The Impact of Medical Therapy on Short- and Long-Term Outcomes of Surgical Therapy for Culture-Positive Infective Endocarditis

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INTRODUCTION

Contemporary population-based studies of infective endocarditis (IE) have shown in-hospital mortality rates between 15 and 22% and 5-year mortality rates approaching 40% in industrialized countries. **Despite improved medical and surgical management, the high mortality rates associated with IE have not declined in the last six decades.**

Valve surgery is indicated for patients with native valve endocarditis who exhibit uncontrolled infection, symptoms of heart failure, or evidence of vegetation on echocardiography. For patients with prosthetic valve endocarditis, the infection is often caused by *Staphylococcus* species and may be particularly severe, with perivalvular abscess formation and valve dehiscence. Therefore, surgery is indicated more frequently for patients with prosthetic valve IE as compared to those with native valve infections.

Although surgical therapy has increased to nearly 50% of all IE patients over the last three decades**, it remains difficult to perform controlled trials to assess clinical outcomes because of the infrequency and severity of IE [1]**. Therefore**, the decision to operate and timing of operation are often based on anecdotal experience and individual clinician preferences.** Observational studies have attempted to assess outcomes associated with the timing of surgery, but results are inconsistent, with recent publications both supporting and refuting the advantage of early surgical intervention. Models for mortality and morbidity associated with surgery in IE patients have been limited by unavailability of certain potentially confounding variables including etiologic organism, valve status (native versus prosthetic), and detailed anatomic data. Additionally, long-term outcomes of surgically treated IE patients are not well known.

The aim of this study is to determine the impact of concurrent medical therapy on the short- and long-term outcomes for surgical therapy of infective endocarditis, in order to aid physicians in their clinical decision-making to treat infective endocarditis.

MATERIALS & METHODS

Design and Setting: Retrospective, observational cohort study conducted from 1990 to 2013. Data were collected from patient charts. Antibiotic therapy was graded as appropriate or inappropriate according to the most recent guidelines of the American Heart Association [2].

Participants: 286 consecutive patients with culture-positive IE by the Duke Modified Criteria [3] undergoing therapeutic valve surgery. 177 (62%) received appropriate antibiotic therapy and 93 (33%) received inappropriate antibiotic therapy. Antibiotic regimens of the 16 (5%) remaining patients could not be assessed.

HYPOTHESIS

H0: There is no difference in survival following surgical therapy for patients receiving inappropriate versus appropriate medical therapy.

H1: There is a significant difference in survival following surgical therapy for patients receiving inappropriate versus appropriate medical therapy.

Follow-up interval: 1 month, 1 year, 5 years, & 10 years

CONTIGENCY ANALYSIS

Table 1. Characteristics of patients given appropriate or inappropriate antibiotics upon presentation for surgical treatment of infective endocarditis

	All patients	Appropriate	Inappropriate	*p* Value
Patients	270	177	93	
Age		48 ± 16	45 ± 13	0.89
Gender				
Male	80	46 (26.0%)	34 (36.6%)	0.07
Female	190	131 (74.0%)	59 (63.4%)	
Race				
White	89	56 (32.2%)	33 (35.9%)	0.80
Black	51	36 (20.7%)	15 (16.3%)	
Hispanic	123	80 (46.0%)	43 (46.7%)	
Asian	3	2 (1.1%)	1 (1.1%)	
IV Drug Abuse				
No	184	113 (63.8%)	71 (76.3%)	0.04*
Yes	86	64 (36.2%)	22 (23.7%)	
Hemodialysis				
No	227	150 (84.7%)	77 (82.8%)	0.67
Yes	43	27 (15.3%)	16 (17.2%)	
HIV				
No	259	170 (96.0%)	89 (95.7%)	0.89
Yes	11	7 (4.0%)	4 (4.3%)	
Hepatitis B or C				
No	206	129 (72.9%)	77 (82.8%)	0.07
Yes	64	48 (27.1%)	16 (17.2%)	
Diabetes				
No	212	141 (79.7%)	71 (76.3%)	0.53
Yes	58	36 (20.3%)	22 (23.7%)	
CHF				
No	71	49 (27.8%)	22 (23.7%)	0.46
Yes	198	127 (72.2%)	71 (76.3%)	
Previous IE				
No	214	152 (85.9%)	62 (66.7%)	<0.001*
Yes	56	25 (14.1%)	31 (33.3%)	
Rheumatic Heart Disease				
No	259	171 (96.6%)	88 (94.6%)	0.62
Yes	11	6 (3.4%)	5 (5.4%)	

