FACTORS THAT ALTER THE RELATIONSHIP BETWEEN PEAK POSTOPERATIVE CKMB AND TROPONIN T AFTER CABG

by

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DISSERTATION

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ABSTRACT
FACTORS THAT ALTER THE RELATIONSHIP BETWEEN PEAK POSTOPERATIVE CKMB AND TROPONIN T AFTER CABG

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Background: *Peak postoperative creatine kinase MB fraction (CKMB) and Troponin T (TnT) levels have been measured after cardiac surgery to assess perioperative myocardial damage, evaluate myocardial protective strategies and predict adverse events. However, the relationship between peak levels of both enzymes has not been fully established in this setting. We compared peak levels of CKMB and TnT in patients after CABG to test the hypothesis that patient and operative characteristics influence the correlation between the values of these biomarkers.*

Objective: *To examine the relationship between peak levels of cTnT and CKMB following CABG in defined subsets of patients with pre-defined comorbidities to test the hypothesis that patient and operative characteristics influence the correlation between the values of these biomarkers.*

Methods: *Data were prospectively collected from 885 consecutive patients undergoing on-pump CABG at a single institution between July 2011 and June 2017. Peak values were selected from all serum levels of CKMB and TnT collected during the hospital stay following surgery. Clinical variables were collected based on definitions in the STS Adult Cardiac Surgery Database version 2.181. Analysis of covariance (ANCOVA) and linear regression models were used to statistically compare the slope of the linear relationship between peak postoperative CKMB and TnT for the patient cohort. Models were created to compare the slopes by pre-defined clinical variables including (1) age, (2) sex, (3) race, (4) current smoking status (5) hypertension, (6) dyslipidemia, (7) ejection fraction (EF), (8) diabetes, (9) renal dysfunction (GFR<60), (10) recent MI, preoperative use of (11) ACE-inhibitors, (12) beta-blockers, and (13) anticoagulants; and operative variables including (1) cross clamp time (< or > 70 min), (2) CPB time (< or > 100 min), and (3) intra-operative blood products transfusion.*

Results: *Overall, the correlation between peak postoperative CKMB and TnT was robust in patients undergoing CABG. However, the slope of the relationship was significantly lower in males, diabetics, patients with dyslipidemia, patients with hypertension, patients with lower EF, patients who received red blood cell transfusions, and patients receiving beta-blockers. The slope was significantly greater in patients with renal dysfunction, current smokers, patients with a recent MI, patients with longer cross clamp times, patients with longer CPB time, and patients receiving ACE-inhibitors.*

Conclusion: *The relationship between CKMB and TnT following CABG appears to be influenced by patient and operative characteristics. These data do not assess which enzyme more accurately reflects myocardial injury, but does suggest conclusions about myocardial damage may be affected by the biomarker selected in the presence of certain variables. Further study to assess the association between these biomarkers and patient outcomes is warranted.*

TABLE OF CONTENTS

CHAPTER 1

Introduction

Peak postoperative creatine kinase MB fraction (CKMB) and Troponin T (TnT) levels have been measured after cardiac surgery to assess perioperative myocardial damage, evaluate myocardial protective strategies and predict adverse events. Several studies have shown that elevated levels of CKMB are associated with adverse postoperative events, especially when peak levels exceed ten times the upper limit of normal during the initial 48 hours after coronary artery bypass graft (CABG) [1].

More recently, other markers, particularly cardiac Troponin T (cTnT) and Troponin I (cTnI), have been suggested to be superior to CKMB in the setting of acute myocardial infarction (AMI), owing to greater specificity for cardiac myocyte damage [2]. In the setting of open heart surgery, cardiac troponin and CKMB have been well established as biomarkers of myocardial injury and have been associated with poorer clinical prognosis when elevated within 24 hours after most cardiac operations [4].

The analysis of cardiac enzyme levels becomes more challenging in cohorts of patients with comorbidities such as renal disease. Troponins are part of the contractile apparatus of the myocyte, and myocardial necrosis is accompanied by release of these structural proteins into the cardiac interstitium. CKMB is present in skeletal muscles and in minor quantities of the intestine, diaphragm, uterus, and prostate, so injury to these major organs may impair the specificity of CKMB. CKMB has been widely used to diagnose myocardial infarction (MI) but also has been elevated in patients with chronic renal failure and skeletal muscle injury, which could falsely diagnose a perioperative ischemic event [5]. TnT has proven a highly sensitive and specific indicator of MI yet has

also been elevated in some patients with renal insufficiency [6].

The release of cardiac enzymes after CABG may relate to graft occlusion, reperfusion injury, inadequate myocardial protection, ischemia during operation, and surgical trauma [7]. However, there has been debate surrounding the clinical interpretation and accuracy of the levels of biomarkers postoperatively. Nevertheless, many cardiac surgery programs collect perioperative biomarker data as a quality assurance measure in order to direct management of patients after cardiac surgery and avoid worse outcomes [4]. However, the relationship between peak levels of both enzymes has not been fully established in the setting of coronary artery bypass surgery.

Purpose

The purpose of this study was to examine the relationship between peak levels of cTnT and CKMB following CABG in defined subsets of patients with pre-defined comorbidities to test the hypothesis that patient and operative characteristics influence the correlation between the values of these biomarkers.

This information may enable us to better understand the assessment of the success or failure of cardio protection in specific cohorts of patients undergoing CABG.

CHAPTER 2

Experimental procedure for this thesis

Data were prospectively collected from 885 consecutive patients undergoing on-pump CABG at a single institution between July 2011 and June 2017. Peak values were selected from all serum levels of CKMB and TnT collected during the hospital stay following surgery. The clinical variables were collected based on definitions in the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database versions 2.73 and 2.81.

Characteristics of the sample were summarized using descriptive statistics. All continuous variables of interest were found to be non-normally distributed; these variables are summarized using medians and ranges. Categorical variables were summarized using frequencies and percentages.

