Congenital Absence of the Left Circumflex Coronary Artery in the Systolic Click Syndrome


SUMMARY

The anatomy of the coronary artery circulation was examined by means of selective coronary arteriography in 19 patients, evaluated because of disabling chest pain and ECG abnormalities, with typical clinical findings of the systolic click syndrome (SCS). In 17 (89.5%), the left circumflex coronary artery (LCCA) was absent; a single marginal branch arose from the left main vessel, but no vessel was present in or near the atroventricular (A-V) groove. In contrast, the LCCA was identified in 74 of 78 control patients (94.9%) considered to have representative normal distribution of coronary artery branches. All but two patients with SCS exhibited reduced contraction of the segment of left ventricular (LV) myocardium surrounding the mitral valve ring (extent of systolic diameter decrease 1.4 ± 3.1% vs normal 31.8 ± 3.4%, P < 0.001), as well as of the LV inflow tract (diameter decrease 16.2 ± 2.5% vs normal 38.6 ± 1.8% P < 0.001); both of these regions of the left ventricle derive their vascular supply from the LCCA. An identical segmental LV contraction disorder was observed in seven patients with functionally single vessel occlusive coronary artery disease involving the LCCA. An incidental finding in this study was a relatively high incidence of absent LCCA (42%) in 19 patients with atypical angina and normal coronary arteriograms. It is concluded that a congenital anomaly of the coronary circulation, with absent LCCA, may be responsible for segmental myocardial dysfunction in some patients with SCS. In turn, this segmental contraction disorder may determine functional abnormality of the mitral valve apparatus.

Previous studies in our laboratories have shown that patients with the systolic click syndrome exhibit a characteristic disorder of left ventricular contraction, with impaired shortening of the inflow tract and, in many instances, systolic expansion of the region of myocardium surrounding the mitral valve ring. The presence of a segmental myocardial abnormality appears to provide a plausible explanation for the occurrence of regional ECG abnormalities, as well as arrhythmias commonly observed in these patients in the absence of evidence of significant mitral valve dysfunction, and may also account for the late systolic timing of mitral incompetence in patients without obvious mitral leaflet abnormality. The possibility was considered that this segmental myocardial contraction disorder, in turn, might be related to an abnormality of the coronary circulation. Accordingly, the anatomy of the coronary circulation was examined by means of selective coronary arteriography in 19 patients with typical manifestations of the systolic click syndrome, and these findings were correlated with alterations in the geometry of ventricular contraction. Similar studies were also carried out in a group of 104 patients who underwent coronary arteriography because of chest pain thought to be angina. The latter group included 19 patients in whom no occlusive coronary disease was demonstrated, as well as seven patients who provided the opportunity to examine the alterations in left ventricular contraction associated with isolated artherosclerotic occlusion of the circumflex coronary artery.

Methods

Nineteen patients (two males, 17 females) ranging in age from 25 to 64 years (mean 46.7 years) with typical clinical manifestations of the systolic click syndrome were included in the present study. These 19 patients represented the minority of our clinical experience in whom the severity of cardiac symptoms, particularly chest pain, required definitive diagnosis and exclusion of coronary artery disease by invasive cardiac study. Each patient reported disabling cardiorespiratory symptoms, including protracted episodes of substernal and left chest pain, the character of which suggested angina, but which was generally more protracted than the pain associated with arteriosclerotic coronary disease. In addition, pain was not directly related to effort, but occurred at some interval after exercise, and often was precipitated by excitement. No patient had experienced a myocardial infarction, although almost all had been hospitalized for observation because of pain. Other symp-
SYSTOLIC CLICK SYNDROME

Symptoms included dyspnea (11 patients), episodic rapid or irregular heart action (seven patients), and syncope (three patients). None gave a history consistent with previous acute rheumatic fever, and none had experienced significant chest trauma.

