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Evaluation of safety and efficacy of trans-radial stenting of left main coronary artery in symptomatic patients

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Introduction: A Significant unprotected left main coronary artery (ULMCA) disease occurs in 3–9% of all patients who undergo coronary angiography [1], and it is regarded as the most prognostically important coronary lesion because of the extent of jeopardized myocardium.
Purpose: To assess the safety and efficacy of using trans-radial approach (TRA) for percutaneous coronary intervention (PCI) and stenting of left main coronary artery (LMN) with over 80% stenosis in symptomatic patients.
Methods: We evaluated clinical outcomes of 170 consecutive patients with LM stenting in period between January 2007 and March 2014. The follow up period was 6 months. The baseline characteristics of the study group were: mean age was 62±10.3 years. Males were 133(78%). Acute coronary syndrome (ACSy) was present in 141(83%) of patients. Patients with ST-segment elevation (STEMI) were 27(16%), and non-STEMI in 19 (11%) and unstable angina (UA) in 93(55%). Cardiogenic shock was present in 2 patients (1.17%).
Results: Trans-radial access was used in 151(89%) of patients, trans-ulnar (TUA) in 10(6%) TFA in 9(5%), using 5F and 6F guiding catheters. Drug-eluting stents were used in 131(77%) of patients treated with standard medication regiment. GP IIB/IIIA inhibitors were administrated only in 7(4%) patients. All procedures were achieved with TIMI 3 flow. Ten patients (6%) died during hospital stay and there was no additional deaths during 6 months follow up period. Nine deaths (5%) were cardiac and one (1,7%) was dye severe gastric bleeding.
Conclusion: Trans-radial stenting of diseased and symptomatic left main is feasible and safe when were performed by experienced high-volume operators. Selection, evaluation of the patient as well as planning of the procedure is crucial.

Keyword: Left Main stenting, trans-radial approach, drug eluting stents.

1. Introduction

The presence of significant narrowing LMCA has remained one of the last bastions of CABG. Nowadays, with the availability of new generation's drug eluting stents and the dramatic reduction in restenosis rates they have provided, the results of LMCA stenting have certainly improved. Several recent observational studies have demonstrated nearly equivalent clinical outcomes with single stent ULM bifurcation revascularization and left main stenting for ostial or shaft disease [2–5]. Nevertheless, approximately 40% of ULM bifurcation treatment involves a two-stent method [6, 7], yet the optimal two-stent technique (e.g., crush, culotte, V- or T-stenting) has not been identified, and the procedure is instead determined more by operator and

institutional preference. The SYNTAX trial compared coronary artery bypass graft surgery (CABG) with percutaneous coronary intervention (PCI) for the treatment of patients with left main coronary disease or three- vessel disease. The five years result of the Syntax trial showed that CABG should remain the standard of care for patients with complex lesions (high or intermediate SYNTAX scores). For patients with less complex disease (low SYNTAX scores) or left main coronary disease (low or intermediate SYNTAX scores), PCI is an acceptable alternative. All patients with complex multivessel coronary artery disease should be reviewed and discussed by both a cardiac surgeon and interventional cardiologist to reach consensus on optimum treatment [8]. The current ACC/AHA guidelines for LMCA stenting are:

IIA LMCA PCI is reasonable in pts with class III angina and >50% LM stenosis who are not eligible for CABG

IIB Stenting of the LMCA as an alternative to CABG may be considered in pts with anatomic conditions that are associated with a low risk of PCI procedural complications and clinical conditions that predict an increased risk of adverse surgical outcomes [9].

The SYNTAX score II (SS II) was developed using baseline features and 4-year follow- up information recorded in the SYNTAX study. In addition to SS and the presence or absence of left main coronary artery disease, this novel score considers age, gender, creatinine clearance, left ventricular ejection fraction, chronic obstructive lung disease and peripheral vascular disease. The predictive accuracy of the score for mortality was validated in the study population and in a multinational registry. In patients with left main coronary artery disease, SS II yielded similar mortality for PCI or CABG surgery in 79.7% of patients, which was significantly lower with CABG surgery in 11.5% and with PCI in 8.8% of patients. With SS II <23, the score predicted significantly lower mortality with PCI in 18.2% of patients and with CABG surgery in 2.7%. With SS II >33, these figures were reversed: 0.7% vs. 19.2%. In patients with three-vessel disease, the SS II yielded similar mortality for PCI or CABG surgery in 58.8% of patients. This prediction was significantly lower with CABG surgery in 40.7% and with PCI in 0.5% of patients. With SS II <23, the score predicted significantly lower mortality with CABG surgery in 19.2% of patients and with PCI in 1.4%. With SS II > 33, the differences were greater: 68.1% vs. 0 % [10].

EXCEL is a large scale, randomized trial of left main PCI versus CABG. In the evaluation of Xience Prime versus coronary artery bypass surgery for effectiveness of left main revascularization. (EXCEL) trial, 2,500 patients with left main disease and SYNTAX score 32, clinically and angiographically eligible for revascularization by either PCI or surgery, will be randomized to Xience Prime (Abbott Vascular, Abbott Park, IL) stenting or CABG. Importantly, the primary combined endpoint of death, myocardial infarction, and cerebrovascular accidents will be assessed at a median follow-up of 3-year [11].

Regarding selection of DES, few comparative studies have evaluated outcomes relative to DES type.

