

Comparison of Off-Pump Coronary Artery Bypass between Octogenarians and Septuagenarians: A Propensity Score Analysis

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Background: Coronary artery bypass grafting (CABG) is being offered increasingly frequently to octogenarians. However, old age is known to be an independent risk factor in CABG. The aim of this study was to compare the outcomes of off-pump coronary artery bypass (OPCAB) between octogenarians and septuagenarians. **Methods:** We retrospectively reviewed the data of 1,289 consecutive patients aged ≥ 70 years who underwent OPCAB at a single institution between 2001 and 2016. We compared the outcomes of 115 octogenarians and 1,174 septuagenarians. Using propensity score matching, based on preoperative clinical characteristics, 114 octogenarians were matched with 338 septuagenarians. **Results:** Propensity score analysis revealed that the incidence of acute kidney injury (14.9% vs. 7.9%, $p=0.028$) and respiratory complications (8.8% vs. 4.2%, $p=0.040$) was significantly higher in octogenarians. The early mortality rate (2.6% vs. 1.0%, $p=0.240$) and 1-year survival rate (89.5% vs. 94.4%, $p=0.097$) were not statistically significant between the groups. However, the 5-year survival rate (67.3% vs. 79.9%, $p<0.001$) was significantly lower in octogenarians. Previous myocardial infarction and a left ventricular ejection fraction $\leq 35\%$ were associated with a poor 1-year survival rate. **Conclusion:** Early and 1-year outcomes of OPCAB in octogenarians were tolerable when compared with those in septuagenarians. OPCAB could be a suitable option for octogenarians.

Key words: 1. Coronary artery bypass grafting
2. Off-pump coronary artery bypass
3. Aged

Introduction

The elderly segment of the Korean population is increasing rapidly, and with increasing life expectancy cardiac surgeons are being asked to consider elderly patients for cardiac surgery. With advances in medical care and the increasing life expectancy of the population, the number of octogenarians undergoing coronary artery bypass grafting (CABG) surgery is

increasing. However, age remains a significant, independent, and unmodifiable risk factor for post-operative complications [1].

Notably, cardiac surgery is no longer uncommon in septuagenarians, and the outcomes of CABG in this population are acceptable. A few studies have suggested that off-pump coronary artery bypass (OPCAB) surgery may reduce morbidity and mortality in high-risk patients, particularly in the elderly pop-

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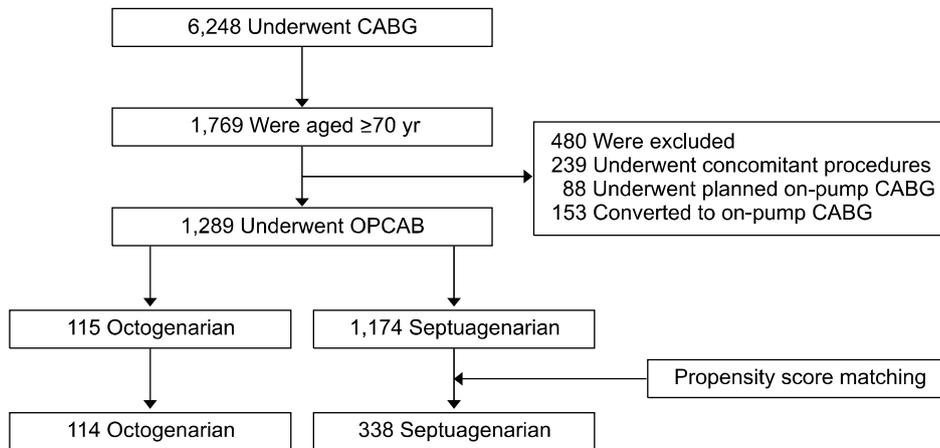


Fig. 1. Flow diagram depicting patient selection. CABG, coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass.

ulation, because it avoids the adverse effects associated with cardiopulmonary bypass (CPB) [2,3]. However, the outcomes of OPCAB are not well-established in octogenarians.

The aim of this study was to compare the outcomes of OPCAB between octogenarians and septuagenarians.

