□ ORIGINAL ARTICLE □

ST 분절 상승 급성 심근 경색증을 가지는 젊은 한국인에 있어서 비만의 정도가 환자의 예후에 미치는 영향

Influence of the Obesity on Clinical Outcomes in the Young Korean Patients with Acute ST-Elevation Myocardial Infarction

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요 약

연구배경: 선행 연구들에서는 비만한 환자들이 비만하지 않은 환자들보다 관동맥 성형 및 스텐트 삽입 후에 더 좋은 임상 결과를 나타내었다. 하지만, 이러한 "비만 패러독스"가 젊은 환자에서도 나타나는 지는 아직 명확하지 않다. 그러므로, 본 저자들은 ST 분절 상승을 보이는 급성 심근경색증으로 관동맥 성형 및 스텐트 삽입을 시행받은 젊은 환자에서 있어서, 비만 정도가 임상 결과에 미치는 영향을 연구하고자 하였다.

방법: ST 분절 상승을 보이는 급성 심근경색증으로 응급 관동맥 성형 및 스텐트 삽입을 시행받은 45세 이하 총 541명의 환자들이 2008년 1월부터 2011년 8월까지 한국인 급성 심근경색증 등록사업에 따라서 등록되었다. 이 환자들은 체질량지수(kg/m²)에 따라 비비만군(체질량지수 < 27.5, 73명), 비만군(27.5 ≤ 체질량지수 < 32.5, 183명), 병적비만군(체질량지수 ≥ 32.5, 285명)으로 분류하였다. 추적관찰에서 이 세 그룹 간에 주요심장사건(사망, 심근경색증 및 표적혈관 재개통)을 비교하였다.

결과: 평균 추적관찰 기간은 384 ± 82일이었다. 세 그룹 간에 나이, 성별, 심혈관 위험인자들 및 좌심실구혈률은 유사하였고, 의미 있는 협착 혹은 경색 연관 관동맥 혈관 숫자도 유사하였다. 심장중환자실에 입원한 기간은 비만군과 병적비만

ABSTRACT

Background: Previous reports have demonstrated that obese patients may have better clinical outcomes after percutaneous coronary intervention (PCI) than non-obese patients; however this "obesity paradox" remains still unknown in young patients. Therefore, we investigated the influence of obesity on the outcomes of young patients with acute ST-segment elevation myocardial infarction (STEMI).

Methods: A total of 541 young patients (≤ 45 year old) with acute STEMI undergoing urgent PCI were enrolled in the Korea Acute Myocardial Infarction Registry between January 2008 and Aug 2011. These patients were categorized according to their body mass index (BMI, kg/m²) as non-obese (BMI < 27.5, N = 73), obese (27.5 ≤ BMI < 32.5, N = 183) and morbidly obese (BMI ≥ 32.5, N = 285). At follow-up, the major adverse cardiac events (MACE; defined as death, myocardial infarction, and target vessel revascularization) were compared among the three groups.

Results: The mean duration of follow-up was 384 ± 82 days. Among the three groups, age, sex, cardiovascular risk factors and left ventricular ejection fraction were similar and number of infarct-related artery or stenotic coronary artery was also similar. The length of stay in the coronary care unit was shorter among the obese and morbidly obese group

군에서, 비비만군과 비교하였을 더 짧았다. 세 그룹 간에 병원 내 사망 그리고 임상경과도 유의한 통계적 차이를 보이지 않았다. 추적관찰에서 주요심장사건과 무관한 1년-생존율도 세 그룹 간에 유의한 차이를 보이지 않았다(비비만군 93%, 비만군 94%, 그리고 병적비만군 95%).

결론: ST 분절 상승을 보이는 급성 심근경색증으로 응급 관동맥 성형 및 스텐트 삽입을 시행 받은 젊은 한국인 환자에서 비만은 임상 결과에 영향을 미치지 않았다.

중심단어: 급성 심근경색증, 젊은 환자, 비만

compared with that of the non-obese group. In-hospital death and clinical outcomes among the three groups were not significantly different. At follow-up, the one-year MACE-free survival rate of those groups was not significantly different (93% in non-obese, 94% in obese and 95% in morbidly obese).

Conclusion: In young patients with STEMI undergoing urgent PCI, influence of obesity on clinical outcomes was not observed as significant in the young Korean patients.

