Predictive factors of intraoperative hemodynamic deterioration during multivessel off-pump coronary artery bypass surgery

Jun Na Hyung

Department of Medicine

The Graduate School, Yonsei University

Predictive factors of intraoperative hemodynamic deterioration during multivessel off-pump coronary artery bypass surgery

Directed by Professor Bae Sun Jun

The Master's Thesis
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the
degree of Master of Medical Science

Jun Na Hyung

December 2007

This certifies that the Master's Thesis

of Jun Na Hyung is approved.

Thesis Supervisor : Bae Sun Joon

[Kwak Young Lan: Thesis Committee Member#1]

[Ha Jong Won: Thesis Committee Member#2]

The Graduate School

Yonsei University

December 2007

ACKNOWLEDGEMENTS

The author thanks Prof. Bae Sun Joon, Prof. Kwak Young Lan, Prof. Ha Jong won, Prof. Shim Jae Kwang and Chun Duk Hee.

<TABLE OF CONTENTS>

<LIST OF TABLES>

<ABSTRACT>

Predictive factors of intraoperative hemodynamic deterioration during multivessel off-pump coronary artery bypass surgery

Jun Na Hyung

Department of Medicine or Medical Science

The Graduate School, Yonsei University

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Introduction

Due to the advances in stabilization devices, surgical technique and anesthetic management strategies, multivessel off-pump coronary artery bypass surgery (OPCAB) has gained increased popularity with comparable safety and early graft patency to conventional on-pump coronary artery bypass grafting (CABG) [1,2]. For complete revascularization during OPCAB, the heart

must be lifted and tilted in order to expose the posterior and lateral wall of the heart. This displacement of the heart causes increase in atrial pressures, decrease in cardiac index (CI) leading to a reduced mixed venous saturation (SvO_2). The positional change of the apex increases the filling pressure and the size of the atria which impairs diastolic filling and causes diastolic dysfunction[5]. These changes may cause significant hemodynamic derangement leading to emergent conversion to on-pump CABG. The patients who required conversion to on-pump have significantly higher operative mortality and morbidity than either completed OPCAB or on-pump CABG patients [6, 7]. Therefore we evaluated the relationship between preoperative patients' characteristics including indices of diastolic function with drop in SvO_2 during grafting as a marker of hemodynamic deterioration during mechanical displacement of the heart and their effects on patients' outcome following multivessel OPCAB

Patients and Methods

A total of 204 consecutive patients scheduled for elective, isolated, multivessel OPCAB at Severance Hospital between March 2006

and September 2007 were studied prospectively. During the period of heart displacement, mean systemic arterial pressure was maintained above 70 mmHg with norepinephrine infusion. SvO_2 was calibrated using venous blood gas analyses, 15 min after the induction and during Y-graft construction and continuously monitored. Patients were allocated into two groups according to SvO_2 values during grafting; 1) patients with $SvO_2 \geq 60\%$, Group 1, 2) patients with $SvO_2 < 60\%$, Group 2. Patients' characteristics and preoperative transthoracic echocardiographic variables including indices of diastolic function were LVEF, degree of MR, LVEDD, LVESD, IVSd, IVSs, LA volume index, and E/E' were assessed. Intraoperative characteristics including operation time, number of grafts performed, total duration of distal anastomoses, and total amount of infused fluid and urine output and postoperative data including 24h postoperative CK-MB level, length of stay in the ICU and total length of postoperative hospitalization were evaluated. To characterize the patients developing decrease in SvO_2 and its effect on postoperative outcome, data between the groups were compared using Chi-square test, Fisher's exact test or independent t-test as

appropriate.

Results

None of the patients required conversion to emergency on-pump CABG. The increased preoperative echocardiographic index of diastolic function (E/E'), advanced age and increased LVEF were independent risk factors of more pronounced hemodynamic deterioration during grafting. The patients who had decreased SvO_2 to below 60% during grafting required significantly longer length of postoperative hospitalization.

Conclusion

The appropriate therapeutic measures, such as use of inotropic support and elective on-pump CABG should be considered in patients with increased preoperative echocardiographic index of diastolic function (E/E'), advanced age and increased LVEF.

