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대동맥에 대한 조작이 없는 무심폐기하 관상동맥 우회술에서 기존의 위험성 예측 시스템의 임상적 유용성 평가에 대한 연구

A study on the performance of the preexisting risk prediction scoring systems in patients undergoing anaortic off-pump coronary artery bypass grafting

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Abstract

A study on the performance of the preexisting risk prediction scoring systems in patients undergoing anaortic off-pump coronary artery bypass grafting

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Background: Risk prediction scoring systems are used to measure perioperative risk and identify high-risk patients. Currently, the Society of Thoracic Surgeons (STS) risk model and European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) are widely used for cardiac surgery. Additionally, the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score II predicts 4-year mortality after coronary artery bypass grafting (CABG). This study aimed to evaluate the performance of preexisting preoperative risk evaluation systems, such as the STS risk model, EuroSCORE II, and SYNTAX score II, for patients undergoing an-aortic off-pump coronary bypass grafting (OPCAB).

Methods*:* Of 1,140 patients had planned to undergo isolated OPCAB preoperatively between January 2010 and June 2017, 1048 patients (isolated anaortic OPCAB: 1043, on-pump conversion: 5) were enrolled in this study. The STS risk score, EuroSCORE II, and SYNTAX score were retrospectively or prospectively calculated with dedicated online software. Calibration of the STS risk model and EuroSCORE II were performed by the risk-adjusted event ratio that was defined as observed events divided by expected events (O/E ratio) and the Hosmer-Lemeshow test. The discrimination powers of the STS risk model and EuroSCORE II were evaluated by the area under the receiver operating characteristic curve (AUC). Student's *t*-test was used to compare SYNTAX score I and II between patients with and without mortality or morbidity.

Results*:* Operative mortality occurred in 10 patients (0.95%). The predicted mortality rates calculated by the EuroSCORE II and STS risk model were 2.58 ± 4.15% and 1.72 ± 2.92%, respectively. The O/E ratio of the EuroSCORE II was 0.370 (confidence interval(CI): 0.177 – 0.681), and the EuroSCORE II significantly overpredicted the operative mortality for patients (P = 0.003). EuroSCORE II showed good discrimination power with an AUC of 0.784. The O/E ratio of mortality in the STS risk model was 0.556 (CI: 0.266 – 1.023), and the STS risk model overpredicted the operative mortality with marginal significance (P = 0.052). However, in the subgroup analysis, the STS risk model significantly overpredicted mortality (O/E ratio: 0.481, CI: 0.193-0.992). Permanent stroke occurred in 6 patients (0.53%). The predicted permanent stroke occurrence rate calculated by the STS risk model was 1.73 ±

1.48%. The O/E ratio was 0.332 (CI: 0.121 – 0.722), and the STS risk model significantly overpredicted the permanent stroke occurrence rate (P = 0.011). In terms of discrimination power for the STS risk model, the AUC for operative mortality and permanent stroke were 0.876 and 0.740, respectively. There was no significant difference in SYNTAX score I value between patients who did and did not experience mortality or morbidity. However, patients with mortality or morbidity showed a significantly higher SYNTAX score II than those without mortality or morbidity.

Conclusions*:* The preexisting risk prediction scoring systems for CABG, the STS risk model and EuroSCORE II, overpredicted the risk of mortality and stroke rate for anaortic OPCAB. These findings suggest the possibility that anaortic OPCAB can lower the operative mortality and occurrence of postoperative stroke than conventional CABG. In addition, these results show that the characteristics of the surgical method, especially whether anaortic OPCAB is performed, should be considered to predict the operative risk for CABG.

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Keywords: risk prediction scoring system, coronary bypass graft grafting, off-pump, anaortic

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1. Introduction

Preoperative risk prediction scoring systems have been used to measure perioperative risk and identify high-risk patients in cardiac surgery. Currently, there are several preoperative risk evaluation systems for predicting the surgical risk of coronary artery bypass grafting (CABG). The Society of Thoracic Surgeons (STS) risk model and European System for Cardiac Operative Risk Evaluation (EuroSCORE) II are widely used scoring systems [1-3]. In addition to these two scoring systems, the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) scores II also predict 4-year mortality according to the procedure and recommend the optimal revascularization method for coronary artery disease [4, 5].

The STS risk models were developed based on the Society of Thoracic Surgeons National Adult Cardiac Surgery Databases (STSNCD). The STS database originated in 1984 as a result of a small group of cardiac surgeons and was established in June 1990 [6]. The first STS risk model was developed in 1994 and calculated the expected operative mortality of isolated CABG based on data from 1984 to 1990 [7]. After that, the STS database published six CABG-only risk stratification models between 1997 and 2003 [8]. Starting in 2003, the STS risk model has calculated not only mortality risk but also the major morbidity risk [9]. The latest update to the STS risk model (version 2.9) was in 2018 and showed nine endpoints, including expected mortality and morbidities, such as permanent stroke, renal failure, reoperation for any cause, prolonged ventilation >24 hours, deep sternal wound infection, major morbidity or mortality, long length of stay (>14 days), and short length of stay (<6 days and alive) [2, 3]. In the validation data, the latest STS risk model showed acceptable calibration and improved discrimination compared to the previous version in patients undergoing CABG [3].

The EuroSCORE was developed based on multinational data from 8 European countries in 1999 and predicted early mortality in cardiac surgery, including CABG [10]. In 2003, the system was updated to the logistic EuroSCORE to correct for underestimations for high-risk patients [11]. The latest update to the EuroSCORE (EuroSCORE II) in 2011 used multinational data from 43 countries. The EuroSCORE II showed good calibration and discrimination (area under the receiver operating characteristic (ROC) curve = 0.8095) in the validation data [1].

The SYNTAX score was developed to evaluate the complexity of coronary artery disease in 2005, and this score was helpful in establishing the optimum revascularization approach in patients with complex coronary artery disease [4]. In 2013, the SYNTAX II score was developed to overcome the limitations of the SYNTAX score, including the absence of an individualized approach and clinical variables [5]. The SYNTAX score II predicts 4-year survival rates through a combination of anatomical and clinical factors, such as age, creatinine clearance, left ventricular function, sex, chronic obstructive pulmonary disease, and peripheral vascular disease. In the external validations using the Drug Eluting stent for Left main coronary Artery disease (DELTA) registry, the SYNTAX II score showed good calibration in patients with three-vessel disease (expected 4-year survival 88.2%, actual 4-year survival 86.2%) [5].

Although these risk prediction systems have been well validated for predicting mortality and morbidity [1, 3, 5], these systems calculate the operative risk of CABG regardless of whether cardiopulmonary bypass (CPB) machines or aortic manipulations are applied. However, currently, many studies have reported the benefits of anaortic off-pump CABG (OPCAB) in terms of postoperative stroke and mortality compared to conventional CABG [12, 13]. This study aimed to evaluate the performance of preexisting preoperative risk prediction scoring systems, such as the STS risk model, EuroSCORE II, and SYNTAX score II, for patients undergoing anaortic OPCAB.

2. Patients and Methods

2.1 Patient characteristics and surgical procedure

The study protocol was reviewed by the institutional review board and was approved as a minimal risk retrospective study (Approval Number: H-1911-041-1076) that did not require individual consent. From January 2010 to June 2017, 1,140 patients had planned to undergo isolated OPCAB preoperatively. Among them, 83 patients with concomitant cardiac or noncardiac procedures and 9 patients with aortic manipulation were excluded, and a total of 1048 patients were enrolled in this study (Figure 1). One thousand forty-three patients underwent anaortic OPCAB, and 5 patients who planned to undergo anaortic OPCAB were converted to on-pump CABG because of hemodynamic instability during anastomosis. The preoperative characteristics of the present study group are summarized in Table 1. The overweight was defined as a body mass index of more than 25 kg/m^2. Chronic renal failure was defined as a glomerular filtration rate of less than 60 mL/min for more than 3 months or a state requiring dialysis. The peripheral arterial disease included claudication, amputation, vascular reconstruction surgery, abdominal aortic aneurysm, and computed tomography imaging of >50% diameter stenosis. The acute coronary syndrome included ST elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina.

The basic surgical procedures and principles of OPCAB have been previously described [14]. The internal thoracic artery was used as the first choice for the graft in almost all patients (n=1044, 99.6%), and the composite graft technique was used for patients with multivessel disease (n=1019, 97.2%). The saphenous vein (SV) has been used as the preferred second conduit of choice to construct composite grafts since 2008 at our institution. The SV was harvested with a “minimal manipulation” technique before October 2013 and was harvested with a “no-touch” technique after October 2013. Transit-time flow measurement (TTFM; Medi-Stim AS, Oslo, Norway) and postoperative early angiographic evaluations were routinely performed. The operative characteristics of the present study group are summarized in Table 2.

2.2 Calculation of the risk prediction scores

The EuroSCORE II was calculated for each patient with dedicated online software to predict operative mortality [15]. The EuroSCORE II was calculated retrospectively by two surgeons (K-B. K, JW. C) before January 2016 and prospectively by a single surgeon (K-B. K) after January 2016. The STS score was calculated using dedicated online software for each patient to predict operative mortality and postoperative outcomes, including renal failure, permanent stroke, prolonged ventilation, deep sternal infection, reoperation, morbidity or mortality, short length of stay and long length of stay; these scores were calculated retrospectively by a single surgeon (JW. C) because the STS score was recently revised to STS Adult Cardiac Surgery Database version 2.9 in 2018 [16]. The SYNTAX scores I and II were calculated for each patient retrospectively before January 2016 by one surgeon (JW. C) and prospectively after January 2016 by one surgeon (K-B. K). The SYNTAX scores could not be calculated for 2 patients without preoperative coronary angiography.

