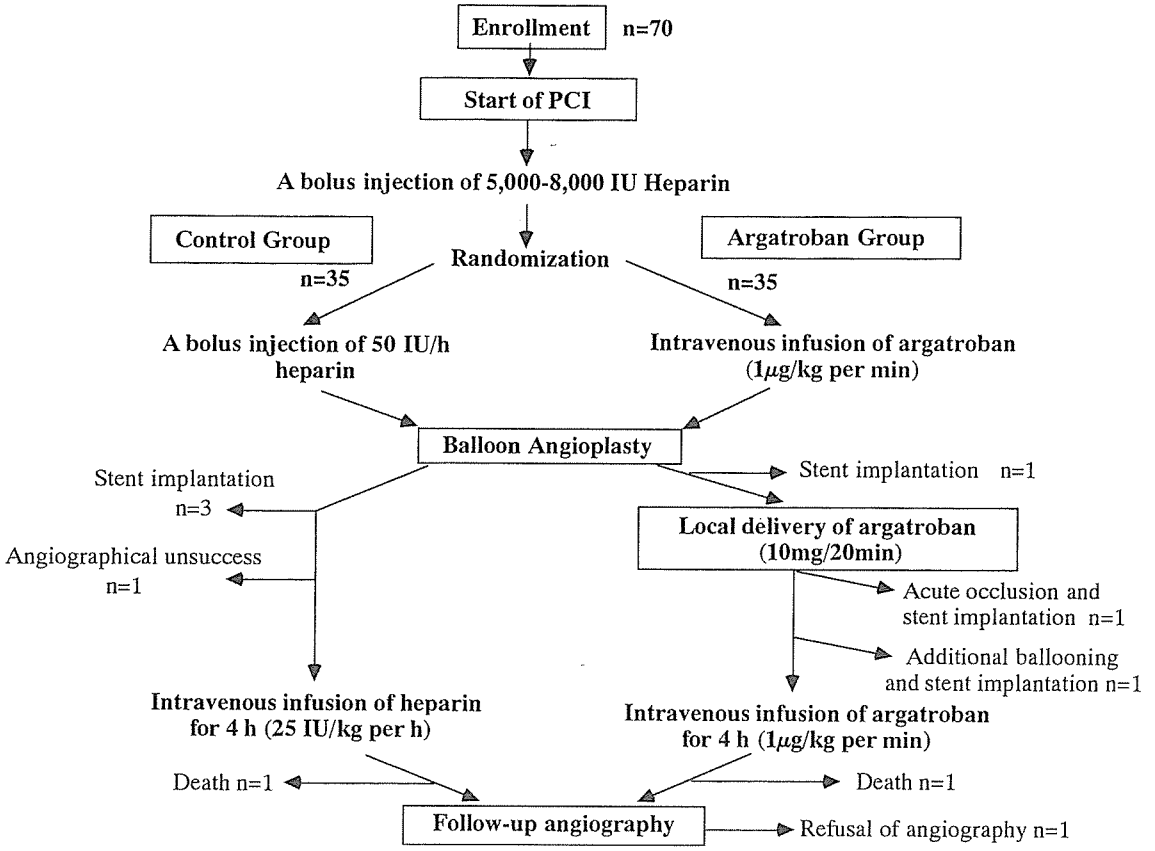

Fig 1. Study protocol and patient flow chart. A bolus of 5,000–8,000 IU heparin was injected intravenously at the start of the percutaneous coronary intervention (PCI) procedure. Patients were randomly assigned to 2 groups: the control group and the argatroban group receiving local delivery of argatroban via a Dispatch™ catheter after PCI. Control group: PCI was performed; the patients received a bolus injection of heparin during the procedure and an intravenous infusion of heparin for 4 h after angioplasty. Argatroban group: intravenous infusion of argatroban was started 30 min before the PCI, followed by local delivery of argatroban into the dilated site using a Dispatch™ catheter, and the postoperative treatment of intravenous infusion of argatroban for 4 h.

according to consecutive sealed envelopes; the control group (n=35) underwent a conventional method of POBA, and the argatroban group (n=35) had the addition of local delivery of argatroban. The exclusion criteria were (1) more than 80 years old or less than 20 years old, (2) a target lesion in a non-protected left main coronary artery, (3) a total occlusive lesion equal to TIMI 0-1 flow, (4) a severely calcified lesion, (5) a diffuse lesion, (6) a target vessel with severe proximal tortuosity, (7) a lesion that restenosed more than once, (8) a bypass graft vessel, (9) an indication for a new device (eg, directional coronary atherectomy, stent, rotational atherectomy or laser ablation), (10) poor left ventricular function (ejection fraction <40%), (11) patients receiving warfarin, (12) patients receiving an intravenous infusion of heparin, (13) a history of gastrointestinal bleeding, thrombocytopenia, or coagulopathy, (14) a history of stroke within the preceding 3 months, (15) acute myocardial infarction within the previous month, (16) patients undergoing thrombolysis within the past 24 h, (17) pregnancy, and (18) other major illness including renal failure and liver dysfunction. Informed consent was obtained from each patient.

PCI Procedure and Adjunctive Therapy

Coronary angiography was performed using the Judkins method, and a bolus of 5,000–8,000 IU heparin was given intravenously after vascular access had been established. In the control group, the POBA was performed in a standard way with a bolus injection of heparin (50 U/kg per h) during the procedure, followed by an infusion of heparin (25 U/kg per h) for 4 h after the POBA. In the argatroban group, an intravenous infusion of argatroban was given (1 μg/kg per min) 30 min before POBA, followed by the local delivery of argatroban (10 mg/20 min) into the dilated site using the Dispatch™ catheter (SIMED Life Systems) after the successful POBA. Postoperatively, the patients received an intravenous infusion of argatroban (1 μg/kg per min) for 4 h (Fig 1). All patients received both Ca antagonist and 81–162 mg of aspirin before the POBA until the follow-up angiography. In addition, β-blockers, long-acting isosorbide dinitrates or nicorandil was administered at the discretion of the treating physician before the POBA until the follow-up coronary angiography. Clinical success of the POBA was defined as angiographic success (residual stenosis <50%) without a major complication (death, myocardial infarction, or emergency coronary-artery bypass surgery) during hospitalization.

Quantitative Coronary Angiographic Analysis

All angiograms were analyzed by a computer-assisted system of quantitative coronary angiographic analysis (QCA; Cardiovascular Measurement System Ver. 3.0

Table 1 Baseline Clinical Characteristics of the Study Patients

	Control group (n=35)	Argatroban group (n=35)	p value
Age (years)	61±8	61±8	NS
M/F	29/6	27/8	NS
Risk factors			
BMI	23.6±2.0	23.5±2.6	NS
Diabetes mellitus	18	12	NS
Hypertension	19	23	NS
Total cholesterol (mg/dl)	185±32	198±36	NS
Prior MI	13	8	NS
Ejection fraction (%)	57±10	58±13	NS
Diseased coronary vessels			
1-vessel disease	23	23	NS
2-vessel disease	11	12	
3-vessel disease	1	0	
Target vessel			
LAD/LCX/RCA	18/13/4	16/16/3	NS

BMI, body mass index; MI, myocardial infarction; LAD, left anterior desending artery; LCX, left circumflex artery; RCA, right coronary artery.

