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PROGNOSTIC IMPACT OF AORTIC- CROSS CLAMP TIME IN CORONARY ARTERY BYPASS GRAFTING SURGERY

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ABSTRACT

Objective: The aim of this study is to estimate the prognostic value of aortic- cross clamping time in predicting outcomes after on-pump CABG and to identify the limits of the safe time. **Patients and Methods:** Retrospective Analytical Prognostic Study conducted for the period four years(January 2017-January 2020) at Tishreen University Hospital and Al-Bassel hospital in Lattakia-Syria. 318 patients who underwent on-pump CABG were included in the study. **Results:** Mean age was 58.8±8.6years, 74.5% were males. When the peak aortic-clamp time during CABG reached 74 min, in hospital mortality could be predicted with an area under the ROC curve of 0.69(95% CI:0.48-0.90) with a sensitivity of 71% and specificity of 64.6%. The time of CPB and operation was longer with increasing cross-clamp time(153.4±27.1 vs. 114.3±26.7, p: 0.0001) and(5.5±0.7 vs. 4.5±0.7, p:0.01) respectively. Using bilateral internal mammary arteries and radial artery was more frequently in patients with longer cross-clamp time($p<0.05$). Aortic- cross clamping time≥74 min was associated with significantly increased risk of mortality(HR: 4.5; 95% CI: 0.1-12.9, P:0.0001), re –exploration due to bleeding(HR: 4.9; 95% CI: 1.3-11.2, P:0.0001), prolonged inotropic dependency(HR: 3.6; 95% CI: 1.3-6.2, P:0.003), In ICU stay (HR: 2.9; 95% CI: 0.2-9.5, P:0.002),and kidney injury(HR: 2.3; 95% CI: 0.9-5.6, P:0.01). **Conclusion:** Prolonged aortic- cross clamping time was associated with increased mortality and morbidity, and this effect increases with increasing this time.

KEYWORDS: Aortic- cross clamping time, on-pump CABG, mortality.

INTRODUCTION

Coronary artery bypass graft (CABG)surgery is still the most commonly performed cardiac surgery procedure worldwide since its first introduction in 1967 by Rene Favaloro.[1,2] CABG treats coronary artery disease(CAD) in certain circumstances, improves blood flow to the heart by creating a new pathway for oxygen rich blood. Consequently, improving quality of life and reducing cardiac-related mortality.[3,4]

The two basic ways of performing CABG are on -pump and off -pump. On-pump causes better revascularization as compared to off -pump CABG, but the resultant inflammatory effects of cardiopulmonary bypass(CPB) machine and aorta manipulation in on-pump CABG cause post-operative morbidity and mortality especially in high risk patients. Complications include mainly: ischemic heart disease, atrial fibrillation, stroke. In addition to, renal, pulmonary, and hematologic complications.[5,6]

Prolonged aortic- cross clamping time causes important physiologic changes that can result in major complications in many systems. These changes include: increasing systemic vascular resistance and decreasing cardiac output.[7,8] The exact reasons are not obvious and may include: decreasing blood volume as a result of hydrostatic pressure-induced transcapilliary fluid shifts, and releasing vasoactive substances.[9] Many clinical studies have demonstrated that aortic- cross clamping time is an independent risk factor for adverse outcome following cardiac surgery. The present study aimed to

determine whether aortic- cross clamping time is associated with increased morbidity and mortality rates after on- pump CABG.

PATIENTS AND METHODS

This is Retrospective Analytical Prognostic Study of a group of patients attending the Cardiovascular Surgery Department's at Tishreen University Hospital and Al-Bassel hospital in Lattakia-Syria during four years period (January 2017 to January 2020), and underwent to on – pump CABG surgery. The following data were recorded: Demographic data including age, sex, and co-morbidities. Blood samples were collected pre-operatively for measurement of renal function. Echocardiogram was performed for all patients for measurement ejection fraction(EF).

Surgical technique: All surgeries were performed under general endotracheal anesthesia, standard cardiopulmonary bypass(CPB) procedure with ascending aortic cannulation, and anterograde cardioplegic solution was used to arrest the heart. The grafts used were left and right internal mammary artery as well as radial artery. The intraoperative variables included CPB time, aortic-clamp time, and number of grafts were recorded. The primary outcome was in-hospital mortality. Secondary outcomes were length of intensive care unit(ICU) and hospital stay and postoperative complications.

