PATHOPHYSIOLOGY AND NATURAL HISTORY
CIRCUMFLEX ARTERY DISEASE

The clinical features of isolated left circumflex coronary artery disease

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ABSTRACT The clinical characteristics of 84 patients with isolated circumflex disease (>70%
luminal stenosis) were reviewed. A total of 66 patients had angina pectoris (mean duration 17.3
months), and 60 had suffered a myocardial infarction. Risk factors averaged 2.2 per patient. In the 84
patients there were 103 discrete circumflex stenoses; 51 stenoses were central (proximal circumflex,
obtuse marginal, and intermediate branches), and 52 were peripheral (distal circumflex, posterolateral,
and posterior descending branches); 48 were total and 55 were subtotal. Left ventricular function
was normal in 21 patients and abnormal in 63 patients, but the mean left ventricular ejection fraction of
the group was normal (59 ± 12%). Eighty-two patients had abnormal electrocardiograms: there were Q
waves in 25, RV pattern in 43, ST-T wave abnormalities in 19, left bundle branch block in two, and
pacemaker rhythm in one. Inferior abnormalities on the electrocardiogram correlated with peripheral
stenoses (p < .02), and lateral abnormalities on the electrocardiogram correlated with central stenoses
(p < .01). The RV pattern of true posterior infarction was seen in both central and peripheral stenoses.
In the 32 patients who underwent thallium scanning, lateral defects were more common with central
stenoses, but posterolateral defects occurred similarly in central and peripheral stenoses. Prognosis was
good. There were two deaths during the mean follow-up time of 17 months (range 1 to 49). The
cumulative survival rate was 100% at 12 months, 97.5 ± 2.9% at 24 months, and 97.5 ± 3.6% at 30
months.


ISOLATED DISEASE of the left circumflex coronary artery is uncommon, and its clinical features have not
been well documented.1-10 As percutaneous transluminal coronary angioplasty is now performed in many
patients, usually those with single-vessel disease, it is pertinent to reexamine the clinical spectrum and prog-
nosis of patients with single-vessel disease of the left circumflex coronary artery.

Methods

Between January 1977 and May 1981, 3900 patients under-
went cardiac catheterization in our laboratory, and 94 of these
patients (2.4%) were found to have significant (≥70%) isolated
disease of the left circumflex coronary artery. We excluded 10
of the 94 patients in whom isolated circumflex disease was
found incidentally at angiography (seven with valvular heart
disease, two with cardiomyopathy, and one with Wolff-Parkin-
son-White syndrome).

Medical records of the remaining 84 patients who presented
with symptoms associated with ischemic heart disease were
examined retrospectively for age, sex, duration and severity of
angina pectoris according to the criteria of the New York Heart
Association,11 history of myocardial infarction, and risk factors
including hypertension, hypercholesterolemia, and family
history.

Coronary angiography. Coronary angiography was per-
formed in multiple projections with the Judkins or Sones tech-
nique. The angiographic estimate of the degree of stenosis was
based on the reduction in luminal diameter as judged in multiple
projections by two experienced angiographers. Significant iso-
lated left circumflex disease was defined as 70% or greater
reduction in luminal diameter of the left circumflex coronary
artery or its major branches, with no stenosis greater than 50%
in the left anterior descending or right coronary arteries and no
stenosis greater than 30% in the left main coronary artery.

The left circumflex coronary system was subdivided into five
segments according to the American Heart Association classifi-
cation11 (figure 1): (1) Proximal left circumflex from its origin
to the takeoff of the obtuse marginal branch; (2) The obtuse
marginal branch; (3) Distal left circumflex, from a point imme-
diately distal to the takeoff of the obtuse marginal branch to the
origin of the posterior descending branch; (4) Posterolateral
branch; (5) Posterior descending branch. When the left coronary
artery divided into three branches, the middle or intermediate

