

## LEFT MAIN CORONARY ARTERY DISEASE AND THERAPY

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Sol ana koroner arterde %50 ve üzerinde darlık olması anlamlı darlık olarak tanımlanır. Korunmamış sol ana koroner arter darlığı tedavisinde internal mammarian arter ile koroner arter bypass yapılması altın standart olmasına rağmen perkütan koroner girişim de yapılabilmektedir. Korunmamış Sol ana koroner arter darlıklarına yapılan balon anjiyoplastide uzun dönem prognoz kötüdür ve mortalite artmaktadır. Seçili vakalarda anjiyoplasti ve stent güvenle uygulanabilir. İlaç kaplı stentler

restenoz ve mortalite açısından uzun dönem sonuçları çıplak metal stentlerde daha üstün bulunmuştur.

**Anahtar kelimeler:** Left main coronary artery disease, Coronary artery bypass grafting, Angioplasty

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### INTRODUCTION

Significant left main coronary artery disease (LMCD) is defined as > 50% narrowing of left main coronary artery. Prognosis is usually poor due to massive ischemia and sudden death. While coronary artery bypass grafting (CABG) is the first-line therapy, Percutaneous coronary intervention (PCI) is emerging as a possible alternative to surgery.

PCI for unprotected left main (ULM) offers a treatment that is both less invasive and with potentially lower risk in patients who are not ideal candidates for CABG because of comorbidity, advanced age, or cardiogenic shock. Prior studies of baremetal stents (BMS) for ULM PCI have involved both low- and high-risk patients as well as those with shock<sup>1-5</sup>.

Although CABG is the treatment of choice for severe left main coronary artery (LMCA) stenosis, the results of a number of multicenter trials have suggested angioplasty with stenting as a possible alternative treatment. Balloon angioplasty of the LMCA has been associated with elevated procedural mortality and with a poor long-term prognosis<sup>6</sup>. Therefore, coronary artery bypass surgery has been the treatment of choice for unprotected LMCA lesions<sup>7</sup> while angioplasty has

been preferred for patients with high surgical risk factors and urgent revascularization requiring cases<sup>8-11,31,32</sup>. Additionally, with the introduction of stents and advancements in antiplatelet agents, LMCA angioplasty is no longer strictly contraindicated as a possible alternative to surgical treatment in particular patients<sup>12</sup>. Traditional balloon angioplasty of the LMCA is associated with increased medium and long term mortality. In O'Keefe et al's series<sup>6</sup>, mortality during treatment in patients undergoing elective angioplasty with or without LMCA protected was 4.3% and 9.1% in the 2 subgroups, respectively. Therefore, conventional LMCA angioplasty has been restricted to patients for whom surgery is a high-risk procedure and to those who need urgent treatment. In addition, the phenomenon of elastic recoil occurs more frequently with LMCA angioplasty because of the preponderance of elastic fibers in arterial walls<sup>10</sup>. The introduction of stents has revolutionized the treatment of coronary artery disease and has increased the number of indications for LMCA angioplasty. The main beneficial effects of stents are to reduce the risk of acute occlusion, to inhibit elastic recoil of the arterial wall, and to decrease the rate of restenosis<sup>13</sup>.

Coronary artery disease with greater than 50% left main stenosis remains a strong indication for early CABG. PCI of left main stenosis in the absence of previous CABG (so-called unprotected left main or ULM) with BMS has been limited by restenosis and sudden cardiac death<sup>1-5,13</sup>. Recently there have been reports of

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the feasibility of treating ULM with drug-eluting stents (DES) with favorable medium-term outcomes. However, these represent selected patients from highly selected centres with a long history of ULM stenting limiting their application to clinical practice.

The experience with BMS for ULM PCI in the multicenter ULTIMA (Unprotected Left Main Trunk Intervention Multicenter Assessment) registry suggested a high early mortality (2% per month among hospital survivors over the first 6 months after hospital discharge), and careful surveillance with coronary angiography was recommended<sup>8</sup>. Patients presenting with MI, ULM occlusion, and cardiogenic shock have lower successful PCI rates (69.7% vs 100%,  $P$  equals 0.040), higher in-hospital mortality (71.4% vs 10%,  $P$  equals 0.0008), and higher 1-year mortality rates ( $P$  equals 0.0064) than stable MI patients regardless of performance of primary PCI with stents<sup>15</sup>. More recently, published studies of left main PCI using DES have reported 6-month or 1-year death rates ranging from 0% to 14%<sup>7,8,12-15,18-22</sup>. Furthermore, In stent restenosis (ISR) appears to be improved with the use of DES versus BMS. One of the larger studies performed to date showed that the 6-month angiographic restenosis rate was significantly lower in the ULM group receiving DES than in those who received BMS (7.0% vs 30.3%,  $P$  less than 0.001)<sup>22</sup>. The lower rate of restenosis of DES compared with BMS has been confirmed in other studies of ULM PCI<sup>21</sup>. The success rate of these interventions can depend on some risk factors.

