特 集 (special edition)

Changes in Myocardial Ischemic Areas by Anesthesia

——Thermographic Determination——

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Abstract

We developed a computerized experimental system that can observe the size of ischemic area of a beating heart using thermography. The ischemic area defined by this system is named TDMIA; Thermographically Determined Myocardial Ischemic Area. This system includes monitoring and filing of heart rate, arterial, pulmonary arterial, and central venous pressures, cardiac output, myocardial pH, end-tidal CO_2, anesthetic gas concentrations and temperatures. In the first experiment, we compared the effects of enflurane and isoflurane on TDMIA in swine utilizing this system. When the anesthetic concentration was changed from 1 MAC to 0.5 MAC, TDMIA decreased significantly together with increases in cardiac output and blood pressure. TDMIA also increased when the anesthetic concentration of either isoflurane or enflurane was increased. We found no significant differences in TDMIA changes between enflurane and isoflurane anesthesia. In conclusion, we advance the theory that isoflurane might have a coronary steal effect and that it might not be different from enflurane. In the second experiment, the possible beneficial effect of nitroglycerin to ischemic areas in the canine model was evaluated with and without dopamine infusions. Nitroglycerin alone (0.5 μg/kg/min and 1 μg/kg/min) had no effect on TDMIA compared to control dogs. Nitroglycerin at 1 μg/kg/min with dopamine (7.5 μg/kg/min) significantly decreased TDMIA. We speculated that the dilating effect of nitroglycerin on the coronary arteries interacted with the positive inotropic effect of dopamine in this experimental method. We conclude that nitroglycerin combined with dopamine would have benificial effects on myocardial ischemic areas in the early phase of acute myocardial infarction in the canine model.

Introduction

The control of coronary circulation is important and indeed mandatory during anesthesia because of the increase in the population of geriatric patients and the increasing range of surgical indications. There are many debates on the selection of the most appropriate anesthesia for those patients who have or might have ischemic heart disease. Controversial points include the choice of anesthetics, effects

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of thoracic epidural anesthesia, how to use coronary dilators during anesthesia, and how to detect ischemic changes during anesthesia and surgery. The ideal answer to these problems, is a method for direct observation of the coronary blood flow and distribution in beating hearts. We have developed a computerized thermographic imaging system which is capable of defining ischemic areas as cold spots on beating hearts (Fig. 1). We used very high performance thermographic equipment. The thermal camera has the following features: the camera can take 30 thermograms in a second, so that, a very clear image can be made while the heart is beating; the smallest thermal resolution is 0.01°C; and the system produces an averaging thermogram from 256 images. We defined the myocardial ischemic area as the cold spot that can be thermographically identified, and named it the TDMIA (thermographically determined myocardial ischemic area). In 1971 Senyk et al. reported cardiothermography as a new method for detecting ischemic areas[1]. After this report some investigators reported that thermographic imaging of ischemic hearts could reliably identify ischemic areas. However, they were uncapable of observing ischemic areas in real time and continuously, because of the primitive nature of their thermographic cameras.

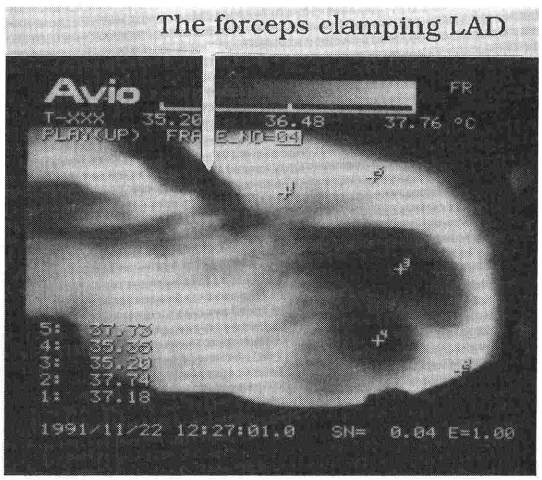

Fig. 1 A typical thermogram of the ischemic change induced by LAD occlusion. Black represents colder temperature. White arrow shows clamping forceps. LAD: left anterior descending coronary artery

