Disruption in the Temporal Sequence of Regional Ventricular Contraction

I. Characteristics and Incidence in Coronary Artery Disease

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SUMMARY While spatial asynchrony at end-systole has been well characterized in patients with coronary artery disease, assessment of regional asynchrony has been hampered by technical constraints. We developed a computer-assisted method for analyzing regional asynchrony from the equilibrium (ECG-gated) radionuclide ventriculogram. Twenty patients with normal contrast left ventriculograms (nine with a normal coronary arteriogram [group 1] and 11 with coronary artery disease [group 2]) and 20 patients with asynchrony during contrast ventriculography (group 3) were studied. The earliest evidence of regional asynchrony occurred in early systole. Regional ejection fraction at one-third systole was 0.32 ± 0.02 (mean ± SEM) in group 1, 0.22 ± 0.01 in group 2 (p < 0.001) and 0.12 ± 0.01 in asynergic regions in group 3 patients (p < 0.001). In group 3, severe forms of regional asynchrony appeared in both early systole and early diastole; five patients (25%) had early systolic paradox, 13 (65%) had regional prolongation of peak ejection fraction and 16 (80%) had reduced percent peak ejection fraction at global end-systole. It appears, therefore, that there is progressively increasing regional asynchrony in patients with increasing severity of coronary artery disease.

A PRINCIPAL FACTOR influencing left ventricular contraction is the adequacy of myocardial blood flow. Tennant and Wiggers were the first to show that a reduction in blood flow after coronary artery ligation resulted in paradoxical expansion of the ventricle during systole. Abnormalities in left ventricular contraction have been further categorized as akinesia, hypokinesis and dyskinesia, depending on the severity of asynergy when wall motion at end-diastole and end-systole have been compared. Asynchrony, a fourth pattern of altered ventricular contraction described by Herman et al., indicates an alteration in the temporal sequence in ventricular contraction. For the most part, quantitative investigations of regional ventricular performance have been limited to two points on the left ventricular volume curve (usually end-systole and end-diastole), because quantitative analysis of regional performance for the entire cardiac cycle is exceedingly time-consuming with standard angiographic techniques. Yet there is reason to suspect that ventricular contraction and the alterations in contraction that occur as a result of coronary artery disease and other pathologic processes might best be understood in terms of the sequential changes in regional myocardial contraction and relaxation that occur throughout the cardiac cycle.

With the development of gated equilibrium radionuclide ventriculography and with the validation of regional ejection fraction as a quantitative index of left ventricular performance, it is possible to quantitatively assess regional left ventricular performance at multiple intervals during the cardiac cycle. In the present study, we analyzed and characterized regional asynchrony, and determined its incidence in patients with coronary artery disease.

Materials and Methods

Patient Population

The study group consisted of 40 consecutive patients referred to the Peter Bent Brigham Hospital for
evaluation of chest pain suggestive of angina pectoris who underwent routine diagnostic cardiac catheterization and agreed to subsequent equilibrium radionuclide ventriculography. The equilibrium radionuclide ventriculogram was performed within 24 hours of the contrast study in all cases.

Radionuclide Data Acquisition

Red blood cells were labeled by injection of unlabeled stannous pyrophosphate (Pyrolite, New England Nuclear Corporation) into an antecubital vein, followed 15–20 minutes later by 25 mCi of technetium-99m as pertechnetate.\textsuperscript{10, 11} Gated radionuclide ventriculograms were obtained using an Anger scintillation camera with a high-sensitivity, 30°, slant-hole collimator (Engineering Dynamics Corporation, Lowell, Massachusetts),\textsuperscript{11} using a technique described previously.\textsuperscript{8} Only cycles within a cardiac cycle length tolerance of \( \pm 100 \) msec were analyzed.

An automated computer algorithm was used to define background correction regions and to position them relative to the hand-drawn left ventricular perimeter (fig. 1). This algorithm has been described in detail elsewhere.\textsuperscript{8} Basically, three rectangular background regions were defined, each three matrix cells wide and having a length equal to one-half the longest vertical dimension of the end-diastolic left ventricular cavity. The background regions were positioned one cell removed from and parallel to the margins of an imaginary rectangle excribed about the ventricular perimeter.

