

## **Comparison of prognostic ability of perioperative myocardial biomarkers in acute type A aortic dissection**

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## Abstract

Stanford type A aortic dissection (AD) is a lethal disease requiring surgery. Evidence regarding the prognostic ability of perioperative myocardiac markers on long-term outcome is limited.

In this cohort study, we measured perioperative myocardiac markers level in 583 surgical patients with type A AD in our hospital between 2015 and 2017. All patients were followed up after surgery for a median period of 864 days to determine short- and long-term mortality.

About one-fifth of patients has a positive preoperative myocardial markers, which was increased significantly after operation. Increase  $\log_{10}$  post-creatine kinase MB isoenzyme (CK-MB) (hazard ratio [HR], 4.64; 95% confidence interval [CI] 1.89–11.43; P=.0008),  $\log_{10}$  post-Tnl (HR, 3.11; 95% CI 1.56–6.21; P=.0013),  $\log_{10}$  post-Mb (HR, 3.00; 95% CI 1.40–6.43; P=.0048),  $\log_{10}$  pre-CK-MB (HR,1.82; 95% CI 1.03–3.21; P=.0377), and upper tertile of post-CK-MB (HR,1.52; 95% CI 1.05–2.20; P=.0261) were the independent risk factor for 30 days mortality adjusted for potential confounders. None of cardiac markers was significantly associated with long-term outcome independent of other factors.

Perioperative myocardiac predicts early outcome in type A AD patients undergoing surgery. Increasing perioperative myocardial markers do not appear to be a predictor for long-term all-cause mortality.

**Abbreviations:** AD = aortic dissection, CI = confidence interval, CK-MB = creatine kinase MB isoenzyme, CPB = cardiopulmonary bypass, HR = hazard ratio, hs-TnI = high sensitivity troponin I, LVEDD = left ventricular end diastolic diameter, Mb = myoglobin, ROC = receiver operating characteristic, UCG = ultrasound cardiogram, URL = upper reference limit.

Keywords: acute type A aortic dissection, perioperative myocardial biomarkers, prognostic ability

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MG and ZW contributed equally to this work.

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## 1. Introduction

Acute aortic dissection (AD) is a rare and lethal cardiovascular disease that has an annual incidence of 3 to 4 per hundred thousand.<sup>[1]</sup> For Stanford A AD, which accounts for two-thirds of AD, emergency surgery is recognized as an effective treatment. Without surgical treatment, the natural death rate of the disease can reach 90% within a month of onset, while for surgical treatment patients the hospital death rate is between 10% and 20%.<sup>[2]</sup> Myocardial markers, including troponin, creatine kinase, and myoglobin (Mb), have been widely confirmed to increase in acute coronary syndrome patients and reflect the severity of myocardial injury.<sup>[3,4]</sup> Recently, many studies have evaluated the prognostic value of perioperative myocardial markers in various cardiac surgery such as valvular surgery, coronary artery bypass grafting (CABG), and congenital heart disease.<sup>[5-7]</sup> However, few patients of thoracic aortic surgery were included in previous studies. Especially for patients with Stanford A AD, small sample evidence is difficult to draw a definitive conclusion. Pattern in perioperative myocardial enzymes changing and determinants of it have been shown to vary from different cardiac surgery.<sup>[8]</sup> Compared with other cardiac surgeries, type A AD surgery has a less frequent direct myocardial incision and coronary artery treatment, but the cardiopulmonary bypass (CPB) duration and aortic clamp time is much longer. Therefore, the changes of perioperative myocardial enzymes of AD and their prognostic effects are worth studying. To address this knowledge gap, we conducted this retrospective cohort study to determine the levels of a series of myocardial

enzymes, including high sensitivity troponin I (hs-TnI), myoglobin (Mb), and creatine kinase isoenzyme-MB (CK-MB), before and after the surgery of acute type A AD, and their prognostic value on short- and long-term all-cause mortality.

## 2. Method

## 2.1. Study design

This study was designed as a retrospective cohort study that continuously collected data on Stanford type A AD patients who underwent surgery in Anzhen Hospital from January 2015 to May 2017. All patients were diagnosed by computed tomography angiography or ultrasound cardiogram (UCG). The exclusion criteria were as follows: patients did not undergo surgery, surgery was performed after 7 days since onset, previous surgical procedures for AD. Demographic data, operation related factors, and UCG funding were obtained as surrogate information of adverse outcomes according to previous studies about surgical risk prognosis in AD.<sup>[9,10]</sup> Patient source provinces and surgeon information were collected as adjustment variables for regression analysis. All participants were prospectively followed up using telephone or text message for a median period of 864 days. All-cause mortality at 30 days and at the end of follow-up was defined as the end point. All data related to the study were obtained after approved by the ethics committee of Anzhen Hospital. The informed consent of this study was obtained through patients or family members at follow-up.

## 2.2. Blood sample test

Preoperative myocardial biomarkers levels were measured within 24 hours before surgery. Postoperative myocardial markers were measured within 72 hours after operation. Data outside this time frame was excluded.

Serum myocardial biomarkers were measured using a chemiluminescence assay (Beckman DX1800 automatic chemical analyzer and AU5400 automatic biochemical analyzer, Coulter, California). The upper reference limit (URL) for the hs-TnI, CK-MB, and Mb were 0.04 ng/mL, 174 U/L, and 6.3 ng/mL, respectively.

### 2.3. Surgical method

As previous reported, we classified type A AD patients into 6 subtypes based on the pathological change of the aortic root and arch.<sup>[11]</sup> Appropriate surgical methods were selected according to different subtypes. In summary, ascending aortic replacement was performed for aortic valve mild involved patients and ascending aortic replacement with concomitant aortic valve/ valsalva sinus plasty or Bentall procedure was performed for moderate to severe aortic valve involved patients. Total aortic arch replacement combined stented elephant trunk implant procedure with the use of deep hypothermia circulatory arrest was performed in patients with severe aortic arch involvement. Patients with mild or nonaortic arch involvement underwent partial aortic arch replacement. Other surgical procedures, such as David or Wheat procedure, were also used when the indications were met, but they are rarely performed in our center. Detailed descriptions of surgical procedures are reported in previous articles.<sup>[12]</sup>

#### 2.4. Statistical analysis

All analyses were performed using statistical packages R (The R Foundation; http://www.Rproject.org version 3.5.2). Continuous variables were expressed as mean±standard deviation or median (quartile range) and classified variables are expressed as frequencies. One-way ANOVA test, Kruskal-Wallis were used to test for significant differences between groups of continuous variables. Blood test results were transferred to log<sub>10</sub> formation before included into regression analyses since they were all nonnormal distributed. Univariate Cox regression analyses were conducted to determine the variables independently associated with outcome. Myocardial biomarkers were stratified into 3 tertiles and variables with P < .1 in univariate analysis were included in multivariate Cox regression analysis. The receiver operating characteristic curves of mortality were plotted to detect the predictive accuracy of myocardial biomarkers. Event analyses were performed using time-to-event data. Data from the last time point of follow-up were used for patients lost in follow-up. The survival curve was plotted with Kaplan-Meier method and log rank analyses were performed. Results of regressions are presented as the hazard ratio (HR) and the 95% confidence interval (CI). Statistical significance was defined as P < .05.

## 3. Results

#### 3.1. Baseline clinical characteristics of participant

A total of 583 people were recruited into the study consist 158 women and 425 men, aged  $48.60 \pm 11.63$  years old. The patient's baseline characteristics are shown in Table 1. The median follow-up period was 864 days (interquartile range 615-1155 days). Sixteen patients lost at 30 days after surgery and 132 patients lost at the end of follow-up. Seventy (12%) patients did not survived 30 days after the operation and 106 (30.7%) patients was confirmed death at the end of follow-up. In hospital complications in the deaths include multiple organ dysfunction syndrome (n=11), respiratory failure (n=15), sepsis (n=8), cerebral infarction or hemorrhage (n=28), cardiovascular adverse events (n=29), and acute renal failure (n=22). Pre- and postoperative myocardial markers were actually measured at average of 13.4 hours before and 6.24 hours after surgery, respectively.

Patients who did not survive 30 days after surgery were older, had higher admission systolic blood pressure, shorter onset time, and had longer operative and CPB time. In terms of perioperative blood tests, patients had lower preoperative hemoglobin, platelet, higher preoperative D-dimer, poorer renal function, and higher postoperative myocardial marker levels were more likely cannot survive 30 days after surgery. There were no significant differences in levels of preoperative myocardial markers, body mass index, UCG parameters, AD subtype, coronary artery disease, and other medical history between 30 days death or not.

#### 3.2. Changes in perioperative myocardial markers

Comparison of preoperative and postoperative myocardial markers revealed a significant increase in myocardial markers after operation. With URL as the critical point, the positive rates of preoperative hs-TnI, CK-MB, and Mb were 22.8%, 32.6%, and 33.1%, respectively. The positive rates of postoperative hs-TnI, CK-MB, and Mb were 99.4%, 97.7%, and 97.2%, respectively (Table 2).