All definitions of operative death and postoperative complications were followed by the STS risk model outcomes except for short and long length of stay [16]. Operative mortality was defined as both of the following: (1) all deaths occurring during the hospitalization in which the operation was performed, even after 30 days, and (2) deaths occurring after discharge from the hospital, but within 30 days of the procedure. Permanent stroke was defined as a confirmed neurological deficit of abrupt onset caused by a disturbance in blood supply to the brain that did not resolve within 24 hours.

Renal failure was defined as acute or worsening renal failure resulting in one or more of the following: (1) an increase in serum creatinine to $\geq$4.0 with an increase of at least 0.5 mg/dl or an increase in serum creatinine to 3-fold the baseline value; and (2) a new requirement for dialysis postoperatively. Prolonged ventilation was defined as a duration of postoperative pulmonary ventilation >24 hours. The hours of ventilation included the time from exiting the operation room to extubation and any additional hours following reintubation. Deep sternal wound infections included sternal wound infections or mediastinitis diagnosed within 30 days of the operation or > 30 days after the procedure but during the hospital stay for surgery. Reoperation was defined as any reoperation for bleeding/tamponade, valvular dysfunction, graft failure, aortic reintervention, or other cardiac reason. Major morbidity or operative mortality was defined as a composite endpoint that included operative mortality, permanent stroke, renal failure, prolonged ventilation, deep sternal wound infection, and reoperation. A short length of stay was defined as a hospital stay of less than 13 days, and a long length of stay was defined as a hospital stay of more than 16 days, referring to the data from Korea's Health Insurance review and assessment service. The performance of the STS risk model and EuroSCORE II were evaluated for calibration of 9 variables (mortality, renal failure, permanent stroke, prolonged ventilation, deep sternal wound infection, reoperation, morbidity or mortality, short length of stay, long length of stay) and calculation of discrimination power. The two types of subgroup analyses were performed. The first subgroup analyses were performed for calibration of the STS risk model for patients who underwent CABG after July 2011 (n = 834), because STS risk model version 2.9 was developed for patients who underwent cardiac surgery between July 2011 and June 2014. The second subgroup analyses were performed for patients with the STS Predicted Risk of Mortaltiy (PROM) score ≥4 to evaluate the performance of the STS risk model and EuroSCORE II for high-risk patients.

For the SYNTAX score, we evaluated the difference in scores between the patients with and without morbidity or mortality following the definition of the STS risk model.

2.3 Statistical analysis

Statistical analyses were performed using IBM SPSS statistical software (version 25.0, IBM Inc., Armonk, NY, USA) and SAS software (version 9.4, SAS Institute, Cary, NC, USA). The risk-adjusted event ratio and the Hosmer-Lemeshow test were used to evaluate the calibration power of the STS risk model and EuroSCORE II. The risk-adjusted event ratio was defined as observed events divided by expected events (O/E ratio). An O/E ratio > 1.0 means that the model underpredicts the event, while an O/E ratio <1.0 means that the model overpredicts the events. If the 95% confidence interval (CI) of the O/E ratio excludes the value of '1.0', it was considered statistically significant [17]. The CI was calculated by the Byar approximation method. The Hosmer-Lemeshow test was used to assess whether the observed event rate matched the expected event rate for the quartiles of the predicted value [18]. The calibration was also assessed by plotting the predicted probability of operative mortality and postoperative complications against the actual probability with 95% CIs for the quartiles of the predicted value. The expected probability is shown on the x-axis, and the actual probability is shown on the y-axis. In the subgroup analyses for the high-risk patients, the only risk-adjusted event ratio was used to evaluate the calibration power of the STS risk model and EuroSCORE II, because the patients and events were too small.

The area under the ROC curve (AUC) was used to evaluate the discrimination power of the STS risk model and EuroSCORE II. The discriminative power is thought to be excellent when AUC≥0.80, very good when 0.75≤AUC<0.8, and acceptable when 0.7<AUC<0.75. Student's *t*-test was used to compare SYNTAX scores I and II between the patients with and without mortality or morbidity. Data are expressed as the mean ± standard deviation, as medians with ranges, or as proportions. A *P* value less than 0.05 was considered statistically significant, and 0.05≤*P* value < 0.1 was considered marginally significant.

3. Results

3.1 Performance of the EuroSCORE II

Operative mortality occurred in 10 patients (0.95%). The causes of operative mortality were septic shock (n = 4), low cardiac output syndrome (n = 3), acute respiratory distress syndrome (n = 2) and limb ischemia (n =1). The predicted mortality calculated from EuroSCORE II was 2.58 ± 4.15%. The O/E ratio of EuroSCORE II was 0.370, and EuroSCORE II significantly overpredicted the operative mortality for patients who underwent anaortic OPCAB (CI: 0.177 – 0.681, Table 3). In the Hosmer-Lemeshow test, there was a significant difference between the predicted mortality calculated by EuroSCORE II (P = 0.003) and actual mortality. The calibration plot showed that the predicted mortality calculated from EuroSCORE II was higher than the actual mortality in all groups (Figure 2(A)). EuroSCORE II showed good discrimination power with an AUC of 0.784 (CI: 0.643 -0.924, Figure 3(B)).

3.2 Performance of the STS risk model

The predicted mortality calculated from the STS risk model was 1.72 ± 2.92%. The O/E ratio of operative mortality in the STS risk model was 0.556, and the STS risk model overpredicted the operative mortality without statistical significance (CI: 0.266 – 1.023). In the Hosmer-Lemeshow test, there was a marginally significant difference between the predicted mortality calculated by the STS risk model and the actual mortality (P = 0.052, Table 3). The calibration plot showed that the predicted mortality calculated by the STS risk model was higher than the actual mortality in the top three quartiles (Figure 2(B)). In terms of discrimination power for operative mortality, the STS risk model showed excellent results, with an AUC of 0.876 (CI: 0.743 – 1.000, Figure 3(B)). In subgroup analyses for patients who underwent anaortic OPCAB after July 2011, the STS risk model significantly overpredicted operative mortality based on the O/E ratio (CI: 0.193 – 0.992, Table 4).

Permanent stroke occurred in 6 patients (0.57%), 5 of whom had an embolic stroke, and one had a hemorrhagic stroke. No patients experienced atrial fibrillation before the stroke. The predicted permanent stroke occurrence rate calculated by the STS risk model was 1.73 ± 1.48%. The O/E ratio was 0.332, and the STS risk model significantly overpredicted the permanent stroke occurrence rate (CI: 0.121 – 0.722, Table 3). There was a significant difference between the predicted occurrence rate of stroke and the actual stroke occurrence rate in the Hosmer-Lemeshow test (P = 0.011). The calibration plot showed that the predicted probability of permanent stroke was higher than the actual probability in all groups (Figure 2(C)).). The discrimination power of the STS risk model for permanent stroke was acceptable, with an AUC of 0.740 (CI: 0.574 – 0.905, Figure 3(C)). Subgroup analyses for patients who underwent anaortic OPCAB after July 2011 also showed that the STS risk model significantly overpredicted permanent stroke based on the O/E ratio and Hosmer-Lemeshow test (CI: 0.149 – 0.889, P = 0.020, Table 5).

The calibrations of other outcomes are summarized in Table 3 and Figure 4. Based on the O/E ratio, the predicted occurrence rates of renal failure, prolonged ventilation, mortality or morbidity, long length of stay, and short length of stay calculated by the STS risk model significantly underpredicted the actual occurrence rate. The Hosmer-Lemeshow test also showed statistically significant differences between the predicted rates of renal failure, prolonged ventilation, mortality or morbidity, long length of stay, and short length of stay and actual occurrence rates.

The discrimination power of the STS risk model for other outcomes are summarized in Table 5, and the ROC curves of the STS risk model for other outcomes are shown in Figure 5. The STS risk model showed excellent discrimination power for renal failure and good discrimination power for deep sternal wound infection and long length of stay. Additionally, the STS risk model showed acceptable discrimination power for prolonged ventilation and mortality or morbidity. However, the STS risk model showed relatively low discrimination power for reoperation and short length of stay.

3.3 Performance of SYNTAX score I and II

The SYNTAX scores I and II for all patients (n = 1046) and patients who experienced mortality or morbidity (n = 199) were 32.3±11.5 and 31.6±11.8, respectively, and 32.8±12.5 and 36.3±12.2, respectively. There was no significant difference in SYNTAX score I between patients who did and did not experience mortality or morbidity (*P* = 0.469). However, patients who developed mortality or morbidity showed significantly higher SYNTAX score II values than those who did not develop mortality or morbidity (*P* <0.001, Table 6).

3.4 Subgroup analyses for high-risk patients

Eighty patients (7.6%) had a STS PROM score of more than 4. Operative mortality occurred in 5 patients (6.3%) and the permanent stroke occurred in 1 patient (1.3%). The O/E ratio of EuroSCORE II was 0.534, and the O/E ratio of operative mortality and permanent stroke in the STS risk model were 0.694

and 0.266, respectively. Although the EuroSCORE II and the STS risk model overpredicted the operative mortality and permanent stroke for high-risk patients, there were no statistically significant (Table 7).

