Percutaneous Coronary Intervention for Left Main Coronary Artery Disease: Is it Time to Change the Guidelines?

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Significant left main coronary artery (LMCA) disease (i.e., stenosis, ≥50% of lumen) is the most lethal form of coronary artery disease. It is present in 3%–5% of patients undergoing coronary angiography.[1] Those who require medical treatment have a poor prognosis, and there is a 3-year mortality rate of 50%.[1] On the other hand, randomized trials carried out at the end of the 1970s demonstrated that survival is significantly improved by revascularization surgery.[2] The favorable outcome of revascularization surgery and the poor results that were initially obtained with percutaneous coronary intervention (PCI), which was associated with elevated short-term and long-term mortality rates (e.g., a 3-year survival rate of 36%),[3] made surgery the treatment of choice for the majority of patients. This is reflected in current clinical guidelines.[4] For example, the guidelines of the Spanish Society of Cardiology (*Sociedad Española de Cardiología*) classify PCI for LCA disease as a class-IIb indication.[5]

Nevertheless, it is necessary to distinguish between two distinct morphological states in LMCA disease: that in which the LMCA is protected by a patent arterial or venous bypass graft that perfuses the left coronary area, and that in which the LMCA is unprotected. In addition, there are also two different clinical circumstances with distinct levels of risk: when the LMCA intervention is elective, and when treatment must be implemented urgently because of acute myocardial infarction (AMI) or because there is either an acute spontaneous occlusion or iatrogenic occlusion resulting from catheter manipulation.

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PROTECTED LEFT MAIN CORONARY ARTERIES

The results of PCIs with stents in protected LMCA are excellent and similar to those obtained at other coronary sites (i.e., 1-year mortality rate, 2%; repeat revascularization rate, 13%),[6] especially if stent implantation is optimized using intravascular ultrasound (IVUS) guidance.[7] In a study carried out by Hong et al,[7] the final cross-sectional area achieved using IVUS was an independent predictor of the occurrence of subsequent events and of the need for repeat revascularization (i.e., 50% for a final cross-sectional area <7 mm^2 and 5% for a final cross-sectional area >9 mm^2).[7] These result have made PCI in protected LMCA a realistic alternative to repeat surgery at the majority of centers.

UNPROTECTED LEFT CORONARY ARTERIES

Percutaneous coronary intervention in an unprotected LMCA is another matter. Improvements in stent implantation techniques and new antithrombotic agents have generated renewed interest in percutaneous treatment of these lesions. Stent implantation has been used as a therapeutic option in unprotected LMCA in selected patients in whom surgery carries a high risk,[6] as a bail-out procedure,[8] and even electively.[9–13]

The short and long-term results reported in two multicenter registries, which were set up between 1993 and 1998 by Ellis et al[14] and Tan et al,[15] are highly variable and dependent on various factors. In particular, results were substantially poorer in patients who presented with an AMI. When this form of presentation was excluded, however, ejection fraction was found to be the most important prognostic factor predicting death during hospitalization.[14] Data from both registries show, however, that results were particularly good for elective treatment in patients with low surgical risk factors and a normal ejection fraction. Nevertheless, overall medium-term results in this very heterogeneous group of patients were poor. The annual

TABLE 1. **Results Obtained by Elective Percutaneous Coronary Intervention in Unprotected Left Coronary Arteries***

Author, Year, and Reference	In-Hospital Results (%)					Follow-up Results (%)			
	n	Procedure Success Rate (%)	Mortality (%)	Need for Surgery (%)	AMI (%)	Time (Years)	Mortality (%)	Restenosis (%)	NRR (%)
Silvestri et al, 2000[9]	140	100	3	–	–	1	8	23	17
Park et al, 2002[11]	63	100	0	0	0	2	3.2	28	10
Takagi et al, 2002[12]	67	97	0	3	7.5	3	11.9	31.4	24.6
Park et al, 2003[13]	270	98	0	–	1.1	3	7.4	21	16.7

*AMI indicates acute myocardial infarction; NRR, need for repeat revascularization.

mortality and revascularization rates were 20% and 25%, respectively. Consequently, early angiographic follow-up is recommended in these patients to help prevent restenosis and late mortality.

ELECTIVE PERCUTANEOUS INTERVENTIONS IN UNPROTECTED LEFT MAIN CORONARY ARTERIES

An increasing number of centers are reporting their experience with elective PCI in unprotected LMCA.[9–13] The results of some studies are summarized in Table 1. Short- and medium-term results are invariably good in selected low-risk patients undergoing stent implantation (i.e., those with a normal ejection fraction who are good candidates for surgery). Moreover, results continue to be better if IVUS is used for treatment optimization.[10] The survival rate can be very high in patients with a normal ejection fraction, and can even exceed 90% at 3 years.[9–13] Therefore, PCI can be considered a realistic alternative to coronary surgery in this type of patient. However, results are poor if the patient is not a good candidate for surgery and there is left ventricular dysfunction.[9–13] In the studies listed in the table, the following independent predictors of mortality were identified: the vessels' reference diameter,[12] the minimum post-stenting lumen diameter,[13] left ventricular dysfunction,[11–13] and high surgical risk score.[12] In summary, these studies present overall good results, but the mid-term rates of cardiac mortality, restenosis, and need for revascularization are still high, which means that survivors must be carefully followed up during the first few months following treatment.