Methods

1) Study population

We retrospectively reviewed the data of 6,248 patients who underwent CABG at Samsung Medical Center between January 2001 and December 2016. Among these patients, 1,769 patients were aged 70 years or older. In this group, 1,289 patients underwent OPCAB. We compared the outcomes between 115 octogenarians and 1,174 septuagenarians. A flow diagram depicting the patient selection process is shown in Fig. 1. Among the 1,530 patients who underwent isolated CABG, 88 patients underwent planned on-pump CABG. Additionally, 153 patients were converted to on-pump CABG during off-pump surgery (132 septuagenarians and 21 octogenarians). The on-pump conversion rate was 10.6% (10.1% for septuagenarians and 15.4% for octogenarians). Using propensity score matching based on preoperative clinical characteristics, 114 octogenarians were matched with 338 septuagenarians. The median follow-up duration was 68.5 months, with a maximum duration of 202.6 months. Information was obtained from the National Registry of Births and Deaths using a unique personal identification number to vali-

date the complete follow-up data regarding mortality. The Institutional Review Board of Samsung Medical Center approved this study, and the requirement for patient consent was waived (IRB approval no., 2018-08-011-001).

2) Revascularization procedures

The internal thoracic arteries were fully skeletonized. With few exceptions, we used the left internal thoracic artery (LITA) *in situ*, and the right internal thoracic artery (RITA) was anastomosed to the LITA as a Y-composite graft. The LITA was anastomosed to the left anterior descending artery and its branches. The RITA was sequentially anastomosed to the branches of the circumflex artery. For right coronary artery revascularization, the RITA was our primary option. The *in situ* right gastroepiploic artery or a saphenous vein graft was used when the length of the RITA was insufficient. Anastomosis was assessed by transit-time flow measurement.

3) Study end points and definitions

The primary outcomes were early, 1-, and 5-year mortality. The secondary outcome measures were postoperative complications, including acute myocardial infarction (AMI), stroke, acute kidney injury (AKI), and respiratory complications.

Early mortality was defined as any death within 30 days postoperatively. Postoperative AKI was defined as an increase in serum creatinine to more than 2-fold higher than baseline. Low cardiac output syndrome (LCOS) was defined as any events involving cardiopulmonary resuscitation, intra-aortic bal-

