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STATISTICAL MODELING OF MORTALITY RISK FOR CONGENITAL HEART DEFECTS

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ABSTRACT. This paper, retrieving surgical data recorded in the Pediatric Cardiac Care Consortium between 1985-2004, identifies an inverse relationship between in-hospital mortality and pediatric cardiac surgical volume in small and medium-sized centers. Similar inverse relationship was found for both low and high complexity cases after stratifying the data by risk category using the Risk Adjustment for Congenital Heart Surgery (RACHS). Given the relationship, a threshold on the volume to reach the lowest attainment of surgical mortality is suggested when is attainable.
Key words: Curvature function; Historic data of Pediatric Cardiac Care Consortium; Mortality risk analysis; Optimal surgical volume.

1. INTRODUCTION

Surgical mortality rates are increasingly used by the various stakeholders in the medical care environment to assess hospital performance for high risk procedures such as cardiac surgeries [4]. For adult open heart procedures, a growing body of evidence indicates that certain surgical procedures exhibit a relationship in which higher volume of patients undergoing a particular procedure at a hospital is associated with lower mortality probability [5, 6]. However, the few studies of the volume-outcome relationship for pediatric cardiac surgery have been mixed in their conclusions [7, 8], so that the role of volume load on mortality remains poorly understood [1, 2, 3, 9, 11]. The first study by Jenkins et al., [3], reported outcomes on 2833 cases from 37 centers in the states of California and Massachusetts based on an administrative database of hospital discharge data from these two states for the years 1988 and 1989 respectively. The study suggested that risk-adjusted in-hospital mortality rates are lower in centers with higher than 300 volumes annually of pediatric cardiac surgeries. In [15] bypassing any discretizations of the hospital surgical volume found a significant inverse between surgical volume and mortality probability for all surgical complexity cases besides the lowest one for centers for a database referring to the New York State. Furthermore, analysis from the Nationwide Inpatient Sample (NIS), the

largest administrative inpatient care database in the United States, concluded that volume alone was only marginally better than a coin flip as discriminator of mortality [7]. However, after adjusting for patient and surgical case-mix, large volume hospitals performing more than 200 procedures per year performed more complex operations and achieved superior results.

Based on the above, the relative importance of hospital surgical volume for pediatric cardiac operations is disputed in particular in the most recent reports. This is not surprising, because there are only few hospitals that with the current low operative risk for congenital heart defects (CHD) have sufficient caseloads to reliably identify quality problems based on mortality rates. An additional limitation in approaching the volume-outcome relationship for CHD is the wide variation of diagnoses and surgical procedures that involves different surgical challenges and entails a wide range of risks to patients. Subsequently, the number of reported outcomes for individual procedures per diagnosis is relatively small and even when accumulating data from multiple institutions, individual procedures frequently cannot reach a sufficient volume to sustain complicated multivariate analyses. In this case, the best analysis option is to combine procedures into groups that are as homogeneous as possible with respect to patient severity of illness and to use the groups as risk factors in a risk-adjustment process. Such a data stratification system is the Risk Adjustment for Congenital Heart Surgery (RACHS) [14, 16]. RACHS has a strong association with in-hospital mortality and as complexity increases; discharge mortality also increases [17, 18]. RACHS method takes under consideration a number of factors that have been identified as risk factors for early surgical mortality including patient age, type of surgical procedure, presence of a major non-cardiac anomaly and combination of cardiac procedures [2, 14, 16].

This paper uses risk adjustment data from a large clinical database, the Pediatric Cardiac Care Consortium (PCCC), encompassing approximately 80,000 consecutive surgeries from 47 small and medium size (less or equal to 300 surgeries per year) centers from different areas across the US and Canada for the period 1985-2004. Unlike previous studies, where discretization methods of the surgical volume were chosen, the volume caseload considered naturally a continuous random variable. The historic data have been grouped into four time periods of five years each. Our data for each such period confirm that hospital surgical volume is positively related to better patient outcomes in terms of in-hospital mortality, and these differences persist for both high and low complexity pediatric cardiac procedures. In addition, the results herein suggest a hospital surgical volume threshold as the critical cut off volume to reach the lowest attainment of surgical mortality for CHD reported by larger volume centers. Beyond this threshold, no significant changes in mortality rates were noted.

