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Digital subtraction angiography: Image-sequence analysis for regional myocardial perfusion dynamics

Tohru TAKEDA
Mitsuo MATSUDA
Takao AKATSUKA*
Takeshi OGAWA
Masaaki KAKIHANA
Ryuichi AJISAKA
Takuji TOMIZAWA
Yasuro SUGISHITA
Iwao ITO
Masayoshi AKISADA

Summary

Digital subtraction angiography with selective coronary injections of contrast media has enabled us to obtain clear images, not only of the artery, but of the capillary and venous phases of the myocardial perfusion. In the present study, densitometry was used to estimate regional myocardial perfusion dynamics in 10 control cases and 11 anterior myocardial infarction cases. The time density curve showed that contrast material increased rapidly in the arterial phase and appeared to be washed out monoexponentially in the venous phase. The time from the onset of contrast medium injection to the maximal density of the contrast medium (Tp), and the time constant obtained from the washout curve (Tc) were analyzed.

In the control group, Tp in the apical region was slightly prolonged as compared with Tp in the anterobasal region, but the difference was not significant (5.2 ± 0.5 vs 4.2 ± 0.4 sec: mean$\pm$SEM). Tc did not definitely change in any portion of the myocardium (anterobasal 5.1 ± 0.5, anterior 4.8 ± 0.5, apex 4.6 ± 0.5 sec, respectively). In anterior myocardial infarction, Tp in the marginal region was significantly prolonged compared to Tp in the control region (6.0 ± 0.3 vs 4.7 ± 0.3 sec, $p<0.01$). Tp was prolonged for more than 10 sec in the infarcted region. Tc in the marginal region was markedly prolonged compared to Tc in the control region (7.4 ± 0.9 vs 4.4 ± 0.5 sec, $p<0.025$). Tc could not be determined in the infarcted regions because data acquisition time of our apparatus was inadequate.

Two indices of Tp and Tc obtained from the time density curve were regarded capable of estimating

Institute of Clinical Medicine, University of Tsukuba, Sakuramura, Ibaraki-ken 305
*Faculty of Engineering, Yamagata University, Yonezawa 992

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regional myocardial perfusion dynamics. Analysis of the DSA image sequence is regarded a very useful method for revealing regional myocardial perfusion dynamics as well as for providing morphological information about the coronary artery.

Key words

Digital subtraction angiography (DSA) Myocardial perfusion dynamics Myocardial infarction
Regional densitometry Arriving time of contrast material Washout time constant

Introduction

Digital subtraction angiography (DSA) has been used to estimate cardiac functions. There have been many attempts to analyze DSA images quantitively using a post-processing computer[1~4]. We have applied DSA to the analysis of regional myocardial perfusions[4~7], during which, we could obtain not only images of the coronary artery, but clear images in the capillary and the venous phases of perfusions after selective coronary arterial injections of contrast media. In myocardial infarction cases, lack of perfusion was demonstrated by lack of contrast material in the capillary phase, and prolonged enhancement of the myocardial wall was shown in the venous phase. Thus abnormal regional myocardial blood flow was presumed from analysis of the DSA images. In this study, regional myocardial perfusion dynamics were analyzed statistically using a regional time density curve obtained from densitometry of DSA images.

Methods

DSA examinations were performed for ischemic and control groups. The ischemic group consisted of 11 patients with old anterior myocardial infarction. The control group consisted of 10 subjects with normal coronary arteriography and normal left ventricular wall motion, but with a history of chest pain. A commercial DSA system (Digiformer-X, Toshiba) was used for these examinations and sequentially-subtracted images were obtained using a continuous mode. Four ml of 76% Urografin® were injected by hand into the left coronary artery. During coronary arteriography, the patient was placed in a 30 degree right anterior oblique position. In inspiration, breath was held for 20 sec. Right atrial pacing was used to maintain a regular heart rate. All examinations were performed after Nitorol® administration.