There have been some attempts to predict success of ULM PCI using customary risk factors such as age, renal failure, coronary calcification, and location of the lesion in the left main coronary artery. In general, younger patients with preserved LV function, noncalcified coronary arteries, and complete delivery of stent, far better. Maintenance of antiplatelet therapy after the procedure is critical, as is the implementation of secondary prevention therapies. Careful postprocedure surveillance with coronary angiography is needed to prevent fatal MI or sudden death that may be associated with ISR with a large area of myocardium in jeopardy; however, the frequency and best method of follow-up are unknown<sup>23</sup>. A researcher from BMS era suggested routine surveillance angiography at 2 and 4 months after PCI<sup>8</sup>. Others advocate routine stress testing or cardiac catheterization at 3 and 6 months even in asymptomatic patients<sup>16,17</sup>. Studies from the DES era have reported performing routine angiography 4 to 8 months after PCI or earlier if clinically indicated by symptoms or documented myocardial ischemia<sup>21,22,31,32</sup>.

Other issues that remain to be resolved are technical issues (e.g., optimal bifurcation stenting technique, stent size), degree of revascularization necessary, cost-effectiveness, and the selection of patients best suited for DES.

Despite use of new treatments for percutaneous intervention, including stent implantation, adjunctive atheroablative techniques and glycoprotein IIb/IIIa inhibitors, the one-year survival rate for stenting of left main disease was reported to be only 88% in the study of Kelley et al<sup>24</sup>. Kelley et al. have reported that one-year mortality rate was 28% for unprotected group when compared with the 5% rate in the protected group<sup>24</sup>. Patients who underwent unprotected LMCA stenting represented a high-risk subgroup, with the majority of the patients in the group classified as poor surgical candidates based on advanced age or other comorbidities. Inclusion of these higher risk patients for unprotected LMCA stenting introduces selection bias, which may help to explain the high one-year mortality of 28% found in the unprotected group when compared to the 5% rate in the protected group. However, the one-year mortality for the protected patients in the Kelley et al study, although similar to previous studies, is still higher than reported rates for non-LMCA procedures<sup>25,26</sup>, which may reflect an increased mortality in patients with well-established coronary artery disease who have previously undergone CABG. Similarly, the one-year MACE rate of 25% for stenting of protected LMCA disease found in Kelley et al. study, comparable to a previous report by Lopez et al<sup>27</sup>, is higher than the one-year event rates of PCI for other coronary lesions<sup>26</sup>. The majority of the patients in Kelley et al. study had a significant stenosis in at least one non-left main vessel, suggesting a heavy atherosclerotic burden which may, in part, explain the poor mortality and MACE rates in addition to the presence of other significant comorbidities.

The Coronary Artery Surgery Study (CASS) demonstrated 1-year and 5-year survival rates of 90% and 85% respectively for surgical revascularization of a left main stenosis, excluding patients having a previous CABG<sup>1</sup>. Recent studies of outcomes for repeat CABG, encompassing both protected left main disease and other coronary lesions, include a peri-operative mortality of 7-10%, and 1 and 5-year survival rates of 86-89% and 76-79% respectively<sup>28,29</sup>. Repeat bypass surgery is also associated with an 8% risk of stroke, wound complications, or reoperation for bleeding<sup>28</sup>.

Recent studies of routine stenting for patients with unprotected LMCA disease have demonstrated differences in procedural results between patients

defined as good or poor surgical candidates. The one-year survival for unprotected LMCA stenting involving good surgical candidates is approximately 95-98%. For poor surgical candidates, survival at one year has ranged from 79-89%<sup>7,10,18,20</sup>. As such, the indication for stent implantation of unprotected LMCA disease likely reflects more emergent indications for immediate revascularization, such as acute myocardial infarction, cardiogenic shock or the presence of other serious comorbidities that preclude a more invasive operation. Long-term survival, in turn, is predominantly dictated by these same adverse clinical variables rather than the procedure itself. Hence, current and previous data should be viewed in that context. However, silent restenosis, manifesting itself as death, rather than recurrence of progressive ischemic symptoms, may be responsible, in part, for the increased mortality noted beyond the initial hospitalization. Evidence of this has been shown in a study by Takagi et al., which demonstrated a 9% mortality rate postulated to be secondary to restenosis in 67 patients undergoing PCI of an unprotected left main lesion<sup>7</sup>. Tan et al. showed a mortality rate of 2% per month over the initial 6 months after PCI of an unprotected LMCA stenosis<sup>8</sup>. A drug-eluting stent could potentially improve some of the late mortality associated with restenosis, but should not affect the high mortality associated with the substantial comorbidity of these patients going into the procedure.