The algorithm also divided the left ventricular perimeter into eight subdivisions by excribing a rectangle around the hand-drawn left ventricular mask. A left ventricular longitudinal axis was then constructed by connecting midpoints of the basal and apical sides of the excribed rectangle. Three quadrisectioning transverse axes within the original left ventricular perimeter completed demarcation of eight intraventricular subdivisions (fig. 1). Intraventricular regions 2 and 3 correspond to the anteroseptal segment of the left ventricle, regions 4 and 5 correspond to the apical segment and regions 6 and 7 correspond to the inferoposterior segment.\textsuperscript{8, *}

The background correction for the regions of the left ventricle was estimated using a weighted average of the counts per cell in each of the three background regions obtained in the end-systolic frame.\textsuperscript{9}

For each 50-msec frame of the composite cardiac cycle, global and regional ejection fraction was determined from the equation:

\[
EF_n = \frac{C_{\text{ED}} - C_n}{C_{\text{ED}} - C_B} \quad (1)
\]

where \( EF_n \) is the fraction of blood ejected from the left ventricle (global \( EF_n \)) or from a region occupied by an anatomic segment of the left ventricle (regional \( EF_n \)) at frame \( n \) after end-diastole. (The conventional global left ventricular ejection fraction is therefore the largest global \( EF_n \) occurring during the cardiac cycle and occurs at global end-systole.) \( C_{\text{ED}} \) is the counts within

the left ventricle or anatomic segment of the left ventricle at end-diastole; \( C_n \) is the counts within the ventricle or region at frame \( n \); \( C_B \) is the background counts for the left ventricle or region of the left ventricle. Curves were then constructed to define the change in \( EF_n \) for the left ventricle and for the six intraventricular regions during the cardiac cycle.

The following indexes of regional asynchrony were defined (fig. 2).

Indexes of Early Systolic Performance

Early systolic paradox (ESP) (negative regional ejection fraction):

\[
ESP = \frac{r_iC_{\text{ED}} - r_iC_n}{r_iC_{\text{ED}} - r_iC_B} \quad (2)
\]

if \( r_iC_{\text{ED}} < r_iC_n \) and where \( r_iC_{\text{ED}} \) is the counts in region \( i \) at end-diastole, \( r_iC_n \) is the counts in that region \( n \) frames after end-diastole and measured one (50–100 msec), two (100–150 msec) and three (150–200 msec) frames after global end-diastole and \( r_iC_B \) is the background counts.

Ejection fraction at one-third systole in region \( r_i \) (\( r_iEF_{1/3} \)):

\[
r_iEF_{1/3} = \frac{r_iC_{\text{ED}} - r_iC_{1/3}}{r_iC_{\text{ED}} - r_iC_B} \quad (3)
\]

where \( C_{\text{ED}} \) is the counts in end-diastole in region \( i \), and \( r_iC_{1/3} \) is the counts one-third of the way between end-diastole and end-systole in region \( r_i \).
Regional asynchrony in CAD/Holman et al.

Figure 2. (A) Regional ejection fraction at one-third systole ($r_{1/3}$EF) is 0.20 for region A and -0.10 for region B. Early systolic paradox (ESP) is present 50, 100 and 150 msec after end-diastole in region B, because the regional ejection fraction is negative at those times (-0.50, -0.10 and -0.05, respectively). A = region A; B = region B; dashed line = entire left ventricle. (B) In region A, ejection fraction at global end-systole equals peak ejection fraction for that region. The percent of peak regional ejection fraction at end-systole ($\% r_{1}EF_{p}$) is therefore 100%. In region B, peak ejection fraction occurs at (3) while ejection fraction at end-systole occurs at (2); therefore, $\% r_{b}EF_{p}$ is (2)/(3). (C) Peak ejection occurs in region A at end-systole; peak ejection time (PET) = 0 msec and PET/gET = 0. In region B, peak ejection (3) occurs 200 msec after end-systole. PET = 200 msec. Because ejection time for the entire left ventricle (gET) = 300 msec, PET/gET = 0.67. (D) Early diastolic relaxation (EDR) is the ejection fraction occurring between end-systole and the frame 50 msec after end-systole. In the normal region A,