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branch was defined as part of the circumflex system and was considered a sixth segment. The site of significant obstruction in the left circumflex coronary artery as defined by the above six segments correlated with electrocardiographic and thallium scan abnormalities. Electrocardiographic abnormalities were correlated with the site of obstruction only in patients with a single obstruction in the left circumflex, whereas thallium scan abnormalities were correlated with the site of obstruction both in patients with only one obstruction (28 patients) or with the most severe obstruction in patients in whom two obstructions were present in the left circumflex (four patients). Patients were also grouped into those with central obstructions (in the proximal circumflex segment, obtuse marginal and intermediate branches) and peripheral obstructions (distal circumflex segment, posterolateral and posterior descending branches), and these two sites of obstruction were correlated also with electrocardiographic and thallium scan abnormalities.

Three angiographic patterns of dominance were recognized: right, left, and balanced, depending on whether the posterior descending branch arose from the right coronary artery, the left circumflex artery, or both, respectively. Left ventricular function. Left ventriculograms were performed in the 30 degree right anterior oblique projection for all patients and in the left anterior oblique projection for 40 patients. The ventriculographic silhouette was divided into five segments in the right anterior oblique projection: anterobasal, anterolateral, apical, diaphragmatic, and posterobasal. The silhouette was divided into two segments in the left anterior oblique projection: posterolateral and septal. Each segment was evaluated qualitatively by the two experienced angiographers for presence of wall motion abnormalities. The systolic wall motion in each segment was classified as normal, hypokinetic (reduced wall motion), akinetic (absence of wall motion), or dyskinetic (paradoxical systolic expansion). Beats immediately following premature contractions were excluded from analysis. Left ventricular end-diastolic size was assessed qualitatively by the two angiographers as normal or enlarged. Left ventricular ejection fraction was calculated according to the single plane area-length method developed by Kennedy et al.

Abnormal left ventricular function was defined as the presence of at least one of the following: (1) ejection fraction less than 50%, (2) segmental or global hypokinesia, akinesia, or dyskinesia, or (3) left ventricular dilatation.

Electrocardiography. The electrocardiograms obtained before coronary angiography were interpreted by two independent observers according to the criteria of the American Heart Association. Electrocardiographic abnormalities, defined as pathologic Q waves, ischemic ST segment depression, and T wave inversion, were classified according to their location as (1) inferior when present in leads II, III, aVF with or without V_{4}, and V_{6}, and (2) lateral when present in leads I and aVL with or without leads V_{3} and V_{5}. True posterior infarction, or the RV pattern (figure 2), was defined by the presence of an initial R wave of 0.04 sec or greater in leads V_{1} or V_{2} and/or R to S amplitude ratio greater than 1 in leads V_{1} or V_{2} in the absence of Wolff-Parkinson-White syndrome, right bundle branch block, or right ventricular hypertrophy. Also assessed were abnormalities previously reported in left circumflex coronary artery disease or posterolateral infarction, including axis deviation, conduction disturbances, notching of the QRS complex in leads V_{1} and V_{2}, upright T wave in leads V_{1} and V_{2}, and reduced R wave amplitude in leads 1 and aVL.

Thallium myocardial scanning. Exercise thallium-201 myocardial perfusion scanning was performed in 32 of the 84 patients within a mean time of 1.9 months from angiography by use of a protocol previously described. Scanning was performed in four views (anterior, 40 degree left anterior oblique, 60 degree left anterior oblique, and left lateral) with a Searle PHO-Gamma mobile camera and low-energy all-purpose parallel-hole collimator. The scans were interpreted at the time of study from the original Polaroid scintiphotographs, without computer enhancement or background subtraction, by the consensus of three experienced observers who had no knowledge of patient data. Each of the four views was diagrammatically divided into three segments as shown in figure 3 and was analyzed for the presence or absence of thallium defects. Furthermore, the lateral segment in the 40 degree left anterior oblique view was divided into upper and lower halves and was analyzed for perfusion defects. Defects in each segment correlated with the location of disease in the individual branches of the circumflex coronary artery.