Key words: Acute myocardial infarction, Young patients, Obesity

Introduction

Prevalence of obesity among the young Easterners, similar to Westerners, has been increasing in epidemic proportions and great concerns.[1,2] Obesity is found to be associated with increased overall mortality, as well as cardiovascular risk factors such as diabetes, hypertension and hyperlipidemia.[3-5] However, several studies have demonstrated an "obesity paradox" after percutaneous coronary intervention (PCI), whereby obesity seems to have better outcomes compared with non-obesity.[6-8] Therefore, recently, obesity seems to be a non-risk factor of overall cardiovascular events in patients with myocardial infarction (MI) which could be explained by more intensive medical treatment, hemodynamic stability, and younger age in Asian patients.[2,9] Until now, data on the impact of obesity, especially in the young Korean patients (≤ 45 year old), on outcomes after urgent PCI for acute ST segment elevation myocardial infarction (STEMI) remain limited. The aim of the present study was to examine the impact of obesity on the clinical outcomes in the young patients with STEMI who underwent urgent PCI in the Korean population.

Methods

Supported by the Korean Circulation Society, KAMIR (Korea Acute Myocardial Infarction Registry) is a prospective multi-center observational study that investigates risk factors for mortality in patients with acute myocardial infarction (AMI) since November 2005 with the aim of establishing universal management guidelines for the prevention of AMI. Online registration of AMI cases is performed in 41 urgent PCI centers that have sufficient experience and volume to perform PCI (www.kamir.or.kr). The study protocol was approved by the ethics committee at each participating institution. The data were registered and submitted online from individual institutions through password-protected electronic case report forms.

Data of 13,472 patients in total were collected from KAMIR since January 2008 to August 2011. Among the patients enrolled in the registry, data of those with consecutive young (≤ 45 year old) acute STEMI cases were analyzed.

We defined STEMI as the presence of ≥ 0.1 mV ST-segment elevation in two contiguous electrocardiogram (ECG) leads with ongoing chest pain with or without an elevation of cardiac enzyme levels above the reference range.

All patients who planned to have primary or rescue PCI were pretreated with 300 mg aspirin and 600 mg clopidogrel. Abciximab was administered at the discretion of the operator: an intravenous preprocedural bolus of 0.25 mg/kg body weight followed by a continuous infusion of 0.125 µg kg^{-1}/min^{-1} for 12 hours (up to a maximum dose of 10 µg/min). During the PCI, an intravenous bolus of unfractionated heparin was given to maintain an activated clotting time of more than 200 sec. A successful PCI was defined as an infarct-related artery stenosis of < 30%, associated with a thrombolysis In Myocardial Infarction flow grade 2 or 3 flow and no requirement for emergent coronary artery bypass (CABG).

For analysis in our study, patients were stratified into three groups based on the recommendation by the World Health Organization for the Asian population[10] : body mass index (BMI, kg/m^2) as non-obese (BMI < 27.5, N = 73), obese (27.5 ≤ BMI < 32.5, N = 183) and morbidly obese (BMI ≥ 33, N = 285).

All patients were discharged with indefinite requirement of aspirin (100 mg) and daily prescription of clopidogrel (75 mg) for 12 months with follow-up visits at 1, 3, 6, and 12 month.

The one-year clinical outcomes included cardiac death, MI, and target vessel revascularization (TVR; defined as repeat revascularization within 5 mm of the treated segment and repeat revascularization of the treated vessel). Major adverse cardiac events (MACE) were a composite of cardiac death, MI, and TVR during one-year of follow-up. The primary endpoint of the study was one-year rates of MACE-free survival. These rates were compared between the three groups during one year of follow-up.

The numeric or categorical data were presented as means ± standard deviation (SD) or number (percentages). The comparisons among three groups were performed using one-way ANOVA (numeric data) or chi-square test (categorical data) for statistical comparisons of clinical characteristics among groups. Survival analysis after urgent PCI was estimated using the Kaplan−Meier method with log rank tests to compare survival among groups. The analyses were performed using SPSS Version 15.0 for Windows (SPSS Inc., Chicago, USA). Statistical significance was defined as $P < 0.05$.