$$EDR = \frac{r_{A}EF_{ES} - r_{A}EF_{ES+1}}{r_{A}EF_{p}} = \frac{0.60 - 0.55}{0.60} = 0.08$$

where $r_{A}EF_{ES}$ is the ejection fraction in region A at end-systole (1); $r_{A}EF_{ES+1}$ is the ejection fraction one frame (50 msec) later (5); and $r_{A}EF_{p}$ is the peak ejection fraction in that region. In region A, $r_{A}EF_{p} = r_{A}EF_{ES}$ and $r_{A}EF_{p}$ also occurs at (1). In region B, $r_{b}EF_{ES} = (4)$, $r_{b}EF_{p} = (4)$, and $r_{b}EF_{ES+1} = (6)$. Therefore,

$$EDR = \frac{0.25 - 0.05}{0.25} = 0.80$$

Similarly, for ejection fraction at one-third systole for the entire left ventricle ($gEF_{1/3}$):

$$gEF_{1/3} = \frac{C_{ED} - gC_{1/3}}{C_{ED} - C_{B}}$$

where $gC_{1/3}$ is the global counts at one-third systole.

Indexes of Early Diastolic Performance

The percent of peak regional ejection fraction at global end-systole ($\% r_{1}EF_{p}$):

$$\% r_{1}EF_{p} = \frac{r_{1}EF_{ES}}{r_{1}EF_{p}} \times 100$$
where \( r_i \text{EF}_{ES} \) is the ejection fraction at end-systole in region \( r_i \) and \( r_i \text{EF}_{p} \) is the highest ejection fraction in that region, occurring at any time after global end-systole.

Peak ejection time (PET): the time after global end-systole to reach \( r_i \text{EF}_{p} \). To compare patients whose heart rates vary, PET was normalized by dividing by the patient’s ejection time (gET), the time from global end-diastole to global end-systole. Thus,

\[
\frac{\text{PET}}{\text{gET}}
\]

Early diastolic relaxation (EDR):

\[
\text{EDR} = \frac{r_i \text{EF}_{ES} - r_i \text{EF}_{ES + 1}}{r_i \text{EF}_{p}}
\]

where \( r_i \text{EF}_{ES + 1} \) is the ejection fraction in region \( i \) one frame (50 msec) after global end-systole. Only regions in which \( \text{EF}_{p} \) occurred at global end-systole or earlier were considered.

The lower of the two values for ESP, \( \text{EF}_{1/3} \), \( \%r_i \text{EF}_{p} \) and EDR, and the higher of the two values for PET/gET in each anatomic segment (anteroseptal, infero-posterior and apical) were used for statistical analysis because the contraction abnormalities may have involved only a portion of an anatomic segment and may not have been detected if averaged with an adjacent, normally contracting region.

**Contrast Angiography Analysis**

For each contrast ventriculographic study, hand-traced right anterior oblique silhouettes of left ventricular end-diastole and end-systole were obtained by an independent observer from projected cineangiograms (16 mm or 35 mm) using previously described techniques. Global ejection fraction was determined for each ventriculogram by the area-length method of Dodge and associates. For 20 patients with biplane ventriculograms, ejection fraction was calculated using the derived minor axis from each of the right and left anterior oblique views and the longest major axis. For 20 patients with single-plane right anterior oblique ventriculograms, ejection fraction was similarly calculated assuming symmetry about the minor axis.