Follow-up. Information about death, myocardial infarction, chest pain resulting in hospitalization, angina, and coronary artery bypass surgery, were obtained from medical records, patients, relatives, or physicians. The outcome for the group was expressed with standard life table survival analysis. The follow-up was 99% complete.

Statistical analysis. Data were analyzed with the Yates corrected chi square test of correlated proportions for unrelated samples and with the McNemar test for related samples.

Results

Clinical presentation. The mean age of the 84 patients with isolated left circumflex coronary artery disease was 49.9 years (range 31 to 73). There were 75 men.
and nine women. A total of 65 patients had angina pectoris (mean duration 17.3 ± 31.7 months), and 60 had suffered a myocardial infarction, 42 with and 18 without previous angina.

Eighty patients had one or more risk factors. Hypercholesterolemia was present in 58%, 52% smoked cigarettes, 38% had hypertension, and 48% had a family history of coronary artery disease. The average number of risk factors was 2.2 per patient and was higher for women than for men (3.1 vs 2.1; p < .05).

**Coronary angiography.** The indications for coronary angiography were angina pectoris in 56 patients, including 39 patients with stable angina and 17 with unstable angina, evaluation of atypical chest pain in two patients, prognostic study after myocardial infarction in 25 patients, and cardiac failure with acute mitral regurgitation after inferior infarction in one patient.

The distribution of stenoses in the left circumflex coronary artery is shown in table 1. A total of 103 discrete and significant stenoses were present in the 84 patients: 66 patients had only a single stenosis, 17 had two, and one had three distinct stenoses. Of the 103 stenoses, 51 were central and 52 were distal (table 1). Forty-eight of the 103 stenoses were total and 55 were subtotal. In the 60 patients with a documented myocardial infarction, 39 stenoses were total and 21 were subtotal, whereas in the 24 patients without infarction, nine were total and 15 were subtotal (p = NS). There were 19 other subtotal stenoses. The pattern of arterial dominance was right in 60%, left in 27%, and balanced in 13% of the patients. Nonsignificant stenoses (≤50%) occurred in the left anterior descending artery.

**FIGURE 3.** Diagrammatic representation of the four views of the thallium scan with the incidence of perfusion defects in patients with single-vessel circumflex disease. In the anterior view, defects were most common in the apical segment (AP ANT) and less common in the anterolateral (ANT LAT) and inferior (INF) segments. In the 40 degree left anterior oblique (LAO) view, defects were most common in the lateral segment (LAT) and less common in the apical (AP 40) and septal (SEPT) segment. In the 60 degree LAO view, defects were most common in the posteroinferior (POST INF) and less common in the apical (AP 60) and anteroseptal (ANT SEPT) segment. In the left lateral view, defects were most common in the posterior (POST) segment and less common in the apical (AP LL) and anterior (ANT) segments.
in 36 patients and in the right coronary artery in 27 patients; nonsignificant stenoses of the left main coronary artery (≤30%) occurred in three patients.

**Left ventricular function.** Left ventricular function was normal in 21 patients (25%) and abnormal in 63 patients (75%). Left ventricular ejection fraction was determined in 72 of the 84 patients and the mean for this group was 59 ± 12%. Sixteen of the 72 patients (22%) had an ejection fraction less than 50%. Ventriculograms showed abnormalities in 62 patients: the diaphragmatic segment was abnormal in 31 patients, the apical segment was abnormal in 26, and the anterolateral segment was abnormal in 25. The posterolateral segment was abnormal in 16 of the 40 patients who also underwent ventriculography in the left anterior oblique view. The left ventricle was dilated in 25 patients. Mitral regurgitation was present in four patients, including one patient with acute regurgitation who was initially in cardiogenic shock.

