Journal of Cardiology 22: 595–605, 1992

Left atrial function in ischemic heart disease assessed by intravenous digital subtraction angiography

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Summary

To investigate changes in left atrial morphology and dimensions during the cardiac cycle, the atrium was visualized by intravenous digital subtraction angiography (DSA).

The study subjects consisted of 22 male patients whose average age was 54.5 ± 8.6 years. They had ischemic heart disease without mitral valve disease and were in sinus rhythm. They were 11 patients with old myocardial infarction (OMI group) and 11 who had chest pain without evidence of infarction (AP group).

DSA was performed in the continuous mode. Contrast material (35 m*l*) was injected at a rate of 18 m*l*/sec via a catheter in the superior vena cava and subtraction images were obtained at a speed of 30 frames/sec in the right anterior oblique projection. The left atrial and left ventricular margins were traced manually, their areas were calculated, and fractional changes in area were analyzed. The left ventricular ejection fraction (LVEF) was calculated by densitometry. Cardiac catheterization was performed in 16 patients and the left ventricular end-diastolic pressure (LVEDP) and mean pulmonary arterial wedge pressure (PAWP) were measured.

The entire left atrium was clearly imaged using DSA. Phase analysis of the time-area curves in the right anterior oblique projection revealed that the left atrial area was maximal during left ventricular end-systole (%LA1 = 100%), it decreased during early left ventricular diastole (%LA2), and then increased slightly again during mid-diastole (%LA3). After left atrial contraction, the minimum area was obtained (%LA4). The left atrium showed a two-stage decrease in the area due to passive emptying and active contraction during left ventricular diastole.

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Received for publication May 3, 1991; accepted November 5, 1991 (Ref. No. 34–26)

Passive emptying (%LA1 − %LA2) was significantly less in the OMI group than in the AP group (6.3±3.6 vs 13.3±4.8%, $p<0.01$, respectively). In all 22 subjects, passive emptying correlated with LVEF ($r=0.70$, $p<0.001$) and LVEDP ($r=-0.58$, $p<0.05$). There was no difference in active contraction (%LA3 − %LA4) between the 2 groups (26.0±5.7% in the OMI group, 28.2±8.4% in the AP group), and it did not correlate with LVEF or LVEDP. The ratio of passive emptying to active contraction [(%LA1 − %LA2)/(%LA3 − %LA4)] correlated with LVEF ($r=0.63$, $p<0.01$). These findings suggested that impaired left ventricular diastolic function and a relative increase in atrial contraction were present in patients with a lower LVEF. The %LA4 correlated with LVEDP and PAWP ($r=0.65$, $r=0.63$, $p<0.01$, respectively).

In conclusion, DSA proved to be a useful method for investigating left atrial morphology and function.

Key words
Digital subtraction angiography   Left atrial imaging   Left atrial function   Ischemic heart disease
Left ventricular dysfunction

Introduction

Though the importance of the atrial contribution to the overall cardiac function has been pointed out[1-4], studies on left atrial function[5-10] are still rather meager compared with those of left ventricular function. One reason is that the diagnostic apparatus and procedures available in the clinical setting have not always provided sufficient direct information on the properties of left atrial function of the intact human heart. Thus, reports on left atrial function were obliged to be based on indirect observations, such as atrial function coupled with left ventricular diastolic function[2,4,11].

Clinically, left atrial morphology and dimensions have been studied by classical left atrial angiocardiography[3,5], echocardiography[4,8,10,12], and radionuclide angiocardiography[7,8]. However, it is not easy to visualize clearly and evaluate the entire left atrium and changes in its shape, size, and function throughout the cardiac cycle[10]. Since 1984, we have used intravenous digital subtraction angiography (DSA) in patients with various cardiac diseases to diagnose morphological and functional abnormalities[13]. As DSA facilitates obtaining good images of the entire left atrium, we used this method to evaluate left atrial function in patients with ischemic heart disease in the present study.

Study population

The subjects consisted of 22 male patients with ischemic heart disease whose mean age was 54.5±8.6 years. Included were 11 patients with chest pain but without evidence of myocardial infarction. This AP group, whose mean age was 54.0±6.3 years, was comprised of 6 patients with effort angina, 3 with angina at rest, and 2 with chest pain syndrome. In addition, 11 patients with documented old myocardial infarction (OMI) were studied (mean age: 55.1±10.4 years). They consisted of 7 patients with anterior infarction, 3 with inferior infarction, and one with lateral infarction. All 22 patients were in sinus rhythm and none of them had mitral valve disease.