Regional ventricular function was assessed by determining left ventricular hemispheric shortening using a previously described technique. Evaluation of superimposed end-diastolic and end-systolic silhouettes allowed identification and localization of abnormally contracting wall segments. Systolic hemispheric shortening of less than 25% was considered abnormal (asynergy). Asynergy was classified as mild hypokinesis (> 15% shortening), severe hypokinesis (5–15% shortening), or akinesis (< 5% shortening and/or presence of a nonmoving or paradoxically moving wall segment). Hemispheric shortening greater than 25% was defined as normokinesis. Presence of both a normokinetic and asynergic hemispheric within a ventricular region was interpreted as asynergy. Coincidence of hypokinetic and akinetic segments within a single region was interpreted as akinesis.

Statistical analysis was performed using the \( t \) test for unpaired data. Data are presented as the mean ± SEM unless otherwise stated.

**Results**

Nine of the 40 patients in this study had normal coronary arteriograms (group 1), 11 had coronary artery stenoses of 50% or greater luminal narrowing but normal contrast ventriculograms at rest (group 2), and 20 had evidence of asynergy on contrast left ventriculography (group 3). All nine patients in group 1 had normal contrast left ventriculograms. Of the 11 patients in group 2, three had one-vessel coronary artery disease, five had two-vessel disease and three had three-vessel disease. In group 3, asynergy was present in the anteroseptal segment in 10 patients, in the apical segment in 17 patients and in the infero-posterior segment in 17 patients. No patients in groups 1 and 2 and all 20 patients in group 3 had a documented myocardial infarction. There were no conduction delays in group 1 patients. One patient in group 2 had an incomplete left bundle branch block and seven patients in group 3 had conduction delays (four with intraventricular conduction delays, one with incomplete left bundle branch block and two with complete left bundle branch block).

**Global Left Ventricular Function**

Global left ventricular ejection fraction determined by radionuclide ventriculography was 0.62 ± 0.03 in group 1 patients, 0.62 ± 0.02 in group 2 patients, and 0.36 ± 0.04 in group 3 patients. Global ejection fraction at one-third systole was 0.33 ± 0.02 in group 1 patients, 0.27 ± 0.01 in group 2 patients (\( p < 0.025 \)) and 0.17 ± 0.02 in group 3 patients (\( p < 0.001 \)).

**Contraction During Early Systole**

Patients in group 1 (normals) had prompt, vigorous contraction throughout the left ventricle soon after the onset of systole. Mean regional ejection fraction in all three regions of the left ventricle at one-third systole was 0.32 ± 0.02 (fig. 3) (using only the lower of the two regional ejection fraction values from each of the three anatomic segments). Regional contraction was less vigorous at one-third systole in group 2 patients. Their mean regional ejection fraction at one-third systole for all left ventricular regions was 0.22 ± 0.02 (\( p < 0.001 \)). In patients with asynergy (group 3), regional ejection fraction at one-third systole was 0.22 ± 0.02 in hypokinetic segments (\( p < 0.001 \) vs group 3 normokinetic segments) and 0.01 ± 0.02 in akinetic segments (\( p < 0.005 \) vs group 3 hypokinetic segments).

Nine of 11 patients in group 2 (82%) had at least one regional ejection fraction at one-third systole outside of the normal range (0.35 ± 0.08 [SD]). Eighteen of 20 patients in group 3 (90%) had at least one regional ejection fraction at one-third systole outside of the normal range. In group 3 patients, regional ejection...
fraction at one-third systole was below the normal range in three of 16 normokinetic segments (19%), 16 of 19 hypokinetic segments (84%) and 24 of 25 akinetic segments (96%).

Abnormalities in early systolic contraction were typically regional. Thus, in group 2, abnormal early systolic ejection was seen in one anatomic segment in six patients, in two segments in two, and in three segments in only one patient.