## Table 1

## Baseline patient characteristics stratified by survived in 30 d or not.

	Survived	Not survived	
Variables, n, %	n=497	n=70	P-value
Age, v	$48.05 \pm 11.29$	$51.39 \pm 12.69$	.016
BMI, ka/m <sup>2</sup>	25.61 + 3.82	25.81 + 4.32	.741
Systolic pressure, mmHq	$125.60 \pm 17.72$	$129.76 \pm 18.50$	.016
Heart rate, bom	82.38 + 13.87	84.73 + 12.97	.129
Hemoglobin, a/L	115.51 + 24.13	$104.40 \pm 26.16$	.002
Creatinine, mmol/L	90.40 (69.90-119.40)	116.30 (88.75–182.20)	<.001
Platelet. $\times 10^9$ /LAAA	112.00 (70.00-185.00)	56.50 (37.70-106.25)	<.001
D-dimer.	1654.00 (830.00-2663.00)	2299.00 (1234.50-3650.00)	.001
Cardiopulmonary bypass time, min	195.00 (162.50-230.00)	213.50 (198.00–256.75)	<.001
Aorta clamp time, min	109.00 (86.00-133.00)	118.00 (101.00-148.25)	.002
Operation time, min	$7.50 \pm 1.68$	8.85+2.09	<.001
Fiect fraction %	$61.89 \pm 6.05$	$62.02 \pm 5.28$	.706
Left ventricular end-diastolic diameter, mm	$50.36 \pm 6.71$	$49.94 \pm 6.45$	.411
l eft ventricular end-systolic diameter, mm	$33.12 \pm 5.48$	$33.67 \pm 5.70$	.651
Aorta sinus diameter, mm	$42.34 \pm 8.09$	$41.09 \pm 9.24$	.247
Ascending aorta diameter, mm	$45.82 \pm 7.29$	44.33 + 7.25	.148
Onset time d	1 00 (0 83-2 00)	1 00 (0 50-1 31)	011
eGER ml /min	87.54 (67.12–114.37)	65.70 (42.80–84.44)	<.001
Preoperative Tol. ng/ml	0.03 (0.02–0.03)	0.05 (0.02–0.30)	291
Postoperative Tnl. ng/ml	4 55 (2 71-7 52)	7 74 (4 98–17 93)	< 001
Preoperative CK-MB ng/ml	1 30 (0 70–24 88)	1.60 (0.70-8.30)	920
Postoperative CK-MB, ng/mL	29 10 (19 98–43 30)	43 50 (26 65–76 45)	< 001
Preoperative myoglobin ng/ml	238 05 (49 77–611 45)	91 90 (27 72–267 90)	348
Postoperative myoglobin, ng/ml	530.00 (269.20–901.00)	901.00 (442.00–3781.10)	< 001
Male gender	364 (73 24%)	52 (74 29%)	853
Hypertension	282 (56 7/%)	42 (60 00%)	808. 808
Diahetes	20 (4 02%)	1 (1 43%)	.000 497
Smoking status	176 (35.41%)	26 (37 14%)	777
COPD	3 (0.60%)	0 (0 00%)	1 000
Valve surgeny history	4 (0.80%)	0 (0.00%)	1.000
	30 (7 64%)	10 (14 28%)	356
Marfan syndrome	5 (1 01%)	0 (0 00%)	1 000
123 Subtune	3 (1.0170)	0 (0.00 %)	580
1	106 (22 60%)	17 (26 15%)	.000
2	227 (48 40%)	27 (41 54%)	
2	136 (29 00%)	21 (32 31%)	
CS subtyne	130 (23.00 %)	21 (02.0170)	1 000
S S	23 (/ 01%)	3 (4 62%)	1.000
C	445 (95 09%)	62 (05 38%)	
According replacement	104 (21 01%)	15 (21 / 3%)	036
Rentall procedure	215 (/3 /3%)	30 (42 86%)	.330
Wheat procedure	1 (0 20%)	1 (1 /13%)	.321
Partial aortic arch ranlacement	27 (5.45%)	1 (1.4576)	1 000
Total arch replacement combined stant elephant trunk implantation	267 (73.84%)	53 (75 71%)	738
Combined CARG	32 (6 50%)	3 (4 /8%)	787
Combined MV/R	7 (1 /1%)	1 (1 /13%)	1 000
Aortic hivelve malformation	10 (2 65%)	1 (1.45%)	1 000
Severe aortic requiraitation	130 (36 87%)	20 (37 0/%)	0.000
Dericardial afflicion	65 (17 20%)	7 (12 06%)	.901
เ ธแอสเนเสเ ซีไไปอีโปไ	03 (17.20%)	1 (12.90%)	.009

BMI = body mass index, CABG = coronary artery bypass grafting, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease, eGFR = estimated glomerular filtration rate, MVR = mitral valve replacement.

## Table 2

Comparison of myocardial markers before and after surgery.

		Preoperative levels			Postoperative levels		
Variables	Positive at URL cut-off, %	Mean concentration level, ng/mL	Quartile range, Q1–Q3	Positive at URL cut-off, %	Mean concentration level, ng/mL	Quartile range, Q1–Q3	<i>P</i> -value
hs-Tnl	22.8	0.03	0.02-0.03	99.4	5.0	2.95-8.72	<.001
Myoglobin	33.1	216.8	48.80-609.90	97.2	631.8	296.65-901.00	<.001
CK-INB	32.6	1.3	0.70-24.45	97.7	30.3	20.50-46.10	<.001

CK-MB = creatine kinase isoenzyme MB, hs-Tnl = high sensitivity troponin I, URL = upper reference limit.

## 3.3. Predictors for short- and long-term mortality

To determine risk factors for short- and long-term mortality, univariate and multivariate Cox regression analyses were performed for all-cause mortality at 30 days and the end of follow-up, respectively. Age, heart rate, systolic blood pressure, operative time, CPB time, perioperative myocardial markers, onset to operative time, preoperative hemoglobin, platelet count, and D-dimer were found to be predictors for 30-day all-cause death in univariate analysis. Multivariate Cox hazard analysis demonstrated that age (HR, 1.03; 95% CI 1.01–1.05; P=.0096), operation time (HR, 1.24; 95% CI 1.01–1.52; P=.0364), Log10 postoperative TnI (HR, 2.50; 95% CI 1.16-5.40 P=.0198), and preoperative CK-MB positive at the best cut-off value (HR, 6.05; 95% CI 1.61–22.66 P=.0076) were independent predictors for 30 days all-cause mortality. As for the mortality at the end of follow-up, high systolic blood pressure (HR, 1.02; 95% CI 1.01-1.04 P = .0081), total aortic arch replacement (HR, 2.12; 95% CI 1.07–4.22 P=.0320), and concurrent coronary artery bypass grafting surgery (HR, 3.12; 95% CI 1.56-6.23 P=.0013) were risk factors while longer time from onset to operation (HR, 0.75; 95% CI 0.60–0.95 P=.0171) was protective factor. Perioperative myocardial markers were not associated with long-term mortality independent of other factors (Table 3).

## 3.4. Prognostic value of myocardial biomarkers for short and long mortality

Adjusted Cox regression model was performed to determine whether perioperative myocardial markers were independently associated with short- and long-term mortality. It was found that postoperative TnI, Mb, and perioperative CK-MB were significantly associated with 30 days mortality after adjusting for age, sex, systolic blood pressure, surgeon, onset time, operation time, estimated glomerular filtration rate, hemoglobin, platelet, and Ddimer. Higher log post-CKMB has the highest risk effect (HR, 4.64; 95% CI 1.89–11.43; P=.0008) followed by log post-TnI (HR, 3.11; 95% CI 1.56–6.21; P=.0013), log post-Mb (HR, 3.00; 95% CI 1.40-6.43; P=.0048), log pre-CK-MB (HR, 1.82; 95% CI 1.03–3.21; P=.0377), and upper tertile of post-CK-MB (HR, 1.52; 95% CI 1.05–2.20; P=.0261). For long-term mortality, multivariate Cox analysis demonstrated that all cardiac biomarkers were not independent predictors after adjusting for age, gender, surgeon, coronary artery disease, operation time, onset time, surgical method, left ventricular end diastolic diameter (LVEDD), and pericardial effusion (Fig. 1).

Receiver operating characteristic curves were plotted to directly compare the diagnostic value of perioperative myocardial biomarkers for 30 days all-cause mortality. Post-TnI showed the largest area under curve of 0.711, followed by post-Mb (0.699), pre-CK-MB (0.694), and post-CK-MB (0.678). Other previously reported risk factors for early AD mortality, such as serum creatinine and D-dimer, showed a weaker ability than myocardial markers in predicting early surgical outcome. The best cut-off values of post-TnI, post-Mb, pre-CK-MB, and post-CK-MB were 5.71 ng/mL, 1665.8 ng/mL, 33.25 ng/mL, and 38.30 ng/mL, respectively (Fig. 2).

Kaplan–Meier analysis showed that patients with upper tertile of perioperative myocardial markers level had a higher shortterm mortality than those with lower tertile (Figs. 3 and 4). In contrast, perioperative myocardial markers did not distinguish long-term mortality. It is interesting that patients with higher perioperative myocardial markers appeared to have lower longterm mortality, but the difference was not significant (Fig. 5).

To verify the consistency of perioperative myocardial markers in predicting early mortality in different subgroups, we performed stratified analysis and calculated the interaction *P* value. The risk effect of high preoperative CK-MB level was significant higher in subgroups of smaller LVEDD, smoking, needing for aortic valve replacement, and shorter onset time. However, in different subgroups, there was no significant difference in the predictive effect of postoperative TnI on early mortality (Supplementary Table 1, http://links.lww.com/MD/ D265).

# 3.5. Factors associated with perioperative myocardial markers

Associations of perioperative myocardial markers levels with clinical variables, and laboratory and UCG variables were shown in Supplementary Table 2, http://links.lww.com/MD/D265. Gender, body mass index, heart rate, severe aortic regurgitation, estimated glomerular filtration rate, and platelet count appeared to be associated with preoperative myocardial enzymes, but none of these variables showed significant association with preoperative myocardial enzymes in multivariate linear regression. As for postoperative troponin I level, multiple linear regression confirmed that preoperative CK-MB, CPB time, and operative time were significantly correlated with it.

## 4. Discussion

Myocardial marker is an important method to diagnose myocardial infarction. However, as the application of rapid high sensitivity assays in routine diagnosis, doctors were more likely to confront with increased myocardial markers patients beside myocardial infarction patients.<sup>[13]</sup> Many studies have found that elevated myocardial markers reflect myocardial injury in addition to infarction, and suggest a worse prognosis.<sup>[14]</sup>

This is the first study to evaluate the effect of perioperative myocardial markers on short- and long-term prognosis of patients undergoing acute type A AD in a large sample. We found that the positive rate of preoperative myocardial markers in acute type A AD surgery patients ranged from one-fifth to onethird. In the majority of patients, postoperative myocardial markers exceeded 99th URL. Some previous studies have found that certain number of acute type A AD patient have a positive troponin (23-54%), <sup>[15-17]</sup> the results of this study consistent with previous reports. However, we doubt whether the rough data of the positive ratio can be compared, because the time from onset to admission varies in different studies, and this data is rarely mentioned in previous studies. As we know, it takes time for cardiac markers to change and peak. For example, serum troponin levels in patients with myocardiac infarction start to rise 3 to 6 hours after onset, peak in 10 to 24 hours, and resume normal in 5 to 7 days. Therefore, more studies considering the time of onset should be carried out in the future to accurately describe the time changes of myocardial markers after the onset of type A AD.

