

# Conservative Medication Follow-up for Over 20 Years of a Patient With Ischemic Heart Disease After Diagnosis of Chronic Total Occlusion of the 3 Main Coronary Arteries

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A 48-year-old man suffered from acute coronary syndrome in 1978. Coronary angiography was performed at that time and showed 99% stenosis of the right coronary artery, 100% of the left circumflex branch, and 50% of the left ascending artery. He received conservative therapy. Five years later (ie, 1983), coronary angiography showed complete occlusions of the 3 major coronary arteries. Rich collateral circulation had developed distal to all 3 major coronary trees. The patient and his family rejected invasive therapies such as coronary-artery bypass graft or percutaneous coronary intervention. Cardiac catheterizations were performed in 1996, 2001, and 2007, but angiographic follow-up studies showed no change in either the coronary atherosclerosis or the collateral circulation. The left ventricular ejection fraction has been maintained at >60%. During the 20-year follow-up, he has had refractory angina, but has not suffered from acute coronary syndrome, congestive heart failure, or critical arrhythmia. (Circ J 2008; 72: 1205–1209)

**Key Words:** Coronary artery disease; Drugs; Ischemia; Occlusion

It is very rare for there to be complete occlusion of the 3 major coronary arteries!<sup>2</sup> Among stable patients, those whose exercise tolerance is severely limited and who have extensive ischemia, as assessed by exercise electrocardiography (ECG) or scintigraphy, have a poor prognosis. Long-term outcomes without revascularization, such as coronary-artery bypass graft (CABG) or percutaneous coronary intervention (PCI), are poor.<sup>3,4</sup>

We report conservative medical follow-up of a case for over 20 years since confirmation of chronic total occlusion of the 3 major coronary arteries. This patient's long-term survival has occurred even in the presence of clinically stable refractory angina that necessitated treatment with sublingual nitroglycerin. To our knowledge, this is an extremely rare case, and we discuss the factors that have led to long-term survival under these severe circumstances.

## Case Report

In 1978, a 48-year-old man presented with chest discomfort. He had risk factors of coronary atherosclerosis related to hypertension, hyperlipidemia, diabetes mellitus, and current smoking. After ECG and serological examinations

(the detailed records were lost), he was diagnosed with acute coronary syndrome, and coronary angiography was performed at that time, revealing 99% stenosis of the right coronary artery (RCA), 100% of the left circumflex branch (LCX) and 50% of the left ascending artery (LAD). He received conservative therapy because he rejected revascularization therapy such as CABG or PCI. After discharge, he had refractory angina after walking for more than 5 min, which was relieved by resting or sublingual nitroglycerin.

Five years later in 1983, coronary angiography showed complete occlusion of the 3 major coronary arteries. There was rich collateral circulation supplying the distal portion of the 3 major coronary trees (Fig 1). Surgical treatment was recommended, but the patient refused it because of the risks involved and the fact that his symptoms remained unchanged.

Thereafter, the patient was followed up at hospital, received medical treatment, and ceased cigarette-smoking. Although his symptoms remained as Canadian Cardiovascular Society (CCS) class III angina, they did not worsen and his activities of daily life remained unchanged during the follow-up period. The results of cardiac catheterization studies performed in 1996 and 2001 were no progression of either the coronary atherosclerosis or the collateral flow.

In 1996 he underwent an abdominal operation for a perforated gastric ulcer, supported by intra-aortic balloon pumping. He also received home oxygen therapy for emphysema since 2003.

Although he still has CCS class III angina, he has no evidence of myocardial infarction, congestive heart failure or arrhythmias. His daily life has become completely independent; he has been walking for more than 10 min every