Materials and Methods

The study protocol was approved by the Hokkaido University School of Medicine Animal Care and Use Committee. Mongrel dogs and swine were anesthetized with thiamylal 25 mg/kg IV and ventilated using 50% O_2 and 50% N_2 mixture with 1 MAC of either isoflurane or enflurane for the preparation of experiments. Vecuronium was used for muscle relaxation. End-tidal CO_2 was maintained between 35 to 40 mmHg. Lactate Ringer's solution was administered at a rate of 10 ml/kg/hr intravenously during the experiment. A left thoracotomy (dogs) or a stenotomy (swine) was performed and the left anterior descending coronary artery (LAD) was dissected from the surrounding tissue. An electromagnetic flowmeter probe was placed around the ascending aorta to measure cardiac output (MFV-3200, Nihon-Kohden, Japan). Arterial pressure, heart rate, esophageal and arterial blood temperatures (Bio View 2F37A, Nihondenki-Sanei, Japan), and end-tidal CO_2 and isoflurane or enflurane concentrations (RGM, Ohmeda, USA) were continuously monitored. A high performance thermographic camera (TVS-2000ME, Avionics, Japan) was used to measure the surface temperatures of beating hearts. All of these data were collected and filed to an engineering work station (HP340C, Hewlett-Packard, USA) (Fig. 2). All animals received 5 min LAD occlusions by a clamp several times after hemodynamic stabilization, and all LAD occlusions were separated by at least 20 min resting time.

〈Experiment 1〉

Six swine were divided into two groups and

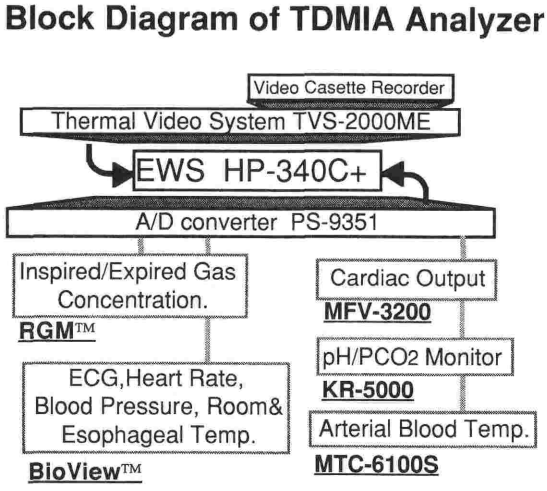

Fig. 2 A block diagram of the TDMIA analyzing system.
EWS: engineering work station

all swine received five min LAD clamping five times. Three swine were anesthetized by isoflurane first, then anesthetized by enflurane. The other group was anesthetized by enflurane first, then by isoflurane. The first occlusion was a trial for setting the thermography, the second was for the baseline measurement of 1 MAC of either isoflurane or enflurane, the third was for 0.5 MAC anesthesia of the same agent as the second occlusion, the fourth was for 0.5 MAC of the other agent, and the fifth was for 1 MAC of the same agent as the fourth occlusion.

〈Experiment 2〉

Fifteen dogs were divided into three groups and all dogs received five min LAD clamping four times. Five dogs served as control (group A), five dogs received nitroglycerin infusion alone (group B) and the other five dogs received nitroglycerin with dopamine infusion (group C) during LAD occlusion which was started 10 min before clamping. The first occlusion was for setting the thermography, the second was for the baseline measurement, the third was for nitroglycerin at 0.5 μg/kg/min with or without dopamine at 5 μg/kg/min (groups B, C), and the

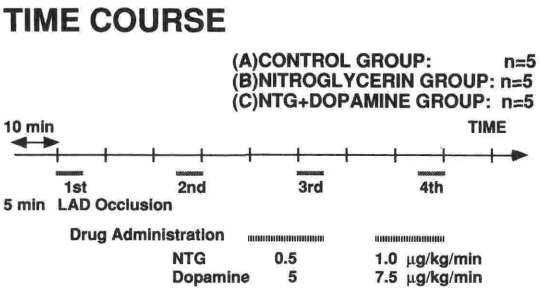

Fig. 3 A protocol of the experiment 2.

forth was for nitroglycerin at 1 μg/kg/min with or without dopamine at 7.5 μg/kg/min infusion (groups B, C). (Fig. 3)

In this study, we defined the TDMIA as the area in which pixels show temperatures of at least 0.5, 0.75, or 1.0°C less than those before the LAD clamping. The TDMIA at the second LAD occlusion served as the baseline value. The engineering work station analyzed the percentage change of the TDMIA every 12 sec. Each thermogram contained 256 frames. In this study, we averaged the %TDMIA for four min in five min LAD clamping, and each %TDMIA number consisted of data from 5120 frames.