Previous studies focus more on the predictive effect of myocardial markers, especially troponin elevate, on the preoperative mortality of type A AD, and found that the preoperative increase of troponin could increase the mortality of type A AD. However, all the patients included in the 4 previous studies

AP: Applementanic Markins         Consistent Applementanic Markins         Consistent Applementanic Marki	Univariate analysis H9, 95% Cl, <i>P</i> -value 1.03 (1.01, 1.05), <i>0.096</i> 1.03 (1.01, 1.05), <i>0.096</i> 1.04 (0.97, 1.12), 2548 1.07 (0.66, 1.12), 2548 1.07 (0.66, 1.12), 2548 1.07 (0.66, 1.12), 2075 1.08 (0.46, 2.52), 8557 1.00 (1.00, 1.03), <i>0.073</i> 1.01 (1.00, 1.03), <i>0.073</i> 1.01 (1.00, 1.03), <i>0.073</i> 0.00 (0.00, 0.11), <i>0.007</i> 1.958 (6.45, 5.948), <i>0.007</i> 1.01 (0.05, 0.11), <i>0.007</i> 1.01 (1.00, 1.10), <i>0.007</i> 1.01 (1.00, 1.10), <i>0.007</i> 1.01 (1.00, 1.10), <i>0.007</i> 1.01 (1.00, 1.10), <i>0.007</i> 1.03 (0.48, 1.68), <i>7.446</i> 1.01 (1.00, 1.01), <i>0.007</i> 1.16 (1.29, 1.65), <i>0.007</i> 1.16 (1.29, 1.65), <i>0.007</i> 1.16 (0.28, 2.88), 8562 1.11 (0.61, 2.28), 8562 1.11 (0.65, 1.38), 9155 1.11 (0.65, 1.38), 9155	Multivariate analysis HR, 95% Cl, <i>P</i> -value 1.03 (1.01, 1.05) .0096 1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (0.15, 1081) 8260 1.45 (0.18) .2416 1.47 (0.98) .8260 0.99 (0.98, 1.00) .0509 0.99 (0.98, 1.00) .0509	Statistics 48.15+11.60 335.7(444%) 25.65+3.88 265.6889%) 16.(3.56%) 16.(3.56%) 16.(3.56%) 41.(9.11%) 155.64+17.57 82.71+4.31 4.(0.89%) 4.(0.89%) 2.05+0.10 2.01+0.33 1.98+0.20 3.20+0.51 2.03300+55.33 114,28+36.70 7.70+1.77 107 (25.18%)	Univariate analysis HI, 95% Cl, <i>P</i> -value 1.00 (0.98, 1.01) .5994 1.07 (0.68, 1.68) .7746 1.01 (0.94, 1.07) .8490 1.27 (0.86, 1.91) .2426 3.43 (1.62, 7.27) .0073 0.96 (0.64, 1.43) .8284 1.00 (0.52, 1.93) .9985 1.01 (1.00, 1.02) .0529 1.00 (1.92) 1.01 .8550 2.55 (0.92, 7.08) .0729 2.55 (0.92, 7.08) .0729 2.55 (0.92, 7.08) .0729	Multivariate analysis HR, 95% Cl, <i>P</i> -value
$Q_{01}$ , $y$ $Q_{01}$ , $y$ $Q_{01}$ , $y$ $Q_{01}$ , $y$ $Q_{01}$ , $Q_{01}$ $Q_{01}$ $Q_{01}$ , $Q_{01}$	1.03 (1.01, 1.05), <b>.0096</b> 1.20 (0.69, 2.11), 5160 1.04 (0.97, 1.12) 25-48 1.07 (0.66, 1.74), 7873 0.37 (0.05, 5.05) 3204 1.03 (0.65, 1.70) 9075 1.03 (0.65, 1.00, 1.03), <b>.0734</b> 1.01 (1.00, 1.03), <b>.0734</b> 1.01 (1.00, 1.03), <b>.0734</b> 1.01 (1.00, 1.01), <b>.0077</b> 1.65 (0.40, 6.83), 4877 0.00 (0.00, hr), 9948 0.01 (0.00, 0.11), <b>.0077</b> 1.95 (6.45, 284), 5.0007 1.95 (6.45, 2.84), 5.0007 1.95 (6.45, 2.94), <b>.0078</b> 1.01 (1.01, 1.01), <b>.0077</b> 1.01 (1.01, 1.01), <b>.0077</b> 1.03 (0.58, 1.88), 5629 1.03 (0.28, 2.88), 8552 1.103 (0.58, 1.83), 9155 1.11 (0.64, 2.28), 8552 1.103 (0.58, 1.83), 9155 1.11 (0.65, 2.28), 8552 1.103 (0.58, 1.83), 9155 1.11 (0.65, 2.28), 8552 1.11 (0.65, 2.28), 8552	1.03 (1.01, 1.05) <b>.0096</b> 1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (015, 108) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	48.15+11.60 335 (74.44%) 25553 388 265 (58.89%) 16 (35.6%) 158 (35.11%) 158 (35.11%) 141 (9.11%) 4 (9.11%) 4 (9.11%) 4 (0.89%) 2.05+0.10 2.01+0.33 1.98+0.20 3.20+0.51 2.03:00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)	1.00 (0.98, 1.01) .5994 1.07 (0.68, 1.68) .7746 1.07 (0.85, 1.91) .2426 3.43 (1.62, 1.91) .2426 3.43 (1.62, 7.27) <b>.0073</b> 0.96 (0.64, 1.43) .8284 1.00 (0.52, 1.93) .9985 1.01 (1.00, 1.02) .0529 1.00 (0.99, 1.01) .8550 2.55 (0.99, 7.08) .0725 1.09 (0.15, 8.05) .9359	
Media $q_{25}(2,30)$ $120$ ( $665$ , $173$ , $753$ $115$ ( $665$ , $173$ , $723$ $120$ ( $655$ , $173$ , $733$ $120$ ( $655$ , $173$ , $733$ $120$ ( $655$ , $173$ , $733$ $120$ ( $655$ , $173$ , $733$ $120$ ( $655$ , $173$ , $733$ $120$ ( $120$ , $133$ , $120$ , $255$ $120$ ( $120$ , $133$ , $120$ , $255$ $120$ ( $120$ , $133$ , $120$ , $255$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $133$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $120$ ( $120$ , $120$ , $237$ $122$ ( $120$ , $120$ , $237$ $122$ ( $120$ , $120$ , $237$ $122$ ( $120$ , $120$ , $237$ $122$ ( $120$ , $110$ , $122$ , $232$ $122$ ( $120$ , $123$ , $122$ , $120$ $122$ ( $120$ , $123$ , $122$ , $120$ $122$ ( $120$ , $123$ , $122$ , $120$ $122$ ( $120$ , $123$ , $120$ $122$ ( $120$ , $123$ , $120$ $122$ ( $120$ , $120$ , $120$ $122$ ( $120$ ,	1.20 (0.69, 2.11) 5160 1.04 (0.97, 1.12) .25.48 1.07 (0.066, 1.74) .25.48 1.03 (0.65, 1.74) .3075 0.37 (0.05, 2.66) .3204 1.03 (0.65, 2.66) .3504 1.03 (0.06, 1.03) .073 1.06 (0.00, 0.11) .0707 1.06 (0.00, 0.11) .0707 0.00 (0.00, 0.11) .0707 1.01 (0.05, 0.11) .0707 0.10 (0.05, 0.11) .0077 1.9.58 (6.45, 5.9.45)0007 0.10 (0.05, 0.11) .0077 1.9.6 (6.45, 5.9.45)0007 1.01 (1.01, 1.01) .0007 1.01 (1.00, 1.101) .0007 1.01 (1.00, 1.101) .0007 1.06 (1.29, 1.65)0007 1.06 (1.29, 1.65)0007 1.16 (1.29, 1.65)0007 1.16 (1.29, 1.65)0007 1.16 (1.29, 1.65)0007 1.16 (0.51, 2.28)6299 1.11 (0.65, 1.38)005 1.11 (0.65, 1.38)0155 1.11 (0.55, 1.38)0155 1.1	1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (0.15, 1081) .8260 1.45 (0.78, 2.69) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	235 (74.4%) 25.65+3.88 265.839%) 16 (3.5.6%) 158 (35.11%) 158 (35.11%) 158 (35.11%) 125.64+17.57 82.77+14.31 4 (0.89%) 2 (0.69%) 2 (0.10 2 (0.10 2 (0.10 2 (0.10 2 (0.10 2 (0.10 3 (25.33) 114.28+36.70 7.70+1.77 7.70+1.77	1.07 (0.68, 1.68), 7746 1.01 (0.94, 1.07), 2426 1.27 (0.85, 1.91), 2426 3.43 (1.62, 7.27), <b>.0073</b> 0.96 (0.64, 1.43), 8284 1.00 (0.52, 1.93), 3985 1.01 (1.00, 1.02), 0.529 1.00 (0.99, 1.01), 8550 2.25 (0.99, 7.08), 0725 2.25 (0.92, 7.08), 0725	
Boli, Name         Substance         Substance <thsubstance< th=""> <thsubstance< th=""> <t< td=""><td>1.04 (0.95, 1.1.42), 25-46 1.07 (0.66, 1.74), 7873 0.37 (0.05, 2.65), 3204 1.03 (0.65, 2.52) 8557 1.08 (0.46, 2.52) 8557 1.00 (1.00, 1.03), 0.07 1.05 (0.46, 6.83), 4877 0.00 (0.00, 0.11), 5.0007 1.05 (0.46, 6.84), 5.0007 0.10 (0.05, 0.11), 5.0007 1.05 (0.48, 1.161), 5.0007 1.01 (1.01, 1.01), 5.0007 1.03 (0.05, 2.84), 5.0007 1.046 (1.29, 1.163), 5.0007 1.01 (1.00, 1.01), 5.0007 1.06 (1.29, 1.163), 7.446 1.01 (1.01, 1.01), 5.0007 1.46 (1.29, 1.163), 7.446 1.01 (1.00, 1.01), 5.0007 1.46 (1.29, 1.163), 5.0007 1.46 (1.29, 1.163), 7.446 1.01 (1.00, 1.01), 5.0007 1.10 (0.58, 1.88), 5.529 1.11 (0.58, 1.88), 9.155 1.11 (0.58, 1.88), 9.15</td><td>1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.45 (0.78, 269) .2416 1.00 (1.00, 1.01) .2368 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b></td><td>25.053+3.88 265 (58.89%) 16 (3.56%) 158 (35.11%) 125.64+17.57 82.77+14.31 43 (9.56%) 4 (0.89%) 2 05+0.10 2.01+0.33 1.98+0.20 3.20+0.51 3.20+0.51 2.03:00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)</td><td>1.01 (0.34, 1.107), 2430 1.27 (0.85, 1.91), 2426 3.43 (1.62, 7.27), <b>0013</b> 0.96 (0.64, 1.43), 8284 1.00 (1.52, 1.93), 9985 1.01 (1.00, 1.02), 0.529 1.00 (1.92), 7.08) 0.729 2.55 (0.92, 7.08), 0.729 2.55 (0.92, 7.08), 0.729 1.09 (0.15, 8.05), 9359</td><td></td></t<></thsubstance<></thsubstance<>	1.04 (0.95, 1.1.42), 25-46 1.07 (0.66, 1.74), 7873 0.37 (0.05, 2.65), 3204 1.03 (0.65, 2.52) 8557 1.08 (0.46, 2.52) 8557 1.00 (1.00, 1.03), 0.07 1.05 (0.46, 6.83), 4877 0.00 (0.00, 0.11), 5.0007 1.05 (0.46, 6.84), 5.0007 0.10 (0.05, 0.11), 5.0007 1.05 (0.48, 1.161), 5.0007 1.01 (1.01, 1.01), 5.0007 1.03 (0.05, 2.84), 5.0007 1.046 (1.29, 1.163), 5.0007 1.01 (1.00, 1.01), 5.0007 1.06 (1.29, 1.163), 7.446 1.01 (1.01, 1.01), 5.0007 1.46 (1.29, 1.163), 7.446 1.01 (1.00, 1.01), 5.0007 1.46 (1.29, 1.163), 5.0007 1.46 (1.29, 1.163), 7.446 1.01 (1.00, 1.01), 5.0007 1.10 (0.58, 1.88), 5.529 1.11 (0.58, 1.88), 9.155 1.11 (0.58, 1.88), 9.15	1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.45 (0.78, 269) .2416 1.00 (1.00, 1.01) .2368 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	25.053+3.88 265 (58.89%) 16 (3.56%) 158 (35.11%) 125.64+17.57 82.77+14.31 43 (9.56%) 4 (0.89%) 2 05+0.10 2.01+0.33 1.98+0.20 3.20+0.51 3.20+0.51 2.03:00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)	1.01 (0.34, 1.107), 2430 1.27 (0.85, 1.91), 2426 3.43 (1.62, 7.27), <b>0013</b> 0.96 (0.64, 1.43), 8284 1.00 (1.52, 1.93), 9985 1.01 (1.00, 1.02), 0.529 1.00 (1.92), 7.08) 0.729 2.55 (0.92, 7.08), 0.729 2.55 (0.92, 7.08), 0.729 1.09 (0.15, 8.05), 9359	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0.37 (0.05, 2.57) 3504 1.03 (0.65, 1.70) 3075 1.08 (0.46, 2.52) 8557 1.08 (0.46, 2.52) 8557 1.01 (1.00, 