All patients exhibited normal blood pressures and were in sinus rhythm. An apical mid or late systolic click was present in 17 patients; in 11 of these patients a late systolic murmur was present which began with the click and extended into the second heart sound. Of the two remaining patients, one exhibited only an intermittent systolic click, while the other had only a late systolic murmur. None exhibited a ventricular filling sound or apical early diastolic rumble to suggest significant mitral regurgitation, and no other valvular abnormalities were detected on examination. No patient had findings suggestive of Marfan's syndrome or gonadal dysgenesis.

Over-all cardiac size and contour were normal in each patient as determined from the chest roentgenogram. The ECG was abnormal in 17 patients, with T wave inversion in leads II, III, and aVF alone (nine patients) or in combination with similar changes in V1 and V6 (six patients), or in leads V1 - V3 (two patients). Echocardiograms were performed in each patient, demonstrating typical posterior mitral leaflet prolapse in only seven instances.

Diagnostic right and left heart catheterization, with left ventricular and selective coronary angiography was carried out in each patient. Left ventricular cineangiograms were performed with injection of radiographic contrast material 0.8-1.0 ml/kg (Hypaque) over a period of 2 sec, using biplane filming in the frontal and lateral projections in 16 patients, and single plane right anterior oblique filming in three patients, at 60-100 frames/sec. The moment of each radiographic exposure was recorded, together with the systemic arterial pressure pulse and ECG, to assure precise identification of end diastole and to document that contractions employed in the analysis of contraction characteristics originated from normal electrical depolarization and were not preceded by extrasystoles.

Left ventricular end-diastolic volume, stroke volume and ejection fraction were derived from measurements of cavity silhouette area and length, corrected for X-ray magnification, using the regression analyses appropriate to biplane and single plane right anterior oblique films. Mitral regurgitant volume was determined by subtracting effective left ventricular stroke volume, derived from an indicator dilution measurement of cardiac output immediately prior to the cineangiogram, from the total left ventricular stroke volume, estimated from the angiogram.

A segmental analysis of left ventricular geometry during contraction was carried out using measurements of dimensions obtained from the cavity silhouette in the lateral or right anterior oblique projections, in a manner described in detail in a previous communication. Briefly, a long axis was drawn from the midpoint of the mitral valve plane to the ventricular apex, and three diameters were then constructed perpendicular to and quadrisecting the long axis. These diameters were designated as proximal (left ventricular inflow), midventricular (minor equatorial), and apical (distal) segment diameter. The mitral valve ring was also measured directly in the lateral projection and its extent of systolic change determined from end-diastolic and end-systolic films. The choice of lateral plane films for these measurements was based first on the general comparability of this view to the right anterior oblique projection used in single plane studies by us and by other investigators, and also on the empirical observation that superimposition of the ventricular cavity on the mitral valve ring, particularly inferiorly, precluded accurate measurement of this diameter in frontal plane films.

Selective coronary arteriograms were exposed in multiple projections to eliminate superimposition of origins of left coronary branches and to visualize the left coronary ostium in profile. The left atrioventricular groove was located by late opacification of the coronary sinus, so that the relation of branches of the left circumflex artery system to the groove could be readily determined.

In order to determine the normal branching pattern of left and right coronary arteries, selective arteriograms were reviewed in 104 patients who were thought to have occlusive major vessel coronary disease, or in whom the study was carried out in the presence of atypical pain to exclude this possibility. Of this group, 19 patients were found to have no occlusive intimal coronary disease. In seven patients, complete occlusion of the left circumflex artery at or near its origin occurred as the sole significant occlusion (six patients) or in association with significant narrowing of the anterior descending vessel (one patient). These seven patients are considered independently, since they provide the opportunity to examine the alterations in left ventricular contraction resulting from acquired loss of blood supply to the periannular left myocardium.

