



Impact and Association of Preoperative Oral Health and Dental Screening Approach on 90-Day Mortality After Cardiac Valve Surgery

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**IMPACT AND ASSOCIATION OF PREOPERATIVE ORAL HEALTH AND DENTAL
SCREENING APPROACH ON 90-DAY MORTALITY AFTER CARDIAC VALVE
SURGERY**

by

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I have reviewed this thesis. It represents work done by the author under my guidance/ supervision.

Primary Mentors: Dr. Nathaniel Treister, DMD; DMSc, Dr. Herve Sroussi, DMD, PhD

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Chapter I- Background

Cardiovascular disease is the largest single most contributor to global mortality and accounts for more than 1/3rd of all deaths. (1) Amongst all, valvular heart disease (VHD) is one of the significant contributors often reported with catastrophic complications. (2) The treatment of choice for the majority of VHD's is surgical valve replacement. (3) Regardless of an extensive improvement in all the sectors of valvular surgeries, post-surgical valvular complications and early mortality remain important concerning issue for both surgeons and patients. (4)

Of all the biological pathways of complications, odontogenic infections as the source of valvular infection is a known phenomenon based on cases reported in the literature. Likewise, the practice of preoperative dental screening (PDS) prior to valve surgery is widely recommended to eliminate the potential source of infection to prevent post-surgical poor outcomes. Due to lack of studies based on the protocol comparison, approach to PDS lacks standardization. Accordingly, individual hospital/institute follows their protocol depending on the experience and the resources available. It remains unclear the extent to which protocols may or may not reduce the risk of valve surgery complications including early mortality, and/or whether or not the protocols themselves pose any risks related to the interventions provided. The potential reason for this ambiguity could be the lack of identified dental characteristic of the patients that would hold an independent impact on the poor post-surgical outcomes. (5) Identification of this dental risk factors can be a potential component to standardize the dental screening approach and help the dentist to render definitive dental treatment prior to the valve surgery. Our paper-1 aims to provide the level of association of two different protocols with early mortality and our paper-2 aims to describes and provide the level of association of individual dental characteristic on early mortality.

Chapter II (Paper1)- Association of PDS Approach with 90-day Mortality after Cardiac Valve Surgery

- Section A: Abstract
- Section B: Introduction
- Section C: Methodology
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Section A: Abstract

Background: Preoperative dental screening (PDS) prior to valvular surgery has been adopted widely by cardiac surgery to prevent poor outcomes associated with infections of oral origin. However, there is limited evidence to guide PDS protocols. This study was designed to understand the differences and association of focused and comprehensive approaches to PDS with post valvular surgery 90-day mortality.

Methods: A retrospective cohort analysis was performed on all adult patients who underwent elective valvular surgery and PDS at two academic medical centers (MGH and BWH) from January 2009 to December 2016. Patients with a history of intravenous drug abuse were excluded. At MGH (n=692), PDS involved a dental examination including full series of diagnostic radiographs and definitive therapy for teeth with active and/or chronic disease (comprehensive protocol). At BWH (n=1143), PDS involved a dental examination that included selective diagnostic radiographs limited to symptomatic teeth and teeth with evidence of active infection (e.g. asymptomatic tooth with associated swelling and suppuration) and intervention only when active signs of disease were observed (focused protocol). Univariate and multivariable analysis were performed to compare 90-day mortality after surgery with the two different approaches.

Results: A total of 1,835 patients met the inclusion criteria and their charts were reviewed. At BWH 1097/1143 (96%) patients received dental clearance at the initial visit with 3.3% (n=38) receiving radiographs. Dental findings included carious teeth (n=197, 17.2%), root tips (n=135, 11.8%), periodontically hopeless teeth (n=27, 2.4%), and periapical infections (n=20, 1.7%); 16 patients (1.4%) were symptomatic. Extractions were performed in 38 patients (3.3%), and 4

(10.5%) had post-extraction complications including pain, bleeding and infection. At MGH 245/692 (35.5%) patients received dental clearance at the initial visit with 94.2% (n=652) receiving radiographs. Dental findings included carious teeth (n=250, 36.1%), root tips (n=118, 17.1%), periodontically hopeless teeth (n=48, 6.9%), and periapical infections (n=149, 21.5%); 40 patients (5.8%) were symptomatic. Extractions were performed in 151 patients (21.8%), and 15 (9.93%) had post-extraction complications including pain, bleeding and infection. There was no significant difference in 90-day mortality between BWH and MGH (n=114, 10% vs n=58, 8.4%, p=0.257). This remained unchanged in a multivariable model after adjusting for demographics and baseline comorbidities (OR focused vs comprehensive:1.32 (95%CI:0.91-1.93), (p=0.14).

Conclusions: There was no difference in 90-day mortality after cardiac valve surgery between patients who underwent a focused versus comprehensive PDS. Further prospective randomized comparative studies are needed to validate and expand on these findings.

Keywords: Preoperative dental screening, perioperative dental treatment, cardiac valve surgery complications, 90-day mortality

Section B: Introduction

Cardiovascular disease is the most significant single contributor to global mortality and accounts for more than 31% of all deaths. (1) Of all, valvular heart disease (VHD) is one of the significant contributors often reported with catastrophic complications. (2) The treatment of choice for the majority of VHD's is surgical valve replacement with either bio-prosthetic or mechanical valves. (3) Although significant improvement has been observed in the design of prosthetic valves regarding both structure and materials, post-surgical valvular complications remain a significant problem that contributes to morbidity and mortality. (4)

Post-surgical valvular infections have been a significant concern for surgeons and patients due to its devastating outcomes, despite an overall low reported incidence ranging from 1 to 6%. (5,6) Odontogenic infections as the source of valvular infection is a widely accepted phenomenon due to reported cases, presenting oral bacteria on the infected valvular region. (7,8) Accordingly, preoperative dental screening (PDS) to identify and eliminate potential oral sources of infection is recommended prior to cardiac valve surgery to reduce the risk of valvular infection and early mortality. (9) There exists no evidence-base guiding PDS protocols which can vary considerably among institutions/hospitals. The objective of this study was to evaluate the association of two different approaches to PDS with 90-day mortality after cardiac valve surgery.

Section C: Methodology

Data Source

All patients for this retrospective chart-based study were identified from the Society of Thoracic Surgeons (STS) data sets of Brigham and Women's Hospital (BWH) and Massachusetts General Hospital (MGH) from the year 2009 to 2016. The Partner's Health Care Institutional Review Board approved the study protocol (protocol number- 2018P000169). All demographic and cardiac valve surgery data were abstracted from the STS data sets of BWH and MGH. Dental screening variables were abstracted from the electronic health record system. All diagnostic approaches involving radiographs and their diagnosis, treatment rendered, complication related to dental treatment requiring a dental consultation and the number of days required for dental clearance was captured for each patient. The data collection was performed using REDCap version 8.5.1. (REDCap consortium).

Study population

All patients aged ≥ 18 years who had an in-hospital PDS completed prior to valvular surgery were included. Valvular surgical procedures included isolated valvular operations, multi-valve, and valve and CABG procedures. Patients who had PDS completed by a community dentist prior to hospital admission, no documented PDS, emergent status for which no dental treatment could be provided, history of systemic infections at the time of hospitalization, or self-reported history of intravenous drug abuse (IVDA) were excluded from the study. The baseline patient characteristics collected included age, sex, race, ethnicity, BMI and relevant comorbidities

including diabetes, hypertension, history of cerebrovascular accident (CVA), history of chronic heart failure (CHF), peripheral artery disease (PVD), and cerebrovascular disease (CVD).