Analysis of covariance (ANCOVA) and linear regression models were utilized to statistically compare the slope of the linear relationship between peak postoperative CKMB and TnT for the patient cohort. The ANCOVA models were created to compare slopes by pre-defined variables including (1) age, (2) sex, (3) race, (4) current smoking status (5) hypertension, (6) dyslipidemia, (7) ejection fraction (EF), (8) diabetes, (9) renal dysfunction (GFR < 60), (10) recent MI, preoperative use of (11) angiotensin-converting-enzyme (ACE) inhibitors, (12) beta-blockers, and (13) anticoagulants. Operative variables (1) cross clamp time (< or > 70 min), (2) CPB time (< or > 100 min), and (3) whether patient received a transfusion of intra-operative blood products were also included. In these models, a lower slope implies less change in CKMB relative to the change in TnT.

Statistical significance is indicated by $p < 0.05$.

CHAPTER 3

Results

Pre-Operative Factors

The slope of the relationship was significantly lower in males, diabetics, patients with dyslipidemia, patients with hypertension, and patients with normal renal function. lower EF (Figures 2, 4, 5, 8, 9). The t-statistic when comparing CKMB to TnT based on sex was -7.72 ($p < 0.001$) with males having less of a change in CKMB relative to a change in TnT (Table 7). In the patient cohort differentiated by the presence of diabetes, the t-statistic was -6.09 ($p < 0.001$) with diabetics having a blunted rise in CKMB when compared to the rise of TnT (Table 9). The t-statistic value was -3.80 ($p < 0.001$) between patients with dyslipidemia and patients without dyslipidemia, and the value was -2.14 ($p = 0.033$) between patients with hypertension and patients without hypertension (Tables 10, 13). Patients who had normal renal function (GFR > 60) had less of a change in the rise of CKMB relative to that of TnT when compared to patients with abnormal renal function (GFR < 60). In this cohort, the t-statistic was -6.42 ($p < 0.001$) (Table 14). However, the slope was significantly greater in patients with higher EF, current smokers, and patients with a recent MI (Figures 7, 6, 10). For cohorts based on EF, current smoking status, and recent MI, the t-statistic values were 15.62 ($p < 0.001$), 3.20 ($p = 0.001$), and 2.61 ($p = 0.009$) with patients with higher EFs, have been smoking currently, and have had a recent MI experiencing a greater change in CKMB relative to that of TnT (Tables 12, 11, 15). In terms of race, the slope of white patients is significantly different from that of African Americans ($p < 0.001$), Hispanic patients ($p < 0.001$), and patients of any other race ($p = 0.036$) (Table 8). There was no statistically significant difference

between values of CKMB and TnT when differentiating patients based on age with a t-statistic of 1.11 ($p = 0.268$) (Table 6).

Pre-Operative Medications

The slope of the relationship was significantly lower in patients receiving beta-blockers, signifying a blunted effect on the change of CKMB relative to that of TnT, when comparing to patients not receiving beta-blockers preoperatively (Figure 13). The slope was significantly greater in patients receiving ACE inhibitors in comparison to patients not receiving ACE inhibitors (Figure 11). There was no significant difference between CKMB and TnT levels when comparing patients who receive anticoagulants or not (Figure 12). The t-statistic values when comparing the rise in CKMB to the increase in TnT were -4.14 ($p < 0.001$), 15.90 ($p < 0.001$), and 1.52 ($p = 0.128$) based on preoperative use of beta-blockers, ACE inhibitors, and anticoagulants, respectively (Tables 18, 16, 17). Of note, these medications are very commonly given to patients with ischemic heart disease.

Intra-Operative Factors

The slope was significantly greater in patients with longer cross clamp times compared to patients with shorter cross clamp times with a t-statistic of 13.77 ($p < 0.001$) (Figure 15, Table 20). Similarly, patients with longer CPB times experienced a greater change in CKMB relative to that of TnT versus patients with shorter CPB times (Figure 14). The t-statistic in the cohort differentiated by CPB time was 12.20 ($p < 0.001$) (Table 19). The relationship in peak postoperative levels of CKMB and TnT was not

significantly altered by intra-operative blood transfusion (t-statistic -1.91, p = 0.057) (Figure 16, Table 21).

Overall, a high number of variables were found to be associated with a significant difference in the relationship between the two biomarkers following CABG.

CHAPTER 4

Conclusions and Recommendations

Myocardial infarction is a recognized complication of coronary bypass surgery. The "Universal Definition" of myocardial infarction categorizes myocardial infarction related to coronary artery bypass grafting as a "type 5“, and a URL (upper range limit of normal) value for troponin and serum CKMB are often determined for an individual lab and population. The definition of perioperative MI following on-pump CABG is 10 times the 99th percentile of that range during the first 72 hours after CABG. This enzyme level reflects significant myocardial cell damage, but the number is not reliable if the patient had an MI in evolution before the operation. New Q waves or new LBBB on ECG, or evidence on imaging of myocardial loss or wall motion defect are supportive of the enzyme elevation criterion [8].

Both CKMB and Troponin have been advocated as markers to detect perioperative myocardial infarction, and some feel they are interchangeable. Our data in this study suggest that this concept should be viewed with caution, as patients with certain preoperative conditions and intra-operative characteristics show significant differences in the behavior of these biomarkers after CABG. While some differences might have a predictable biologic mechanism (for example, renal clearance of the two biomarkers may differ in patients with renal dysfunction), the reason behind these variations is not known in most instances.

It is interesting to note the amount of factors that have been found to have a statistically significant difference in the relationship of CKMB and TnT levels. This suggests that there are numerous components to a patient’s medical profile that alter the

change seen in these two well-established cardiac biomarkers. This may affect the ability of the physician to diagnose an adverse outcome such as a myocardial infarction.

Also of note, patients who sustained in-hospital postoperative adverse events did not have a different relationship between peak biomarker levels compared to those experiencing no adverse outcomes. This is perhaps consistent with prior studies that have observed that even long–term outcomes (LV ejection fraction 6 months after CABG) were similar between patients who had early significant enzyme elevation and those who did not.