Data were analyzed with the Stat View statistical analysis program, using two-way repeated measures analysis of variance and Student's *t* test. Differences were considered to be statistically significant if the P value was less than 0.05.

Results

〈Experiment 1〉

There were no significant differences in %TDMIA between enflurane and isoflurane anesthesia. (Fig. 4)

〈Experiment 2〉

In group A, the TDMIA changed to 111±16% (mean±SEM) (3rd occlusion) and 104±17% (4th occlusion). In group B, the TDMIA changed to 87±18% (3rd occlusion) and 106±17% (4th occlusion). In group C, the

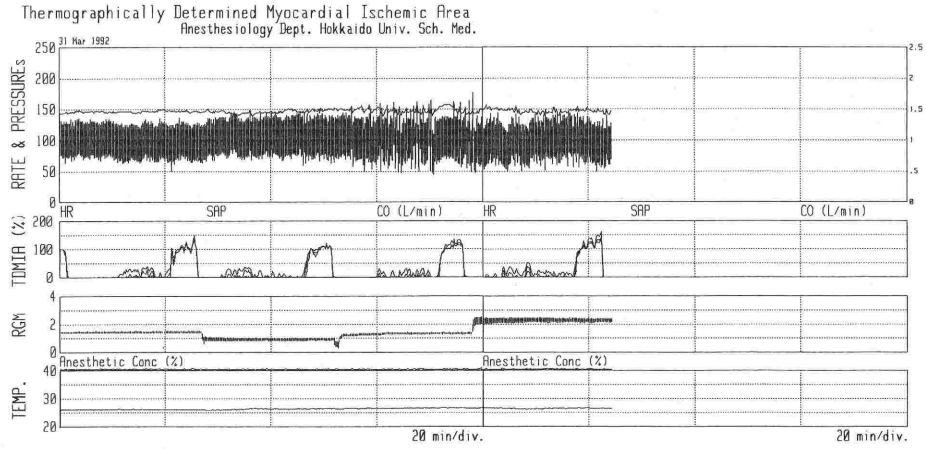

Fig. 4 A computer display of TDMIA analyzing system.
A typical result of experiment 1.
In the top window, there are trends of heart rates and blood pressures. In the next window, there is % change of TDMIA. In this experiment, the ischemic areas at the first LAD occlusion was defined 100% TDMIA.
In the next window, anesthetic gas concentrations were displayed. In this experiment, isoflurane 1 MAC, 0.5 MAC, enflurane 0.5 MAC, and 1 MAC were displayed in order. In the bottom window, esophageal and room temperatures were displayed.

TDMIA changed to 73±14% (3rd occlusion) and 54±10% (4th occlusion) that was significantly different compared to the baseline measurement and groups A and B (Fig. 5).

Systolic blood pressure increased by 24% (4th occlusion) in group C while it decreased 8% (4th occlusion) in group B. Diastolic pressure also increased by 12% (3rd occlusion) and 31% (4th occlusion) in group C. Heart rates did not change significantly in all groups. Cardiac output decreased by 6% (3rd occlusion) in group B. (Table 1)

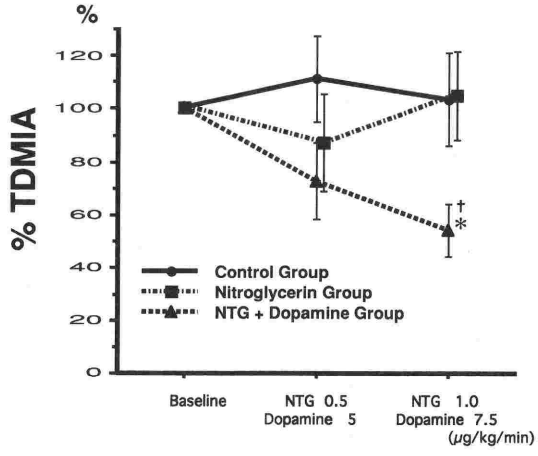

Fig. 5 TDMIA changes in the experiment 2
NTG: nitroglycerin, * $p<0.05$ Paried to Baseline, † $p<0.05$ Paired Control and Nitroglycerin Group