PDS approach

BWH PDS approach involved a detailed dental examination and selective diagnostic radiographs limited to teeth with symptoms and/or evidence of active infection (i.e. suppuration, fistula). Extractions were performed when there were active signs of infection including pain, swelling, tenderness on percussion, suppuration, and fistula formation (focused protocol). MGH PDS approach involved a detailed dental examination including a full series of diagnostic radiographs for all patients. Extractions were performed when there were active signs of infection, long-standing chronic infections (asymptomatic and/or without active signs of infection) and in teeth with the potential to develop infections (comprehensive protocol).

Outcomes

The primary outcome was 90-day mortality. Secondary outcomes included reinfection requiring re-operation, post-operative dental origin infective endocarditis, post-operative pneumonia, post-operative septicemia, length of hospital stay and all-cause mortality. Assessment of all-cause mortality was accomplished by linking the STS population generated by this project with NDI data. All the demographics, comorbidities, valvular history, post-surgical valvular outcomes were defined as per the STS data specification version 2.9.

Statistical approach

Data are shown as mean $\pm$ SD for continuous and n (%) for categorical and tested between centers with Students t-test and Chi-square tests. As patients were not randomized to the hospital

sites, we performed a multivariable logistic regression model to obtain the independent association of PDS approach at both hospitals on 90-day mortality. The multivariable model incorporated baseline covariates that were significantly different in the univariate model and clinically relevant factors (were chosen from domain knowledge such as Elixhauser Comorbidity Index). Following the criteria, we adjusted for age, sex, race, BMI, diabetes, hypertension, history of CHF, CVD, PVD, CVA, pre-operative steroid, perfusion time, valve procedure performed and moderate/severe valvular insufficiency. Data from this model is shown as Odds Ratios (OR) and 95% CI's for categorical variables and beta coefficient for continues variables. All analysis was performed with SAS version 9.4 (Cary, NC) and STATA version 15.2, with a p value of 0.05 marking statistical significance.

Section D: Results

Demographics and clinical characteristics

Total of 1835 patients (BWH=1143 and MGH= 692) of the 2322 subjects met the inclusion criteria and were therefore included in the analysis. (Figure 1). We excluded the patients with history of IVDU and systemic infection due to their dominant effect on the 90-day mortality as well as the post-surgical valvular outcomes. The study participants showed more men (58.9%) than women, with a mean age of 69 ± 14.5 years. Self-reported race was predominantly Caucasian (91.8%). There was no significant difference observed between BWH vs MGH in CVA (8.6% vs 10.5%) [$p=0.158$] and CVD (16.6% vs 20.5%) [$p=0.336$]. Notable and statistically significant differences were seen in the prevalence of PVD (10.8% vs 14%) [$p=0.037$] and CHF (75.7% vs 60%) [$p=<0.001$] between the two hospitals. These differences were accounted in the multivariable analysis.

Valvular history, diagnosis and procedures

There were 40 patients who reported to have a history of pre-operative infective endocarditis of dental origin (2.3% at BWH and 2% at MGH). 235 patients represented 12.8% of the cohort (BWH 11.8%; MGH 14.5%) had a previous history of valvular surgery. The prevalence of valvular disease at BWH and MGH including that of aortic stenosis (52.9% vs 59.7%), mitral stenosis (6.4% vs 11%) and tricuspid valve stenosis (0.2% vs 0.1%) and of valvular insufficiency are presented in Table 2. Emergent surgery (2.9%) and salvage surgery (0.1%) were observed at BWH. The valve surgeries performed at BWH vs MGH were planned coronary artery bypass graft (CABG) (35.8% vs 35.1%), unplanned CABG (64.2% vs 64.7%), aortic valve replacement (64.7%

vs 21.9%), mitral valve replacement (20.7% vs 4.6%), tricuspid valve replacement (2% vs 0.6%) and pulmonic valve replacement (0.5% vs 1.3%). While comparing both the sites, a statistically significant difference was observed in the mean perfusion time, preoperative steroid, aortic stenosis, mitral stenosis, surgery type and the valvular replacement surgeries (Table 2).

Preoperative dental screening approach

Preoperative dental screening data is summarized in Table 3. At BWH 1097/1143 (96%) patients received dental clearance at the initial visit with 3.3% (n=38) receiving radiographs. Dental diagnosis included carious teeth (n=197, 17.2%), root tips (n=135, 11.8%), periodontally hopeless teeth (n=27, 2.4%), and periapical infections (n=20, 1.7%); 16 patients (1.4%) were symptomatic. Extractions were performed in 38 patients (3.3%), with four patients experiencing post-extraction complications including bleeding (n=1) and pain requiring dental visit (n=3). At MGH 245/692 (35.5%) patients received dental clearance at the initial visit with 94.2% (n=652) receiving radiographs. Dental findings included carious teeth (n=250, 36.2%), root tips (n=118, 17%), endodontically treated tooth (n=315, 45.5%), periodontally hopeless teeth (n=48, 6.9%), and periapical infections (n=149, 21.6%); 40 patients (5.8%) were symptomatic. Extractions were performed in 151 patients (21.8%), with 15 experiencing post-extraction complications including bleeding (n=10), infection (n=2) and pain requiring dental visit (n=9). While comparing the sites, there was a significant difference observed between dental complaint, carious teeth, root tips, endodontically treated teeth, periodontally hopeless teeth, partially erupted third molars, radiograph obtained, periapical infections, treatment prior to valve surgery, dental antibiotics and extractions.

Primary outcome

The primary outcome was to compare 90-day mortality after cardiac valve surgery with the two different PDS approaches. On univariate analysis, there was no significant difference observed in 90-day mortality between the two hospitals (n=114, 10% vs n=58, 8.4%) [p=0.257] and it remained unchanged in multivariable model after adjusting for demographics and baseline comorbidities (OR focused vs comprehensive:1.32 (95%CI:0.91-1.93) [p=0.14]. (Table 4)

Secondary outcomes

Our secondary outcomes were to compare the post-surgical valvular reinfection (requiring re-operation, post-operative dental origin infective endocarditis, post-operative pneumonia, post-operative septicemia, length of hospital stay) and all-cause mortality after cardiac valve surgery with the two different PDS approaches. On univariate analysis, statistically significant differences were observed between the two hospitals for re-operation due to reinfection (p=<0.001), postoperative pneumonia (p=<0.001), postoperative septicemia (p=0.0065) and length of hospital stay (p=<0.001). There was no statistically significant difference between BWH vs MGH in post-operative IE of dental origin (p=0.159) and all-cause mortality (p=0.671). (Table 5)

Section E: Discussion

Preoperative dental screening (PDS) prior to cardiac valve surgery is a widely accepted approach intended to reduce the risk of post-surgical valvular complications which can result in early mortality. (7) Although widely implemented in most medical centers and institutions, there is a lack of standardization of what a PDS should entail resulting in institution-specific protocols that are not evidence-based. To address the gap of knowledge described above, we conducted a comparative study of two different PDS protocols which differed in the scope of the diagnostic imaging and dental treatments rendered. One was more extensive and required that dental radiographs be obtained for all patients, and that all hopeless teeth be extracted prior to valve surgery. The other protocol was more limited in scope and based on the elimination of all clinically evident sources of odontogenic infection and pain, with dental radiographs obtained for symptomatic teeth or teeth with evidence of active infection. Our data indicated that there was no statistically significant difference in 90-mortality between the two centers despite these different PDS approaches.

