

Prevalence of Unfavorable Angiographic Characteristics for Percutaneous Intervention in Patients With Unprotected Left Main Coronary Artery Disease

Michael Ragosta,* MD, Sandra Dee, MD,
Ian J. Sarembock, MB, ChB, MD, Lewis C. Lipson, MD,
Lawrence W. Gimple, MD, and Eric R. Powers, MD

Objectives: The goal of this study was to determine the proportion of patients with left main coronary disease (LMCD) with unfavorable characteristics for percutaneous coronary intervention (PCI). **Background:** Published series suggest that LMCD can be treated percutaneously, however, the proportion of patients in whom PCI is an option based on angiographic criteria is unknown. **Methods:** In 13,228 consecutive coronary angiograms, 476 (3.6%) patients had $\geq 60\%$ stenosis of the left main. In 232 patients with unprotected LMCD, the clinical characteristics and angiograms were reviewed with six features chosen as “unfavorable” for PCI: (1) Bifurcation LMCD, (2) occlusion of a major coronary, (3) ejection fraction $<30\%$, (4) occlusion of a dominant RCA, (5) left dominant circulation, and (6) coexisting three-vessel disease. Treatment modality and 1 year mortality were determined. **Results:** The mean age was 69 years and 68% were male. Unfavorable characteristics were common with at least one unfavorable characteristic seen in 80%. Bifurcation disease was the most common unfavorable characteristic observed (53%) and coexisting three-vessel disease was seen in 38%. Treatment consisted of CABG in 205 (88%), medical therapy in 24 (10%) and PCI in 3 (1%). Among patients referred for CABG, 1 year survival was 88% with similar rates of survival for those with favorable characteristics (86%) compared to those with at least one unfavorable characteristic (88%). **Conclusions:** Most patients with LMCD have at least one unfavorable characteristic for PCI suggesting that PCI may be a technically difficult option for most patients with LMCD. © 2006 Wiley-Liss, Inc.

Key words: atherosclerosis; coronary bypass surgery; coronary angiography

INTRODUCTION

Patients with significant atherosclerotic narrowing of the left main coronary artery have a survival advantage with CABG compared to medical therapy, and thus, CABG is the predominant treatment modality for patients with left main coronary disease (LMCD) [1,2]. Percutaneous coronary intervention (PCI) using balloon angioplasty was abandoned as a treatment option for LMCD, because of high in-hospital mortality and unacceptable long-term outcome [3,4]. The introduction of coronary stents to interventional cardiology led to renewed interest in PCI for LMCD. Several published case series showed that stenting of LMCD was associated with high rates of procedural success and acceptable midterm results [5–12]. However, restenosis remained a significant limitation and might manifest as unheralded sudden cardiac death. The important dis-

covery that drug-eluting stents significantly reduce in-stent restenosis [13,14] has sustained the interest in PCI for LMCD.

Cardiovascular Division, Department of Internal Medicine, University of Virginia Health System, Charlottesville, Virginia

*Correspondence to: Michael Ragosta, MD, Director, Interventional Cardiology, Associate Professor of Medicine, Cardiovascular Division, Department of Medicine, P.O. Box 800158, University of Virginia Health System, Charlottesville, VA 22908-0158.
E-mail: mr8b@virginia.edu

Received 7 July 2005; Revision accepted 1 February 2006

DOI 10.1002/ccd.20709

Published online 4 August 2006 in Wiley InterScience (www.interscience.wiley.com).

The left main stem is an attractive site for PCI because of its proximal location and larger reference diameter. However, there are several potential features that might make LMCD unfavorable for PCI. These include clinical characteristics that increase the risk of PCI such as patient instability or reduced ventricular function as well as angiographic characteristics such as heavy calcification, involvement of the bifurcation of the left main stem, and the presence of other coronary disease such as total coronary occlusion in other vessels not treatable by PCI. Bifurcation disease is a particularly important feature since optimal percutaneous methods for its treatment have proven elusive [15–17].

To date, the published case series consist of highly selected patients with LMCD both in terms of anatomy and clinical suitability for the procedure. It is difficult to know the general applicability of PCI to patients with LMCD. Thus, the purpose of this study was to determine the proportion of patients with LMCD with unfavorable angiographic and clinical characteristics for PCI in a consecutive population of patients referred for coronary angiography and to determine patient outcomes in a modern series of consecutive LMCD patients treated surgically.