Methods

DSA

Intravenous cardiac digital subtraction angiography was performed on all 22 patients, and a commercially available DSA system (Digiformer-X, Toshiba) was used for the examinations. With this system and a 10-bit A/D converter, X-ray TV images were logarithmically amplified and digitized into a 512×512 pixel matrix with an 8-bit depth at standard TV rates (30 frames/sec). Before injection of any contrast material, an average image of one second duration (30 frames) was obtained and stored in computer memory as a digital mask image. Immediately after the mask image was stored, 35 m*l* contrast material (Urografin 76) was injected intravenously at a speed of 18 m*l*/sec through a 5 F catheter (Mallinckrodt) placed in the superior vena cava via an antecubital vein. Sequentially-subtracted images were obtained in the continuous mode. Successive frames of the TV image were subtracted from the mask image in real time, and these subtracted images were stored using an analog video disc recorder. DSA images were obtained for 15–20 seconds in the right anterior oblique (30 degrees) projection, with the patients in suspended inspiration and lying supine. Then, levo-phase images were obtained, in which the left atrium and ventricle were clearly visualized.

On the DSA images, margins of the left atrium and ventricle were manually traced and the projected areas of the left atrium and ventricle were computed using a commercially available medical image analyzer (Cardio-200, Kontron). In tracing the left atrium, the left auricle was excluded from calculation of the left atrial area. In each patient, the changes in left atrial and ventricular areas during one cardiac cycle were plotted and analyzed. To compensate for the magnification constants which differ from patient to patient and are apt to lead to erroneous calculations of absolute areas, we also calculated fractional changes in the area during one cardiac cycle. The maximal areas of the left atrium and left ventricle were regarded as 100% in each cycle. The left ventricular ejection fraction (LVEF) was computed from the DSA images by densitometry using a medical image processor (GMS-55A, Toshiba).

Cardiac catheterization

In 16 patients, 8 from each group, standard cardiac catheterization was performed, including pressure measurements, cardiac output measurements, biplane left ventriculography, and coronary cineangiography. The left ventricular end-diastolic pressure (LVEDP) and mean pulmonary arterial wedge pressure (PAWP) were compared with the data obtained by DSA.

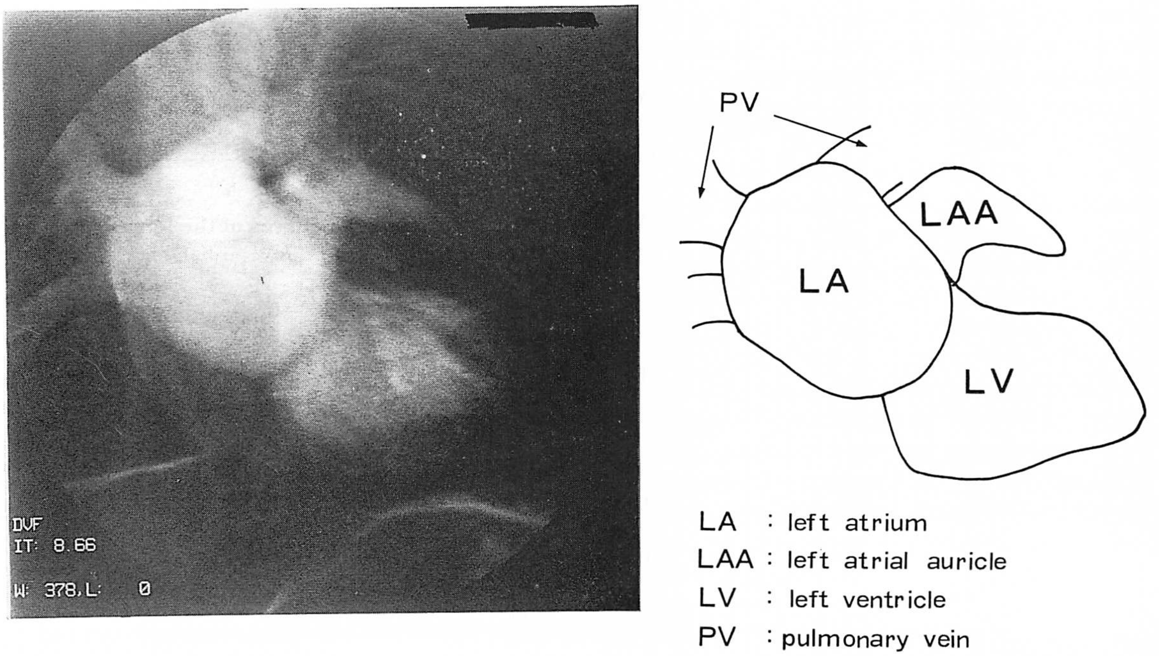

Fig. 1. Visualization of the left atrium by DSA (Case 19, myocardial infarction).