Key words : OPCAB, SvO2, emergency conversion to on-pump CABG, hemodynamic, diastolic dysfunction

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I. INTRODUCTION

Due to advances in stabilization devices, surgical technique and anesthetic management strategies, multivessel off-pump coronary artery bypass surgery (OPCAB) has gained increased popularity with comparable safety and early graft patency to conventional on-pump coronary artery bypass grafting (CABG) [1,2]. Also, increasing number

of studies validated advantages of OPCAB over on-pump CABG with regard to shorter postoperative stay in the intensive care unit (ICU), less transfusion requirement and cardiac enzyme release [2,3,4].

For complete revascularization during OPCAB, the heart must be lifted and tilted in order to expose the posterior and lateral wall of the heart. This displacement of the heart causes increase in atrial pressures, decrease in cardiac index (CI) leading to a reduced mixed venous saturation (SvO_2). Also the stabilization devices induce further decrease in cardiac output by compressing the ventricular wall and causing wall motion abnormality. The positional change of the apex increases the filling pressure and the size of the atria which impairs diastolic filling and causes diastolic dysfunction. [5]. These changes may cause significant hemodynamic derangement leading to emergent conversion to on-pump CABG.

Not surprisingly, patients who were intended for an off-pump strategy and then required conversion to on-pump have significantly higher operative mortality and morbidity than either completed OPCAB or on-pump CABG patients [6, 7]. This data mandates identification of risk factors in patients undergoing OPCAB that would help prevent the need for emergency conversion to on-pump CABG.

It has been proposed to consider conversion to on-pump CABG, when

CI < 2.0 L/min/m^2 and/or SvO_2 < 60% for more than 15 min in spite of any aggressive therapy. Hemodynamic deterioration caused by mechanical displacement of the heart during grafting is mainly the result of impairment of diastolic filling and dysfunction [5]. Therefore, patients with pre-existing diastolic dysfunction would be more prone to undergo significant hemodynamic deterioration, and evaluation of relationship between preoperative indices of diastolic function and intraoperative hemodynamic deterioration should also be assessed.

We therefore evaluated the relationship between preoperative patients' characteristics including indices of diastolic function with drop in SvO_2 during grafting as a marker of hemodynamic deterioration during mechanical displacement of the heart and its effect on the outcome of patients undergoing multivessel OPCAB.

II. PATIENTS AND METHODS

Following the approval of institutional review board and patients' consent, 204 consecutive patients scheduled for elective, isolated, multivessel OPCAB at Severance Hospital between March 2006 and September 2007 were studied prospectively.

All patients received 0.05 to 0.1 mg/kg of morphine intramuscularly as premedication 1 hour before the operation and cardiac medications except diuretics and antiplatelet agents were continued until the morning of the surgery. On arrival in the operating room, standard monitoring devices were applied, including a pulmonary artery catheter (Swan-Ganz CCombo CCO/SvO_2; Edwards LifeSciences, Irvine, Calif), which was inserted via the right internal jugular vein before induction of anesthesia. Anesthesia was induced with intravenous midazolam (2.0-3.0 mg) and sufentanil (1.5-3.0 μg/kg) and maintained with sevoflurane (0.4%-1.0%) and continuous infusion of sufentanil (0.5-1.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Neuromuscular blockade was achieved by administering rocuronium (0.9 mg/kg) and maintained with continuous infusion of vecuronium (1-2 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Isosorbide dinitrate 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ was infused in all patients throughout the study period. The patient's lung was ventilated with a tidal volume of 8-10 mL/kg, and inspiratory/expiratory ratio of 1:2, and an inspiratory pause 10% of total inspiration time at a rate of 8 to 12

breaths/min in 40% oxygen with air. After the induction of anesthesia, a transesophageal echocardiography probe was inserted to assess global cardiac performance, and to detect newly developing segmental wall motion abnormalities as well as changes in the severity of mitral regurgitation during mechanical displacement of the heart. Intravascular volume replacement was managed with crystalloid and colloid solutions to maintain the pulmonary capillary wedge pressure between 8 and 14 mmHg according to the baseline values before enucleation of the heart. Central blood temperature measured by the pulmonary artery catheter was maintained above 36℃ with a warm mattress, forced warm air blanket and fluid warmer as necessary.

