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Clinical validity of wash-out time constant images obtained by digital subtraction angiography

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Summary

Functional images of left ventricular myocardial perfusion were obtained using the washout time constant obtained from the analysis of digital subtraction angiograms (DSA). The results were compared with those of left ventriculography to evaluate its clinical validity. DSA examinations were performed in eight patients with old anterior myocardial infarction and in 10 control subjects. Washout time constant images of the left ventricular wall were nearly homogeneous in normal cases. On the contrary, regional heterogeneity on the washout time constant images was observed in cases of anterior infarction. The abnormal region in the washout time constant image corresponded well to the area of abnormal percent wall thickening, whereas the extent of the abnormal wall motion area tended to be broader than that of the abnormal washout time constant area or area of abnormal percent wall thickening. Thus, the washout time constant images obtained by DSA may comprise a reliable means of estimating the extent of ischemia in the myocardium.

Key words

Digital subtraction angiography　Regional myocardial perfusion　Dynamic image analysis　Functional image　Washout time constant

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Introduction

Recently digital subtraction angiography (DSA) has been used to evaluate ventricular function and myocardial perfusion[1~13]. After arterial injection of contrast material, DSA can clearly delineate coronary arterial images, and capillary and venous phase images in sequence. We have already performed the regional densitometry of these images to estimate the dynamics of regional myocardial perfusion, and have analyzed the time density curves. In the venous phase, contrast material disappears monoexponentially. In that study, the calculated washout time constant derived from this curve proved to be a valid parameter for differentiating the ischemic regions from the normal regions[8], and it was assumed that a single compartmental model should be available for analysis of this phenomenon. In the present study, a washout time constant image was constructed and compared with left ventriculograms to evaluate the clinical validity of this image.

Methods and materials

1. Patients

DSA examinations were performed in eight patients with old anterior myocardial infarction and in ten control subjects. The eight patients consisted of seven men and one woman whose ages ranged from 48 to 67 years (57±7 years old, mean±SD). The angiograms of all patients showed marked stenosis (more than 90%) in the left coronary artery. Control subjects consisted of four men and six women whose ages ranged from 36 to 68 years (52±10 years old, mean±SD). All control subjects had normal coronary arteriograms, normal exercise cardiac scintigrams, and normal left ventricular wall motion, though each of them had a history of chest pain.

2. Data acquisition system and data processing procedure

A commercial DSA system (Digiformer-X, Toshiba) was used for these examinations. Selective coronary angiography was performed using the Judkins technique. Sequentially subtracted images were obtained by using a continuous mode with 4 ml 76% Urografin manually injected into the left coronary artery. During coronary arteriography, the patients were placed in a 30 degree right anterior oblique position and maintained motionless. Breath was held in inspiration for 20 sec. Right atrial pacing was performed to maintain a regular heart rate. All examinations were performed after Nitorol® administration.

For digital processing, X-ray TV images were logarithmically amplified and digitized using a 10 bit AD converter, into 512×512 pixel matrices with an 8 bit depth at standard TV rates (30 frames/s) using DSA. Before the injection of contrast material, an "averaged" image of the heart over one sec (30 frames) was obtained and stored in the image memory as a digital mask image. Immediately after the mask was stored, contrast material was injected. Each successive frame of the X-ray TV image was subtracted from the mask image in real time, and these subtracted images were converted to analog signals and stored on an analog video disc recorder.

3. Image synthesis of washout time constant

Regional myocardial perfusion images were synthesized by a post-processing computer (**Fig. 1**). A total of 600 frames of digital subtraction images with 512×512×8 bits were obtained by the DSA system. The memory capacity of the post-processing computer (GMS-55A) was limited, therefore, each of the blocks of image data was compressed to a 64×64 matrix with an 8 bit depth. A large general purpose computer (FACOM M-380) was used to calculate and construct the washout time constant images in brief computation times. Densitometry was performed sequentially at each pixel of the condensed digital image; then a regional time density curve was obtained. Small periodic density changes were observed in those pixels corresponding to the cardiac cycle and they were thought to represent the myocardium. The time of the maximal point in each cardiac cycle corresponded to the end-diastolic phase. No cyclic density changes were observed in the lung field

