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①Incidence and Clinical Predictors of Stent Restenosis and Early Stent Occlusion in Patients with Acute Myocardial Infarction treated by Bare Metal Stents: Importance of Infarct location and Serum Creatinine Level

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Incidence and Clinical Predictors of Stent Restenosis and Early Stent Occlusion in Patients with Acute Myocardial Infarction treated by Bare Metal Stents: Importance of Infarct location and Serum Creatinine Level

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Abstract

Background: Bare Metal Stents (BMS) have been commonly used for recanalization of an infarct-related artery in Japanese patients with Acute Myocardial Infarction (AMI). We sought to examine predictors of binary restenosis and early Stent Occlusion (SO) in these patients.

Methods: Among 242 consecutive patients with AMI treated by BMS implantation as reperfusion therapy, 226 underwent either ischemia-driven or follow-up coronary angiography within 8 months. Restenosis change in the stented segment was found in 56. Among them, 10 patients had early SO on an angiogram. Multivariate analysis was performed to obtain predictors of restenosis and early SO.

Results: Predictors for restenosis were Left Anterior Descending Artery (LAD) involvement (odds ratio (OR) 2.32, p=0.024), serum creatinine (SCr) on admission (OR 1.29 per 0.1mg/dl increase, p=0.001), and stent size (OR 0.43 per 0.5mm increase, p=0.001). Those for early SO were left main trunk or LAD involvement (OR 27.0, p=0.029), SCr (OR 1.65 per 0.1mg/dl increase, p=0.005) and leukocyte count (OR 1.28 per 1,000/microliter increase, p=0.037) on admission. SCr was significantly higher in patients with early SO than in those with restenosis (median 1.05, Interquartile Range (IQR) 0.80-1.10 vs. median 0.80, IQR 0.70-1.00, p=0.035).

Conclusion: In patients with AMI treated with BMS, both restenosis and early SO were increased by anterior wall involvement and elevation of SCr level. Higher SCr may be subject to more occlusive changes. It is suggested that in early SO, an inflammatory mechanism may be involved.

Keywords: Acute myocardial infarction; Bare metal stent; Stent occlusion; Restenosis

Introduction

Emergency percutaneous coronary intervention has become an established standard reperfusion therapy for patients with Acute Myocardial Infarction (AMI), especially since cardiologists started to use stents, which can stabilize coronary patency. As compared to uncoated Bare Metal Stents (BMS), many studies [1-7] have shown that Drug-Eluting Stent (DES) implantation at the infarct-related lesion can reduce target lesion revascularization markedly during a 1 to 3 year follow-up period. However, there is accumulating evidence that raises concerns regarding a higher risk of stent thrombosis after DES placement, especially in the setting of AMI [3-6, 8, 9]. Compared with restenosis without complete occlusion, unexpected abrupt coronary closure caused by Stent Occlusion (SO) may need urgent recanalization because it can involve sudden hemodynamic deterioration, leading to death.

This risk can be avoided to a great extent if BMS is used appropriately for reperfusion therapy by knowing the predictors of stent restenosis and SO. In Japan, the Ministry of Health, Labor, and Welfare did not accept DES use in the setting of AMI by the medical care insurance system for a long time. Here, under such circumstances, we report the predictors of binary restenosis and early SO at infarct-related lesions treated with BMS in patients with AMI.

Methods

Patients

Between October 1999 and March 2013, 242 consecutive patients with AMI underwent emergency percutaneous coronary intervention as reperfusion therapy within 24 hours of symptom onset and received uncoated BMS at the infarct-related lesion to successfully obtain Thrombolysis in Myocardial Infarction trial 3 flow grade with residual stenosis of <50%. AMI was diagnosed when patients complained of chest pain of ≥ 20 minutes but ≤ 24 hours duration that was unresponsive to sublingual nitroglycerin and was associated with ST segment elevation ≥ 1 mm in ≥ 2 contiguous ECG leads or ST depression in leads V1 to V4 consistent with posterior wall infarction. Those whose body temperature exceeding 38°C, who were too restless for catheterization, or who had bleeding tendency due to hepatic or hematologic disorder were excluded.

Groups

Among these 242 patients, 226 underwent either ischemia-driven or planned follow-up coronary angiography within 8 months. Thus,

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this study was performed in these patients (182 men and 44 women, mean age, 63 ± 10 years). All patients gave written informed consent. Comparisons were performed between patients with and without either angiographic restenosis or early SO.

Therapeutic method

Percutaneous coronary intervention was only performed for The Infarct-Related Artery (IRA). After the procedure the patients were transferred to the coronary care unit and monitored. Heparin was continuously infused to maintain the activated clotting time ≥ 200 seconds for ≥ 24 hours. At the same time, intravenous isosorbide dinitrate and nicorandil were administered. Patients received oral aspirin (100 mg/ day), either ticlopidine (200 mg/day) or clopidogrel (75 mg/ day), and calcium antagonist after the procedure. If recurrent chest pain unrelieved by nitrates lasted ≥ 20 minutes and was accompanied by ≥ 1 mm ST elevation or depression in the infarct-related territory, the patient underwent emergency angiography and, if necessary, additional coronary intervention.

Clinical observation indicators

Coronary artery diameters were measured on end-diastolic frames and percent diameter stenosis was calculated after maximal dilation obtained by isosorbide dinitrate administration. It was defined as follows: (reference diameter – minimal luminal diameter)/reference diameter × 100. A diseased vessel was defined as one with >70% narrowing. Binary restenosis was defined as >50% luminal narrowing at the infarct-related lesion, including the implanted stent and 5 mm proximal and distal to the stent edges of the target vessel on the follow-up angiogram. Early SO was defined as stent thrombotic occlusion within the stented segment, confirmed with angiographic proof of vessel occlusion within 30 days after the index procedure. This study complied with the Declaration of Helsinki and was approved by the ethics committee of our institution.