Results

The normal branching pattern of the coronary arterial tree was determined from selective arteriograms in 78 patients in whom angina occurred as the result of occlusive coronary artery disease. In 74 of these patients (94.9%) the left circumflex coronary artery (LCCA) coursed in, or near and parallel to, the atroioventricular groove, extending to or beyond the obtuse margin and giving rise to at least two marginal branches to the lateral and infero-lateral left ventricular (LV) free wall (fig. 1, left panel; fig. 2, left panel). In only four patients (5.1%) was the atroioventricular groove branch of the circumflex system absent. A left dominant circulation, in which the posterior descending artery arose from the left circumflex vessel was present in 15% of those 78 patients.

Patients with the Systolic Click Syndrome (SCS)

In contrast to the normal group, in 17 of 19 patients with SCS (89.5%) no atroioventricular groove branch of the LCCA was identified (fig. 1, right panel); the circumflex artery system was represented by a marginal branch alone (fig. 3), branching either proximally (fig. 2, right panel) or distally (fig. 2, middle panel) over the lateral LV wall. In only two patients with SCS was a normal atroioventricular groove branch of the LCCA seen. The left anterior descending vessel exhibited a normal distribution in all patients. Similarly, right coronary arteriograms showed no differences in branching between the control group and patients with SCS. In particular, no compensatory continuation of the right coronary artery to the infero-posterior
The branching pattern of the left circumflex coronary artery (LCCA) and its anatomic relation to the left atrioventricular groove, as identified by the coronary sinus (CS), is illustrated schematically in a patient with normal coronary anatomy (left) and in the two branching patterns observed in the 17 patients with the systolic click syndrome in the present study in whom the atrioventricular groove branch of the LCCA was absent.

Figure 2

region of the left atrioventricular groove was observed in patients with SCS.

The extent of shortening of the midventricular and apical segment diameters, measured in the lateral or RAO projection, averaged $34.4 \pm 1.9\%$ and $36.8 \pm 2.2\%$, respectively, in patients with SCS, values comparable to those observed in patients with normal LV contraction ($40.3 \pm 2.2\%$ and $46.8 \pm 2.7\%$, respectively). However, shortening of the proximal, or inflow segment diameter was substantially reduced in patients with SCS, averaging $16.2 \pm 2.5\%$, as compared to $38.6 \pm 1.8\%$ in patients with normal LV contraction ($P < 0.001$) (fig. 4). This region of myocardium is that normally supplied by the LCCA. Of interest, the extent of contraction of this segment was normal or only slightly reduced in the two patients with SCS who exhibited a normal A-V groove branch of the circumflex coronary artery (23.0 and 43.5\%). In addition, the contraction characteristics of the perian-

Figure 1

Selecte left coronary angiographic frames exposed in the right anterior oblique projection are illustrated in a patient with normal coronary arterial anatomy (left panel) and in a typical patient with the systolic click syndrome (right panel). Note the absence of the atrioventricular groove branch of the left circumflex artery, readily apparent in the patient with normal branching pattern, in the patient with the systolic click syndrome.

nular myocardium, or mitral valve ring (MVR), were consistently abnormal in patients with SCS, with either reduced contraction (nine patients), or no change or systolic expansion (ten patients); the average systolic change in MVR diameter in this group was $1.4 \pm 3.1\%$ compared to systolic shortening averaging $31.8 \pm 3.4\%$ in patients with normal LV contraction (fig. 5).

Patients with Isolated Arteriosclerotic Occlusion of the Proximal Circumflex Coronary Artery

In seven patients complete occlusion of the LCCA occurred at or near its origin as the result of arteriosclerotic disease. One of these patients also exhibited significant occlusive disease involving the left anterior descending artery, while in the remaining six patients only nonocclusive intimal disease was observed in vessels other than the LCCA. Examination of regional contraction characteristics demonstrated normal shortening of mid-ventricular and apical segment diameters in all but one of these seven patients (27.1 to 42\%, mean 32\%, and 9 to 43\%, mean 31\%, respectively); proximal segment shortening was clearly reduced in four patients, however (4.6 to 22\%, mean 12.9\%), and MVR diameter change was reduced, or the MVR actually expanded, in all seven ($-10.4$ to $+14\%$, mean $-4.8\%$). All of these patients exhibited posterior mitral leaflet prolapse on cineangiography (fig. 6). Five had apical mid-systolic clicks, six had apical late systolic murmurs, and one had a holosystolic murmur of mitral regurgitation.

