

INTRODUCTION

- PWID patients are underrepresented in current literature but represent a significant proportion of patients hospitalized with infective endocarditis
- The rates of infective endocarditis (IE) are increasing, particularly in PWIDs¹
- There has been debate in the literature about the predominant site of infection (e.g., right-sided predominance in PWIDs^{2,3} and causative organism (whether staphylococcal infections predominate)⁴
- PWIDs are less likely to be considered for surgical treatment given the higher risk of re-infection and significant mortality related to prosthetic valve IE^{4,5}
- It is unclear which PWID patients are ideal surgical candidates^{5,6,7}

CLINICAL QUESTIONS

- What variables influence all-cause mortality in first episode endocarditis in PWIDs?
- What are the demographic and clinical differences between PWIDs and non-PWIDs with first episode infective endocarditis?
- What is the effect of surgical treatment in first episode endocarditis in PWIDs?

METHODS

- Retrospective chart review between February 2007-March 2016 (analysis in Nov 2017)
- Included: adult inpatients (>18) admitted at LHSC (Victoria Hospital or University Hospital)
- Excluded: patients who did not meet criteria for "Definite Endocarditis" per Modified Duke's Criteria, patients with prior infective endocarditis
- EMR allowed comprehensive data collection and long term follow-up
- Patients missing mortality data were excluded from analysis
- Statistical analysis was performed using R Version 1.1.383
- Chi-square and Wilcoxon tests used to compare proportions
- Cox Regression used for survival analysis; covariates of interest were statistically associated with mortality or clinically relevant and all were screened to no violation of proportional hazards assumption

RESULTS

Table 1: Variables Associated with All-Cause Mortality in First Episode Infective Endocarditis Among PWIDs

Variable	Mortality (n=68)	P-value	RR (95%CI)
Age at Death (median, IQR)	36.5 (29-44)	0.04	
Sex		0.12	
Male	41 (60.3%)		1.26 (0.97-1.64)
Female	27 (39.7%)		0.76 (0.54-1.06)
Surgery	13 (19.1%)	>0.99	0.98 (0.54-1.79)
Leave Against Medical Advice	5 (7.4%)	0.01	0.34 (0.14-0.84)
Site of Infection		<0.001	
Right Sided IE	30 (44.1%)		0.61 (0.45-0.81)
Left Sided IE	28 (41.2%)		1.98 (1.28-3.08)
Bilateral IE	8 (11.8%)		3.18 (1.08-9.31)
Causative Organism		0.27	
<i>S. aureus</i> *	48 (48.5%)		0.88 (0.74-1.04)
Polymicrobial	6 (22.1%)		1.69 (0.59-4.83)
Other	14 (25.0%)		1.24 (0.64-2.41)
Opioid Substitution Therapy	9 (13.2%)	0.43	0.34 (0.43-1.33)
Substance Use		0.11	
Opioid	20 (29.4%)		1.72 (1.06-2.80)
Stimulant	5 (7.4%)		0.79 (0.30-2.11)
Polysubstance	30 (44.1%)		0.81 (0.62-1.06)
Referral to Addiction Treatment	5 (11.8%)	0.001	0.28 (0.12-0.69)