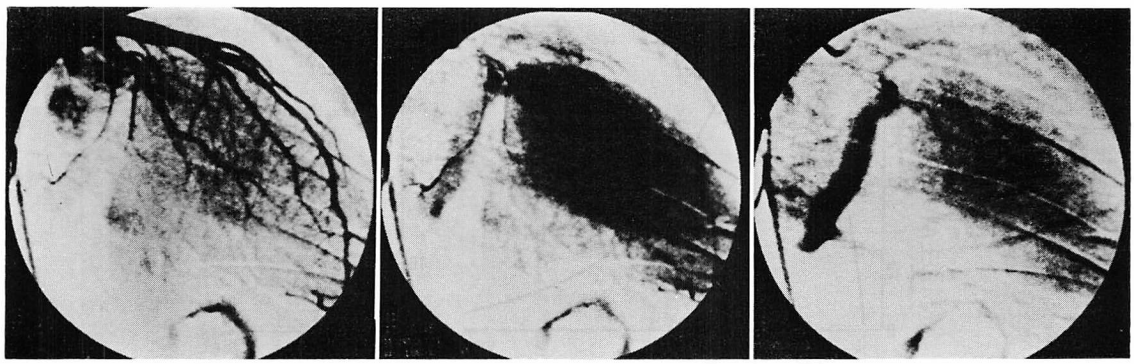
X-ray TV images were logarithmically amplified and digitized by a 10 bit A/D converter into a 512×512 pixel matrix with an 8 bit depth at standard TV rates (30 frames/s). Before any contrast material was injected, an average image during one sec (30 frames) was obtained and stored in the memory of the computer as a digital mask image. Immediately after the mask was stored, contrast material was injected. Successive frames of the TV image were subtracted from the mask image in real time, and these subtracted images were stored on an analog video disc recorder.

Typical subtracted images in the arterial, capilary and venous phases are shown in **Fig. 1.** Densitometry was performed at regions of interest (ROI), and a regional time-density curve was obtained. In the case of a normal coronary arteriogram, ROI was set at the anterobasal region, anterior region, and at the apex. In the case of anterior myocardial infarction, ROI was set at the non-infarcted region, infarcted region, and marginal region. The marginal region was set at the point where the peak density ranged between 40–70% of normal regions. The time density curves in each region were then analyzed using two parameters (Tp and Tc).

These parameters were analyzed by the paired t test, and by the chi-square test (statistical significance was assumed when $p<0.05$). All values were expressed as mean$\pm$standard error means (SEM).

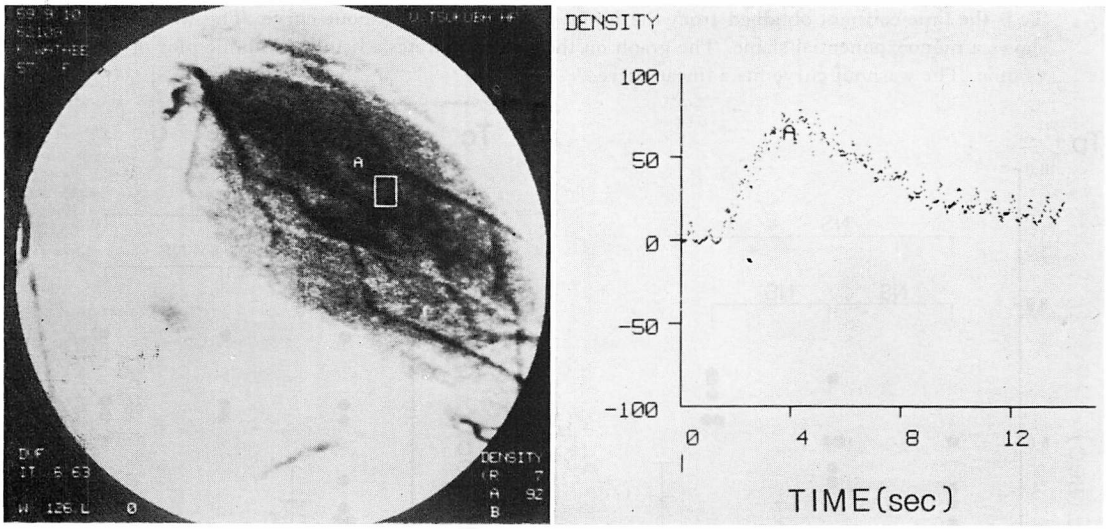
Results

Fig. 2 shows the regional time density curve at a ROI in a normal DSA image of an anterior