On the other hand, the increased mortality risk associated with elective surgery for LMCA disease should be considered. Data from the Cleveland Clinic[16] and the Coronary Artery Surgery Study (CASS) registry[17] show mortality rates during hospitalization of 2.3% and 4.6%, respectively, and medium-term mortality rates of 11% at 1 year[16] and 15% at 5 years.[17] These figures are comparable with those obtained in some PCI studies: Sylvester et al[9] found a mortality rate during hospitalization of 3% in 140 patients undergoing elective treatment; Tan et al[15] observed no in-hospital deaths and registered a 1-year mortality rate of 3.4% in low-risk patients, who formed 32% of the total; and Takagi et al[12] reported a 3-year cardiac mortality rate of 4.2% in patients for whom surgery presented a low risk.

Unfortunately, patients who are good candidates for surgery are also good candidates for PCI. Surgery could still be the treatment of first choice for many patients with LMCA disease, especially if it is associated with multivessel disease and ventricular dysfunction. However, elective percutaneous revascularization is, according to data from the studies mentioned above, a realistic alternative in selected low-risk patients and should be indicated for inoperable patients with severe symptoms. Consequently, patients must be selected judiciously if results are to be optimized. Therefore, further studies are needed to define which patients are really inoperable and which of those patients will benefit from PCI.

URGENT PERCUTANEOUS INTERVENTIONS IN UNPROTECTED LEFT MAIN CORONARY ARTERIES FOR ACUTE MYOCARDIAL INFARCTION

Cardiogenic shock occurs as a complication of AMI in 75%–80% of patients in whom the LCA is the affected vessel.[18] The "LMCA cardiogenic shock syndrome" described by Quigley et al[19] is an extremely serious condition in which AMI is accompanied by cardiogenic shock and severe LMCA stenosis. The mortality rate is 100% with conservative treatment and 89% with PCI and surgery.[19] The use of stents, platelet glycoprotein IIb/IIIa inhibitors, in particular abciximab, and hemodynamic support techniques, in particular intra-aortic balloon counterpulsation (IABC), have improved results with these procedures. Since PCI has been accepted as the best treatment for AMIs, experience with treating unprotected LMCA in these circumstances has increased.

In a multicenter study carried out by Marso et al,[20] 40 patients with LMCA disease and AMI (92% of whom were in shock) were treated by PCI; a stent was used in 43%, IABC was used in 87%, and abciximab, in 13%. The procedure was angiographically success-

ful in 88% and the in-hospital mortality rate was 55%. Significantly, the 1-year mortality rate in patients with this serious condition was 43%. Moreover, results in the post-hospitalization phase were good, with only one death occurring after discharge.

De Luca et al[18] have described a large series of patients (n=24) with AMI and LMCA disease (63% of whom were in shock) who were treated at a single center by PCI; a stent was used in 58%, IABC was used in 100%, and abciximab, in 21%. Angiographic success was achieved in 67% of the cases and the in-hospital mortality rate was 58%. As in Marso et al's study, the prognosis for survivors during follow-up was good. There was no difference in long-term mortality between those treated by PCI alone and those who additionally underwent surgical revascularization.

It is not clear from the current literature which of the 2 methods (i.e., PCI or surgery) is preferable in patients with AMI and LMCA disease, with or without shock. Unlike PCI, urgent surgery is not always an option. Even when it is available, preparation can take longer than the patients' hemodynamic condition permits. In contrast, in the context of primary PCI for treatment of AMI, with which many centers have accumulated great experience, PCI can be used to restore coronary flow and improve hemodynamics within minutes and, thereby, save lives. Accordingly, the use of PCI with stenting is the preferred revascularization strategy in patients with AMI and LMCA disease. The effectiveness of this form of treatment is indisputable and current AMI guidelines from the American College of Cardiology and the American Heart Association include it as a class-I indication.[21]

CURRENT SITUATION IN SPAIN

Currently, PCI in the LMCA forms part of daily practice in Spain. In 2002, 493 procedures were carried out (1.42% of all PCIs), 70% of which were performed in unprotected LCAs.[22]

