)	0 (0.0%)	3 (1.7%)	0.568
Others	11 (4.7%)	2 (3.2%)	9 (5.2%)	0.732
Culture Negative	70 (29.9%)	19 (30.6%)	51 (29.7%)	0.883
Valve culture positivity	18 (7.7%)	2 (3.2%)	16 (9.3%)	0.167
Duration of total antibiotic treatment (days)	33 (27-41)	29 (21-37)	35 (28-42)	<0.001
Patients with vegetation (initial)	218 (93.2%)	58 (93.5%)	160 (93.0%)	0.999
Median maximal vegetation size (cm)	1.10 (0.70-1.60)	1.10 (0.70-1.80)	1.10 (0.70-1.60)	0.816

Table 2. Postoperative outcomes of patients with infective endocarditis who underwent valve surgery

| Postoperative outcomes | Total (n=234) | Postoperative antibiotics duration | | p value |
		≤2wks (n=62, 26.5%)	>2wks (n=172, 73.5%)	
overall mortality	30 (12.8%)	8 (12.9%)	22 (12.8%)	0.982
overall reoperation	11 (4.7%)	4 (6.5%)	7 (4.1%)	0.488
overall recurrence	10 (4.3%)	5 (8.1%)	5 (2.9%)	0.135
New-onset heart failure	25 (10.7%)	10 (16.1%)	15 (8.7%)	0.105
New conduction abnormality	19 (8.1%)	2 (3.2%)	17 (9.9%)	0.100
Paravalvular complication	33 (14.1%)	6 (9.7%)	27 (15.7%)	0.243
Embolic complication				
CNS involvement	67 (28.6%)	18 (29.0%)	49 (28.5%)	0.935
Renal failure	20 (8.5%)	5 (8.1%)	15 (8.7%)	0.874
PAOD	3 (1.3%)	0 (0.0%)	3 (1.7%)	0.568
Other systemic emboli	20 (8.5%)	5 (8.1%)	15 (8.7%)	0.874

Table 3. Univariable and multivariable analysis of overall mortality in patient with infective endocarditis by Cox Proportional-Hazards Model

| Characteristics | N | Univariable analysis | | | Multivariable analysis | | |
		HR	95% CI	p-value	HR	95% CI	p-value
Sex							
Male	155	1					
Female	79	0.906	0.398-2.066	0.815			
Prosthetic valve	27	3.466	1.232-9.749	0.018	2.957	1.221-7.161	0.016
Multiple valve involvement	46	1.218	0.493-3.010	0.669			
Previous infective endocarditis	8	0.650	0.122-3.463	0.613			
Charlson comorbidity index		1.249	1.120-1.392	<0.001	1.231	1.111-1.364	<0.001
Microbiology							
S.aureus	17	1.746	0.493-6.185	0.388			
Unknown	70	1.368	0.588-3.183	0.467			
Postoperative antibiotics duration							
≤ 2 weeks	62	1					
> 2 weeks	172	0.867	0.374-2.013	0.741			
New onset HF	25	3.515	1.283-9.627	0.014	3.575	1.341-9.528	0.011
New onset CNS complication	67	2.681	1.291-5.570	0.008	2.661	1.299-5.454	0.007
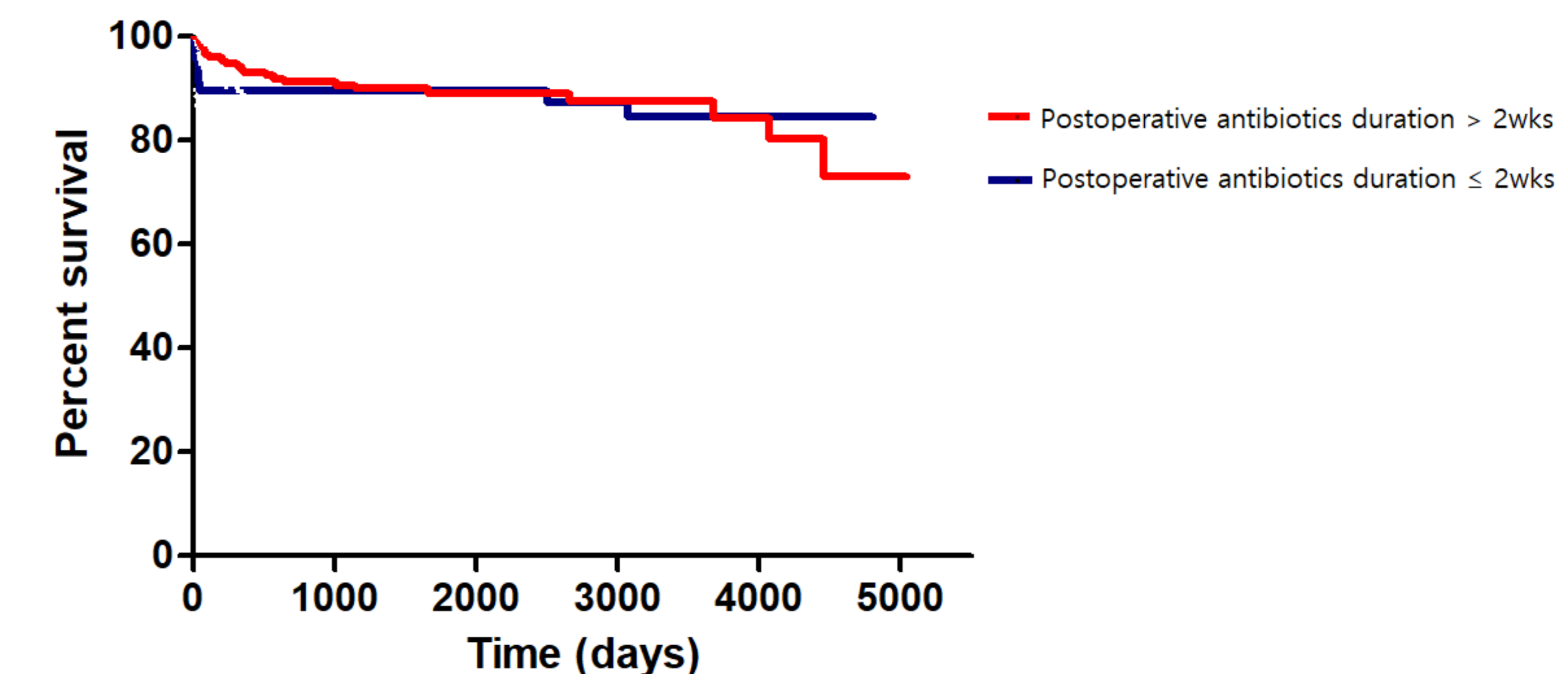
Figure 1. Kaplan-Meier curve for overall mortality in patients with infective endocarditis according to the duration of postoperative antibiotic usage