All surgical procedures were performed by one surgeon through a median sternotomy. During the period of heart displacement, mean systemic arterial pressure was maintained above 70 mmHg either with a 10° to 20° Trendelenburg position and/or norepinephrine infusion. Intracoronary shunt was inserted in all patients during grafting at the left anterior descending coronary artery. Criteria for emergency conversion to on-pump CABG were one or more of the following conditions despite aggressive therapy; 1) fall in mean arterial pressure to < 50 mmHg, 2) intractable ventricular arrhythmias, 3) persisting changes in ST segments, 4) increase in mean pulmonary artery pressure to near systemic mean

arterial pressure, 5) left ventricular distention with bradycardia, 6) SvO_2 < 60% for more than 15 min.

A cell salvage device was used and salvaged blood was re-infused to the patient before the end of the operation. Allogenic packed red blood cells were transfused when the hemoglobin level was below 8 mg/dL throughout the study period. All patients were transferred to the ICU after the operation.

SvO_2 was calibrated using venous blood gas analyses, 15 min after induction of anesthesia and during Y-graft construction and continuously monitored (Vigilance,™ Edwards Lifesciences LLC, Irvine, CA, USA) throughout the study period. Patients were allocated into two groups according to SvO_2 values during grafting; 1) patients with $SvO_2 \geq 60\%$, Group 1, 2) patients with $SvO_2 < 60\%$, Group 2.

Preoperative patients' characteristics including age, gender, body surface area, history of MI within 1 month, presence of unstable angina, cardiothoracic ratio on the chest PA, serum creatinine and creatine kinase-MB (CK-MB) level were assessed. Preoperative transthoracic echocardiographic variables including indices of diastolic function were LVEF, degree of mitral regurgitation, left ventricular end-diastolic and systolic diameter (LVEDD, LVESD), interventricular septal thickness in diastole and systole (IVSd, IVSs), left atrial (LA) volume index, and the

ratio of mitral velocity to early diastolic velocity of the mitral annulus (E/E') were also assessed. Intraoperative characteristics including operation time, number of grafts performed, total duration of distal anastomoses, and total amount of infused fluid and urine output and postoperative data including 24h postoperative CK-MB level, length of stay in the ICU and total length of postoperative hospitalization were evaluated.

Statistical analysis was performed with SPSS 12.0 software (SPSS, INC, Chicago, Ill). To characterize the patients developing decrease in SvO_2 and its effect on postoperative outcome, data between the groups were compared using Chi-square test, Fisher's exact test or independent t-test as appropriate. Predictive factor for SvO_2 decline during OPCAB were evaluated using multivariate logistic regression with. A p value of less than 0.05 was considered statistically significant.

III. RESULTS

OPCAB could be successfully performed in all 204 patients with none of the patients requiring conversion to emergency on-pump CABG.

Number of patients allocated to Group 1 and 2 were 154 and 50 respectively.

Preoperative patients' characteristics were similar between the groups (Table 1). In intergroup comparisons of preoperative transthoracic echocardiographic variables, E/E' value was significantly higher in Group 2 (Table 2). In univariate analysis for predictors of drop in SvO_2, age, gender, presence of unstable angina, cardiothoracic ratio, creatinine, CK-MB, LVEF, degree of mitral regurgitation, LA volume index and E/E' were found to be significant risk factors. In multivariate logistic regression analysis of these variables, only age, LVEF and E/E' were found to be independent predictors of SvO_2 decline below 60% during OPCAB (Table 3).

Intraoperative characteristic were similar between the groups (Table 4).

In intergroup comparisons of postoperative variables, patients in Group 2 required significantly longer length of postoperative hospitalization (Table 5).

Table 1. Comparison of patients' characteristics.

	Group1 (n =154)	Group 2(n =50)
Age (years)	63.7±7.8	66.2±7.3
Gender (M/F)	114/40	26/24
Body surface area (m^2)	1.7±0.1	1.7±0.2
Myocardial infarction within 1 month	36	12
Unstable angina	36	10
Cardiothoracic ratio	52.6±5.8	54.9±6.6
Creatinine (mg/dL)	1.2±1.3	1.6±2.4
Creatine kinase-MB (ng/ml)	3.4±4.8	4.7±6.6

Data are expressed as mean Data are expressed as mean ± SD or number of patients and all p values were not significant. Group1, patients with $SvO_2 \geq 60\%$ during grafting; Group 2, patients with $SvO_2 < 60\%$ during grafting.

Table 2. Comparison of preoperative echocardiographic variables.