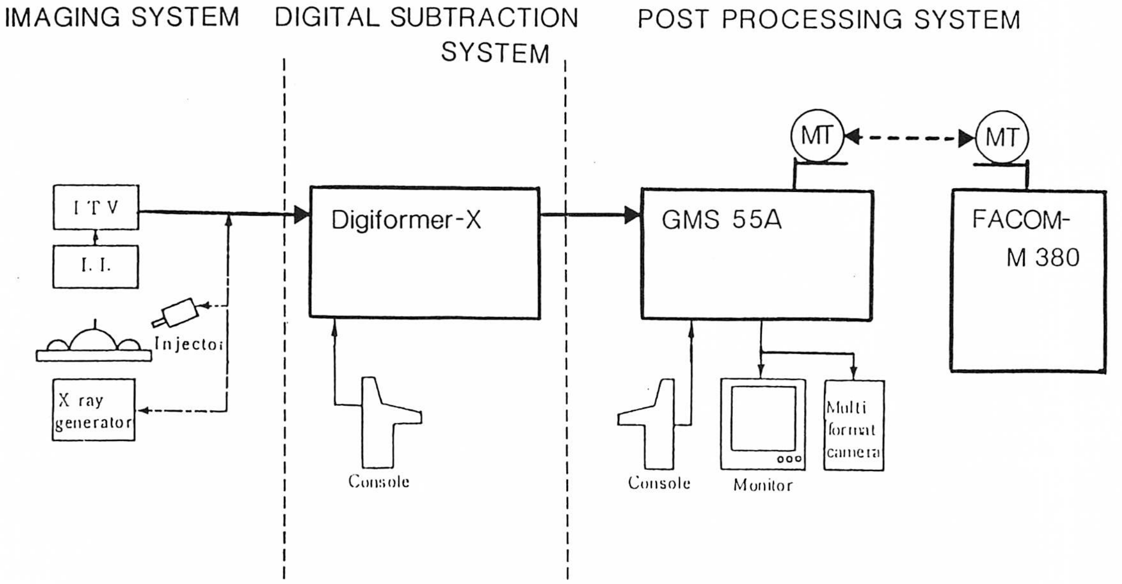

Fig. 1. Block diagram of the experimental system.

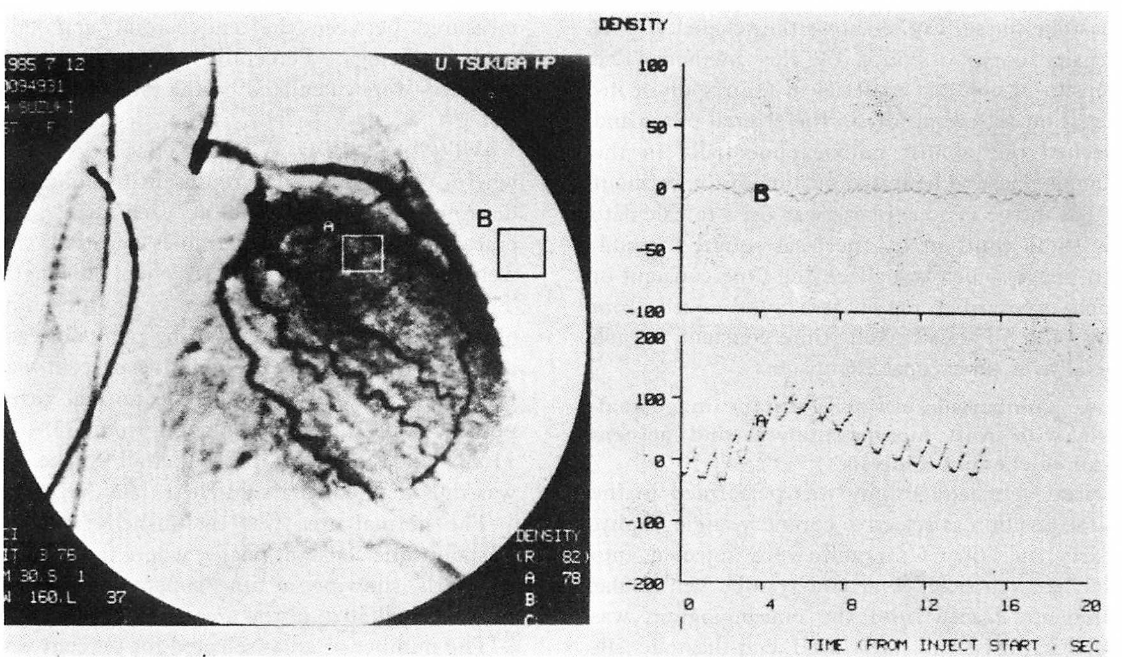

Fig. 2. Regional areas for densitometry and their time density curves.
A: myocardium, B: lung.