Results

The basic characteristics of the patients are listed in Table 1. The mean age of these groups was 40 years old

Table 1. Baseline clinical characteristics

	Non-obese (N = 73)	Obese (N = 183)	Morbidly Obese (N = 285)	P-value
Age (years)	40 ± 3	39 ± 4	40 ± 3	0.320
Male, n (%)	72 (98.6)	183 (98.6)	265 (93.0)	0.532
Body mass index (kg/m^2)	25.1 ± 2.2	29.6 ± 0.6	32.6 ± 1.7	< 0.001[*]
Risk Factor				
Previous MI, n (%)	5 (6.8)	19 (10.4)	16 (6.3)	0.263
Hypertension, n (%)	20 (27.4)	60 (32.8)	75 (26.3)	0.309
Diabetic Mellitus, n (%)	12 (16.4)	26 (14.2)	32 (11.2)	0.407
Dyslipidemia, n (%)	11 (15.1)	22 (12.0)	37 (13.0)	0.806
Current smoker, n (%)	55 (75.3)	153 (83.6)	243 (85.3)	0.126
Family History, n (%)	13 (17.8)	35 (19.1)	35 (12.3)	0.110
Physical Findings				
Systolic BP (mmHg)	130 ± 25	133 ± 30	132 ± 25	0.771
Diastolic BP (mmHg)	82 ± 16	85 ± 18	83 ± 17	0.417
Heart Rate (beats/min)	76 ± 14	77 ± 17	79 ± 18	0272
LVEF (%)	55 ± 10	54 ± 10	54 ± 10	0.827
Killip Class III-IV, n (%)	14 (19.2)	26 (14.2)	45 (15.8)	0.382
Sinus rhythm, n (%)	58 (93.5)	161 (93.1)	247 (93.9)	0.489
Lab finding				
Glucose (mg/dL)	150 ± 72	149 ± 63	154 ± 72	0.729
Creatinine (mg/dL)	0.9 ± 0.1	1.0 ± 0.8	1.0 ± 1.0	0.752
Total cholesterol (mg/dL)	206 ± 50	197 ± 41	204 ± 46	0.196
High density lipoprotein- cholesterol (mg/dL)	43 ± 16	40 ± 10	41 ± 9	0.120
Low density lipoprotein- cholesterol (mg/dL)	131 ± 41	123 ± 37	132 ± 42	0.101
NT-pro BNP (pg/mL)	236 ± 408	507 ± 143	459 ± 124	0.266

Data were expressed as mean ± standard deviation or number (%). One-way ANOVA (for numeric data) or Chi-square test (for categorical data) was performed.

MI, myocardial infarction; BP, blood pressure; LVEF, left ventricular ejection fraction; NT-pro BNP, N-terminal pro-brain natriuretic peptide.

* significant difference.

and follow-up duration was 384 ± 82 days. A significant proportion of all patients were obese, male and current smokers but, similar in each group. There were no significant differences between the groups concerning previous MI, hypertension, diabetes mellitus, dyslipidemia and family history of MI. The mean ejection fraction and laboratory findings were similar among the three groups. There were no significant differences among the three groups regarding symptom-to-door and door-to-balloon time. Table 2 shows that angiographic and procedural

Table 2. Angiographic and procedural characteristics

	Non-obese (N = 73)	Obese (N = 183)	Morbidly Obese (N = 285)	P-value
Infarct-related artery, n (%)				0.637
Left anterior descending artery	46 (65.7)	105 (58.7)	163 (60.6)	
Left circumflex artery	16 (22.9)	53 (29.6)	69 (25.7)	
Right coronary artery	8 (11.4)	19 (10.6)	30 (11.2)	
Number of stenotic coronary artery, n (%)				0.436
coronary one vessel	28 (40.0)	81 (45.3)	124 (46.4)	
coronary two vessel	13 (17.1)	42 (23.5)	56 (21.0)	
coronary three vessel	30 (42.9)	55 (30.7)	83 (31.1)	
Lesion Type[†], n (%)				0.554
A/B1	16 (25.4)	47 (29.6)	78 (32.2)	
B2/C	47 (74.6)	112 (70.4)	164 (67.8)	
Infarct-related artery TIMI flow[‡], n (%)				0.009[*]
0~1	61 (83.6)	121 (66.1)	186 (65.3)	
2~3	12 (16.4)	62 (33.9)	99 (34.7)	
Post-procedure TIMI flow[‡], n (%)				0.385
0~1	2 (0.3)	4 (0.5)	8 (1.9)	
2~3	70 (95.8)	164 (94.2)	247 (97.6)	
Drug eluting stent, n (%)	66 (90.4)	161 (87.9)	247 (86.6)	0.439
Stent diameters, mm	3.4 ± 0.5	3.3 ± 0.5	3.3 ± 0.4	0.454
Stent size, mm	21 ± 7	22 ± 7	22 ± 7	0.903
Stent numbers, n	1.3 ± 0.6	1.3 ± 0.7	1.3 ± 0.7	0.702