Table 2 Baseline Lesion Characteristics of the Study Patients

	Control group (n=35)	Argatroban group (n=35)	p value
ACC/AHA classfication			
A	5	5	
B	29	29	NS
C	1	1	
De novo lesion	32 (94%)	28 (80%)	NS
Reference vessel diameter (mm)	2.89±0.46	2.89±0.39	NS
Minimal lumen diameter (mm)	0.86±0.24	0.83±0.19	NS
Lesion length (mm)	6.00±3.69	5.25±3.77	NS
Lesion characteristics			
Eccentricity	29 (83%)	27 (77%)	NS
Calcification	12 (34%)	16 (46%)	NS
Ostial lesion	4 (11%)	5 (14%)	NS
Proximal tortuosty	2 (6%)	1 (3%)	NS
Angled lesion	4 (11%)	4 (11%)	NS
Bifurcation	7 (20%)	6 (17%)	NS

(CMS), Medical Imaging Systems Inc, Leiden, the Netherlands). CAG was performed before, immediately after, and 3 months after the POBA (follow-up) as described in detail elsewhere![9] All angiographic analyses were performed in a blinded fashion by an experienced physician. The % diameter stenosis (%DS) and minimal lumen diameter (MLD) of the target lesion were determined quantitatively. The diameter of a Judkins catheter was measured using a precision micrometer (No. 293-421-20; precision 0.001 mm, Mitutoyo Co, Kawasaki, Japan) to obtain a calibration factor in the 'Free French' mode in the image calibration of the CMS program. The calibration factor (CF) was adjusted between 0.08 and 0.1 mm/pixel using digital zoom according to the CMS manual![20] The complex edit mode (gradient field transform: GFT) was used in the case of a complex lesion, as described in detail elsewhere![21]

Angiographic restenosis after POBA was defined as a %DS greater than 50% on the follow-up angiogram. Clinical restenosis was defined as the recurrence of ischemia and/or target lesion revascularization within the period before the follow-up angiography.

Endpoints

The following endpoints were prospectively defined. Restenosis was the primary endpoint. Secondary endpoints included death, acute myocardial infarction (symptoms, ECG changes, and creatine kinase >twice the upper normal limit) and coronary revascularization (coronary bypass surgery, or repeated POBA and/or coronary stenting). Repeat revascularization of the target lesion (target lesion revascularization) was defined as angioplasty or bypass surgery performed because of restenosis of the target lesion in association with recurrent angina, objective evidence of myocardial ischemia, or both. The principal safety endpoints were abrupt vessel closure, stroke, major bleeding, or the need for vascular surgery. Major bleeding was defined as intracranial hemorrhage or overt bleeding associated with a decrease in hemoglobin of more than 5 g/dl.

Statistical Analyses

The data are presented as mean±SD (standard deviation). Differences in angiographical parameters (%DS and MLD) between the 2 groups before POBA, immediately after all procedure and during the follow-up were compared by unpaired t-test. Statistical comparisons of differences in categorical data between the 2 groups were performed using the chi-square test. Differences were considered significant when $p<0.05$. The clinical follow-up analyses were performed on an intention-to-treat basis and on-treatment-analyses. Moreover, angiographic follow-up analyses were performed using on-treatment-analyses.

Table 3 In-Hospital Outcomes of the Study Patients

	Control group (n=35)	*Argatroban group (n=35)*	*p value*
Stent required (%)	*3 (8.6)*	*3 (8.6)*	*NS*
Acute occlusion (%)	*0 (0)*	*1 (2.8)*	*NS*
Additional ballooning (%)	*0 (0)*	*1 (2.8)*	*NS*
Angiographical nonsuccess (%)	*1 (2.8)*	*0 (0)*	*NS*
Acute myocardial infarction (%)	*0 (0)*	*0 (0)*	*NS*
Emergency CABS (%)	*0 (0)*	*0 (0)*	*NS*
Death (%)	*0 (0)*	*0 (0)*	*NS*

CABS, coronary artery bypass surgery; MI, myocardial infarction.

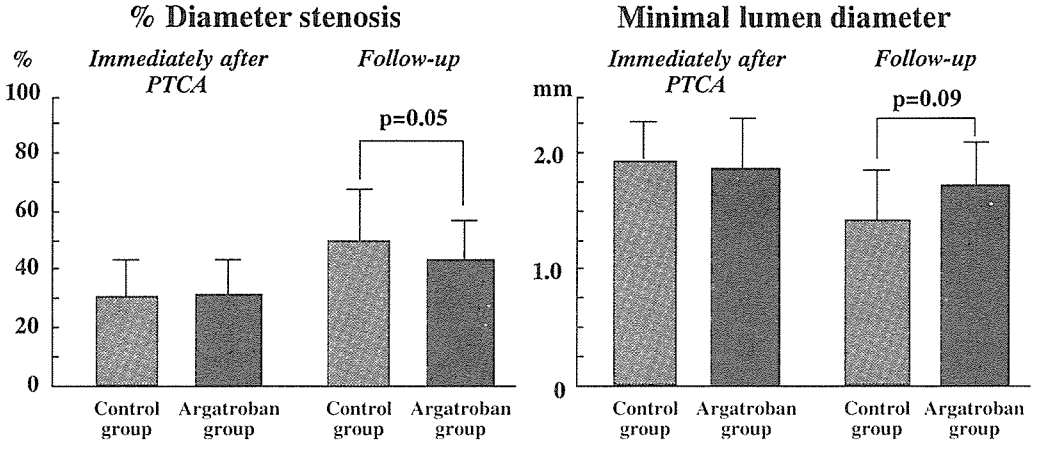

Fig 2. There were no significant differences between the 2 groups in % diameter stenosis or minimal lumen diameter immediately after PCI. Angiographic parameters including % diameter stenosis and minimal lumen diameter were marginally better in the argatroban group than in the control group at follow-up.

Results

Patient Population (Fig 1)

Four patients in the argatroban group were excluded from the follow-up CAG; 1 underwent stent implantation because of a major coronary dissection before the local delivery of argatroban, 1 had an abrupt vessel closure during the local delivery of argatroban, 1 required additional ballooning and stent implantation, and 1 refused to undergo the follow-up CAG with negative exercise thallium-201 stress imaging. Four patients in the control group were also excluded from the follow-up CAG: 3 required stent implantation because of major coronary dissection after the balloon angioplasty, and 1 had residual %DS >50% (angiographically unsuccessful). During the course of the study, 2 patients died suddenly (control 1, argatroban 1) before the follow-up angiography; the 1 in the argatroban group had cardiac sudden death after balloon angioplasty on day 60 (the patient had an old myocardial infarction with left ventricular dysfunction) and the patient in the control group died suddenly on day 60 after the balloon angioplasty (suspected rupture of a thoracic aortic aneurysm). In total, 10 patients (5 in each group) were excluded from the follow-up angiography.

Baseline Clinical and Lesion Characteristics

Tables 1 and 2 summarize the baseline clinical and lesion characteristics; there were no significant differences between the 2 groups in this study.

In-Hospital Outcome

The in-hospital outcomes are summarized in Table 3. An acute occlusion in the treated segment during the local delivery of argatroban using a Dispatch™ catheter was observed in 1 patient, requiring implantation of a Palmaz-Schatz stent. There were no major complications during the procedure in either group.

Quantitative CAG Analyses at Follow-up

Fig 2 compares the results of the angiographic analyses between the 2 groups. There were no significant differences between the 2 groups in %DS (Control group: 30.9±10.9%, Argatroban group: 31.7±9.6%) or MLD (Control group: 1.95±0.3 mm, Argatroban group: 1.92±0.35 mm) immediately after procedure. However, after 3 months, the angiographic parameters of %DS (Control group: 51.3±16.2%, Argatroban group: 43.5±14.6%) and MLD (Control group: 1.36±0.46 mm, Argatroban group: 1.57±0.47 mm) were marginally better in the argatroban group than in the control group (p=0.05 and p=0.09, respectively). The mean difference in coronary MLD (net gain) between the post-procedure and follow-up angiograms was 0.51±0.44 mm in the control group, and 0.72±0.50 mm in the argatroban group (p=0.09).