Table 1. Preoperative demographics and clinical characteristics

Characteristic	Overall patients (n=1,289)			Propensity-matched patients (n=452)		
	Octogenarians (n=115)	Septuagenarians (n=1,174)	p-value	Octogenarians (n=114)	Septuagenarians (n=338)	p-value
Age (yr)	81.77±1.84	73.52±2.68		81.76±1.84	73.83±2.86	
Male sex	78 (67.8)	735 (62.6)	0.315	77 (67.5)	218 (64.5)	0.556
New York Heart Association class			0.050			0.933
I	63 (54.8)	680 (57.9)		63 (55.3)	186 (55.0)	
II	31 (27.0)	377 (32.1)		31 (27.2)	97 (28.7)	
III	17 (14.8)	93 (7.9)		17 (14.9)	45 (13.2)	
IV	4 (3.5)	24 (2.0)		3 (2.6)	11 (3.2)	
Medical history						
Hypertension	87 (75.7)	829 (70.6)	0.303	86 (75.7)	253 (74.7)	0.873
Diabetes mellitus	44 (38.3)	545 (46.4)	0.114	43 (37.7)	136 (40.4)	0.615
Dyslipidemia	27 (38.3)	357 (30.4)	0.149	27 (23.7)	91 (26.9)	0.448
Previous stroke	16 (13.9)	223 (19.0)	0.225	16 (14.0)	51 (15.2)	0.750
Chronic kidney disease	6 (5.2)	61 (5.2)	1.000	6 (5.3)	17 (5.1)	0.953
Dialysis	0 (0.0)	28 (2.4)	0.180	0 (0.0)	0 (0.0)	1.000
Chronic obstructive pulmonary disease	3 (2.6)	47 (4.0)	0.627	3 (2.6)	9 (2.6)	1.000
Peripheral artery disease	9 (7.8)	114 (9.7)	0.624	9 (7.9)	25 (7.3)	0.829
Previous MI	10 (8.7)	123 (10.5)	0.661	10 (8.8)	24 (7.0)	0.532
Carotid artery disease	48 (41.7)	360 (30.7)	0.020	47 (41.2)	147 (43.6)	0.644
Previous percutaneous coronary intervention	16 (13.9)	212 (18.1)	0.325	16 (14.0)	37 (10.8)	0.392
LVEF (%)	56.27±13.60	57.47±12.23	0.318	56.50±13.43	56.29±13.50	0.886
LVEF ≤35%	12 (10.4)	78 (6.6)	0.183	11 (9.6)	40 (11.7)	0.538
Mitral regurgitation grade			0.042			0.598
0	19 (16.5)	173 (14.7)		19 (16.7)	47 (13.7)	
1	57 (49.6)	720 (61.3)		56 (49.1)	190 (56.3)	
2	31 (27.0)	241 (20.5)		31 (27.2)	80 (23.5)	
3	8 (7.0)	40 (3.4)		8 (7.0)	22 (6.4)	
Recent MI	25 (21.7)	170 (14.5)	0.053	24 (21.1)	70 (20.8)	0.938
Unstable angina	57 (49.6)	517 (44.0)	0.298	56 (49.1)	167 (49.3)	0.978
Left main disease	31 (27.0)	230 (19.6)	0.079	30 (26.3)	86 (25.4)	0.854
Three-vessel disease	84 (73.0)	848 (72.2)	0.939	83 (72.8)	244 (72.2)	0.911
Emergency operation	9 (7.8)	53 (4.5)	0.175	9 (7.9)	31 (9.1)	0.708

Values are presented as mean±standard deviation for continuous data or number (%) for categorical data. MI, myocardial infarction; LVEF, left ventricular ejection fraction.

loon pump (IABP) support, or extracorporeal membrane oxygenation support. Respiratory complications were defined as prolonged mechanical ventilation over 1 week, or any event involving reintubation or tracheostomy.

4) Statistical analyses

Measurements were expressed as means±standard deviation or as frequencies and proportions. Intergroup comparisons were performed using the Pearson

chi-square and the Fisher exact tests for categorical variables, the unpaired Student t-test for normally distributed continuous variables, and the Mann-Whitney U-test for non-normally distributed continuous variables. All tests were 2-tailed.

Propensity score analysis was performed to control for selection bias based on 20 baseline covariates (sex, the New York Heart Association [NYHA] functional classification, hypertension, diabetes mellitus, dyslipidemia, stroke history, chronic kidney disease,

Table 2. Operative data

Variable	Overall patients (n=1,289)			Propensity-matched patients (n=452)		
	Octogenarians (n=115)	Septuagenarians (n=1,174)	p-value	Octogenarians (n=114)	Septuagenarians (n=338)	p-value
Distal anastomosis	3.86±1.28	3.98±1.20	0.316	3.88±1.28	3.91±1.17	0.787
Type of grafts						
Left ITA	115 (100.0)	1,161 (98.9)	0.519	114 (100.0)	337 (99.7)	0.561
Right ITA	103 (89.6)	1,067 (90.9)	0.766	103 (90.4)	305 (90.2)	0.966
Right gastroepiploic artery	7 (6.1)	131 (11.2)	0.128	7 (6.1)	32 (9.4)	0.305
Radial artery	1 (0.9)	21 (1.8)	0.727	0 (0.0)	8 (2.3)	0.083
Saphenous vein graft	18 (15.7)	200 (17.0)	0.805	18 (15.8)	63 (18.6)	0.509
Bilateral ITA use	103 (89.6)	1,055 (89.9)	1.000	103 (90.4)	304 (89.9)	0.898

Values are presented as mean±standard deviation for continuous data or number (%) for categorical data. ITA, internal thoracic artery.