Statistical analysis

Continuous variables were tested for normal distribution using the Shapiro-Wilk test. Data with normal distribution are presented as the mean ± SD; non-normally distributed data are presented as the median and interquartile range (IQR). Between-group comparisons of normally distributed variables were made with two-sided Student's t test for unpaired data, and those of variables not normally distributed were made by the Mann-Whitney test. Categorical variables were compared with the chi-square or Fisher's exact test (whenever an expected cell value was <5). Multivariate logistic regression analysis was performed to correlate binary restenosis and early SO with clinical and angiographic variables. The model was built entering variables that demonstrated $p \leq 0.15$ in univariate analysis by means of a stepwise forward selection procedure. Statistical significance was accepted as $p<0.05$. All tests were performed by SPSS 11J statistical software (Tokyo, Japan).

Results

Binary restenosis and SO

Among 226 study patients who received BMS implantation as reperfusion therapy, 56 had binary restenosis, including reocclusion in the stented portion confirmed on either ischemia-driven or planned follow-up coronary angiogram. Ten patients had early SO and underwent another coronary intervention successfully. Among them, however, two patients with left main coronary artery occlusion died due to pneumonia or multi-organ failure secondary to cardiac pump failure 33 days and 4 months after BMS implantation, respectively. Beyond 30 days, very late SO occurred in another two patients with right coronary artery occlusion (2.5 and 9 years after coronary intervention) requiring reperfusion therapy.

Predictors of binary restenosis

No significant intergroup differences were present with regard to coronary risk factors and infarct size, although the percentage of male and aged patients tended to be greater and that of hyperlipidemia tended to be smaller in the restenosis group than in the non-restenosis group (Table 1).

Laboratory examinations on admission showed significantly higher Serum Creatinine (SCr) (p=0.012) and slightly higher C-reactive protein (p=0.065) in the restenosis group. (Table 2).

In this group, the frequency of the Left Anterior Descending Artery (LAD) as IRA was significantly higher (64% vs. 44%, p=0.009) and implanted BMS size was significantly smaller (p <0.001) (Table 3).

Multivariate analysis, which excluded gender, age, hyperlipidemia, and C-reactive protein on admission in the final model, revealed an SCr level on admission (odds ratio (OR) of 1.29 per 0.1 mg/dl increase, p=0.001), LAD involvement (OR 2.32, p=0.024), stent size (OR 0.43 per 0.5 mm increase, p=0.001) as three independent correlates of binary restenosis (Table 4).

	Restenosis group(n=56)	Non-restenosis group(n=170)	p	Early SO group(n=10)	Non-early SO group(n=216)	p
Men (%)	49(88)	133 (78)	0.129	10 (100)	172 (80)	0.216
Age (yrs)	65.3 ± 9.4	62.7 ± 10.5	0.103	61.9 ± 11.4	63.4 ± 10.2	0.647
Current smoker (%)	26 (46)	93 (55)	0.282	4 (40)	115 (53)	0.523
Hypertension (%)	33 (59)	82 (48)	0.165	5 (50)	110 (51)	1.000
Hyperlipidemia (%)	29 (52)	110 (65)	0.085	4 (40)	135 (63)	0.189
Diabetes mellitus (%)	16 (29)	50 (29)	0.905	3 (30)	63 (29)	1.000
Hyperuricemia (%)	6 (11)	18 (11)	0.979	2 (20)	22 (10)	0.288
Prior MI (%)	2 (4)	9 (5)	1.000	0 (0)	11 (5)	1.000
Previous CABG (%)	0 (0)	1 (1)	1.000	0 (0)	1 (1)	1.000
Cardiogenic shock (%)	7 (13)	16 (9)	0.507	3 (30)	20 (9)	0.069
Peak CK (IU/l)	3173 (1659-4586)	3180 (1979-5201)	0.452	4004.(2078-7547)	3161 (1835-4935)	0.372
Peak CKMB (IU/l)	268 (177-469)	308 (166-461)	0.618	258 (198-635)	298 (165-459)	0.703

Abbreviations: CABG: coronary artery bypass grafting; MI: myocardial infarction; SO: stent occlusion

Table 1: Baseline characteristics of the study population.

	Restenosis group(n=56)	Non-restenosis group(n=170)	p	Early SO group(n=10)	Non-early SO group(n=216)	p
Glucose (mg/dl)	154 (135-206)	166 (139-211)	0.397	163 (137-258)	165 (138-210)	0.818
Creatinine (mg/dl)	0.8 (0.7-1.0)	0.8 (0.6-0.9)	0.012	1.1 (0.8-1.1)	0.8 (0.6-0.9)	0.003
CRP (mg/dl)	0.16 (0.08-0.37)	0.12 (0.06-0.27)	0.065	0.08 (0.05-0.24)	0.13 (0.06-0.30)	0.382
Hemoglobin (g/dl)	14.5 ±1.6	14.4 ± 1.7	0.568	14.5 ± 1.2	14.4 ± 1.7	0.914
Platelets (/microl)	22.9 (20.1-26.3)	23.1 (19.6-27.4)	0.688	25.3 (21.6-28.8)	23.0 (19.6-27.2)	0.357
White Blood Cells (/microl)	11000 (8610-13430)	10000 (7660-12730)	0.207	13650 (8840-16450)	10300 (8110-12700)	0.041
Neutrophils (/microl)	7060 (5420-10080)	6650 (4620-9380)	0.356	10450 (4820-12660)	6830 (4780-9340)	0.121
Lymphocytes (/microl)	2100 (1540-3010)	2070 (1250-3010)	0.692	2010 (1670-3650)	2080 (1360-3000)	0.703
Monocytes (/microl)	525 (407-762)	509 (341-732)	0.409	565 (380-864)	509 (380-734)	0.457
Eosinophils (/microl)	68 (25-163)	89 (20-160)	0.482	22 (2-134)	87 (24-162)	0.112

Abbreviations: CRP: C-reactive protein; SO: stent occlusion

Table 2: Laboratory findings on admission.