Discussion

In the early phase of an acute myocardial infarction (AMI), the size of ischemic areas may change depending on the collateral circulation. Simultaneous analysis of changes in ischemic areas and hemodynamic variables by the thermographic system was applied to an experimental AMI model. The surface temperature of a heart is thought to represent a combination of the blood temperature and the coronary blood flow. Unless that is an actual change in the blood temperature, it follows that the surface temperature represents the blood flow. This thermographic system can thus observe directly the size of an ischemic area in real time.

Table 1 Hemodynamic variables in the experiment 2

		Baseline	3rd Occlusion	4th Occlusion
Systolic BP				
mmHg	(A)Control	127(9)	129(10)	128(11)
	(B)Nitroglycerin	125(5)	118(5)	115(4)*
	(C)NTG+Dopamine	123(4)	134(9)	153(11)*
Diastolic BP				
mmHg	(A)Control	89(7)	90(8)	88(9)
	(B)Nitroglycerin	85(4)	84(5)	83(4)
	(C)NTG+Dopamine	83(5)	93(7)*	109(9)*
Heart Rate				
bpm	(A)Control	151(6)	153(5)	150(7)
	(B)Nitroglycerin	146(8)	141(8)	141(7)
	(C)NTG+Dopamine	146(12)	151(14)	148(11)
Cardiac Output				
L/min	(A)Control	1.64(.26)	1.62(.28)	1.83(.39)
	(B)Nitroglycerin	1.26(.18)	1.19(.17)*	1.14(.18)
	(C)NTG+Dopamine	1.35(.22)	1.40(.18)	1.39(.13)

mean(SEM) * $p<0.05$ Paired to Baseline

The ischemic area used to be measured pathologically and biochemically after autopsy, by coronary angiography or by nuclear medical technics in vivo. These methods could not measure changes of ischemic areas continuously in real time.

In 1983 Reiz et al. reported on the coronary steal phenomenon induced by isoflurane anesthesia[2]. After this report there were many debates on anesthesia for patients with ischemic heart disease. In 1987 Buffington et al. reported their results of experiments on coronary steal induced by isoflurane[3]. This report prompted some famous exchanges of correspondence in Anesthesiology in 1987[4-8]. Hatano et al. showed that isoflurane dilated small coronary arteries more than large coronary arteries compared to halothane in vitro[9]. This relation is same as that of adenosine and nitroglycerin[10]. Adenosine and isoflurane dilate small coronary arteries, so that in theory they can induce the coronary steal phenomenon.

In 1991 Slogoff et al. reported that there were no differences in the incidence of ECG-monitored ischemic changes between isoflurane, halothane, enflurane, and sufentanil anesthesia for coronary artery bypass graft surgery in 955 patients[11]. Leung et al. reported similar results in isoflurane and sufentanil anesthesia using transesophageal echocardiography and Holter ECG in 186 high risk patients[12].

In the present study, our results showed that there was no difference between the effect of isoflurane and enflurane anesthesia on the size of ischemic areas in the early phase of AMI. These fidings are consistent with the clinical reports of Slogoff et al. and Leung et al.

Dopamine is often used combined with nitroglycerin in early phase of AMI, because nitroglycerin alone sometimes produces further decreases in cardiac output and blood pressure. The use of nitroglycerin during surgery on patients with ischemic heart disease is still controversial. In this study, the benefit of nitroglycerin and dopamine infusions to myocardial ischemic areas was evaluated in the canine model.

Although nitroglycerin alone dilates the coronary arteries, it did not decrease the TDMIA significantly (Fig. 5). Our results indicated that combined infusion of nitroglycerin and dopami-

ne decreased the TDMIA. The hemodynamic effects of dopamine with nitroglycerin may increase coronary blood flow even in the ischemic area, through collateral vessels.

We conclude that dopamine combined with nitroglycerin may have beneficial effects on myocardial ischemic areas in the early phase of AMI. The prophylactic use of nitroglycerin may reduce the ischemic area if blood pressure and cardiac output are well maintained within a physiological range.

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