4. Discussion

This study reported three main findings. First, as preexisting risk prediction scoring systems, the EuroSCORE II and the STS risk model overpredict the mortality for patients undergoing anaortic OPCAB. Second, the STS risk model overpredicts the occurrence rate of permanent stroke for patients undergoing anaortic OPCAB. Third, the SYNTAX score II is associated with the occurrence of mortality or morbidity, but the SYNTAX score I is not.

Currently, the EuroSCORE II and STS risk models are widely used risk prediction scoring systems. EuroSCORE II predicts operative mortality after all cardiac surgeries, and the STS risk model predicts 9 early clinical outcomes, including mortality and permanent stroke, after six common cardiac procedures.

The first STS risk model was established in 1994 and calculated the expected mortality for isolated CABG [7]. This model was constructed using the records of 80,881 patients undergoing CABG between 1984 and 1990 and was based on a Bayesian algorithm, which has advantages in handling incomplete data. The next version was made in 1997 using information from more than 300,000 patients undergoing isolated CABG between 1990 and 1994 [19]. Logistic regression techniques were used to create this model, and there was a good correlation between the predicted and observed mortality in simple comparisons and subgroup validations. After that, the next version was developed in 1998 using the 1995 STS National Adult Cardiac Surgery Database (STS NCD). This model showed good discrimination power (C index: 0.786) but overestimated the risk for the high-risk patient deciles (p value of Hosmer-Lemeshow: 0.0004) [20]. The model was revised in 1999 using the 1996 STS NCD. This model showed excellent performance across all risk groups (C index: 0.774, p value of Hosmer-Lemeshow test: 0.99) [21]. The next version was developed in 2002 using the records of more than 1 million patients undergoing isolated CABG between 1990 and 1999 and calculated the predicted risk based on 23 preoperative risk factors [22]. The other model, developed in 2002, started to predict other clinical outcomes. This risk model predicted the expected length of hospital stay and the risk of short or prolonged hospitalization [23]. In 2003, the STS risk model started a system to predict mortality and major morbidities simultaneously. First, this model calculated operative mortality and five major endpoints: permanent stroke, renal failure, reoperation, prolonged ventilation (>48 hours), and deep sternal wound infection [24]. In 2009, the STS risk model was revised again and predicted nine endpoints, including major morbidity or mortality, long length of stay, and short length of stay [25]. The latest update to the STS risk model (version 2.9) was in 2018 and predicted nine endpoints for commonly performed adult cardiac surgical procedures: isolated CABG, isolated aortic valve replacement, isolated mitral valve repair or replacement, aortic valve replacement plus CABG, and mitral valve repair or replacement plus CABG [2,3]. The latest STS risk model calculates the predicted risk for isolated CABG based on 65 preoperative risk factors, including medications and blood tests [3].

The additive EuroSCORE was developed in 1999 based on the records of 13,302 patients based on multinational data from 8 European countries and predicted operative mortality based on 17 preoperative risk factors in cardiac surgery [10]. The 17 risk factors included nine patient-related factors, four cardiac-related factors and four operation-related factors. This system showed good performance (C index: 0.76, p value of Hosmer Lemeshow test: <0.68). In 2003, the system was updated to the logistic EuroSCORE because the EuroSCORE showed a trend of underestimating the operative risk in very high-risk patients [11]. The latest update to the EuroSCORE (EuroSCORE II) was in 2011 and incorporated the multinational data of 43 countries and 22,381 patients. EuroSCORE predicted operative mortality based on 10 patient-related factors, 5 cardiac-related factors, and 3 operation-related factors [1].

These two systems showed good calibration and discrimination in the validation data [1,3]. However, these risk prediction scoring systems have not been considered to calculate scores for aortic manipulation or used for CPB. Therefore, we evaluated whether these preexisting risk prediction scoring systems can appropriately predict the perioperative risk for patients undergoing anaortic OPCAB.

In this study, the EuroSCORE II and STS risk model (for subgroups) overpredicted the operative mortality for patients undergoing anaortic OPCAB. Although the advantage of OPCAB for mortality remains controversial [26, 27], our study showed the possibility that anaortic OPCAB has an advantage in terms of early mortality compared to conventional CABG. These results might be due to anaortic OPCAB being performed by a dedicated surgical team for OPCAB, reduced occurrence of permanent stroke, and intrinsic features of not using CPB.

Although the EuroSCORE II and STS risk model overpredicted the operative mortality for patients undergoing anaortic OPCAB, the STS risk model (1.72%) calculated a predicted mortality that was closer to the actual mortality (0.95%) than the EuroSCORE II (2.58%). There are two possible factors that could affect this result. First, the two systems have different model designs. The STS score was developed using patients who only underwent isolated CABG, but the EuroSCORE II was developed using patients who underwent all kinds of cardiac surgery, and the operation type was considered a risk factor. The STS risk model calculated the predicted values based on 65 risk factors, but EuroSCORE II calculated the value based on 18 risk factors. Second, the latest STS risk model was developed for patients who underwent cardiac surgery between July 2011 and June 2014, and EuroSCORE II was developed for patients who underwent cardiac surgery in 2010. These differences may have allowed the STS risk model to calculate a more accurate prediction for operative mortality.

Anaortic OPCAB has theoretical benefits regarding the occurrence of stroke because this technique can prevent damage caused by CPB and aortic manipulation, such as emboli caused by gaseous or fat particles or atherosclerotic embolization [13, 28, 29]. Some previous studies showed a decrease in the risk of stroke after OPCAB [12, 30, 31], and recently, a meta-analysis by Zhao and colleagues showed that anaortic OPCAB could decrease the risk for postoperative stroke, especially in high-risk patients [12]. In this study, the STS risk model significantly overpredicted the occurrence rate of permanent stroke with an O/E ratio of 0.332. This result means that anaortic OPCAB could have a protective effect on permanent stroke compared to conventional CABG.

Unexpectedly, the STS risk model underpredicted the occurrence rate of acute renal failure, prolonged ventilation, and mortality or morbidity. There are some possible explanations for these results. First, our postoperative protocol included routine early angiography for all patients, which might lead to a higher incidence of acute renal failure than the predicted value. Second, the relatively long operation could be related to a higher incidence of acute renal failure and prolonged ventilation. Prolongation of the operation to train residents and fellows could increase the possibility of intraoperative volume overloading. Third, our postoperative strategy, which favored extubation during the regular working period, might affect the prolongation of intubation. Fourth, the STS risk model for predicting prolonged ventilation is likely inaccurate in Asians. When the latest STS risk model was developed, only

2.8% of patients (12,076/439,092) were Asian people [3]. Moreover, since they have lived in different lifestyles, the Asians included in the model development cannot represent Asians living in Asia. Fourth, although most cases of acute renal failure and prolonged ventilation do not cause sequelae, these cases affect the higher incidence of mortality or morbidity.

In terms of hospital stay, the criteria to discriminate short and long stays were different from the definitions of the STS risk model because of the different health insurance systems between the USA and South Korea. The value of 16 days, which is the criterion for long stays, corresponded to the top 75%, and 13 days, which is the criterion for short stays corresponded to the bottom 25%. According to a previous study performed using STS NCD in 2002, 52.5% (260,908/496,797) of patients had a short stay, and 5.2% (26,008/496,797) of patients had a long stay [23]. This means that our criteria using quartiles (bottom 25% and top 75%) for short and long stays may be too low. If the criteria were set similarly to the values of the previous study, the occurrence of short stays would increase, and the occurrence of long stays would decrease.

According to the current guidelines, the SYNTAX score is used to recommend the type of revascularization for patients with left main disease or three-vessel disease [32, 33]. The SYNTAX score I was developed to grade the anatomical complexity of coronary lesions in patients [4], and the SYNTAX score II, which is a combination of anatomical and clinical factors, such as age, creatinine clearance, left ventricular function, sex, chronic obstructive pulmonary disease, and peripheral vascular disease, predicts 4-year survival rates [5].

Previous studies found that the SYNTAX score I was an independent predictor of long-term outcomes in patients treated with percutaneous coronary intervention (PCI) [32], but the association between anatomical complexity of the coronary artery and clinical outcomes after CABG remains uncertain. Previous studies showed that there was no significant association between the SYNTAX score and major adverse cardiopulmonary events, including death, myocardial infarction, stroke, and repeat revascularization [4, 5, 34]. This study also confirmed the findings of previous studies regarding the association between the anatomical complexity of the coronary artery and clinical outcomes after CABG. In this study, there was no significant difference in SYNTAX score I value between patients with and without mortality or morbidity, but there was a significant difference in SYNTAX score II values between patients with and without mortality or morbidity. These findings suggest that anatomical complexity cannot affect the early clinical outcomes after CABG, but the clinical comorbidity of patients can be associated with early adverse outcomes.

4.1 Limitations

The present study has several limitations. First, most of operations were performed by single surgeon at a single institution. Therefore, this could limit the generalization of these results to all surgeons and hospitals. A multicenter study involving many surgeons performing both on-pump and off-pump

CABG will be required to evaluate the performance of preexisting risk models for anaortic OPCAB. Second, the number of events was too small to evaluate the calibration of the models, especially for deep sternal wound infection, using the Hosmer-Lemeshow test. Therefore, the risk-adjusted ratio was mainly used for the calibration of the models, and there were some differences between the risk-adjusted ratios and Hosmer-Lemeshow tests.