	Group 1	Group 2
Left ventricular ejection fraction (%)	54.7±15.3	57.8±14.1
Mitral regurgitation (grade)	0.57±0.3	0.73±0.5
Left ventricular EDD (mm)	51±6	51.3±5.5
Left ventricular ESD (mm)	36.3±7.7	35.8±6.8
Thickness of IVSd (mm)	9.7±1.9	9.6±1.6
Thickness of IVSs (mm)	12.5±2.2	12.4±2
Left atrial volume index (ml/m^2)	26.4±8.5	28.4±10.1
E/E’	13.7 ± 6.3	16.1 ± 5.1*

Data are expressed as mean Data are expressed as mean ± SD. Group1, patients with $SvO_2 \geq 60\%$ during grafting; Group 2, patients with $SvO_2 < 60\%$ during grafting; EDD, end-diastolic diameter; ESD, end-systolic diameter; IVSd, interventricular septum in diastole; IVSs, interventricular septum in systole; E/E’, ratio of mitral velocity to early diastolic velocity of the mitral annulus. *, $p < 0.05$.

Table 3. Multivariate analysis for predictors of SvO_2 decline during grafting.

	Odds ratio	95% Confidence interval	P-value
Age	1.098	(1.009, 1.195)	0.0301
Gender (F vs. M)	1.471	(0.508, 4.263)	0.4771
Unstable angina	0.889	(0.203, 3.900)	0.8765
Cardiothoracic ratio	1.033	(0.940, 1.135)	0.5036
Creatinine	1.176	(0.723, 1.915)	0.5134
Creatine kinase-MB	1.032	(0.945, 1.127)	0.4823
Left ventricular ejection fraction	1.068	(1.005, 1.135)	0.0349
Degree of mitral regurgitation	1.971	(0.587, 6.617)	0.2727
Left atrial volume index	1.054	(0.998, 1.123)	0.1093
E/E’	1.133	(1.028, 1.249)	0.0119

E/E’, ratio of mitral velocity to early diastolic velocity of the mitral annulus.

Table 4. Comparison of operative characteristics.

	Group 1	Group 2
Duration of operation (min)	370±56	371±66
Number of grafts performed (n)	3.2±0.9	3.5±0.8
Duration of distal anastomosis (min)	16±8	15±4
Amount of infused fluid (ml)	3904.4±1183.3	3920.5±1293.9
Amount of urine output (ml)	952.3±597.6	1019.3±855.7

Data are expressed as mean Data are expressed as mean ± SD. Group1, patients with $SvO_2 \geq 60\%$ during grafting; Group 2, patients with $SvO_2 < 60\%$ during grafting.

Table 5. Comparison of postoperative variables.

	Group 1	Group 2
24h postoperative CK-MB (ng/ml)	10.8±18.8	8.9±5.6
Length of stay in the ICU (days)	3.6±1.4	5.9±11.4
Length of postoperative hospitalization (days)	13 ± 6.1	18 ± 13.8

Data are expressed as mean Data are expressed as mean ± SD. Group1, patients with $SvO_2 \geq 60\%$ during grafting; Group 2, patients with $SvO_2 < 60\%$ during grafting; CK-MB, creatine kinase-MB; ICU, intensive care unit. *, $p < 0.05$.

IV. DISCUSSION

In this study, we evaluated the predictors for SvO_2 decline as a marker of hemodynamic deterioration during OPCAB and the age, LVEF and echocardiographic index of diastolic function were the independent risk factors for SvO_2 decline during grafting. Additionally, the patients experiencing SvO_2 decline below 60% required significantly longer length of postoperative hospitalization, despite the fact that SvO_2 decline was only less than 15 minutes.

Advances in stabilizing devices and anesthetic techniques have enabled complete revascularization in OPCAB with comparable safety and graft patency to on-pump CABG [1,2]. Furthermore, OPCAB has several theoretical advantages to on-pump CABG, including less inflammatory reaction, avoidance of emboli related to cannulation and more physiologic myocardial preservation [9]. In accordance, a number of studies have pointed out better outcomes of OPCAB including lower myocardial enzyme release, better neurological outcome, fewer blood transfusion and shorter length of postoperative recovery [10,11,12].