With increasing abnormalities of the contrast ventriculogram in patients with coronary artery disease, the severity of the early systolic contraction abnormalities also increased. Only six of 76 segments (7.9%) that were normokinetic by contrast ventriculography showed early systolic paradox two (100-150 msec) or three (150-200 msec) frames after end-diastole. In group 3 patients, five of 19 hypokinetic segments (26.3%) and 12 of 25 akinetic segments (48.0%) showed early systolic paradox. The severity of paradox when present was greatest in the akinetic segments (−0.05 ± 0.02 in normokinetic segments with early paradox vs −0.08 ± 0.06 in hypokinetic segments and −0.14 ± 0.03 in akinetic segments). Of the segments showing early paradox in group 3 patients, eight still showed paradox at end-systole and nine had positive regional ejection fraction at end-systole.

Contraction During End-systole and Early Diastole

Regional contraction at end-systole was synchronous in group 1 patients (fig. 4). The mean normalized time for each region to reach peak ejection fraction after global end-systole (PET/gET) was 0.06 ± 0.03 of the global ejection time (fig. 5). Thus, regional peak ejection occurred very close to global end-systole. No region in group 1 patients required more than 100 msec after global ejection fraction to reach peak ejection fraction. Regional contraction in group 2 patients was also synchronous at end-systole (0.06 ± 0.02). In patients with asynergy, the time after global end-systole for normokinetic regions to reach maximum ejection fraction was 0.08 ± 0.04 of global ejection time, which is similar to PET/gET in patients in groups 1 and 2. However, hypokinetic and akinetic segments were significantly delayed, and reached peak contraction well into global diastole (0.28 ± 0.05 and 0.41 ± 0.05 of the global ejection time, respectively) (fig. 6). PET/gET was prolonged (> 2 sd from the mean value for group 1 patients) in one of 16 nor-
mokininetic (6%), eight of 19 hypokinetic (42%) and 15 of 25 akinetic segments (60%) in group 3 patients. No patients in groups 1 and 2 and 13 of 20 patients in group 3 (65%) had abnormally elevated PET/g ET.

Synchrony in normokinetic segments was also observed using %rEFp as an index (fig. 7). In group 1 patients, regional ejection fraction was 95.3 ± 0.8% of its peak at global end-systole. Similarly, in group 2 patients, regional ejection fraction was 95.7 ± 0.9% of peak at global end-systole. In patients with asynergy (group 3), regional ejection fraction was 96.8 ± 1.4% of peak at global end-systole in normokinetic segments. However, in asynergic regions, %rEFp was significantly reduced at end-systole. This reduction was significantly greater in akinetic than in hypokinetic segments (54.0 ± 7.6% vs 84.2 ± 5.2%, p < 0.005). Percent of peak regional ejection fraction at global end-systole was reduced (< -2 SD from the normal mean) in none of nine group 1 patients, in one of 11 group 2 patients (9%) and in 16 of 20 group 3 patients (80%). In group 3, %rEFp was reduced in two of 16 normokinetic segments (12%), eight of 19 hypokinetic segments (42%) and 18 of 25 akinetic segments (72%). The reduction in %rEFp was usually due to delayed regional contraction. Thus, in 19 of 31 regions with significantly reduced %rEFp (61.3%), PET/g ET was significantly increased.

Early diastolic relaxation was 0.10 ± 0.02 in group 1, 0.11 ± 0.02 in group 2 and 0.15 ± 0.08 in group 3 patients (p = NS). Only two patients, both in group 3, had regional early diastolic relaxation values more than 2 SD above the mean value.

Paradox at end-systole was present in five patients (six anatomic regions). In four of these regions, some contraction occurred after end-systole, and ejection fraction during early or mid-diastole was positive (less blood volume than at end-diastole) (range 0.05 –0.19). In two regions (one patient), paradox continued throughout diastole and regional ejection fraction was negative during diastole as well as at end-systole. This patient had severe diffuse left ventricular asynergy and a global ejection fraction of 0.11. In another patient, ejection fraction in the apex was negative in early systole and during diastole, but was zero at end-systole (blood volume equal to that at end-diastole). In four of these six patients, presence of scar tissue was confirmed at autopsy in one patient, at aneurysmectomy in two and at surgery in one. Five of the six patients had an aneurysm, which was confirmed by contrast ventriculography in two patients, at surgery in two and at autopsy in one.