	Restenosis group(n=56)	Non-restenosis group(n=170)	p	Early SO group(n=10)	Non-early SO group(n=216)	p
Multi-vessel disease (%)	28 (50)	71 (42)	0.281	7 (70)	92(43)	0.109
Target (%) (LMCA/LAD/RCA/Cx)	3/36/12/5 (5/64/21/9)	0/75/77/18 (0/44/45/11)	<0.001	3/6/1/0 (30/60/10/0)	0/105/88/23 (0/49/41/11)	<0.001
LAD (%)	36 (64)	75 (44)	0.009			
LMCA or LAD (%)				9 (90)	105 (49)	0.019
Proximal segment (%)	34 (61)	88 (52)	0.244	6 (60)	116 (54)	0.756
Bifurcation lesion (%)	22 (39)	55 (32)	0.901	4 (40)	73 (34)	0.738
Initial TIMI flow grade 0/1 (%)	47 (84)	132 (78)	0.315	7 (70)	172 (80)	0.437
Poor collaterals (%)	33 (59)	114 (67)	0.268	6 (60)	141 (65)	0.743
IABP support (%)	5 (9)	9 (5)	0.181	3 (30)	11 (5)	<0.001
Time to PCI (min)	236 (196-367)	244 (179-381)	0.849	218 (199-343)	245 (180-379)	0.816
Single stent placement (%)	54 (96)	164 (97)	1.000	10 (100)	208 (96)	1.000
Stent size (mm)	3.00 (2.50-3.00)	3.00 (3.00-3.50)	<0.001	3.00 (2.50-3.50)	3.00 (2.75-3.50)	0.407
Stent length (mm)	15 (13-18)	15 (14-18)	0.453	15 (12-18)	15 (14-18)	0.455

Abbreviations: Cx: left circumflex artery; IABP: intra-aortic balloon pumping; LAD: left anterior descending artery; LMCA: left main coronary artery; PCI: percutaneous coronary intervention; RCA: right coronary artery; SO: stent occlusion; TIMI: Thrombolysis in Myocardial Infarction

Table 3: Angiographic and procedural characteristics of the study population.

	OR	95% CI	p
Serum creatinine (mg/dl)			
(per 0.1mg/dl increase)	1.29	1.11 to 1.50	0.001
Stent size (mm)			
(per 0.50mm increase)	0.43	0.26 to 0.70	0.001
LAD as IRA	2.32	1.12 to 4.80	0.024

Abbreviations: CI: confidence interval; IRA: infarct-related artery; LAD: left anterior descending artery; OR: odds ratio

Table 4: Predictors of binary restenosis.

Predictors of early SO

No significant differences were present among baseline patient demographics and infarct size between the early SO and non-early SO groups, although patients complicated with cardiogenic shock were slightly more frequent (p=0.069) in the early SO group (Table 1). Laboratory examinations on admission showed significantly higher SCr (p=0.003) and white blood cell count (p=0.041), slightly higher numbers of neutrophils (p=0.121), and slightly lower numbers of eosinophils (p=0.112) in the early SO group (Table 2). In this group, the percentages of either left main coronary artery or LAD involvement (p=0.019) and usage of intra-aortic balloon pumping (p <0.001) were significantly higher and multi-vessel disease tended to be more frequent (p=0.109) (Table 3). Multivariate analysis, which excluded cardiogenic shock and neutrophil count on admission in the final model, revealed the SCr level on admission (OR 1.65 per 0.1mg/dl increase, p=0.005), left main coronary artery or LAD involvement (OR 26.97, p=0.029), white blood cell count (OR 1.28 per 1,000/microliter increase, p=0.037) as three independent correlates of early SO (Table 5).

Here, use of intra-aortic balloon pumping was not included as an independent variable in the analysis because this was significantly more frequently recorded in patients with left main coronary artery or LAD involvement (11.1% vs. 3.3%, p=0.030), indicating a high correlation between the two factors and also, it was at cardiologists' discretion and thus possibly biased. Because the incidence of early SO was quite low, reclassification method was applied for above 3 factors; net reclassification improvement was 0.605, 0.495, and 0.428 for the SCr level, left main coronary artery or LAD involvement, and white blood cell count, respectively (p < 0.001 for each).

	OR	95% CI	p
Serum creatinine (mg/dl)			
(per 0.1mg/dl increase)	1.65	1.17 to 2.33	0.005
LMCA or LAD as IRA	26.97	1.41 to 514.59	0.029
White blood cells			
(per 1000/microl increase)	1.28	1.02 to 1.61	0.037
Multi-vessel disease	5.57	0.89 to 34.90	0.067
Eosinocytes			
(per 20/microl increase)	0.88	0.73 to1.06	0.174

Abbreviations: CI: confidence interval; IRA: infarct-related artery; LAD: left anterior descending artery; LMCA: left main coronary artery; OR: odds ratio.

Table 5: Predictors of early stent occlusion.

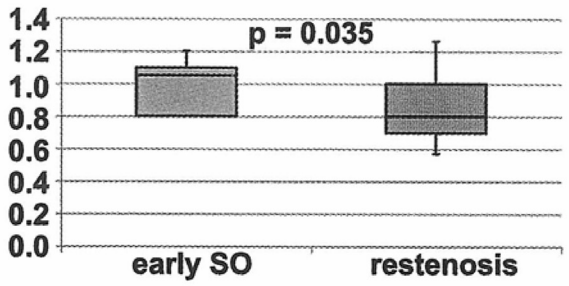

Figure 1: Comparison of serum creatinine levels (mg/dl) on admission between patients with early stent occlusion (n=10) and those with binary restenosis other than stent occlusion (n=46).
Central horizontal lines indicate median values. Lower and upper edges of boxes indicate 25th and 75th percentiles, and lower and upper bars indicate 10th and 90th percentiles. SO: stent occlusion.