Restenosis Rates, Target Lesion Revascularization, and Clinical Follow-up Data

Fig 3 compares the restenosis rates in the 2 groups. The lesion restenosis (%DS >50%) rates were 27% in the argatroban group and 56% in the control group (p=0.02). The clinical restenosis rates were 14% in the argatroban group and 37% in the control group (intention-to-treat analysis; Table 4, p=0.03). The target lesion revascularization rates were 14% in the argatroban group and 34% in the control

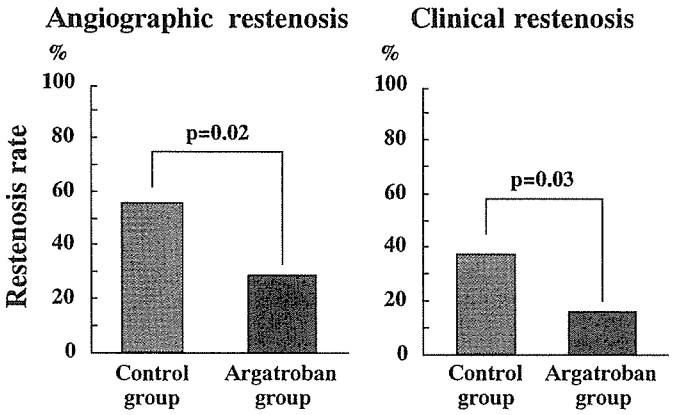

Fig 3. Angiographic restenosis occurred in 5 of the 30 patients in the argatroban group (27%) and 12 of the 30 patients in the control group (56%). Clinical restenosis occurred in 5 of the 35 patients in the argatroban group (14%) and 13 of the 35 in the control group (37%).

Table 4 Clinical Outcome at Follow-up of the Study Patients

	Control group (n=35)	*Argatroban group (n=35)*	*p value*
Clinical restenosis	*13**	*5*	*0.03*
Target vessel revascularization	*12*	*5*	*0.05*
Vasospastic angina	*0*	*1*	*NS*
Myocardial infarction	*0*	*0*	*NS*
Death	*1*	*1*	*NS*
Any clinical event	*14*	*7*	*0.07*

Clinical restenosis included recurrence of ischemia and/or angina and target vessel revascularization.
**Includes one case of recurrence of ischemia (silent) without target vessel revascularization.*

Table 5 Clinical Outcome at Follow-up of the Study Patients According to on-Treatment Analysis

	Control group (n=31)	*Argatroban group (n=32)*	*p value*
Clinical restenosis	*12**	*5*	*0.03*
Target vessel revascularization	*11*	*4*	*0.06*
Vasospastic angina	*0*	*1*	*NS*
Myocardial infarction	*0*	*0*	*NS*
Death	*1*	*1*	*NS*
Any clinical event	*13*	*7*	*0.08*

Clinical restenosis included recurrence of ischemia and/or angina and target vessel revascularization.
**Includes one case of recurrence of ischemia (silent) without target vessel revascularization.*

group (intention-to-treat analysis; Table 4, p=0.05). Moreover, Table 5 shows the clinical outcome at follow-up of the study patients on-treatment-analysis. Seven cases (6 stent implantations and 1 unsuccessful procedure during initial angioplasty) were excluded in Table 5 according to on-treatment-analysis. The clinical restenosis rates at follow-up were 17% (n=5) in the argatroban group and 40% (n=12) in the control group according to on-treatment-analysis after exclusion of 10 cases (n=30, respectively; p=0.04). The details of those 10 cases are as follows: 6 stent implantations during procedure, 1 unsuccessful procedure, 2 deaths, and 1 refusal of follow-up CAG.

Discussion

Previous and Present Trials Regarding the Prevention of Restenosis

No definitively effective prevention of restenosis by systemic administration of drugs has been observed in previous clinical trials. Several types of drug therapy, such as anticoagulants (heparin, warfarin) and antiplatelet therapy (aspirin, dipyridamole, ticlopidine, prostacyclin, and thromboxane A_2 inhibitor), fish oil, and steroids have failed to reduce the restenosis rate in most clinical trials[22–24] Recently, trapidil and cholesterol-lowering agents have been shown to be promising in preventing restenosis after coronary angioplasty[25] but patients must take these drugs for several months after angioplasty.

In contrast, coronary stenting has been shown to be effective in preventing restenosis after coronary angioplasty[26,27] and the drug eluting stent has been developed in recent years[28] Nevertheless, adjunctive anticoagulation and/or antiplatelet therapy is required for 1 month after coronary stenting, resulting in occasional bleeding complications. Accordingly, a new procedure with a low rate of adverse effects and no need for adjunctive therapy after discharge has been sought. In the present randomized, controlled study, local delivery plus intravenous infusion of argatroban reduced both the angiographic and clinical restenosis rates after coronary angioplasty. There was no increase in bleeding risk with the argatroban treatment. The restenosis rate in the argatroban group in this trial (27%) was similar to that in the stent group of the STRESS trial (32%; NS)[27] despite the fact that the reference vessel diameter was smaller (2.89±0.39 mm) than that in the STRESS trial (3.03±0.42 mm; p=0.07). The restenosis rate in the

control group in the present study was similar to that in the control group of the CAVEAT trial (56% vs 57%)[29]

Mechanism of Restenosis and Thrombin Activation

The mechanism of restenosis after PCI is considered to be a healing process after a balloon injury. Immediately after arterial injury with a balloon catheter, many factors lead to the activation of medial smooth muscle cells (SMC), but there are 3 major ones. First, elastic recoil is a pivotal factors after mechanical trauma to the abnormal vessel wall and stretching of the normal vessel wall (ie, arterial remodeling). Second, the formation of thrombus on the intimal surface and inside the disrupted plaque is an important part of the restenosis process. The intensity of thrombus formation could serve to reduce the initial gain in lumen both by adding to the plaque mass and by elaborating more growth factors.[30] Third, the most intense interest has been on the impact of mitogenic factors (basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and SMC-derived growth factor (SDGF)) released by platelets, monocytes, and by components of the intact parts of the vascular wall, including the SMC. In vitro and in vivo studies have shown that injury to the endothelium and the vessel wall causes increased thrombin production.[31] Thrombin, in particular, may play a significant role in the initiation of the restenosis process, because the regulation of these growth factors has been reported to be modulated by thrombin via a thrombin receptor.[32,33] Moreover, thrombin activates a variety of vascular and inflammatory cell types that promote wound healing.[10,32] Thus, the inhibition of the initial thrombin activation may exert a potent preventative effect on restenosis after POBA.

Direct Thrombin Inhibitors and Restenosis

The direct thrombin inhibitors, such as r-hirudin, hirulog, hirugen and D-Phe-Pro-Arg-chloromethylketone (PPACK), are expected to reduce the restenosis rate after PCI,[11,34] and several relevant experimental studies have been performed in recent years. Rogasta et al reported that the 2-h systemic infusion of hirudin failed to reduce cell proliferation within the first 7 days, whereas the 2-h infusion of hirulog improved the late angiographic luminal dimensions and reduced the cross-sectional area narrowing by plaque in rabbits compared with heparin controls after angioplasty.[12] They suggested that (1) hirudin inhibits cellular migration rather than proliferation, and (2) hirudin reduces mural thrombosis, resulting in less thrombus incorporation into the plaque. However, Serruys et al reported that the systemic administration of r-hirudin failed to reduce restenosis in a clinical study (HELVETICA study).[35] This discrepancy between the experimental study (Rogasta et al[12]) and the clinical study (Serruys et al[35]) may be explained by a difference in the local concentration of hirudin at the target lesion. Accordingly, it is expected that the local delivery of a high concentration of a direct thrombin inhibitor using a drug delivery device would reduce restenosis without increasing adverse effects in the clinical setting. However, there has not a previous clinical prospective randomized trial using a direct thrombin inhibitor and a local delivery device for preventing restenosis after angioplasty.