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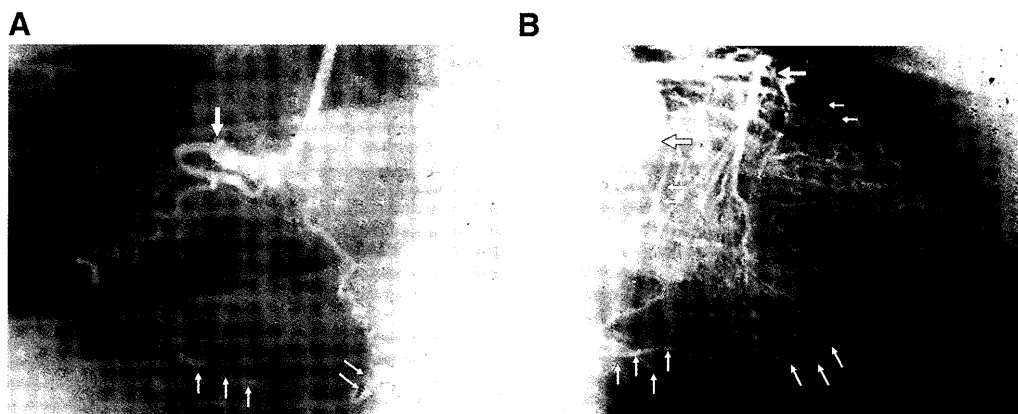


Fig 1. Coronary angiogram in 1978. (A) Left anterior oblique projection shows total occlusion of the right coronary artery (white arrow) and rich collateral vessels (small white arrows). (B) Right anterior oblique caudal projection shows the left coronary artery and total occlusion of the left anterior descending artery and left circumflex branch (white arrows), as well as rich collateral circulation to the distal site of the 3 main coronary trees (small white arrows).

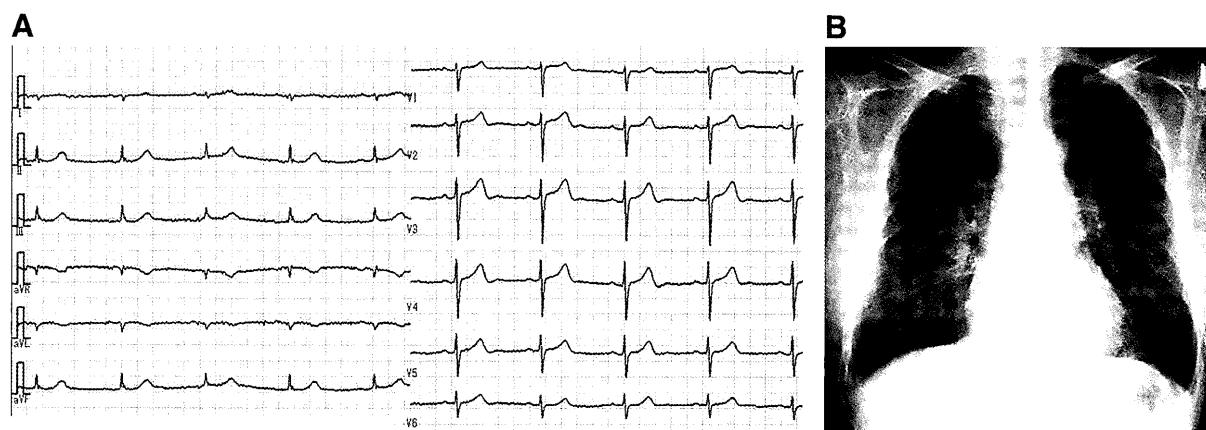


Fig 2. (A). Electrocardiogram showing no poor R wave progressions or ST changes. (B) Chest radiograph showing clear lung fields, and a cardiothoracic ratio of 48%.