The paper is organized as follows. Section 2 describes the data, and its stratification according to RACHS. Section 3 gives an outline of the results whose statistical analysis are discussed in Section 4. Section 5 addresses future questions which need to be determined based on the data entries from the PCCC database.

2. DATA SOURSES AND RISK CATEGORY STRATIFICATION

The historic data for the period 1985-2004 are aggregated from the Pediatric cardiac Care Consortium (PCCC). The PCCC registry collects clinical data from centers

perform- ing pediatric cardiac operations [12]. Due to the wide range of diagnoses and surgical procedures, we stratify the data into 6 groups such that conditions with similar expected mortality rates will be in the same group. Such a risk classification system is the Risk Adjusted Classification for Congenital Heart Surgery (RACHS). RACHS is a discrete index taking values from 0 to 6, where RACHS = 1 is assigned to the surgical procedures with the lowest risk of death and RACHS = 6 to the corresponding procedures with the highest risk for death. Conditions which cannot be stratified according to this method and remained unclassified, are assigned RACHS=0.

The outcome data for each five-year period are summarized in Table 1. The use of the database data for research purposes has been approved by the Institutional Review Board of the University of Minnesota.

Period	1985-1989	1990-1994	1995-1999	2000-2004
Number of Participating Centers	21	27	32	47
Number of Surgeries	10,924	15,884	24,495	30,204
Outlier Centers	3	3	4	6
% of surgeries from outlier centers	5%	4.5%	2.8%	2%
% of surgeries with RACHS=0	18.9%	14.5%	9%	12.2%

Table 1: Description for each 5-year period

3. RESULTS

This section outlines the results of this manuscript. Figures 1(a)-1(d) are graphical representations of the relationship between the surgical volume and the mortality probability within each 5-year period after removing any outlier within each period. We observe from Figures 1(a) and 1(b) that during the periods 1985-1989 and 1990-1994, there is a linear decreasing dependency between the mortality risk and the volume. For the two consecutive periods, 1995-1999 and 2000-2004, the decreasing dependency changes to a power law (Figures 1(c) and 1(d)). Figure 3 compares the four different patterns of the relationship volume-outcome. It is clear that the closer to the present year, the lower the mortality risk becomes. On the other hand, one may note that after approximately 1,200 surgeries the mortality probability of the period 1985-1989 is lower than the corresponding mortality probability of the period 1990-1994. An explanation for the fact is on the size of the centers which participated in the study during the early years of 1985-1989. Indeed, only one center recorded more than 1,200 surgeries during that period. If this center is ignored, then the general pattern of higher mortality during the past years is satisfied.