Statistical analysis

Student's t-test and first order regression analysis were performed. Correlation coefficients were also determined. A p value less than 0.05 was regarded significant, and data were expressed as means±SD.

Results

Intravenous cardiac DSA facilitated visualization of the entire left atrium (**Fig. 1**).

Time-area curves of the left atrium and left ventricle during one cardiac cycle are shown in **Fig. 2,** which is a representative example for the AP group. The left atrial area was maximal (LA1) at the end of left ventricular systole. It then passively decreased during early left ventricular diastole (LA2) and increased slightly again during ventricular mid-diastole (LA3). Subsequently, it decreased to the minimal value after active atrial contraction (LA4). Thus, the left atrium exhibited a bimodal decrease in area, consisting of "passive" and "active" decreases, during left ventricular diastole.

Similar changes in the left atrial area were demonstrated in the OMI patients (**Fig. 3**), but the passive decrease in the area (from LA1 to LA2) was relatively little and the decrease by active atrial contraction from LA3 to LA4 was relatively great.

Fig. 4 shows representative images of the 4 phases of the atrial cycle obtained by DSA examinations. At left atrial end-systole (LA4), contraction of the left atrial auricle was also clearly demonstrated.

We expressed the fractional changes in the left atrial area according to the formula:

$\%LAi = (LAi/LA1) \times 100\ (\%)\ (i = 1, 2, 3, 4)$,

where LAi is the area measured in phase LAi.

Comparison of the AP and OMI groups

There was no significant difference in age between the AP and OMI groups. The heart rate during the DSA examination was 71.0±8.6 bpm in the AP group and 68.7±7.5 bpm in the OMI group (p=ns). There was also no significant difference in the mean arterial blood pressure (MBP). However, there was a significant difference in the LVEF between the 2 groups (AP: 75.4±6.7% and OMI: 55.1±10.8%, $p<0.001$). There were also significant differences in LVEDP and PAWP between the 2 groups (**Table 1**).

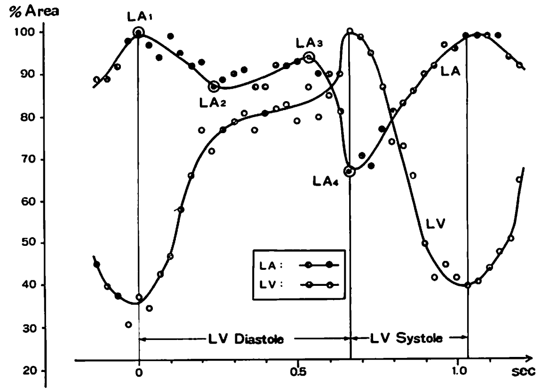

Fig. 2. Time-area curves of the left atrium and left ventricle (Case 4, angina pectoris).

LA=left atrium; LV=left ventricle; LA1, LA2, LA3, LA4=the 4 phases of LA area.

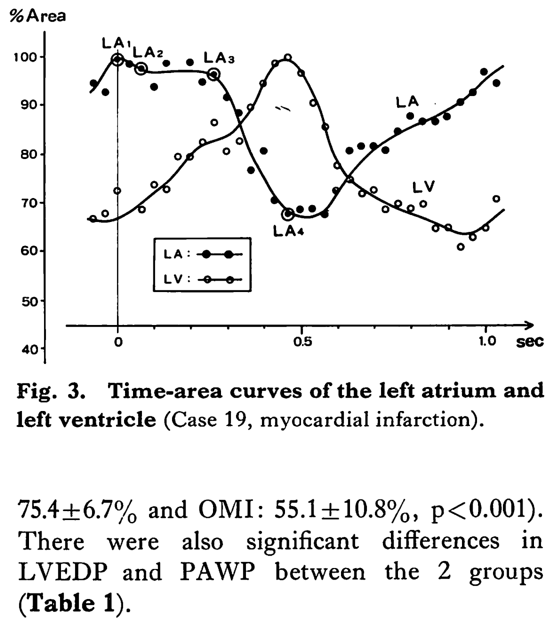

Fig. 3. Time-area curves of the left atrium and left ventricle (Case 19, myocardial infarction).