5. Conclusion

The preexisting risk prediction scoring systems for CABG, the STS risk model and EuroSCORE II, overpredicted the risk of mortality and stroke rate for anaortic OPCAB. These findings suggest the possibility that anaortic OPCAB can lower the operative mortality and occurrence of postoperative stroke than conventional CABG. In addition, these results show that the characteristics of the surgical method, especially whether anaortic OPCAB is performed, should be considered to predict the operative risk for CABG.

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Figure 1. Summary flow diagram of enrolled patients. (CABG = coronary artery bypass grafting)

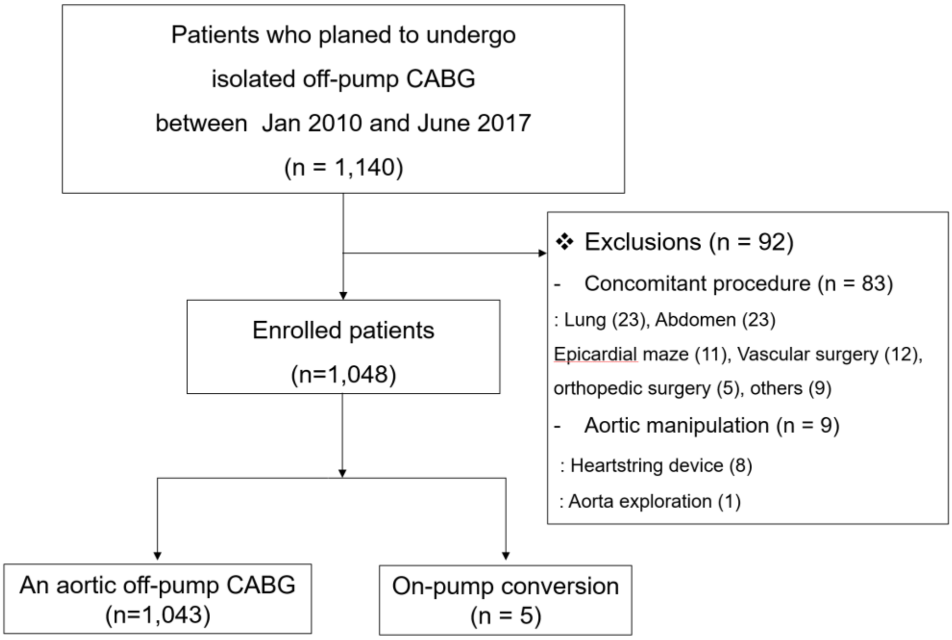
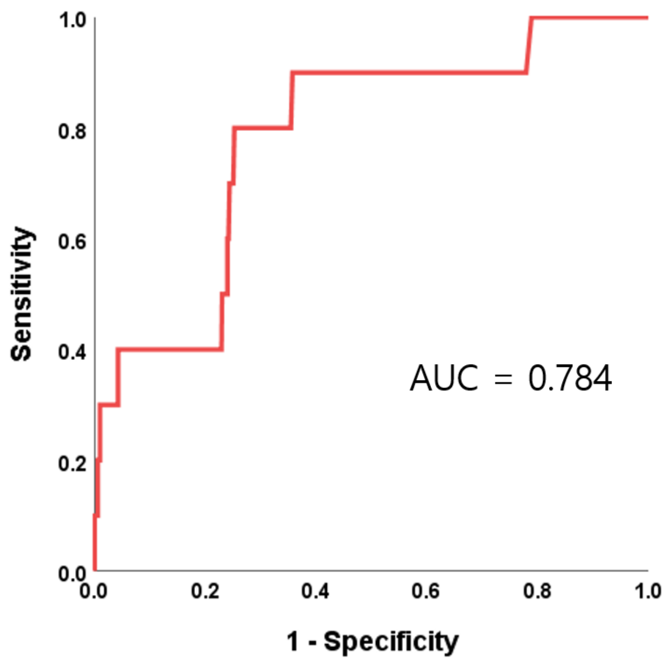
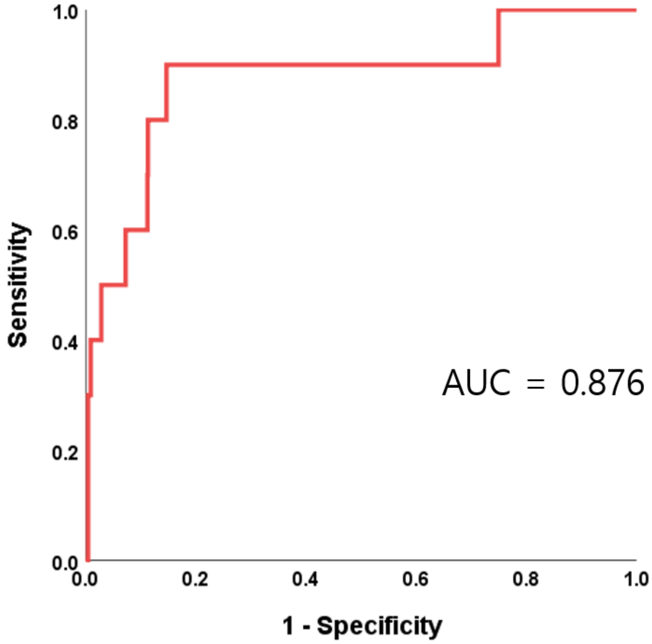


Figure 2. Receiver operating characteristic (ROC) curve of the (A) EuroSCORE II, (B) mortality calculated by the STS risk model, and (C) permanent stroke calculated by the STS risk model.

(A) ROC curve for EuroSCORE II



(B) ROC curve for mortality (STS)



(C) ROC curve for permanent stroke

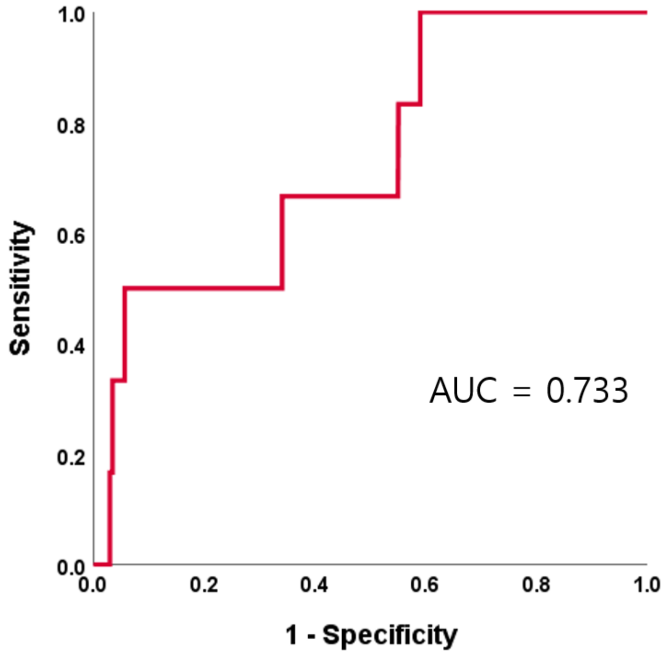
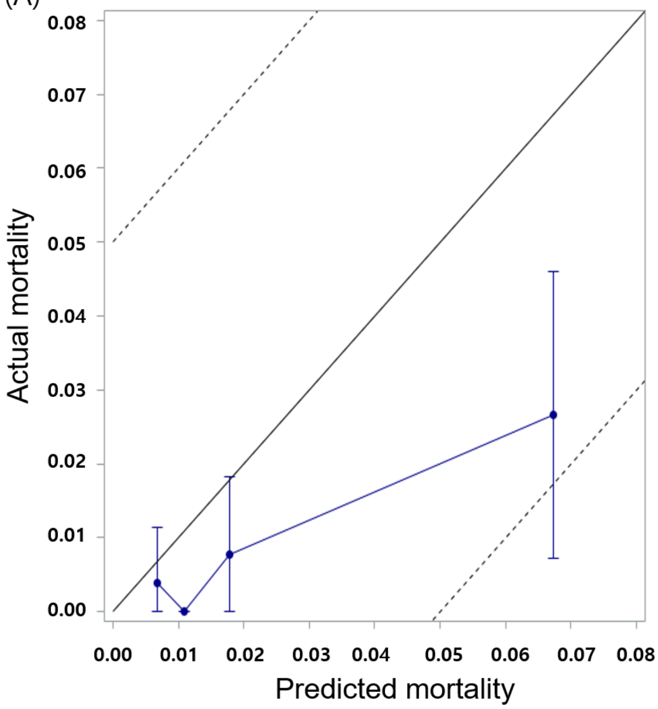
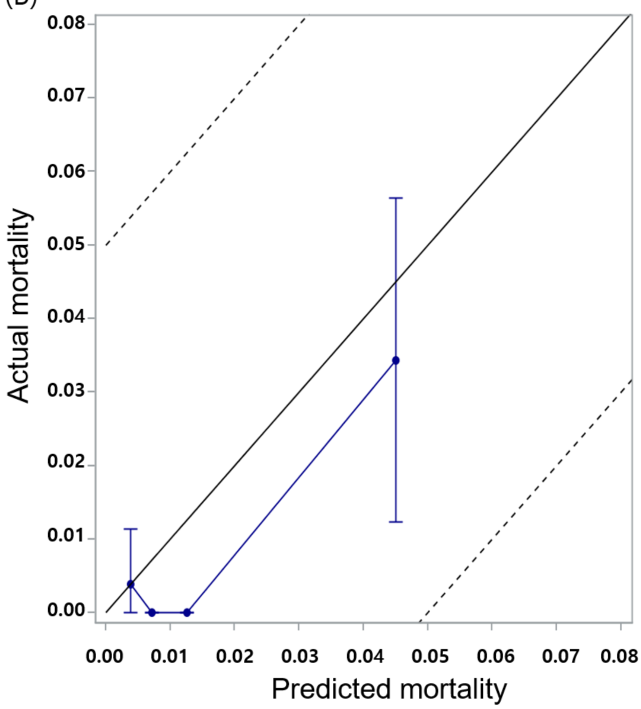