In our study we included 1835 patients (BWH=1143 and MGH=692). Patients with history of IVDU and systemic infections were excluded from the study. The rationale supporting these exclusions is that oral health was less likely to affect 90-day mortality in the context of an overwhelmingly dominant factor such as IVDU or systemic infection. While the study populations at the two centers were almost similar, the reported dental findings and subsequent treatment rendered were notably different. Our study demonstrated the similarities in the patient's characteristics at both the hospital site; regardless there was a wide difference in the dental findings

and the treatment rendered prior to the valve surgery. Dental findings like dental caries, root tips, endodontically treated teeth, periodontically hopeless teeth, partially erupted teeth, and periapical signs of infection were detected more with the comprehensive approach at MGH in comparison to focused approach at BWH. Accordingly, the treatment like extractions and restorations rendered with comprehensive approach was markedly more in comparison to the focused approach. With no restriction, a noticeable difference was observed between the number of PDS dental visits at each site. Majority of the patients undergoing a focused approach got cleared in a single visit while most of the patients undergoing comprehensive approach required two PDS visits. We believe that these results were driven by the nature of the PDS approach implemented and/or due to the difference in the number of resources available at each hospital site. In our opinion, the extensiveness of the dental approach not only adds the dental and the hospitalization cost to the patients, but it also delays the planned valvular surgery. This delayed surgery can lead to the development of poor post-surgical valvular complications and in some cases early mortality.

On considering the hard event as a concerning outcome from the care teams and patient's perspective, this study primarily focused on answering the association between the two different PDS approach and its 90-day mortality. Our study demonstrated no association between the exposure and outcome after adjusting for the potential risk factors. However, there was a significant difference observed in our secondary findings. We noted that the infectious complications post valvular surgery was significantly different for the patient undergoing two different PDS approach. The post-surgical valvular reinfection and post-operative pneumonia were observed significantly higher in the patients undergoing comprehensive approach to PDS while post-operative septicemia was observed more in the patients undergoing the focused approach. We believe that the extensive dental treatment and its resultant increased hospitalization stay might be

a key component in driving the higher number of complications observed with the comprehensive approach. Post-surgical septicemia was found to be significantly higher with the focused approach, and this might have been due to the limited approach especially, for the patient undergoing urgent valve surgery. Despite the secondary findings being intriguing, the analysis reported is based on the univariate model due to the paucity of secondary events. These secondary outcomes might or might not be directly associated with the difference in the PDS approach but might be due to confounding variables which could derive from the difference in the overall clinical practices at the two hospitals.

In our belief, a standardized, quick and effective dental screening that treats the teeth with only active infection might be an intuitive approach for the entire care team as well as from the patient's aspect given the no difference in the primary and secondary outcomes. Ultimately, this can be only answered after conducting a randomized control clinical trial.

This study had a number of limitations that must be considered. Some of these limitations include those inherent to retrospective studies and include missing data. This missing data can be one of the possible reasons of lesser outcome events in our study. Likewise, due to missing data and lesser frequency of secondary outcomes, this study restricts the ability to perform the multivariable analysis to prevent over fitting of the model. Due to the nature of the eligibility criteria, the study restricts in answering its applicability on the patients with systemic infections and a history of intravenous drug abuse. As the nature of the study design, comparison of individual clinical practices and hospital environment between the hospital sites might have played a potential bias which cannot be adjusted using the present data. Since the STS baseline score were unavailable, inter-comparison of our findings with STS data cannot be reported. The variables relying on STS datasets suffer from limitations such as subjectivity and institution specific

approaches but that reliance on STS is widely accepted in the scientific literature with ample of evidence supporting its validity despite its limitations. Considering all these challenges inherent of a retrospective chart-based study, further prospective randomized study is needed to expand and validate the study findings.

Section F: Conclusions

There was no difference observed in 90-day mortality after cardiac valve surgery between patients who underwent a focused versus comprehensive PDS approaches. Further prospective comparative studies are needed to validate and expand the findings of this study.