*includes methicillin sensitive and methicillin resistant *S. aureus*

Table 2: Characteristics of First Episode IE in PWIDs versus Non-PWID Patients

	PWID (n=202)	Non-PWID (n=168)	p-value
Age	34.41±9.96	59.44±14.85	<0.001
Sex			0.006
Male	105 (51.9%)	112 (66.6%)	
Female	97 (48.0%)	56 (33.3%)	
HIV	16 (7.9%)	3 (1.8%)	0.73
Hepatitis C	141 (70.5%)	2 (1.2%)	<0.001
Pre-existing Heart Disease			<0.001
Congenital	0	25 (14.7%)	
Intracardiac Device	1 (0.5%)	11 (6.5%)	
Health Care Associated	0	20 (11.8%)	0.004
Site of Infection			<0.001
RSIE	125 (61.9%)	17 (9.4%)	
LSIE	55 (27.7%)	145 (87.6%)	
Bilateral IE	13 (6.4%)	4 (2.9%)	
Prosthetic Valve	2 (1.0%)	34 (20%)	<0.001
Organism			<0.001
MSSA	113 (55.9%)	38 (22.4%)	
MRSA	43 (21.3%)	15 (8.8%)	
CONS	1 (0.5%)	21 (12.4%)	
VGS	4 (2.0%)	48 (28.2%)	
Non-VGS	5 (2.5%)	10 (5.6%)	
Enterococci	11 (5.5%)	20 (11.8%)	
Enterobacter	1 (0.5%)	1 (0.6%)	
HACEK	0	2 (1.2%)	
Pseudomonas	2 (1.0%)	1 (0.6%)	
Fungal	1 (0.5%)	1 (0.6%)	
Polymicrobial	13 (6.4%)	4 (2.4%)	
Culture negative	5 (2.5%)	3 (1.7%)	
Other	1 (0.5%)	4 (2.4%)	
Recurrence	Total 59 (29.2%)	7 (4.1%)	<0.001
ICU Admission	78 (38.6%)	87 (51.2%)	0.01
Left AMA	34 (16.8%)	0	<0.001
Treatment			<0.001
Intramuscular	2 (1.0%)	0	
Intravenous	162 (80.2%)	165 (98.2%)	
Oral	38 (18.8%)	0	
Surgery*	39 (19.3%)	95 (56.5%)	<0.001
Procedure			<0.001
Device	2 (5.1%)	11 (11.6%)	
Valve Repair	18 (46.2%)	19 (20%)	
Valve Replacement	17 (43.6%)	57 (60%)	
Repair & replacement	2 (5.1%)	6 (6.3%)	

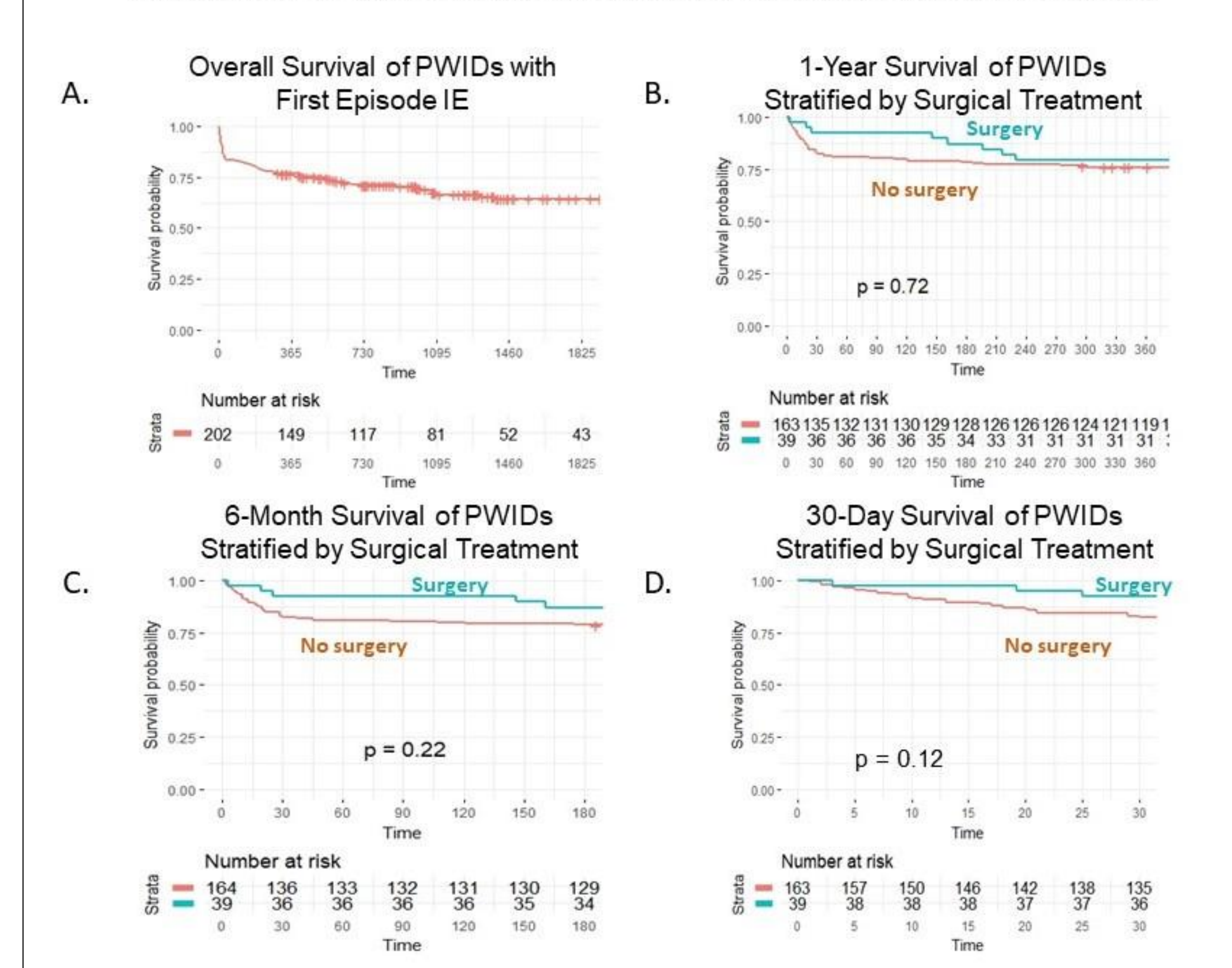
*among PWIDs treated surgically they were more likely to have conduction delay, CHF, myocardial or aortic root abscess, be managed in the ICU and left sided or bilateral IE (data not shown)