Figure 3. Calibration plot of the (A) EuroSCORE II, (B) mortality calculated by the STS risk model and (C) permanent stroke calculated by the STS risk model

(A)



(B)


0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
Actual mortality
0.00 0.01 0.02 0.03 0.04 0.05 0.06 0.07 0.08
Predicted mortality

(C)

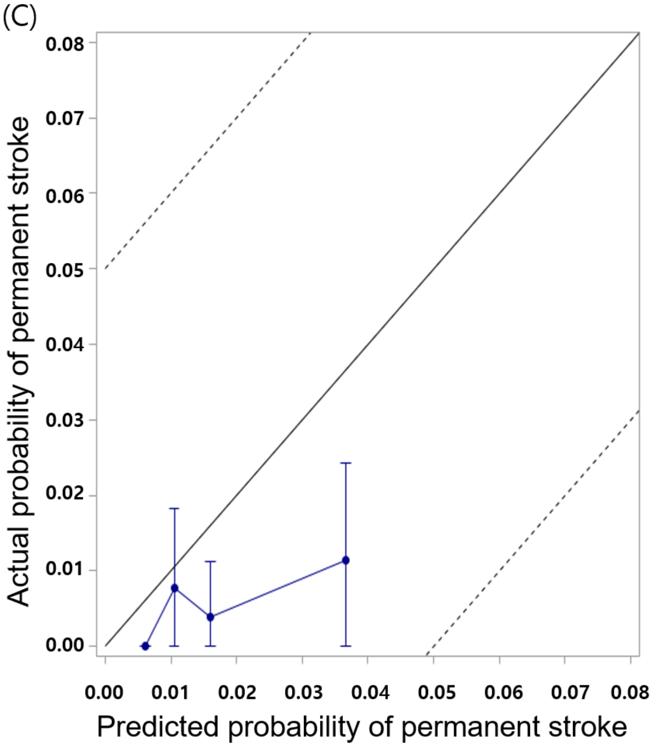
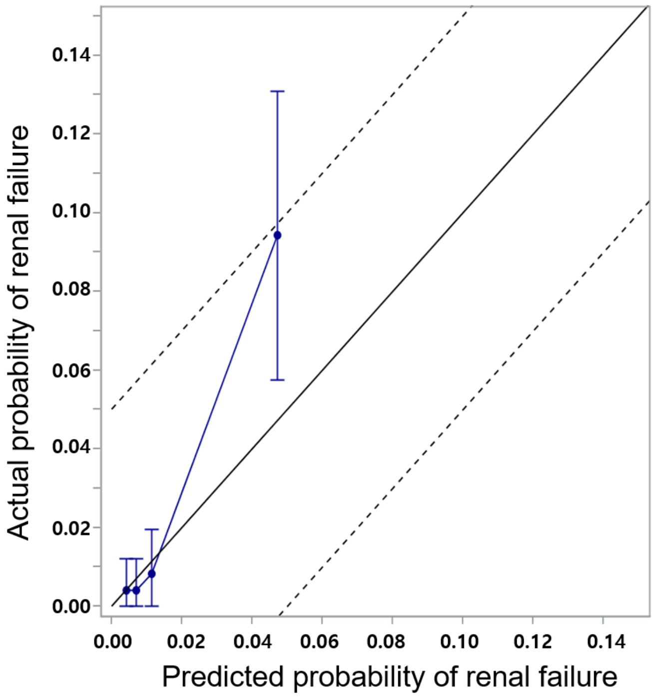
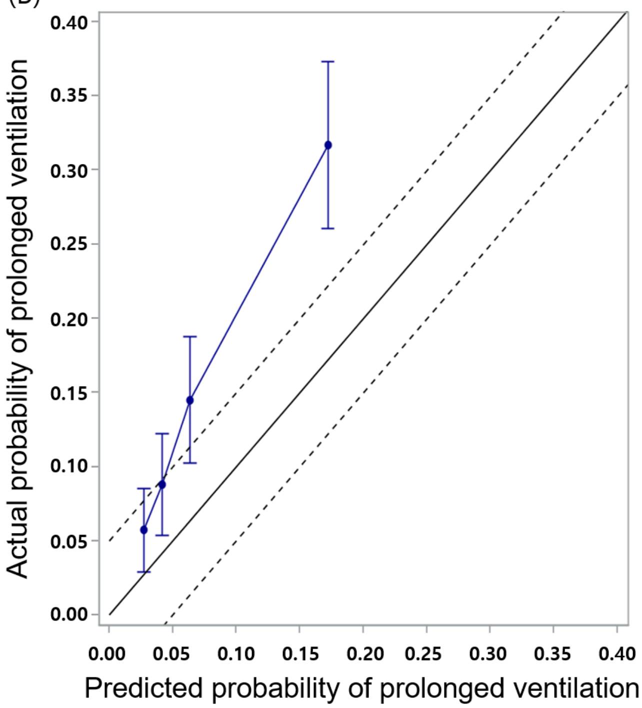

0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
Actual probability of permanent stroke
0.00 0.01 0.02 0.03 0.04 0.05 0.06 0.07 0.08
Predicted probability of permanent stroke

Figure 4. Calibration plot of (A) renal failure, (B) reoperation, (C) deep sternal wound (DSW) infection, (D) prolonged ventilation, (E) mortality or morbidity, (F) long length of stay, and (G) short length of stay calculated by the STS risk model.

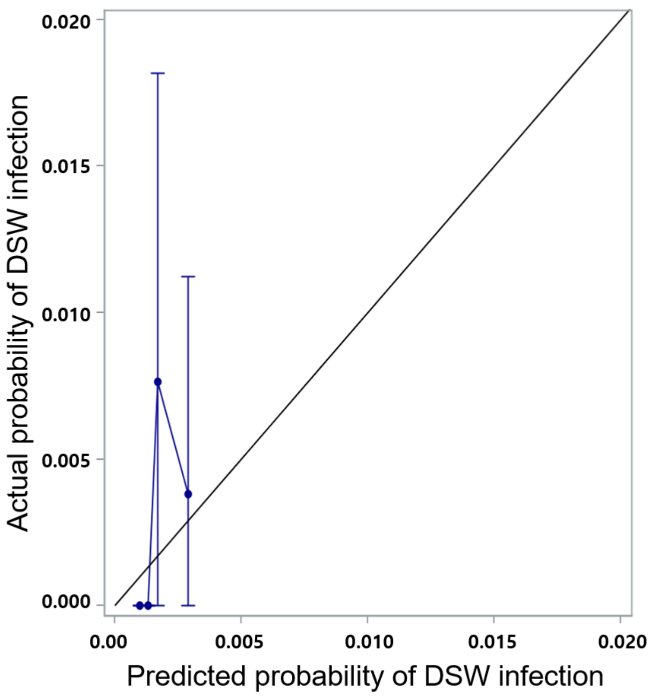
(A)



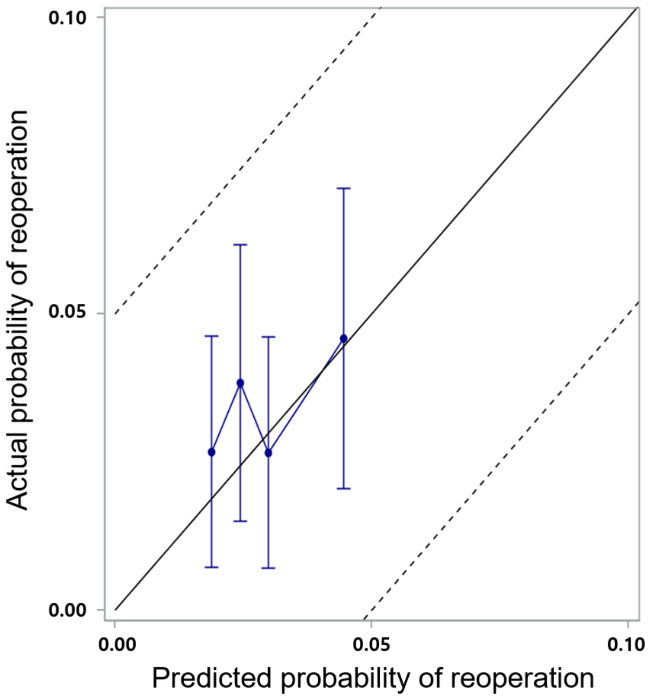
(B)


0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Actual probability of prolonged ventilation
0.00 0.05 0.10 0.15 0.20 0.25 0.30 0.35 0.40
Predicted probability of prolonged ventilation