Data were expressed as mean ± standard deviation or number (%). One-way ANOVA (for numeric data) or Chi-square test (for categorical data) was performed.
* significant difference.
† Type A/B1 was considered as low risk lesion but, type B2/C as high risk lesion according to ACC/AHA coronary lesion classification 1988.
‡ Grading system of coronary artery flow using TIMI(Thrombolysis In Myocardial Infarction), 0 = no perfusion, 1 = penetration without perfusion, 2 = partial reperfusion, 3 = complete perfusion, procedural success was defined as TIMI 2~3.

Table 3. In-hospital management

	Non-obese (N = 73)	Obese (N = 183)	Morbidly Obese (N = 285)	P-value
CCU stay, days	3.4 ± 2.9	2.7 ± 2.0	2.5 ± 1.1	0.004[*]
Vasopressor, n (%)	30 (31.5)	58 (32.4)	97 (34.8)	0.873
Aspirin, n (%)	72 (98.6)	179 (98.3)	276 (97.8)	0.892
Clopidogrel, n (%)	72 (98.6)	177 (97.7)	273 (96.3)	0.871
Unfractional heparin, n (%)	44 (88.6)	162 (89.9)	253 (89.9)	0.351
β blocker, n (%)	23 (72.1)	133 (73.2)	208 (73.9)	0.784
Angiotensin-converting enzyme inhibitor, n (%)	21 (47.5)	87 (48.3)	136 (48.9)	0.631
Angiotensin receptor blocker, n (%)	8 (14.3)	23 (13.1)	37 (13.8)	0.964
Statin, n (%)	42 (52.5)	96 (53.6)	153 (54.9)	0.712

Data were expressed as mean ± standard deviation or number (%). One-way ANOVA (for numeric data) or Chi-square test (for categorical data) was performed.
CCU, coronary care unit.
* significant difference.

Table 4. Clinical outcomes

	Non-obese (N = 73)	Obese (N = 183)	Morbidly Obese (N = 285)	P-value
In-hospital death, n (%)	0 (0)	2 (0)	2 (0.0)	0.783
Out-of-hospital outcome, n (%)				
1-year MACE	5 (6.8)	13 (7.1)	15 (5.3)	0.690
Cardiac Death	2 (2.7)	4 (2.1)	4 (1.4)	0.698
MI	5 (6.8)	9 (4.9)	14 (4.9)	0.786
TVR	1 (1.3)	5 (2.7)	7 (2.5)	0.810

Data were expressed as number (%). Chi-square test was performed.
MACE, major adverse cardiac event; MI, myocardial infarction; TVR, target vessel revascularization.
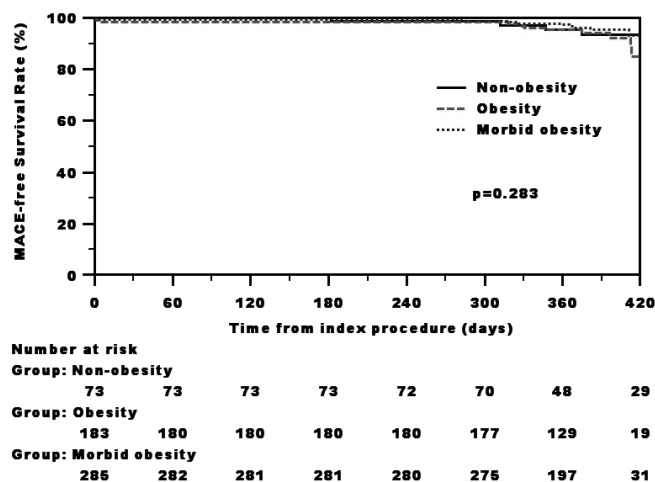
Fig. 1. One-year Kaplan-Meier estimates of MACE-free survival rate among the three groups. MACE, major adverse cardiac event.