1.03) .073 1.01 (1.00, 1.03) .073 0.01 (0.00, 0.11) .0707 0.00 (0.00, 0.11) .0007 0.10 (0.05, 0.13) .0007 0.10 (0.05, 0.13) .0007 1.10 (1.01, 1.01) .0007 1.10 (1.00, 1.01) .0007 1.46 (1.29, 1.65) .0007 1.46 (1.29, 1.65) .0007 1.46 (1.29, 1.65) .0007 1.46 (1.29, 1.65) .0007 1.10 (0.028, 2.88) .7446 1.11 (0.61, 2.28) .6299 Reference 0.90 (0.28, 1.83) .6693 0.33 .275) .9155 1.11 (0.68, 1.83) .6915 1.11 (0.68, 1.83) .6915 1.11 (0.68, 1.83) .6915 1.11 (0.68, 1.83) .6913 0.39 (0.35, 2.75) .9115	1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (0.15, 10.81) .8260 1.45 (0.78, 2.69) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	16 (3.56%) 158 (35.11%) 158 (35.11%) 125.64+17.57 82.77+14.31 43 (9.56%) 4 (0.89%) 2 .05+0.10 2 .01+0.33 1.98+0.20 3.20+0.51 2.03:00+55.33 114.28+36.70 7.70+1.77 107 (25.18%)	3.43 (1.62), 7.27), 0.073 3.43 (1.62), 7.27), 0.073 0.96 (0.64, 1.43), 8284 1.00 (1.52, 1.93), 9985 1.01 (1.00, 1.02), 0.529 1.00 (0.99, 1.01), 8550 2.55 (0.99, 7.08), 0.72 2.55 (0.99, 7.08), 0.72 1.09 (0.15, 8.05), 9359	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1.03 (0.63, 1.70), 3075 1.08 (0.46, 2.52) 8557 1.02 (1.00, 1.03), 1070 1.63 (0.40, 6.83), 4877 1.61 (1.00, 1.03), 1070 1.65 (0.40, 6.83), 4877 0.00 (0.00, 0.11), 5.0007 0.01 (0.00, 0.11), 5.0007 0.10 (0.05, 0.11), 5.0007 19.96 (6.45, 5.945) <.0007 19.96 (6.45, 5.945) <.0007 1.01 (1.01, 1.01), 5.0007 1.01 (1.01, 1.01), 5.0007 1.46 (1.29, 1.65), 5.0007 1.46 (1.29, 1.65) <.0007 1.46 (1.29, 1.65) <.0007 1.46 (1.29, 1.65) <.0007 1.60 (0.25, 1.63), 5.299 1.01 (0.61, 2.28), 5.299 1.13 (0.53, 1.38), 9155 1.11 (0.65, 1.38), 9155 1.11 (0.58, 1.38), 5915 1.11 (0.58, 1.38), 5915 1.11 (0.58, 1.38), 5915 1.11 (0.58, 1.38), 5915	1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (0.15, 10.81) .8260 1.45 (0.78, 2.69) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	158 (35.11%) 41 (9.11%) 125.64+17.57 82.77+14.31 43 (9.56%) 4 (0.89%) 2 05+0.10 2.01+0.33 1.98+0.20 3.20+0.51 3.20+0.51 203.00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)	0.96 (0.64, 1,43) .8284 1.00 (0.52, 1,93) .9985 1.01 (1.00, 1.02) .0529 1.00 (0.99, 1.01) .8550 2.55 (0.99, 7.08) .0725 1.09 (0.15, 8.05) .9359	1.60 (0.51. 4.99) .4191
Static pressure mittery $26, 6, 82^{\circ}$ $108, 0.46, 2.55$ $101, (000, 103, 0.734)$ $101, (001, 147), 0037$ Static pressure, mittery $56, 80, 0.83, 837$ $0.01, 000, 0.103, 1070$ $0.01, 147, 0037$ Hear rate, hom $5, 0.68, 836, 0.100, 0.00, 100, 101, 940, 8272 + 133, 55         0.01, 000, 0.11, 147, 0037 0.010, 000, 111, 100, 2003           Marta synthem         5, 0.08, 836, 0.100, 0.00, 100, 101, 940, 8272 + 133, 55         0.010, 000, 0.11, 147, 0037 0.010, 0.01, 147, 1032           Log10 patterie         5, 0.08, 830, 50, 000, 0.01, 100, 100, 100, 100, 100, 1$	1.08 (0.46, 2.52) 8557 1.02 (1.00, 1.03) .0734 1.01 (1.00, 1.03) .0734 1.61 (1.00, 1.03) .073 1.65 (0.40, 6.83) .487 0.00 (0.00, 1.11) .007 0.10 (0.00, 0.11) .007 0.10 (0.00, 0.11) .007 1.10 (1.01, 1.01) .007 1.228 (1.36, 3.86, .0078 1.01 (1.01, 1.01) .0077 1.46 (1.29, 1.165) .0077 1.10 (0.58, 1.83) .0663 0.030 (0.28, 1.83) .0663 0.330 .035, 2.75) .9814	1.01 (0.99, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (0.15, 1081) .8260 1.45 (0.78, 269) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	41 (9.11%) 125 64+ 17.57 82.77 + 14.31 43 (9.56%) 4 (0.89%) 2.05 + 0.10 2.01 + 0.33 1.98 + 0.20 3.20 + 0.51 2.03 00 + 55.33 114.25 + 36.70 7.70 + 1.77 107 (25.18%)	1.00 (0.52, 1,93) .9985 1.01 (1.00, 1.02) .0529 1.00 (0.99, 1.01) .8550 2.55 (0.992, 7.08) .0722 1.09 (0.15, 8.05) .9359	
System pressue, mmhg $1260, -117.73$ $100, 100, 103, 103$ $101, 000, 113, 2003$ $101, 000, 113, 2003$ Derif rate, upm $8223+117.73$ $100, 100, 113, 2003$ $101, 000, 113, 2003$ $101, 000, 113, 2003$ Current are, upm $25, 0.86\%$ $0.01, 0.00, 0.11, 2.0007$ $0.10, 0.01, 1.203$ $2034$ $1.01, 0.00, 1.13, 2003$ Current are, number $5, 0.86\%$ $0.01, 0.00, 0.11, 2.0007$ $0.10, 0.01, 1.25, 0.2054$ $1.47, 0.032, 0.003$ $1.26, 0.02, 0.263, 2346$ Logrith cannary memory $233, 0.457, 322$ $1.01, (101, 101), 0.0027$ $0.09, 0.003$ $1.24, (101, 1.52), 0.0264$ Arch cannary memory $233, 0.457, 322$ $1.01, (101, 010), 0.0027$ $0.09, 0.003$ $1.01, 0.001, 0.0027$ Current are, min $233, 0.457, 323$ $1.01, (101, 101), 0.0027$ $0.09, 0.039$ $1.01, 0.01, 0.15, 2.203$ Arch cannary mem, min $233, 0.457, 323$ $1.01, (101, 101), 0.0027$ $1.24, (101, 1.52), 0.0264$ 23, Subper $111, 0, 0.01, 0.00, 0.013, 0.0024$ $1.24, (101, 1.52), 0.0264$ $1.24, (101, 1.52), 0.0264$ 23, Subper $1.12, 0.027, 0.027$ $1.24, (101, 1.52), 0.0264$ $1.24, (101, 1.52), 0.0264$	1.02 (1.00, 1.03) .0134 1.01 (1.00, 1.03) .0734 1.56 (0.40, 6.83) 4877 0.00 (0.00, 1n1) .9948 0.01 (0.00, 0.11) <.0007 0.10 (0.05, 0.13) <.0007 19.59 (6.45, 59.45) <.0007 19.59 (6.45, 59.45) <.0007 1.01 (1.01, 1.01) <.0007 1.01 (1.01, 1.01) <.0007 1.01 (1.00, 1.01) <.0007 1.01 (1.00, 1.01) <.0007 1.01 (1.02, 1.03) <.0037 1.03 (0.28, 2.88) .5529 1.03 (0.28, 2.88) .8552 1.11 (0.68, 1.83) .6653 0.39 (0.35, 2.75) .9814	1.01 (0.39, 1.02) .3710 0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (0.15, 10.81) .8260 1.45 (0.78, 2.69) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	125.64+17.57 82.77 +14.31 43.(9.56%) 4 (0.89%) 2.05 + 0.10 2.01 + 0.33 1.98 + 0.20 3.20 + 0.51 3.20 + 0.51 3.20 + 0.51 7.70 + 1.77 107 (25.18%)	1.01 (1.00, 1.02) .0529 1.00 (0.99, 1.01) .8550 2.55 (0.92, 7.08) .0722 1.09 (0.15, 8.05) .9359	
Cuto consistent         Sez.24:13:56         1.00         1.00         1.00         1.00           Matrix syntome         Sez.24:13:56         1.00         0.00         0.00         0.01         1.00         1.00           Matrix syntome         5         0.88%         0.00         0.00         1.00         0.11         0.00         0.11         0.00         0.11         0.00         0.11         0.00         0.11         0.00         0.11         0.00         0.01         0.13         0.00         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.0	1.01 (1.00, 1.03), 1.070 1.65 (0.40, 6.83), 4.877 0.00 (0.00, 1nf), 9.948 0.01 (0.05, 0.19) <.0007 0.10 (0.05, 0.19) <.0007 1.928 (6.45, 59.45) <.0007 1.928 (6.45, 59.45) <.0007 1.01 (1.01, 1.01) <.0007 1.01 (1.00, 1.01) <.0007 1.01 (1.00, 1.01) <.0007 1.01 (1.00, 1.01) <.0007 1.01 (1.01, 1.01) <.0007 1.01 (1.02, 1.03) <.029 Reference 0.30 (0.48, 1.88) 5.299 Reference 0.30 (0.28, 1.83) 6.693 0.39 (0.35, 2.75) 9.914 0.30 (0.35, 2.75) 9.914	0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (015, 101) .8260 1.45 (0.78, 2.69) 2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	22.// +14.31 82.// +14.31 4 (3 (9.56%) 4 (3 (9.56%) 2.01 +0.33 1.98 +0.20 3.20 +0.51 3.20 + 55.33 114.25 + 36.70 7.70 +1.77 107 (25.18%)	1.00 (0.394, 1.01) .8550 2.55 (0.92, 7.08) .0722 1.09 (0.15, 8.05) .9359	1.02 (1.01, 1.04) <b>.0081</b>
Martin syndom $5,0.65\%$ $0.00,000,000,000,000,000,000,000,000,00$	0.00 (0.00) m0) 3948 0.01 (0.00) m1) 3948 0.01 (0.05, 0.19) <.0007 0.10 (0.05, 0.19) <.0007 19.59 (6.45, 58.45) <.0007 1.01 (1.01, 1.01) <.0007 1.01 (1.00, 1.01) <.0007 1.01 (1.00, 1.01) .0077 1.46 (1.29, 1.65) <.0007 1.46 (1.29, 1.65) <.0007 0.39 (0.28, 2.28) .6299 1.03 (0.28, 1.83) .6663 0.39 (0.35, 2.75) .9814	0.10 (0.01, 1.47) .0937 1.27 (0.15, 1.17) .1052 1.27 (0.15, 1.08) .2460 1.45 (0.78, 2.69) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	4.0 (8.20%) 4.0 (8.99%) 2.05 + 0.10 2.01 + 0.33 1.98 + 0.20 3.20 + 0.51 203.00 + 55.33 114.25 + 36.70 7.70 + 1.77 107 (25.18%)	1.09 (0.15, 8.05) .9359	0 38 (0 0E 3 16) 3796
Logio hemedolin $2.05+0.10$ $0.01$ $0.005$ $0.10$ $0.001$ $1.47$ $0.052$ Logio hemedolin $1.201$ $0.005$ $0.19$ $0.005$ $0.19$ $0.001$ $0.11$ $0.001$ $0.11$ $0.001$ $0.11$ $0.001$ $0.11$ $0.015$ $0.93$ $0.946$ $0.946$ $0.946$ $0.946$ $0.946$ $0.946$ $0.011$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.010$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$	0.01 (0.06, 0.11) <-0007 0.10 (0.05, 0.19) <-0007 19.53 (6.45, 59.45) <-0007 2.29 (1.36, 3.38) .0078 1.01 (1.01, 1.01) <-0007 1.01 (1.00, 1.01) <-0007 1.01 (1.00, 1.01) <-0007 1.46 (1.29, 1.65) <-0007 Reference 0.30 (0.48, 1.68) <-228) .529 1.18 (0.61, 2.28) .6293 8.8562 1.03 (0.28, 1.83) .6683 0.39 (0.28, 1.83) .6683 0.39 (0.35, 1.18) .9155 1.11 (0.66 1, 3.23) .6593 0.39 (0.35, 2.75) .9314	0.10 (0.01, 1.47) .0937 0.46 (0.18, 1.17) .1052 1.27 (0.15, 1031). 8260 1.45 (0.78, 2.56) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	2.05+0.10 2.01+0.33 1.98+0.20 3.20+0.51 203.00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)		U.JU (U.UJ, J.10) JI 20