Section G: Figures and Tables

Figure 1- Consort diagram

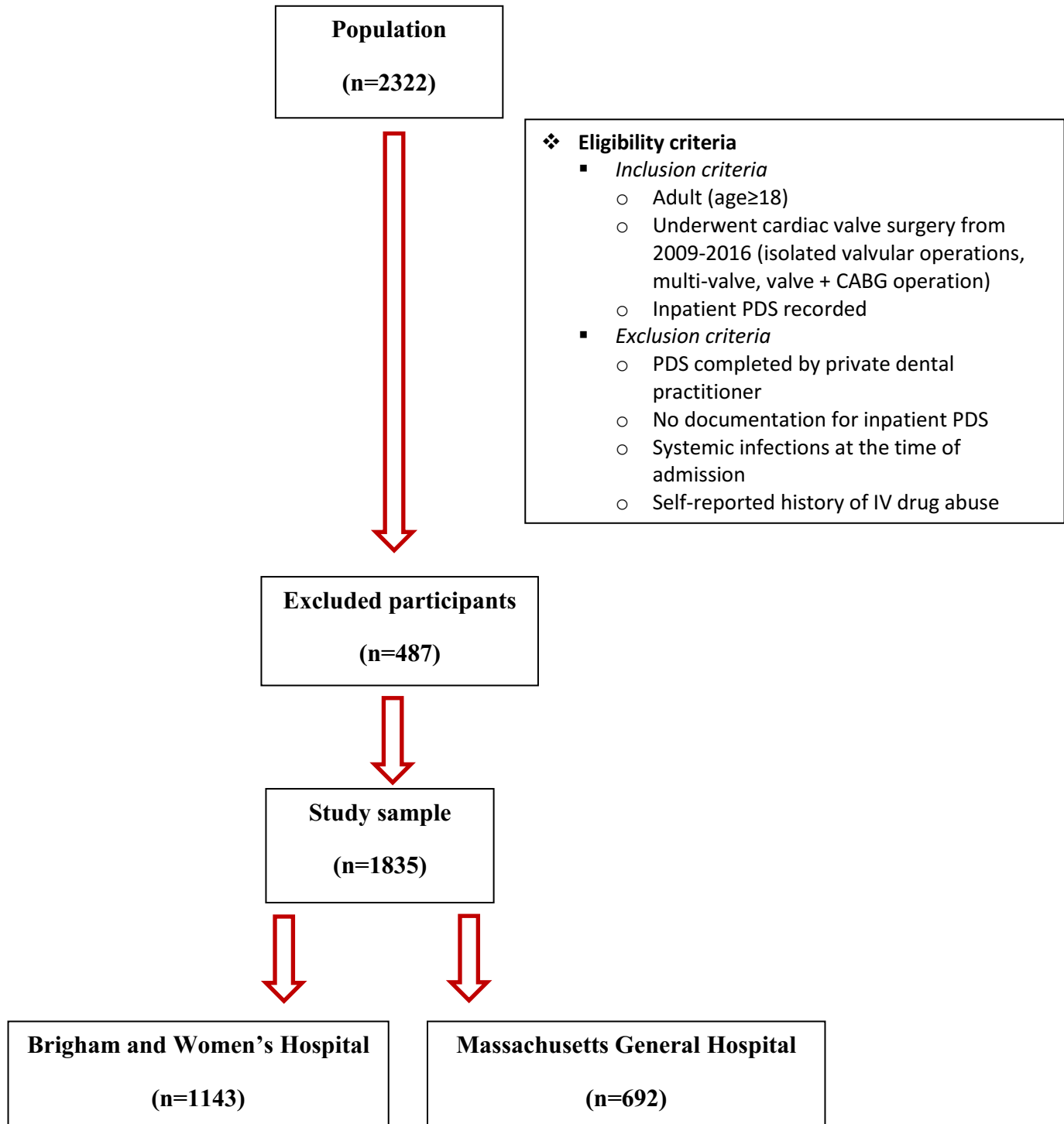


Table 1- Demographics and clinical characteristics

Variables	Total (n=1835)	Hospitals		P value
		BWH (n=1143)	MGH (n=692)	
Age (mean±SD)	69 ± 14.5	69.4 ± 14.2	68.7 ± 14.7	0.329
Sex				0.393
Male	1081 (58.9%)	665 (58.2%)	416 (60.2%)	
Female	753 (41.8%)	478 (41.8%)	275 (39.8%)	
Race				0.002
Caucasian	1685 (91.8%)	1070 (93.6%)	615 (88.9%)	
African American	58 (3.2%)	34 (3%)	24 (3.5%)	
Asian	35 (1.9%)	13 (1.1%)	22 (3.2%)	
Native American	2 (0.1%)	1 (0.1%)	1 (0.1%)	
Others	55 (2.9%)	25 (2.1%)	30 (4.3%)	
BMI	28.1± 7.2	28.2±6.5	28.2±8.2	0.625
Diabetes	510 (27.8%)	311 (27.2%)	199 (28.8%)	0.473
Hypertension	1363 (74.3%)	850 (74.4%)	513 (74.1%)	0.911
History of CVA	171 (9.3%)	98 (8.6%)	73 (10.5%)	0.158
History of CHF	1280 (69.8%)	865 (75.7%)	415 (60%)	< 0.001
History of PVD	220 (12%)	123 (10.8%)	97 (14%)	0.037
History of CVD	332 (18.1%)	190 (16.6%)	142 (20.5%)	0.336

Table 2- Valvular history, diagnosis and procedures at BWH and MGH

Variables	Total (n=1835)	Hospitals		P value
		BWH (n=1143)	MGH (n=692)	
Previous valvular surgery	235 (12.8%)	135 (11.8%)	100 (14.5%)	0.100
Pre-operative IE of dental origin	40 (2.2%)	26 (2.3%)	14 (2%)	0.811
Perfusion time (mean±SD)	166.7 ± 84	169.5 ± 93.3	162.0 ± 68	0.013
Pre-operative steroid	59 (3.2%)	28 (2.4%)	31 (4.5%)	0.017
Aortic stenosis	1018 (55.4%)	605 (52.9%)	413 (59.7%)	0.004
Mitral stenosis	149 (8.1%)	73 (6.4%)	76 (11%)	<0.001
Tricuspid stenosis	3 (0.2%)	2 (0.2%)	1 (0.1%)	0.875
Aortic valve insufficiency				0.330
Moderate	223 (12.2%)	131 (11.5%)	92 (13.3%)	
Severe	157 (8.6%)	100 (8.7%)	57 (8.2%)	
Mitral valve insufficiency				0.931
Moderate	402 (21.9%)	244 (21.3%)	158 (22.8%)	
Severe	423 (23.1%)	258 (22.6%)	165 (23.8%)	
Tricuspid valve insufficiency				0.103
Moderate	332 (18.1%)	201 (17.6%)	131 (18.9%)	
Severe	132 (7.19%)	69 (6%)	63 (9.1%)	
Surgery type				<0.001
Elective surgery	834 (45.4%)	654 (57.2%)	180 (26%)	
Urgent surgery	967 (52.7%)	455 (39.8%)	512 (74%)	
Emergent surgery	33 (1.8%)	33 (2.9%)	0	
Salvage surgery	1 (0.1%)	1 (0.1%)	0	
CABG				0.422
Planned	652 (35.5%)	409 (35.8%)	243 (35.1%)	
Unplanned	1182 (64.4%)	734 (64.2%)	448 (64.7%)	
Aortic valve replacement	891 (48.6%)	739 (64.7%)	152 (21.9%)	<0.001
Mitral valve replacement	269 (14.7%)	237 (20.7%)	32 (4.6%)	<0.001
Tricuspid valve replacement	27 (1.5%)	23 (2%)	4 (0.6%)	<0.001
Pulmonic valve replacement	15 (0.8%)	6 (0.5%)	9 (1.3%)	0.591

Table 3- PDS approach at BWH and MGH

Variables	Total (n=1835)	Hospitals		P value
		BWH (n=1143)	MGH (n=692)	
<i>Diagnostic approach</i>				
Dental complaint	56 (3.1%)	16 (1.4%)	40 (5.8%)	<0.001
Partial denture	127 (6.9%)	83 (7.3%)	44 (6.3%)	0.464
Complete denture	213 (11.6%)	140 (12.2%)	73 (10.5%)	0.272
Carious teeth	447 (24.4%)	197 (17.2%)	250 (36.1%)	<0.001
Root tips	253 (13.8%)	135 (11.8%)	118 (17%)	0.001
Endodontic treatment	330 (18%)	15 (1.3%)	315 (45.5%)	<0.001
Periodontally hopeless teeth	75 (4.1%)	27 (2.4%)	48 (6.9%)	<0.001
Partially erupted third molars	16 (0.9%)	2 (0.2%)	14 (2%)	<0.001
Radiograph taken	690 (37.6%)	38 (3.3%)	652 (94.2%)	<0.001
Periapical signs of infection	169 (9.2%)	20 (1.7%)	149 (21.5%)	<0.001
<i>Treatment rendered</i>				
Treatment prior to valvular surgery	191 (10.4%)	39 (3.4%)	152 (22%)	<0.001
Dental antibiotic prophylaxis	46 (2.5%)	11 (1%)	35 (5.1%)	<0.001
Restoration	7 (0.4%)	3 (0.3%)	4 (0.6%)	0.287
Extraction	189 (10.3%)	38 (3.3%)	151 (21.8%)	<0.001
Total number of visits				<0.001
1	1342 (73.1%)	1097 (96%)	245 (35.5%)	
2	368 (20.1%)	28 (2.4%)	340 (49.2%)	
3	85 (4.6%)	5 (0.4%)	80 (11.6%)	
4	24 (1.3%)	3 (0.3%)	21 (3%)	
Post-extraction related complications	19 (1%)	4 (10.5%)	15 (9.9%)	<0.001

Table 4- Primary outcome

Outcomes	Total (n=1835)	Hospitals		Model	OR*	95%CI	P value
		BWH (n=1143)	MGH (n=692)				
90-day mortality	172 (9.4%)	114 (10%)	58 (8.4%)	Univariate	0.83	0.59-1.15	0.257
				#Multivariable	1.32	0.91-1.93	0.14

*Odds Ratio (OR), 95%CI and p value=BWH vs MGH

#adjusted- age, sex, race, BMI, diabetes, hypertension, history of CHF, CVD, PVD, CVA, pre-operative steroid, perfusion time, valve procedure performed and moderate/severe valvular insufficiency

Table 5 - Secondary outcomes

Outcomes	Total (n=1835)	Hospitals		Effect estimates	95%CI	P value
		BWH (n=1143)	MGH (n=692)			
Reoperation due to reinfection	24 (1.3%)	6 (0.5%)	18 (2.6%)	0.11	0.07-0.18	< 0.001
Post-operative IE of dental origin	10 (0.5%)	4 (0.3%)	6 (0.9%)	2.49	0.70-8.86	0.159
Post-operative pneumonia	42 (2.3%)	15 (1.3%)	27 (3.9%)	3.65	1.96-6.78	< 0.001
Post-operative septicemia	24 (1.3%)	19 (1.7%)	5 (0.7%)	2.77	1.55-4.95	0.006
Length of hospital stay	16.6 ± 12	15.9 ± 12.0	17.8 ± 11.9	1.84 (B- coef)	0.71-2.97	< 0.001
All-cause mortality	509 (27.7%)	321 (28.1%)	188 (27.2%)	0.96	0.77-2.97	0.671

Odds Ratio (OR), 95%CI and p value= BWH vs MGH

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Chapter III (Paper 2)- Impact of dental characteristics on 90-day mortality after cardiac valve surgery

- Section A: Abstract
- Section B: Introduction
- Section C: Methodology
- Section D: Results
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Section A: Abstract

Background- Odontogenic infections/ poor oral hygiene is one of the risk factors for developing post-surgical valvular complications. The magnitude and the impact to which these infections affect the post-surgical outcome especially early mortality remains unclear. This study was designed to evaluate the association of individual dental characteristic with the 90-day mortality.