Table 3: Unadjusted and Adjusted Cox Proportional Hazards Model for Mortality in First Episode Infective Endocarditis in PWIDs

	Unadjusted HR	95% CI	p-value	Adjusted HR*	95% CI	p-value
Treatment (Ref=Medical)						
Surgery	0.89	0.49-1.64	0.72	0.44	0.23-0.84	0.01
Site of Infection (Ref=Right Sided IE)						
Left Sided IE	2.92	1.76-4.87	<0.001	3.26	1.82-5.84	<0.001
Bilateral	3.96	1.80-8.68	<0.001	4.51	2.01-10.1	<0.001
Leave Against Medical Advice (Ref=Did Not LAMA)						
LAMA	0.34	0.14-0.85	0.02	0.47	0.18-1.19	0.11
Referral to Addiction Treatment (Ref=No)						
Referral	0.28	0.11-0.69	0.006	0.29	0.12-0.73	0.008

*adjusted for age and sex

Kaplan Meier Survival Curves for PWIDs with First Episode Infective Endocarditis



DISCUSSION

- Right sided IE occurs more commonly in PWIDs (62%), adding to the evidence that these patients predominantly have tricuspid valve endocarditis (related to endothelial injury from particulate matter)¹, and left-sided or bilateral infection is associated with higher mortality in PWIDs⁸
- Previous data regarding surgery and survival is difficult to interpret; it was suggested that the high mortality seen in PWID surgical patients reflects the high mortality associated with ongoing drug use^{7,9}
- Addition treatment is underutilized in PWIDs (40/202, 19.8%) but is associated with reduced mortality
- Cardiac surgery is not significantly associated with mortality on univariate analysis; additional variables need to be considered. Surgical patients were more likely to have left sided or bilateral disease and on multivariate analysis surgery was associated with reduced mortality
- In selected PWID patients consider surgery (particularly for left sided or bilateral infections) in conjunction with a multidisciplinary team (preferably involving addiction specialists)
- Interestingly, leaving AMA was associated with lower mortality on univariate analysis but not on adjusted multivariable analysis; potentially, patients who were less ill (less left sided or bilateral disease, less embolic disease or metastatic infections) were more likely to be well enough to sign out AMA. Oral Therapy may have been efficacious in these patients

CONCLUSIONS

- PWIDs have predominantly right sided IE, and the vast majority of first episode cases are caused by *S. aureus* (77.2%)
- Further study is necessary to identify PWID patients who may benefit from cardiac surgery
- Referral to addiction services should be an emphasis as it is associated with reduced mortality

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