Coronary artery bypass graft surgery provides better survival in patients with acute coronary syndrome or ST-segment elevation myocardial infarction experiencing cardiogenic shock after percutaneous coronary intervention: A propensity score analysis

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Objective: The objective of this study was to find the best treatment strategy in patients who had acute coronary syndrome and ST-segment elevation myocardial infarction sustaining cardiogenic shock.

Methods: Patients having cardiogenic shock owing to acute coronary syndrome and ST-segment elevation myocardial infarction who required hemodynamic support with intra-aortic balloon counterpulsation were retrospectively retrieved from the clinical information system in a tertiary medical center in Taiwan. A propensity score-based matching process was applied to find equalized groups with documented involvement of more than 2 coronary vessels who received percutaneous coronary intervention only (PCI only group) and who underwent subsequent coronary artery bypass graft surgery after percutaneous coronary intervention (PCI+CABG group). A logistic regression model was used to find the factors associated with 30-day mortality.

Results: The propensity analysis identified 44 patients in the PCI only group (35 men, 65 ± 2 years, and 9 women, 75 ± 4 years) and the other 44 patients in the PCI+CABG group (31 men, 67 ± 2 years, and 13 women, 71 ± 2 years) who had comparable baseline characteristics. The 30-day mortality, 40.9% in the PCI only group and 20.5% in the PCI+CABG group, was positively associated with percutaneous coronary intervention only (odds ratio, 3.33; 95% confidence intervals, 1.14–10.0; $P = .03$), increased age (odds ratio, 1.06 for each year; 95% confidence intervals, 1.01–1.12; $P = .01$) and a need to use extracorporeal membrane oxygenation (odds ratio, 9.64; 95% confidence intervals, 2.19–42.4; $P < .001$).

Conclusions: This study has shown the survival benefit of surgical intervention in high-risk patients with acute coronary syndrome or ST-segment elevation myocardial infarction who had cardiogenic shock after percutaneous coronary intervention. (J Thorac Cardiovasc Surg 2009;138:1326-30)

Cardiogenic shock complicates the course of 5% to 15% of patients with acute myocardial infarction¹⁻³ and accounts for a large percentage of mortality from myocardial infarction.^{2,4} Initial stabilization of cardiogenic shock with intra-aortic balloon pumping (IABP) was associated with a 20% absolute risk reduction in mortality.⁵⁻⁷ The Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO)-1 trial and the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial also showed that early revas-

cularization resulted in improved survival in the patients with cardiogenic shock compared with medical treatment alone.^{8,9}

However, there is no consensus whether percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) results in better outcome. Some guidelines suggest that primary PCI is preferred to CABG for patients with 1- or 2-vessel coronary artery disease and technically suitable lesions.¹⁰ Immediate CABG is the preferred treatment for left main or severe 3-vessel disease. In the analysis from the SHOCK trial, CABG and PCI were associated with equivalent outcomes, although patients undergoing CABG had more comorbid diseases such as diabetes and multivessel involvement.¹¹ However, owing to the critical conditions in the patients with cardiogenic shock, it is difficult, if not impossible, to conduct a randomized trial to compare the effects of emergency PCI or CABG.

Therefore, the objective of this study was to assemble patients having cardiogenic shock treated with either PCI only or PCI with subsequent CABG (PCI+CABG) who were comparable in baseline characteristics and disease severity so as to determine the survival difference between the two treatment strategies.

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Received for publication Oct 23, 2008; revisions received Feb 24, 2009; accepted for publication March 20, 2009; available ahead of print June 11, 2009.

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0022-5223/\$36.00

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doi:10.1016/j.jtcvs.2009.03.038

Abbreviations and Acronyms

ACS	= acute coronary syndrome
ALKK	= Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte
CABG	= coronary artery bypass graft surgery
95% CI	= 95% confidence intervals
ECMO	= extracorporeal membrane oxygenation
GUSTO	= Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries
IABP	= intra-aortic balloon pumping
OR	= odds ratio
PCI	= percutaneous coronary intervention
SHOCK	= SHould we emergently revascularize Occluded Coronaries for cardiogenic shock
STEMI	= ST-segment elevation myocardial infarction
TIMI	= Thrombolysis In Myocardial Infarction

METHODS**Study Design**

We conducted a nonrandomized study comparing survival between patients with cardiogenic shock owing to ST-segment elevation myocardial infarction (STEMI) or acute coronary syndrome (ACS) treated with PCI only and PCH+CABG in a tertiary medical center in Taiwan. A propensity score method was used to elucidate factors associated with high probability for getting CABG. The score was further applied to find subsets within both groups so that potential covariates were comparable, aiming to make retrospective study cohorts like an evenly distributed randomized trial.