However, OPCAB has two unique problems regarding the hemodynamic instability during grafting. Firstly, the heart must be displaced to expose the anastomotic site therefore altering the geometry of the heart leading to hemodynamic instability. Displacement of the

heart during anastomosis causes hemodynamic consequences such as increase in atrial and filling pressures, decrease in cardiac output, reduced SvO_2 as well as functional mitral regurgitation due to distortions of the mitral annuli [5]. Secondly, temporary interruption of coronary blood flow is required to provide bloodless anastomotic conditions, which may cause various degree of myocardial damage [5,18,21]. In clinical practice, period of target vessel occlusion is usually confined to approximately 15 min and the mechanical as well as ischemic insult to the myocardium is usually well tolerated in most patients [1,2,5]. However, some patients do not tolerate the mechanical and ischemic burden imposed on the myocardium and require emergent conversion to on-pump CABG. This may expose patients to significantly higher morbidity and mortality, especially when patients have to be prepared for cardiopulmonary bypass while the diseased coronary artery has already been dissected and occluded [7]. Not surprisingly, patients who underwent conversion to on-pump CABG have significantly higher operative mortality and morbidity than patients underwent either completed OPCAB or on-pump CABG patients [6,7]. These findings suggest the need for identifying predictors of hemodynamic deterioration to avoid emergent conversion to on-pump CABG, hence improving the patients' outcome. Among the suggested criterias for considering

conversion to on-pump CABG after positioning the heart for grafting, CI and SvO_2 are one of the major determinants [5,14]. Importance of maintaining CI and SvO_2 as an indicator of adequate circulation has been emphasized. In OPCAB, distortion of the tricuspid annulus from heart displacement may result in various degree of tricuspid regurgitation or even stenosis and CI measured with right-sided pulmonary artery catheter during mechanical displacement of the heart might be unreliable during distal coronary anastomosis [5]. In contrast to CI, SvO_2 measured by the pulmonary artery catheter is not affected by changes in normal geometry of the heart during grafting and provides reliable index of global oxygen delivery/requirement relationship [22]. As long as the metabolic rates of the major organs remain constant, it could be a more reliable index of adequate cardiac output. Thus, we defined hemodynamic deterioration as SvO_2 decline below 60% during coronary anastomosis in this study.

In the current literature, no comprehensive data exists regarding predictors of hemodynamic instability and conversion to on-pump CABG. Reported risk factors include low LVEF (< 25%), prior history of myocardial infarction, congestive heart failure, left ventricular hypertrophy and low body mass index [6,7,8]. However, these studies did not include indices of diastolic function. The resultant myocardial

dysfunction from displacement of the heart is mainly diastolic dysfunction [5,23]. Thus, patients with pre-existing diastolic dysfunction would be more prone to undergo significant hemodynamic deterioration during grafting and evaluation for predictors of hemodynamic instability encompassing indices of diastolic function seems to be necessary. The E/E' value derived from tissue doppler echocardiography has been demonstrated to be a relatively load-independent index, which correlates well with left ventricular filling pressures, and is considered as a reliable index for diagnosing diastolic dysfunction [19,20]. Along with E/E' value, LA volume index and IVSd have also been validated to be practical values for diastolic function grading [24]. We included several indices of diastolic function to evaluate the predictors for hemodynamic deterioration and this is the first study demonstrating the relationship between preoperative diastolic function and hemodynamic deterioration presented by SvO_2 decline during OPCAB. The fact that increased E/E' value is an independent risk factor for SvO_2 decline supports the hypothesis that patients with pre-existing diastolic dysfunction are more prone to undergo significant hemodynamic deterioration.

Other independent risk factors were advanced age and increased LVEF. The age has been well validated as a risk factor associated with increased patients' morbidity and/or mortality after CABG [25]. Although

advanced age has not been identified as predictors of hemodynamic instability in previous studies [6,7,8], it may be associated with increased LA size, reduced threshold for cell calcium overload, and decreased cardiovascular reserve [26]. Thus it is not surprising that increased age is associated with significant hemodynamic deterioration.

The finding that increased LVEF is a risk factor for significant hemodynamic deterioration during grafting is somewhat surprising. Mishra, et al.[8] have demonstrated that low LVEF (< 25%) was associated with conversion to on-pump CABG. In other studies assessing increased morbidity and/or mortality in patients converted to on-pump CABG, neither preserved or decreased LVEF was not a predictor for emergent conversion [6,7]. Possible explanations for this observed discrepancy between the result of our study and others include; 1) adaptation of major organs to low cardiac output state and thereby resulting in 2) relative preservation of SvO_2 during grafting. Further studies for the evaluation of possible reasons seem to be needed.