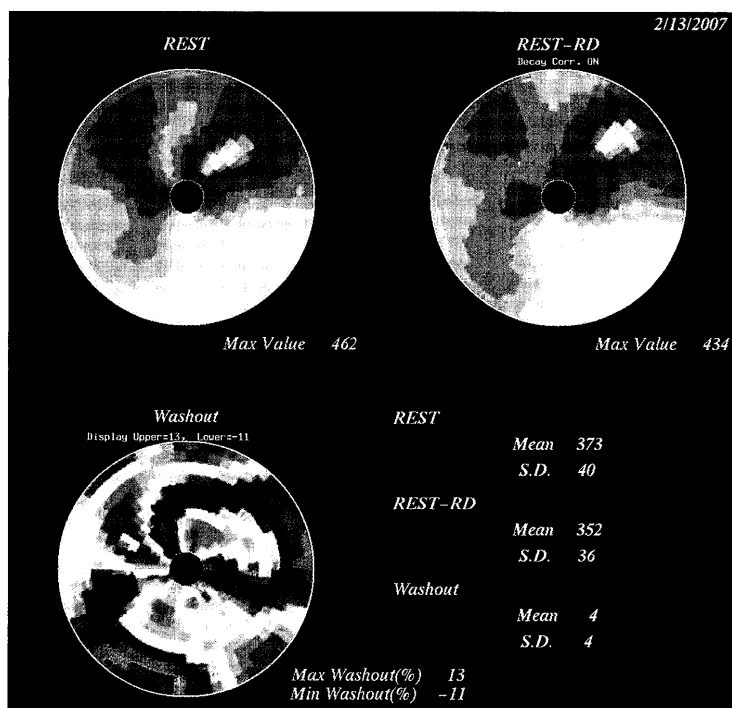


Fig 3. Bull's eye image from thallium-201 single-photon emission computed tomography at rest. There is no decreased uptake in the relatively early and late phases, but there is diffuse deterioration of the washout rate.