dialysis, chronic obstructive pulmonary disease, peripheral arterial disease, previous myocardial infarction [MI], carotid artery disease, previous percutaneous coronary intervention, left ventricular ejection fraction [LVEF] \leq 35%, mitral regurgitation grade, recent MI, unstable angina, left main disease, 3-vessel disease, and emergency operation). The predicted probabilities were calculated using binary logistic regression analysis and were subsequently used as the propensity score. The propensity score model discrimination was assessed with c-statistics, and the model calibration fit was assessed with Hosmer-Lemeshow statistics. One-to-three matching based on the nearest neighbor algorithm with a caliper of 0.025 resulted in 2 balanced groups with standardized mean differences of less than 10% and variance ratios near 1.0. Some patients could only be matched to 1 or 2 counterparts. After matching, we assessed the balance of the covariates between groups using the standardized mean difference and the appropriate statistical tests.

We used weighted Kaplan-Meier curves and weighted Cox proportional hazards modeling to test the difference in mortality between the groups. Comparisons were completed with Cox regression models with robust standard errors that accounted for the clustering of matched pairs. The proportional hazards assumption was confirmed by testing the weighted Schoenfeld residuals. A p-value $<$ 0.05 was considered to indicate statistical significance. Statistical analysis was carried out using R software ver. 3.4.3 (<https://www.r-project.org/>).

Results

The preoperative demographic and clinical characteristics of each group are shown in Table 1. In the unmatched population, statistically significant intergroup differences were observed in the NYHA functional classification, the presence of carotid artery disease, and the mitral regurgitation grade. In the matched population, no factors were significantly different. Intergroup differences in the operative data are shown in Table 2. No statistically significant differences were observed.

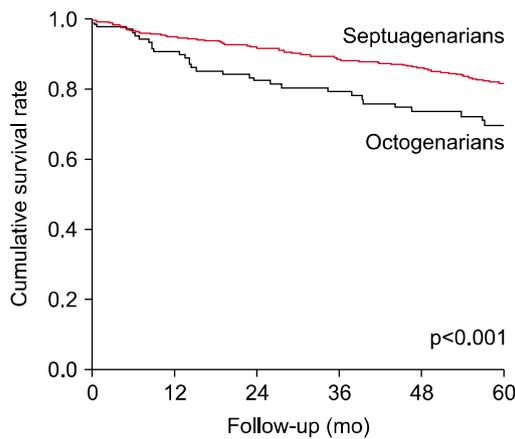
The intergroup differences in early postoperative outcomes are shown in Table 3. In the unmatched patients, the early mortality rate was higher in octogenarians than in septuagenarians (2.6% versus 0.6%, $p=0.073$), although this difference was statistically insignificant. However, the incidence rates of atrial fibrillation (27.8% versus 18.1%, $p=0.015$), AKI (14.8% versus 7.5%, $p=0.011$), LCOS (4.3% versus 0.9%, $p=0.007$), postoperative IABP support (2.6% versus 0.3%, $p=0.005$), and respiratory complications (8.7% versus 4.1%, $p=0.041$) were significantly higher in octogenarians.

In the matched patients, the early mortality rate (2.6% versus 1.0%, $p=0.240$) did not show a statistically significant difference between groups. No significant intergroup differences were observed in the incidence rates of atrial fibrillation (28.1% versus 22.1%, $p=0.200$), postoperative AMI (0.9% versus 0.3%, $p=0.418$) and stroke (0.0% versus 0.6%, $p=0.407$). However, the incidence rates of AKI (14.9% versus 7.9%, $p=0.028$), LCOS (4.4% versus 1.3%, $p=0.010$),