The present study has demonstrated that the intracoronary local delivery of argatroban, in addition to a 4-h intravenous infusion, prevents restenosis following POBA. Argatroban has been reported to inhibit platelet activation by fibrin- or clot-incorporated thrombin more effectively than does hirudin.[16] The reason that both local delivery and continuous intravenous infusion of argatroban were used in the present study was to inhibit thrombin activity, which may increase immediately after angioplasty before the local delivery of argatroban, because there was a time delay (approximately 10 min) between the first balloon inflation and the local delivery of argatroban (thrombin receptors have been reported to appear on a SMC within a few min after balloon injury[12]). The present findings, together with the report of Rogasta et al,[13] suggest that direct thrombin inhibition may successfully inhibit cell migration in the initiation of restenosis in human patients.

Local Drug Delivery Device

Several local delivery balloon catheters have been designed. The double-balloon catheter was the first percutaneous drug delivery device. Other drug delivery devices such as the Wolinsky perforated-balloon catheter, a microporous balloon, a channel catheter, and the Transport coronary angioplasty catheter have been developed since then. More recently, the drug delivery devices known as the Infusasleeve™, a hydrogel-coated balloon, and the Dispatch™ catheter have become available.[36] The hydrogel-coated balloon does not have a perfusion port to support distal blood flow during balloon inflation. Imanishi et al reported that the local delivery of argatroban using a hydrogel-coated balloon reduced intimal thickening after balloon injury in an experimental study.[37] The Dispatch™ catheter consists of an over-the-wire, non-dilatation catheter with a spiral inflation coil and a perfusion port on its distal tip. There are several advantages of this system for the drug delivery. First, this device allows distal coronary perfusion during balloon inflation for a sufficiently longer time compared with other drug delivery catheters. Second, this system makes it easier to deliver the drug than a hydrogel-coated balloon catheter, because in the case of the hydrogel-coated balloon, the drug must first penetrate the hydrogel-balloon surface. Third, the pharmacokinetic validity of the local delivery of argatroban using a Dispatch™ catheter has been established. Anabuki et al confirmed that the local delivery of argatroban using a Dispatch™ catheter resulted in the intramural deposition of high concentration argatroban without any arterial damage.[38] This new device has been used for the prevention of reocclusion after revascularization in patients with acute myocardial infarction and unstable angina pectoris.[18,39] However, there are no other clinical reports on the prevention of restenosis using the Dispatch™ catheter except for one small non-randomized trial.[10] Thus, this is the first prospective randomized controlled trial using the Dispatch™ catheter and argatroban to prevent restenosis following POBA. Moreover, it is expected that these local delivery devices may be available not only for direct thrombin inhibitor but also gene therapy in the future.[40]

Study Limitations

First, it is unclear whether the local delivery of argatroban using a Dispatch™ catheter is effective in patients with small vessels (<2.5 mm). Second, this study was designed as an open-label randomized trial in the light of safety concerns. Although a double-blind design may be better, it is not easy to use a specific device such as the Dispatch™ catheter in a double-blind manner. Because no

obvious benefit of long-term inflation in preventing restenosis was found in a previous study;[41] the long-term inflation (20 min) with the Dispatch™ catheter is unlikely to be responsible for the significant reduction of restenosis in the present study. Third, this trial was performed at a single center, with a small number of patients. Further study is necessary with a larger number of patients in a double-blind, randomized, multicenter trial with a placebo group (local delivery of normal saline using a Dispatch™ catheter). We are now planning to conduct such a trial in Japan. Fourth, the effect of the exclusively local delivery of argatroban remains undetermined, because postoperative intravenous infusion of argatroban was combined with the intracoronary local delivery in the present study. Further study is necessary to assess the 'pure' efficacy of the local delivery of argatroban. Moreover, further study is necessary to assess the efficacy for stenting lesions in the present stenting era. Final, the present study did not evaluate local delivery direct pressure, although it is reported that high, local delivery pressure is a key determinant of vascular damage and intimal thickening.[42] Further study is needed to examine the local drug delivery pressure during infusion of argatroban in the clinical setting.

Conclusions

The local delivery of argatroban using a Dispatch™ catheter was observed to be safe and effective in preventing restenosis after balloon angioplasty.

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Circ J 2004; **68:** 304–307

Exercise-Induced Hepatocyte Growth Factor Production in Patients After Acute Myocardial Infarction

—— Its Relationship to Exercise Capacity and Brain Natriuretic Peptide Levels ——

Satoshi Yasuda, MD; Yoichi Goto, MD; Hiroshi Takaki, MD; Yasuhide Asaumi, MD; Takeshi Baba, MD; Shunichi Miyazaki, MD; Hirohi Nonogi, MD

Background The hepatocyte growth factor (HGF) is a multifunctional cytokine with cardioprotective properties and potent myogenic activity for vascular endothelium. In patients after acute myocardial infarction, exercise training has the beneficial effects on cardiovascular adaptations. We hypothesized that exercise induces HGF production in those patients. If this hypothesis is correct, HGF production may be associated with clinical parameters of cardiovascular function.

Methods and Results In 20 patients after acute myocardial infarction, HGF levels in the pulmonary artery (HGF_{PA}) and aorta (HGF_{Ao}) were determined at rest and during supine submaximal exercise, with cardiac output (CO) measured by catheterization. Exercise-induced HGF production was calculated by using the following equation: $[(HGF_{PA}-HGF_{Ao})\times CO$ during exercise$]-[(HGF_{PA}-HGF_{Ao})\times CO$ at rest]. On a separate day, peak oxygen uptake ($\dot{V}O_2$) was determined during a symptom-limited upright cardiopulmonary exercise test. Exercise increased HGF production (from 1.6±3.0 to 9.0±6.3 μg/ml, $p<0.001$). Exercise-induced HGF production was inversely related to peak $\dot{V}O_2$ ($r=-0.664$, $p<0.01$) and positively related to levels of brain natriuretic peptide (BNP), a biochemical marker for post-infarction ventricular remodeling ($r=0.686$, $p<0.01$).

Conclusions Exercise significantly increases HGF production. This phenomenon may play an important role in post-infarction patients, particularly with reduced exercise tolerance and elevated BNP levels. (*Circ J* 2004; **68:** 304–307)

Key Words: Exercise; Growth substances; Myocardial infarction; Rehabilitation

Hepatocyte growth factor (HGF), originally identified and cloned as a potent mitogen for hepatocyes, has mitogenic, motogenic, morphogenic, and anti-apoptotic activities in a variety of cells through its receptor, c-Met.[1,2] HGF is a unique growth factor to act protectively against endothelial dysfunction,[3–5] myocardial ischemia/infarction and remodeling.[6–8] Thus, the HGF system (HGF and its receptor c-Met) is attracting increasing attention in the field of cardiovascular pathophysiology.[9]

In patients with acute myocardial infarction (AMI), exercise training has the beneficial effects on cardiovascular systems.[10] Cardiac effects include attenuation of post-infarction ventricular remodeling,[11,12] for which brain natriuretic peptide (BNP) is a useful biochemical marker.[13] Vascular effects include an increase in the density of skeletal-muscle capillaries[14] and improvement in endothelial-dependent vasodilation,[15,16] which are important determinants for exercise tolerance and symptoms.

In the present study, we hypothesized that exercise induces HGF production, mediating the beneficial effects of exercise training in patients with AMI. If so, HGF production may be associated with clinical parameters of cardiovascular function.