Patients with Atypical Angina and Normal Coronary Arteries

Nineteen patients evaluated by means of selective

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Selective left coronary arteriograms are shown in the left anterior oblique (left panel) and right anterior oblique (right panel) projections in a patient with the systolic click syndrome.

arteriography because of angina-like chest pain were found to have no evidence of occlusive coronary disease. Pain in these patients was only variably related to effort, and most commonly occurred at some interval after exercise. It tended to occur with emotional stress, and was more protracted than typical angina. Nitroglycerin resulted in pain relief in some patients. All but two had undergone unrevealing evaluation for esophageal and other gastrointestinal disease including the Bernstein test, acid barium esophagram, and oral cholecystogram. Submaximal treadmill exercise testing revealed ECG changes consistent with myocardial ischemia in five patients. None had a systolic apical click.

In this group, eight patients (42.1) had no atrioventricular groove branch of the LCCA, while in the remaining 11 patients coronary arterial branching followed the normal pattern. Six of the eight patients

Figure 4
The average extent of shortening of proximal, mid-ventricular, and apical left ventricular chamber diameters are shown in a group of patients with normal ventricular contraction (left panel) and in the 19 patients with the systolic click syndrome (SCS, right panel). The standard deviation for each measurement is indicated by the vertical bars.
in whom the LCCA was absent exhibited localized reduced contraction of the inflow tract (13.5 to 28.7%, mean 22.9 ± 2.1%).

Discussion

While a substantial body of information is available from anatomic studies concerning normal coronary arterial branching patterns and their relative incidence, it was elected in the present study to compare the coronary arteriograms from a control group of 78 patients with presumably representative normal coronary anatomy with the coronary anatomy in patients with SCS. The principal advantage of using a control group in which a comparable method of anatomic study was employed was that it was possible to determine precisely normal variations in the relation of the LCCA to the atrioventricular groove, and thus to identify deviations in this relation with certainty in patients with SCS. The incidence of absent LCCA in our control group is substantially lower than that in larger anatomic studies (average approximately 15%). However, these studies are based on clinically undefined populations which may have included a significant number of patients with SCS or atypical chest pain. It should be noted, too, that the incidence of left dominant coronary circulation in the present study was identical to the generally accepted figure of 15%, providing further evidence that the incidence of absent LCCA in the control population was not falsely low.

In the present study, a remarkably consistent pattern of distribution of left coronary artery branches, differing substantially from that in the control group, was observed in patients with SCS. This unusual coronary anatomy, with absence of the LCCA, has not previously been recognized, although in describing coronary arteriograms as normal, it is noted that previous investigators have not made reference to the distribution of vessels, but rather to their caliber and to the absence of changes suggesting intimal disease.

It has been reported in qualitative descriptions that patients with SCS exhibit an unusual pattern of LV contraction. Little quantitative information has been presented to document the nature of this contraction abnormality. While Scampordonis and coworkers have recently described several different disorders of contraction in this syndrome, the use of nonanatomic axes in their analysis limits the usefulness of their study. It is apparent, at least in those ventricular cavity drawings illustrated in their report, that the papillary muscles were often excluded from the cavity silhouettes. The means of identification of the sinus origin of the angiographic beats from which silhouettes were taken, and the determination that such beats were not the result of or subsequent to ventricular extrasystoles, is not stated in their study. We would interpret the majority of silhouettes illustrated in this study as showing reduced contraction or noncontraction of the MVR and periannular myocardium, which we have found to be a virtually consistent defect in patients with SCS. The strikingly high incidence of absence of the LCCA in this group of patients suggests the possibility that this contraction disorder may be related to a chronic regional abnormality of myocardial perfusion. It is of interest in this connection that in a number of patients with an acquired defect in perfusion of this segment of myocardium resulting from isolated, complete arteriosclerotic occlusion of the proximal LCCA, an identical disorder of LV contraction was observed. These patients also exhibited some degree of posterior mitral leaflet prolapse which was associated with typical systolic click and late systolic murmur. None
had significant occlusive disease involving the right coronary artery.