Control         <	0.10 (0.05, 0.19) <.0001 19.53 (6.45, 59.45) <.0001 2.23 (1.36, 3.86) 0018 1.01 (1.01, 1.01) <.0001 1.01 (1.00, 1.01) <.0001 1.46 (1.29, 1.65) <.0001 Reference 0.30 (0.48, 1.65) <.0001 Reference 0.30 (0.28, 2.28) .6529 Reference 0.30 (0.28, 2.28) .6529 1.11 (0.68, 1.38) .6563 1.11 (0.68, 1.38) .6563 0.39 (0.35, 2.75) .9514	0.46 (0.18, 1,17) .1052 1.27 (0.15, 10.81) 8260 1.45 (0.78, 269) 2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	2.01 + 0.33 1.98 + 0.20 3.20 + 0.51 203.00 + 55.33 114.25 + 36.70 7.70 + 1.77 107 (25.18%)	0.32 (0.05, 2.19) .2455	
Logic creatine $139 + 0.20$ $193 + 0.20$ $139 + 0.20$ $127$ (0.15, 10.51, 10.51, 256) $2416$ Cardiounionary bypass time, min $320 + 0.49$ $220$ (1.00, 1.01), $2007$ $100$ (1.00, 1.01), $2007$ $100$ (1.00, 1.01), $2039$ Anta clamp time, min $7.70 + 1.79$ $1.46$ (1.29, 1.65) < $.2007$ $100$ (1.00, 1.01), $2039$ Anta clamp time, min $7.70 + 1.79$ $1.46$ (1.29, 1.65) < $.2007$ $1.29$ (0.01, 0.01), $2039$ Anta clamp time, min $129$ (23.50%) $1.46$ (1.29, 1.65) < $.2007$ $1.29$ (0.01, 0.01), $2039$ Anta clamp time, min $129$ (23.50%) $1.46$ (1.29, 1.65) < $.2007$ $1.24$ (1.01, 1.152) .0394           2         Subtype $1.29$ (23.50%) $1.46$ (1.29, 1.65) < $.2007$ $1.24$ (1.01, 1.52) .0394           2         Subtype $1.29$ (23.50%) $1.86$ (0.12, 2.89) $.236$ $1.29$ (0.11, 2.29) $.5299$ 2         Subtype $1.29$ (0.12, 2.89) $.236$ $1.36$ (0.12, 2.89) $.236$ $1.36$ (0.11, 2.29) $.5299$ 2         Subtype $1.29$ (0.12, 2.89) $.257$ $1.36$ (0.12, 2.29) $.239$ $1.36$ (0.12, 2.29) $.239$ 2         Subtype $2.23$ (1.66, 1.29) $.103$ $.232$	19.59 (6.45, 59.45) <.0001 2.29 (1.36, 388), 0003 1.01 (1.01, 1.01) <.0007 1.01 (1.00, 1.01) <.0007 1.46 (1.29, 1.65) <.0007 Heference 0.90 (0.48, 1.68), 7446 1.18 (0.61, 2.28) .6299 Reference 0.90 (0.28, 2.88) .8562 1.03 (0.58, 1.83, 1.9155 1.11 (0.68, 1.83) .6663 0.99 (0.35, 2.75) .9814	1.27 (0.15, 10.81) .8260 1.45 (0.78, 2.69) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	1.98+0.20 3.20+0.51 203.00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)	1.31 (0.72, 2.36) .3778	
Log 10 - Drand Cubic Duration         Log 10 COOT         Log 10 COOT </td <td>2.28 (1.36), 3.86), 2007 1.01 (1.01, 1.01) &lt; .0007 1.01 (1.00, 1.01) &lt; .0007 1.46 (1.29, 1.65) &lt; .0007 Reference 0.90 (0.48, 1.68), 7.446 1.18 (0.61, 2.28), 5.299 Reference 0.90 (0.28, 2.88), 5.652 1.03 (0.58, 1.83), 5.653 1.11 (0.68, 1.83), 5.653 0.39 (0.35, 2.75), 9.814</td> <td>1.45 (0.16, 2.19) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.100) .0509 1.24 (1.01, 1.52) <b>.0364</b></td> <td>3.20.40.51 203.00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)</td> <td>0.74 (0.29, 1.90) .5306</td> <td></td>	2.28 (1.36), 3.86), 2007 1.01 (1.01, 1.01) < .0007 1.01 (1.00, 1.01) < .0007 1.46 (1.29, 1.65) < .0007 Reference 0.90 (0.48, 1.68), 7.446 1.18 (0.61, 2.28), 5.299 Reference 0.90 (0.28, 2.88), 5.652 1.03 (0.58, 1.83), 5.653 1.11 (0.68, 1.83), 5.653 0.39 (0.35, 2.75), 9.814	1.45 (0.16, 2.19) .2416 1.00 (1.00, 1.01) .2358 0.99 (0.98, 1.100) .0509 1.24 (1.01, 1.52) <b>.0364</b>	3.20.40.51 203.00+55.33 114.25+36.70 7.70+1.77 107 (25.18%)	0.74 (0.29, 1.90) .5306	
Constraint         Constraint <thconstraint< th="">         Constraint         Constra</thconstraint<>	1.01 (1.00, 1.01), <b>2017</b> 1.46 (1.29, 1.65) <. <b>2007</b> 1.46 (1.29, 1.65) <. <b>2007</b> 8 Reference 0.30 (0.48, 1.68) .7446 1.18 (0.61, 2.28) .6299 Reference 0.30 (0.28, 2.88) .8562 1.03 (0.58, 1.84) .9155 1.11 (0.68, 1.83) .6563 0.39 (0.35, 2.75) .9814	0.09 (0.38, 1.00) .0509 0.99 (0.38, 1.00) .0509 1.24 (1.01, 1.52) <b>.0364</b>	140500 + 20.50 7.70 + 1.77 107 (25.18%)	0.99 (0.66, 1.48) .9438 0 00 /0 00 1 00) <b>0015</b>	1 00 /0 00 1 00/ 31/12
Operation fine, min $7.70 + 1.79$ $1.46$ (i.29, i.65) < .0001 $1.24$ (i.01, i.52) .0364           123 Subtype         123 Subtype         124 (i.01, i.52) .0364         123 Subtype         124 (i.01, i.52) .0364           133 Subtype         258 ( $4.74\%$ )         Reference         138 ( $661$ , 228) .6293         138 ( $661$ , 228) .5295           2 Subtype         258 ( $4.74\%$ )         Reference         258 ( $4.74\%$ )         138 ( $661$ , 228) .5852           C Subtype         2 Subtype         258 ( $4.74\%$ )         Reference         252 ( $55.26\%$ )         0.90 ( $0.28$ , 2.88) .5852           C Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype           C Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype           C Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype           C Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype           C Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype           S Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype         2 Subtype           S Subtyp	1.46 (1.29, 1.65) <.0001 Reference 0.90 (0.48, 1.68) .7446 1.18 (0.61, 2.28) .6299 Reference 0.90 (0.28, 2.88) .8562 1.10 (0.58, 1.83) .6563 0.111 (0.68, 1.83) .6563 0.111 (0.68, 1.83) .6563	1.24 (1.01, 1.52) <b>.0364</b>	7.70 + 1.77 107 (25.18%)	0.99 (0.99, 1.00) .0108	1.00 (0.99, 1.01) .9815
123 Subtype       123 Subtype         1       123 Subtype         2       259 (47.18%)       0.90 (0.48, 1.68), 7446         2       259 (47.18%)       0.90 (0.48, 1.68), 7446         3       161 (29.33%)       1.18 (0.61, 2.28), 6299         5       55 subtype       25 (47.4%)       Reference         5       5 subtype       25 (47.4%)       Reference         5       5 subtype       26 (4.74%)       1.18 (0.61, 2.28), 6299         5       5 (5.51%)       0.90 (0.58, 1.38), 9155       3614         7       252 (65.51%)       0.90 (0.58, 1.38), 9155       3614         7       252 (65.51%)       0.90 (0.58, 1.39), 6475       3614         7       26 (4.73%)       1.14 (0.65, 1.39), 6475       3614         7       0.90 (0.56, 1.13), 5014       3665       3716         8enhall procedure       25 (6.10%)       1.14 (0.65, 1.39), 6475       3716         8enhalt protectore       26 (4.74%)       1.14 (0.65, 1.39), 6475       3716         8enhalt protectore       26 (4.74%)       1.14 (0.65, 1.39), 6475       3716         8enhalt protectore       26 (4.74%)       1.14 (0.65, 1.39), 6475       3716         8enhalt protectore       26 (4.71, 3.39%) <td< td=""><td>Reference 0.90 (0.48, 1.68) .7446 1.18 (0.61, 2.28) .6299 Reference 0.90 (0.28, 2.88) 8562 1.10 (0.58, 1.83) .6563 1.11 (0.68, 1.83) .6563 0.99 (0.35, 2.75) .9814</td><td></td><td>107 (25.18%)</td><td>0.87 (0.77, 0.99) .0295</td><td>1.00 (0.78, 1.29) .9759</td></td<>	Reference 0.90 (0.48, 1.68) .7446 1.18 (0.61, 2.28) .6299 Reference 0.90 (0.28, 2.88) 8562 1.10 (0.58, 1.83) .6563 1.11 (0.68, 1.83) .6563 0.99 (0.35, 2.75) .9814		107 (25.18%)	0.87 (0.77, 0.99) .0295	1.00 (0.78, 1.29) .9759
1         129 (23.50%)         Reference           2         23 (47.18%)         0.90 (0.48, 168), 7446           3         3         161 (29.33%)         1.18 (0.61, 2.20), 6239           5 subtype         5         56 (4.74%)         Reference           5         3         161 (29.33%)         1.18 (0.61, 2.20), 6239           5         55 (51%)         0.90 (0.28, 184) .9155         1.88           5         5         55 (51%)         0.90 (0.28, 184) .9155         1.11 (0.68, 139) .6475           8         Partial acrit: arch replacement         22 (51%)         0.90 (0.35, 2.75) .9814         1.14 (0.65, 1.99) .6475           Bernal procedure         22 (51%)         0.90 (0.35, 2.75) .9814         1.14 (0.65, 1.99) .6475         0.90 (0.35, 2.75) .9814           Combined Abs         1.14 (0.65, 1.99) .6475         0.99 (0.35, 2.75) .9814         1.16 (0.16, 8.47) .8902           Combined Abs         8 (1.37%)         1.14 (0.65, 1.99) .6475         0.99 (0.35, 1.03) .5364           Combined Abs         8 (1.37%)         1.16 (0.96, 1.09) .6475         0.99 (0.96, 1.03) .2465           Combined Abs         8 (1.37%)         1.16 (0.5) .109 .4003         1.16 (0.16, 8.47) .8902           Combined Abs         8 (1.37%)         0.59 (0.16) 1.00 .103 .41175         1.16 (0.10 .	0.90 (0.48, 1.68) .7446 1.18 (0.61, 2.28) .5299 Reference 0.90 (0.28, 2.88) .8562 1.03 (0.28, 1.83) .6563 1.11 (0.68, 1.83) .6563 0.99 (0.35, 2.76) .9814		107 (25.18%)		