The Effect of Conduction Delays on Asynchrony

In group 3, patients with conduction delays tended to have more severe asynchrony than patients with normal conduction, but the differences were not significant. (gEF1/3 0.12 ± 0.02 vs 0.19 ± 0.02, p = NS; PET/g ET 0.52 ± 0.07 vs 0.35 ± 0.07, p = NS). Group 3 patients with conduction delays also tended to have more severe reductions in overall performance (global ejection fraction 0.26 ± 0.04 vs 0.41 ± 0.04, p = NS). Conduction delays did not necessarily accompany early diastolic asynchrony. Thus, group 3 patients without conduction defects had significant early diastolic asynchrony (PET/g ET 0.35 ± 0.07 vs 0.17 ± 0.04 for groups 1 and 2, p < 0.005).

Relationships Between Early Systolic and Early Diastolic Abnormalities

While early systolic abnormalities were present in most patients with coronary artery disease, previous infarction was usually required before early diastolic abnormalities were demonstrated. Thus, while early regional ejection fraction at one-third systole was reduced in 16 of 33 anatomic segments (48.5%) in patients with coronary artery disease (group 2), only one of 33 of these segments (3%) was abnormal during early diastole. In group 3 patients, 10 of 44 asynergic segments (22.7%) had significantly reduced regional ejection during early systole but no abnormalities of early diastole. When the indexes of early diastolic function were abnormal, regional ejection fraction during early systole was usually reduced (30 of 32 segments [93.8%]).

Discussion

Left ventricular movement proceeds uniformly and continuously throughout the cardiac cycle in normal man. The effects of coronary artery disease on regional ventricular function have been studied by subjective analysis of the cineventriculogram or quantitatively at discrete points in the cardiac cycle (usually at end-diastole and end-systole). As a result, only effects due to advanced coronary artery disease that occur at end-systole have been studied extensively. In this study, equilibrium radionuclide ventriculography was adapted to provide quantitative information on regional ventricular contraction throughout the cardiac cycle.

The results of the present study confirm earlier reports that the earliest demonstrable effect of coronary artery disease on left ventricular performance occurs during early systole. Almost all patients
with coronary artery disease had depressed performance in the first third of systole. Global left ventricular ejection fraction during early systole is reduced in most patients with coronary artery disease, including the majority of patients with normal ventricular contraction at end-systole. This phenomenon is regional, occurring most frequently in regions with significant coronary stenoses. Most patients with coronary artery disease but without asynchrony when wall motion is assessed at end-systole have abnormalities in early systole limited to one or two anatomic segments of the left ventricle.

Multiple factors are presumably responsible for these observations. There is some variability in the time sequence of regional left ventricular contraction even in normal subjects. There is also considerable individual variability in the time sequence of activation of various regions of the ventricle. This presumably relates to variability in the sequence of electrical activation, or other considerations, such as ventricular volume and fiber orientation, that play important roles in determining ventricular geometry.

The changes in the ejection pattern shown in the current study in patients with coronary artery disease are qualitatively different from effects due to patient variability. Abnormal regions were not delayed as much in the onset of ejection as they were in the completion of ejection. The degree of ejection of abnormal segments was typically less than that of normal segments early in systole, although by end-systole many of the abnormal regions were able to achieve normal peak ejection fractions. This undoubtedly relates to the high intraventricular pressure early in systole, with resulting high wall tension. Myocardial regions perfused by stenotic vessels have limited functional reserve, and their degree of shortening is determined by the relative afterload. Thus, it is not unreasonable to expect compromised left ventricular regions to delay active shortening until wall tension has begun to decrease later in systole. While the overall degree of regional contraction may be normal, the pattern of shortening is not.