The presence of a segmental myocardial abnormality provides one possible explanation for the occurrence of regional ECG repolarization abnormalities and ventricular arrhythmias in those patients with SCS in whom evidence of mitral valve incompetence is minimal or absent. In addition, several observations in this and previous studies suggest that the myocardial abnormality may play an etiologic role in mitral valve prolapse. The late systolic timing of mitral regurgitation is not readily attributable to a leaflet abnormality alone, since it would seem reasonable to expect that mitral prolapse resulting from a leaflet abnormality would occur soon after the onset of contraction with the rapid rise in intraventricular pressure. The possibility might be considered that, as in patients with diaphragmatic myocardial infarction who develop late-systolic mitral regurgitation, an abnormality of the inferior LV wall or papillary muscle might account for the inability of these structures to sustain support of the posterior leaflet throughout contraction.\textsuperscript{11, 12} In contrast to patients with diaphragmatic infarction, however, each of our patients with SCS exhibited a normal coronary arterial distribution to the inferior wall, and a presumably normal vascular supply to the inferior papillary muscle. It has been noted that a segmental ventricular contraction disorder in patients with arteriosclerotic occlusion of the LCCA identical to that in SCS may be associated with mitral leaflet prolapse. This suggests the alternative possibility that failure to reduce the cross sectional area of the mitral orifice and thus mitral "sail" area during systole, and the consequent maintenance of high levels of tension throughout contraction, places an unsupported load on the papillary muscles, resulting in their early relaxation in mid to late systole.

It is apparent from published arteriograms in previous reports, as it was in our series, that not all patients with SCS exhibit absence of the LCCA. Indeed, in view of the diverse circumstances in which the systolic click and murmur have been described, including diaphragmatic myocardial infarction, chest trauma, acute rheumatic fever, atrial septal defect, and even hypertrophic subaortic stenosis, it seems reasonable to assume that this unique auscultatory complex can be taken to represent only the posterior displacement of the mitral leaflets in midsystole, which may occur as the result of several mechanisms. Undoubtedly the patients included in the present report represent a select group, inasmuch as all had experienced significant symptoms, particularly chest pain; none was studied because of the ECG abnormality or auscultatory findings alone. Nonetheless, the striking incidence of absence of the LCCA in patients in whom there was only minimal evidence of mitral leaflet abnormality, or "ballooning," suggests this defect may be an important etiologic factor in the production of the SCS.

Figure 6

Selective left ventricular cineangiographic frames exposed in the lateral projection at end-diastole (left panel) and end-systole (right panel) in a patient with isolated arteriosclerotic occlusion of the left circumflex coronary artery. Note the lack of contraction in the region of the mitral valve ring.
An incidental finding in the present study was the observation that absence of the LCCA occurs considerably more frequently in patients evaluated for angina in whom coronary arteriograms demonstrate no evidence of occlusive intimal disease. Indeed, the atypical chest pain many of the patients described, with anginal character but of protracted duration and inconsistent relation to effort, was similar to that described by many patients with SCS. Further, many of these patients also exhibited reduced contraction of the inflow tract and MVR, differing from patients with SCS only in the absence of a click or murmur. These observations suggest that SCS may, in fact, represent only part of the clinical spectrum associated with a common congenital coronary arterial anomaly.

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