Methodology- A retrospective cohort analysis was performed on all adult patients who underwent valvular surgery and preoperative dental screening at Massachusetts General Hospital from January 2009 to December 2016. All valve surgery and dental data were procured using STS data set and electronic health record system of MGH respectively. Patients with a self-reported history of intravenous drug use and systemic infections were excluded from the study. We performed univariate and multivariable analysis for all the dental characteristics using logistic regression model. Odds Ratios (OR) and 95% CI's were reported, and the significance level was 5%.

Result- A total of 692 patients met the inclusion criteria of which, 58 (8.4%) patients died within 90-days and 634 (91.6%) patients survived after the valve surgery (within 90 days). Among the 90-day mortality group and survived patients, the mean ($\pm$ SD) age was 73.9 ± 13.3 years vs 68.1 ± 14.2 years with more females ($n=32$, 55.2% vs $n=243$, 38.3%). Although dental characteristics including dental complaint ($n=1$, 1.7% vs $n=39$, 6.2%), total number of teeth present (19.7 ± 8.1 vs 21.1 ± 7.8), complete denture ($n=9$, 15.5% vs $n=64$, 10.1%), partial denture ($n=1$, 1.7% vs $n=43$, 6.8%), carious teeth ($n=18$, 31% vs $n=232$, 36.5%), root tips ($n=5$, 8.6% vs $n=113$, 17.8%), total number of asymptomatic root tips (0.3 ± 0.9 vs 0.6 ± 1.6), endodontically treated teeth ($n=26$, 44.8% vs $n=289$, 45.5%), periodontally hopeless teeth ($n=3$, 5.2% vs $n=45$, 7.1%) and tenderness on percussion ($n=2$, 3.4% vs $n=17$, 2.7%) varied amongst the group, the univariate and

multivariable analysis showed no significant association of dental/ oral health characteristics with 90-day mortality.

Conclusion- There was no significant association noted between dental characteristics and 90-day mortality. Further large prospective comparative studies are needed to validate and expand these findings.

Keywords- Dental characteristic, odontogenic infections, post-surgical valvular complication

Section B: Introduction

Infectious complications following cardiac valve surgery are serious and can lead to early mortality. (1,2) Oral cavity bacteria, including bacteria associated with odontogenic infections, are believed to be a potential risk factor for post-valve surgery complications. (3,4) In order to reduce the risk of developing post-surgical valvular complications, preoperative dental screening protocol is followed with the intent of removing any potential source of infections. (5) Despite the widespread adoption of this practice, the overall evidence-based literature is deficient and lacks data demonstrating the impact of individual odontogenic infections/oral health characteristic on the post-surgical valvular outcomes. (6) As a result, the current screening practice is arbitrary, changing from one hospital/ institute to another. This ambiguity in this dental screening itself can be a potential risk factor for poor valve-surgery outcomes. In order to address this gap, there exists a strong need for identification of odontogenic infection/ dental characteristics that holds the risk of developing poor post-surgical valvular outcomes. The objective of this study was to describe and evaluate the association of an individual odontogenic infection/dental characteristic with early mortality (within 90-days) after cardiac valve surgery.

Section C: Methodology

Data Source

The data presented in this study for secondary analysis is abstracted from Brigham and Women's Hospital (BWH) and Massachusetts General hospital (MGH). All demographic and valvular surgery data were abstracted from the Society of Thoracic Society (STS) data sets of MGH from the year 2009 to 2016. All dental data for the study was collected from electronic health record system of MGH using REDCap version 8.5.1. (REDCap consortium). The study protocol was approved by the Partner's Health Care Institutional Review Board (protocol number-2018P000169).

Study population

All patients aged ≥ 18 years who underwent any type of valvular surgery and/or procedure preceded by in-hospital preoperative dental screening (PDS) were included. Patient with no dental screening, dental screening conducted by private dental office, the patient with an emergent case where no dental screening performed, the self-reported case of systemic infection and intravenous drug use were excluded from the study. The baseline patient characteristics collected included age, sex, race, BMI, clinically relevant comorbidities including diabetes, hypertension, history of cerebrovascular accident (CVA), history of chronic heart failure (CHF), peripheral artery disease (PAD), cerebrovascular disease (CVD), valvular diseases, nature of surgery and type of valve surgeries performed.

Outcome

The outcome was 90-day mortality

Statistical approach

Data are shown as mean $\pm$ sd for continuous and n (%) for categorical and tested between the patients died within 90-days and survived patients (within 90-days) with Students t-test and Chi-square tests. We performed univariate analysis for all the dental characteristics. The variable that showed statistically significant difference (<0.05) between the comparison groups were adjusted in the multivariable analysis. Data from the logistic regression model is shown as Odds Ratios (OR) and 95% CI's. Analysis to study the impact of comorbidities on the association of dental characteristic on outcome 90-day mortality was performed. The comorbidities were selected based on similar approach as the multivariable model. Considering diabetes as a most clinically relevant comorbidity based on the domain knowledge, analysis to study the impact of diabetes was also performed. All analysis was performed with STATA version 15.1, with a p value of 0.05 marking statistical significance.

Section D: Results

Demographics and clinical characteristics

The demographic and clinical characteristic presented in Table 1 describes the overall as well as the characteristic features of patients stratified by 90-day mortality outcome. Out of 2322 patients from the original cohort, the study included a total of 692 patients (Figure 1). Of 692 patients, 58 (8.4%) patients died within 90-days and 634 (91.6%) patients survived (within 90-days) after the valve surgery. Amongst the 90-day mortality group and the survived patients with majority of self-reported Caucasian race (n=52, 89.7% vs n=563, 88.8%), there was a significant difference observed between the mean age (73.9 ± 13.3 years vs 68.1 ± 14.2 years) [p value=0.010] and sex (male=26, 44.8% and females=32, 55.2% vs male=390, 61.5% and females=243, 38.3%) [p value= 0.012]. BMI was similar between the groups (26.8 ± 5.7 kg/m² vs 28.4 ± 8.4 kg/m²).

Amongst the 90-day mortality group and the patient survived, CHF (n=43, 74.1% vs 372, 58.6%) [p value=0.021] and PVD (n=51, 25.9% vs n=82, 12.9%) [p value= 0.007] were observed to be significantly different. The burden of other comorbidities including diabetes, hypertension, CVA and CVD remained similar between the groups. The burden of valvular disease including aortic stenosis (n=34, 58.6% vs n=379, 59.3%) and mitral stenosis (n=6, 10.3% vs n=70, 11%) were similar between the groups. Majority of the patient treated across the groups needed urgent valve surgeries (n=44, 75.9% vs n=468, 73.8%) with comparatively lesser elective surgeries (n=14, 24.1% vs n=166, 26.2%), regardless, no significant difference was marked between the groups. Although majority of these patients received aortic valve procedure (n=12, 20.7% vs n=157, 24.8%) followed by mitral valve procedure (n=5, 8.6% vs n=59, 9.3%), tricuspid valve

procedure (n=11, 18.1% vs n=65, 10.3%) and pulmonic valve procedure (n=1, 1.7% vs n=8, 1.3%), no significant difference was noted across the groups.