Ethical consideration: All patients were provided a complete and clear informed consent after discussion about the study. This study was performed in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations(SD), median, Frequency and percentages. Independent t student test or Mann Whitney test was used to compare 2 independent groups. Differences among different groups were examined with using chi- square test or Fisher exact test. The receiver operating characteristics(ROC) curves were constructed, and the area under curve(AUC) was established to assess the ability of peak aortic-clamp time in predicting outcomes of on-pump CABG. The cutoff value for peak aortic-clamp time was determined with ROC curves using Youden index. Multiple logistic regression analysis was performed to estimate independent predictive factors for mortality. This model included risk factors first identified through univariate analysis. P value <0.05 was considered as statistically significant.

RESULTS

A total of 318 patients who presented to the Department of Cardiovascular surgery from January 2017 to January 2020 were included in the study. The mean age of patients who enrolled in the study was 58.8±8.6 years, 74.5% of the patients were males. The AUC of ROC was 0.69(95% CI:0.48-0.90), Figure1.

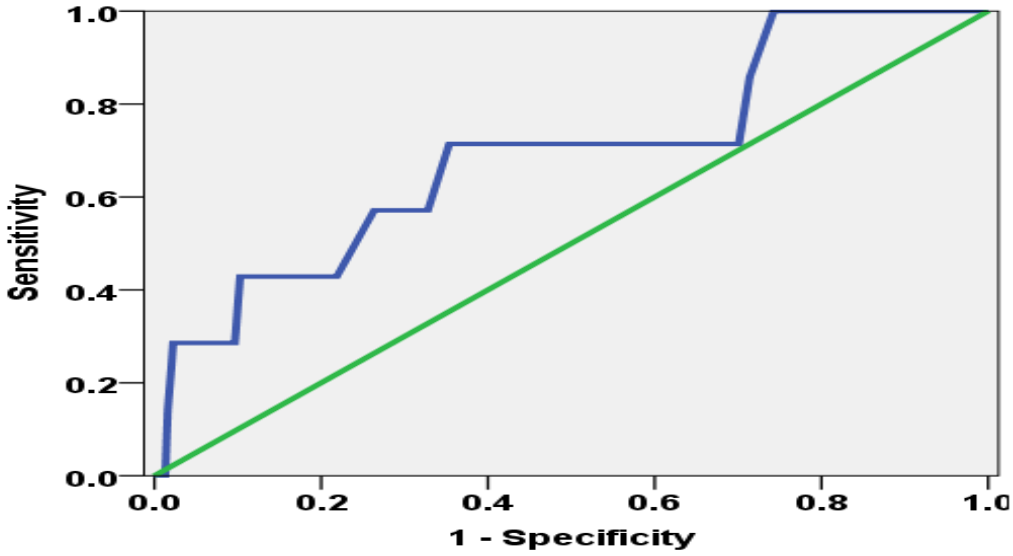

Figure 1: Receiver operating characteristics curve presenting ability of peak aortic-clamp time in predicting mortality after on-pump CABG.

The best cutoff value of aortic-clamp time that can be used to predict in-hospital mortality was 74 min with sensitivity 71% and specificity 64.6%. Based on this cutoff value, patients were divided into two groups: <74 min and ≥74 min. The baseline characteristics of patients are as given in table(1). The mean EF was significantly lower in group 2 compared to group 1(50.7±10.4 vs. 54.4±9.1, p:0.001). Creatinine levels were higher in the group 2, but without significant differences(1.8±0.3 vs. 1.05±0.2, p:0.1). There were no statistically significant differences between the two groups regarding to; age, sex, and co-morbidities(p>0.05).

Table 1: Demographic characteristics of the study population.

Variables	Group 1 <74 min(203)	Group 2 ≥74 min (115)	P value
Age(years)	59.6±8.5	57.6±8.6	0.05
Sex Male Female	 150(73.9%) 53(26.1%)	 87(75.7%) 28(24.3%)	 0.7
Co-morbidities Diabetes mellitus Atrial fibrillation Pulmonary diseases Cerebrovascular accident(CVA) Left coronary stem stenosis Previous cardiovascular surgery Previous stent placement	 87(42.9%) 1(0.5%) 12(5.9%) 11(5.4%) 16(7.9%) 2(1%) 27(13.3%)	 52(45.2%) 1(0.9%) 8(7%) 4(3.5%) 16(13.9%) 2(1.7%) 14(12.2%)	 0.6 0.6 0.7 0.4 0.08 0.5 0.7
Laboratory findings Creatinine levels	 1.05±0.2	 1.8±0.3	 0.1
Echocardiographic findings EF	 54.4±9.1	 50.7±10.4	 0.001