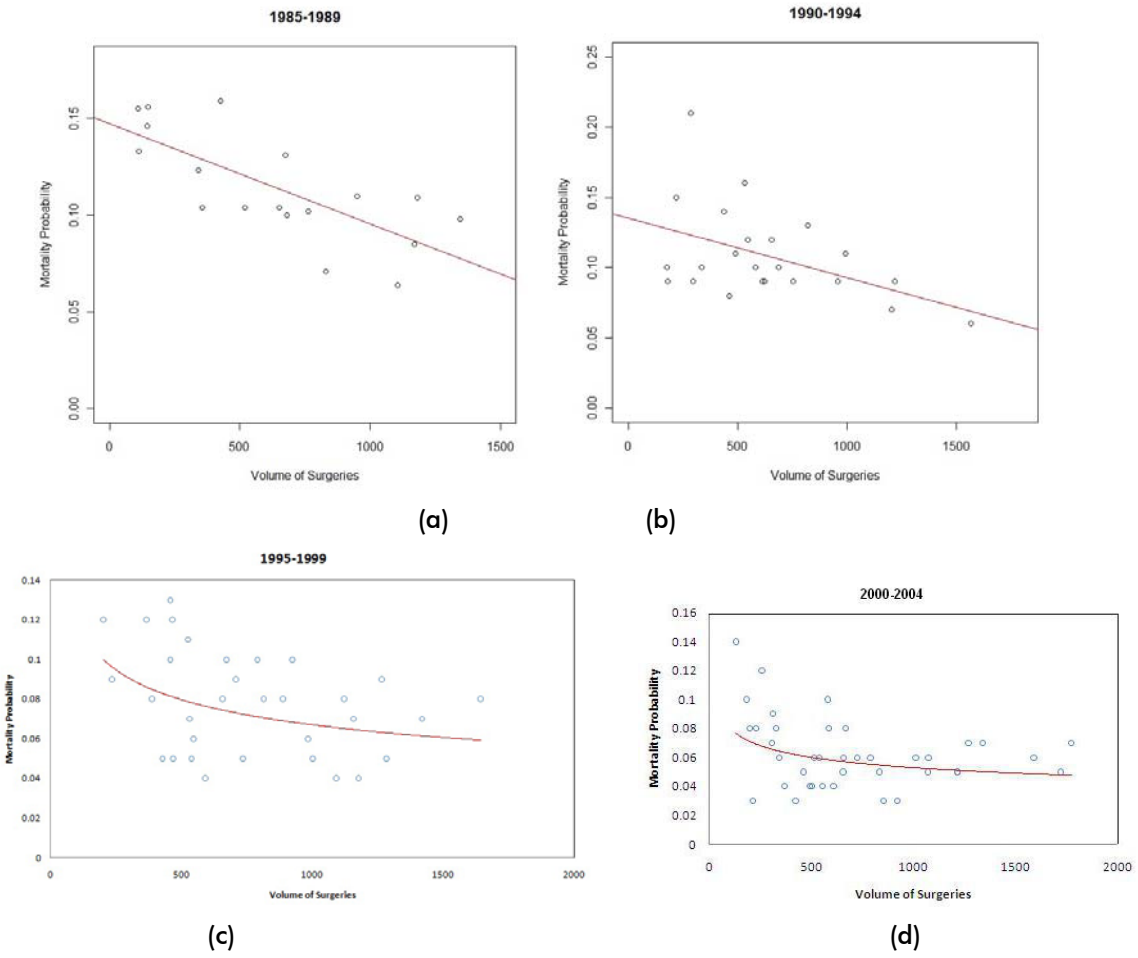


Figure 1. Historic PCCC data between 1985-2004. Each subfigure is the plot of each 5-year period, and the line declares the pattern which is followed within each period.

4. STATISTICAL ANALYSIS

4.1. **All data.** The goal of this paper is to examine whether an increase of the number of surgeries is a real evidence of a change in the probability of surgical mortality for CHD repair. In other words, whether it could be explained merely as a consequence of random variation in the historic data from 1985-2004. The statistical analysis was run via the statistical package R. The reader may refer to [13, 19] for an extensive study of statistical modeling and its application in medicine particularly.

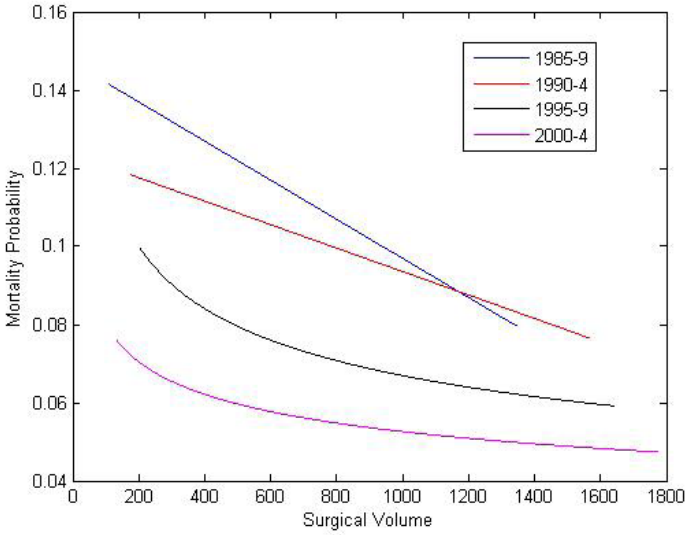


Figure 2. Comparison of the four different patterns within each period.