We compared the changes in the left atrial area between the AP and OMI groups (**Fig. 5**). In the OMI patients, the %LA2 was significantly greater than in the AP patients (93.7±3.6 vs 86.7±4.7%, $p<0.01$, respectively). Therefore, the passive decrease in area (100−%LA2) was not so great in the OMI patients as in the AP patients (6.3±3.6 vs 13.3±4.8%,

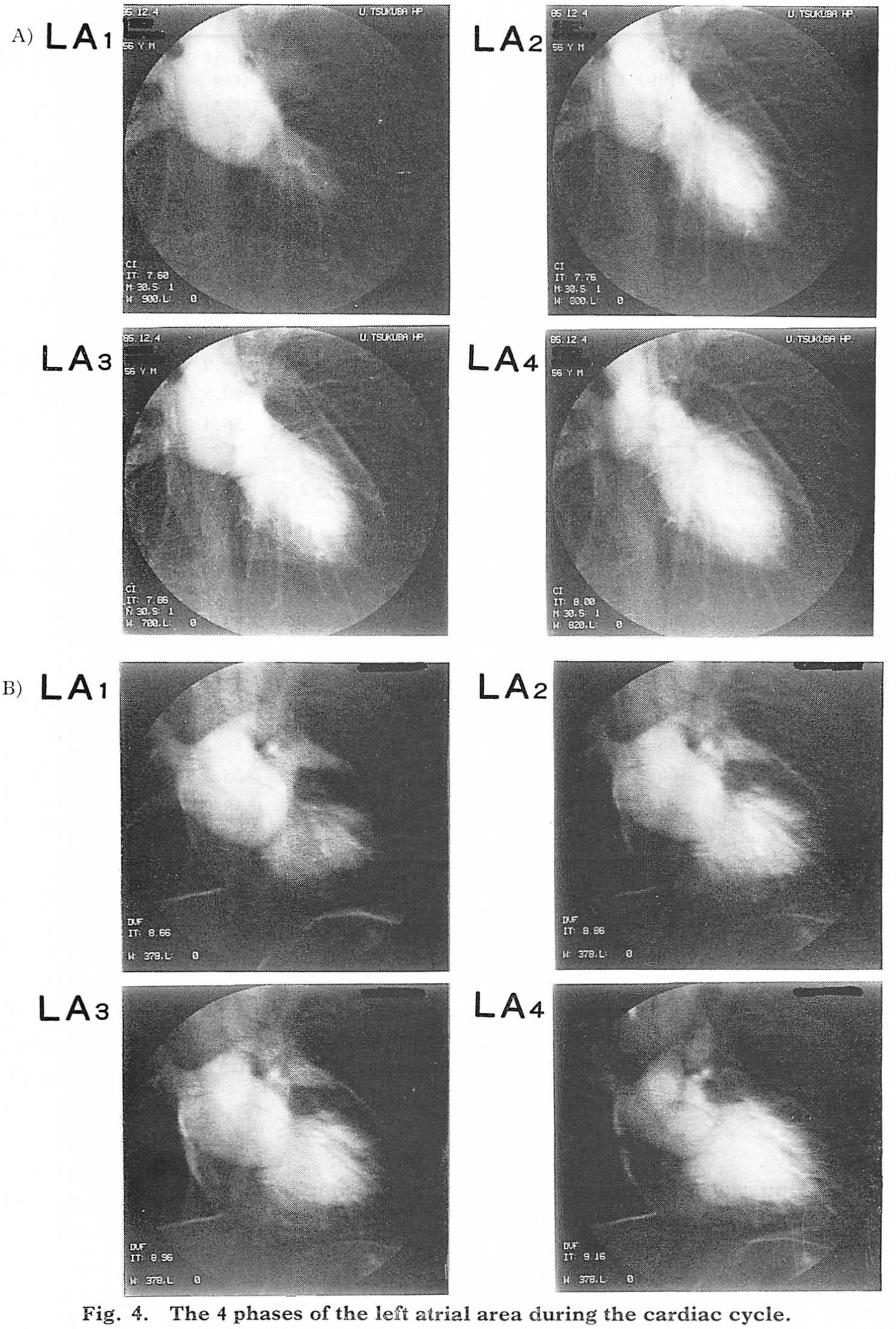

Fig. 4. The 4 phases of the left atrial area during the cardiac cycle.