As shown below in table(2); there were significant differences between two groups regarding to number and type of grafts, in which the mean number of distal anastomoses was higher in group2(3.8±0.7 vs. 3.1±0.6, p:0.002), bilateral internal mammary arteries and radial artery were more frequently used in group2 compared to group 1($p<0.05$). The operation time and CPB time were longer in group2; (5.5±0.7 vs. 4.5±0.7,p:0.01) and(153.4±27.1 vs. 114.3±26.7, p: 0.0001) respectively. There were no significant differences between two groups regarding to the type of Cardioplegia.

Table 2: Intraoperative parameters of the study population.

Variables	Group 1 <74 min(203)	Group 2 ≥74 min(115)	P value
Number of distal anastomoses	3.1±0.6	3.8±0.7	0.002
Bilateral internal mammary arteries	2(0.9%)	8(6.9%)	0.04
Radial artery	13(6.4%)	14(12.2%)	0.04
Cardioplegia • Crystalloid • Blood	 84(41.4%) 119(58.6%)	 43(37.4%) 72(62.6%)	 0.4
Operation time(hour)	4.5±0.7	5.5±0.7	0.01
CPB time(min)	114.3±26.7	153.4±27.1	0.0001
EF(after surgery)	46.4±8.2	41.2±8.2	0.002

Prolonged inotropic dependency, re –exploration due to bleeding, and kidney injury were significantly more frequently in group2:(17.4% vs. 5.4%), (11.3% vs. 1.5%), and (5.2% vs. 1.5%), respectively. In hospital stay was significantly longer in group2 (7.1±2.6 vs. 5±1.9, p: 0.0001), as well as in ICU stay(3.1±2.2 vs. 2.3±1.3,p:0.01). Mortality rate was higher in patients with aortic-clamp time≥74 min(4.3% vs.1%, p:0.03), Table 3.

Table 3: Primary and secondary outcomes.

Variables	Group 1 <74 min(203)	Group 2 ≥74 min(115)	P value
Prolonged inotropic dependency	11(5.4%)	20(17.4%)	0.001
CVA	4(2%)	2(1.7%)	0.8
Use of Intra –aortic balloon pump	6(3%)	4(3.5%)	0.7
Re –exploration due to bleeding	3(1.5%)	13(11.3%)	0.0001
Atrial fibrillation	24(11.8%)	15(13%)	0.7
Sternal wound infection	1(0.5%)	1(0.9%)	0.6
Kidney injury	3(1.5%)	6(5.2%)	0.04

In hospital stay(days)	5±1.9	7.1±2.6	0.0001
In ICU stay	2.3±1.3	3.1±2.2	0.01
Death	2(1%)	5(4.3%)	0.03

Patients with longer aortic-clamp time(≥74 min) were associated with higher risk of mortality(HR: 4.5; 95% CI: 0.1-12.9, P:0.0001), Re –exploration due to bleeding(HR: 4.9; 95% CI: 1.3-11.2, P:0.0001), prolonged inotropic dependency(HR: 3.6; 95% CI: 1.3-6.2, P:0.003), In ICU stay (HR: 2.9; 95% CI: 0.2-9.5, P:0.002), and kidney injury(HR: 2.3; 95% CI: 0.9-5.6, P:0.01), Table(4).

Table 4: The effect of prolonged aortic-clamp time on the clinical outcomes.

Variables	HR	P value
Prolonged inotropic dependency	3.6[1.3-6.2]	0.003
Death	4.5[0.1-12.9]	0.0001
In ICU stay	2.9[0.2-9.5]	0.002
Re –exploration due to bleeding	4.9[1.3-11.2]	0.0001
Kidney injury	2.3[0.9-5.6]	0.01

The previous HRs were represented in the Figure(2)