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Division of Cardiology, Department of Medicine, National Cardiovascular Center, Osaka, Japan

Mailing address: Satoshi Yasuda, MD, PhD, Division of Cardiology, Department of Medicine, National Cardiovascular Center, 5-7-1 Fujishiro-dai, Suita 565-8565, Japan. E-mail: syasuda@hsp.ncvc.go.jp

Methods

Study Patients

The study group included 20 male patients (aged 61± 12 years [mean±SD]) after AMI. The infarction site was anterior in 13 patients (65%), and inferior/lateral in 7 patients (35%). All patients underwent reperfusion therapy (percutaneous transluminal coronary angioplasty in 17 patients and intravenous administration of tissue-type plasminogen activator in 3 patients) on admission. The peak level of serum creatine kinase was 2,995±2,043 [mean± SD] U/L. The severity of heart failure ranged from New York Heart Association functional class I to II. The baseline patient characteristics are summarized in Table 1. No patients had liver (elevated levels of aminotransferases), kidney (elevated levels of creatinine or urea), or lung dysfunction (restrictive or obstructive pattern in spirometry). No patients had prior myocardial infarction. Medications remained unchanged during the entire study.

The study was approved by the institutional review committee. The protocol was fully explained, and all patients gave their written informed consent to participate in the study.

Table 1 Baseline Characteristics of Patients

NYHA, n (%)	
I	*12 (60)*
II	*8 (40)*
LVEF (%)	*43±9*
LVEDVI (ml/m²)	*70±11*
LVEDP (mmHg)	*13±6*
Coronary risk factors, n (%)	
Diabetes mellitus	*11 (55)*
Hyperlipidemia	*9 (45)*
Hypertension	*7 (35)*
Medications, n (%)	
ACE-inhibitor	*11 (55)*
Ca^{2+}-antagonist	*12 (60)*
Nitrates	*9 (45)*
Aspirin	*20 (100)*
Diuretics	*8 (40)*
Digoxin	*7 (35)*
β-blockers	*4 (20)*

NYHA, New York Heart Association classification; LVEF, left ventricular ejection fraction; LVEDVI, left ventricular end-diastolic volume index; LVEDP, left ventricular end-diastolic pressure; ACE, angiotensin-converting enzyme; Ca^{2+}, calcium.

Table 2 Changes in Hemodynamics and HGF Levels in Response to Supine Exercise

	Baseline	*Peak exercise*	*p value*
HR (beats/min)	*68±11*	*117±17*	*<0.001*
Aosyst (mmHg)	*126±17*	*169±20*	*<0.001*
PAsyst (mmHg)	*34±7*	*58±14*	*<0.001*
PAdiast (mmHg)	*11±4*	*19±5*	*<0.001*
CO (L/min)	*6.8±1.6*	*14.7±3.9*	*<0.001*
HGF_{PA} (ng/ml)	*7.72±3.50*	*7.82±3.53*	*NS*
HGF_{Ao} (ng/ml)	*7.45±3.32*	*7.14±3.14*	*NS*
ΔHGF(PA–Ao) (ng/ml)	*0.27±0.44*	*0.68±0.58*	*<0.01*
CO×ΔHGF (μg/min)	*1.6±3.0*	*9.0±6.3*	*<0.001*
$S\dot{V}O_2$ (%)	*67±4*	*34±10*	*<0.001*

HGF, hepatocyte growth factor; HR, heart rate; Ao, aorta; PA, pulmonary artery; syst, systolic pressure; diast, diastolic pressure; CO, cardiac output (by the thermodilutional method); ΔHGF (PA–Ao), the difference in HGF levels between pulmonary artery and aorta; $S\dot{V}O_2$, mixed venous O_2 saturation.
p values were assessed with the paired student t-test.

Cardiac Catheterization and Supine Exercise Test

From the right brachial artery through a 6F sheath, chronic phase coronary angiography and left ventriculography were performed according to the conventional Judkins technique, 28±7 [mean±SD] days after the onset of myocardial infarction[17] Heparin was initially administered at a dose of 5,000 IU into the distal brachial artery. For angiographic evaluation of left ventricular volumes, ventricular silhouettes in 30° right anterior oblique projections were digitized with an ANCHOR ventriculography analysis system (Siemens-Elema, Solna, Sweden). By the area-length method, the left ventricular end-systolic and end-diastolic volume indices and ejection fraction were calculated. Left ventricular pressure was measured with a 2F high-fidelity micromanometer catheter (model SPC-320; Miller Instruments, Houston, TX, USA) advanced into the left ventricle via the lumen of a 6F pig tail catheter.

A 7.5 F Swan-Ganz thermodilution catheter (Opticath®; Abbott Laboratories, North Chicago, IL, USA) was inserted through the left subclavian vein, to measure cardiac output (CO) and pulmonary artery (PA) pressure.

After sampling blood and measuring hemodynamic parameters at baseline, the supine bicycle exercise test was performed by using a Siemens Ergometry System 930B, and the mixed venous O_2 saturation ($S\dot{V}O_2$), and pressure of the PA and aorta (Ao) were monitored. We also monitored arterial blood O_2 saturation continuously using a Biox III pulse oximeter (Omeda, Louisville, KY, USA). The workload was increased at 3-min intervals in 30-W increments followed by a 0-W bicycling period for 1 min. The exercise was finished at 30 W in 2 patients, 60 W in 8 patients and 90 W in 10 patients. This final workload was the submaximal level for each patient, because the peak heart rate was approximately 80% of the maximal heart rate achieved at the symptom-limited cardiopulmonary exercise test, as described below. Before and immediately after the supine exercise test, blood samples were taken from the PA and the Ao. The samples were centrifuged at 4°C and stored at –80°C until assayed.

Cardiopulmonary Exercise Test

On a separate day (3±1 [mean±SD] days before the cardiac catheterization), patients underwent the symptom-limited cardiopulmonary exercise test (CPX), with determination of peak oxygen uptake ($\dot{V}O_2$), workload and heart rate. The exercise test was performed on a calibrated, electronically braked bicycle in an upright position (Examiner, Lode B.V., Groningen, Netherlands). Ramp protocols began at a workload of 0 W for 1 min and increased in 15-W increments at 1-min intervals. Expired gas analysis was performed by using a respiromonitor AE-280 (Minato Products, Tokyo, Japan). The $\dot{V}O_2$ was measured on a breath-by-breath basis, and was averaged over contiguous 30-s intervals, except at peak exercise, when 18-s averaging was used.

Hepatocyte Growth Factor Measurements

Hepatocyte growth factor levels in the pulmonary artery (HGF_{PA}) and aorta (HGF_{Ao}) were determined with specific enzyme-linked immunosorbent assay kits (Otsuka Assay Laboratories, Tokushima, Japan). Microtiter plates coated with an anti-HGF murine monoclonal antibody were incubated with standard HGF or serum samples, and an anti-HGF rabbit polyclonal antibody was added. After adding first the anti-rabbit goat immunoglobulin G-peroxidase conjugate and then o-phenylene diamine, the absorbance was read at 492 nm using a plate reader[18] The sensitivity of the HGF kit was 0.1 ng/ml. This assay system detects only bioactive, heterodimeric (mature) forms of HGF in the blood samples[18,19] Previous studies have demonstrated that there is a strong (r=0.986) positive correlation between HGF levels measured by this assay system and those measured by bioassay (determined by stimulating DNA synthesis of rat hepatocytes in primary cultures)[18,19]

The BNP levels were determined with a specific immunoradiometirc assay kit (Shionogi Co, Osaka, Japan), as previously reported[17] The sensitivity of this BNP kit is 2 pg/ml. Brain natriuretic peptide has been considered as a biochemical marker of ventricular remodeling after myocardial infarction.

Data Analysis

Exercise-induced HGF production (μg/min) was calculated by using the following equation:

$[(HGF_{PA}-HGF_{Ao})\times CO$ at peak exercise$]-[(HGF_{PA}-HGF_{Ao})\times CO$ at rest$]$.