Based on the universal enzyme definition, the fraction of patients from our patient population who would be deemed to have sustained a perioperative MI by CKMB criteria was 9%. By the same definition, the fraction of patients who would have sustained a perioperative MI by TnT criteria was >90%. Not surprisingly, this has prompted some authors to revise the troponin-based definition in patients undergoing cardiac surgery [9]. When enzyme levels were compared between patients who developed new Q waves or new LBBB with those who did not, the differences were not striking. This may mean that elevated cardiac biomarkers after CABG reflect perioperative injury that may be reversible and not necessarily associated with MI.

The relationship between CKMB and TnT following CABG appears to be influenced by patient and operative characteristics. These data do not assess which enzyme more accurately reflects myocardial injury, but do suggest conclusions about myocardial damage may be affected by the biomarker selected in the presence of certain variables. Further study to assess the association between these biomarkers and patient outcomes is warranted. Additionally, other criteria such as angiographically documented

new graft or native coronary artery occlusion or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality can be analyzed with peak level of CKMB and TnT.

LIST OF TABLES

Table 1: Demographics

Variable	n (%)	Median (IQR)
Age		60 (54-67)
Sex; female	210 (24)	
Race		
White, non-Hispanic	370 (42)	
Black, non-Hispanic	154 (18)	
Hispanic	271 (31)	
Other	82 (9)	

Table 2: Comorbidities

Variable	n (%)	Median (IQR)
CVD	144 (16)	
Diabetes	522 (59)	
Dyslipidemia	804 (91)	
Current smoker	350 (40)	
Ejection fraction		52 (40-61)
Heart failure	348 (40)	
Hypertension	802 (91)	
Liver disease	77 (9)	
PAD	118 (13)	
Pre-op creatinine		1.0 (0.8-1.3)
Pre-op renal dysfunction (GFR < 60)	407 (46)	
Pre-op EKG; new waves	55 (7)	
Recent MI (within 21 days)	284 (33)	

Table 3: Medications

Table 3: Medications

Variable	n (%)	Median (IQR)
ACE inhibitors	408 (47)	
Anticoagulants	268 (30)	
Aspirin	794 (90)	
Beta blockers	742 (88)	

Table 4: Operative Characteristics

Table 4: Operative characteristics

Variable	n (%)	Median (IQR)
Emergent/urgent status	269 (30)	
Cardiopulmonary bypass time (min)		115 (91-146)
Cross clamp time (min)		74 (59-96)
Intra-operative transfusion	555 (63)	

Table 5: Post-operative Outcomes

Table 5: Post-operative outcomes

Variable	n (%)	Median (IQR)
Peak CKMB		23.3 (16.2-38.2)
Peak troponin T		0.7 (0.4-1.3)
In-hospital post-op event	544 (61)	
Post-op EKG; new waves	34 (4)	

Table 6: Effect of Age on the Association of CKMB and Troponin T
Assessment of whether the relationship between the enzymes changes with relation to age. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 6 indicate that age does not significantly alter the relationship ($p = 0.268$).

Table 6: Effect of age on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	9.01	2.67	3.37	0.001
Age	0.01	0.14	0.09	0.928
Age | TnT	0.05	0.04	1.11	0.268

Table 7: Effect of Sex on the Association of CKMB and Troponin T
Assessment of how sex affects the relationship between the enzymes. CKMB is the outcome variable for the model, and the three predictors include main effects for sex and Troponin T as well as an interaction effect between sex and troponin. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 7 indicate that sex does significantly alter the relationship ($p < 0.001$).

Table 7: Effect of sex on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	20.77	1.26	16.46	< 0.001
Sex	9.66	3.42	2.82	0.005
Sex | TnT	-10.70	1.39	-7.72	< 0.001

Table 8: Effect of Race on the Association of CKMB and Troponin T
Assessment of how race affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 8 indicate that race does significantly alter the relationship ($p < 0.001$). Specifically, we find that the slope for white patients is significantly different from that of black patients ($p < 0.001$), Hispanic patients ($p < 0.001$), and patients of any other race ($p = 0.036$).

Table 8: Effect of race on the association of CKMB and Troponin T

Variable	F-statistic	p
TnT	544.64	< 0.001
Race	0.15	0.932
Race | TnT	35.30	< 0.001

Table 9: Effect of Diabetes on the Association of CKMB and Troponin T
Assessment of how diabetes affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 9 indicate that diabetes does significantly alter the relationship ($p < 0.001$).

Table 9: Effect of diabetes on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	15.24	0.76	19.94	< 0.001
Diabetes	1.22	2.83	0.43	0.665
Diabetes | TnT	-6.41	1.05	-6.09	< 0.001

Table 10: Effect of Dyslipidemia on the Association of CKMB and Troponin T
Assessment of how dyslipidemia affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 10 indicate that dyslipidemia does significantly alter the relationship ($p < 0.001$).

Table 10: Effect of dyslipidemia on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	18.87	1.90	9.90	< 0.001
Dyslipidemia	9.36	5.37	1.74	0.082
Dyslipidemia | TnT	-7.55	1.98	-3.80	< 0.001

Table 11: Effect of Smoking on the Association of CKMB and Troponin T
Assessment of how smoking affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 11 indicate that smoking does significantly alter the relationship ($p = 0.001$).

Table 11: Effect of smoking on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	15.80	0.66	23.93	< 0.001
Current smoker	-3.86	2.61	-1.48	0.139
Current smoker | TnT	3.82	1.19	3.20	0.001

Table 12: Effect of Ejection Fraction on the Association of CKMB and Troponin T
Assessment of how ejection fraction affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 12 indicate that ejection fraction does significantly alter the relationship ($p < 0.001$).