With increasingly severe manifestations of coronary artery disease, accompanied in our patients by a prior episode of myocardial necrosis, contraction abnormalities appear in early diastole. Regional ventricular functional is delayed, reaching maximal ejection during isovolumetric relaxation, when the remaining ventricle has begun to relax. These segments fail to attain maximum contraction at global end-systole. The contribution of these regions to ventricular ejection is reduced, limited by the extent of ejection at end-systole rather than by the peak ejection fraction in that region.

With the development of early diastolic asynchrony, the severity of the early systolic abnormalities increases. Not only is early systolic ejection fraction reduced in almost all of these segments, but also early systolic paradox is observed in many of them. In the majority of segments with early systolic paradox, the paradox is reversed later in the cardiac cycle. End-systolic measurements of ventricular contraction will indicate normal contraction or, at most, hypokinesis in many of these regions.

With even more severe left ventricular damage, paradox beginning in early systole extends into diastole. Even with end-systolic paradox, some regions contract during early diastole, suggesting that these anatomic segments contain a mixture of fibrous scar tissue and viable muscle. With more extensive fibrosis, paradox is seen even during early diastole. Some asynergic segments that are paradoxical in both early systole and early diastole may show an increase in ejection fraction during end-systole, with the ejection fraction rising to zero at end-systole. This phenomenon probably represents passive movement of that ventricular segment at end-systole caused by contraction of the remaining ventricle.

It appears, therefore, that there is progressively increasing regional asynchrony in patients with increasing severity of coronary artery disease (fig. 8). Many patients with coronary artery stenoses will have what appears to be normal left ventricular wall motion when end-diastole and end-systole are compared, but who nonetheless have impaired performance because they have reduced ejection early in systole. When myocardial necrosis develops, more severe abnormalities of regional asynchrony appear, with overt asynchrony at end-systole, early systolic paradox or delayed contraction. Extensive areas of myocardial scar, often with the clinical features of an aneurysm, are frequently associated with the most severe abnormalities of asynchronous regional left ventricular wall contraction. The changes in the ejection pattern shown in the current study in patients with coronary artery disease are qualitatively different from effects due to patient variability. Abnormal regions were not delayed as much in the onset of ejection as they were in the completion of ejection. The degree of ejection of abnormal segments was typically less than that of normal segments early in systole, although by end-systole many of the abnormal regions were able to achieve normal peak ejection fractions. This undoubtedly relates to the high intraventricular pressure early in systole, with resulting high wall tension. Myocardial regions perfused by stenotic vessels have limited functional reserve, and their degree of shortening is determined by the relative afterload. Thus, it is not unreasonable to expect compromised left ventricular regions to delay active shortening until wall tension has begun to decrease later in systole. While the overall degree of regional contraction may be normal, the pattern of shortening is not.

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**Figure 8. Alterations in the temporal sequence of left ventricular contraction.**
motion, and paradox is evident throughout systole. Conduction delays are not a prerequisite for regional asynchrony, because both early systolic and early diastolic abnormalities occurred in most of our coronary artery disease patients with normal conduction.

A quantitative assessment of the temporal changes in left ventricular contraction is made possible by adapting the equilibrium-gated radionuclide ventriculogram to obtain quantitative measurements of regional ventricular performance throughout the cardiac cycle. Because regional ejection fraction is based on changing count rates, a three-dimensional perspective of changes in left ventricular blood volume is obtained. Regional ejection fraction is independent of the constraints of contrast ventriculography, which assesses wall motion only at points of the ventricle tangential to the x-ray beam.

One of the major difficulties with any measurement of regional wall motion, and only partially obviated by our technique, is the need for a fixed reference system for the measurement of relative wall motion.24 Various strategies for defining an appropriate reference system for analyzing regional wall motion during contrast ventriculography have been suggested,25-27 but virtually all are limited by the fact that in the contrast-filled left ventricle no single fixed point on the ventricular wall can be tracked throughout the cardiac cycle, except possibly the apex and aortic valve midpoint.24 The radionuclide method of the current study offers the distinct advantage of not being dependent on precise endocardial identification throughout the cardiac cycle, because regional function is determined by analysis of regional time-activity curves, and thus is independent of geometric constraints.