2         233 (47.18%)         0.30 (0.48, 1.06) .746           3         CS subtype         233 (47.18%)         0.30 (0.48, 1.06) .746           5         S subtype         26 (4.74%)         Reference           5         C         522 (95.26%)         0.30 (0.28, 2.88) .8562           6         4.74%)         Reference         26 (4.74%)           7         0.00 (0.58, 1.84) .9155         1.16 (0.61, 2.28) .629           8         1.17 (0.66, 1.99) .6475         0.39 (0.35, 2.75) .9814           Partial aortic arch replacement         22 (5.1%)         0.39 (0.35, 2.75) .9814           Partial aortic arch replacement         23 (5.1%)         0.39 (0.35, 2.75) .9814           10tal arch replacement         23 (5.1%)         0.39 (0.35, 2.75) .9814           10tal arch replacement         23 (5.1%)         0.39 (0.35, 1.39) .6475           0.00 mined CABG         8 (1.37%)         1.14 (0.65, 1.99) .6475           Combined ABG         8 (1.37%)         1.16 (0.61, 1.23) .6239           Combined ABG         8 (1.37%)         1.16 (0.61, 1.23) .6234           Combined ABG         8 (1.37%)         0.39 (0.36, 1.09) .6475           Combined ABG         8 (1.37%)         0.39 (0.36, 1.09) .6475           Combined ABG         8 (1.37%)         0.39	0.30 (0.45, 1.06), / 446 1.18 (0.61, 2.28) .6299 Reference 0.30 (0.28, 2.88) .8562 1.03 (0.58, 1.84) .6955 1.11 (0.68, 1.83) .6953 0.39 (0.35, 2.76) .9814			Reference	
CS         Subple         Contract         Contract <thcont< th=""> <thcont< th=""> <thcont< th=""></thcont<></thcont<></thcont<>	1.10 (0.01, 2.20) .0239 Reference 0.30 (0.28, 2.88) .8562 1.11 (0.65, 1.84) .9155 1.11 (0.653, 1.84) .9155 0.39 (0.35, 2.76) .9814		196 (46.12%)	1.84 (1.09, 3.09) <b>.0222</b> 1.15 (0.62, 2.14) 6477	3.12 (1.46, 0.64) .0032 1 25 /0 57 2 2 4/ 4057
Second restrict of the first of th	Reference 0.50 (0.28, 2.88) .8562 1.03 (0.58, 1.84) .9155 1.11 (0.661, 1.83) .6693 0.99 (0.35, 2.76) .9814				1.00 (0.01, 0.64)
C         522 (95.26%)         0.90         0.28, 2.88)         3.662           Assending replacement         122 (21.00%)         1.03         0.58, 1.84)         9155           Bentall procedure         122 (21.00%)         1.03         0.58, 1.84)         9155           Bernall procedure         25 (43.03%)         1.11         (0.68, 1.89)         .6633           Bernall procedure         23 (5.51%)         0.91 (0.68, 1.89)         .6633         .609%)         .71 (0.68, 1.89)         .6633           Combined stent         33 (5.51%)         0.19 (0.65, 1.99)         .647         .890         .647         .890         .647         .890         .647         .890         .647         .890         .647         .890         .647         .890         .647         .890         .647         .890         .647         .890         .646         .747         .980         .747         .947         .890         .747         .747         .947         .890         .747         .947         .890         .747         .947         .890         .747         .747         .747         .747         .747         .747         .747         .747         .747         .747         .747         .747         .747         .747	0.90 (0.28, 2.88) .8562 1.03 (0.58, 1.84) .9155 1.11 (0.68, 1.83) .6693 0.99 (0.35, 2.75) .9814		20 (4.71%)	Reference	
Ascending replacement         122 (21,00%)         1.03 (0.58, 1.84) (0.155)         0.915           Bentall procedure         250 (43,03%)         1.11 (0.68, 1.89) (663)         0.693 (0.53, 0.57) (0.99) (647)           Partial aronic arch replacement         23 (5.51%)         0.99 (0.55, 1.99) (647)         0.99 (0.55, 1.99) (647)           Partial arch replacement         32 (5.51%)         0.99 (0.55, 1.99) (647)         0.475           Rephant trunk implantation         35 (6.09%)         0.59 (0.18, 1.88) (3716)         0.19 (0.57, 0.9) (647)           Combined CABG         8 (1.37%)         1.14 (0.65, 1.99) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647, 0.9) (647	1.03 (0.58, 1.84) .9155 1.11 (0.68, 1.83) .6693 0.99 (0.35, 2.75) .9814		405 (95.29%)	2.61 (0.64, 10.65) .1814	
Bentall procedure         250 (43.03%)         1.11 (0.68, 1.83) .6633         2683           Partial and cach replacement         23 (5.51%)         0.39 (3.53, 2.75) .9814         32 (5.51%)         0.39 (3.55, 2.75) .9814           Total ach replacement         32 (5.51%)         0.39 (0.55, 1.99) .6475         33 (5.51%)         0.39 (0.55, 1.99) .6475           Total ach replacement         33 (5.09%)         0.59 (0.18, 1.88) .3716         3716           Combined CABG         35 (6.09%)         0.59 (0.18, 1.88) .3716         3716           Combined CABG         35 (6.09%)         0.59 (0.18, 1.88) .3716         3716           Combined CABG         35 (6.09%)         0.59 (0.18, 1.88) .3716         3716           Combined CABG         35 (6.09%)         0.59 (0.18, 1.88) .3716         3716           Combined CABG         35 (6.09%)         0.59 (0.18, 1.88) .3716         3716           Combined MNR         8 (1.37%)         1.15 (0.16, 8.47) .8902         3812           Left ventricular end-diastolic diameter, mm         32.24 + 6.73         0.90 (0.95, 1.02) .3584         3.417           Aorta situs diameter, mm         32.24 + 7.32         0.98 (0.95, 1.02) .3587         3.48) .433         3.48) .433           Aorta situs diameter, mm         32.17 + 8.21         0.98 (0.97, 1.02) .343         0.81 (0.67	1.11 (0.68, 1.83) .6693 0.99 (0.35, 2.75) .9814		96 (21.38%)	1.27 (0.82, 1.98) 2895	
Partial antic actri replacement $32$ (5.51%) $0.39$ (0.35, 2.75). 9814           Total actri replacement $31$ (73.33%) $1.14$ (0.65, 1.99). 6475 $31$ (73.33%)           Total actri replacement $31$ (73.33%) $1.14$ (0.65, 1.99). 6475 $31$ (73.33%)           Combined CABG $35$ (6.09%) $0.59$ (0.18, 1.88). 3716 $37$ (6.09%) $0.53$ (0.18, 1.88). 3716           Combined MNR $81$ (1.37%) $1.15$ (0.16, 8.47). 8902 $1.15$ (0.16, 8.47). 8902 $1.01$ (0.96, 1.03). 5364           Elect fraction, % $61.94.5.31$ $1.00$ (0.96, 1.03). 5364 $1.02$ (0.97, 1.03). 3364           Actribute and-diastolic diameter, mm $33.23.5.5.6$ $1.02$ (0.97, 1.02). 2436 $0.34$ (0.05, 2.436           Aorta situs diameter, mm $32.77.46$ $0.38$ (0.97, 1.02). 2436 $0.81$ (0.67, 0.97). 0230           Aorta situs diameter, mm $32.24.5.32$ $0.98$ (0.97, 1.02). 2436 $0.81$ (0.67, 0.97). 0230           Aorta situs diameter, mm $32.17.46$ $0.38$ (0.96, 1.02). 2436 $0.81$ (0.67, 0.97). 0230           Aorta situs diameter, mm $32.77.46$ $0.38$ (0.96, 1.02). 2336 $0.81$ (0.67, 0.97). 0230           Aorta situs diameter, mm $22.17.46.7$ $0.28$ (0.96, 1.07)	0.99 (0.35, 2.75) .9814		184 (40.98%)	0.71 (0.46, 1.08) .1116	
Iotal actin teplacement combined stent         431 (3.3.3.3%)         114 (JJDS, 1.99), 16475         69475           elephant trunk implantation         35 (6.09%)         0.59 (0.18, 1.88), 3716         3716           Combined CABG         8 (1.37%)         1.15 (0.16, 8.47), 8902         3716           Combined CABG         8 (1.37%)         1.15 (0.16, 8.47), 8902         3716           Combined CABG         8 (1.37%)         1.01 (0.96, 1.05), 7417         366           Elect fraction, %         51.94 + 6.73         0.90 (0.51, 1.02), 3564         3103, 3564           Cut withcular end-diastoic diameter, mm         53.23 + 5.50         0.98 (0.97, 1.09), 4403         4318, 4334           Aorte biavale mater, mm         33.23 + 5.50         0.98 (0.94, 1.02), 2436         0.81 (0.67, 0.97), 0.230           Aorte biavale mater, mm         42.17 + 8.21         0.98 (0.97, 1.03), 3484         4384         0.81 (0.67, 0.97), 0.230           Aorte biavale mater, mm         45.64 + 7.32         0.98 (0.97, 1.03), 3986         0.81 (0.67, 0.97), 0.230         0.81 (0.67, 0.97), 0.230           Aorte biavale         1.72 (48.79)         0.98 (0.97, 1.03), 3986         0.81 (0.67, 0.97), 0.230           Onset time, d         92.17 + 467         0.88 (0.96, 1.17), 3945         0.81 (0.67, 0.97), 0.230           Pericarcial effusion         1.			26 (5.79%)	0.52 (0.19, 1.43) .2064	