**TABLE 2**

<table>
<thead>
<tr>
<th>Electrocardiographic pattern</th>
<th>No. of stenoses</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q waves</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Isolated ST-T wave</td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td>abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV pattern associated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with Q waves</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>RV pattern associated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with ST-T wave</td>
<td></td>
<td></td>
</tr>
<tr>
<td>abnormalities</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Ventricular pacing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rhythm</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Normal ECG</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Electrocardiography.** Electrocardiograms were normal in two patients and were abnormal in 82 patients (table 2). Q waves were present in 35 patients, isolated ST-T wave abnormalities were present in 25 patients, and the RV pattern was present in 43 patients, 24 of whom had Q waves and 19 had ST-T wave abnormalities. Two patients had left bundle branch block, and one patient with sick sinus syndrome had a ventricular pacemaker rhythm.

The site of electrocardiographic abnormalities is shown in table 2. Q waves occurred more often in leads II, III, and aVF (inferior pattern) and less often in leads I and aVL (lateral pattern). ST-T wave abnormalities occurred similarly in inferior and lateral leads. Associated abnormalities in leads V₁ and V₃ were present in 55 of the 84 patients (65%). An electrocardiogram from a patient with inferior, lateral, and RV patterns is shown in figure 2. Conduction disturbances were frequently seen, including an intraventricular conduction block in 75 patients (89%), slurring of either the descending or ascending limbs of the QRS complex in V₁ and/or V₃ in 48 patients (57%), left-axis deviation in 13 patients (15%), and upright or isoelectric T waves in V₁ in 79 patients (94%).

Electrocardiographic abnormalities were documented for 61 of the 66 patients who had only a single stenosis in the circumflex coronary artery. In these 61 patients, the site of stenosis correlated with the site of electrocardiographic changes (table 3). The inferior pattern was most common in patients with stenosis in the distal circumflex segment (18 of 19 patients), whereas the lateral pattern was most common in patients with stenosis in the obtuse marginal branch (nine

**TABLE 3**

<table>
<thead>
<tr>
<th>Location of stenosis</th>
<th>Infarct Location</th>
<th>ECG pattern</th>
<th>RV pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>32</td>
<td>17 (53%)</td>
<td>21 (66%)</td>
</tr>
<tr>
<td>Proximal LCX</td>
<td>17</td>
<td>11 (65%)</td>
<td>8 (47%)</td>
</tr>
<tr>
<td>Obstructive</td>
<td>10</td>
<td>3 (30%)</td>
<td>9 (90%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>5</td>
<td>3 (60%)</td>
<td>4 (80%)</td>
</tr>
<tr>
<td>Peripheral</td>
<td>29</td>
<td>21 (86%)</td>
<td>10 (34%)</td>
</tr>
<tr>
<td>Distal LCX</td>
<td>19</td>
<td>18 (95%)</td>
<td>5 (26%)</td>
</tr>
<tr>
<td>Posterolateral</td>
<td>8</td>
<td>5 (62%)</td>
<td>5 (62%)</td>
</tr>
<tr>
<td>Posterolateral</td>
<td>2</td>
<td>2 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>42 (69%)</td>
<td>31 (51%)</td>
</tr>
</tbody>
</table>

LCX = left circumflex coronary artery.

*p < .05 compared with the inferior pattern in peripheral stenoses.

*p < .01 compared with the lateral pattern in peripheral stenoses.

*p = NS compared with the RV pattern in peripheral stenoses.
of 10 patients) and intermediate branch (four of five patients). The inferior electrocardiographic pattern was more frequent in patients with peripheral stenoses (25 patients, 86%) than in patients with central stenoses (17 patients, 53%; p < .02). By contrast, the lateral electrocardiographic pattern was more frequent in patients with central stenoses (21 patients, 66%) than in patients with peripheral stenoses (10 patients, 34%; p < .01). The RV pattern was present in 15 patients (47%) with central stenoses and in 17 patients (58%) with peripheral stenoses (p = NS).

**FIGURE 4.** Thallium scan of a 49-year-old man with a single circumflex obstruction in the proximal segment. Defects, illustrated in the diagrammatic representations in black, are present in the apical, lateral, posteroinferior, and posterior segments. Abbreviations as for figure 3.