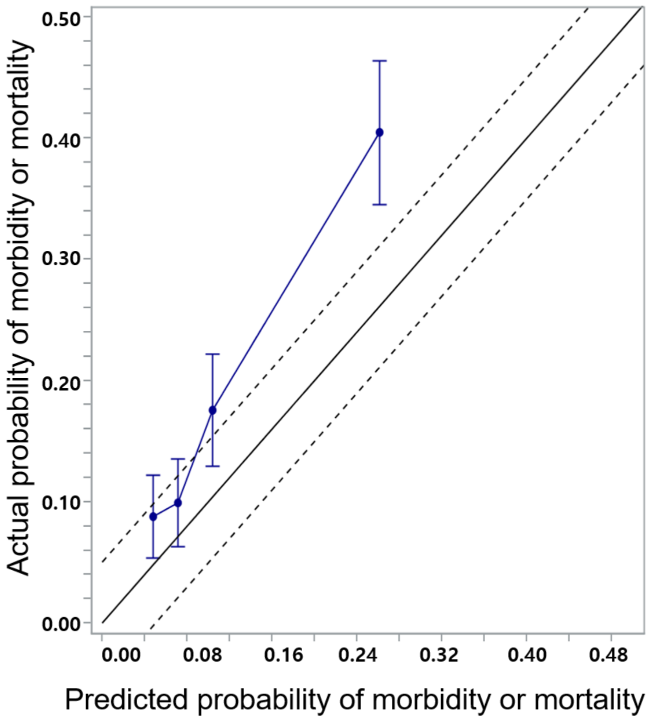
(C)


0.020
0.015
0.010
0.005
0.000
Actual probability of DSW infection
0.00 0.005 0.010 0.015 0.020
Predicted probability of DSW infection

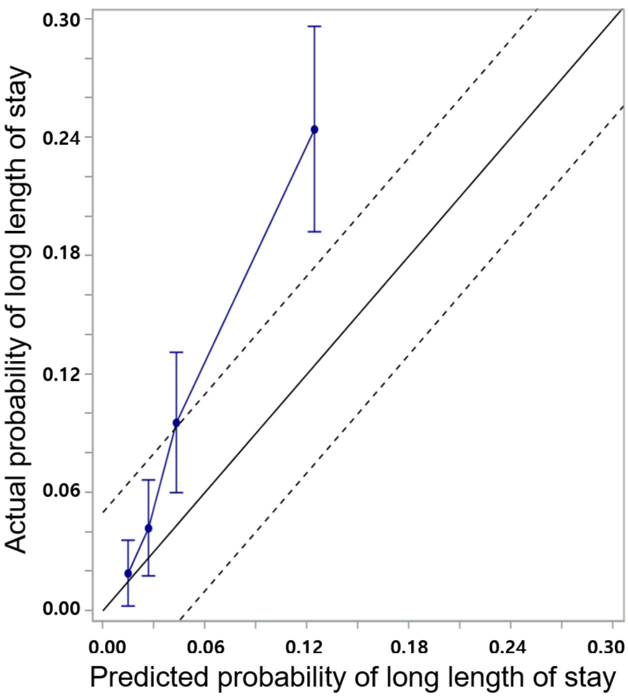
(D)


0.10
0.05
0.00
Actual probability of reoperation
0.00
0.05
0.10
Predicted probability of reoperation

(E)


0.50
0.40
0.30
0.20
0.10
0.00
Actual probability of morbidity or mortality
0.00
0.08
0.16
0.24
0.32
0.40
0.48
Predicted probability of morbidity or mortality

(F)


0.30
0.24
0.18
0.12
0.06
0.00
Actual probability of long length of stay
0.00
0.06
0.12
0.18
0.24
0.30
Predicted probability of long length of stay

(G)

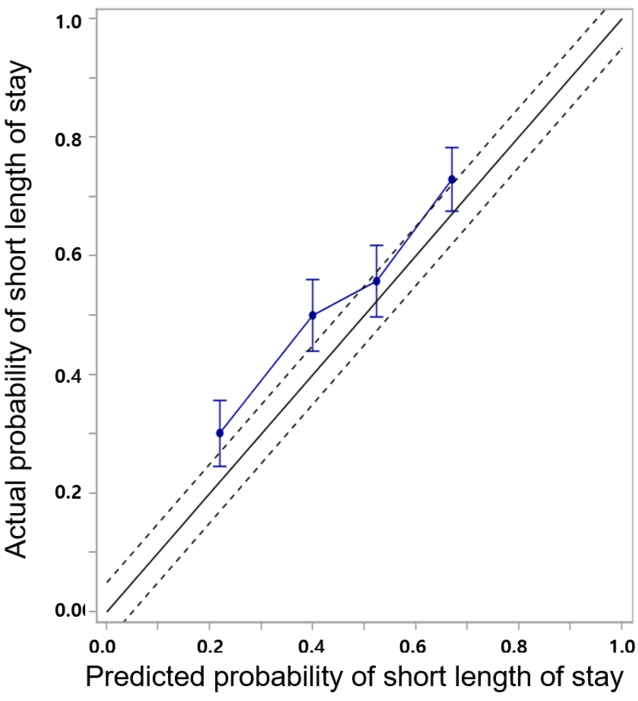
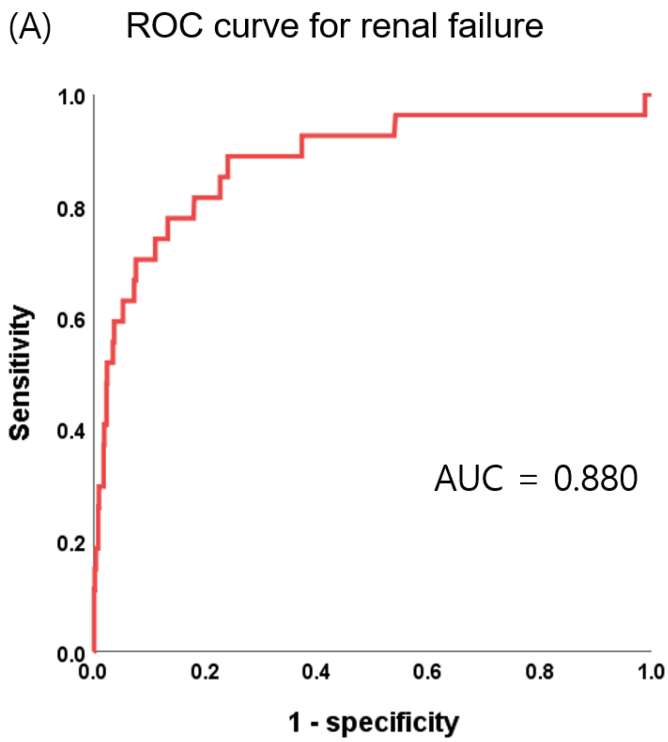
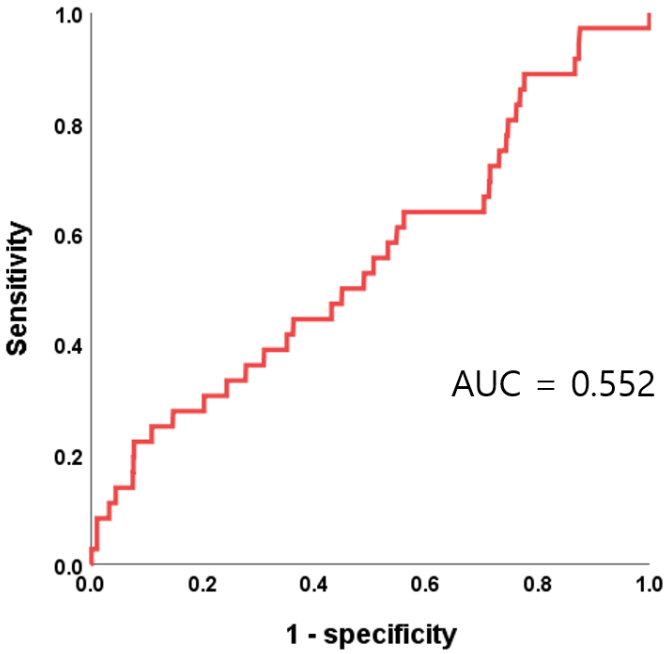

1.0
0.8
0.6
0.4
0.2
0.0
Actual probability of short length of stay
0.0
0.2
0.4
0.6
0.8
1.0
Predicted probability of short length of stay

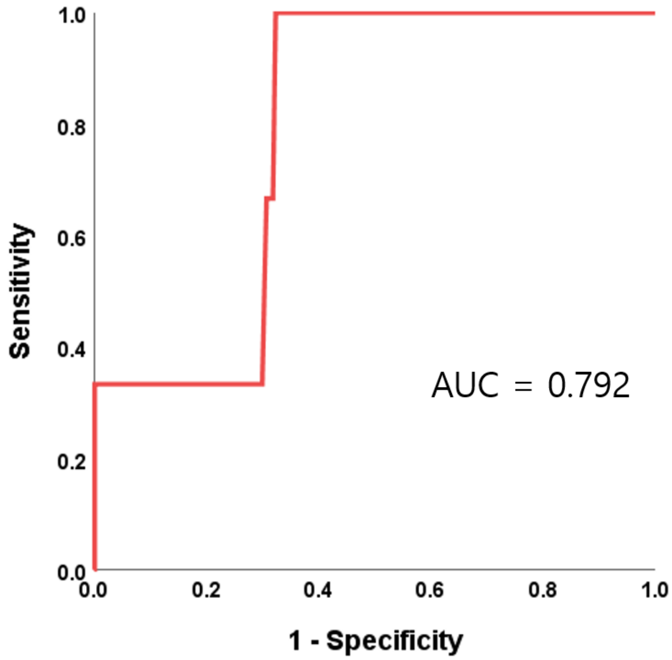
Figure 5. Receiver operating characteristic (ROC) curves of (A) renal failure, (B) reoperation, (C) deep sternal wound (DSW) infection, (D) prolonged ventilation, (E) mortality or morbidity, (F) long length of stay, and (G) short length of stay calculated by the STS risk model.