* Statistically significant (p<0.05)

Table 2. Comparison of surgical procedures between patient groups given appropriate or inappropriate antibiotic treatment

	All patients	Appropriate	Inappropriate	*p* Value
Procedures	269	177	92	
Prosthetic Valve				
No	221	150 (84.7%)	71 (76.3%)	0.09
Yes	49	27 (15.3%)	22 (23.7%)	
Left Heart IE				
No	37	23 (13.0%)	14 (15.2%)	0.62
Yes	232	154 (87.0%)	78 (84.8%)	
Left Heart IE only				
No	68	42 (23.7%)	26 (28.3%)	0.42
Yes	201	135 (76.3%)	66 (71.7%)	
Aortic Valve				
No	143	91 (51.4%)	52 (56.5%)	0.43
Yes	126	86 (48.6%)	40 (43.5%)	
Mitral Valve				
No	110	71 (40.1%)	39 (42.4%)	0.72
Yes	159	106 (59.9%)	53 (57.6%)	
Right Heart IE				
No	213	143 (80.8%)	70 (76.1%)	0.37
Yes	56	34 (19.2%)	22 (23.9%)	
Right Heart IE only				
No	244	162 (91.5%)	82 (89.1%)	0.52
Yes	25	15 (8.5%)	10 (10.9%)	
Tricuspid Valve				
No	219	145 (81.9%)	74 (80.4%)	0.77
Yes	50	32 (18.1%)	18 (19.6%)	
Pulmonary Valve				
No	258	171 (96.6%)	87 (94.6%)	0.42
Yes	11	6 (3.4%)	5 (5.4%)	
Multiple Valve IE				
No	197	126 (71.2%)	71 (77.2%)	0.29
Yes	72	51 (28.8%)	21 (22.8%)	

Table 3. Comparison of infectious organisms between patient groups given appropriate or inappropriate antibiotic treatment

	All patients	Appropriate	Inappropriate	*p* Value
Procedures	319	177	142	
Multiple Organism				
No	299	169 (95.5%)	130 (91.5%)	0.15
Yes	20	8 (4.5%)	12 (8.5%)	
MRSA				
No	298	164 (92.7%)	134 (94.4%)	0.54
Yes	21	13 (7.3%)	8 (5.6%)	
MSSA				
No	260	135 (76.3%)	125 (88.0%)	0.01*
Yes	59	42 (23.7%)	17 (12.0%)	
S. epidermidis				
No	284	156 (88.1%)	128 (90.1%)	0.57
Yes	35	21 (11.9%)	14 (9.9%)	
Coagulase-Negative Staph				
No	308	170 (96.0%)	138 (97.2%)	0.58
Yes	11	7 (4.0%)	4 (2.8%)	
S. viridans				
No	260	128 (72.3%)	132 (93.0%)	<0.001*
Yes	59	49 (27.7%)	10 (7.0%)	
β-Hemolytic Strep				
No	305	169 (95.5%)	136 (95.8%)	0.90
Yes	14	8 (4.5%)	6 (4.2%)	
Enterococcus				
No	284	160 (90.4%)	124 (87.3%)	0.38
Yes	35	17 (9.6%)	18 (12.7%)	
Other Gram-positive				
No	310	171 (96.6%)	139 (97.9%)	0.49
Yes	9	6 (3.4%)	3 (2.1%)	
Gram-negative				
No	312	174 (98.3%)	138 (97.2%)	0.50
Yes	7	3 (1.7%)	4 (2.8%)	
HACEK				
No	317	175 (98.9%)	142 (100.0%)	0.20
Yes	2	2 (1.1%)	0 (0.0%)	
Fungi				
No	309	174 (98.3%)	135 (95.1%)	0.01*
Yes	10	3 (1.7%)	7 (4.9%)	