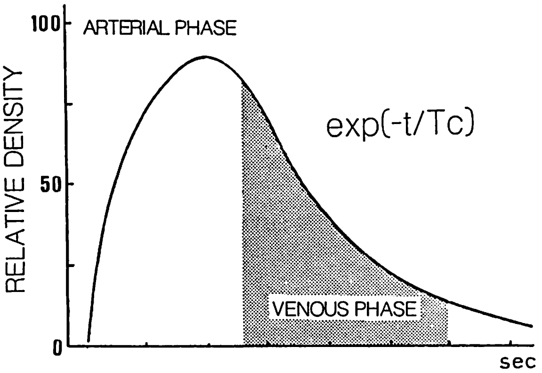

Fig. 3. Regional time density curve at the end-diastolic phase.

Contrast material is washed out monoexponentially, and an initial portion of washout curve (dotted zone) is used to calculate the washout time constant.

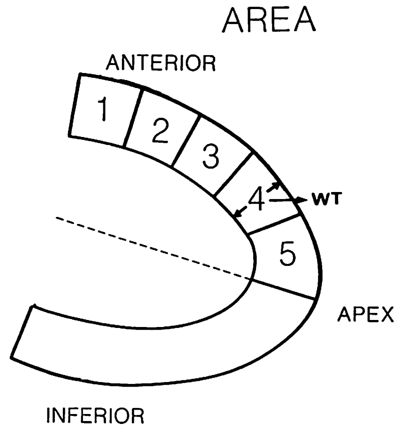

Fig. 4. Five areas of interest for comparison of analyzing procedure.

(**Fig. 2**). A smoothed time density curve was drawn from the original time density curve on the myocardial region by connecting each maximal point; i.e., points corresponding to the end-diastolic phase. **Fig. 3** shows the schematic time density curve obtained by this method. The density of contrast material in the region of interest increased rapidly in the arterial phase and washed out almost monoexponentially in the venous phase. The initial portion of the washout curve in the venous phase was used to calculate the time constant by the least square method. An image which visualized the time constant of each myocardial region was synthesized from the value of the washout time constant at each pixel as a time constant image.

4. Comparison of time constant image analysis with wall motion analysis and percent wall thickening analysis

Left ventriculography was performed in the same position as selective coronary angiography. Forty ml 76% Urografin were injected into the left ventricle. The end-systolic ventricular silhouette traced from the cineangiogram was superimposed on the traced end-diastolic silhouette. Regional wall motion determined by comparisng end-systolic and end-diastolic tracings was semiquantitatively assessed by two experienced observers as normal, hypokinesis, akinesis, and dyskinesis. Wall motion analysis was performed in five areas as illustrated in **Fig. 4.**

At the end-systolic and end-diastolic phases, the thickness of the myocardial wall (WT) was measured between the endocardial and epicardial tracings. Percentile changes of wall thickness were calculated by the following equation:

$$WT\ (\%) = (WTs - WTd)/WTd \times 100,$$

where WTs and WTd represent systolic and diastolic wall thicknesses at each area. The epicardial and endocardial lines of each area were divided into three parts equal in length. The average value of percent wall thickening obtained from two corresponding points of each area, was used as a representative percent wall thickening at each area. In the normal cases, percent wall thickening ranged from 35% to 116%, and abnormal percent wall thickening was thus defined as a value less than 30%.

The normal area was established from the washout time constant image, where the number of pixels showing a time constant below 6.1 sec exceeded 50% in the area of interest.

The number of areas selected for percent wall thickening analysis and washout time constant analysis was the same as that used for wall motion analysis.