Serum creatinine level as a common factor in both restenosis and early SO

As shown in Tables 4 and 5, SCr level on admission was an adjusted correlate of both restenosis and early SO. Subsequently, we compared SCr levels between the patients with early SO and those with restenosis but not due to early SO. SCr was significantly higher in the early SO group than in the restenosis group (median 1.05, interquartile range (IQR) 0.80-1.10 vs. median 0.80, IQR 0.70-1.00, p=0.035). (Figure 1).

Discussion

In Japan, the DES use in patients with AMI was contraindicated for a long time in the medical care insurance system by the Ministry of Health, Labor, and Welfare because of its unconfirmed long-term safety, but this restriction was relaxed recently. Thus, AMI has been treated mostly with BMS in the Japanese population.

Many studies [1-7] have shown that uncoated BMS placement is inferior to DES use in terms of reducing target lesion or vessel revascularization during a 1 to 3 year follow-up period after emergency stent implantation at the site of coronary occlusion. No significant difference was observed between BMS and DES in terms of the incidence of death and recurrent AMI [1,2,6,10-12]. On the other hand, accumulating data began to show a higher risk of stent thrombosis in those treated with DES over a 1-year follow-up period [3,6,9]. Kalesan et al. [8] demonstrated in meta-analysis that 1 year after AMI treatment, very late SO is significantly more likely to occur in patients receiving DES than in those with BMS placement. The risk ratio of definite stent thrombosis was 2.10 for DES vs. BMS subsequent to year 1 and interestingly, it was more prominent in trials with industry-independent funding (risk ratio=3.99). In contrast to restenosis without complete occlusion, once unexpected abrupt coronary closure caused by SO takes place, it may require urgent recanalization because such patients can be complicated with hemodynamic deterioration, leading to death. If such an unexpected event occurs quite a long time after stent implantation when less attention is paid by both cardiologists and patients themselves and antiplatelet agents may be reduced as a result of symptomatic stability, more cautious and closer management must be continued for a longer period of time once patients with AMI are treated with DES, which obviously is accompanied by more financial cost. Thus, it is of importance to elucidate predictors of restenosis and SO in patients receiving BMS as reperfusion therapy for AMI. Selection of patients who can be treated by BMS with a high probability of long-term coronary patency will enable safer and less costly supervision by limiting cases receiving DES, especially beyond 1 year after treatment.

Some studies have reported patient-related clinical factors such as hypertension and diabetes mellitus as predictors of stent restenosis [13,14]. Procedure-related factors such as minimal stent cross-sectional area, stent length, and multiple stenting have been reported as predictors of stent restenosis in many studies [13,15,16] although these factors are influenced by the known lesion-specific predictors of restenosis; vessel diameter <3.5 mm and lesion length [13,14]. In our study, stent size was relevant to restenosis but not to early SO. Consistent with previous reports, we support the idea that BMS can be used for large coronary vessels, whereas in smaller vessels DES might be selected with less frequency of target vessel revascularization.

As shown previously [17] we found an increased restenosis rate when LAD was treated as IRA. We also found that left main coronary artery or LAD involvement was an adjusted predictor of early SO. Namely, AMI, including the anterior region, is associated with both events. Brener et al. [18] reported that the anterior location of AMI was a predictor of death and reinfarction 30 days after primary angioplasty. According to the study by Beinart et al. [19] Killip class >1 on admission was an independent predictor of early SO after coronary stenting during acute coronary syndrome. Interestingly, Smit et al. [20] reported in a previous study that in primary angioplasty for AMI, both LAD as the target vessel and Killip class >1 at presentation were unadjusted predictors of early SO. However, they also showed that after multivariate analysis, the latter was the only independent predictor. Since anterior AMI is more likely to be associated with lower left ventricular function [17] it is likely that LAD involvement promotes early SO through hemodynamic compromise and thereby microcirculatory disturbance of the distal peripheral coronary bed leading to reduced coronary flow reserve. Moreover, since a bigger thrombus can be formed in the IRA of larger caliber, LAD may contain more clot burden to release vasoactive materials such as platelet-derived growth factor, promoting vascular smooth muscle proliferation.

We found that the leukocyte count on admission is another independent predictor of early SO. Since leukocyte increase was shown to be related to microvascular injury [21] and infarct size [22], it is suggested that the increase of white blood cell could serve as a contributing factor to early SO by way of inflammatory reactions producing impaired microvascular perfusion and more necrotic change, leading to left ventricular dysfunction. C-reactive protein on admission, in contrast, was not selected as a predictor here; its elevation follows the leukocyte recruitment and thus, may not be useful as an early-stage surrogate biomarker.

Lastly, we also discovered that the SCr level on admission is an independent predictor of both stent restenosis and early SO. This may

be explained as renal dysfunction is associated with the presence of patient-related predictors of stent restenosis; hypertension and diabetes. In addition, patients complicated with early SO exhibited higher SCr than those with restenosis, although IQR for the former was still in the normal range (Figure 1). Renal insufficiency was reported to increase early, late and very late stent thrombosis [23]. It tended to increase the early SO rate in the setting of ST-elevated AMI treated with DES [24], where renal insufficiency was defined as SCr ≥ 115 micromol/L (=1.3 mg/dl). According to our findings, it is suggested that the higher SCr is on admission, the more occlusive coronary change should be expected and more attention should be paid after primary stenting even if it is not as high as to be regarded as renal dysfunction.