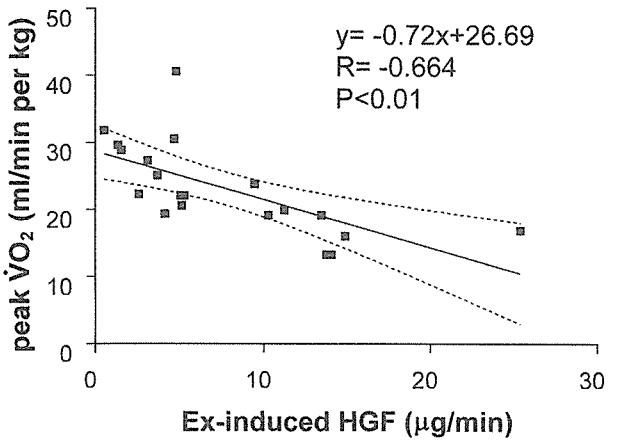

Fig 1. Correlation of the exercise (Ex)-induced hepatocyte growth factor (HGF) production with peak oxygen uptake (peak $\dot{V}O_2$) in 20 patients after acute myocardial infarction (AMI).

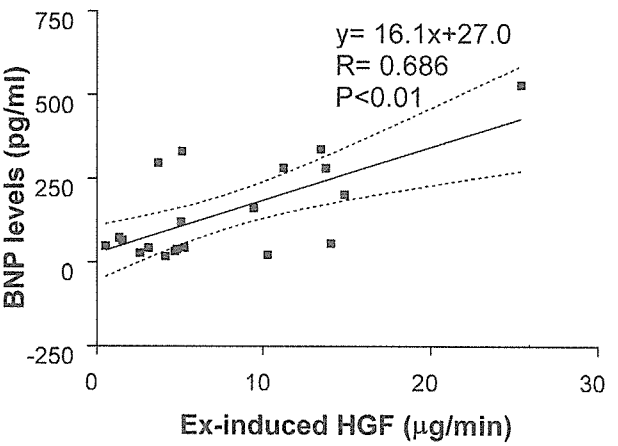

Fig 2. Correlation of the exercise Ex-induced HGF production with brain natriuretic peptide (BNP) levels.

The χ^2 test was used for comparison of categorized variables. The Student's t-test or Mann-Whitney U-test rank test was used for comparisons of mean values to determine significance of difference between the 2 groups. Linear regression curves and correlations were calculated according to the least squares method. All data are presented as mean±SD. Differences were considered significant at $p<0.05$.

Results

Changes in Hemodynamics and HGF in Response to Supine Exercise

Table 2 shows the changes in hemodynamics and HGF levels, at baseline (=before exercise) and at peak exercise during the catheterization. At baseline, there were no significant differences in HGF levels between PA and Ao. The supine exercise (74±18 W in intensity, 10±2 min in duration) significantly increased heart rate, Ao pressure, PA pressure, and CO, whereas it decreased $S\dot{V}O_2$. Although the absolute HGF levels in PA and Ao appear unchanged, the difference in HGF levels between PA and Ao (ΔHGF) significantly increased by approximately 3-fold after the exercise. When assessed based on the fold change compared with the baseline level, exercise increased the HGF_{PA} to 1.02±0.11-fold ($p<0.05$), but did not change HGF_{Ao} (0.96±0.09-fold). Finally, in the patients of the present study, exercise-induced HGF production ([ΔHGF×CO at peak exercise]−[ΔHGF×CO at baseline]) was calculated to be 7.4±6.3 μg/min, on average.

Correlations With HGF Production

Peak $\dot{V}O_2$, workload and heart rate determined during the symptom-limited upright cardiopulmonary exercise text (CPX) performed on a separate day were 23±7 ml/min per kg, 130±37 W, and 140±24 beats/min, respectively.

As shown in Fig 1, exercise-induced HGF production correlated inversely with peak $\dot{V}O_2$ ($r=-0.664$, $p<0.01$). Eight patients with peak $\dot{V}O_2<20$ ml/min per kg had greater exercise-induced HGF production (13.4±5.9 vs 3.9±2.4 μg/min, $p<0.05$) and higher prevalence of angiographically significant stenosis in major coronary arteries (>60%) (50 vs 8%, $p<0.05$) in comparison with the remaining 12 patients with $\dot{V}O_2\geq20$ ml/min per kg.

Also, as shown in Fig 2, exercise-induced HGF production correlated positively with BNP levels at baseline ($r=0.686$, $p<0.01$). However, there were no significant relations with cardiac function at rest (left ventricular end-diastolic volume index and ejection fraction), percentage increase in heart rate, Ao pressure and PA pressure in response to the submaximal supine exercise (data not shown).

Discussion

The major finding of the present study is that HGF production is induced during exercise in accordance with the severity of exercise intolerance and the increase in BNP levels.

In patients after AMI, exercise training is now emerging as an important component of the therapy[10,20] It attenuates post-infarction ventricular remodeling, which is associated with heart failure and increased mortality,[21] and is accompanied by an elevated level of BNP.[13] Regular exercise training also increases the density of skeletal muscle capillaries[14] and induces repetitive increases in vascular blood flow and shear stress,[22] thereby improving endothelium-dependent vasodilation.[15,16] Both central (cardiac) and peripheral (skeletal muscle and vascular) effects of exercise training may consequently improve exercise tolerance and symptoms.[10] From the data obtained in the present study, a causal relationship cannot be clearly determined. However, the several effects of exercise training are potentially mediated through HGF in patients after AMI.

As shown in Table 2, exercise increases the concentration gradients of HGF levels between PA and Ao, indicating exercise-induced HGF production. The vessel wall may be a potential source of circulatory HGF.[23] Fig 1 shows that exercise-induced HGF production is associated with reduced peak $\dot{V}O_2$. In particular, patients with peak $\dot{V}O_2<20$ ml/min per kg were sensitive towards the HGF response to exercise. These patients with reduced exercise capacity had a higher prevalence of coronary artery stenosis. Myocardial ischemia appears to be one of the determinants for exercise capacity and is known to induce upregulation of non-cardiac HGF systems.[24] HGF promotes angiogenesis as a potent growth factor of endothelial cells[25] and promotes the functional recovery of nitric-oxide-mediated vasodila-

tion;[26] thus improving myocardial blood flow. Also, as shown in Fig 2, exercise-induced HGF production is associated with increased levels of BNP. The HGF may be systemically released during exercise in response to left ventricular dysfunction and may exert wound healing and cardioprotective actions against myocardial ischemia/infarction.[27,28] In a mouse myocardial infarction model, HGF gene therapy attenuated left ventricular remodeling and dysfunction.[28]

The recent clinical studies also suggest a possibility that HGF may contribute to improving myocardial ischemia and dysfunction. In the CAPTURE (c7E3 Anti-Platelet Therapy in Unstable REfractory angina) trial studying the patients with acute coronary syndromes, elevated HGF levels are associated with reduced incidence of death and myocardial infarction.[29] In another study in patients with coronary artery disease, elevated coronary sinus HGF levels were associated with collateral formation and with left ventricular dysfunction.[30] Thus, interventions that enhance HGF levels could be beneficial in the management of those patients. Exercise is a potential approach. However, further studies are required to determine whether short-term benefits of exercise could translate into long-term effects.[20]

In conclusion, the present study provides a novel aspect of exercise training as cytokine-mobilization. HGF may have a therapeutic implication in patients after AMI.