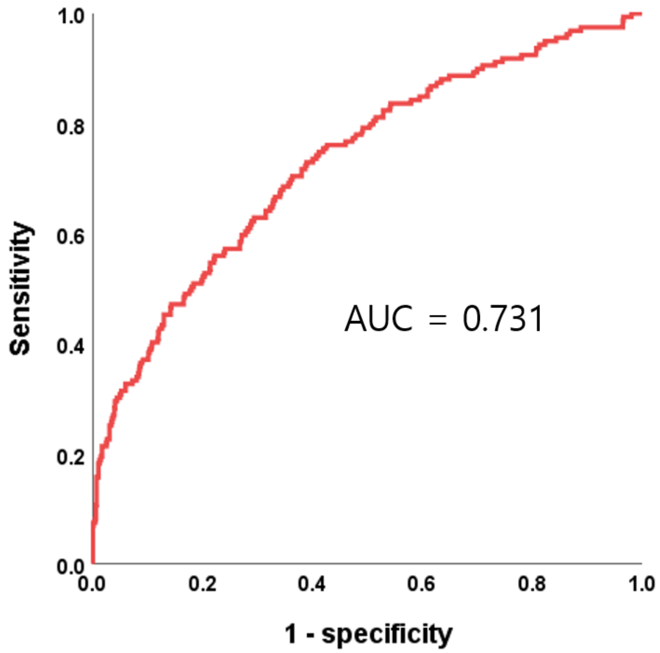
(B) ROC curve for reoperation



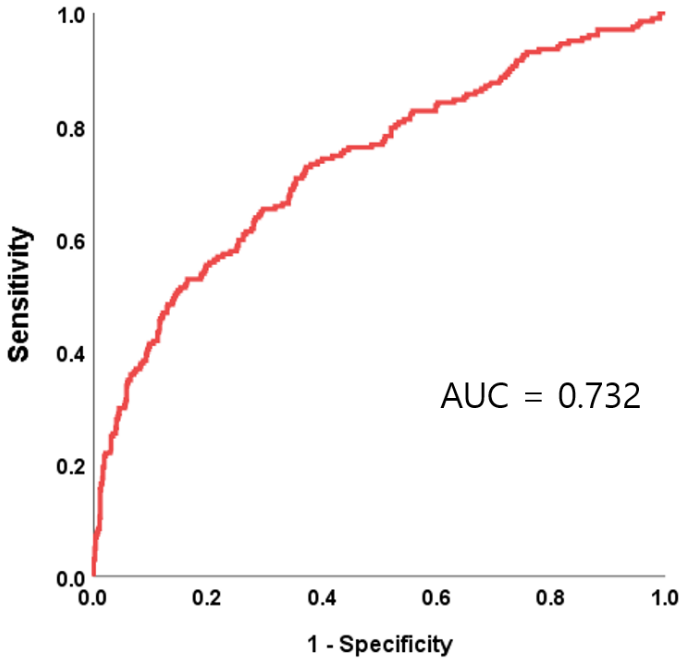
(C) ROC curve for DSW infection



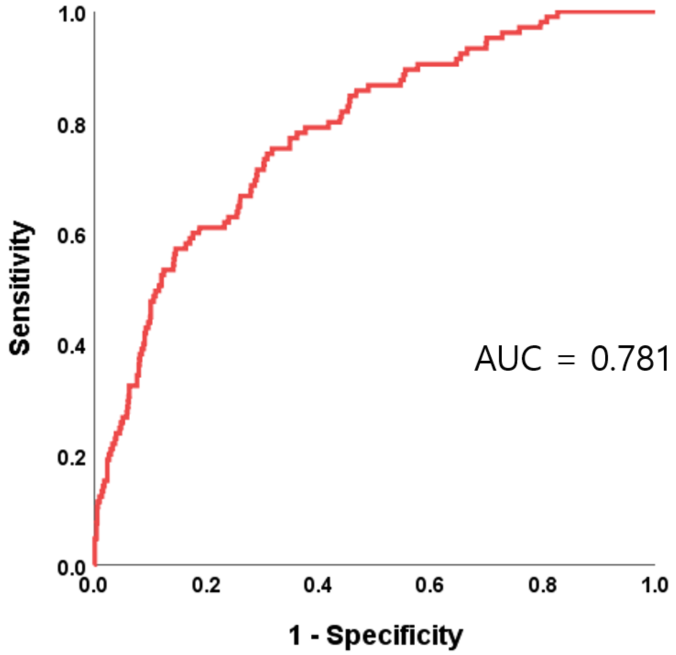
(D) ROC curve for prolonged ventilation



(E) ROC curve for mortality or morbidity



(F) ROC curve for long length of stay



(G) ROC curve for short length of stay

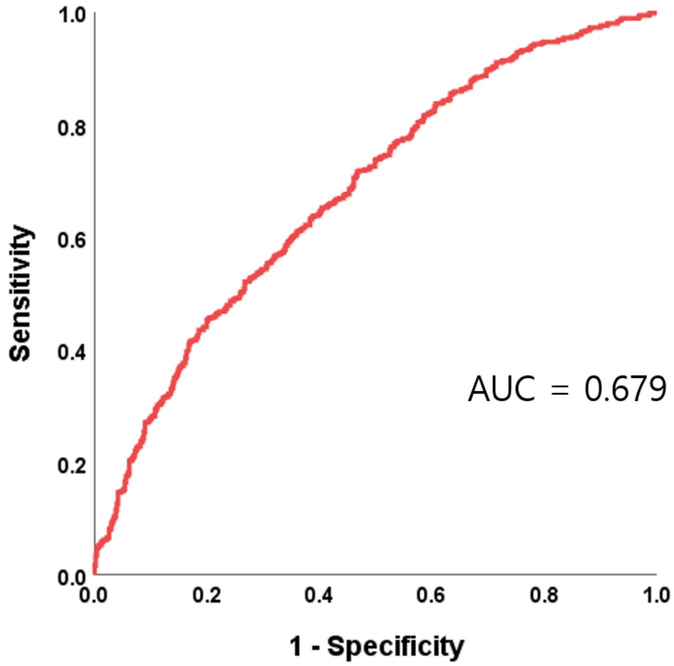


Table 1. Preoperative characteristics and risk factors of the study patients

Variables	Total (n = 1048)
Age (y)	66.0 ± 10.0
Male, n (%)	794 (75.8)
Risk factors, n (%)	
Overweight (body mass index> 25 kg/m^2)	416 (39.7)
Smoking	337 (32.2)
Hypertension	747 (71.3)
Diabetes mellitus	522 (49.8)
Dyslipidemia	333 (31.8)
History of stroke	142 (13.5)
Chronic renal failure (GFR <60 mL/min)	164 (15.6)
Chronic obstructive pulmonary disease	32 (3.1)
Peripheral vascular disease	248 (23.7)
Left ventricular dysfunction (LVEF <30%)	79 (7.5)
Redo surgery	32 (3.1)
Emergency operation	17 (1.6)
Diagnosis	
Acute coronary syndrome	686 (65.5)
Stable angina	362 (34.5)
Three vessel disease with left main disease	294 (28.1)
Three vessel disease without left main disease	459 (43.8)
Two vessel disease with left main disease	92 (8.8)
Two vessel disease without left main disease	157 (15.0)
Single vessel disease	46 (4.4)

Data are presented as the mean ± SD or n (%).

GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction.

Table 2. Operative and early clinical results

Variables	Total (n = 1048)
Off-pump CABG	1043 (99.5)
Number of anastomoses per patient	3.4 ± 1.0
Composite grafts	1019 (97.2)
Use of internal thoracic artery	1044 (99.6)
Conduits used	
Left internal thoracic artery	1001 (95.5)
Right internal thoracic artery	113 (10.8)
Right gastroepiploic artery	13 (1.2)
Radial artery	1 (0.1)
Saphenous vein	968 (92.4)

Data are presented as the mean ± SD or n (%).