The observation that patients who had decreased SvO_2 to below 60% during grafting required significantly longer length of postoperative hospitalization draws interesting challenges in anesthetic management. The drop in SvO_2 during grafting was usually transient, confined to 15 min and it was restored to above 60% after completion of grafting in all

patients. Use of inotropic support before complete revascularization might be hazardous by increasing oxygen consumption of the myocardium as well as intracellular calcium concentration making patients more vulnerable to ischemia-reperfusion injury.

In conclusion, improving SvO_2 by use of inotropic support during grafting results in similar postoperative cardiac enzyme release and decrease in the length of postoperative hospitalization, merits further study.

V. CONCLUSION

We prospectively assessed the preoperative predictors for significant hemodynamic deterioration presented as SvO_2 decline below 60% during coronary anastomosis including indices of diastolic function in 204 patients undergoing multivessel OPCAB. As a result, we found that increased preoperative echocardiographic index of diastolic function (E/E'), advanced age and increased LVEF were independent risk factors of more pronounced hemodynamic deterioration during grafting. Furthermore, patients who had decreased SvO_2 to below 60% during grafting required significantly longer length of postoperative hospitalization. Upon these results, appropriate therapeutic measures, such as use of inotropic support, or elective on-pump CABG should be considered in this subset of patients.

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< ABSTRACT(IN KOREAN)>

체외순환 없는 관상동맥우회술시 혈역학적 불안정을 예측할 수 있는 수술 전 요인들에 대한 분석 연구

<지도교수 배선준>

연세대학교 대학원 의학과

전나형

서론

심장수술에 있어서 수술 기법, 마취 유지 방법, 고정장치의 발전에 따라 체외순환 없는 관상동맥우회술(off-pump coronary artery bypass graft surgery, OPCAB)이 각광 받고 있으며 체외순환을 사용하는 관상동맥우회술과 비교하여 유사한 안전성과 우회로의 개통성를 보인다[1,2]. 하지만 체외순환을 하지 않을 경우 우회로 조성과 수술부위 확보를 위한 심장의

변위는 심방압 증가, 심박출지수 감소, 혼합정맥혈 산소포화도(SvO2) 감소를 초래하며 심방의 충만압 증가와 크기 증가는 이완기 장애로 이어진다. 체외순환 없는 관상동맥 우회술시 응급으로 체외순환으로 전환하는 경우 환자의 이환율과 사망률이 현저히 증가한다. 본 연구에서는 OPCAB을 시행 받았던 환자들을 OPCAB중 혈역학적 변화가 가장 심한 둔각 변연지 문합시 SvO2가 60% 이하와 이상으로 유지되었던 군으로 나누어 수술 전 심실의 이완기 기능을 나타내는 지표들을 포함한 여러 인자들을 비교하고 SvO2의 저하와의 연관성을 조사하였다.

대상 및 방법

본원에서 OPCAB을 시행받은 204명의 환자들을 대상으로 둔각 변연지 문합중 1. $SvO_2 < 60\%$ 인 군과 2. $SvO_2 \geq 60\%$ 인 군으로 나눈 후 이미 알려진 체외순환으로의 전환을 고려해야 하는 지표들과 수술전 심초음파에서 이완기 장애를 나타내는 지표 및 좌심실 비대 정도 등을 두 군간 비교하여 혈역학적 불안정을 예측할 수 있는 요인들을 비교하고 SvO2의 저하와의 연관성을 분석하였다.

결과

문합시 혈역학적 불안정과 연관이 있는 인자들은 연령, 수술전 좌심실 박출분율 그리고 좌심실 이완기 충만압을 나타내는 지표 (E/E')로 나타났으며 문합중 혼합정맥혈 산소포화도가 60%이하로 감소되었던 환자들이 입원일수가 유의하게 많은 것으로 관찰되었다.

고찰 및 결론

관상동맥 문합 중 발생하는 SvO2의 저하와 이로 인한 혈역학적 불안정의 가능성이 높은 고령, 수술전 좌심실 박출분률과 좌심실 이완기 충만압이 증가된 환자에 있어서는 수술중 심장수축 촉진제의 사용등 적절한 치료가 중요하며 수술전 선택적 체외순환 관상동맥우회술의 가능성 또한 고려해 보아야 한다.

핵심되는 말: 체외순환 없는 관상동맥 우회술, 혼합정맥혈 산소포화도, 혈역학적 변화, 심실의 이완기 기능