Regional ejection fraction at end-systole has been validated as a quantitative index of left ventricular performance.9 The extension of this technique to evaluate ejection throughout the cardiac cycle provides, in addition, a method for assessing regional asynchrony quantitatively. It has three advantages over global measurements of left ventricular performance obtained either with contrast ventriculography or with more traditional approaches to radionuclide ventriculography: 1) Asynchrony can be localized and correlated with the presence of end-systolic asynergy. 2) The sensitivity for the detection of contraction abnormalities is increased. 3) An index of relative ventricular contractility can be obtained.

Ventricular performance is dependent not only on the inotropic state of the myocardial contractile fibers, but also on preload, afterload and ventricular geometry.28 As a result, noninvasive global indexes such as ejection fraction, mean normalized systolic ejection rate and mean velocity of circumferential fiber shortening do not measure the contractile state of the human heart distinct from the effects of the loading condition of the ventricle.4 Intraventricular pressure measurements would be necessary to obtain a truly quantitative index of left ventricular contraction. However, because the regional indexes of asynchrony described in this study are normalized to their corresponding global measurement, they represent a relative index of contractility. While an absolute measurement of contraction is still not possible, contraction in a given left ventricular segment can be compared with that in other segments in the same patient. This characteristic of the regional ejection fraction technique has enabled us to investigate the characteristics and prevalence of left ventricular asynchrony in patients with coronary artery disease.

This study provides a framework for the quantitative assessment of the disruption in the temporal sequence of regional ventricular contraction. These indexes can now be applied to coronary artery disease patients during physiologic stress such as exercise, during pharmacologic interventions and during acute phases of their disease, such as acute myocardial infarction and angina pectoris.

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Comparison of Early Systolic and Holosystolic Ejection Phase Indexes by Contrast Ventriculography in Patients with Coronary Artery Disease

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SUMMARY To compare the discriminant ability of early systolic and holosystolic ejection phase indexes to detect abnormalities of left ventricular performance, the contrast ventriculograms of 20 control patients and 55 patients with coronary artery disease (at least 70% stenosis of one or more major coronary arteries) were analyzed. All subjects were studied to evaluate chest pain, and none was taking propranolol or anti-hypertensive drugs. Several ejection phase indexes were evaluated, using holosystole, the first third of systole and the first half of systole. In the patients with coronary disease, 14 (25%) had one-vessel disease, 13 (24%) had two-vessel disease and 28 (51%) had three-vessel disease. In general, the ejection fraction was more useful than indexes based on velocity of ejection. Ejection fraction was lower in the coronary patients than in normal subjects for holosystole (0.62 ± 0.14 vs 0.70 ± 0.08, p < 0.01), for the first third of systole (0.20 ± 0.06 vs 0.36 ± 0.05, p < 0.01), for the first half of systole (0.24 ± 0.09 vs 0.53 ± 0.05, p < 0.001). Fourteen patients with coronary artery disease (25%) had a depressed holosystolic ejection fraction, 36 (65%) had a depressed first-half ejection fraction and 52 (94%) had a depressed first-third ejection fraction. We conclude that early ejection phase indexes, particularly the first-third ejection fraction, are more useful than holosystolic indexes in identifying resting abnormalities of left ventricular function.

EJECTION PHASE INDEXES of left ventricular performance are often more useful in discriminating normal from abnormal function than indexes derived from the isovolumic phase of contraction.1,2 In patients with coronary heart disease, wall motion abnormalities may be present at midsystole without being apparent at the end of systole,3 observations that were extended in a study by Johnson et al.4 to include an assessment of the volume of blood ejected during the first third of systole. These studies suggested that a variety of measures of the early ejection phase often are abnormal, even when all of the holosystolic indexes are normal. To further compare the relative power of early systolic and holosystolic indexes to detect ventricular dysfunction, and to elucidate which period during systole is most useful, we analyzed the contrast ventriculograms in 20 control subjects and 55 patients with coronary heart disease.
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