In the current era, stenting for protected LMCA disease is still associated with increased mortality and MACE rates compared to PCI of other coronary lesions, but offers a possible alternative to a repeat bypass surgery. Prospective studies of these two treatment strategies seem warranted. Stenting for unprotected LMCA disease in a high-risk population is associated with a poor one-year survival and should only be considered in the absence of other revascularization options. Further studies are needed to definitively define the role of stenting for unprotected LMCA disease.

Although findings published in the medical literature, especially in patients undergoing elective treatment, have encouraged an increase in indications for LMCA angioplasty, randomized controlled studies are needed before the technique can be recommended as an alternative treatment for those without contraindications to surgery. It should be emphasized that patients who are good candidates for revascularization surgery are usually also good candidates for angioplasty. Therefore, those for whom angioplasty is appropriate must be carefully selected. In

patients undergoing elective angioplasty, results are more favorable when the lesion is not bifurcated and the LMCA is relatively long than when the lesion affects a short LMCA and involves the bifurcation<sup>30</sup>. In patients with AMI in cardiogenic shock, angioplasty is probably the only therapeutic option despite the poor results.

In conclusion, CABG using IMA grafting is the "gold standard" for treatment of ULM disease and has proven benefit on long-term outcomes. LMCA angioplasty with stent implantation is a safe procedure in selected patients. Elective angioplasty in individuals with a protected LMCA is associated with a relatively low incidence of major cardiac events. The use of DES has shown encouraging short-term outcomes, but long-term follow-up is needed. Nevertheless, the use of PCI for patients with significant ULM stenosis who are candidates for revascularization but not suitable for CABG can improve cardiovascular outcomes and is a reasonable revascularization strategy in carefully selected patients.

## REFERENCES

1. Caracciolo EA, Davis KB, Sopko G, et al.. Comparison of surgical and medical group survival in patients with left main equivalent coronary artery disease. Long-term CASS experience. *Circulation* 1995;91:2335-44.
2. García-Robles JA, García E, Rico M, et al.. Emergency coronary stenting for acute occlusive dissection of the LCA. *Cathet Cardiovasc Diagn* 1993;30: 227-29.
3. Karam C, Fajadet J, Cassagneau B, Laurent JP, Joran C, Laborde JC, et al.. Results of stenting of unprotected LCA stenosis in patients with high surgical risk. *Am J Cardiol* 1998;82:975-78.
4. Macaya C, Alfonso F, Iñiguez A, et al.. Stenting for elastic recoil during coronary angioplasty of the left main coronary artery. *Am J Cardiol* 1992;70:105-107.
5. Ramírez Moreno A, Cardenal Piris R, Guzmán Herrera M, et al. Dissection espontánea del tronco coronario izquierdo tratada mediante implantation de múltiples stents. *Rev Esp Cardiol* 2003;56:417-20.
6. Park SJ, Kim YH, Lee BK, et al.. Sirolimus-eluting stent implantation for unprotected left main coronary artery stenosis: comparison with bare metal stent implantation. *J Am Coll Cardiol* 2005;45:351-56.
7. Takagi T, Stankovic G, Finci L et al.. Results and long-term predictors of adverse clinical events after elective percutaneous interventions on