Table 12: Effect of ejection fraction on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	-7.74	1.35	-5.75	< 0.001
EF	-0.35	0.09	-4.14	< 0.001
EF | TnT	0.48	0.03	15.62	< 0.001

Table 13: Effect of Hypertension on the Association of CKMB and Troponin T
Assessment of how hypertension affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 13 indicate that hypertension does significantly alter the relationship ($p = 0.03$

Table 13: Effect of hypertension on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	16.01	1.98	8.10	< 0.001
Hypertension	9.26	5.18	1.79	0.074
Hypertension | TnT	-4.40	2.05	-2.14	0.033

Table 14: Effect of Renal Function on the Association of CKMB and Troponin T
Assessment of how renal function (based on the GFR) affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 14 indicate that renal function does significantly alter the relationship ($p < 0.001$).

Table 14: Effect of renal function on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	15.32	0.75	20.37	< 0.001
Renal function	5.63	2.81	2.01	0.045
Renal function | TnT	-6.77	1.05	-6.42	< 0.001

Table 15: Effect of a Recent MI on the Association of CKMB and Troponin T
Assessment of how a recent MI (within the previous 21 days) affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 15 indicate that hypertension does significantly alter the relationship ($p = 0.009$).

Table 15: Effect of a recent MI on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	10.77	0.69	15.67	< 0.001
Recent MI	-5.92	3.09	-1.91	0.056
Recent MI | TnT	2.90	1.11	2.61	0.009

Table 16: Effect of ACE Inhibitors on the Association of CKMB and Troponin T
Assessment of how ACE inhibitors affect the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 16 indicate that ACE inhibitors do significantly alter the relationship ($p < 0.001$).

Table 16: Effect of ACE inhibitors on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	7.99	0.54	14.89	< 0.001
ACE inhibitors	-17.17	2.60	-6.61	< 0.001
ACE inhibitors | TnT	18.28	1.15	15.90	< 0.001

Table 17: Effect of Anticoagulants on the Association of CKMB and Troponin T
Assessment of how anticoagulants affect the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 17 indicate that anticoagulants do not significantly alter the relationship ($p = 0.128$).

Table 17: Effect of anticoagulants on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	11.31	0.68	16.53	< 0.001
Anticoagulants	-4.25	3.13	-1.36	0.175
Anticoagulants | TnT	1.69	1.11	1.52	0.128

Table 18: Effect of Beta-blockers on the Association of CKMB and Troponin T
Assessment of how beta-blockers affect the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 18 indicate that beta-blockers do significantly alter the relationship ($p < 0.001$).

Table 18: Effect of beta blockers on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	17.78	1.63	10.93	< 0.001
Beta blockers	12.28	4.65	2.64	0.008
Beta blockers | TnT	-7.14	1.73	-4.14	< 0.001

Table 19: Effect of Bypass Time on the Association of CKMB and Troponin T
Assessment of how cardiopulmonary bypass time affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 19 indicate that bypass time does significantly alter the relationship ($p < 0.001$).

Table 19: Effect of bypass time on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	-1.52	1.13	-1.35	0.176
Bypass time	0.04	0.03	1.41	0.159
Bypass time | TnT	0.09	0.01	12.20	< 0.001

Table 20: Effect of Cross Clamp Time on the Association of CKMB and Troponin T
Assessment of how cross clamp time affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 20 indicate that cross clamp time does significantly alter the relationship ($p < 0.001$).

Table 20: Effect of cross clamp time on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	-2.79	1.11	-2.51	0.012
Cross clamp time	-0.14	0.04	-3.19	0.001
Cross clamp time | TnT	0.20	0.01	13.77	< 0.001

Table 21: Effect of an Intra-operative Blood Transfusion on the Association of CKMB and Troponin T
Assessment of how an intra-operative blood transfusion affects the relationship between the enzymes. The overall model is found to be statistically significant ($p < 0.001$), and the results in Table 21 indicate that an intra-operative blood transfusion does not significantly alter the relationship ($p = 0.057$).

Table 21: Effect of an intra-operative blood transfusion on the association of CKMB and Troponin T

Variable	Estimate	StErr	t-statistic	p
TnT	17.25	2.98	5.79	< 0.001
Blood transfusion	11.34	3.46	3.28	0.001
Blood transfusion | TnT	-5.77	3.03	-1.91	0.057

LIST OF FIGURES

Figures 1: Marginal Effect Plot demonstrating the Effect of Age on the Association of TnT and CKMB

This plot visualizes the fitted model for a set of fixed ages, which were selected based on the 25th, 50th, and 75th percentiles. Figure 1 demonstrates that the slopes are similar (as the interaction analysis indicates), and we can conclude that the association between CKMB and troponin is not altered by age.

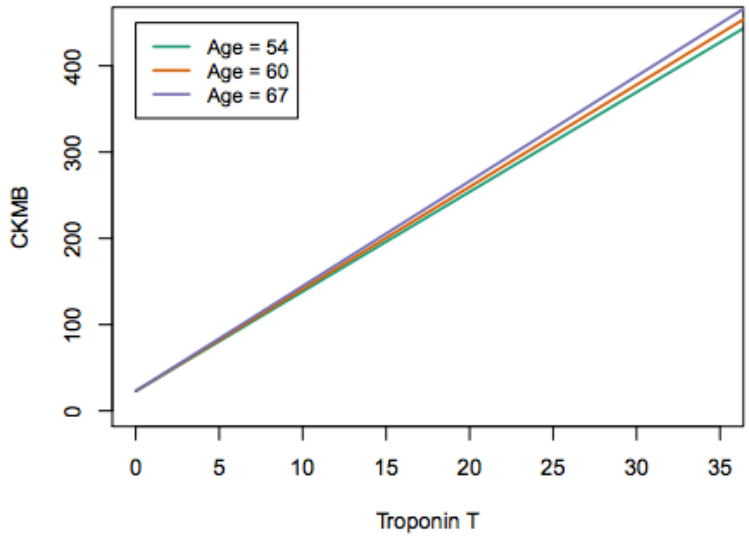

Figure 1: Marginal effect plot demonstrating the effect of age on the association of TnT and CKMB

Figure 2: Marginal Effect Plot demonstrating the Effect of Sex on the Association of TnT and CKMB

This plot visualizes the association between the enzymes for both sexes. Figure 2 demonstrates that the slope of the enzyme relationship differs by sex, and thus, we can conclude that the association between CKMB and troponin is significantly altered by the sex of the patient.