Table 3. Early postoperative outcomes

Variable	Overall patients (n=1,289)			Propensity-matched patients (n=452)		
	Octogenarians (n=115)	Septuagenarians (n=1,174)	p-value	Octogenarians (n=114)	Septuagenarians (n=338)	p-value
Early mortality	3 (2.6)	7 (0.6)	0.073	3 (2.6)	4 (1.0)	0.240
In-hospital mortality	3 (2.6)	9 (0.8)	0.146	3 (2.6)	4 (1.3)	0.363
Atrial fibrillation	32 (27.8)	212 (18.1)	0.015	32 (28.1)	75 (22.1)	0.200
Acute myocardial infarction	1 (0.9)	2 (0.2)	0.638	1 (0.9)	1 (0.3)	0.418
Stroke	0	10 (0.9)	0.662	0	2 (0.6)	0.407
Acute kidney injury	17 (14.8)	88 (7.5)	0.011	17 (14.9)	27 (7.9)	0.028
Mediastinitis	1 (0.9)	5 (0.4)	1.000	1 (0.9)	1 (0.3)	0.418
Low cardiac output syndrome	5 (4.3)	11 (0.9)	0.007	5 (4.4)	4 (1.3)	0.010
Cardiopulmonary resuscitation	3 (2.6)	11 (0.9)	0.238	3 (2.6)	3 (0.9)	0.088
Extracorporeal membrane oxygenation	1 (0.9)	4 (0.3)	0.932	1 (0.9)	2 (0.6)	0.741
Intra-aortic balloon pump	3 (2.6)	3 (0.3)	0.005	3 (2.6)	3 (0.7)	0.045
Respiratory complications	10 (8.7)	48 (4.1)	0.041	10 (8.8)	14 (4.2)	0.040
Reoperation due to bleeding	2 (1.7)	12 (1.0)	0.813	2 (1.8)	2 (0.6)	0.253
Hospital stay (day)	13.53±20.27	10.07±28.94	0.211	13.51±20.35	10.27±17.35	0.139

Values are presented as number (%) for categorical data or mean±standard deviation for continuous data.

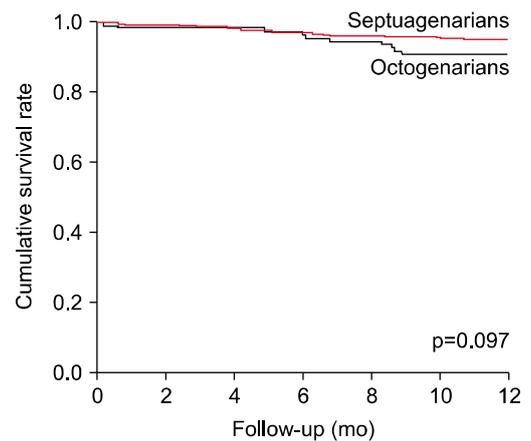


No. at risk	0	12	24	36	48	60
Octogenarians	114	102	82	71	60	49
Septuagenarians	338	318	291	250	220	188

Fig. 2. Kaplan-Meier estimates of 5-year survival rates in the propensity-matched patients.

postoperative IABP support (2.6% versus 0.7%, $p=0.045$) and respiratory complications (8.8% versus 4.2%, $p=0.040$) were significantly higher in octogenarians.

The 5-year survival rate (67.3% versus 79.9%, $p<0.001$) was significantly lower in octogenarians (Fig. 2), although the 1-year survival rate (89.5% versus 94.4%, $p=0.097$) was not statistically significant between groups (Fig. 3). The median survival was 7.2



No. at risk	0	1	2	3	4	5	6	7	8	9	10	11	12
Octogenarians	114	111	111	110	107	102	102	102	102	102	102	102	102
Septuagenarians	338	333	330	325	321	320	318	318	318	318	318	318	318

Fig. 3. Kaplan-Meier estimates of 1-year survival rates in the propensity-matched patients.

years in octogenarians and 9.4 years in septuagenarians.

Multiple Cox regression showed that previous MI (hazard ratio, 2.511; $p=0.044$), carotid artery disease (hazard ratio, 2.541; $p=0.016$), and LVEF $\leq 35\%$ (hazard ratio, 3.499; $p=0.002$) were predictors of 1-year mortality (Table 4).