Dental characteristics of 90-day mortality patients vs survived patients.

Dental characteristics amongst the 90-day mortality patient and the survived patients (within 90-days) is described in Table 2. Dental complaint (n=1, 1.7% vs n=39, 6.2%), partial denture (n=1, 1.7% vs n=43, 6.8%), carious teeth (n=18, 31% vs n=232, 36.5%) and root tips (n=5, 8.6% vs n=113, 17.8%) were noted less, whereas, patient with complete denture (n=9, 15.5% vs n=64, 10.1%) were observed more in the 90-day mortality group in comparison to survived patients. Total number of teeth (19.7 ± 8.1 vs 21.1 ± 7.8), endodontically treated teeth (n=26, 44.8% vs n=289, 45.5%), periodontically hopeless teeth (n=3, 5.2% vs n=45, 7.1%) and tenderness on percussion (n=2, 3.4% vs n=17, 2.7%) were observed comparable amongst the groups. Impacted teeth, dental pain, purulence, swelling, symptomatic root tips were not observed amongst the 90-day mortality group. Overall, there was no statistically significant difference observed in the individual dental characteristic between the groups.

Univariate analysis of dental characteristics on 90-day mortality

Table 3 shows univariate analysis of dental characteristic on 90-day mortality. Of those in 90-day mortality and the survived patients, there was no significant difference observed between dental complaint [OR=0.26, 95%CI=0.03-1.98, p value=0.197], presence of complete denture [OR=1.63, 95%CI=0.76-3.47, p value=0.24], presence of partial denture [OR=0.24, 95%CI=0.03-1.78, p value=0.163], carious teeth [OR=0.77, 95%CI=0.43-1.38, p value=0.395], root tips

[OR=0.43, 95%CI=0.17-1.11, p value=0.082], endodontically treated teeth [OR=0.96, 95%CI=0.54-1.66, p value=0.912], periodontically hopeless teeth [OR=0.71, 95%CI=0.21-2.37, p value=0.582] and tenderness on percussion [OR=1.29, 95%CI=0.29-5.75, p value=0.733].

Multivariable analysis of dental characteristics on 90-day mortality

Table 4 shows multivariable analysis of dental characteristic on 90-day mortality. Of those in 90-day mortality and the survived patients, there was no significant difference observed between dental complaint [OR=0.25, 95%CI=0.03-1.94, p value=0.189], presence of complete denture [OR=1.41, 95%CI=0.65-3.07, p value=0.380], presence of partial denture [OR=0.20, 95%CI=0.02-1.52, p value=0.582], carious teeth [OR=0.84, 95%CI=0.46-1.53, p value=0.582], root tips [OR=0.42, 95%CI=0.16-1.10, p value=0.079], endodontically treated teeth [OR=0.86, 95%CI=0.49-1.50, p value=0.606], periodontically hopeless teeth [OR=0.74, 95%CI=0.22-2.54, p value=0.641] and tenderness on percussion [OR=1.04, 95%CI=0.29-6.62, p value=0.671].

Subgroup analysis

Table 5 shows the impact of comorbidities (subgroup) on the association of dental characteristic on 90-day mortality. In the CHF group, between the patient who died in 90 days in comparison to the patient survived within 90days, we observed no statistically significant difference between dental complaint (n=1, 1.7% vs n= 24, 3.7%) [p value=0.281], complete denture (n=6, 10.3% vs n=37, 5.9%) [p value=0.414], partial denture (n=1, 1.7% vs n=28, 4.4%) [p value= 0.205], carious teeth (n=18, 9% vs n=140, 22.1%) [p value= 0.120], root tips (n=4, 6.9% vs n=69, 10.9%) [p value= 0.132], endodontically treated teeth (n=21, 36.2% vs n=161, 25.4%) [p

value= 0.487], periodontically hopeless teeth (n=3, 5.2% vs n=24, 3.7%) [p value= 0.895] and tenderness on percussion (n=3, 5.2% vs n=14, 2.2%) [p value= 0.314].

In the PVD group, between the patient who died in 90 days in comparison to the patient survived within 90 days, we observed no statistically significant difference between dental complaint (n=0 vs n=7, 1.1%), complete denture (n=4, 6.9% vs n=14, 2.2%) [p value= 0.380], partial denture (n=0 vs n=6, 0.9%), carious teeth (n=6, 10.3% vs n=30, 4.7%) [p value= 0.801], root tips (n=3, 5.2% vs n=12, 1.9%) [p value= 0.597], endodontically treated teeth (n=5, 8.6% vs n=41, 6.5%) [p value= 0.235], periodontically hopeless teeth (n=0 vs n=9, 1.4%), and tenderness on percussion (n=1, 1.7% vs n=2, 0.3%) [p value= 0.385].

In the diabetes group, between the patient who died in 90 days in comparison to the patient survived within 90days, we observed no statistically significant difference between dental complaint (n=0 vs n=7, 1.1%), complete denture (n=3, 5.2% vs n=26, 4.1%) [p value= 0.969], partial denture (n=0 vs n=1, 1.7%), carious teeth (n=9, 15.5% vs n=72, 11.4%) [p value= 0.832], root tips (n=1, 1.7% vs n=40, 6.3%) [p value= 0.058], endodontically treated teeth (n=9, 15.1% vs n=74, 11.7%) [p value= 0.910], periodontically hopeless teeth (n=1, 1.7% vs n=18, 2.8%) [p value= 0.430], and tenderness on percussion (n=1, 1.7% vs n=8, 1.3%) [p value= 0.956].

Section E: Discussion

Many patients scheduled for cardiovascular surgery have poor oral hygiene status/ dental characteristics. (5,7) Accordingly, preoperative dental clearance is widely accepted phenomenon in order to eliminate potential source of dental infection to prevent poor valve surgery outcomes. (5) Diagnosis of which infection being a potential risk for developing post-surgical valvular complications remains ungauged due to lack of evidence-based data. Our study was designed to focus on early mortality (within 90-days), a major concerning post-surgical valvular outcome. In this study we described and evaluated the association of individual odontogenic infection/ dental characteristic of those undergoing comprehensive preoperative dental screening approach with the 90-day mortality. Our data indicated that dental characteristics had no significant association with 90-day mortality.

In our study, we excluded patients with high risk of mortality (history of IVDU and systemic infection) and only included patients who underwent comprehensive PDS at MGH. Of overall 692 included patients, 58 (8.9%) patient died within 90-days and 634 (91.6%) survived (within 90-days) in which we observed majority of patients with self-reported Caucasian race amongst the group with a significantly higher mean age and majority of female gender in the 90-day mortality group in comparison to patient who survived (within 90-days). Except more case of CHF and PVD, all other comorbidities were comparable amongst the 90-day mortality group and the survived patient (within 90-days). The burden of valvular disease, valvular surgeries performed, and the nature of surgery remained comparable between the group.