Study Limitations

This is a single-center, retrospective study with a relatively small number of patients, and confirmation by a larger study is warranted. For the same reason, other variables could have been selected as independent predictors of binary stent restenosis or early SO. We did not evaluate later SO here due to its low incidence providing with only weak statistical power in a small population. We found here that stent size is only related to restenosis, not to early SO. In contrast, the anterior location and higher SCr level were correlated with both events. Thus, DES can be used for IRA with reference diameter ≤ 3.0 mm; however, the large amount of intracoronary thrombus in patients with AMI may predispose them to stent malapposition because of stent under sizing or thrombus resolution. This may increase the incidence of later SO. Thus, a randomized study comparing DES and BMS should be performed to elucidate whether the benefit of DES placement in primary reperfusion therapy can be safely maintained for years or whether it is also prone to early SO in those with higher normal or abnormal SCr values, elevated white blood cell counts, or anterior involvement at AMI presentation. The stent type might be cautiously selected considering that very late stent thrombosis is more frequent with DES implantation than BMS over 1 year after the procedure [8]. It could be an option to implant BMS initially as reperfusion therapy with a subsequent angiographic follow-up at 6 months when stent restenosis is most likely to occur [25,26]. DES can be implanted at this stage for more pathologically stabilized in-stent restenosis mainly consisting of neointimal hyperplasia and little thrombotic component.

Conclusion

In patients with AMI treated with BMS, both binary restenosis and early SO were increased by anterior wall involvement and elevation of SCr. Higher SCr may be subject to more occlusive changes even if its value is within the normal range. It is also suggested that in early SO, the inflammatory mechanism reflected by the leukocyte count may be involved while vessel size is not as related as it is to stent restenosis.

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＜循環器内科＞

①急性肺血栓塞栓症により心肺停止をきたした2症例

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第 27 回 心臓性急死研究会

急性肺血栓塞栓症により心肺停止をきたした 2 症例

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Successfully resuscitated two cases from acute pulmonary embolism

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Key words
心肺停止
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§　抄録

急性広範型肺塞栓症で心停止後に PCPS 装着し緊急手術で救命した 2 症例を報告する．

症例 1：64 歳女性．急性散在性脳脊髄炎のため当院脳外科に入院しステロイドパルス療法が施行された．退院当日の朝，車イス移乗後呼吸困難が出現した．緊急造影 CT で，左右肺動脈中枢側に多量の血栓像を認めた．人工呼吸管理しショック状態を安定化させた後に，緊急手術のため他院へ救急搬送された．救急車内で CPA となり他院救急外来に引き継ぎ CPR を 1 時間半継続し PCPS 装着後，肺動脈塞栓除去術が施行された．術後経過良好で退院した．

症例 2：64 歳女性．両膝痛を我慢していた．ある朝，胸部絞扼感，呼吸困難出現した．倒れているところを家族が発見し救急要請した．救急隊到着時，ショック状態で，救急車内で CPA となり CPR 開始し心拍再開した．当院到着後再び CPA となり，気管挿管し PCPS を装着後，意識回復した．造影 CT で，左右肺動脈一次/二次分枝に血栓を認めた．緊急手術のため他院へ搬送され，肺動脈塞栓除去術が施行された．経過良好で退院した．

§　はじめに

急性広範型肺塞栓症は急性の右心不全から心原性ショックと多臓器不全を起こしやすい．多量の浮遊性血栓が肺動脈を閉塞することで右心不全を急激に悪化させ，約 90％の患者が症状出現後 2 時間で心肺停止となるといわれている[1)]．ショック例の死亡率は 16～25％と高く，心肺蘇生を要した循環虚脱例では 52～65％にも上る[2,3)]．心肺停止をきたすような重篤な肺塞栓症に対する治療として，外科的血栓摘除術が推奨されているが，当院のように心臓外科のない施設では外科医との連携が患者の生命線となることがある．

今回，急性広範型肺塞栓症による心肺停止患者に経皮的人工心肺補助装置(PCPS)を装着し，近隣の心臓血管外科と連携して外科的血栓摘除術を施行し，神経学的予後良好で退院した 2 症例を経験したので報告する．

§　症例 1

患者：64 歳　女性．

既往歴：髄膜炎，子宮がん，腰椎圧迫骨折，変形性膝関節症，骨粗鬆症．

現病歴：X 年 10 月眩暈，日中傾眠出現．歩行が突進様，仮面様顔貌となり，症状が急速に進行した．10 月 15 日当院脳神経外科受診し，パーキンソン症候群疑われ緊急入院した．入院後の腰椎穿刺などから，急性散在性脳脊髄炎(ADEM)と診断された．10 月 18 日から

3日間第1回目の，11月7日から3日間第2回目の，ステロイドパルス療法施行された．以降内服ステロイドを服用し11月30日で終了した．次第に神経学的状態が改善し，歩行器にて50 m歩行も可能となり12月12日リハビリ目的転院予定であった．転院予定日のAM 8：50ポータブルトイレ移動中に，眩暈と気分不良が出現した．ベッドに横になったのちに，腹痛を訴え，呼吸困難も出現した．

意識レベルはJCS Ⅰ-3，血圧80 mmHg，SpO_2 80%後半で顔面蒼白と四肢冷感著明であった．O_2マスク3 L/分を開始したがSpO_2が上昇せずリザーバーマスクで10 L/分にしたが呼吸状態改善しなかったため，AM 9：16バッグバルブマスクで補助換気開始した．その後，呼吸状態改善しリザーバーマスクで10 L/分