A) Case 6, angina pectoris.

B) Case 19, myocardial infarction.

Table 1. Clinical data and left atrial areas

Case	No.	Age (yrs)	HR (bpm)	MBP (mmHg)	LVEF (%)	LVEDP (mmHg)	PAWP (mmHg)	LA1 (cm^2)	%LA2 (%)	%LA3 (%)	%LA4 (%)
AP group	1	44	72	93	79	10	8	44.3	81.6	83.4	61.8
	2	42	72	89	70	11	6	48.1	86.2	93.2	65.8
	3	56	64	78	67	10	3	42.6	88.5	91.9	40.7
	4	55	68	89	82	11	6	37.7	90.3	96.2	67.1
	5	60	59	83	80	6	2	38.4	87.7	91.9	63.5
	6	56	72	87	78	7	7	42.7	84.5	80.9	56.9
	7	56	80	75	83	6	2	36.2	86.6	89.7	57.1
	8	60	81	81	74	16	9	33.3	94.2	96.2	71.1
	9	57	88	102	72	—	—	34.9	93.3	92.8	74.5
	10	47	62	89	77	—	—	40.5	77.2	77.1	55.7
	11	61	63	82	76	—	—	36.4	83.4	86.0	55.3
Mean±SD		54.0 ±6.3	71.0 ±8.6	86.2 ±7.2	75.4 ±6.7	9.6 ±3.1	5.4 ±2.5	39.5 ±4.3	86.7 ±4.7	89.0 ±6.0	60.9 ±8.8
OMI group	12	38	65	87	57	15	11	32.6	91.0	94.7	63.3
	13	44	76	90	56	10	5	30.7	93.5	85.1	61.3
	14	49	81	86	60	18	14	29.1	88.5	94.1	72.8
	15	54	62	101	54	8	4	32.5	93.4	93.7	55.5
	16	61	60	86	66	13	7	28.4	95.4	95.7	77.1
	17	74	60	91	48	—	—	32.1	98.3	91.0	63.8
	18	46	70	98	54	—	—	54.7	86.9	90.6	59.7
	19	67	65	89	52	16	8	34.2	96.4	96.3	71.0
	20	63	66	80	57	19	10	38.2	93.0	89.6	70.9
	21	50	82	127	30	18	12	38.9	99.0	94.5	72.6
	22	60	69	87	49	—	—	25.5	95.1	103.8	75.1
Mean±SD		55.1 ±10.4	68.7 ±7.5	92.9 ±12.1	55.1 ±10.8	14.6 ±3.7	8.9 ±3.3	34.2 ±7.5	93.7 ±3.6	93.6 ±4.5	67.6 ±6.8
AP vs OMI		ns	ns	ns	$p<0.001$	$p<0.02$	$p<0.05$	ns	$p<0.01$	ns	ns ($p=0.07$)

AP=angina pectoris; OMI=old myocardial infarction; HR=heart rate; MBP=mean blood pressure; LVEF=left ventricular ejection fraction; LVEDP=left ventricular end-diastolic pressure; PAWP=mean pulmonary arterial wedge pressure; LA1=maximal left atrial area; %LA2, %LA3, %LA4=left atrial fractional area in the phase LAi (i=2, 3, 4).

$p<0.01$, respectively).

There was no significant difference in the decrease in left atrial area accomplished by active atrial contraction (%LA3−%LA4) between the 2 groups (AP: 28.2±8.4% vs OMI: 26.0±5.7%, p=ns). The minimal area after active atrial contraction (%LA4) in the OMI group was 67.6±6.8%, and that in the AP group was 60.9±8.8% (p=0.07, ns). The ratio of passive atrial emptying to active atrial contraction [(100−%LA2)/(%LA3−%LA4)] was lower in the OMI group than in the AP group (0.25±0.15 vs 0.51±0.25, $p<0.02$, respectively), and a relative increase in active atrial contraction was observed in the OMI group (**Table 2**).

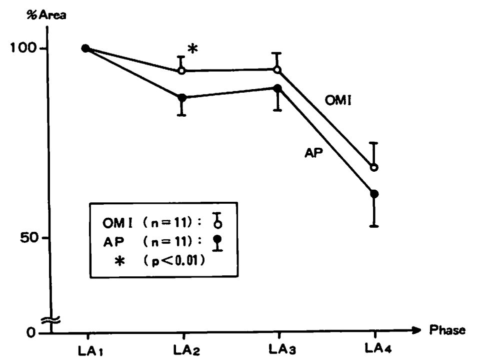

Fig. 5. Changes in left atrial area between the AP and OMI groups.