parameters were not significantly different among the three groups. Especially, most of the patients in each group had infarct-related artery involving the left anterior descending territory (65.7%, 58.7%, and 60.6%) and successful revascularization after procedure (95.8%, 94.2%, and 97.6%). Total 474 (87.6%) patients with STEMI who had urgent PCI were treated with drug-eluting stent. The length of stay in the CCU was shorter for morbidly obese and obese patients than for non-obese patients (2.5 days, 2.7 days and 3.4 days, respectively). However, there was no significant difference among the groups regarding the use of inotropics, aspirin, clopidogrel, heparin, beta blockers, angiotension-converting enzyme inhibitors or angiotension receptor blocker and statin (Table 3). During the follow-up period, there was no significant difference among groups in the in-hospital death or one-year MACE (Table 4). In addition, there was no significant difference in the MACE-free survival rate (93% in non-obese, 94% in obese and 95% in morbidly obese) among the three groups in the Kaplan-Meier Curve (P = 0.283) (Fig. 1).

Discussion

In our study, non-obese, obese and morbidly obese patients with STEMI treated with urgent PCI had similar MACE free survival rate during the one-year follow-up period.

With growing recognition that obesity adversely influences traditional cardiovascular risk factors, such as hypertension, dyslipidemia, diabetes mellitus, the American Heart Association defined obesity as a strong predictor for cardiovascular events[3] and suggested that it is essential to control obesity.[1] However, some studies have reported better clinical outcomes in obese patients after PCI compared with non-obese patients, an interaction termed "obesity paradox".[11] There have been few explanations for obesity paradox phenomenon. First, guideline-recommended medical treatment (beta blockers, angiotensin-converting enzyme inhibitors, and statins)

were prescribed more frequently for obese patients. Second, obese patients had higher blood pressure, lower Killip class, and higher left ventricular ejection fraction compared with non-obese patients, indicating they were in a relatively more stable hemodynamic state. Third, physicians had a tendency to use medications more aggressively for younger patients that may have had a favorable effect on the cardiovascular outcomes because age is an independent risk factor for overall mortality. However, in our study, guideline-recommended medical treatment, blood pressure, killip class and left ventricular ejection fraction were similar between the non-obese and obese groups in the young adult population, therefore, we were better able to distinguish the influencing factors for cardiovascular outcome.

Recent studies demonstrated obese patients seem to have a lower incidence of cardiovascular events than non-obese patients regarding PCI in patients with STEMI.[7-9,12,13] A meta analysis also reported that non-obesity was associated with an increased relative risk (RR) for cardiovascular mortality (RR 1.45 [95% CI 1.16~1.81]), whereas obesity showed a low risk for cardiovascular mortality (RR 0.88 [95% CI 0.75~1.02]).[12] Recently, German DES DE study showed that non-obesity would be associated with MACE-free survival of 90%, obesity with 92%, and severe obesity with 92% respectively.[14]

According to our result of the young patients with STEMI who underwent urgent PCI and were followed up for the first year, the MACE-free survival rate was 93% in non-obese group, 94% in obese group and 95% in morbidly obese group (Table 4, Fig. 1). In the Asian report[2], obese patients with STEMI were often younger and male which offered better baseline characteristics. Conversely, non-obese patients with STEMI had poor profiles, therefore, clinical follow-up results demonstrated that obese patients had better prognosis compared to non-obese patients.[11,15] Most of the patients in our study were young and male but, non-obese patients also had good profiles compared to the Asian report. Therefore, we were able to investigate whether or not obesity paradox was also observed in young Korean patients with STEMI having urgent PCI.

In fact, previous studies did not prove the mechanism of the obesity paradox. In addition, some reports revealed that there was no evidence for obesity paradox after

treatment with drug-eluting stents in a routine clinical practice.[14,16] However, basic research already demonstrated that fat tissue in obese patients produce proatherogenic adipokines, oxidative stress, and inflammation and lead to endothelial dysfunction subsequent to cardiovascular events.[17-19]

Our study also demonstrated that the young Korean patients with STEMI were not associated with the obesity paradox. Compared with obesity or morbid obesity, non-obesity had also similar rates of MACE-free survival during follow-up (Table 4, Fig. 1).

This study had limitation of nonrandomized, observational study. Severity of obesity was estimated by using the BMI at the time of first admission without any information on weight change. Apart from weight, both waist circumference and waist to- hip ratio were unavailable.

Conclusion

In our study, the one-year MACE-free survival rates of either obese or morbidly obese young patients with acute STEMI who underwent urgent PCI were not significantly different from those of non-obese counterparts. Further, obesity paradox was not observed in the young Korean patients. However, our conclusion should be confirmed through a multi-center, randomized, prospective study.

Conflict of Interest

None declared

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