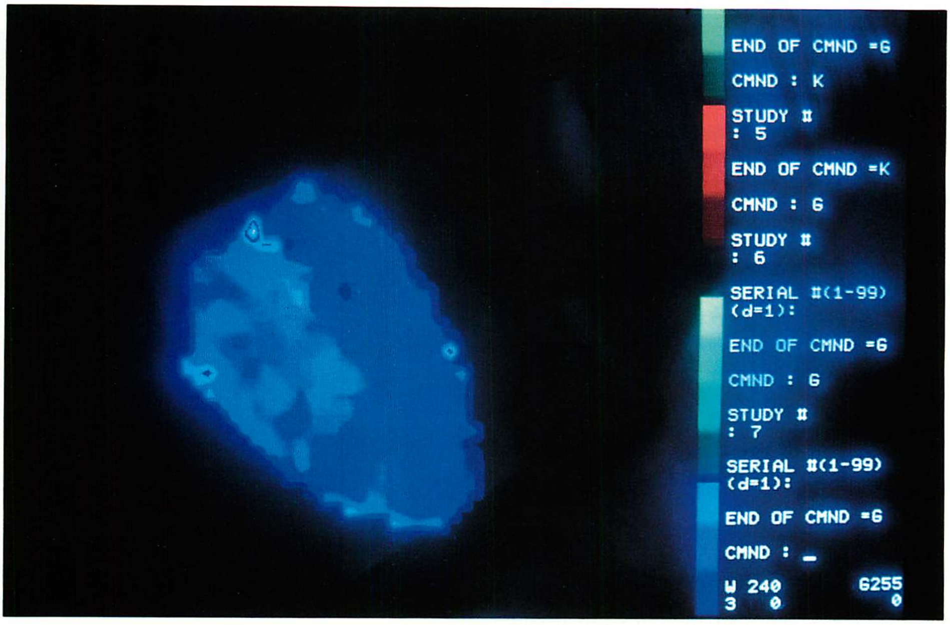

Fig. 5. The washout time constant image in a normal case.
The left ventricular wall perfused by the left coronary artery is nearly homogeneous as shown in blue.

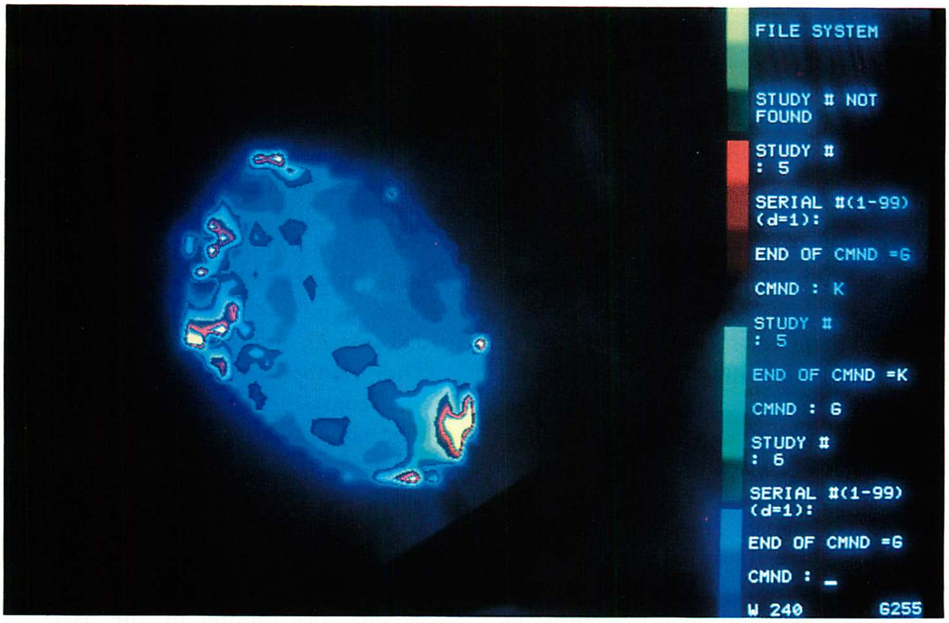

Fig. 6. The washout time constant image in a case of anterior myocardial infarction.
Abnormal perfusion is seen at the apical region.

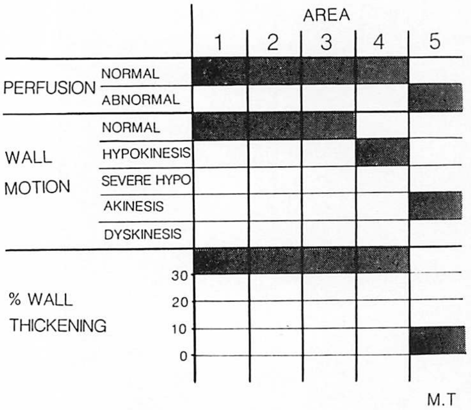

Fig. 7. Comparison of the three analyzing procedures for the case shown in Fig. 6.