For the first two periods, 1985-1989 and 1990-1994, and after removing the appropriate outliers, linear regression analysis is used. It is established with p – value = 0.005 and p – value = 0.0156 respectively that the predicted mortality probability with respect to surgical volume is given as:

(1) $\hat{p}_m = \alpha + \beta V$

where $\hat{p}_m$, V are the predicted mortality risk and surgical volume respectively. The different values for α, β for the two different periods, 1 and 2, are in Table 4.1.

Period	Trend	p-value
1	$p_m = -5*10^{-5}V + 0.147$	0.0005
2	$p_m = -5*10^{-5}V + 0.1$	0.0156
3	$p_m = 0.372V^{-0.249}$	0.0426
4	$p_m = 0.186V^{-0.182}$	0.045

Table 2.Models expressing the PCCC data within each period and their corresponding p-value.

Next, observing the scatterplots for the periods 1995-1999 and 2000-2004 as displayed in Figure 1(c) and Figure 1(d) respectively, one may conclude that it is not easily identified a trend between the surgical volume and mortality probability. Proceeding to a natural logarithmic transformation of the data a statistically significant linear relationship between the two transformed data for both 5-year periods is established, and using the inverse transformation, this relationship is given via a power law as below:

(2) $\hat{p}_m = exp(\tilde{\alpha})V^{\tilde{\beta}}$

where $\hat{p}_m$, V are the predicted mortality risk and surgical volume respectively. The different values for $\tilde{\alpha}$, $\tilde{\beta}$ and the corresponding p−values for the two periods 3 and 4, are found in Table 4.1.

4.2. **Stratified data by RACHS.** The Risk Adjusted classification for Congenital Heart Surgery (RACHS) was developed as a tool to compare in-hospital mortality for children undergoing CHD surgery with the purpose of quality improvement. Given the PCCC historic data, there is no much information for the highest RACHS scores, and thus we dichotomize the RACHS score by low, score 1-3, and high, score 4-6. We proceed by analyzing the data the same way as it was explained in Section 4.1. For the first two periods, one may employ linear regression and the relationship is expressed as in (1). After transforming the data of the third and the forth period, a statistically significant association expressed via a power law (see (2)) between the surgical volume and the probability of surgical mortality for CHD repair within each group is revealed. Defining $(V_l, p_{m,l})$, $(V_h, p_{m,h})$ the volume and mortality probability for low RACHS and high RACHS correspondingly, we have the following patterns as explained on Table 3 and Table 4.

Period	Trend	p-value
1	$P_{m,l} = -5*10^{-5}V_l + 0.111$	0.008
2	$P_{m,l} = -5*10^{-5}V_l + 0.1$	-0.0149
3	$P_{m,l} = 0.33V_l^{-0.304}$	0.046
4	$P_{m,l} = 0.179V_l^{-0.26}$	0.046

Table 3. Models expressing the PCCC data with low RACHS within each period and their corresponding p-value.

Period	Trend	p-value
1	$P_{m,l} = -0.002V_h + 0.513$	0.026
2	$P_{m,l} = -5*10^{-4}V_h + 0.4$	0.041
3	$P_{m,l} = 0.877V^{-0.276}$	0.029
4	$P_{m,l} = V_h^{-0.28}$	0.003

Table 4. Models expressing the PCCC data with high RACHS within each period and their corresponding p-value.

4.3. **Establishing the optimal number of surgeries.** This section investigates the optimal number of surgeries after which there is not a drastic change in the decay rate of the probability of surgical mortality. Clearly, there is not such a cut-off value for the first two periods, since the rate is constant and equals to the slope of the regression line, $-5*10^{-5}$.