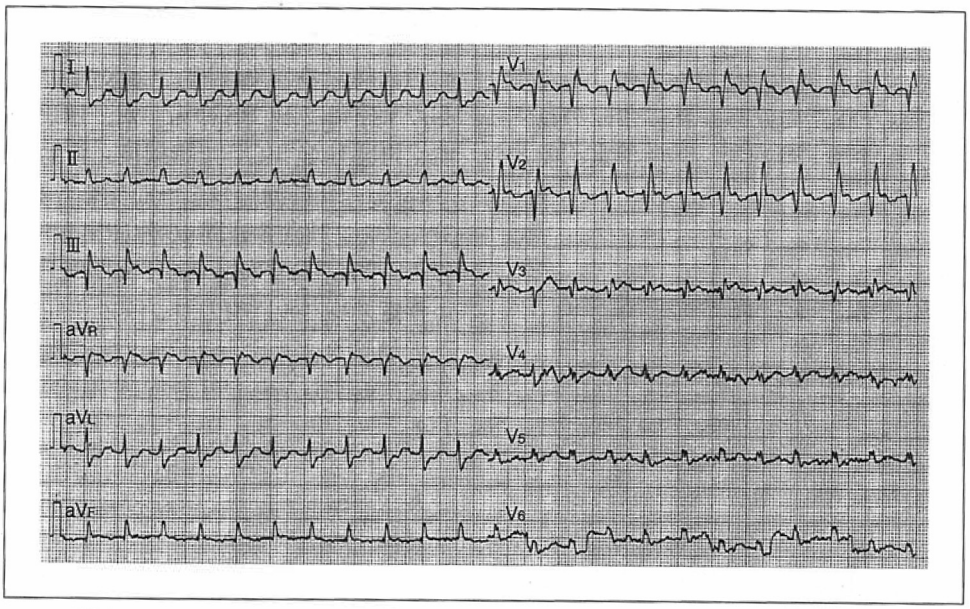

図1　症例1　急性期心電図

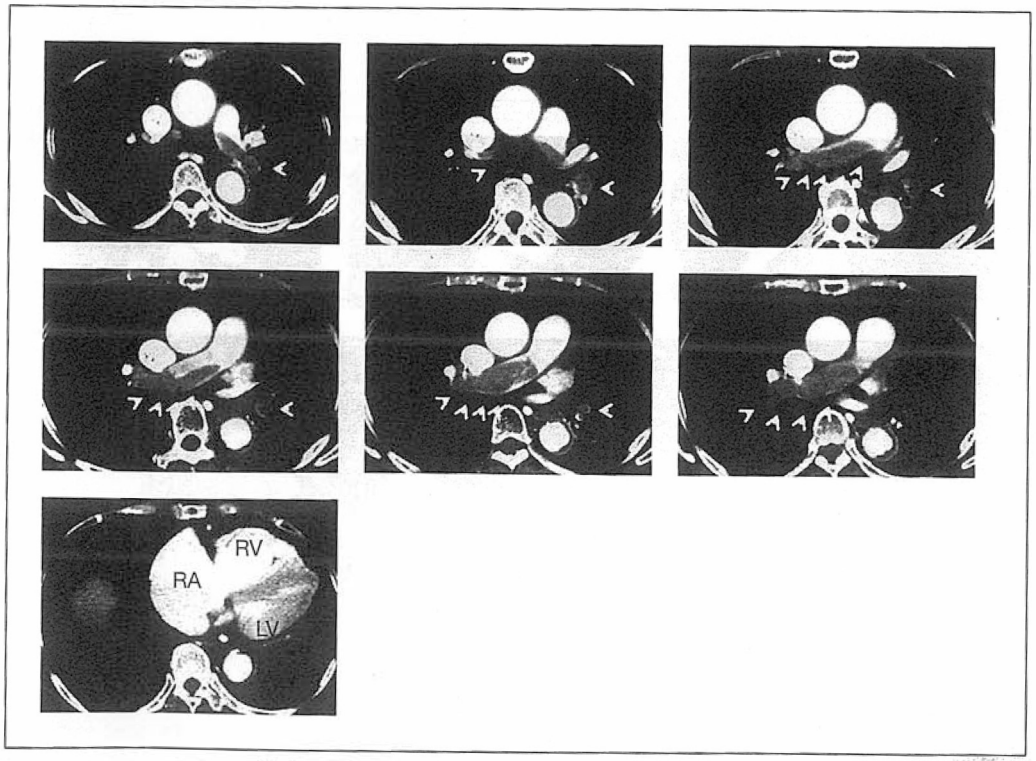

図2　症例1　造影CT検査
多量の血栓を矢頭(≺)で示す

で SpO_2 93%，BP＝87/71 mmHg，HR112 であった．血圧上昇せず，アルブミネート，ドパミン開始した．AM 9：30 ECG 施行し，Ⅰ誘導で深いS波，Ⅲ誘導でQ波と陰性T波，V1-2 誘導で陰性T波認めた(**図 1**)．心エコー施行し右心系拡大を認め，肺血栓塞栓疑いであった．わずかな三尖弁閉鎖不全からは圧較差 30 mmHg であった．AM 9：50 胸腹部-下肢造影 CT 施行した(**図 2**)．左右肺動脈中枢側を占める著明な血栓像を認め，急性肺血栓塞栓症と診断した．静脈相の CT では，右に比べて左大腿静脈が著明に拡張を認めたが血栓が存在せずここから肺動脈血栓塞栓を起こしたと推測された．左大腿/左膝窩の深部静脈に血栓がわずかに残存していた．AM 10：30 血圧，SpO_2測定不能となり，10：45 意識レベル低下し気管挿管施行した．ドブタミン開始した．

肺動脈内に巨大な血栓を認め，カテーテルによる破砕術や血栓吸引は効果がないと判断し外科的血栓摘出術を選択した．カテコラミン 2 剤併用し，強心薬と人工呼吸器管理下で血圧 90 台，SpO_2 94%に保たれたため PCPS は装着せず，AM 10：50 近隣の県立広島病院心臓血管外科に緊急手術の依頼をした．AM 11：51 緊急塞栓摘出術のため救急搬送された．