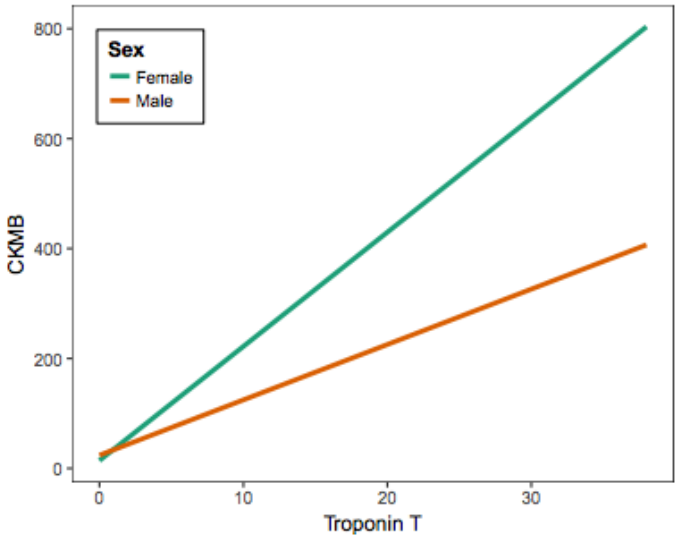

Figure 2: Marginal effect plot demonstrating the effect of sex on the association of TnT and CKMB

Figure 3: Marginal Effect Plot demonstrating the Effect of Race on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by race, and thus, we can conclude that the association between CKMB and troponin is significantly altered by the race of the patient.

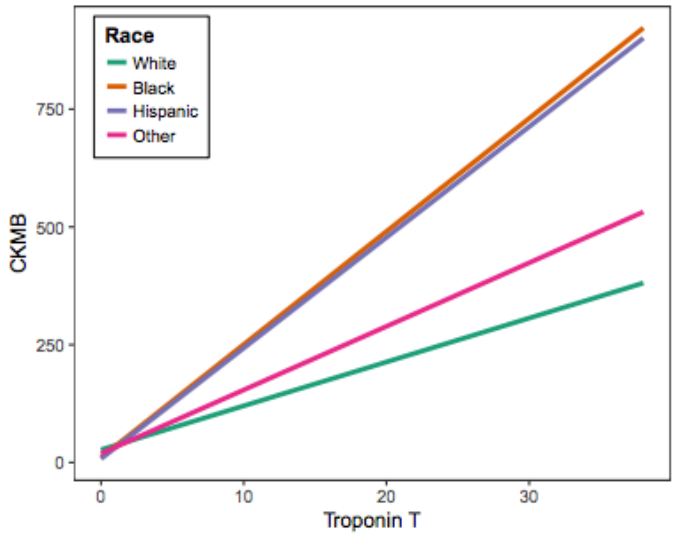

Figure 3: Marginal effect plot demonstrating the effect of race on the association of TnT and CKMB

Figure 4: Marginal Effect Plot demonstrating the Effect of Diabetes on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient is diabetic, and thus, we can conclude that the association between CKMB and troponin is significantly altered by the presence of diabetes.

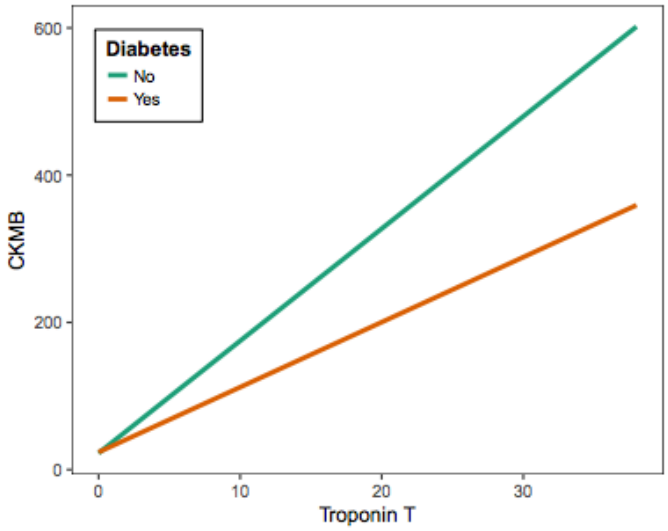

Figure 4: Marginal effect plot demonstrating the effect of diabetes on the association of TnT and CKMB

Figure 5: Marginal Effect Plot demonstrating the Effect of Dyslipidemia on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient has dyslipidemia, and thus, we can conclude that the association between CKMB and troponin is significantly altered by the presence of dyslipidemia.

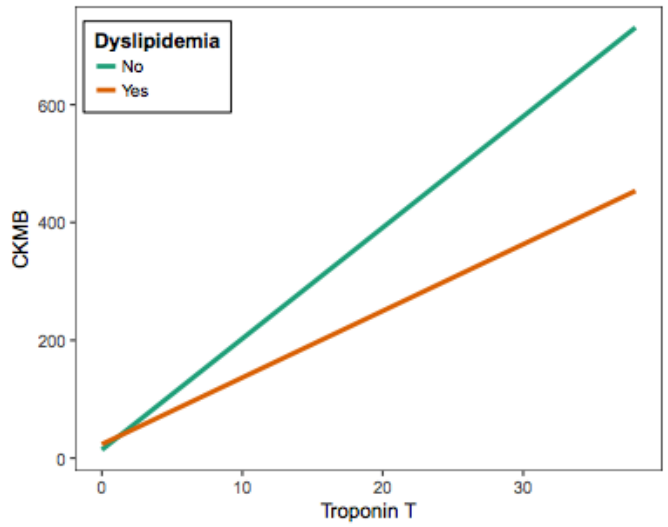

Figure 5: Marginal effect plot demonstrating the effect of dyslipidemia on the association of TnT and CKMB

Figure 6: Marginal Effect Plot demonstrating the Effect of Smoking on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient currently smokes, and thus, we can conclude that the association between CKMB and troponin is significantly altered by this variable.