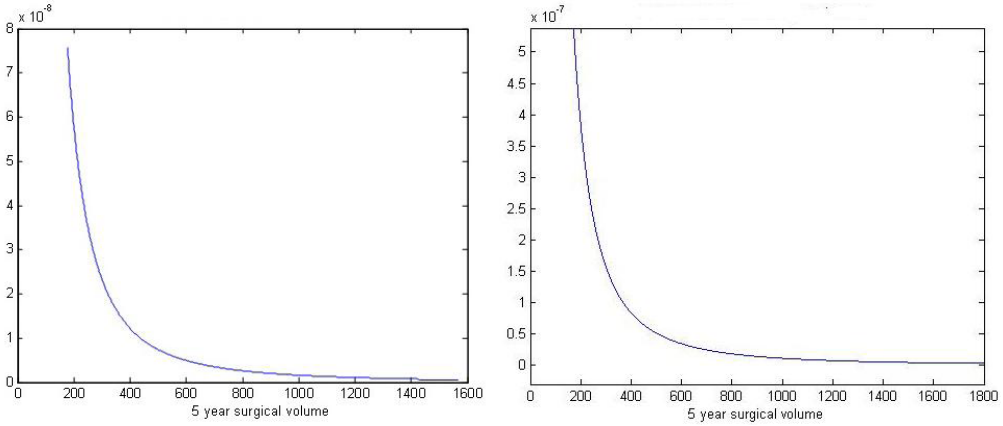
The two consecutive periods 1995-1999, 2000-2004 achieve such an optimal number which will calculated using the curvature function of the two power law expressions which model the relationship between surgical volume and mortality risk. Generally, the curvature, k(x) for a function f(x), is given by the following expression:

$$k(x) = \frac{|f''(x)|}{(1+f'(x)^2)^{3/2}} \quad (3)$$

where f' and f'' are the first and second derivatives of the function f respectively. One mayrefer to [10] and references therein for an extensive study of curvatures. For the special case where f is given as in (2) the curvature is of the following form,

$$k(x) = \frac{|exp(\tilde{\alpha})\tilde{\beta}(\tilde{\beta}-1)x^{\tilde{\beta}-2}|}{(1+exp(2\tilde{\alpha})\tilde{\beta}^2x^{2(\tilde{\beta}-1)})^{3/2}} \quad (4)$$

Substituting in (4) the exact values for $\tilde{\alpha}$, $\tilde{\beta}$ as they are given in Table 4.1, the curvature functions with respect to 5 year surgical volume for each period (periods 3 and 4) are displayed in Figure 3(a) and Figure 3(b) respectively.



(a) (b)

Figure 3. Curvature function for period 3 and period 4.

Given Figure 3(a) and Figure 3(b), one may conclude that after 1,000-1,200 surgeries for the period 1995-1999 and after 850 to 1,000 surgeries for the period 2000-2004, the decreasing rate does not change drastically.

5. DISCUSSION

Sufficient progress has occurred in surgically repairing physiologically important congenital cardiac defects so that operations for congenital heart defects can now be performed with a relatively low risk of mortality.

However, many studies have demonstrated considerable differences in mortality among institutions performing cardiac surgery in children and young adults. The outcome of surgery is influenced by many factors, including patient-related risk factors, human factors and natural variations.

The primary purpose of this study was to analyze a large database such that any bias is removed and to conclude the impact of cardiac center case load on in-hospital mortality. We reported the outcome events from approximately 80,000 surgeries for congenital heart disease from 47 small and medium size centers across the US participating in the clinical database of the Pediatric Cardiac Care Consortium (PCCC), within the period 1985-2004. The surgical procedures were stratified by the validated Risk Adjustment in Congenital Heart Surgery (RACHS) method. Surgical volume was used as a continuous random variable to avoid the pitfalls of deciding a priori what constitutes small and large volumes within these types of centers. The statistical analysis suggested a decay between mortality probability and surgical volume. Depending on the period this decay was expressed through a linear or a power law expression. Given the large number of outcome events

available in this study a secondary purpose was to identify whether there is a minimum number of surgeries beyond which there is no change in the risk of surgical mortality and in this case to define the threshold demarcating the lowest attainment in terms of surgical mortality. Using the curvature, this threshold was found to be 1,000-1,200 surgeries for the period 1995-1999 and 850 to 1,000 surgeries for the period 2000-2004.

Future analysis is required on the behavior the unclassified data (RACHS=0). Also, more random variables such that the length of hospitalization or several demographics of the patients and their health history, should be incorporated in order to have a more complete picture of the mortality probability.

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