Arterial phase Capillary phase Venous phase

Fig. 1. Myocardial perfusion images in arterial, capillary and venous phases.



ROI Time density curve

Fig. 2. Regional area of interest for densitometry (ROI: left) **and its time density curve** (right).

wall. The time density curve of regional myocardial perfusion shows that the contrast material increases rapidly in the arterial phase and is washed out monoexponentially in the venous phase. In 10 normal cases, we ascertained the washout curve to be monoexponential in the venous phase using a chi-square test. We used two parameters (Tp and Tc) to evaluate the regional myocardial perfusion dynamics of normal and ischemic cases (**Fig. 3**). The arriving time Tp is defined as the time elapsed from the onset of contrast injection to the point at which maximal contrast density is achieved. Tc is defined as the time constant of the washout exponential curve as obtained in the venous phase.

In the control group, Tp in the apical region was slightly prolonged compared with Tp in the anterobasal region, but the difference was not significant (5.2 ± 0.5 sec vs. 4.2 ± 0.4 sec: mean $\pm$SEM) (**Fig. 4**). Tc does not change definitively at any portion of the myocardium (anterobasal 5.1 ± 0.5, anterior 4.8 ± 0.5, apex 4.6 ± 0.5 sec,

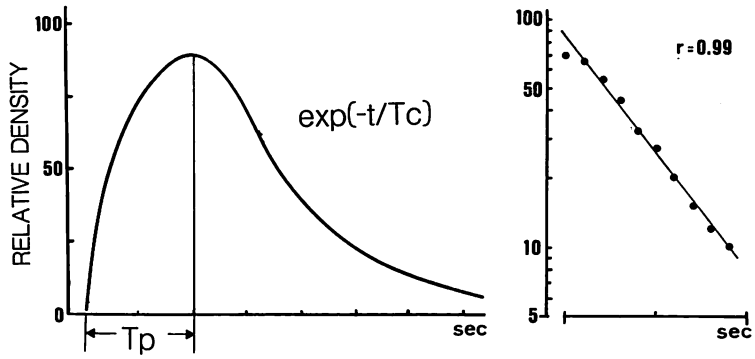


Fig. 3. The two indices, Tp and Tc, used to evaluate the regional myocardial perfusion dynamics.

Tp is the time from the onset of injection of contrast material to the peak density of the material. Tc is the time constant obtained from the initial portion of the washout curve. The washout curve shows a monoexponential shape. The graph on the right illustrates a hemilogarithmic plot of density vs time. The washout curve fits a linear curve.

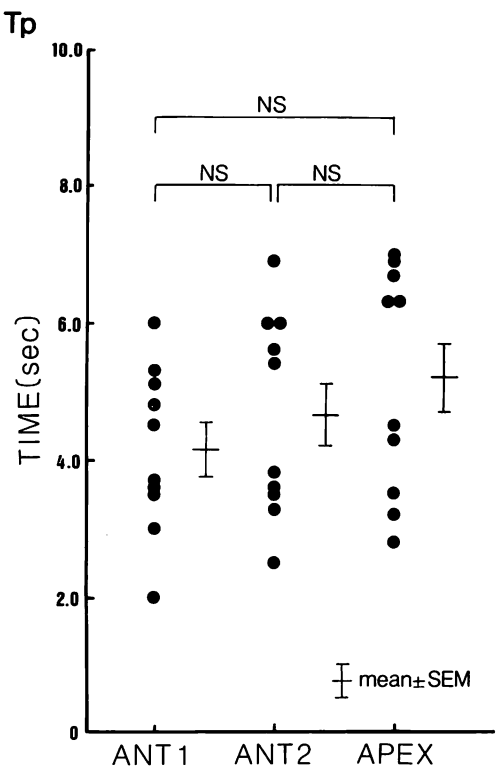


Fig. 4. Regional change in Tp.