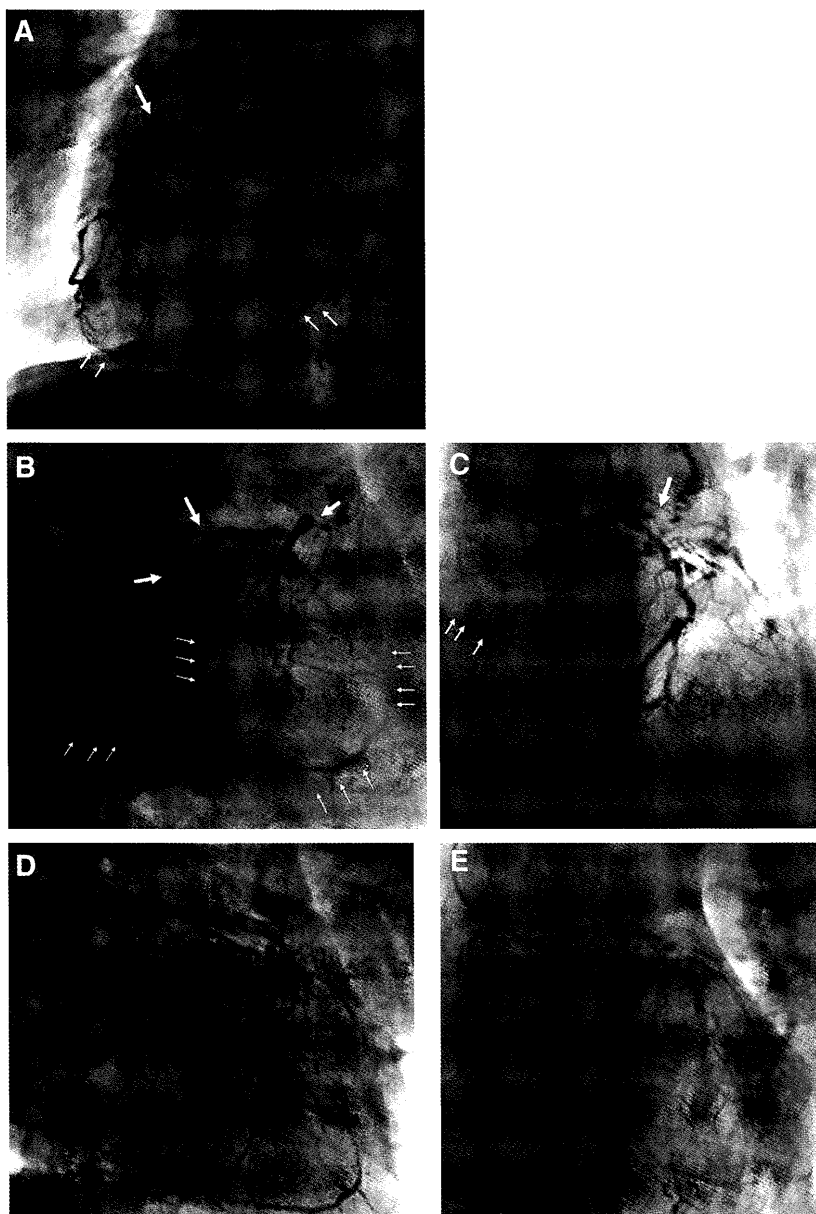


Fig 4. (A) Left anterior oblique projection showing total occlusion of the right coronary artery (white arrow) and rich collateral vessels (small white arrows). (B) Straight caudal projection showing the left coronary artery and total occlusion of the left anterior descending artery and left circumflex branch (white arrows), as well as rich collateral circulation to the distal site of the 3 main coronary trees (small white arrows). (C) Straight cranial projection clearly shows total occlusion of the left anterior descending artery and the left circumflex branch (white arrows), and the development of a septal branch and collateral flow to the distal site of the posterior descending artery (small white arrows). (D) Right anterior oblique caudal projection (D) and frontal projection (E) in the late phase show the rich and complicated collateral circulation.

day, taking a rest every few steps with sublingual nitroglycerin. At present, he takes the following oral medicines daily: aspirin, 81 mg once; ticlopidine, 100 mg twice; atenolol, 50 mg once; slow release nifedipine, 20 mg twice; long-acting isosorbide dinitrate, 20 mg 3 times plus a 40-mg transdermal patch; enalapril, 2.5 mg once; pravastatin, 10 mg twice; gliclazide, 40 mg once; metformin, 250 mg once.

At the latest examination, his blood pressure was 100/60 mmHg and his heart rate was 60 beats/min with a regular rhythm. Neither heart murmur nor crackles were audible. Resting ECG was normal limits (no poor R wave progression and no ST change) (Fig 2A). Chest X-ray showed a 48% cardiothoracic ratio and no congestion in the lung fields (Fig 2B). Laboratory assessment revealed total cholesterol of 136 mg/dl, high-density lipoprotein cholesterol of 35 mg/dl, and triglycerides of 147 mg/dl. Fasting blood sugar was 83 mg/dl, and hemoglobin A<sub>1c</sub> was 5.6%. The serological creatinine level was 1.04 mg/dl, and creatinine clearance (Cockcroft-Gault formula) was 54.0 ml/min. The level of B-type natriuretic peptide was 36.7 pg/dl. We recommended

that he undergo a stress test, but he declined because of the probability of experiencing chest pain. Myocardial single-photon emission computed tomography at rest identified no decreased uptake in the relatively early and late phases, but a diffuse deterioration of the washout rate, suggestive of myocardial ischemia (Fig 3).

Coronary angiography in February 2007 demonstrated chronic total occlusion of the proximal RCA, 75% stenosis of the proximal and chronic total occlusion of the mid LAD, and chronic total occlusion of the proximal LCX. There was a rich and complicated collateral circulation to the distal area of the major coronary tree; for example, from the septal branch to the posterior descending, from the left atrium branch to the posterior lateral, and from the posterior descending to the distal LAD, and also from the conus branch to the distal LCX. There was a collateral bridge proximal to the distal LCX and the RCA (Fig 4). Left ventriculography revealed almost normal wall motion. These findings were almost unchanged from those of past catheterizations.

## Discussion

The prognosis of stable angina has improved with advances in the understanding of its pathophysiology and of pharmacologic therapy. Mortality rates vary depending on the number of diseased vessels, the severity of the obstruction, the status of left ventricular infarction, and the presence of complex arrhythmias.<sup>4</sup> It is reported that patients with 3-vessel disease have more mildly stenotic or nonstenotic plaques that are potential sites for acute coronary events than those with 1-vessel disease.<sup>5</sup> The 10-year survival rates of 3-vessel disease treated medically were 64.2% in previous reports in Japanese, in whom cardiac death occurred in 36.9% and nonfatal cardiac events developed in 30.9%; in patients with angina pectoris, the survival rate decreased as the number of totally-occluded arteries increased.<sup>6</sup> From this point of view, patients should receive coronary revascularization, although the indications are often debated. Randomized trials have shown that over follow-up periods of several years, the mortality and infarction rates for PCI and CABG are generally comparable.<sup>3,7,8</sup> CABG rather than PCI may have been the better revascularization therapy for the present patient, because there are total occlusions of 3 coronary arteries and inability to successfully pass a guidewire into the true distal lumen is the most frequent cause of failed PCI.