**Thallium-201 myocardial perfusion scanning.** Thallium-201 scanning was performed in 32 of the 84 patients. The incidence of perfusion defects in individual segments is shown diagrammatically in figure 3. In 32 patients perfusion defects were most common in four segments: apical in the anterior view (AP ANT), 69% of patients; lateral in the 40 degree left anterior oblique view (LAT), 72%; posteroinferior in the 60 degree left anterior oblique view (POST INF), 84%; posterior in the left lateral view (POST), 75%. The thallium scan of a patient with isolated circumflex coronary disease is shown in figure 4.

The site of perfusion defects in the 32 patients correlated with the site of the single stenosis (28 patients) or the most severe stenosis (four patients) in the circumflex coronary artery (figure 5). Thallium defects in the LAT segment were more common in patients with central stenoses (17 of 21 patients, 81%) than in patients with peripheral stenoses (five of 11 patients, 45%; p < .05). Thallium defects in AP ANT, POST INF, and POST segments occurred similarly in both groups. Thallium defects in the inferior segment of the anterior view (INF) (anterior view) occurred in four of 11 patients with peripheral stenoses and in another three patients with proximal circumflex stenoses, but
did not occur in any patients with obtuse marginal or intermediate branch stenoses. Stenoses of the intermediate branch did not produce a consistent pattern of thallium defects.

The LAT defects were further divided into those involving the upper, the lower, or the entire segment. One patient had thallium defects only in the upper LAT segment, 10 patients had defects only in the lower LAT segment, and in 12 patients, defects involved both upper and lower portions of the LAT segment. No clear correlation could be established between location of defects in upper, lower, or both parts of LAT segment and sites of stenoses in individual segments of left circumflex coronary artery or the pattern of arterial dominance.

Follow-up. Follow-up was dated from angiography, and the median time for the 84 patients was 17 months (range 1 to 49). There were two cardiac deaths, which occurred at 13 and 32 months. The cumulative life table survival rate for the 84 patients was 100% at 12 months, 97.5 ± 2.9% at 24 months, and 97.5 ± 3.6% at 30 months (figure 6).

Seventeen patients (16 men and one woman) underwent coronary artery bypass surgery; 16 underwent this surgery because of angina pectoris and one because of cardiac failure resulting from inferior myocardial infarction and acute mitral regurgitation. All were alive and well at a mean of 28 months (range 1 to 39). Another four patients were hospitalized because of angina, and one patient suffered myocardial infarction. Fifty-two patients were angina free (37 on medical therapy and 15 after coronary artery surgery) at the time of the last follow-up.

Discussion

Isolated left circumflex coronary disease is infrequently shown at angiography. Our prevalence of disease of 2.4% agrees with that of other reports.1-9, 18, 24, 25 Patient selection in this study is similar to that of previous reports of patients with single-vessel disease, except that 30% of our patients were studied as part of a prognostic study of survivors of myocardial infarction 60 years of age or less; this may account for the lower incidence of angina.5, 6, 26 Isolated disease of the left circumflex coronary artery does not appear to cause severe left ventricular dysfunction, as the mean ejection fraction in our patients was 59%, and this is in accord with the previous reports.5, 18, 24, 27

Electrocardiographic abnormalities were present in nearly all of our patients with isolated left circumflex disease and occurred in the inferolateral leads (inferior pattern in leads II, III, aVF, V5, and V6,) anterolateral leads (lateral pattern in leads I, aVL, V5, and V6), and right precordial leads (RV pattern in leads V1 and V2), as reported previously.17, 28, 29 Although electrocardiographic abnormalities were most common in the inferior leads, inferior electrocardiographic changes can also occur in patients with right coronary artery disease and are not specific.27 The lateral pattern and RV pattern are more specific for circumflex disease,4 and the left circumflex arterial system was therefore subdivided into six segments to determine whether these more specific patterns correlated with disease in specific segments of the circumflex system.