METHODS

Between July 1, 1999 and December 31, 2002, 13,228 patients underwent coronary angiography at the University of Virginia Health System cardiac catheterization laboratories at three hospitals (University of Virginia Hospital, Martha Jefferson Hospital, and Augusta Medical Center). A database query was performed and 476 (3.6%) patients were found to have $\geq 60\%$ narrowing of the left main coronary artery noted on the angiographic report. This determination was made based on visual analysis of the angiogram by experienced angiographers at the time of the procedure. In 200 of these patients, a patent saphenous vein or internal mammary graft was present to one or more branches of the left coronary artery (“protected” left main disease). In the remaining 276 patients without prior bypass surgery (“unprotected” left main disease), the coronary angiograms were available and suitable for angiographic analysis in 232 patients and formed the basis of this study.

Clinical characteristics were extracted from a prospectively collected, predefined point-of-care clinical database used by the Cardiac Catheterization Laboratories of the University of Virginia Heart Center (Clinical Automated Office Solutions, Intelligent Business Solutions, Winston-Salem, NC) using data definitions from the American College of Cardiology/National Cardiovascular Data RegistryTM [18] as shown in Table I.

TABLE I. Clinical Characteristics (n = 232)

Age	69 \pm 11
Male	157 (68) ^a
Status	
Elective	97 (42)
Urgent	125 (54)
Emergent	9 (4)
Ejection fraction	(52 \pm 15)%
IABP use	41 (18)
Angina class III or IV	153 (66)
Co-morbidity	
Hypertension	155 (67)
Diabetes	65 (28)
Hypercholesterolemia	149 (64)
COPD	41 (18)
Prior CVA	39 (17)
PVD	38 (16)
Tobacco abuse	
Former	67 (29)
Active	70 (30)
Prior MI	45 (19)
Recent MI	59 (25)
Creatinine > 2 mg/dl	9 (4)

IABP, intra-aortic balloon pump; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; PVD, peripheral vascular disease; MI, myocardial infarction.

^aValues in parentheses are indicated in percentages.

The angiograms were reviewed and assessed for the location of the left main stem lesion (ostium, midportion, distal end), the presence of severe calcification, eccentricity of the lesion, coronary dominance and whether the lesion of the left main stem involved the bifurcation. A lesion was classified as involving the left main bifurcation if it involved both the distal portion of the left main artery and the origin of the left circumflex, ramus, and/or left anterior descending arteries. The extent of significant ($>50\%$) proximal or midvessel narrowing in other, major coronary vessels (dominant RCA, LCX and/or ramus intermedius, and LAD) and the presence of total coronary occlusion in the proximal portion of these major epicardial coronary arteries were determined. Ejection fraction was determined from left ventriculography or from noninvasive estimation.

Six characteristics were defined as “unfavorable” for left main coronary intervention. Lesion characteristics that have been associated with suboptimal acute and long-term success from PCI included (1) presence of a bifurcation left main coronary stenosis and (2) presence of total occlusion of a major epicardial coronary (RCA, LAD, or LCX). Other angiographic or patient characteristics that are associated with an increased risk of the procedure due to the potential for hemodynamic compromise during left main intervention included (3) ejection fraction $<30\%$ [4,11] and (4) the presence of total occlusion of a proximal, dom-

TABLE II. Angiographic Characteristics (n = 232)

Coronary dominance	
Right	208 (90) ^a
Left	17 (7)
Mixed dominance	7 (3)
Location and characteristics of left main disease	
Ostial	94 (41)
Mid	47 (20)
Distal	138 (59)
Bifurcation	123 (53)
Calcification	112 (48)
Eccentric	158 (68)
Quantitative angiography of left main (n = 220)	
Reference (mm)	4.38 ± 0.65
MLD (mm)	1.55 ± 0.27 mm
Lesion length (mm)	5.48 ± 1.91 mm
Percent diameter stenosis (%)	64 ± 7
Presence of >50% stenosis in other arteries	
LAD	149 (64)
LCX	138 (59)
RCA	184 (79)
Ramus intermedius	14 (6)

MLD, minimal luminal diameter; LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery.^aValues in parentheses are indicated in percentages.

inant RCA or (5) the presence of a left dominant circulation. The sixth unfavorable angiographic characteristic included the presence of extensive coexisting coronary artery disease defined as stenosis >50% in all three major epicardial coronary arteries (LAD, LCX and/or ramus intermedius, and RCA) in addition to the left main stenosis.

Quantitative coronary angiography was performed on the left main stem to assess reference diameter, minimal luminal diameter, and lesion length. Reference diameter was the diameter of the angiographically normal caliber left main coronary artery proximal or distal to the lesion.

The treatment received by the patient (CABG, PCI or medical therapy) was determined by chart review in all patients. Clinical follow-up was obtained by review of the medical records to determine all cause mortality in 1 year.