しかし，救急車内で CPA となり CPR を開始した．搬送先病院の救急外来で CPR を約 1 時間半継続し，心カテ室にて PCPS 挿入した．PCPS 開始後，心拍はすぐ再開した．ICU で待機後，肺動脈塞栓除去術施行された．両側肺動脈の黒色血栓を一塊に摘出しえた(**図 3**)．ポンプ時間 3 時間 46 分(PM 3：36-PM 7：22)，心停止時間 59 分(PM 4：22-PM 5：21)であった．翌日朝より意識レベル回復しコンタクト可能となった．後日，下大静脈フィルター留置(永久留置)した．第 30 病日当院に転院しリハビリを行い，その後車いすにて退院した．

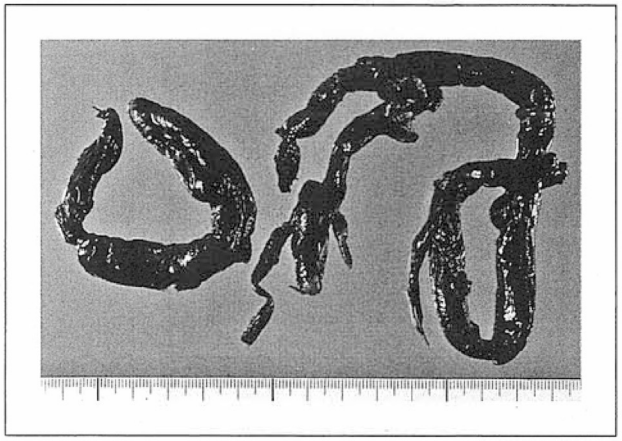

図 3　症例 1　摘出血栓肉眼像

§　症例 2

患者：64 歳　女性．

既往歴：高血圧，脂質異常症，痛風にて内服治療中 X-2 年　右膝関節半月板断裂手術．

現病歴：以前より，右膝の痛みがあったが我慢していた．下肢浮腫は気がつかなかった．発症 1 週間前に

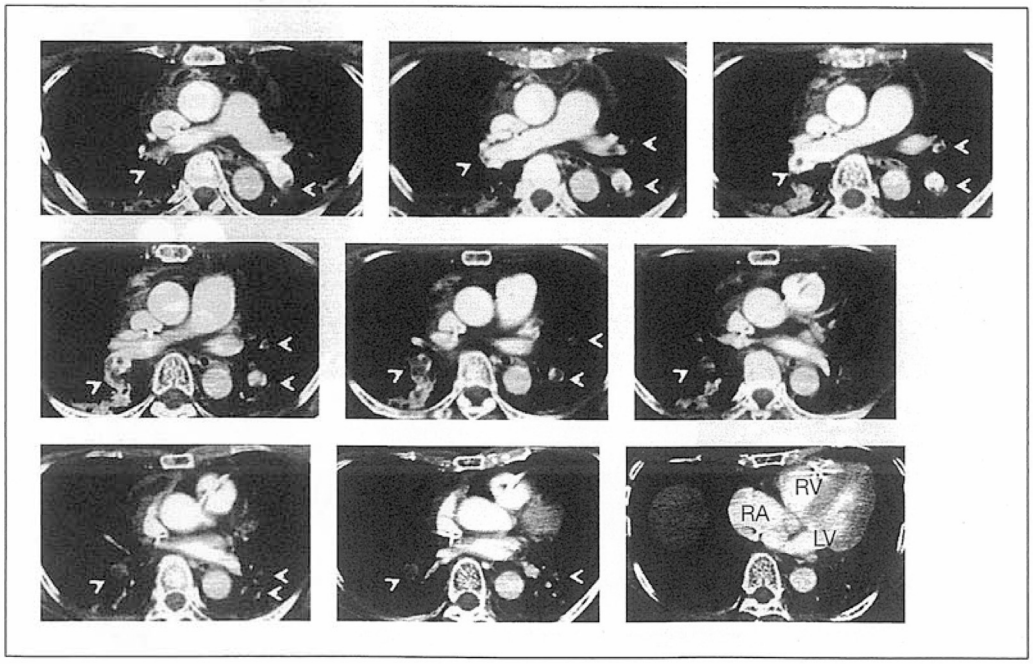

図 4　症例 2　造影 CT 検査
多量の血栓を矢頭(≺)で示す

左胸痛があり近医受診したが心電図などに異常なく経過観察となった．X年12月20日(症例1発症日の8日後)早朝トイレに行き胸部絞扼感，呼吸困難出現し，救急車を呼ぼうと歩いたところで意識消失し転倒した．顔面に出血して倒れているところを家族が発見し救急要請した．AM 7：31 救急隊到着時，会話可能であった．橈骨動脈は触知できず，酸素飽和度・血圧測定不可であった．AM 7：54 当院に救急搬送中CPAとなりCPR開始した．AM 7：56 呼吸再開，体動あったが，AM 7：57 再度CPAとなりCPR再開した．AM 8：00 CPR継続され当院到着した．

ECGモニターでPEAと診断した．CPRを継続したまま，AM 8：10 静脈ルート確保後，アドレナリン投与した．AM 8：20 機械式胸骨圧迫装置LUCAS装着し心カテ室に移動し，AM 8：25 PCPSを装着した．その後，気管挿管，冠動脈造影を施行したが冠動脈に異常はなかった．その後，心拍再開し，自発呼吸も出現した．急性肺血栓塞栓症が疑われ，確定診断のためAM 9：15 造影CT施行した(**図4**)．左右肺動脈一次/二次分枝を占拠する多量の血栓を認め，急性肺血栓塞栓症と診断した．静脈相のCTでは，左下肢静脈末梢のみ拡張し，左膝窩静脈の遠位部に残存血栓認めた．CPAの蘇生例でPCPS装着後の状態であり，緊急血栓摘出術の適応ありと判断した．AM 9：30 救急センターに戻り，近隣の県立広島病院心臓血管外科に緊急手術の依頼をした．AM 10：00 呼名にて開眼あり．BP＝135/96 mmHg　HR＝113回/分となったため，鎮静薬投与した．AM 10：25 同病院へ救急搬送された．