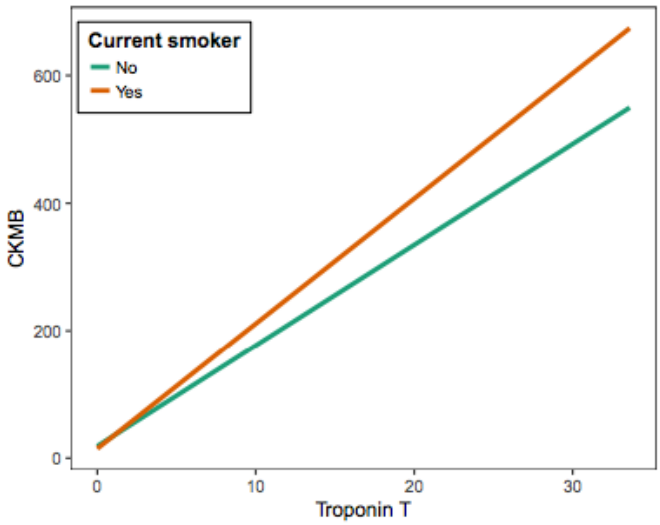

Figure 6: Marginal effect plot demonstrating the effect of smoking on the association of TnT and CKMB

Figure 7: Marginal Effect Plot demonstrating the Effect of EF on the Association of TnT and CKMB

This plot visualizes the fitted model for a set of fixed ejection fractions, which were selected based on the 25th, 50th, and 75th percentile. It demonstrates that the slopes differ (as the interaction analysis indicates), so we can conclude that the association between CKMB and troponin is altered by the ejection fraction.

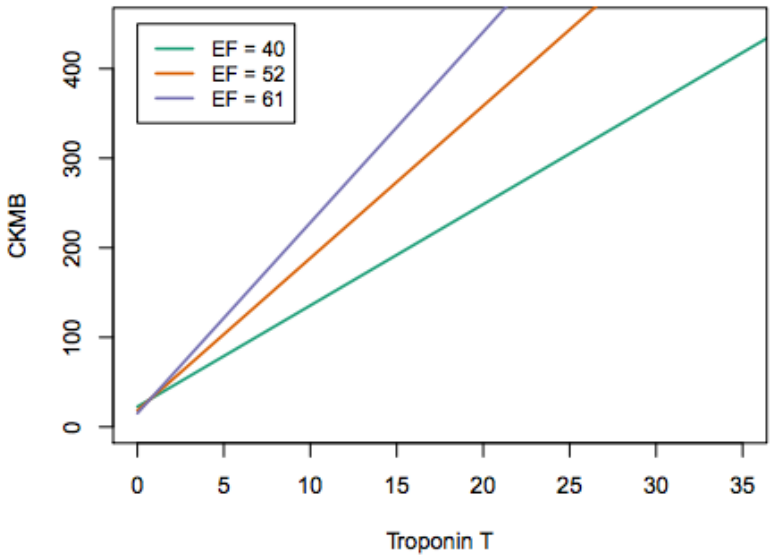

Figure 7: Marginal effect plot demonstrating the effect of EF on the association of TnT and CKMB

Figure 8: Marginal Effect Plot demonstrating the Effect of Hypertension on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient is hypertensive, and thus, we can conclude that the association between CKMB and troponin is significantly altered by hypertension

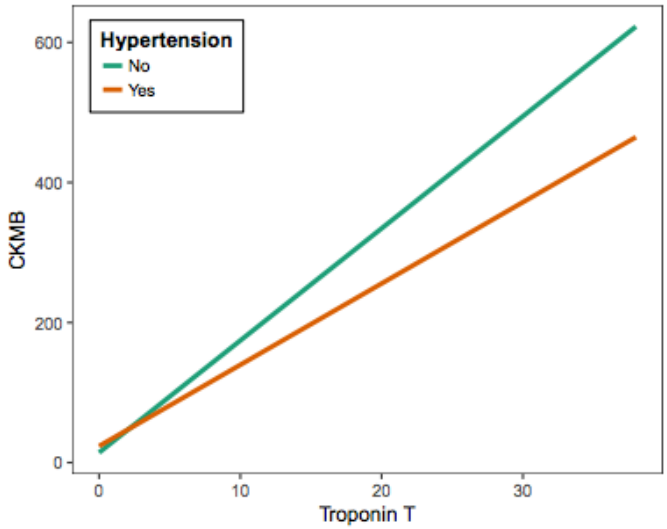

Figure 8: Marginal effect plot demonstrating the effect of hypertension on the association of TnT and CKMB

Figure 9: Marginal Effect Plot demonstrating the Effect of Renal Function on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient has normal renal function, and thus, we can conclude that the association between CKMB and troponin is significantly altered by renal function.

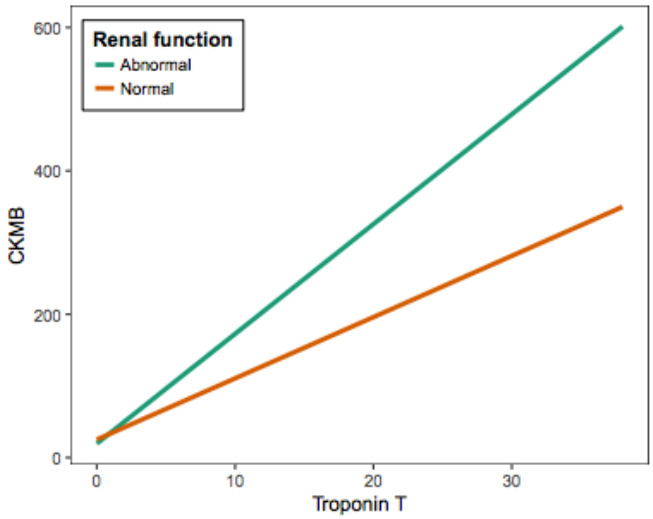

Figure 9: Marginal effect plot demonstrating the effect of renal function on the association of TnT and CKMB

Figure 10: Marginal Effect Plot demonstrating the Effect of a Recent MI on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient has experienced a recent MI, and thus, we can conclude that the association between CKMB and troponin is significantly altered by that condition.