Table 4. Clinical predictors of mortality in the matched patients

Variable	Multivariate analysis	
	Hazard ratio (95% confidence interval)	p-value
Previous myocardial infarction	2.511 (1.025–6.151)	0.044
Carotid artery disease	2.541 (1.187–5.440)	0.016
Left ventricular ejection fraction \leq 35%	3.499 (1.554–7.879)	0.002

Discussion

Korean society is rapidly aging, and the average life expectancy has already exceeded 80 years. Patients with coronary artery disease are also aging, and although CABG is indicated in many elderly patients, age is a major concern in such cases. Octogenarians remain at a higher risk for in-hospital mortality and postoperative complications after cardiac surgery than younger patients [4]. Cardiovascular risk factors in elderly patients include aortic calcification, stiff vessels, diminished cardiovascular response to exercise, and intolerance to anemia. Other age-related changes influence the performance status and physiological reserve of other systems [5]. However, following improvements in operative techniques and perioperative care, age is no longer a contraindication for CABG [6]. Cardiac surgery in septuagenarians is no longer uncommon, and outcomes of CABG in septuagenarians are acceptable. However, CABG in octogenarians still requires careful consideration [7].

Our hospital follows the off-pump protocol in all possible cases. Theoretically, OPCAB is preferable to conventional CABG because it involves less aortic manipulation and avoids the systemic inflammatory response associated with CPB. Although OPCAB has not shown proven superiority over on-pump surgery, it is associated with reduced mortality and stroke rates in high-risk patients, including octogenarians [8-13].

We compared the outcomes of OPCAB between octogenarians and septuagenarians. Our results show that OPCAB can be performed safely in octogenarians. Despite higher rates of AKI, LCOS, and respiratory complications, no significant intergroup difference was observed in early mortality. The rates of other morbidities and the 1-year survival rate were acceptable. No stroke was observed in any patient. Therefore, OPCAB can be safely performed in octogenarians, as well as in septuagenarians.

In our study, octogenarians showed higher rates of AKI, LCOS, and respiratory complications. All 4 octogenarians who experienced LCOS did not survive. Even in patients with a similar preoperative medical history in terms of CKD, dialysis, and COPD, octogenarians suffered more postoperative complications. This means that frailty and reduced reserve capacity due to aging cannot be ruled out solely based on the preoperative diagnosis of diseases [14]. Therefore, our recent preoperative risk evaluation has included a careful assessment of the estimated glomerular filtration rate and pulmonary function testing to identify high-risk patients. A future study should include these factors.

Likosky et al. [15] reported a study involving 54,397 patients who underwent isolated CABG surgery between 1987 through 2006. This cohort included 2,661 patients aged 80–84 years and 587 patients aged \geq 85 years. The median survival time was 7.4 years in patients aged 80–84 years and 5.8 years in patients aged \geq 85 years. Our findings concur with these results. The median survival of octogenarians was 7.2 years.

The 5-year survival rate was significantly lower in octogenarians than in septuagenarians. We compared octogenarians to septuagenarians because cardiac surgery in septuagenarians is no longer uncommon, and the outcomes of CABG in septuagenarians are acceptable. However, life expectancy differs between septuagenarians and octogenarians.

In year 2016, the life expectancy at age 82 in the general population was 7.1 years for Korean males and 8.9 years for Korean females [16]. In our study, the average age of octogenarians was 81.77 years, and 67.8% of octogenarians were male. The median survival of the octogenarians was 7.2 years. Our outcomes were not excessively inferior compared to the general population. Age alone should not be a precluding factor [17]. Further studies are warranted to compare the outcomes of OPCAB between octoge-

narians and the general population.

There are several limitations of this study. First, this was a retrospective nonrandomized study performed at a single institution. Thus, even after propensity score matching, the effect of unidentified confounders cannot be completely excluded. Second, details regarding causes of death were unavailable. Disease-specific death rates would provide a better understanding of the long-term results. Finally, we only included patients who underwent off-pump surgery, and did not include and compare patients who underwent conversion to on-pump surgery.

In conclusion, the early and 1-year outcomes of OPCAB in octogenarians were tolerable when compared with those in septuagenarians. OPCAB could therefore be a suitable option for octogenarians. Further investigations are warranted to compare the long-term outcomes between octogenarians and the general population.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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