Slight Tp prolongation at the apex in control patients is shown.

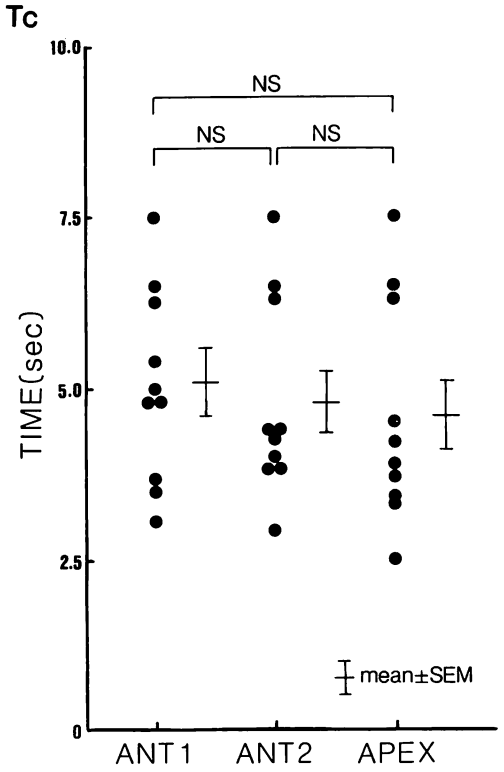


Fig. 5. Regional change in Tc.

There is no change in Tc in any portions of the myocardium in control patients.

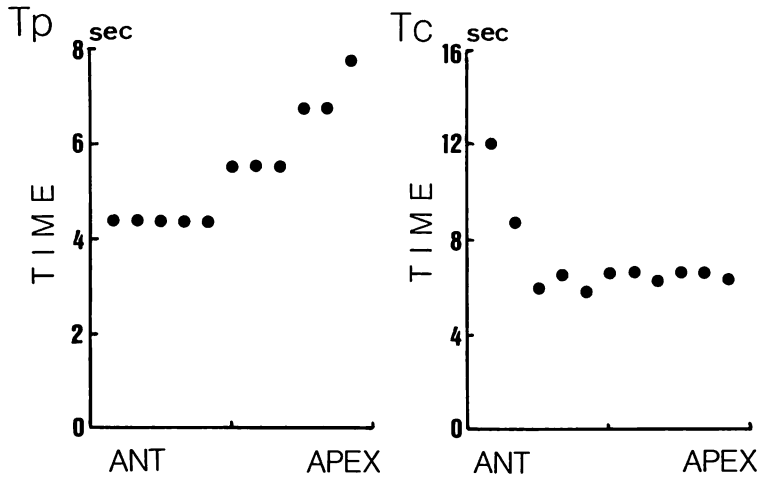


Fig. 6. Regional change of Tp and Tc in a control case.
Tp is prolonged towards the apex. However, Tc does not change significantly in any portions of the left ventricle except false prolongation of Tc in the anterobasal region which may be caused by superimposing contrast material on the right ventricle and the pulmonary artery.

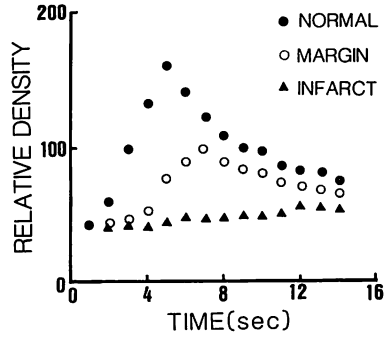


Fig. 7. The time density curve in a case of anterior myocardial infarction.