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【厚生労働科学研究】
院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床試験（J-PULSE）ホームページ
URL：http://j-pulse.umin.jp/

☆トップページ

☆ キャンペーンの活動と目的

J-PULSE 【厚生労働科学研究】院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床試験

キャンペーンの活動と目的
主任研究者からのメッセージ
(国立循環器病センター　野々木　宏)
J-PULSEの目的と
これまでの成果
心臓マッサージと
AEDを用いた心肺蘇生法(ビデオ画像)
講習会、講演についてのお知らせ
心肺蘇生法講習会 実施医体 公開講座の紹介など
資料
(J-PULSEニュースレター、AEDパンフレット等)
HOMEへ

「あなたの勇気がいのちを救う」
心臓マッサージとAEDでつなぐ命の輪キャンペーン

活動の目的

目の前で突然倒れ、亡くなられる方の大半は心臓病が原因です。
その多くは、病院外で発生しており、その場に居合わせた方がすばやく心肺蘇生法を開始し、AED(自動体外式除細動器)を使用して応急処置を行うことで、助かるチャンスが生まれます。
今回のキャンペーン活動を通じ、1人でも多くの方に心肺蘇生法やAED(自動体外式除細動器)の使いを知って頂き、救命処置に参加していただきたいと思っています。

活動の概略

このキャンペーンは、2006年8月から行います。キャンペーンを通じて一般市民の方の救命意識がどの程度向上したか評価するために、キャンペーン期間の前後にアンケート調査を行います。
キャンペーン期間中、読売テレビにてテレビCM(放送予定はこちら)を放映します。また、心肺蘇生法やAEDの使い方解説ビデオを作成し、ホームページ上で自由に閲覧していただけるようにしました。また、心肺蘇生法の中でもっとも重要である胸骨圧迫心臓マッサージとAEDの使用方法を習得していただくための講習会の開催も予定しています。

キャンペーン前
アンケート実施

テレビCM・ホームページでの
情報提供

キャンペーン後
アンケート実施

キャンペーン実施期間

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☆ 主任研究者からのメッセージ

J-PULSE 【厚生労働科学研究】院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床試験

厚生労働科学研究 院外心停止対策研究班 (J-PULSE)
apanese opulation-based tstein-style study with basic and advanced ife upport ducation

私たちの目指すところ

主任研究者 野々木 宏

心臓発作の現状を理解しましょう

心臓発作(急性心筋梗塞が代表的)は、専門病院へ入院すると治療方法の進歩により治療成績は良好で、最近では死亡する率は5%以下となってまいりました。
ところが、心筋梗塞の死亡率の全体は30%近くあり、その半数以上は院外での死亡です。
すなわち病院へ到着するまでに死亡しています。大多数は発病から1時間以内に突然亡くなっています。
多くは心停止時に心室細動が生じていると考えられます。

救命には傍にいる方の助けが必要です

院外で突然心停止になったときには、救命の連鎖と呼ばれる一連の行為が時間の遅れなく実行される必要があります。救命の連鎖には、迅速な通報、心肺蘇生法の迅速な開始、迅速な電気的除細動の適用、迅速な専門的な治療の4つからなります。
特に前半の3つは一次救命処置と呼ばれ、一般の方から医療従事者まで誰でも実施可能です。心室細動の唯一の救命方法は電気的除細動であり、救命率をあげるためには、発見すれば早期に通報し心肺蘇生法を実施しながら電気的除細動器の到着を待つ必要があります。
院外では心停止から5分以内、院内では3分以内の除細動の適用が推奨されています。それには医療従事者(院内では医師、院外では救急救命士)による通常の手動式電気的除細動器の適用では達成ができません。
傍に居る人が、設置された自動体外式除細動器(AED)を使用することで達成ができることです。

AEDは誰でも使用が可能となりました

2004年に厚生労働省は、非医療従事者による自動体外式除細動器(AED)使用を認可しました。
そのため国立循環器病センターは、率先してその普及にあたり、適切な場所への設置、講習会を実施し救命の連鎖を確立することが使命であり、厚生労働科学研究費により、AEDの普及とその効果の検証をテーマとして班研究(主任研究者:野々木 宏)が開始され、普及対策とその効果の検証を国際標準とされるウツタイン登録を使用して行うことになりました。
院内心停止例への対応とともに広くその普及をアピールすることが目的です。

AEDの診療の中での位置づけ

AEDは非医療従事者を含め誰でも即時に使用が可能であることから、院外、院内を問わず使用が可能です。
音声ガイドに従えば簡単に操作ができますので、講習を受けることは必修ではありません。ただ、一度でも講習を受け、操作方法や心肺蘇生法を学んでおければ安心して自信を持って応急処置が可能と思います。
多くの方が講習会を受けられ、心肺蘇生法とAEDの扱い方に慣れていただき、一人でも多くのかたを救命可能となることを望んでやみません。

☆ J-PULSE の目的とこれまでの成果

J-PULSE 【厚生労働科学研究】院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床試験

キャンペーンの活動と目的

主任研究者からのメッセージ
(国立循環器病センター　野々木　宏)

[illegible]
これまでの成果

心臓マッサージと
AEDを用いた心肺蘇生法(ビデオ画像)

講習会、講演についてのお知らせ
心肺蘇生法講習会 実施施設 公開講座の紹介など

資料
(J-PULSEニュースレター、AEDパンフレット等)

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J-PULSEの目的とこれまでの成果

J-PULSEとは？

『院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床研究』を行う厚生労働科学研究班です。
Japanese Population-based Utstein-style study with basic and advanced Life Support Educationの頭文字をとって研究班の名称としています。

J-PULSEの目的

1. 病院の外で起こっている心臓突然死の実態調査を行い、病院外救急医療を客観的に評価することができるシステムを構築すること。
2. 心肺蘇生とAEDの普及とその効果を客観的に評価し、病院外で突然心停止となった方の救命率を向上させること。

J-PULSE　研究課題

1. AED普及とその効果に関する研究：ウツタイン様式を用いた解析(J-PULSE1)
2. 難治性心室細動に対する抗不整脈薬の効果に関する研究(J-PULSE2)
3. 循環器救急医療におけるモバイルテレメディシンの普及とその効果に関する研究(J-PULSE3)
4. 心肺蘇生法普及における教育方法に関する研究(J-PULSE4)
5. 大血管疾患の疫学と救急システム構築に関する研究(J-PULSE5)

J-PULSE　これまでの成果

- 国際基準にのっとった病院外心停止例の登録・データ解析システムの構築
- 病院外心停止症例(約30,000例)に関する基礎データの解析
- 胸骨圧迫心臓マッサージのみの心肺蘇生法の効果の検証
- 市民の自動体外式除細動器(AED)・救命の連鎖に関する認知を高めるためのキャンペーンの効果の検証
- 病院内心停止登録方法の確立とIT化
- 市民の蘇生参加の障害の検証
- 胸骨圧迫心臓マッサージのみに単純化した心肺蘇生法教育の開発と検証

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☆ 心臓マッサージと AED を用いた心肺蘇生法（ビデオ画像）

J-PULSE 【厚生労働科学研究】院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床試験

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資料
（J-PULSEニュースレター、AEDパンフレット等）

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心臓マッサージとAEDを用いた心肺蘇生法

もし目の前で人が倒れたとき、何をしたらいいのでしょうか？
とっさに何ができますか？
ここでは、そんな疑問にお答えするための、皆さんに行っていただきたい救命処置の解説ビデオをお見せします。

ここで紹介するのは胸骨圧迫心臓マッサージのみを続けて行い、AEDが到着次第AEDを用いて除細動（電気ショック）を行うというものです。

J-PULSE研究班では、一般市民の方が救急隊到着までの間に行う心肺蘇生は胸骨圧迫心臓マッサージだけでも従来の人工呼吸付の心肺蘇生と同等の効果があることを明らかにしました。心臓マッサージのみの単純な心肺蘇生法を普及させることで、心停止となった方の多くが救命処置を受け、救われることを願っています。

みなさん目の前で倒れている人がいたら勇気を持って手を差し伸べて下さい。

＊従来どおり、人工呼吸を行うことができる方は行っていただいても構いません。

解説ビデオ　本映像の編集および加工は禁止致します

ストリーミング再生（WMP、7分、単位:bps）

300k
20MB

【映像ファイルのダウンロード・閲覧手順】
映像再生ボタンを右クリックし、「対象をファイルに保存」機能を使用して、映像をダウンロード保存していただくことも可能です。
ダウンロードしたファイルをダブルクリックするとプレイヤーが立ち上がり映像がスタートします。