Left atrial function in the whole study population (Table 2)

Passive atrial emptying: Among all 22 patients, the decrease in left atrial area by passive atrial emptying (100−%LA2) showed a correlation with LVEF ($r=0.70$, $p<0.001$, **Fig. 6**). There was also a correlation between passive atrial emptying (100−%LA2) and LVEDP ($r=-0.58$, $p<0.05$, $n=16$), but there was no significant correlation between passive atrial emptying (100−%LA2) and PAWP ($n=16$).

Active atrial contraction: In all groups, the decrease in left atrial area produced by active atrial contraction (%LA3−%LA4) did not correlate significantly with LVEF (**Fig. 7**) or LVEDP. However, there was a correlation between the change due to active atrial contraction (%LA3−%LA4) and PAWP ($r=-0.56$, $p<0.05$, $n=16$).

Passive atrial emptying and active atrial contraction: The ratio of passive atrial emptying to active atrial contraction [(100−%LA2)/(%LA3−%LA4)] correlated with LVEF ($r=0.63$, $p<0.01$, $n=22$), but there was no significant correlation between this ratio and LVEDP or PAWP. A decrease in relative atrial emptying by the passive mechanism, i.e., a relative increase in the contribution of active atrial contraction, was observed in patients with lower LVEF values.

Minimum left atrial area: There was no correlation between the minimum left atrial area after active atrial contraction (%LA4) and LVEF. However, %LA4 correlated with LVEDP and PAWP ($r=0.65$, $p<0.01$, **Fig. 8**; $r=0.63$, $p<0.01$, **Fig. 9**, respectively), and its value was greater in patients with an elevated LVEDP or PAWP.

Discussion

Intravenous DSA facilitated visualizing the entire left atrium (**Fig. 1**) and investigating changes in its shape and size during the cardiac cycle (**Figs. 2–4**). The shape, size, and function of the left atrium have been previously investigated by classical cineangiography[3,5], echocardiography (including Doppler echocardiography)[4,9,10,12] and radionuclide angiocardiography[7,8]. Since the DSA method provides clear images obtained by the central intravenous injection of contrast material, it is unnecessary to inject contrast material directly into the left atrium or pulmonary artery. Thus, this method

Table 2. Changes in left atrial area and left ventricular performance

	Passive emptying (100−%LA2)	Active contraction (%LA3−%LA4)	(100−%LA2) / (%LA3−%LA4)	%LA4
*AP (n=11) vs OMI (n=11)	p<0.01	ns	p<0.02	ns (p=0.07)
**LVEF (n=22)	r=0.70, p<0.001	ns	r=0.63, p<0.01	ns
**LVEDP (n=16)	r=−0.58, p<0.05	ns	ns	r=0.65, p<0.01
**PAWP (n=16)	ns	r=−0.56, p<0.05	ns	r=0.63, p<0.01

* unpaired t-test; ** correlation coefficient analysis.

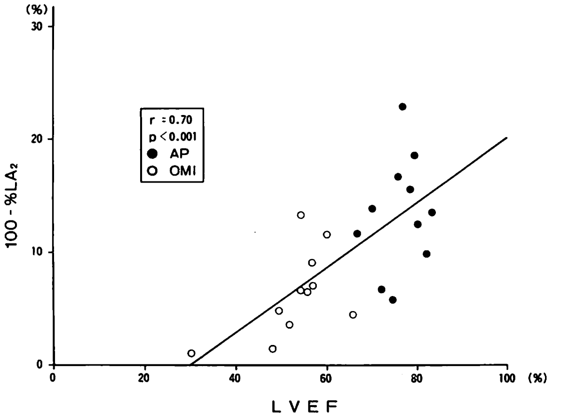

Fig. 6. **Passive atrial emptying vs left ventricular ejection fraction** (LVEF).