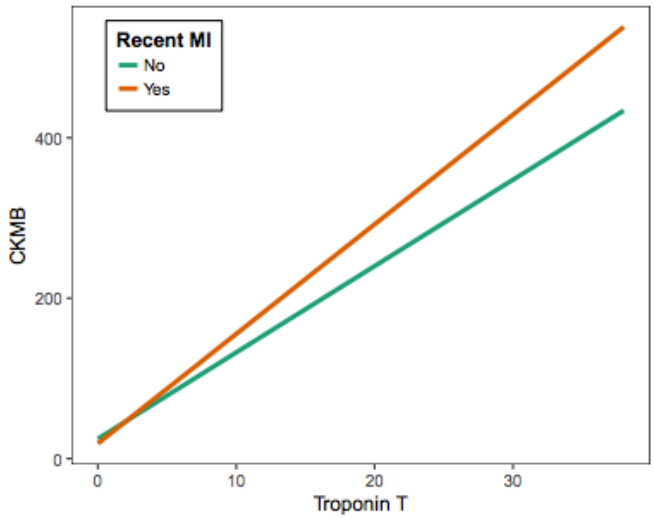

Figure 10: Marginal effect plot demonstrating the effect of a recent MI on the association of TnT and CKMB

Figure 11: Marginal Effect Plot demonstrating the Effect of ACE Inhibitors on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient uses ACE inhibitors, and thus, we can conclude that the association between CKMB and troponin is significantly altered by that medication.

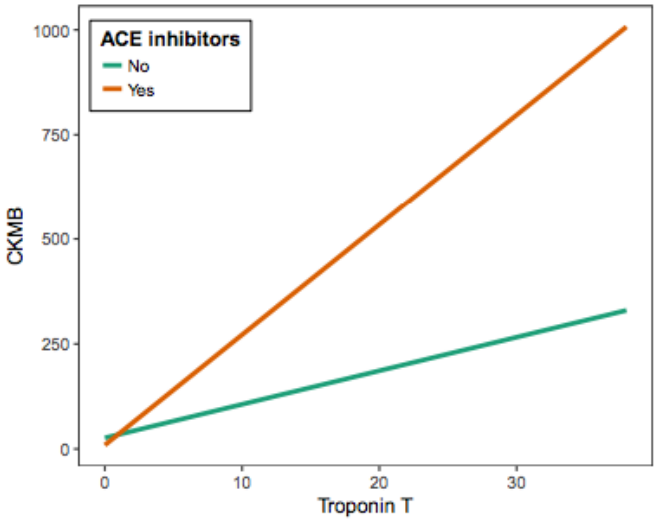

Figure 11: Marginal effect plot demonstrating the effect of ACE inhibitors on the association of TnT and CKMB

Figure 12: Marginal Effect Plot demonstrating the Effect of Anticoagulants on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship does not differ by whether a patient uses anticoagulants, and thus, we can conclude that the association between CKMB and troponin is not significantly altered by that medication.

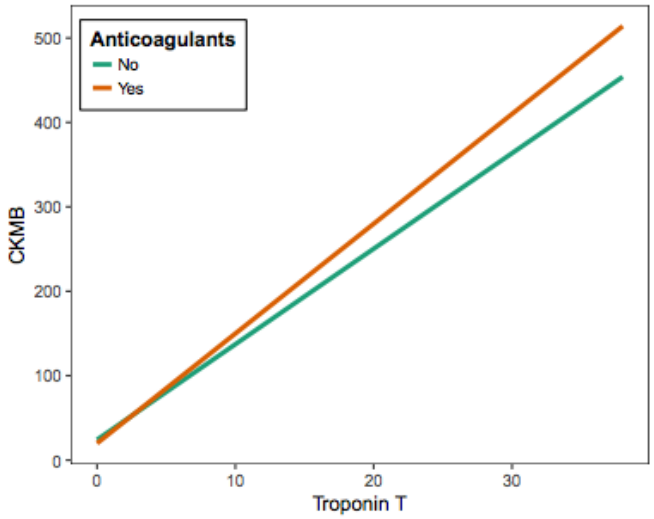

Figure 12: Marginal effect plot demonstrating the effect of anticoagulants on the association of TnT and CKMB

Figure 13: Marginal Effect Plot demonstrating the Effect of Beta-Blockers on the Association of TnT and CKMB

This plot demonstrates that the slope of the enzyme relationship differs by whether a patient uses beta-blockers, and thus, we can conclude that the association between CKMB and troponin is significantly altered by that medication.

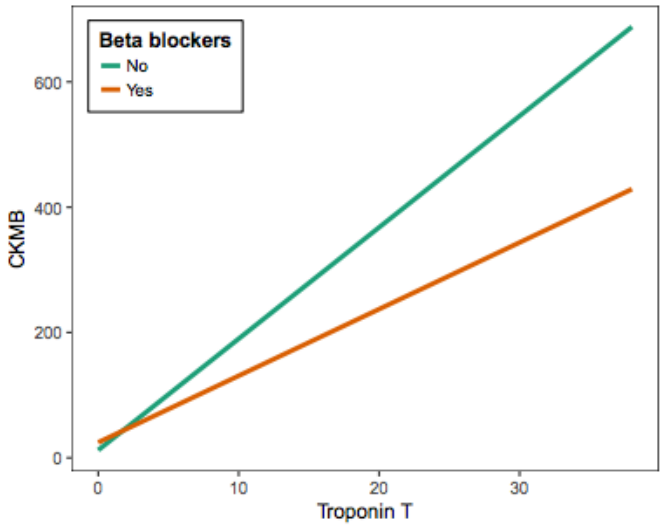

Figure 13: Marginal effect plot demonstrating the effect of beta blockers on the association of TnT and CKMB

Figure 14: Marginal Effect Plot demonstrating the Effect of Cardiopulmonary Bypass Time on the Association of TnT and CKMB

This plot visualizes the fitted model for a set of fixed times, which were selected based on the 25th, 50th, and 75th percentiles. It demonstrates that the slopes differ (as the interaction analysis indicates), and thus, we can conclude that the association between CKMB and troponin is altered by the time spent on bypass.