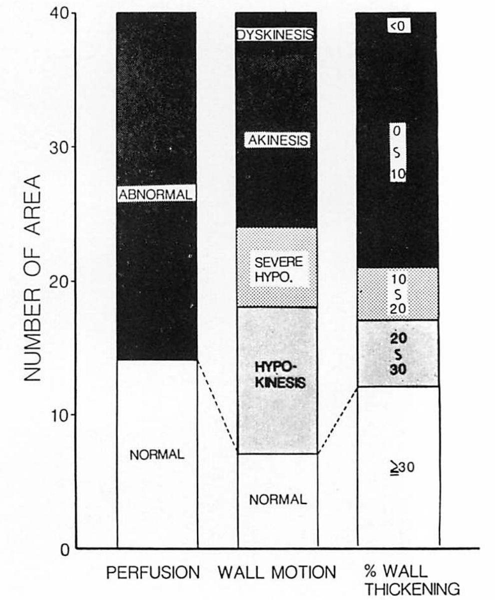

Fig. 8. Comparison of three analyzing procedures for 8 cases of anterior myocardial infarction.

Results

Fig. 5 shows the washout time constant image of a normal case. Sixteen steps of color representation were used to describe washout time constant images. The left ventricular wall perfused by the left coronary artery is shown nearly homogeneously in blue (time constant ranging from 3.0 sec to 4.5 sec). However, in the inferobasal regions, the washout time constant image is light blue (time constant ranging from 4.5 to 6.0 sec). This difference expressed the prolonged time constant value of the myocardium.

Washout time constant images of a case of old anterior myocardial infarction are shown in **Fig. 6.** Abnormal perfusion is demonstrated in the apical region. This 61-year-old man had dual LAD, and complete obstruction in the long LAD (#7). Myocardial infarction was limited to the apical region. Here, the washout time constant image was compared to the wall motion and percent wall thickening using the procedure previously explained. **Fig. 7** shows the results of the comparison made in the case shown in **Fig. 6.** The abnormal region in the washout time constant image appear in area 5. The wall motion abnormality appear in area 4 (hypokinesis) and in area 5 (akinesis). The abnormal percent wall thickening appear in area 5. Thus, the abnormal regions in the washout time constant images corresponded well to the apparent ischemic regions according to the percent wall thickening abnormality. The regions with abnormal wall motion tended to be broader than the abnormal regions as estimated by washout time constant images and percent wall thickening.

Ten control subjects demonstrated no abnormalities in either wall motion or percent wall thickening. Forty areas in eight patients with old anterior infarction were examined (**Fig. 8**). The number of abnormal areas of washout time constant images was 26 (65%). Wall motion abnormalities were demonstrated as hypokinesis in 11 areas, severe hypokinesis in 6 areas, akinesis in 13 areas and dyskinesis in 3 areas. The total percentage of abnormal areas was 82%. Abnormality in percent wall thickening was demonstrated in 28 areas (70%). The detailed distribution of the assessments corresponding to each area is shown in **Table 1.** The regions of abnormal washout time constant

Table 1. Detailed distribution of the judgements corresponding to the area for the cases of anterior myocardial infarction

		Area				
		1	2	3	4	5
Perfusion	Normal	7	5	1	1	
	Abnormal	1	3	7	7	8
Wall motion	Normal	3	3	1		
	Hypokinesis	5	2	3	1	
	Severe hypokinesis		3	1	1	1
	Akinesis			3	6	4
	Dyskinesis					3
%wall thickening	30~	7	3	1	1	
	20~	1	3	1		
	10~		2	1		1
	0~			5	7	5
	~0					2

images corresponded well to those of abnormal percent wall thickening as in the case shown in **Fig. 7.**

Discussion

Assessment of regional myocardial perfusion abnormalities is important for evaluating ischemic heart disease. Selective coronary angiography is widely used to predict disturbances of coronary blood flow caused by stenosis, but this method cannot directly reveal the dynamics of regional myocardial perfusion. Recent developments in radiography and computer technology have facilitated evaluating not only anatomical information about the coronary artery, but the dynamics of regional myocardial perfusion, as well. Previously, we proposed the washout time constant as a parameter for estimating regional myocardial perfusion by DSA images[8]. In the present study, the images of washout time constants are constructed and used as diagnostic information.