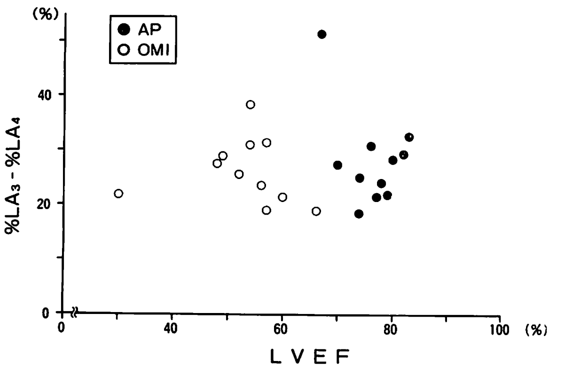

Fig. 7. Active atrial contraction vs LVEF.

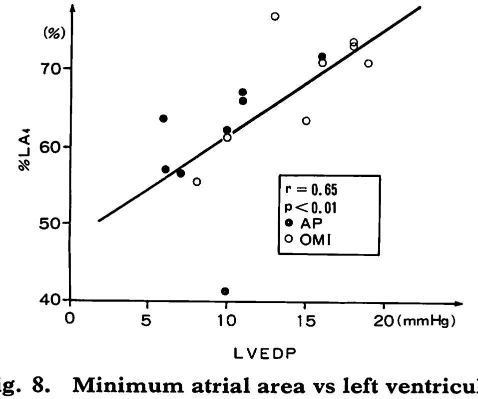

Fig. 8. **Minimum atrial area vs left ventricular end-diastolic pressure** (LVEDP).

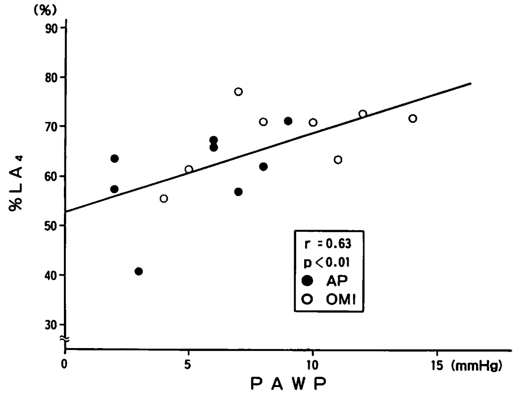

Fig. 9. **Minimum atrial area vs pulmonary arterial wedge pressure** (PAWP).

is less invasive and more simple than conventional cineangiography. Furthermore, the DSA method has considerable benefits with respect to image processing.

Echocardiography is generally a non-invasive, simple and excellent method for cardiac evaluation. However, it is sometimes impossible to obtain an adequate acoustic window for good visualization of the region of interest in obese patients, the elderly, patients with pulmonary disease, and in patients who have undergone cardiac surgery. It is not always easy to obtain an image of the entire left atrium in one section to facilitate observation of changes occurring during the cardiac cycle[10].

Radionuclide angiocardiography does not seem to provide sufficient spatial and temporal resolution for analyzing left atrial function by the summation of many heart beats[7].

DSA facilitates visualizing the entire left atrium, including the left auricle and the roof of the atrium (**Fig. 1**). In the present study, we only analyzed images obtained in the right anterior oblique projection, because our DSA system did not allow biplane image acquisition or electrocardiogram-gated acquisition. More precise analysis would have been possible if left anterior projections and ECG-gated images had been studied.

In the present study, we mainly analyzed the fractional changes of the left atrial area. With

DSA, as with conventional cineangiography, it is also possible to calculate the absolute value of the left atrial area in a right anterior oblique projection with the magnification constant of the image taken into consideration. However, it is not very easy to determine the exact value of the magnification constant for each patient. Therefore, to avoid errors induced by variations in magnification constant, we analyzed the fractional changes in the left atrial area.

The left atrium has 3 functions; it acts as a reservoir, a pump, and a conduit[5-7]. Indirect evaluations of left atrial function have consisted of analyses of left ventricular diastolic function using left ventricular angiography[2], radionuclide angiocardiography[14-16], and Doppler echocardiography[4,11]. It is difficult to separate the left atrial reservoir and conduit functions in studies based on left ventricular diastolic function. However, DSA enabled direct analysis of the left atrial function during the cardiac cycle. The left atrium showed a bimodal decrease in area during left ventricular diastole (passive atrial emptying and active atrial contraction)[3,6,7] (**Figs. 2, 3, 5**), and these changes seemed to reflect the reservoir and pump functions of the left atrium. The left atrium showed a slight increase in area during atrial diastasis in the AP patients, but not in the OMI patients (**Figs. 2, 3, 5**). Therefore, the atrial reservoir function in early left ventricular diastole (%LA1−%LA2) was separated from its reservoir function prior to left atrial contraction (%LA3−%LA2).