CABG, coronary artery bypass grafting;

Table 3. Calibration of the STS risk model and EuroSCORE II for all patients

Variables (n = 1048)	Observed events	Score	Expected events	O/E ratio (95% CI)	P*
EuroSCORE II	10 (0.95)	2.58±4.15	27.0	0.370 (0.177 – 0.681)	0.003
STS risk model					
Mortality	10 (0.95)	1.72±2.92	18.0	0.556 (0.266 – 1.023)	0.052
Permanent stroke	6 (0.57)	1.73±1.48	18.1	0.332 (0.121 – 0.722)	0.011
Renal failure (n=975)	31 (2.96)	1.75±3.43	17.1	1.762 (1.188 – 2.515)	<0.001
Reoperation	37 (3.7)	2.95±1.16	30.9	1.167 (0.817-1.614)	0.2137
Deep sternal wound infection	3 (0.35)	0.17±0.01	1.8	1.653 (0.332-4.829)	0.048
Prolonged ventilation	160 (15.25)	7.61±8.85	79.8	1.993 (1.695-2.328)	<0.001
Morality or morbidity	201 (19.18)	12.11±11.81	126.9	1.583 (1.372-1.818)	<0.001
Long length of stay	106 (10.1)	5.23±6.43	54.8	1.917 (1.568-2.320)	<0.001
Short length of stay	547 (52.1)	45.32±17.50	475.0	1.152 (1.057-1.252)	<0.001

* P value was calculated by Hosmer-Lemeshow test

Table 4. Calibration of the STS risk score for subgroups

Variables (n = 834)	Observed events	Score	Expected events	O/E ratio (95% CI)	P*
Mortality	7 (0.8)	1.74±2.77	14.5	0.481 (0.193-0.992)	0.055
Permanent stroke	5 (0.7)	1.76±1.45	14.7	0.340 (0.110-0.794)	0.020
Renal failure (n = 795)	24 (3.0)	1.81±3.53	14.0	1.717 (1.100-2.555)	0.007
Reoperation	30 (3.6)	2.94±1.15	24.5	1.223 (0.825-1.746)	0.240
Deep sternal wound infection	1 (0.1)	0.17±0.01	1.4	0.685 (0.009-3.813)	0.333
Prolonged ventilation	125 (15.0)	7.51±8.30	62.6	1.996 (1.661-2.378)	<0.001
Morality or morbidity	160 (19.2)	11.95±10.85	99.7	1.605 (1.366-1.874)	<0.001
Long length of stay	93 (11.2)	5.24±6.08	43.7	2.128 (1.718-2.607)	<0.001
Short length of stay	407 (48.8)	44.69±17.48	372.7	1.092 (0.989-1.204)	0.008

* P value was calculated by Hosmer-Lemeshow test

Table 5. Discrimination power of the STS risk model and EuroSCORE II

Variables (n = 1048)	Area under the ROC curve (95% CI)	P
EuroSCORE II	0.784 (0.643 - 0.924)	0.002
STS risk model		
Mortality	0.876 (0.743 - 1.000)	<0.001
Permanent stroke	0.733 (0.540 – 0.926)	0.049
Renal failure (n=772)	0.880 (0.800 – 0.961)	<0.001
Reoperation	0.552 (0.451 – 0.653)	0.285
DSW infection	0.792 (0.624 – 0.959)	0.081
Prolonged ventilation	0.731 (0.687 – 0.776)	<0.001
Morality or morbidity	0.732 (0.691 – 0.772)	<0.001
Long length of stay	0.781 (0.736 – 0.827)	<0.001
Short length of stay	0.679 (0.647 – 0.712))	<0.001

DSW, deep sternal wound; ROC, receiver operating characteristic.

Table 6. Association between SYNTAX score and mortality or morbidity

Variables	Patients with mortality or morbidity (n = 199)	Patients without mortality or morbidity (n = 847)	P
SYNTAX score I	32.8±12.5	32.1±11.3	0.469
SYNTAX score II	36.3±12.2	30.5±11.3	<0.001

Table 7. Calibration of the STS risk model and EuroSCORE II for high risk patients

Variables (n = 80)	Observed events	Score	Expected events	O/E ratio (95% CI)
EuroSCORE II	5 (6.3)	11.7±9.7	9.36	0.534 (0.172 – 1.247)
STS risk model				
Mortality	5 (6.3)	9.0±6.9	7.2	0.694 (0.224 – 1.621)
Permanent stroke	1 (1.3)	4.7±2.6	3.76	0.266 (0.003 – 1.48)
Renal failure (n=62)	6 (9.7)	8.8±9.7	5.45	1.101 (0.402 – 2.396)
Reoperation	7 (8.8)	5.4±1.9	4.32	1.62 (0.649 – 3.339)
DSW infection	1 (1.3)	0.3±0.2	0.24	4.167 (0.054 – 23.18)
Prolonged ventilation	40 (50.0)	30.1±17.8	24.08	1.661 (1.187 –2.262)
Morality or morbidity	48 (60.0)	42.2±20.2	33.76	1.422 (1.048 – 1.885)
Long length of stay	29 (36.3)	21.8±12.3	17.44	1.663 (1.113 – 2.388)
Short length of stay	17 (21.3)	12.6±5.8	10.08	1.687 (0.981– 2.7)

* P value was calculated by Hosmer-Lemeshow test

DSW, deep sternal wound.

국문초록

대동맥에 대한 조작이 없는 무심폐기하 관상동맥 우회술에서 기존의 위험성 예측 시스템의 임상적 유용성 평가에 대한 연구

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서론: 수술 후 위험도를 점수로 예측하는 시스템은 환자의 수술 위험도를 측정하고, 고위험군 환자를 확인하는데 이용된다. 현재 STS 위험도 예측 모델과 EuroSCORE II는 심장 수술 환자에서 널리 이용되고 있으며, SYNTAX score II 는 관상동맥 우회술 후 4년 사망률을 예측한다. 이 연구에서는 현재 존재하고 있는 위험도 예측 시스템인 STS 위험도 예측 모델, EuroSCORE II, SYNTAX score II가 대동맥 조작이 없는 무심폐기하 관상동맥 우회술 환자에서 임상적 유의성을 보이는지 평가해 보도록 하겠다.

방법: 2010년 1월부터 2017년 6월까지, 수술 전 무심폐기하 관상동맥 우회술을 계획한 1,140명의 환자 중, 대동맥 조작이 없는

무심폐기하 관상동맥 우회술을 시행한 1043명의 환자와 수술 중 심폐기를 가동하게 된 5명의 환자를 포함하여 총 1048명의 환자를 대상으로 하였다. STS score, EuroSCORE II, SYNTAX score II는 인터넷 프로그램을 이용하여 후향적 또는 전향적으로 계산되었다. STS 위험도 모델과 EuroSCORE II의 calibration은 실제 발생한 사건 수를 예측 발생 사건 수로 나눈 risk-adjusted event ratio (O/E ratio) 와 Hosmer-Lemeshow 검사를 이용하여 평가하였고, 분별력은 ROC curve의 면적 (AUC)을 통하여 평가하였다. Student's t-test는 수술 후 사망 또는 합병증이 발생한 환자와 그렇지 않은 환자에서 SYNTAX score I 과 II를 비교하는데 이용되었다.

결과: 수술 후 사망은 10명(0.95%)에서 발생했다. EuroSCORE II와 STS 위험도 모델로 계산한 예측 사망률은 각각 2.58 ± 4.15%, 1.72 ± 2.92% 이였다. EuroSCORE II는 사망률을 통계적으로 의미있게 높게 평가 했으며 (P = 0.003), O/E ratio는 0.370 (신뢰구간: 0.177-0.681) 이었다. EuroSCORE II는 AUC가 0.784로 좋은 분별력을 보여주었다. STS 위험도 모델의 사망률에 대한 O/E ratio는 0.556 (신뢰구간: 0.266 - 1.023) 였으며, 예측 사망률은 실제 발생에 비하여 높게 계산되었으며, 통계적으로 경계성 유의성을 보였다 (P = 0.052). 그러나 하위집단 분석에서 STS 위험도 모델은 사망률을 통계적으로 의미있게 높게 예측하였다. (O/E ratio: 0.481, 신뢰구간: 0.193-0.992). 수술 후 영구적 뇌졸중은 6명(0.53%)에서 발생했으며, STS 위험도 모델로 예측한

영구적 뇌졸중 발생률은 1.73 ± 1.48%이었다. O/E ratio는 0.332 (신뢰구간: 0.121 – 0.722) 였고, STS 위험도 모델은 영구적인 뇌졸중 발생을 통계적으로 의미있게 높게 예측하였다 (P = 0.011). STS 위험도 모델의 사망률과 영구적 뇌졸중 발생률에 대한 분별력은 AUC가 각각 0.876, 0.740이었다. 수술 후 사망 또는 합병증이 발생한 환자와 그렇지 않은 환자의 SYNTAX score를 비교하였을 때, 두 그룹에서 SYNTAX score I은 차이를 보이지 않았으며 (P =0.469), SYNTAX score II는 수술 후 사망 또는 합병증이 발생한 환자에서 유의하게 높게 나타났다 (P<0.001).

결론: 관상동맥 우회술에 대한 기존의 위험도 예측 시스템인 STS 위험도 모델과 EuroSCORE II는 대동맥 조작이 없는 무심폐기하 관상동맥 우회술에서 사망률과 뇌졸중 발생률을 실제보다 높게 예측했다. 이러한 결과는 무심폐기하 관상동맥 우회술이 기존의 관상동맥 우회술보다 사망률과 뇌졸중 발생을 낮출 수 있다는 가능성을 시사한다. 또한, 이러한 결과는 관상동맥 우회술의 수술 위험도를 예측할 때 대동맥 조작이 없는 무심폐기하 관상동맥 우회술 같은 수술의 방법적 특성이 반드시 고려되어야 함을 보여준다.

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주요어: 수술 위험도 예측 시스템, 관상동맥 우회술, 무심폐기, 대동맥 무조작

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