Subjects and Materials

Our institution, a 2400-bed university-affiliated tertiary teaching hospital equipped with a 227-bed intensive care unit and 40 emergency department observatory units, is a tertiary referral center for cardiovascular emergency. All the discharge notes during the period from 2002 to 2004 in the clinical information system were downloaded, and eligible patients who had STEMI or ACS (unstable angina and non-STEMI) complicated by cardiogenic shock caused by left ventricular dysfunction were retrieved. Cardiogenic shock was defined by either clinical or hemodynamic data. The clinical criteria included systolic blood pressure less than 90 mm Hg for more than 1 hour not responsive to fluid administration alone and end-organ hypoperfusion (urine output $< 0.5 \text{ mL} \cdot \text{h}^{-1} \cdot \text{kg}^{-1}$ or cool extremities). Hemodynamic criteria included cardiac index below $2.2 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ of body surface area and pulmonary capillary wedge pressure more than 18 mm Hg. Exclusion criteria were recent intracranial hemorrhage (< 6 months), recent trauma or major operation, active bleeding, and unsuitability for revascularization. Patients with a mechanical complication of myocardial infarction such as ventricular septal defect, papillary muscle rupture, or myocardial rupture were also excluded. The onset of shock had to be within 36 hours of myocardial infarction. All patients received IABP and PCI within 12 hours after onset of STEMI or after onset of symptoms of cardiogenic shock in patients with ACS. The decision to undergo subsequent CABG after PCI in these patients remaining in shock depended on the attending cardiologists' discretion, clinical conditions, and the preference of the family.

Demographic, hemodynamic, and mortality data were also derived from paper and electronic medical records. Laboratory data were retrieved from the laboratory information system.

Propensity Score Methods

Propensity score matching is a method used to balance observed covariates in the two treatment groups, that is, PCI only and PCH+CABG.¹² In this study, propensity score is the conditional probability for getting CABG, as a binary dependent variable, under a set of measurements. All baseline characteristics and parameters, potentially related to survival, were included in a logistic regression model as covariates. This matching process made observational studies imitate a randomized trial and reduced selection bias in the study cohorts.¹³

Age, sex, initial cardiac enzyme level (troponin I $> 50 \text{ ng/mL}$ or not), Killip classification, left ventricular ejection fraction, hemoglobin level, diabetes, hypertension, renal function, and the need for extracorporeal membrane oxygenation (ECMO) were added into a nonparsimonious multivariable logistic regression model to predict the decision to perform CABG. The predicted probability derived from the logistic equation was used as the propensity score for each individual.

Study Cohort Assembly

Patients with cardiogenic shock who received PCH+CABG therapy or who received PCI only were pooled together and sorted according to their propensity score in an ascending order. Subjects for whom an appropriate match within an acceptable rank range could not be found were excluded from further analysis.

Statistical Analysis

A logistic regression model was used to perform the propensity match under SPSS 13.0 (SPSS Inc, Chicago, Ill). Odds ratio (OR) and 95% confidence intervals (95% CI) were used to represent the predilection for a subject to be treated with CABG. Patients with lower and higher propensity scores were excluded from further analysis if an appropriate match could not be found. After the 1:1 matched groups were assembled, the propensity scores of both PCH+CABG and PCI only groups were reported. Baseline patient characteristics were compared with χ^2 test (for categorical data) or with the Student *t* test (for continuous variables). The χ^2 test was used to compare the 30-day mortality between the two groups. Another logistic regression model was used to find the factors, in addition to CABG, associated with 30-day mortality.