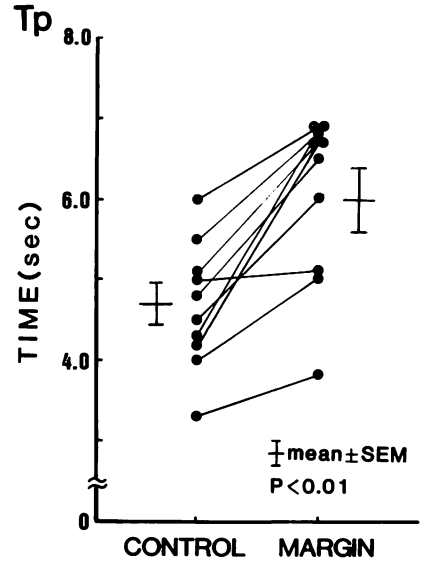


Fig. 8. Tp changes in the ischemic group.
Tp is definitively prolonged at the marginal regions.

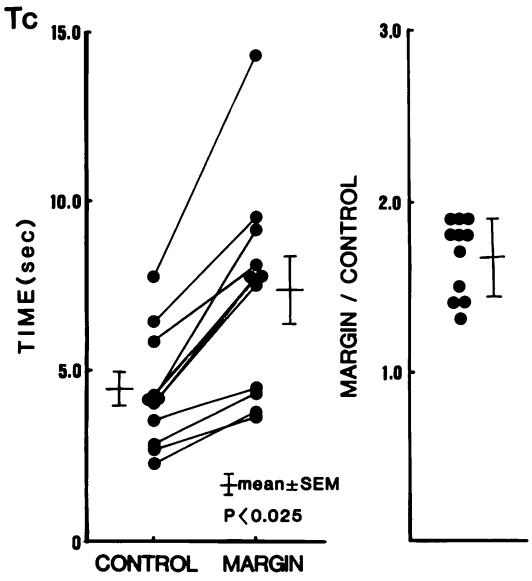


Fig. 9. Tc changes in the ischemic group.
Tc is markedly prolonged at the marginal regions.

Table 1. Evaluation of perfusion dynamics by two parameters

	Tp	Tc
CONTROL	ANT→APEX	ANT→APEX
MARGIN	↑	↑↑
INFARCT	↑↑	—

respectively) (**Fig. 5**). In a detailed analysis at 11 points from the basal region to the apex, it was shown that Tp was progressively prolonged and Tc was nearly invariable in any portions of the myocardium except at the basal regions where it has a slightly larger value (**Fig. 6**).

In case of anterior myocardial infarction, the time density curve in the marginal region indicated that Tp was prolonged and the washout time of the contrast material was also prolonged compared with that in a control region (**Fig. 7**). The peak density of contrast material had a relatively low value in the infarcted and marginal regions compared with normal ones. This was especially true in the infarcted regions, Tp was prolonged more than 10 sec, and the washout curve could not be completely analyzed because of limitations in data acquisition by our apparatus. Then comparative studies were performed only in the marginal region for the ischemic group in order to show regional myocardial perfusion dynamics. Tp in the marginal region was significantly prolonged compared to Tp in the control region (6.0 ± 0.3 sec vs. 4.7 ± 0.3 sec, $p<0.01$) (**Fig. 8**). The ratio of Tp (Tp ratio) in the marginal region to that in the control region was about 1.3. The Tc in the marginal region was markedly prolonged compared to the Tc in the control region (7.4 ± 0.9 sec vs. 4.4 ± 0.5 sec, $p<0.025$) (**Fig. 9**). The ratio of Tc (Tc ratio) in the marginal region to that in the control region was about 1.7.