Although studies and metanalysis have reported the frequency of periodontal disease with other deleterious dental characteristics as a common finding in patients scheduled for valvular

surgery, (5,6,7,8) there lacks data suggesting the magnitude to which odontogenic infections and dental characteristic impacts on the post valvular surgical outcomes. Of all post-surgical valvular outcomes, early mortality is a major concerning issue for both patient and the care team. Accordingly, our study was designed to understand the impact of odontogenic infections and dental characteristics on the early mortality. Although, amongst the 90-day mortality group and the survived patient there was a varying difference in the frequency of dental characteristic including dental complaint, total number of teeth present, complete dentures, partial dentures, carious teeth, root tips, total number of asymptomatic root tips, endodontically treated teeth, periodontically hopeless teeth and tenderness on percussion, no statistically significant difference was observed amongst the group. When assessed for the association between the observed dental characteristics and the outcome 90-day mortality, the result for unadjusted and adjusted model remained similar and was not statistically significant. The probable reason for no significant result could be a smaller number of sample size and the event rate in the outcome. To further verify the impact of dental characteristics on the outcomes, we assessed for the impact of clinically relevant comorbidities on the association of dental characteristic on 90-day mortality. We observed no significant impact for relevant clinical comorbidities. This study had a number of limitations. One of the major limitations was the missing data from both STS data set of hospital and the dental data. Since the study excluded high risk group patients (IVDU and systemic infections), the result of this study restricts its application on these group. Due to the unavailability of the STS mortality scores, inter-comparison of our findings with STS data cannot be reported. As a nature of retrospective study, we cannot adjust for the hospital/center effect on our findings. Further large prospective studies are needed to validate these findings.

Section F: Conclusion

In conclusion, the study could not demonstrate an association between the individual dental characteristics and 90-day mortality in patients undergoing cardiac valve surgery. This was also true in patients with comorbidities (PVD, CHF, diabetes) which are known to represent risk factors for poorer survival. Further large prospective studies are needed to validate these findings.

Section G: Figures and Tables

Figure 1- Consort diagram

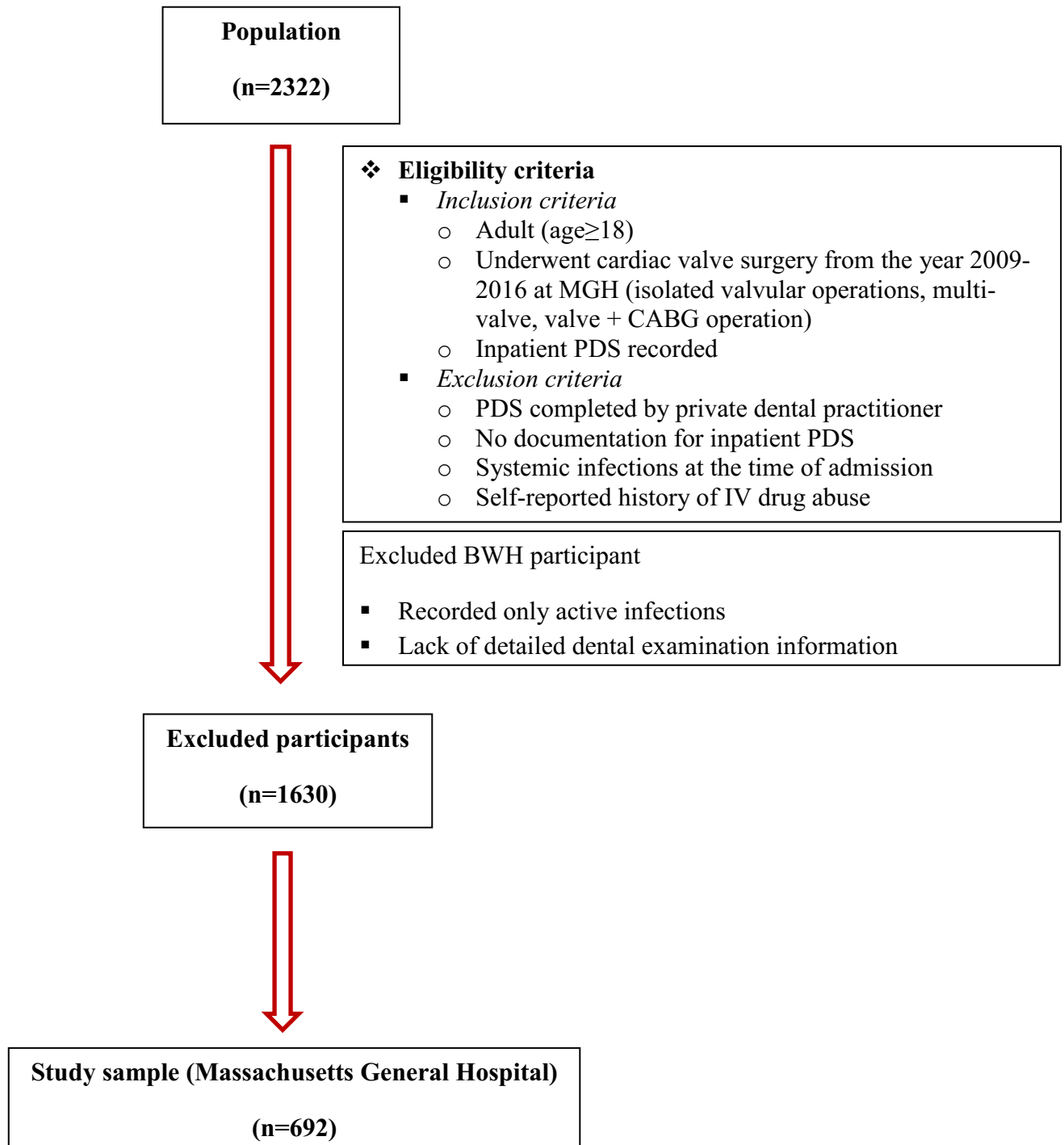


Table 1- Baseline characteristics

Variables	All patient (n=692)	90-day mortality		P value
		Died (n=58)	Survived (n=634)	
Age (mean±SD)	68.7 ± 14.7	73.93 ± 13.3	68.97 ± 14.2	0.010
Sex				0.012
Male	416 (60.2%)	26 (44.8%)	390 (61.5%)	
Female	275 (39.8%)	32 (55.2%)	243 (38.3%)	
Race				0.961
Caucasian	615 (88.9%)	52 (89.7%)	563 (88.8%)	
African American	24 (3.5%)	2 (3.4%)	22 (3.5%)	
Asian	22 (3.2%)	1 (1.7%)	21 (3.3%)	
Others	30 (4.3%)	3 (5.2%)	27 (4.3%)	
BMI (mean±SD)	28.2±8.2	26.8 ± 5.7	28.4 ± 8.4	0.152
Diabetes	199 (28.8%)	21 (36.2%)	178 (28.1%)	0.190
Hypertension	513 (74.1%)	47 (81%)	466 (73.5%)	0.210
History of CVA	73 (10.5%)	7 (12.1%)	66 (10.4%)	0.698
History of CHF	415 (60%)	43 (74.1%)	372 (58.6%)	0.021
History of PVD	97 (14%)	15 (25.9%)	82 (12.9%)	0.007
History of CVD	142 (20.5%)	15 (25.9%)	127 (20%)	0.293
Valvular disease				
Aortic stenosis	413 (59.7%)	34 (58.6%)	379 (59.3%)	0.774
Mitral stenosis	76 (11%)	6 (10.3%)	70 (11%)	0.870
Nature of surgery				0.734
Elective	180 (26%)	14 (24.1%)	166 (26.2%)	
Urgent	512 (74%)	44 (75.7%)	468 (73.8%)	
Type of valve procedure				
Aortic valve procedure	169 (24.4%)	12 (20.7%)	157 (24.8%)	0.762
Mitral valve procedure	64 (9.2%)	5 (8.6%)	59 (9.3%)	0.759
Tricuspid valve procedure	76 (10.1%)	11 (18.1%)	65 (10.3%)	0.117
Pulmonic valve procedure	9 (1.3%)	1 (1.7%)	8 (1.3%)	0.863