The studies carried out by Martí et al[23] and López-Palop et al,[24] which are reported in this issue of Revista Española de Cardiología, are testimony to this new reality. The patient populations involved in the 2 studies were similar: poor surgical candidates. Moreover, the percentages of patients who underwent elective surgery (71% and 73%, respectively) or urgent surgery for AMI (29% and 27.5%, respectively) were also comparable. Nor did the PCI techniques used differ substantially: stents were used in 100% and 95%, respectively; abciximab in 21% and 36%, respectively; and IABC in 24% and 40%, respectively. Nevertheless, the studies differed in one important respect. Martí et al's study included 15 patients with protected LMCA (39% of the total), whereas all patients in López-Palop et al's study had unprotected LMCA. This difference could explain the different results obtained: immediate success in 97%[23] and 92%,[24] respectively, and in-hospital mortality rates of 15.8%[23] and 29%,[24] respectively (3.7% and 20%, respectively, during elective surgery, and 45% and 55%, respectively, during urgent surgery). Medium-term follow-up demonstrated cardiac mortality rates of 8%[23] (all deaths occurred in patients with unprotected LMCA) and 12%,[24] respectively. Almost all deaths took place in the first few months following PCI. Recurrent ischemia occurred during the first few months of follow-up in 13.2%[23] and 22%[24] of patients in the 2 studies, respectively. Repeat revascularization was required in 7%[23] and 17%[24], respectively, and was almost always carried out by repeat PCI. Very few of the serious events reported in the first year took place late in the year. An urgent indication for PCI was found to be a predictor of in-hospital mortality in both studies, and the presence of an unprotected LCA was a predictor in Martí et al's study. In addition, the presence of left ventricular dysfunction was associated with a nonsignificant tendency towards greater mortality.

These data are comparable with those reported in the literature. In particular, the data on mortality with urgent procedures are equivalent to those quoted by Marso et al[20] and de Luca et al.[18] Nevertheless, the results obtained in patients undergoing elective procedures, particularly in López-Palop et al's study, are poorer than those reported in other recent studies with patients at a high surgical risk. The authors attribute these poor results to the particular type of patient treated: many were of advanced age and the incidence of comorbid complaints was high.

STUDY LIMITATIONS

The main limitation of the majority of studies on PCI in the LCA, including those featured in this issue, is that they involved heterogeneous patient populations and clinical situations (e.g., protected and unprotected LMCA, and elective and urgent procedures). This heterogeneity reflects the reality of everyday practice but makes the analysis of the results difficult.

Other study limitations are the infrequent use of glycoprotein IIb/IIIa inhibitors and IABC, which should probably be employed more often in these high-risk procedures. Moreover, IVUS was not used very often in these studies. The results of elective PCI in the LCA could be improved by using IVUS, especially in cases involving bifurcated LMCA.[7,10] In addition, the difficulty of carrying out angiography to evaluate the severity of LMCA disease is well known. The use of IVUS could aid decision-making in patients with intermediate lesions (i.e., greater than 50%) since revascularization surgery does not improve survival in these cases.[17]

Previously, the occurrence of restenosis has been the principle factor limiting medium-term results with PCI. In patients with LMCA A disease who were treated using a stent, however, in-hospital results have been very satisfactory. Nevertheless, the mortality rate increases during the first 6 months after treatment. The occurrence of adverse events has been attributed to atherosclerosis progression and to restenosis, which frequently leads to deleterious symptoms. If restenosis were to have a solution, long-term results appear to improve in these patients. The introduction into the therapeutic armamentarium of stents coated with agents such as sirolimus and paclitaxel and their ability to reduce restenosis has raised expectations about the future treatment of LMCA disease. However, previous studies with drug-eluting stents have generally excluded treatment of the LMCA. Still, some experience with the use of sirolimus-eluting stents in the LMCA has been described in two recent studies reported by Arampatzis et al.[25,26] The results obtained were very promising. The first study included 31 unselected patients, some of whom underwent elective treatment while others underwent urgent treatment for AMI and cardiogenic shock. The in-hospital mortality rate was 13%. During a 5-month follow-up period, the repeat revascularization rate was 4%, but there were no other cardiac events.[25] These results are particularly good considering that the study involved unselected patients treated in "daily practice in the real world." The second study, which was carried out using the same type of stent, involved 16 patients who underwent elective treatment, nine of whom had an unprotected LCA that, in the majority of cases, affected the distal bifurcation.[26] The in-hospital and 1-year results were excellent: no deaths, one non-Q-wave AMI, and one repeat revascularization because of restenosis (8%).[26]

The situation is likely to become clearer in the future as the number of indications for this type of stent increases progressively and as the results of studies that are already underway (e.g., case registers of inoperable patients treated using such stents) become available. The difficulties encountered in the past in completing randomized studies that compared the results of surgery and PCI in LMCA disease could have been resolved in practice by using drug-eluting stents, given their potential to remain patent.

CONCLUSIONS

When carried out by skilled practitioners, percutaneous coronary intervention is now a realistic alternative to surgery in protected LMCA and in selected groups of low-risk patients with unprotected LMCA. Moreover, currently it is the best form of treatment for patients with AMI, with or without cardiogenic shock, and for inoperable symptomatic patients.

There is a need for studies comparing results obtained by PCI (using drug eluting stents) with those obtained by coronary surgery so that current indications for the treatment of this vessel can be revised.

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