Moriuchi et al reported that the ejection fraction, a mid-portion occlusion, good collateral supply, and a history of angina pectoris are important factors in survival, and in particular, good collateral supply to the LAD from the RCA may be important at 8 years, as noted in 10 of 15 patients receiving conservative medical treatment for occlusions of the 3 major coronary arteries.<sup>2</sup> Hosokawa et al reported a patient with a low ejection fraction (22%) who was receiving conservative therapy for occlusions of the 3 major coronary arteries and who had suffered an acute myocardial infarction more than 10 years ago, and they suggested that a well-developed collateral supply made it possible for the patient to survive with this ischemic history.<sup>9</sup> In those previous reports, a good base-line cardiac function, rich collateral circulation, and a history of prolonged ischemia are some of the mortality-related factors in patients receiving conservative treatment for occlusion of 3 major coronary arteries. The present case also included these factors.

Prolonged ischemia might cause ischemic preconditioning. Brief episodes of ischemia and reperfusion reduce size of the infarct by one-quarter to one-eighth.<sup>10,11</sup> The preconditioning effect is determined by a combination of factors: the duration of the ischemia, the duration of the preconditioning reperfusion, and the duration of subsequent ischemic episodes following reperfusion. Using a PCI model in humans Matsubara et al demonstrated that ischemia of 180 s, but not of 60 s, followed by 5 min of reperfusion, led to a preconditioning effect without recruitment of collateral flow.<sup>12</sup> Therefore, a long history of ischemic events may induce a preconditioning effect. Previous reports have demonstrated that preconditioning without recruitable collateral circulation clinically and electrocardiographically lessened myocardial ischemia, but failed to preserve left ventricular function, whereas preconditioning with recruitable collateral circulation greatly reduced myocardial ischemia.<sup>13</sup> In the present case, preconditioning might have played an important role in myocardial protection and the patient's survival; both preconditioning and development of collateral circulation may have played important roles in the ad-

aptation to ischemic conditions.

The combination of lifestyle modification and medical treatment also assisted in long-term survival. Intensive pharmacologic therapy and lifestyle intervention as an initial management strategy in patients with stable coronary artery disease can reduce the risk of cardiovascular events as much as PCI.<sup>14</sup> These treatments aim to reduce myocardial the oxygen demand, improve the oxygen supply, treat cardiac risk factors such as hypertension, diabetes, and hyperlipidemia, and control exacerbating factors that may precipitate ischemia.

Aspirin,  $\beta$ -blockers, angiotensin-converting enzyme inhibitors, low-density lipoprotein-lowering therapy, sublingual nitroglycerin, calcium antagonists, and long-acting nitrates as a substitute for  $\beta$ -blockers were recommended as class I in a guideline in which there is evidence or general agreement that a given procedure or treatment is useful and effective.<sup>4</sup> Ticlopidine has not been shown to decrease adverse cardiovascular events, but it does decrease platelet function in patients with stable angina.<sup>15,16</sup> Nicorandil, a potassium channel activator, has pharmacologic properties similar to those of nitrates and may be effective in the treatment of stable angina.<sup>17</sup> Furthermore, it has a pharmacological ischemic preconditioning effect.<sup>12</sup>

The home oxygen therapy for emphysema had the additional benefit of improving the oxygen supply and thus reducing myocardial ischemia. Additionally, insofar as he has angina, though considerably limited by refractory symptoms, he has been continuing to exercise, which is not only be good for glycemic control, but has also helped maintain maximum oxygen uptake and exercise capacity, considered to be an index of mortality.<sup>18-20</sup>

For most patients, the goal of treatment is complete, or nearly complete, elimination of anginal chest pain and return to normal activities with a functional capacity of CCS class I angina. This goal should be accomplished with minimal side-effects, as well as reducing the risk of mortality and morbid events. Because of the variation in symptom complexes among patients and their unique perceptions, expectations, and preferences, and the evidence of patients such as the present subject with more severe angina and several coexisting medical problems, some patients may be satisfied with a reduction in symptoms that enables the performance of only limited activities of daily life.

However, recognizing the danger to the patient suggested by the baseline data, we treat such patients more vigorously. This is a rare and valuable case of survival for over 20 years with stable symptoms. It is necessary to continue careful follow-up of this patient, paying attention to complications such as worsening angina, heart failure, and arrhythmias.

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