expanding         35 (6.09%)         0.59 (0.18, 1.88)         3716           Combined CABG         8 (1.37%)         1.15 (0.16, 8.47)         8902           Combined CABG         8 (1.37%)         1.16 (0.96, 1.05)         7.417           Combined MNR         51.44 + 6.73         0.09 (0.95, 1.00)         3.5364           Left ventricular end-diastolic diameter, mm         33.23 + 5.50         1.02 (0.97, 1.03)         3.5364           Aorts binake main         33.23 + 5.50         0.98 (0.96, 1.02)         2.436         4.334           Aorts binake main         42.17 + 8.12         0.98 (0.94, 1.02)         2.436         4.334           Aorts binake malformation         1.12 (2.48%)         0.44 (0.06, 3.40)         4.334         0.81 (0.57, 0.97)         0.230           Aorts binake malformation         1.72 + 1.748         0.38 (0.97, 1.02)         2.436         0.81 (0.67, 0.97)         0.230           Aorts binake malformation         1.72 (4.87%)         0.98 (0.96, 1.01)         0.81 (0.67, 0.97)         0.231	1.14 (0.65, 1.99) .64/5		340 (75.56%)	2.12 (1.22, 3.68) <b>.0077</b>	2.12 (1.07, 4.22) .0320
Combined MR         Sol (0.105, 371)         U.S. (0.16, 347)         Sol (0.35, 741)           Combined MR         8 (1, 37%)         1.15 (0.16, 347)         3802           Elect fraction, %         61, 965, 53()         1.10 (0.96, 1.05)         7417           Left ventricular end-systolic diameter, mm         50.41+6.73         0.99 (0.95, 1.03)         5364           Left ventricular end-systolic diameter, mm         53.23+5.50         1.02 (0.97, 1.08)         4403           According acria diameter, mm         33.23+5.50         1.02 (0.97, 1.08)         4403           According acria diameter, mm         33.23+5.50         1.02 (0.97, 1.03)         5364           According acria diameter, mm         33.23+5.50         0.98 (0.94, 1.02)         23387           According acria diameter, mm         33.23+5.50         0.98 (0.94, 1.02)         2348)           According acria diameter, mm         41.74+6.79         0.98 (0.97, 1.02)         0.98 (0.97, 0.97)           According acria diameter, mm         1.79+1.76         0.88 (0.57, 1.03)         0.81 (0.57, 0.97)         0.230           Acric biving acria diameter, mm         22.17+46.79         0.98 (0.97, 0.99)         0.99 (0.96, 1.01)         5011           Pericardial effusion         777/2000         0.92 (0.56, 1.27)         0.99 (0.96, 1.01) <t< td=""><td>0 E0 (0 1 0 3 00) 0716</td><td></td><td>(1000 9) 10</td><td></td><td>010156 6000 0010</td></t<>	0 E0 (0 1 0 3 00) 0716		(1000 9) 10		010156 6000 0010
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	U.33 (U.16, 1.00) .37 10 1 15 (N 16 8 47) 89N2		51 (0:30%) 6 (1 33%)	0.04 (2.04, 0.01) <.000	<b>6100.</b> (62.0 ,00.1) 21.6
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1.01 (0.96, 1.05) .7417		61.98 + 5.72	0.97 (0.94, 1.01) .1920	
Left vertricular end-systolic diameter, mm         33.23+5.50         1.02         0.97         1.008         .4.403           Aorta sinus diameter, mm         33.23+5.50         1.02         0.96         (0.95, 1.02)         .3867           Ascending aorta diameter, mm         45.64+7.32         0.98         (0.94, 1.02)         .2486           Ascending aorta diameter, mm         45.64+7.32         0.98         (0.94, 1.02)         .2486           Ascending aorta diameter, mm         45.64+7.32         0.98         (0.94, 1.02)         .2486           Ascending aorta diameter, mm         45.64+7.32         0.98         (0.74, 1.03)         .9386           Ascenting anti formation         1.79+1.76         0.87         (0.39, 1.01)         .5011           Distributer         0.217+46.79         0.98         (0.97, 0.99)         .0001         1.00         0.98, 1.01)         .5011           Pericardial effusion         1.74+6.79         0.98         (0.97, 0.99)         .0001         .010         .031         .031         .031         .031         .031         .031         .031         .031         .031         .031         .0230         .031         .031         .031         .031         .031         .031         .031         .031         <	0.99 (0.95, 1.03) .5364		50.14+6.62	0.95 (0.92, 0.99) .0104	0.99 (0.94, 1.05) .8322
Aorta sinus diameter, mm         42.17+8.21         0.98         (0.95, 1.02)         3587           Ascending and adameter, mm         42.17+8.21         0.98         (0.94, 1.02)         3587           Ascending and adameter, mm         45.64+7.32         0.98         (0.94, 1.02)         24.86           Ascending and adameter, mm         45.64+7.32         0.98         (0.94, 1.02)         24.86           Onset time, d         17.9+17.6         0.48         (0.06, 3.48)         0.81         (0.67, 0.97)         0.230           Onset time, d         1.79+17.6         0.87         (0.74, 1.03)         0.986         0.81         (0.17, 0.99)         0.001         1.00         (0.98, 1.01)         5011           Pericardial effusion         22.17+46.79         0.98         (0.97, 0.99)         <.0001	1.02 (0.97, 1.08) .4403		33.09 + 5.30	0.98 (0.93, 1.03) .4619	
Ascending arta diameter, mm 45.64+7.32 0.98 (0.94, 1.02), 24.36 Acrit bialve malformation 15 (2.48%) 0.04 (0.06, 3.40), 4369 (0.57, 0.97), <b>0.230</b> 0.81 (0.67, 0.97), <b>0.230</b> 0.87 (1.03), 0.986 (0.97, 0.93) (0.67, 0.97), <b>0.237</b> 0.87 (1.03), 0.986 (0.97, 0.93) (0.98, 1.01), 5011 Pericardial effusion 72 (16.22%) 0.88 (0.97, 0.99) <- <b><i>MOOT</i></b> 1.00 (0.98, 1.01), 5011 Pericardial effusion 72 (16.22%) 0.98 (0.56, 1.71), 3945 (0.97, 0.935 (0.97, 0.935 (0.97, 0.935)) <- <b><i>MOOT</i></b> 1.00 (0.98, 1.01), 5011 Pericardial effusion 72 (16.22%) 0.98 (0.56, 1.71), 3945 (0.97, 0.945 (0.97, 0.945))	0.98 (0.95, 1.02) .3587		42.00+7.73	0.97 (0.94, 1.01) .1069	
Aprile branch and the dimension         1.1 (2.48%)         0.44 (0.00, 3.48)         0.340 (3.434)         0.341 (3.67, 0.97)         0.230           Onset time, d         1.79 +1.76         0.98 (0.74, 1.03)         0.986         0.81 (0.67, 0.97)         0.971 (3.611           Onset time, d         2.17 + 46.7         0.98 (0.97, 0.99)         0.98 (0.97, 0.99)         0.0001         1.00 (0.98, 1.01)         5011           Pericardial effusion         72 (16.22%)         0.98 (0.56, 1.71)         9345         1.00 (0.98, 1.01)         5011           Severe aortic regurgitation         164 (37.02%)         0.98 (0.56, 1.71)         9345         1.00 (0.98, 1.01)         5011           Log10 presperative Thi         0.10 (-1.11         0.56 (0.25, 1.20)         1.317         260 (1.16, 5.40)         0.48           I conf 0 costnerative Thi         0.71 + 0.47         463 (7.77) <-0.007	0.98 (0.94, 1.02) .2436		45.52 + 7.51	1.00 (0.97, 1.03) .8603	
Unset unit, a         1.79+1.1/b         U.St (U.74, 1.05), U986         U.St (U.57, U37), U37, U37), U37, U37, U37, U37, U37, U37, U37, U37	0.44 (0.06, 3.48) .4354		9 (2.06%)	1.58 (0.49, 5.11) .4406	
even, inclumin Pericardia effusion 72 (16.22%) 0.38 (v.37, 1.34) (5557 1.00 (v.36, 1.01) (5011 1.20 (v.36, 1.20) (1317 1.20 (v.36, 1.01) (5011 1.20 (v.36, 1.01) (5011 1.20 (v.36, 1.20) (1317 1.20 (v.36, 1.20) (1311 1.20 (v.36, 1.20) (0.26) (0.26) (1211 1.20 (v.36, 1.20) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.26) (0.	0.87 (0.74, 1.03) .0986	0.81 (0.67, 0.97) <b>.0230</b> 1 00 0 08 1 01) <b>5</b> 011	1./6+1./3	0.89 (0.78, 1.02) <b>.0990</b> 1 00 /1 00 -1 00) 8813	U. / 5 (U.6U, U.95) .U1/1
$\begin{array}{cccccc} restructured entration restructure r$	0.30 (0.31, 0.39) <001	1.00 (0.36, 1.01) .3011	93.U2 + 40.03 57 /16 010/	1.00 (1.00, 1.00) .0012 1.61 (0.04 - 2.75) .0707	1 F6 (0 74 2 76) 2422
Log10 province row regregation for the row rest in the row	0.02 (0.07, 1.04) .000/ 0.08 (0.56 1.71) 0345		J/ (10.01.%) 121 (35.80%)	1.01 (0.34, 2.7.0) .0797 1 1 8 (0 75 1 84) 4829	1.30 (0.14, 3.20) .2432
1 m10 nottinertive Tul 0 71 + 0 47 4 68 (2 76 7 77) < 0001 2 50 (1 16 5 40) 0198	0.55 (0.25, 1.20) .1317		$-0.14 \pm 1.16$	0.79 (0.57, 1.10) ,1680	
	4.63 (2.76, 7.77) <.0001	2.50 (1.16, 5.40) <b>.0198</b>	0.68 (0.45, 1.04) 0.0758	0.68 (0.45, 1.04) .0758	0.66 (0.32, 1.33) .2442
Log10 preoperative myoglobin 2.60 + 0.60 3.44 (2.02, 5.86) <.0001	3.44 (2.02, 5.86) < <b>.0001</b>	•	2.59 + 0.63	0.74 (0.51, 1.06) .0961	
Log10 postoperative myoglobin 2.78+0.44 5.51 (3.03, 10.04) <-0001	5.51 (3.03, 10.04) < <b>0001</b>		2.78 + 0.45	0.60 (0.30, 1.17) .1336	
Log10 preoperative CAMB 112+076 389 (233, 647) < 2007 1.81 (0.74, 4.42) ,1952	3.89 (2.33, 6.47) <.0001	1.81 (0.74, 4.42) .1952	1.13 +0.75	0.87 (0.67, 1.12) .2818	
	0.01 (4.29, 11.32) <.001	6 05 /1 61 00 66) 0076	1.46 + 0.38	U.83 (U.5U, I.4U) .4938 1 21 /0 82 1 20) 21E0	
Treuberative UN-1/10 - 2001 - 2014 (30:34.76) 3.12 (2.24, 0.10) - 2012 (1.21, 22:00) - 2010	0.12 (2.24, 0.10) <	0.00 (1.01, 22.00) .00/0	(0/. / C.C+) 1.02	1.21 (0.02, 1.19) .3430	