Table 2- Dental characteristics

Dental characteristics	Overall (n=692)	90-day mortality		P value
		Died (n=58)	Survived (n=634)	
Dental complaint	40 (5.8%)	1 (1.7%)	39 (6.2%)	0.167
Total number of teeth present (mean±SD)	20.9 ±7.9	19.7 ± 8.1	21.1 ±7.8	0.196
Prosthesis				
Complete denture	73 (10.5%)	9 (15.5%)	64 (10.1%)	0.200
Partial denture	44 (6.4%)	1 (1.7%)	43 (6.8%)	0.130
Carious teeth	250 (36.1%)	18 (31%)	232 (36.5%)	0.394
Root tips	118 (17.1%)	5 (8.6%)	113 (17.8%)	0.074
Total number of asymptomatic root tips (mean±SD)	0.5±1.5	0.3 ± 0.9	0.6 ± 1.6	0.196
Endodontically treated teeth	315 (45.5%)	26 (44.8%)	289 (45.5%)	0.912
Periodontically hopeless teeth	48 (6.9%)	3 (5.2%)	45 (7.1%)	0.581
Impacted third molars	14 (2%)	0	14 (2.2%)	-
Dental pain	10 (1.4%)	0	10 (1.6%)	-
Purulence	5 (0.7%)	0	5 (0.8%)	-
swelling	2 (0.3%)	0	2	-
Symptomatic root tips	4 (0.6%)	0	4 (0.6%)	-
Tenderness on percussion	58 (8.4%)	2 (3.4%)	17 (2.7%)	0.602

Table 3- Univariate analysis

Dental characteristics	OR	95%CI	P value
Dental complaint	0.26	0.03-1.98	0.197
Prosthesis			
Complete denture	1.63	0.76-3.47	0.204
Partial denture	0.24	0.03-1.78	0.163
Carious teeth	0.77	0.43-1.38	0.395
Root tips	0.43	0.17-1.11	0.082
Endodontically treated teeth	0.96	0.54-1.66	0.912
Periodontically hopeless teeth	0.71	0.21-2.37	0.582
Tenderness on percussion	1.29	0.29-5.75	0.733

Odds ratio (OR), 95%CI and P value= died vs survived

Table 4- Multivariable analysis

Dental characteristics	OR	95%CI	P value
Dental complaint	0.25	0.03-1.94	0.189
Prosthesis			
Complete denture	1.41	0.65- 3.07	0.380
Partial denture	0.20	0.02-1.52	0.122
Carious teeth	0.84	0.46-1.53	0.582
Root tips	0.42	0.16- 1.10	0.079
Endodontically treated teeth	0.86	0.49- 1.50	0.606
Periodontically hopeless teeth	0.74	0.22 -2.54	0.641
Tenderness on percussion	1.04	0.29-6.62	0.671

Adjusted for Age, sex, CHF and PVD. Odds ratio (OR), 95%CI and P value= died vs survived

Table 5- Impact of comorbidities (subgroups) on the association of dental characteristic on 90-day mortality

Comorbidities	Dental characteristics	90-day mortality		P value
		Died (n=58)	Survived (n=634)	
CHF	Dental complaint	1 (1.7%)	24 (3.7%)	0.281
	Complete denture	6 (10.3%)	37 (5.9%)	0.414
	Partial denture	1 (1.7%)	28 (4.4%)	0.205
	Carious teeth	11 (18.9%)	140 (22.1%)	0.120
	Root tips	4 (6.9%)	69 (10.9%)	0.132
	Endodontically treated teeth	21 (36.2%)	161 (25.4%)	0.487
	Periodontically hopeless teeth	3 (5.2%)	24 (3.7%)	0.895
	Tenderness on percussion	3 (5.2%)	14 (2.2%)	0.314
PVD	Dental complaint	0	7 (1.1%)	-
	Complete denture	4 (6.9%)	14 (2.2%)	0.380
	Partial denture	0	6 (0.9%)	-
	Carious teeth	6 (10.3%)	30 (4.7%)	0.801
	Root tips	3 (5.2%)	12 (1.9%)	0.597
	Endodontically treated teeth	5 (8.6%)	41 (6.5%)	0.235
	Periodontically hopeless teeth	0	9 (1.4%)	-
	Tenderness on percussion	1 (1.7%)	2 (0.3)	0.385
Diabetes	Dental complaint	0	7 (1.1%)	-
	Complete denture	3 (5.2%)	26 (4.1%)	0.969
	Partial denture	0	11 (1.7%)	-
	Carious teeth	9 (15.5%)	72 (11.4%)	0.832
	Root tips	1 (1.7%)	40 (6.3%)	0.058
	Endodontically treated teeth	9 (15.1%)	74 (11.7%)	0.910
	Periodontically hopeless teeth	1 (1.7%)	18 (2.8%)	0.430
	Tenderness on percussion	1 (1.7%)	8 (1.3%)	0.956

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Chapter IV- Summary

Preoperative dental screening is a widely accepted phenomenon to prevent poor post-surgical valvular complications. Since, there lacks a standardized approach, practice of PDS remains arbitrary. The most common approach known to the authors are focused approach (limited radiographic diagnosis and treatment of teeth with active infections) and comprehensive approach (detailed radiographic diagnosis and treatment of teeth with active/chronic infections). There lacks data that presents the magnitude to which these protocol impacts early mortality (90-day mortality). Our paper 1 was focused to evaluate the association of PDS approach to 90-day mortality. Our primary finding suggests that focused PDS approach and comprehensive approach is not associated with 90-day mortality. The secondary findings showed that focused PDS approach is associated with increased risk of septicemia and lesser complications of pneumonia, and re-infections. While, comprehensive PDS approach was found to be associated with increased in length of hospitalization, higher number of pneumonia and reinfection cases. The secondary findings of our study were based on unadjusted analysis and likely needs further validation with larger prospective study.

Lack of identified dental characteristics that might hold an independent impact on the poor post-surgical outcomes can be one of the reasons for an ambiguous PDS approach. Our paper-2 focused to study the association of dental characteristic with early mortality patients (90-day mortality). Our results showed no significant association of dental characteristic with 90-day mortality. There was no impact of comorbidities observed on the association of dental characteristics on the 90-day mortality.

Chapter V- Discussion and perspectives

Due to lack of evidence-based data, impact of preoperative dental screening (PDS) methods and dental characteristic on the early mortality post valve surgery is still unclear. Through our paper-1 and paper-2, we focused to answer this gap. We observed no significant association of two types of PDS and dental characteristics with 90-day mortality.

Following are the strengths, limitation and future perspective of the study:

Strengths- The study was conducted using the original hospital-based data of two well renowned tertiary care hospitals of Boston, Massachusetts having the largest available cohort with long term stable standing and defined PDS approach. *Limitations-*As a retrospective, one of the major limitations was the missing data at both the hospital sites. Accordingly, we could adjust our outcomes with limited risk factors. Due to the fewer events in the outcomes, the study restricts the ability to perform the multivariable analysis to prevent over fitting of the analytical model. Since the STS baseline score were unavailable, inter-comparison of our findings with STS data cannot be reported. The study finding cannot be applied to patients with self-reported systemic infections and a history of intravenous drug abuse due to their exclusion from the study. As the nature of the study design, comparison of individual clinical practices and hospital environment between the hospital sites might have played a potential bias which cannot be adjusted using the present data. *Future directions-* Future studies can be directed in understanding the association of different protocols on the high-risk subgroup of the population, comparative analysis on the preoperative dental screening approach between the hospital setups and private community practice, level of association of PDS approach and the post-surgical infectious outcomes, association of dental

characteristic with the post-surgical valvular infectious outcomes, identification of dental risk factors in the subgroup of the population stratified by high risk diseases.