RESULTS

Initially, 86 patients receiving PCH+CABG and 69 patients receiving PCI only owing to multiple-vessel diseases and cardiogenic shock were enrolled. Age was 66.7 ± 11.1 years in the PCH+CABG group and 67.6 ± 13.8 years in the PCI only group (Table 1). The average time from symptom onset to shock was 7.2 ± 7.0 hours in the PCI group and 5.7 ± 5.4 hours in the PCH+CABG group. There were no significant differences between the two groups ($P = .275$). Mortality rate was statistically lower in the CABG group at 7 days (11.1% vs 21.4%; $P = .02$) and 30 days (17.1% vs 35.7%; $P < .001$).

Propensity analysis showed the odds with which a patient would or would not receive subsequent CABG if certain clinical characteristics existed. Vessel condition (3-vessel disease or left main involvement) was shown to be one of the determining factors that led to subsequent CABG (OR,

TABLE 1. Baseline characteristics and mortality in patients with PCI and subsequent CABG or with PCI only, before propensity score–based matching

	PCI+CABG	PCI only	<i>P</i> value
No. of patients	86	69	
Age (y)	66.7 ± 11.1	67.6 ± 13.8	.63
Male (%)	72.1	76.8	.58
Hypertension (%)	38.4	49.3	.19
Diabetes mellitus (%)	32.6	36.2	.73
Troponin I > 50 (%)	36.0	49.3	.25
LVEF < 40% (%)	82.6	69.6	.14
Killip			.02
I or II (%)	24.4	24.6	
III (%)	25.6	36.2	
IV (%)	46.5	39.1	
ECMO use (%)	15.1	10.1	.36
Diseased vessel			.002
Two-vessel disease (%)	17.4	42.0	
Three-vessel disease (%)	54.7	44.9	
LM + 3-vessel disease (%)	27.9	13.0	
LVEF (%)	36.4 ± 11.2	33.5 ± 13.7	.52
Hemoglobin (g/dL)	12.0 ± 2.0	11.8 ± 2.0	.73
Creatinine (mg/dL)	1.6 ± 1.5	3.1 ± 11.4	.26
Propensity score	0.6453 ± 0.1971	0.4421 ± 0.2040	<.001

PCI, Percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; LVEF, left ventricular ejection fraction; ECMO, extracorporeal membrane oxygenation; LM, left main coronary artery.

2.4; $P = .003$; 95% CI, 0.14–4.2). Initial left ventricular ejection fraction less than 40% (OR, 0.34; $P = .059$; 95% CI, 0.11–1.04) and initial troponin I more than 50 ng/mL (OR, 0.43; $P = .084$; 95% CI, 0.17–1.11) were less prone to require CABG, with a borderline significance. Parameters such as sex, age, renal function, diabetes, hypertension, ECMO use, non-STEMI, or STEMI did not seem to affect the decision in choosing CABG. All the predictors remained in the model and were used to calculate the propensity score for CABG. Propensity score was 0.6453 ± 0.1971 in patients receiving CABG and 0.4421 ± 0.2040 in patients receiving PCI. The propensity in predisposing to the selection of CABG was statistically significant ($P < .001$).

The propensity score–matching process selected 44 patients receiving PCI+CABG and the other 44 patients receiving PCI only for further analysis. The average time of CABG after PCI in PCI+CABG group was 2.8 days, a range from 1 to 19 days. Twenty patients received cardioplegic arrest and on-pump CABG, and the others received beating-heart and off-pump CABG. The average number of revascularized vessels via initial PCI was 1.3 (3-vessel revascularization in 3 patients, 2 vessels in 22, and 1 vessel in 63). The average number of revascularized vessels via subsequent CABG was 2.6 (3 vessels in 28 patients and 2 vessels in 16). There were 4 patients with moderate to severe mitral insufficiency in the PCI group and 2 patients with moderate to severe mitral insufficiency in the PCI+CABG group. One patient received mitral valve repair during CABG. The mean age was 68.5

TABLE 2. Baseline characteristics and mortality in patients with PCI and subsequent CABG or with PCI only, after propensity score–based matching