Statistical Analysis

Data were analyzed with RS/1 software (RS/1 Version 6.0.1, copyright 1999, Domain Manufacturing Corporation, Burlington, MA). All normally distributed data were expressed as mean ± 1 standard deviation; data not normally distributed were expressed as median (25th, 75th percentile). Comparisons between groups were performed and group differences of continuous factors were compared using Wilcoxon signed rank tests. Group differences of categorical variables were

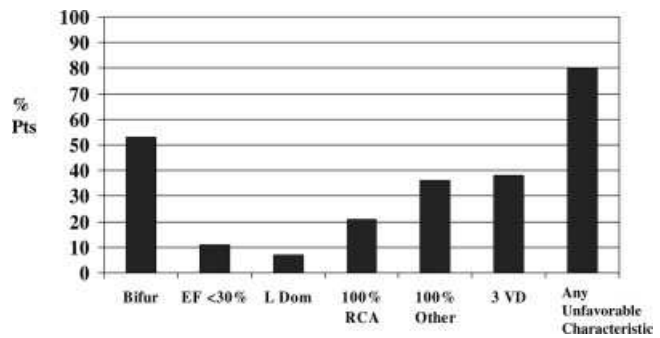


Fig. 1. Prevalence of unfavorable characteristics for percutaneous intervention in patients with left main coronary disease. Bifur, bifurcation disease; EF, ejection fraction; L Dom, left dominant circulation; RCA, right coronary artery; 3 VD, three vessel coronary disease.

compared using χ^2 -tests or, in the cases of small cell sizes, Fisher's exact test. All *P*-values are from two-sided tests.

RESULTS

The clinical characteristics of the 232 patients included in this study are shown in Table I. Overall, patients with LMCD tended to be elderly (mean age 69 years) and predominantly male (68%). Angina Class 3 or 4 was observed in 66% of patients. The catheterization procedure was performed electively (as an outpatient evaluation) in 42% and as an urgent procedure (as part of an in-patient evaluation) in 54%; only 4% had angiography performed as an emergency procedure. An intra-aortic balloon pump was placed after angiography in 18% of patients.

The angiographic data are summarized in Table II. Disease was present in at least one of three locations as follows: ostium in 41%, midportion in 20% and at the distal end of the left main stem in 59%. In 53% of patients the disease represented a bifurcation stenosis involving also the LAD and/or the LCX or ramus arteries. A high proportion of patients had >50% narrowing in other coronary arteries with nearly 80% of patients demonstrating significant disease in the RCA in addition to LMCD. Other than the LMCD, 17% of patients had single vessel disease, 35% had two vessel disease and 38% had three vessel disease. Only 9% of patients had isolated LMCD.

The prevalence of the six prespecified unfavorable characteristics for PCI are summarized in Fig. 1. The most commonly observed unfavorable feature was the presence of a bifurcation stenosis that was found in more than half of the patients. There was also a high prevalence of total occlusion of one or more major

TABLE III. Comparison of Clinical Characteristics

Variable	Favorable anatomy	Unfavorable anatomy	<i>P</i> value
<i>n</i>	41	164	
EF (%)	58 ± 11%	51 ± 16	0.0001
Age (y)	65 ± 13	70 ± 10	0.008
Prior MI (%)	30	48	0.03
Male (%)	56	70	0.08
DM (%)	20	30	0.20
Creatinine (mg/dl)	1.0 (0.7, 1.3)	1.0 (0.7, 1.3)	0.99

EF, ejection fraction; MI, myocardial infarction; DM, diabetes mellitus.

epicardial arteries. Overall, 80% of patients had at least one of the six unfavorable characteristics for PCI of the left main stem. The clinical characteristics of patients with unfavorable angiographic characteristics were compared to those with favorable angiographic characteristics (Table III). Patients with unfavorable angiographic characteristics were older, had a lower ejection fraction, and included a higher proportion of patients with prior MI.

Following angiography, 205 (88%) patients were referred for CABG, 24 (10%) patients were treated medically and 3 (1%) patients were treated with coronary stents. Among patients referred for CABG, 3 died in-hospital while awaiting CABG. Clinical follow-up was obtained in 200/202 (99%) of the remaining patients at 30 days and in 181/202 (90%) at one year. The overall survival in 1 year was no different between patients with favorable angiographic characteristics (86%) compared to those with unfavorable angiographic characteristics (88%).

DISCUSSION

The role of PCI for revascularization of complex coronary disease has expanded in recent years because of improvements in devices and adjunctive pharmacology. Percutaneous intervention of the left main stem has attracted a great deal of attention and numerous case series have reported outcomes following stenting of LMCD [5–12]. These series typically are small and consist of highly selected patients. In general, the procedural success rates approach 100% and the in-hospital rate of major adverse events is low, particularly in nonemergent patients. However, the rate of major adverse events after hospital discharge is disturbingly high. One of the larger series describing the outcome of consecutive left main stem stenting reported a 1 year mortality of 24.2% [11]. Another series consisting of elective patients undergoing left main PCI reported angiographic restenosis rates of 31% at 5 months and 6/67 (9%) patients suffered a cardiac death within 6

months [12]. As a consequence of these concerns, CABG remains the predominant mode of revascularization for LMCD. In fact, the guidelines from the American Heart Association and the American College of Cardiology characterize PCI of the left main stem as a Class 3 indication for any patient who is a candidate for coronary revascularization surgery [19].