- unprotected left main coronary artery. *Circulation* 2002;106:698-702.
8. Tan WA, Tamai H, Park SJ, et al. ULTIMA Investigators. Long-term clinical outcomes after unprotected left main trunk percutaneous revascularization in 279 patients. *Circulation* 2001;104:1609-14.
  9. Ellis SG, Tamai H, Nobuyoshi M, et al. Contemporary percutaneous treatment of unprotected left main coronary stenoses: initial results from a multicenter registry analysis 1994-1996. *Circulation* 1997;96:3867-72.
  10. Black A, Cortina R, Bossi I, et al. Unprotected left main coronary artery stenting: correlates of midterm survival and impact of patient selection. *J Am Coll Cardiol* 2001;37:832-88.
  11. Marso SP, Steg G, Plokker T, et al. Catheter-based reperfusion of unprotected left main stenosis during an acute myocardial infarction (the ULTIMA experience). Unprotected Left Main Trunk Intervention Multi-center Assessment. *Am J Cardiol* 1999;83:1513-17.
  12. Agostoni P, Valgimigli M, Van Mieghem CA, et al. Comparison of early outcome of percutaneous coronary intervention for unprotected left main coronary artery disease in the drug-eluting stent era with versus without intravascular ultrasonic guidance. *Am J Cardiol* 2005;95:644-47.
  13. Valgimigli M, van Mieghem CA, Ong AT, et al. Short- and long-term clinical outcome after drug-eluting stent implantation for the percutaneous treatment of left main coronary artery disease: insights from the Rapamycin-Eluting and Taxus Stent Evaluated At Rotterdam Cardiology Hospital registries (RESEARCH and T-SEARCH). *Circulation* 2005;111:1383-89.
  14. O'Keefe JH Jr, Hartzler GO, Rutherford BD, et al. Left main coronary angioplasty: early and late results of 127 acute and elective procedures. *Am J Cardiol* 1989;64:144-47.
  15. Sakai K, Nakagawa Y, Kimura T, et al. Primary angioplasty of unprotected left main coronary artery for acute anterolateral myocardial infarction. *J Invasive Cardiol* 2004;16:621-25.
  16. Silvestri M, Barragan P, Sainsous J, et al. Unprotected left main coronary artery stenting: immediate and medium-term outcomes of 140 elective procedures. *J Am Coll Cardiol* 2000;35:1543-50.
  17. Park SJ, Hong MK, Lee CW, et al. Elective stenting of unprotected left main coronary artery stenosis: effect of debulking before stenting and intravascular ultrasound guidance. *J Am Coll Cardiol* 2001;38:1054-60.
  18. Park SJ, Park SW, Hong MK, et al. Long-term (three-year) outcomes after stenting of unprotected left main coronary artery stenosis in patients with normal left ventricular function. *Am J Cardiol* 2003;91:12-16.
  19. de Lezo JS, Medina A, Pan M, et al. Rapamycin-eluting stents for the treatment of unprotected left main coronary disease. *Am Heart J* 2004;148:481-85.
  20. Arampatzis CA, Lemos PA, Hoye A, et al. Elective sirolimus-eluting stent implantation for left main coronary artery disease: six-month angiographic follow-up and 1-year clinical outcome. *Catheter Cardiovasc Interv* 2004;62:292-96.
  21. Chieffo A, Stankovic G, Bonizzoni E, et al. Early and mid-term results of drug-eluting stent implantation in unprotected left main. *Circulation* 2005;111:791-95.
  22. Park SJ, Kim YH, Lee BK, et al. Sirolimus-eluting stent implantation for unprotected left main coronary artery stenosis: comparison with bare metal stent implantation. *J Am Coll Cardiol* 2005;45:351-56.
  23. Sadeghi HM, O'Neill WW, Grines CL. Percutaneous intervention of unprotected left main coronary artery. *J Interv Cardiol* 2003;16:281-88.
  24. Michael P. Kelley, Bruce D. Klugherz, Seyed M. Hashemi, et al. One-year clinical outcomes of protected and unprotected left main coronary artery stenting. *Eur Heart J*. 2003;24:1554-59.
  25. Williams DO, Holubkov R, Yeh W et al. Percutaneous coronary intervention in the current era compared to 1985-86: The National Heart, Lung, and Blood Institute Registries. *Circulation*. 2000;102:2945-51.
  26. Kiemeneij F, Serruys PW, Macaya C et al. Continued benefit of coronary stenting versus balloon angioplasty: five-year clinical follow-up of Benestent-I trial. *J Am Coll Cardiol*. 2001;37:1598-1603.
  27. Lopez JJ, Ho KKL, Stoler RC et al. Percutaneous treatment of protected and unprotected left main coronary stenoses with new devices: immediate angiographic results and intermediate-term follow-up. *J Am Coll Cardiol*. 1997;29:345-52.
  28. Christenson JT, Schmuziger M, Simonet F. Reoperative coronary artery bypass procedures: risk factors for early mortality and late survival. *Eur J Cardiothorac Surg*. 1997;11:129-33.
  29. Weintraub WS, Jones EL, Morris DC et al. Outcomes of reoperative coronary bypass surgery versus coronary angioplasty after previous bypass surgery. *Circulation*. 1997;95:868-77.

30. Brueren BRG, Ernst JMPG, Sutorp MJ, et al. Long-term follow up after elective percutaneous coronary intervention for unprotected non-bifurcational left main stenosis: is the time to change the guidelines? *Heart* 2003;89:1336-39.
31. Pershukov I, Batyraliev T, Niyazova-Karben Z, Kadayıfci S, Ozgul S, Sengul H, Akgul F, Petrakova L, Peresypko M, Preobrazhenskii D, Sidorenko B. Direct Coronary Stenting of Unprotected and Protected Left Main Stenoses. Proceeding of the Interamerican Congress of Cardiology, Toronto, Ontario, October 24-29, 2003, Canada. p.136
32. Niyazova-Karben Z, Pershukov I, Batyraliev T, Serceloik A, Sidorenko B. Long-term Outcome of direct Coronary Stenting of Left Main Stenoses. Proceeding of XIII th International Symposium on Atherosclerosis, September 28-October 2, 2003, Kyoto, Japan. *J Atherosclerosis*,4/2 (2003) suppl, p. 29.