	PCI+CABG	PCI only	<i>P</i> value
No. of patients	44	44	
Propensity scores	0.5363 ± 0.1807	0.5355 ± 0.1809	.98
Age (y)	68.5 ± 10.1	67.0 ± 14.1	.57
Male (%)	79.5	70.5	.46
Hypertension (%)	45.5	43.2	.83
Diabetes mellitus (%)	38.6	34.1	.66
Troponin I > 50 (%)	50.0	47.7	.97
LVEF (%)			.40
>40%	15.9	6.8	
<40%	6.8	6.8	
Unknown (%)	77.3	86.4	
Killip			.72
I or II (%)	27.3	20.5	
III (%)	27.3	29.5	
IV (%)	45.5	50.0	
ECMO use (%)	13.6	15.9	.76
Diseased vessel			.44
Two-vessel disease (%)	25.0	34.1	
Three-vessel disease (%)	59.1	45.5	
LM + 3-vessel disease (%)	15.9	20.5	
LVEF (%)	32.8 ± 11.1	29.6 ± 14.4	.62
Hemoglobin (g/dL)	12.1 ± 2.1	12.0 ± 2.1	.77
Creatinine (md/dL)	1.7 ± 1.5	1.7 ± 1.2	.98

PCI, Percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; LVEF, left ventricular ejection fraction; ECMO, extracorporeal membrane oxygenation; LM, left main coronary artery.

± 10.1 years in the PCI+CABG group and 67.0 ± 14.1 years in the PCI only group ($P = .57$). The percentage of initial troponin I more than 50 ng/mL and the percentage of initial left ventricular ejection fraction less than 40% were similar in both groups ($P = .97$ and $P = .40$, respectively). The distribution of vessel status and other baseline characteristics were comparable (Table 2). Propensity score was 0.5363 ± 0.1807 in the PCI+CABG group and 0.5355 ± 0.1809 in the PCI only group ($P = .98$).

The 7-day mortality was of no significant difference between the PCI+CABG and the PCI only groups (15.9% vs 25%; $P = .29$). The 30-day mortality was statistically lower in the PCI+CABG group (20.5% vs 40.9%; $P = .03$). Multivariate logistic regression model found that the 30-day mortality was negatively associated with CABG (OR, 0.30; 95% CI, 0.10–0.88; $P = .03$) and positively associated with increased age (OR, 1.06 for each year; 95% CI, 1.01–1.12; $P = .01$) and a need to use ECMO (OR, 9.64; 95% CI, 2.19–42.4; $P < .001$).

DISCUSSION

Although patients with more coronary vessel involvement and less extent of myocardial damage were prone to undergoing CABG, the results of this study have demonstrated an

observed survival benefit in the patients with cardiogenic shock receiving PCI and subsequent CABG. In the propensity analysis, PCI followed by CABG has still provided survival benefit over PCI only.

The postoperative mortality in cardiogenic shock has been documented principally as a result of delay of operation (beyond 18 hours) leading to progression of preoperative organ failure or progression of underlying cardiac disease.¹⁴ Our patients received revascularization by PCI within 12 hours after STEMI or 12 hours after shock in non-ST-elevated ACS. The early intervention in our patients (average time of CABG after PCI was 2.8 days) made the 30-day mortality not inferior to prior studies.

In the GUSTO-I study, the 30-day mortality in the 406 patients who underwent early catheterization was 38%.⁸ In the SHOCK trial, the 30-day mortality rate in early revascularization patients was 46.7%.⁹ Our patients treated with PCI only had the same mortality rate (40.9%) as reported in previous large trials, but the patients treated with PCI+CABG had a lower mortality rate (20.5%). In the SHOCK registry, CABG and PCI were associated with equivalent outcomes even if there was significantly more comorbidity (diabetes and multivessel diseases) in the CABG group.¹¹ The similar outcomes, despite the worse condition in patients undergoing CABG, may reflect in part the higher rate of complete revascularization (CABG 87% vs PCI 23%).¹¹ In our study, patients in both groups received early revascularization by immediate IABP and emergency PCI after cardiogenic shock. The ability to achieve further complete revascularization by CABG may explain the better outcome in this group, given equal left ventricular function and diseased vessel status in both groups.