Passive left atrial emptying for the OMI group was less than that for the AP group (**Fig. 5**). It was also decreased in patients with left ventricular dysfunction who had a decrease in LVEF (**Fig. 6**) or an elevated LVEDP. This change in atrial emptying seemed to reflect changes in early left ventricular diastolic function in the patients with left ventricular systolic dysfunction[14,16].

Active atrial contraction, which occurs during left ventricular end-diastole, did not decrease in the patients with left ventricular dysfunction. The ratio of left atrial passive emptying to active contraction [(100−%LA2)/(%LA3−%LA4)] had a positive correlation with LVEF (**Table 2**). This suggested the increased importance of active atrial contraction in the patients with left ventricular dysfunction[1-3].

The minimum left atrial area after active contraction (%LA4) showed a positive correlation with both LVEDP and PAWP (**Figs. 8, 9**), supporting the hypothesis that Starling's law is operative not only in the left ventricle but in the left atrium as well[1,3].

In the present study, we evaluated the difference of left atrial function between the AP and OMI groups, and also analyzed left atrial function in 22 patients. However, the left atrial function of normal subjects without myocardial infarction or chest pain was not assessed in this study. Comparison of left atrial function of patients with heart disease and of normal subjects should be made in the future.

Clinical implication

DSA facilitated visualizing the entire left atrium and evaluating changes in its shape, size and function during the entire cardiac cycle in patients with ischemic heart disease. A bimodal decrease in the left atrial area (passive emptying and active contraction) was clearly demonstrated in these patients, all of whom were in sinus rhythm.

In the patients with left ventricular dysfunction due to ischemic heart disease, passive left atrial emptying was decreased and the importance of active left atrial contraction (pump function) was increased.

DSA proved to be a useful method for evaluating the left atrium and its functions.

要　　約

経静脈性 DSA による虚血性心疾患における左房機能の解析

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虚血性心疾患患者に，経静脈性 digital subtraction angiography (DSA) を行ない，左房の全体像を描出し，心周期に伴う形態変化を観察し左房機能を解析した．僧帽弁疾患がない洞調律の虚血性心疾患(男22例，平均年齢54.5±8.6歳)を対象とした．内訳は陳旧性心筋梗塞11例 (OMI群) と心筋梗塞のない胸痛患者11例 (AP群) の2群である．Continuous mode を用い DSA を行なった．上大静脈に留置したカテーテルから造影剤35 ml を毎秒 18 ml で注入し，右前斜位30度で毎秒30フレームの差分画像を得た．左房と左室の輪郭をトレースし，その面積を求め，面積変化を百分率で表わして検討した．左室駆出分画 (LVEF) は densitometry により算出した．16例では心臓カテーテル検査を実施し，左室拡張終期圧 (LVEDP)，平均肺動脈楔入圧 (PAWP) を得た．

DSA により左房の全体像が良好に描出された．時間-面積曲線では，左房面積は左室収縮終期に最大値 (%LA1=100%) をとり，左室拡張早期に受動的減少を示し (%LA2)，左室拡張中期に面積をやや増した後 (%LA3)，左房の能動的収縮により減少し最小値 (%LA4) をとった．すなわち，左房面積は左室拡張期に二段階の減少 (受動的および能動的) を示した．

受動的収縮 (%LA1−%LA2) は OMI 群で AP 群より低値を示し (6.3±3.6 対 13.3±4.8%, $p<0.01$)，全症例においては LVEF と正の相関 ($r=0.70$, $p<0.001$)，LVEDP と負の相関 ($r=-0.58$, $p<0.05$) を示した．能動的収縮 (%LA3−%LA4) は2群間で有意差を認めず(OMI群:26.0±5.7%，AP群:28.2±8.4%)，全症例においても LVEF, LVEDP と相関を示さなかった．受動的収縮と能動的収縮の比 [(%LA1−%LA2)/(%LA3−%LA4)] は LVEF と正の相関を示した ($r=0.63$, $p<0.01$)．LVEF 低下例では左室拡張早期機能も障害され，左房の能動的収縮が相対的に高まることが示された．%LA4 は LVEDP および PAWP と正の相関を示した(それぞれ $r=0.65$, $r=0.63$, $p<0.01$)．DSA により左房の全体像がよく描出でき，左房の形態と機能の解析が可能であった．

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