Using two indices, Tp and Tc, we could evaluate the dynamics of regional myocardial perfusion as shown in **Table 1.**

Discussion

Currently, selective coronary arteriography is the most important imaging modality for determining the diagnosis, prognosis and indications for operations for ischemia. This method can clearly visualize the extension and distribution of coronary arterial obstruction, stenosis and any collateral vessels. However, conventional coronary arteriography cannot reveal the degree of myocardial perfusion which has been compromised by a coronary stenotic lesion. Furthermore, it cannot reveal the presence of lesions in small vessels ($<200\ \mu m$) and abnormalities in the microcirculation. DSA can not only capture arterial images but capillary and venous phase images as well by utilizing merits such as excellent contrast resolution, and good temporal and spatial resolution. Moreover, it is

feasible for DSA images to perform many kinds of quantitative analyses, using densitometry. To evaluate regional myocardial perfusion dynamics, we applied DSA with selective contrast material in the coronary artery. Two indices derived from regional time density curves, i. e. the arrival time of contrast material (Tp) and the time constant of the washout curve (Tc) were analyzed.

In control subjects, the arrival time (Tp) in the apex showed slight prolongation compared with that in the base. Though this prolongation had no statistical significance, it may be consistent with delay in the arrival of contrast material at the apex, caused by the direction of coronary blood flow from the basal region to the apex. In cases of anterior myocardial infarction, Tp was significantly prolonged in the ischemic regions. This phenomenon may be caused by delayed blood flow due to stenosis or obstruction in the coronary artery.

In the venous phase, contrast material was washed out exponentially. The time constant of the washout curve was calculated to evaluate regional myocardial perfusion because a single compartmental model was applicable to analyzing the exponential washout curve of the contrast material[8]. A similar method of analysis has been used to evaluate regional myocardial blood flow with the Xenon-133 washout technique[9~12]. In the present study, Tc showed a slightly greater value at the basal portion of the anterior wall, when Tc was constant in other regions in the control group. Because the contrast material was washed out of the coronary sinus into the right ventricle and pulmonary artery, superimposition of the contrast material may have occurred in the left ventricular basal region—thus prolongation of Tc may have been apparent. In cases of myocardial infarction, marked prolongation of Tc was evident in marginal regions. This phenomenon may be caused by reduction of coronary blood flow volume and decreased flow velocity in ischemic regions, caused by coronary arterial stenosis and increased impedance of regional vessels due to pathological changes. Both Tp and Tc had large values in ischemic regions. The Tc ratio in the marginal region was about 1.7, whereas the Tp ratio in the marginal region was about 1.3. Tc may be a more sensitive index than Tp for detecting abnormalities of regional myocardial perfusions.

For many years, investigators have been trying to develop a precise method to measure myocardial blood flow. Some approaches to evaluating regional myocardial perfusions have incorporated diffusible inert gases (Xenon-133, Kripton-85)[9~15,17] or radioisotope-labeled microspheres[16]. Notably, the use of Xenon-133 and a multiple-crystal scintillation camera had been the only technique for estimating regional myocardial blood flow in unanesthetized humans. This Xenon washout analysis introduced by Cannon et al[10,12] could reveal reduced myocardial blood flow in ischemic regions. In the present study using DSA, we were likewise able to detect regional ischemia. In spite of its capability of evaluating regional myocardial blood flow, the Xenon washout method has not been widely used because it cannot make repeated flow measurements due to the ready solubility of Xenon in fat, necessitating very expensive equipment, and it cannot measure the transmural distribution of left ventriclar perfusions. Once the patient holds his breath, the DSA method can estimate not only regional myocardial perfusion dynamics but morphological abnormalities in the coronary arteries such as stenosis, obstruction and any collaterals with readily available DSA equipment. Moreover, it can be performed repeatedly.

Vogel et al[18] described a new DSA technique for evaluating coronary blood flow using regional myocardial contrast appearance time (MCAT), the time from onset of contrast injection to its appearance in regions of the myocardium, and coronary flow reserve using contrast medium-induced hyperemia[18,19]. They demonstrated good correlation between the regional blood flow index determined by DSA and the coronary blood flow as obtained by the thermodilution technique. MCAT was substantially comparable to Tp.

Results using our DSA method with respect to Tp resembled those of Vogel. Our study developed further the analysis of the washout curve of contrast material in the venous phase, to estimate regional myocardial perfusion. Tc can also reveal abnormalities of regional myocardial perfusions, and it appears to be a more sensitive index than Tp.