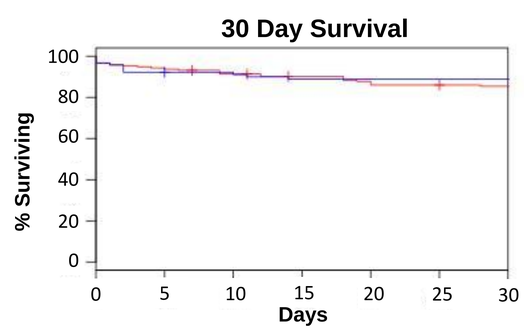
* Statistically significant (p<0.05)

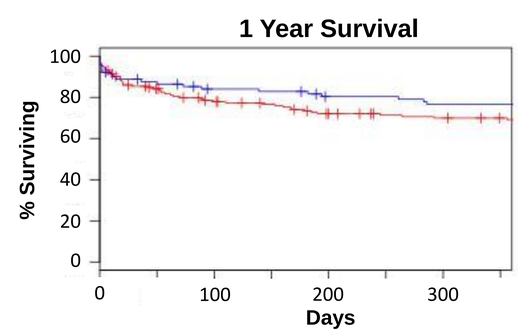
KAPLAN-MEIER SURVIVAL ANALYSIS

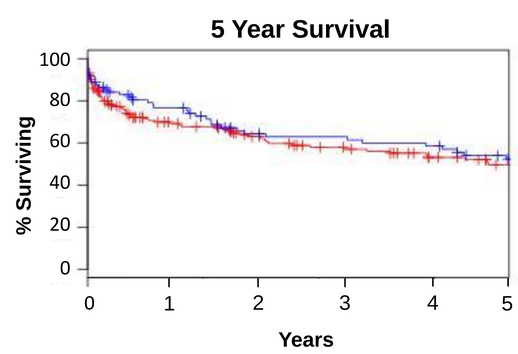
Appropriate antibiotic regimen

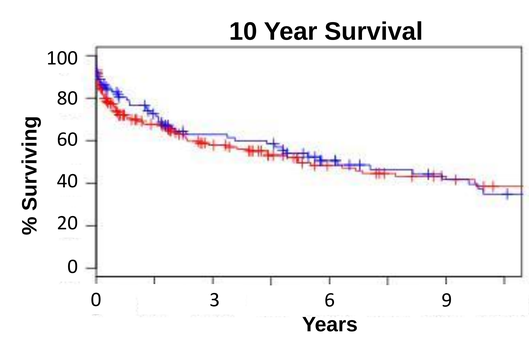
Inappropriate antibiotic regimen

Difference between curves:
p = 0.795









SURVIVAL RESULTS

Period	Appropriate Antibiotics	Inappropriate Antibiotics
	% Surviving (95% Conf. Int.)	
Operative	97	97
1 Month	85 (80,90)	88 (81,95)
1 Year	69 (62,77)	76 (67,85)
5 Years	48 (40,58)	52 (42,65)
10 Years	37 (28,50)	33 (24, 50)

CONCLUSIONS

- Patients were **grouped by appropriateness of medical therapy** before and after receiving surgery to treat infective endocarditis
- Contingency analysis revealed **few differences between groups** in PMH, race, gender, affected valves, microbiology, and other potential risk factors.
- **Survival was virtually equivalent between groups** at key end points (operative, 1 month, 1 year, 5 years, & 10 years). We cannot reject H0.
- **It appears that short-term and long-term survival of patients undergoing valve surgery to treat Infective Endocarditis are not affected by the appropriateness of prior medical therapy.**
- Further analysis may reveal other variables predictive of short or long-term mortality in these patients.

REFERENCES

[1]Durack DT. Evaluating and optimizing outcomes of surgery for endocarditis. JAMA 2003;290:3250-1.

[2] Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for health-care professionals from the Committee on Rhuematic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Disease Society of America. Circulation 2005; 111(23):e394-e434

[3] Hoen B and Duval X. Infective endocarditis. N Engl J Med 2013;368:1425-1433

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