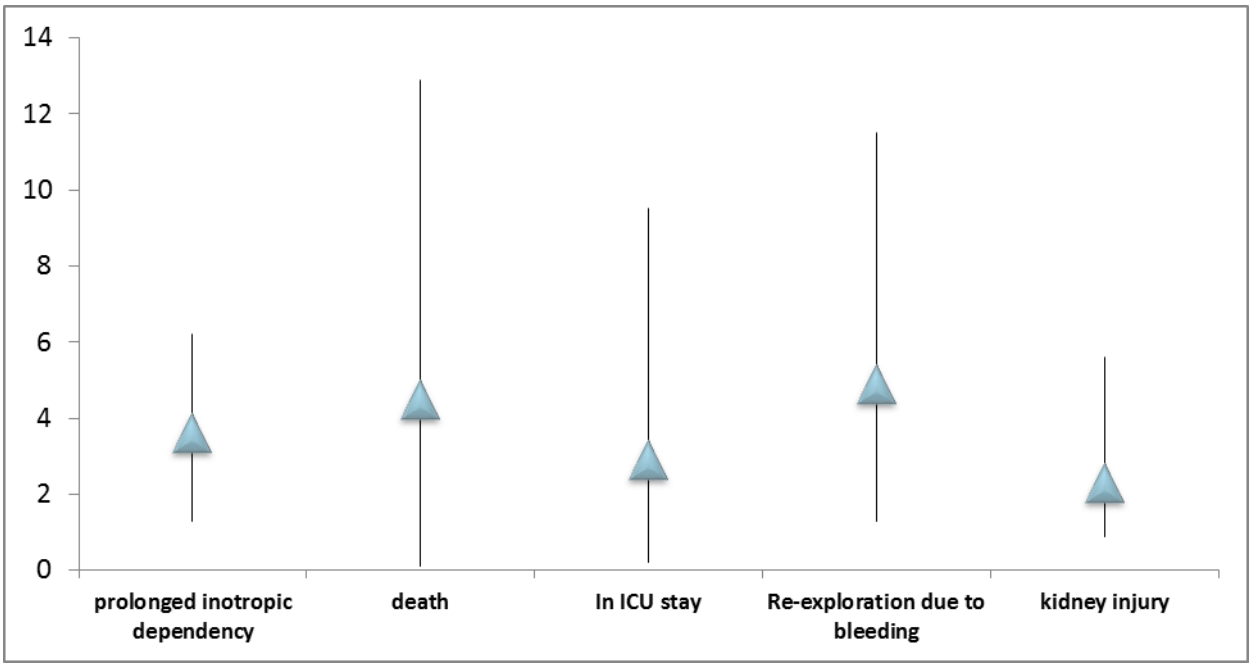

Figure (2) Multivariate analysis shows effects of prolonged aortic-clamp time on the clinical outcomes in the study population.

DISCUSSION

This study aimed to determine how aortic-clamp time is associated with both early morbidity and mortality among patients undergoing on pump CABG.

The results of the current study of 318 patients showed that most patients were males. The cutoff value of aortic-clamp time 74 min was a significant predictor of mortality. Prolonged aortic-clamp time correlated significantly with decreased EF, prolonged CPB time, and increased the number of distal anastomoses that used. Patients with prolonged aortic-clamp time were at increased risk of death and some complications included prolonged ICU stay, kidney injury, prolonged inotropic dependency, and re –exploration due to bleeding.

The exact mechanisms that can explain the association between prolonged aortic-clamp time and observed mortality and morbidity are very few. Firstly, ischemic injury resulted from prolonged aortic-clamp time that is still noted to affect directly on mortality rate after surgery in spite of better myocardial protection. Secondly, increasing in catecholamine(epinephrine and norepinephrine) release levels during cross-clamping of aorta, and this effect could be amplified by the prolonged time.[10,11] These results are comparable to the findings reported by the limited previous studies that evaluated the prognostic effect of aortic cross-clamping time on outcomes in patients undergoing on-pump CABG.

Mohamed *et al*., (2017) showed that mechanical ventilation time was up to one day in 83.33% of patients undergoing to on-pump CABG when the mean time of cross clamp was 73 min, and with increasing the time (135 min), the post-operative ventilation was up to three days in 16%.[12]

Vito *et al*., (2018) recognized that a peak aortic cross-clamping time higher than 75 min was an independent predictor of prolonged treatment with inotropes, use of intra-aortic balloon pump and extracorporeal membrane oxygenation, acute kidney injury, ICU stay> 2days and mortality.[13]

In summary, aortic cross-clamping time is an independent predictor of postoperative mortality and morbidity despite recent surgical and technical advances. Prior knowledge on this effect can help in preventing these complications.

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