※お使いの回線によっては、ダウンロードに時間がかかる場合がございます。ご了承ください。

Windows Media Player
動画の再生には、プレーヤーソフトウエアのWindows Media Player(無料)、が必要となります。
左の画像をクリックし、手順に従ってインストールしてください。

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☆ 講習会、講演についてのお知らせ

心肺蘇生法講習会 実施団体 公開講座の紹介など

J-PULSE 【厚生労働科学研究】院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床試験

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資料
(J-PULSEニュースレター、AEDパンフレット等)

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講習会、講演についてのお知らせ

1. Berg教授講演会 ※終了しました

『心肺蘇生法の新しい潮流:最新のトピックスから』

ROBERT A. BERG, M.D.
(Associate Dean for Clinical Affairs The University of Arizona, College of Medicine)

院外心停止例の心脳蘇生に対して、胸骨圧迫のみの新しい蘇生法を提唱しておられます。
大阪ウツタイン登録に対しても大きな関心を寄せられ、多くのご指導をいただいている方です。
心肺蘇生法に関する最新の情報について解説をいただけます。
同時通訳がありますので、心肺蘇生法にご興味のある方は、皆様お誘いあわせの上、是非ご参加下さいますようお願い申し上げます。
※ 同時通訳、軽食の準備のため参加のお申込を頂けますようお願い致します。
ポスターはこちら

日 時	2006年12月14日(木) 18時~20時 ※同時通訳あり
場 所	千里ライフサイエンスビル 5階 ライフホール 地下鉄御堂筋線 千里中央駅 徒歩5分 大阪府豊中市新千里東町1丁目4番2号 TEL:06-6873-2000
対 象	医師、看護師、救命士 など
参加要領	下記内容を記載の上、事務局までメールでお申込下さい。 1. 参加人数、2. 参加者名(代表者)、3. 所属、4. 職業 J-PULSE事務局(Berg教授講演会) ※終了しました

2. 市民公開講座 ※終了しました

『あなたの勇気が命を救う 心臓突然死の実態とその対策』

家庭や学校、職場、路上など病院の外で起こる突然の心停止(院外心停止)の状況と院外心停止に対する活動についてわかりやすく説明するとともに、一般市民の方も使用できる自動体外式除細動器(AED)について解説いたします。
★ AEDと簡単な心肺蘇生法体験コーナーもあります。
ポスターはこちら

日 時	2007年1月14日(日)14時~16時
場 所	千里朝日阪急ビル 4階 A&Hホール 大阪モノレール 千里中央駅 徒歩5分 大阪府豊中市新千里東町1丁目5番3号 TEL:06-6873-2608
座 長	野々木 宏 (国立循環器病センター 心臓血管内科・緊急部)
	『高槻における救命対策について:高槻キャンペーン』 森田 大 先生(大阪府三島救命救急センター 所長)
	『大阪府におけるウツタイン登録の状況について』

☆ 資料（J-PULSE ニュースレター、AED パンフレット等）

J-PULSE 【厚生労働科学研究】院外心停止者の救命率向上に対する自動体外式除細動器を用いた心肺蘇生法の普及とエビデンス確立のためのウツタイン様式を用いた大規模臨床試験

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心肺蘇生法講習会 実施医体 公開講座の紹介など

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J-PULSEの作成した資料・教材

▶ 映像ダウンロード ▶ AEDマップ ▶ AEDの使い方パンフレット ▶ ニュースレター

映像ダウンロード

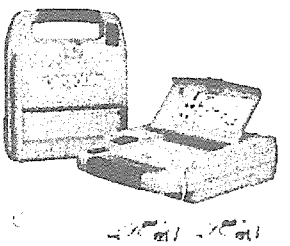
ダウンロードはこちらから 「心臓マッサージとAEDを用いた心肺蘇生法」
20MB(WMP、7分)

AEDマップ

AED(自動体外式除細動器)設置施設一覧
[J-PULSE 分担研究者] 大阪府済生会千里病院千里救命救急センター　向仲　真蔵先生

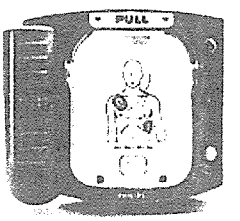
AEDの使い方パンフレット

日本光電



日本光電へはこちらから
パンフレット(PDF:957KB)

フィリップス社



フィリップス社へはこちらから
パンフレット(PDF:931KB)

メドトロニック社 CR Plus

メドトロニック社へはこちらから
パンフレット(PDF:939KB)

パンフレットは2枚綴りになります。両面印刷し、二つ折りにして御覧下さい。
パンフレットの送付を希望される方は、こちらから申し込み用紙(MS Word形式)をダウンロードし、FAXにてお申込下さい。

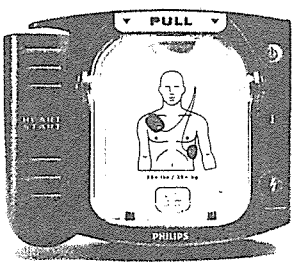
J-PULSEニュースレター

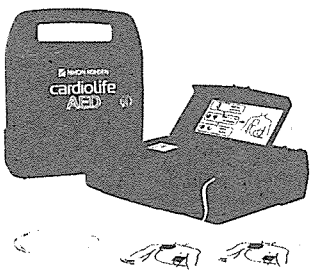
2005/06/29 vol.1(PDF:57KB)
2005/11/28 vol.2(PDF:198KB)
2006/03/23 vol.3(PDF:356KB)
2006/07/12 vol.4(PDF:109KB)

Get Reader PDFファイルを閲覧・プリントアウトするためには、Adobe(R) Adobe(R) Reader(無料)が必要です。

あなたの勇気がいのちを救う

AED

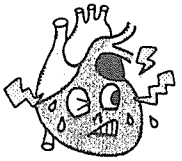




心臓マッサージとAEDを知ろう！

目の前で人が倒れたら、あなたなら何をしますか？

その人を助けるのは、あなたの勇気です

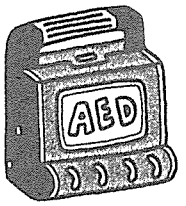


「心臓突然死って何？」

心臓病による死亡の多くは、病院の外で突然おこります。その方を救うためには、そばに居合わせた方の協力が不可欠なのです。

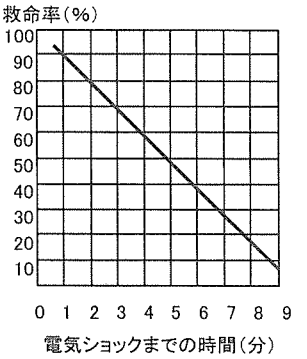
「何をしたらいい？」

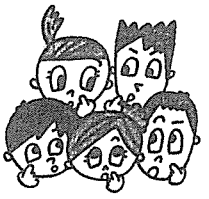
目の前で人が倒れたら勇気を出して、声を掛けて下さい。もし意識がなければ、近くの人に119番通報とAEDを持ってくるように頼みます。正常な息がなければ心臓が止まっているので直ちに心臓マッサージを始めて下さい。そしてAEDが到着次第、使って下さい。



「AEDって何？」

心臓突然死の多くは「心室細動」という心臓病が原因です。これを治すために心臓に電気ショックを与える器械のことをAED（自動体外式除細動器）と言います。AEDは，自動的に電気ショックが必要であるか否かを判断してくれます。電気ショックが1分遅れると救命率が10%低下すると言われており（右図）、少しでも早くAEDを使用する必要があります。





「AEDって誰が使うの？」

それはあなたかもしれません。早く電気ショックを行うために、突然倒れた方のそばにいる人が使用する必要があります。

「心臓マッサージとAED」

AEDの効果を十分に発揮するために、AEDをつけるまでの間、必ず心臓マッサージも行って下さい。