転院後，引き続き肺動脈塞栓除去術施行された．左肺動脈上葉枝および下葉枝，右肺動脈上葉/中葉/下葉枝の黒色血栓を摘出した．ポンプ時間3時間52分(PM 2：04-PM 5：56)，心停止時間2時間(PM 2：37-PM 4：37)であった．翌日より問いかけにうなずきが可能であった．後日，下大静脈フィルター留置(永久留置)した．第28病日当院転院しリハビリを行い，後日独歩退院した．

§ 考察

重症肺塞栓症のため心停止をきたしPCPSを装着後，外科的血栓摘除術を施行され，神経学的予後良好で退院した2症例を報告した．症例1は搬送途中に心停止をきたしたため，PCPS装着までCPRを長時間行うこととなった．発症時の状態が不安定であったことや，緊急手術といっても手術が即座に準備できるわけではないので，当院でPCPSを装着して搬送すべきであった．2例目は，心停止の状況で搬送されたが，来院後25分でPCPSが装着された．到着時刻が午前8時で多くのスタッフが出勤していたことが幸運であったと考えられる．

日本循環器学会の肺血栓塞栓症および深部静脈血栓症の診断，治療，予防に関するガイドライン(2009年改訂版)によると[4]，循環動態が不安定な場合は，呼吸循環サポートを行い，それでも循環虚脱した場合にはPCPSを装着する．PCPSは短期間の生命維持装置であり，原因除去のための根本治療を行う必要があり，その後，血栓溶解療法，カテーテル治療，外科的血栓摘出術を行う．PCPSを装着した状態での血栓溶解療法は，後腹膜出血などのリスクが高くなり，また，血流が肺動脈をバイパスするため血流が不十分であり，単独治療としては適切ではないと考える．カテーテル治療では血栓を完全に吸引することは不可能であるが，血栓を破砕して血流を部分的に再開させることで肺動脈圧を低下させ治療効果が出てくる．しかし，PCPS装着時は同様に肺動脈をバイパスするので，肺血流は十分に確保できず血栓が溶解されない可能性がある．よって，PCPS装着時の治療として外科的血栓摘出術が最も良い適応と考えられる．

前述ガイドラインによれば，わが国では2000年から2006年までの7年間に，急性肺血栓塞栓症539例に対して外科的血栓摘除術が行われ，その在院死亡率は21.2%であった．手術成績は，患者が昇圧剤に抵抗性でショック状態になり多臓器不全に陥る前に行われると最も成績が良い．心停止後に行われる手術は生存率がさらに低くなると思われる．よって，PCPS装着前の効果的な蘇生が持続されていることが，心停止に陥った傷病者の術後成績に大きく関係する．当院のように心臓血管外科がない病院から患者を紹介する場合は，その患者を診ていない状態にもかかわらず二つ返事で受け入れてくれる心臓外科の存在が大切であり，我々もPCPS装着までのCPRの質を高めることが大切であろう．PCPSを装着することで手術までの時間的余裕が生まれるが，心臓外科が手術を行っていない状況や施設の手術室が空いている状況のどちらも満たされていないと救命の連鎖がつながらない．今回，偶然にも8日間で2例の肺塞栓症による心停止を経験したが，2例とも高次脳機能に問題なく生存退院した．外科医との連携および，質の高いCPRを継続してPCPS装着に継げること大切さを実感した．

§ 結語

心停止をきたした致死性の肺血栓塞栓症に対し，外科的血栓摘出術を行い脳機能カテゴリー(CPC)1で退院した2症例を報告した．発症早期から良質の心肺蘇生を継続し，PCPSを装着して循環動態維持を図り，

なおかつ，心臓血管外科と連携して迅速に塞栓除去術に移行できれば救命しうる可能性が高い．

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§ 質疑応答

座長：加藤林也(名古屋掖済会病院)

加藤(座長：名古屋掖済会病院)　ありがとうございました．ただいまの演題につきまして，ご討議をおねがいします．この2症例ともCPAの状態が搬送の時にもありましたが，心リズムは心静止ですか，VFですか．

住居　いいえ，どちらもPEAでした．血圧が下がって意識がなくなったという状況でした．

加藤　2例とも良好な結果で良かったと思いますけども，最後におっしゃったように，ただちに手術で対応するという心臓外科のバックアップがなければ，助からない症例だと思います．平日の日勤帯というのは実は盲点でありまして，通常，心臓外科が手術をやっていて，スタッフやオペ室が確保できないということが，実際にはありますので，案外夜間とか，そういった時のほうが対応してくれることがあります．自院での緊急症例でも連絡を受けてから，手術の準備をするので，基本的には他院の症例であっても搬送に伴う不備といったようなことがなく，なおかつ，連携がよければ受け入れ不可能という懸念は解消されると思います．

住居　加藤先生のおっしゃるとおりです．広島でもとくに月曜日の朝は，すべての病院が心臓外科のオペが行われているという状況です．その時に解離性動脈瘤症例が搬送されて，非常に厳しい状況になったことがあります．緊急手術を要する疾患の中でも，急性肺血栓塞栓症の場合はPCPSを入れれば多少の時間の余裕ができるので，緊急手術までの待機時間を稼ぐことができる．もしくは場合によっては血栓のカテーテル的な治療でなんとかそこをしのぐというようなことになろうかと思います．

加藤　解離に比べるとPCPSといった対応で時間稼ぎが少しできるのは，肺塞栓のひとつの特徴だと思いますね．貴重なご発表でしたが，先生どうもありがとうございました．