Washout time constant images of the left ventricle were nearly homogeneous in the normal cases except at the basal region, where heterogeneity indicating prolonged time constants was demonstrated. Such regions were not used in our comparative studies. This phenomenon might be caused by superimposed contrast material, which originated from the coronary sinus in the right ventricle and in the pulmonary artery[8]. In a case of myocardial infarction, regional heterogeneity was demonstrated on washout time constant images in the ischemic region.

From comparative studies of washout time constant images, wall motion analysis, and percent wall thickening analysis it can be concluded that the ischemic regions assessed by washout time constant images agreed well with those assessed by percent wall thickening analysis, whereas the ischemic regions assessed by abnormal wall motion tended to be broader than those assessed by the former two methods. Wall motion analysis is less precise than percent wall thickening analysis in discriminating between infarcted and noninfarcted zones and could lead to some overestimations of infarct sizes[15~20]. Kerber et al[15] reported that such overestimations of wall motion abnormality might be due to passive alteration of the motion of the normally perfused area by the severe dyskinesis of the adjacent ischemic myocardium.

In the present study, the threshold of the abnormal time constant of the regional myocardium was established as 6.1 sec from data of our previous study[8]. Holman et al[21], using the Xenon washout study, reported that there was considerable overlap of regional specific flow values (corresponding to washout time constants) obtained at rest in patients with normal coronary arteriograms and values obtained in those with moderate or even severe coronary artery disease. However, they indicated that the regional specific flow index measured during reactive hyperemia induced by contrast material may be more sensitive than that measured during baseline studies to detect hemodynamically significant coronary arterial lesions in man[21]. For our DSA study only a small amount of contrast material was used, so that reactive hyperemia cannot be induced sufficiently to differentiate ischemic from normal regions[22]. Thus, using the maximal reactive hyperemic technique, more precise information can be obtained about regional myocardial perfusion and coronary flow reserve by DSA examinations.

In the washout method, it is assumed that a steady flow state exists during the time of measurement, i.e., the Kety-Schmidt principle[23,24]. However, the injection of contrast material results in an unsteady state with an initial decrease in blood flow, followed by a subsequent increase in flow, and then a return to normal flow[14,21,22]. Therefore, the Kety-Schmidt principle does not strictly apply. However, our previous study[8] showed that the washout curve was fitted to the exponential curve statistically. Thus the initial portion of the washout curve approximates the monoexponential curve, and the image of the washout time constant is constructed from these curves.

Other approaches have been tried in attempting to estimate regional myocardial perfusion using DSA[3,10~14]. Vogel[12] made parametric images using the ECG-gated DSA images in the arterial and capillary phases. Dual parameter functional images were generated using color and intensity coding to represent contrast arrival times and contrast densities, respectively. These parametric images have proved helpful in determining the physiological significance of intermediate coronary artery stenosis. For 50% diameter stenosis they seem to be the best criteria for determining the physiological significance of the stenosis. Vogel proposed to evaluate the coronary flow reserve by contrast-induced reactive hyperemia.

In the future, many types of parametric images must be used to assess the physiological significance of stenosis, abnormalities of the microcirculation, and coronary flow reserve, using DSA.

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要　約

選択的冠状動脈造影により得られた経時的なDSA 画像のうち，特に静脈相画像に注目し，造影剤の指数関数的な洗い出し曲線から求めた時定数を用いて，局所心筋における血液灌流状態の画像表現を行い，その臨床的評価を試みた.

虚血性心疾患を疑われた患者 18 例，すなわち冠状動脈造影で明らかな狭窄を示さなかった健常例 10 例，および前壁心筋梗塞例 8 例を対象とした. DSA 装置により画像を収集し，後処理用コンピューターおよび汎用大型計算器を用い，画像処理を行った. 76% Urografin 4 ml を用手的に冠状動脈に注入し，右前斜位 30 度より透視モードを用い撮影した. 計算器解析では，画素数を 64×64 ピクセルに圧縮して用いた.

健常例では局所心筋における血流にむらは見られず，ほぼ一様な血流状態を示した. 前壁梗塞例では，梗塞周辺部で明らかな血流異常が示された. 左室造影法との比較では，局所心筋の血流異常部位は壁運動異常部位および percent wall thickening の異常部位と良く対応し，なかでも，percent wall thickening との対応が特に良好であった.

DSA を用いて得られた局所心筋の血流画像は，左室造影法で推定した心筋虚血部位の広がりと程度を明瞭に描出することができ，臨床診断上，非常に有用であると考えられた.

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