The widespread implementation of drug-eluting stents has rekindled an interest in left main stem intervention. Several recent reports have shown very favorable rates of restenosis with drug eluting stents in left main disease [20–24]. One study comparing sirolimus-eluting stents to bare metal stents, found the rate of major adverse cardiac events at 1 year to be only 2% in the drug eluting stent group compared to 19% in the bare metal stent group [24].

Restenosis is not the only obstacle to the widespread acceptance of PCI for the treatment of LMCD. Patients with LMCD may have anatomic features or additional disease that is difficult or impossible to treat by percutaneous techniques. Given these considerations, the published case series of highly selected patients undergoing PCI for LMCD provide little information on how many patients with LMCD are good candidates for PCI. Furthermore, it is important to establish the outcomes of unselected patients with LMCD treated surgically in the modern era to serve as a standard by which to compare the outcomes of patients treated percutaneously. The present study provides insight into these important issues.

A major finding of this study is that most patients with LMCD have at least one undesirable angiographic feature for PCI. More than half of the patients had a bifurcation stenosis. Bifurcation lesions can be particularly challenging to treat percutaneously and are associated with lower success and higher restenosis rates [15–17]. Another important observation is that LMCD is frequently associated with extensive coronary disease in other vessels. Nearly three-fourths of the patients had significant two- or three-vessel coronary disease in addition to the left main stenosis and 36% had total occlusion of at least one other coronary artery. Only 9% of patients had isolated left main stem coronary artery disease. Focusing solely on the technical feasibility of a left main stem intervention fails to place the entity of LMCD in the proper perspective.

The outcomes of unselected patients with LMCD treated with surgery are usually good. In the present cohort, the 1 year all-cause mortality was 12% for those treated with CABG. In the Collaborative Study in Coronary Artery Surgery (CASS) study, the 1 year mortality for patients with left main narrowing >60% treated with surgery was 4 and 9% for patients >65

years old [2]. The 1 year mortality in the Veterans Administration Cooperative Study was 6% [1]. Our unselected cohort of patients with left main disease were significantly older and had a higher prevalence of comorbid conditions than the highly selected population of patients enrolled in the above-mentioned clinical trials and thus a higher 1 year all-cause mortality. The reported 1 year mortality following left main stem intervention varied from 0% in a selected, low risk, nonbifurcation stenosis population to 20.2% in a more heterogeneous and higher risk cohort [9–11,24–26]. The selection bias inherent to these studies makes it impossible to compare the outcomes of CABG versus left main intervention without a randomized trial.

There are several limitations to this study. First, not all interventionalists would necessarily agree on the six angiographic features chosen as “undesirable for PCI.” Some of these features may not be considered insurmountable obstacles by all interventionalists and many of these features do not necessarily prohibit a PCI procedure. However, most will agree that the selected features raise the risk and lower the acute and long-term clinical success of the procedure and thus are important to characterize. Another limitation relates to whether or not our cohort is truly representative of patients with left main stem disease. This is difficult to know since there is very little published data regarding the nature of this entity in unselected patients. Our patients were identified from over 13,000 consecutive coronary angiograms performed in six catheterization laboratories at three hospitals; one tertiary care hospital (four labs) and two community hospitals (two labs). Most of the angiograms were obtained at the tertiary care hospital which may lead to a higher proportion of patients with advanced disease. However, the proportion of patients with left main disease was similar to another report identifying LMCD in 4.3% of patients undergoing catheterization for chest pain syndromes [27]. Our finding of extensive coronary disease in association with LMCD is similar to a recent report which identified significant, coexisting coronary disease in 94.5% of patients with LMCD [28].

Given the high proportion of bifurcation stenoses, left main stem PCI might become more conventional once better treatment for bifurcation lesions is established. It is not clear that drug-eluting stents will overcome the problem of in-stent restenosis for bifurcation disease as the restenosis rate in one trial using sirolimus was 25.7% at 6 months [29]. New stents dedicated to bifurcation disease are under development but their role remains untested [30]. Given the complexity of the disease and the accepted standard with surgery, it is apparent that randomized clinical trials are necessary to define the role of PCI in the treatment of

unprotected LMCD. The data presented in this study provides some important groundwork for planning these trials.

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