To evaluate coronary flow reserve, Vogel et al[18,19] used contrast medium-induced reactive hyperemia to emphasize the coronary blood flow. Bassan et al[20] reported that within seconds after intracoronary injection of only 3 ml 76% Renografin, an increase in coronary sinus flow began, peaking at an average of 53% above control values in 5–10 seconds[20]. They also reported slight differences in response to contrast injections between patients with normal coronary arteries and those with obstructive coronary artery diseases. Although the difference was insignificant to permit assessment of degree of impairment of the coronary arterial bed[20], results of our study may have been affected by reactive hyperemia induced by contrast media. The difference in hyperemic changes between normal and ischemic regions may reinforce those of DSA indices.

Pertinent to this method, there are a few points for careful consideration. Use of the subtraction method causes misregistration artifacts which disturb the analysis. Since the injection of contrast material is performed manually, it is unstable and sometimes results in errors in measurements of Tp and Tc. Vogel et. al., reported temporal sampling inaccuracies caused by manual injections to be about a 12% precision error[18]. DSA is not capable of distinguishing epicardial from endocardial blood flow, because of overlapping.

Conclusion

DSA can easily reveal not only morphological abnormalities of the coronary arteries but abnormalities of regional myocardial perfusion dynamics as well. Two parameters, the arriving time Tp and the washout time constant Tc, from the DSA image sequence, are very useful for quantitatively evaluating regional perfusions. Thus, it is thought that this method will be widely used in the future clinically to evaluate decreased myocardial perfusions in regions of the myocardium distal to coronary artery lesions. This method will also be useful in evaluating in detail the effects of collateral vessels under a variety of conditions, not only at rest but during interventions which either increase myocardial oxygen consumption or induce coronary vasodilatation.

Digital subtraction angiography による局所心筋血流状態の定量的解析

筑波大学臨床医学系
武田　徹，松田光生，赤塚孝雄，
小川　剛，垣花昌明，鰺坂隆一，
富沢巧治，杉下靖郎，伊藤　巌，
秋貞雅祥

選択的冠状動脈造影に DSA を適用することにより，経時的に心筋灌流の動脈相，毛細管相および静脈相に対応する画像を得ることが可能となる．局所心筋における血流動態の定量的解析を目的として，局所心筋の濃度計測を行ない，造影剤注入開始より造影剤濃度が最高値に到達するまでの時間 (Tp)，および Tp 以降の造影剤が指数関数的に洗い出されることに注目し，この洗い出し曲線より得られた時定数 (Tc) の 2 つのパラメーターについて検討した．

検査対象は健常例 10 例，前壁心筋梗塞例 11 例である．

健常群では Tp は前壁部で 4.2±0.4 [SEM] 秒から心尖部で 5.2±0.5 秒とごく軽度の延長を示したが，Tc は心基部で 5.1±0.5，前壁で 4.8±0.5，心尖部で 4.6±0.5 秒で，部位による変化はほとんど見られなかった．前壁心筋梗塞例での Tp は，健常部心筋では 4.7±0.3 秒，梗塞周辺部では 6.0±0.3 秒であったが，梗塞部では造影剤濃度上昇速度が遅く，Tp が 10 秒以上と有意に延長していた．Tc は健常部では 4.4±0.5 秒，

梗塞周辺部では 7.4±0.9 秒で，著明な延長が見られた．梗塞部位では，現在の装置における記録時間上の制約のため，Tp の十分な解析は不可能であった．

DSA 画像の経時的計測から求めた Tp 及び Tc は，健常部と梗塞部及び梗塞周辺部で明らかな差を示した．本指標により，局所心筋の血流動態を定量的に解析しうる可能性が示唆される．DSA は冠状動脈の形態的な異常だけでなく，局所心筋の血流動態を一度の検査で得ることが出来る点で，非常に有力な手法と考えられた．

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