Figure 1. Impact of myocardial biomarkers levels on postoperative short and long-term mortality. CI=confidence interval, CK-MB=creatine kinase MB isoenzyme, HR=hazard ratio, Mb=myoglobin, post=postoperative, pre=preoperative, TnI=troponin I.

included surgical and nonsurgical patients.<sup>[18]</sup> Therefore, it is not possible to accurately evaluate the short- and long-term prognosis of preoperative myocardial markers in surgical patients, and it is not possible to guide the surgical decisionmaking. Only surgical patients were included in this study, and independent effect of preoperative myocardial markers on early mortality was confirmed. Interestingly, patients with higher perioperative myocardial markers showed a reduced trend in terms of long-term mortality, although the difference was not statistically significant. For the first time, we found some subgroups that affect the prediction effect of preoperative myocardial enzymes on early mortality, such as smoking, LVEDD, and onset time. This means that if the patient smoked, had a smaller left ventricular end-diastolic diameter, or had a



Figure 2. ROC curve of myocardial biomarkers for postoperative short-term mortality. AUC=area under curve, ROC=receiver operating characteristic.

shorter onset time, the elevation of myocardial enzymes should be more noteworthy, since its risk effects are significantly increased. Previous studies have reported that smoking is associated with increased troponin in response to subclinical myocardial injury, and mortality is significantly increased when smoking is coupled with increased troponin.<sup>[19]</sup> The conclusion that smaller LVEDD is more dangerous seems to be contrary to clinical experience because larger LVEDD seems to represent heart enlargement and poor cardiac function. We believe that this is because most patients with AD have chronic hypertension. Left ventricular hypertrophic cardiomyopathy suggests long-term poor blood pressure control. Once myocardial enzyme elevation occurs, it indicates a higher risk of early mortality after surgery. The relationship between ventricular thickness and prognosis in patients with AD is still unclear, which needs further study.<sup>[20]</sup> The mechanism by which shorter onset increases the risk of cardiac enzymes is unknown, we hypothesized that survival bias leads to this result. Patients with high myocardial enzyme died rapidly in the early stage of the disease, while patients with low myocardial enzyme level and at low risk remained. This results in a decreased risk of early death from myocardial enzymes over time.<sup>[2]</sup> Therefore, we believe that patients with high myocardial enzymes should not be delayed or wait for myocardial markers to decline, but should undergo prompt surgery in time and reverse the cause of myocardial injury.

The preoperative elevation of myocardial markers in patients with type A AD is mainly a result of coronary ischemia caused by blood pressure fluctuations, severe aortic regurgitation caused by type A dissection involving the aortic sinus, and cover of coronary ostia by intimal flap. But all of these conditions reversed in timely surgery, such as aortic sinus plasty or Bentall surgery. Therefore, in this study, postoperative myocardial markers were found to have stronger risk effects on the early mortality. But the prediction effect of preoperative myocardial markers on the early mortality of surgery is also acceptable and has a greater significance in clinical application.

In cardiac surgery, even without perioperative myocardial infarction, there is an increase in postoperative myocardial markers.<sup>[21]</sup> CPB and cardiac arrest caused by cardioplegia fluid



can lead to myocardial injury. Ischemia and reperfusion injury may also result in postoperative myocardial injury and necrosis. The reasons for the increase of myocardial markers after different cardiac surgery vary. Myocardial enzymes increased the most after valvular surgery and decreased to normal for a longer time. Compared with other cardiac surgery, AD surgery takes much longer time of extracorporeal circulation and aortic occlusion, the increase of postoperative myocardial markers is mainly attributed to the myocardial injury caused by CPB. In our study, the increase of postoperative TnI was mainly correlated with the increase of CPB, operative time, and preoperative CK-MB. Compared with other cardiac surgeries, type A AD surgery requires longer CPB time, operation time, and aortic clamp time, especially for total aortic arch replacement. Although our study did not focus on CPB related variables, we believe that a more detailed study should focus on CPB parameters such as





cardioplegia fluid solution, delivery of cardioplegic solution, and temperature of hypothermia with circulatory arrest. In order to review the current CPB strategy for aortic surgery, myocardial markers are not only associated with myocardial structural injury, but also reflect cardiac function.<sup>[22,23]</sup> In this study, the leading causes of death at 30 days were cardiovascular adverse events, including low cardiac output syndrome, fatal arrhythmias, myocardial infarction, tamponade, and aortic rupture. However, the long-term mortality to the end point of follow-up was mainly related to diabetes, coronary heart disease, and other chronic morbidity, and the death was less related to short-term myocardial injury after surgery, and perioperative myocardial markers could not predict long-term prognosis.

With the mature of the early diagnosis and surgical technology of aortic disease, current research hot spots are to shorten diagnosis delay, shorten delay from onset to surgery, and evaluate long-term outcome in different subgroups.<sup>[24,25]</sup> Myocardial markers, as a widely used screening tool for chest pain units, are often detected in the initial diagnosis of aortic disease. Especially the widespread of standardized sensitive assay, it is possible to test for perioperative myocardial markers in routine diagnosis and treatment of all patients with AD. Although myocardial markers could not predict the long-term all-cause mortality of patients undergoing AD, they could significantly predict the short-term prognosis. Therefore, we believe that myocardial marker examination, especially postoperative myocardial marker examination in the intensive care unit, should be a routine examination item for patients with type A AD. Because this can detect small area of myocardial injury or perioperative myocardial infarction in advance, and guide the timely response measures such as angiography or extracorporeal membrane oxygenation support.

Previous studies on perioperative myocardial enzymes and long-term mortality in cardiac surgery have drawn different conclusions. Bojan et al found that troponin can only predict long-term mortality in patients without effective intraoperative myocardial protection and suffer from perioperative myocardial infarction.<sup>[26]</sup> Bottio et al found that cardiac surgery patients with troponin greater than  $35 \,\mu$ g/L or cardiac insufficiency at discharge would recover after 1 year of follow-up.<sup>[27]</sup> In our study, no significant relationship was found between perioperative myocardial markers and long-term mortality after AD, suggesting that the increase in perioperative myocardial enzymes in patients with AD was mainly attributed to CPB and the recoverable temporary myocardial injury caused by preoperative acute ischemia. Although our study demonstrated that preoperative elevated myocardial enzymes increased postoperative mortality, currently, coronary artery involvement by dissection is an indication of the need for emergency surgical management of AD. Therefore, the association between myocardial enzymes and mortality after AD should be a prompt for careful observation and timely response and should not interfere with surgical treatment decisions.

## 5. Limitaion

This study based on a large type A AD patient sample of single center in China. Whether the results can be applied to other races requires other research verification. In addition, it is worth noting that previous studies also suggest that the continuous increase of myocardial enzymes 24 hours after surgery reflects the occurrence of perioperative myocardial infarction. But in our study, the postoperative mean measurement time of myocardial enzyme was 6 hours in the early postoperative period, so more studies should be carried out to further verify whether postoperative late myocardial enzyme elevation is also irrelevant to long-term prognosis.

### 6. Conclusion

Both preoperative and postoperative cardiac biomarkers levels were independent predictor for early mortality in Stanford A AD. Early postoperative myocardial markers, including hs-TnI, CK-MB, and Mb, reflect both preoperative myocardial ischemia and intraoperative CPB injury, have better efficacy in predicting early mortality. Comparative analysis showed postoperative hs-TnI had stronger prognostic value for early mortality to CK-MB and Mb. Neither preoperative nor postoperative myocardial markers can predict the long-term all-cause mortality after Stanford A AD surgery. The causes of perioperative changes of myocardial markers in patients with AD deserve further study to identify high-risk groups and take early action.

## Author contributions

**Conceptualization:** Ming Gong, Wenjian Jiang, Hongjia Zhang. **Data curation:** Zining Wu.

Formal analysis: Zining Wu.

Funding acquisition: Hongjia Zhang, Ming Gong, Wenjian Jiang. Methodology: Ming Gong.

Project administration: Ming Gong.

Supervision: Ming Gong, Hongjia Zhang.

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