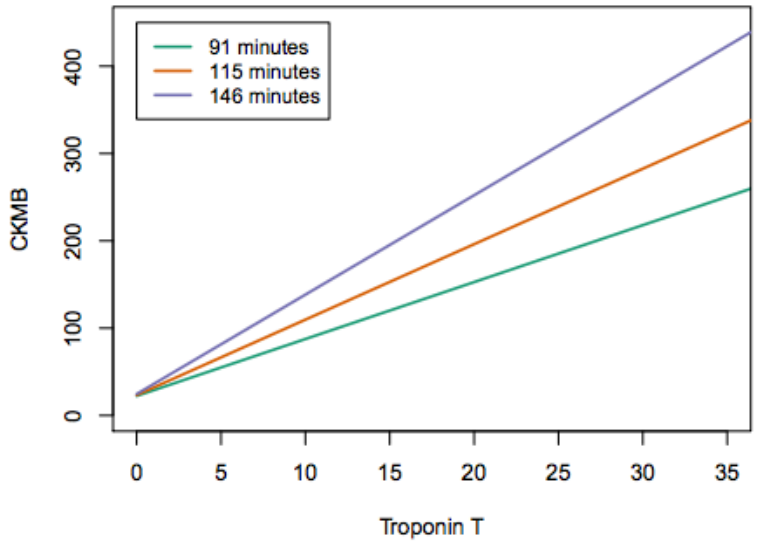

Figure 14: Marginal effect plot demonstrating the effect of cardiopulmonary bypass time on the association of TnT and CKMB

Figure 15: Marginal Effect Plot demonstrating the Effect of Cross Clamp Time on the Association of TnT and CKMB

This plot visualizes the fitted model for a set of fixed times, which were selected based on the 25th, 50th, and 75th percentiles. It demonstrates that the slopes differ (as the interaction analysis indicates), and thus, we can conclude that the association between CKMB and troponin is altered by cross clamp time.

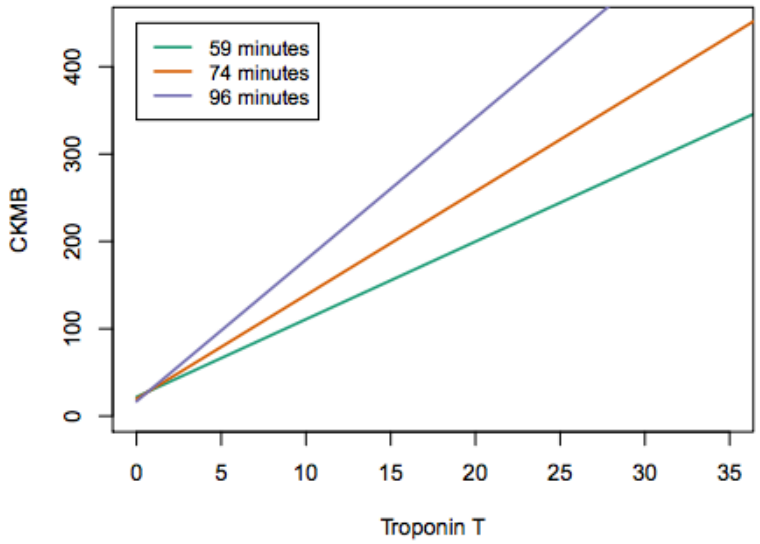

Figure 15: Marginal effect plot demonstrating the effect of cross clamp time on the association of TnT and CKMB

Figure 16: Marginal Effect Plot demonstrating the Effect of Intra-operative Blood Transfusions on the Association of TnT and CKMB
This plot demonstrates that the slope of the enzyme relationship does not differ by whether a patient received a transfusion, and thus, we can conclude that the association between CKMB and troponin is not significantly altered by that factor.

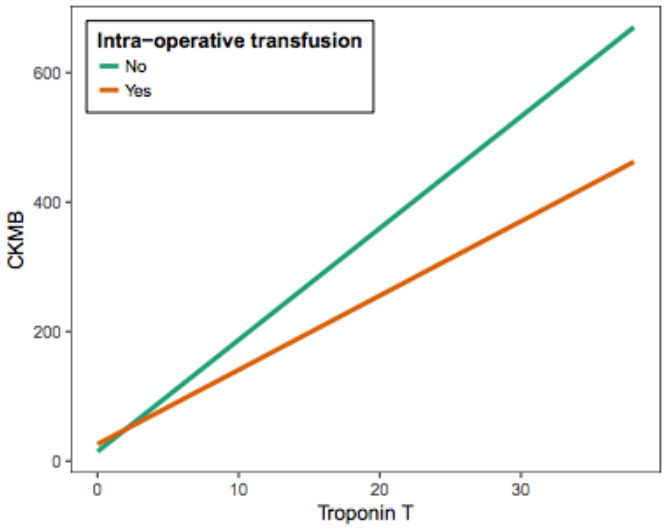

Figure 16: Marginal effect plot demonstrating the effect of intra-operative blood transfusions on the association of TnT and CKMB

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VITAE

Kinjal Mukesh Mehta (August 27th, 1993 - present) was born in Dallas, Texas. She completed her undergraduate education in Biology and Spanish at Texas A&M University. She is about to graduate from medical school at UT Southwestern Medical Center in Dallas, Texas. Throughout her medical school education, she has been actively involved in research. She started this particular research project approximately 3 years ago with the Department of Cardiovascular and Thoracic Surgery and has continued to work on this research. She has been inducted into the Gold Humanism Honor Society and is a part of many organizations. She is now working to finish her Distinction in Research. Following her passion in Obstetrics & Gynecology, she will start her residency training here at UT Southwestern.

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