The in-hospital mortality after PCI in cardiogenic shock is related to the degree of reperfusion achieved in the infarct-related artery.^{4,15} Among 276 patients in the nonrandomized SHOCK registry undergoing PCI, the mortality for Thrombolysis In Myocardial Infarction (TIMI) 3, TIMI 2, and TIMI 1/0 flow was 33%, 50%, and 86%, respectively.¹⁵ A report from the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK) primary PCI registry in Germany also demonstrated the same mortality relationship to TIMI flow.¹⁶ Although we did not have thallium or coronary angiographic images after CABG, complete revascularization was one of the reasonable explanations of better survival.

Remote muscle contraction maintained cardiac contractility in myocardial infarction. Improved availability of vessels was a key element toward secondary salvage of remote muscle, which carried the day in relationship to survival. Allen and associates¹⁷ reported that surgical intervention at the time of acute myocardial infarction, using controlled reperfusion, salvaged contractile recovery of regions supplied both by the infarct vessel and by remote muscle. As compared with CABG, PCI seems to cause more dyskinetic non-

reperfused segments to develop akinesis and thereby renders the infarct-related muscle unable to recover.¹⁷ The subsequent CABG after PCI might have benefit to the remote muscle. Besides, the infarct-related region may have lost function (immediately after the acute myocardial infarction), progressively dilated, and impaired remote muscle function owing to geometric process.¹⁸ Surgical intervention by CABG with ventricular restoration is reported to reduce late mortality and morbidity. Although our patients did not receive ventricular restoration, the timely surgical intervention provided an alternative treatment option in cardiogenic shock.

The analysis in our propensity score-matched study showed that CABG was an independent factor associated with better outcome, but old age and ECMO use were associated with worse outcome. In the SHOCK registry, the notable exception of higher survival with early revascularization was a differential treatment effect by age.¹⁹ The younger patients (<75 years old) derived a large benefit from early revascularization, in contrast to an apparent lack of benefit for those 75 years of age and older. We also demonstrated that age was one of the important independent factors associated with worse survival in our study, compatible with the SHOCK registry. Because the number of patients with age equal to or more than 75 years was not large enough in our cohort, we were conservative to conclude that PCI+CABG was still better than PCI only in the elderly patients.

The fact that ECMO use was associated with a poor outcome might be related to more severe conditions in the patients who needed it. Besides, ECMO use provided no benefit to coronary blood flow, and it only earned “additional time” for physicians to achieve complete revascularization in cardiogenic shock.²⁰ In previous studies, patients in cardiogenic shock on admission had higher in-hospital mortality than those in whom shock developed after hospitalization.^{21,22} However, in our analysis, the initial Killip classification was not an independent factor related to survival once the cardiogenic shock later developed.

Limitations

The propensity analysis would exclude the patients with high or low propensity score owing to lack of adequate control. Further studies will be needed to find the optimal mode of revascularization in those who are at an extreme risk so that CABG is the last resort and in those whose hemodynamics can be maintained so that CABG will not be considered a necessity. We found that increased vessel involvement (3-vessel and left main disease) was more likely to necessitate CABG, and some of these patients with a high propensity score might have been excluded.

In addition, we considered that all of the patients having cardiogenic shock after PCI and requiring IABP had very grave hemodynamic conditions. Possible prognostic factors

at the moment, such as general conditions, vessel conditions, and comorbid conditions (eg, renal function), were matched by propensity score. The remaining factors that led to the decision for CABG were family preference, financial problems, and social stigma, which we assumed were not associated with the outcome. However, this propensity-score-based method cannot replace the evidence provided by a full-scale randomized trial. Further prospective studies may be needed to further examine our results.

CONCLUSIONS

This study has demonstrated the survival benefit of surgical intervention in the high-risk patients with ACS or STEMI who had cardiogenic shock and required IABP after PCI. Further studies will be needed to identify the mechanism of benefit of surgical intervention, such as complete revascularization.

We thank those doctors and health providers in National Taiwan University Hospital who provided high quality of care to the patients with cardiogenic shock. The assistance by Professor Feipei Lai, Miss Man-Hsiang Chang, and the Information Systems Office of National Taiwan University Hospital is much appreciated.

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