In contrast to the findings of Gensini et al.21 suggesting that most stenoses are proximal, about half of our 103 individual stenoses were central and half were peripheral. The sites of stenoses reflect the sites of predilection for atherosclerosis in patients with isolated circumflex disease and include proximal and distal circumflex segments and proximal portions of the major branches. The portions of the branches of circumflex coronary artery beyond the major bifurcation were usually free of segmental stenoses, as has been previously observed.12 Also, in contrast to the findings of Gensini,13 the first few millimeters of the circumflex artery were free of significant obstruction in all patients, and no ostial circumflex stenoses were seen.

In this study of patients with isolated circumflex disease, the pattern of electrocardiographic abnormalities and distribution of thallium defects appears to reflect the site of stenosis in the circumflex system. The electrocardiographic data were based on information obtained from 61 patients with solitary stenoses in the
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circumflex system so that the patterns of electrocardiographic abnormalities could be related to stenoses in individual segments of the circumflex coronary artery. Our study is the first to show electrocardiographic and angiographic correlations for patients with isolated circumflex disease. The data from the thallium scans were obtained from 32 patients, and perfusion defects in individual segments correlated with either a single stenosis or the most severe stenosis in the left circumflex system when more than one stenosis was present.

A stenosis in the obtuse marginal branch of the circumflex was associated with the lateral pattern of electrocardiographic abnormalities and with thallium defects in the LAT segments of the 40 degree left anterior oblique view, previously shown to be specific for circumflex disease, as well as with defects in the POST INF and POST segments. This is predictable because the obtuse marginal branch of the circumflex usually supplies the posterolateral myocardium. In contrast, disease in the proximal segment of the circumflex was associated with both lateral and inferior electrocardiographic patterns and with thallium defects in the LAT, INF, POST INF, and POST segments; this association may reflect the fact that the proximal circumflex supplies both the posterolateral and posteroinferior myocardium. Disease of the intermediate branch, also considered a central stenosis, demonstrated no distinctive electrocardiographic or thallium scan characteristics.

A peripheral stenosis distal to the takeoff of the obtuse marginal branch was usually associated with the inferior pattern of electrocardiographic abnormalities and thallium defects in POST INF, POST, and INF segments. Thallium defects in the LAT segment were uncommon. This is consistent with the fact that the distal circumflex supplies blood to the posteroinferior myocardium. The posterolateral branch, however, may contribute to the blood supply of the posterolateral myocardium, and stenosis of the posterolateral branch, although classified as peripheral, may explain the lateral electrocardiographic pattern and thallium defects in the LAT segment found in some patients with peripheral circumflex stenoses. In a small number of patients, stenoses confined to the posterior descending branch were associated with inferior electrocardiographic patterns and thallium defects in POST INF and POST segments.

The prognosis was excellent as 97.5% of our patients with isolated left circumflex disease survived at a mean of 2½ years. This could have been influenced by several factors since 20% of the patients underwent coronary bypass surgery and 30% were studied prognostically after myocardial infarction. Longer follow-up studies, up to 12 years, in smaller series show that single-vessel circumflex disease has a mortality of 2.0% to 4.2% per year, compared with mortality for patients with disease of the right coronary artery of 0.3% to 3.0% and with mortality for patients with disease of the left anterior descending artery of 2.0% to 5.6%. The mortality is reported to be higher for patients with more severe stenoses and for patients who have minor disease in the other coronary arteries. The high survival rate for our patients may be due to the relatively young age of our patients (mean 49.9 years), since age reflects mortality and morbidity in coronary artery disease, or may be due to the better recent medical and surgical treatment of coronary artery disease.

Clinical implications. Isolated circumflex disease may be suspected by the use of clinical and electrocardiographic criteria, but cannot be definitely diagnosed. Exercise thallium scanning in a subset of these patients may identify isolated circumflex disease. Because of the overall good prognosis, normal left ventricular function, and the good response to medical therapy, initial treatment for these patients should be medical. Since a significant number of patients required later surgery for their symptoms, percutaneous transluminal coronary angioplasty should be considered for those who do not respond to medical therapy.

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