In the randomized ISAR-LEFT MAIN trial [14], PCI with either sirolimus eluting stents (SES) or paclitaxel-eluting stents (PES) were associated with similar 2-year clinical events in both stent groups (target lesion revascularization, 9.2% PES vs 10.7% SES; P=0.47). Although to date no studies have compared newer-generation DES to PES or SES in ULM PCI, ongoing trials are comparing newer-generation DES to CABG. The Nordic-Baltic-British Left Main Revascularization trial is randomizing 1,200 patients with ULM and SYNTAX score less than 22 to CABG or DES with end points of major adverse cardiac events (MACE) at 2 years and death at 5 years.

In the Milan experience 5-Year Outcomes Following Percutaneous Coronary Intervention

With Drug-Eluting Stent Implantation Versus Coronary Artery Bypass Graft for Unprotected Left Main Coronary Artery Lesions were compared. In this single-center observational experience, there was still no difference in the occurrence of MACE between elective PCI with DES implantation and CABG in ULMCA lesions, at a median clinical follow- up of 61.9 months (IQR: 57.8 to 67.2 months). This study confirmed a possible advantage of PCI in the composite end point of death, MI, and/or stroke, whereas a benefit in reducing the need for repeated revascularization was still observed in CABG. Adverse cardiac and cerebrovascular events between elective PCI with DES implantation and CABG in unprotected left main coronary artery lesions in this single-center experience. There was an advantage of PCI in the composite end point of death, MI, and/or stroke, whereas a benefit in the need for re-intervention was still found in CABG [12].

Risk scores are useful in determining the early and late outcomes after PCI and CABG for ULM disease, and discriminating between these two modalities for the individual patient [13]. The Euro-SCORE and Parson-net score, which are typically used to risk stratify CABG candidates, have been applied both prospectively and retrospectively to patients undergoing ULM PCI. An analysis from the MAIN COMPARE trial demonstrated that the EuroSCORE≥6 was an independent predictor of mortality in ULM patients who undergo both percutaneous and surgical revascularization [14]. Similarly, increasing Parson-net score was also identified as a significant predictor of major adverse cardiac and cerebrovascular events [14].

2. Methods

We evaluated clinical outcomes of 170 consecutive patients with LM stenting in the period between January 2007 and March 2014. The baseline characteristics of the study group were: mean age was 62±10,23 years; males were 78% (Table 1).

Table 1.

Baseline	LM Stenting (N=170)
Age (years)	62 +/- 10.23
Male gender	132 (78 %)

Acute coronary syndrome (ACSy) was present in 141(83%) of patients. Patients with ST-segment elevation (STEMI) were 27(16%), and non-STEMI in 19(11%) and unstable angina (UA) in 93(55%). Cardiogenic shock was present in 2(1.17%) patients (Table 2).

Table 2.

Clinical	LM Stenting
UA	93 (55 %)
Non-STEMI	19 (11 %)
STEMI	27 (16 %)
Shock	2 (1.17 %)

Previous coronary intervention had 66(39%) patients, 76(45%) had prior MI and 32(19%) were diabetics. Other risk factors are shown in table three

Table 3.

Risk factors	LM Stenting (N=170)
Prior IM	76 (45 %)
Prior PCI	66 (39 %)
DM	32 (19 %)
HTA	117 (69 %)
Smoker	49 (29%)
Positive family history of VD	29 (17 %)
HLP	50(29 %)

3. Results: Drug eluting stents (DES) were used in 131(77%) of patients treated with standard medications regiment. Trans-radial access was used in 85% of patients, using 5F and 6F guiding catheters. All procedures were achieved TIMI 3 flow. GP-IIB/IIIA inhibitors were used only in 7(4%) patients with large thrombus burden. Other procedure related details are shown in table 4.

Table 4.

Procedure	LM Stenting
DES	131 (77 %)
Stent diameter (mm)	3.6 +/- 0.38
Stent length	17.85 +/- 6.0
Pressure (atm.)	17.4 +/- 3.1 8
TIMI 3	139 (95 %)
TIMI 2	7 (5 %)
Reo-Pro	7 (4%)
TRA	135 (85 %)

Ten (10) patients (6%) died during in hospital stay and there were no additional deaths during 6 months follow up period. Nine deaths were cardiac and one was dye severe gastric bleeding (Table 5).

Table 5.

MACE	Death	Live
In hospital mortality	10 (6 %)	160
Syntax score	24.6 +/- 8.5	22.31 +/- 9.3
STEMI	7	10
Distal LM	4	7
Shock	1	1
Reo-Pro	4	3

4. Discussion

Until recently, PCI of ULMCA stenosis was considered a class III indication with level of evidence C in the clinical practice guidelines [15–17]. In the most recent American College of Cardiology/American Heart Association guidelines, PCI of ULMCA stenosis has been upgraded to a class IIb indication with level of

evidence B. It is stated that PCI of ULMCA stenosis may be considered as an alternative to CABG in patients with anatomic conditions associated with a low risk of procedural complication. This restriction connected to the overall anatomical complexity reflects the results of the SYNTAX trial, which has clearly demonstrated an association between coronary lesion complexity and clinical outcomes in the subset of patients undergoing PCI. Also in the European Society of Cardiology guidelines for myocardial revascularization,

PCI of ULMCA stenosis has been upgraded compared to previous recommendations. In particular, three elements should be considered when deciding the optimal strategy of revascularization between CABG and PCI: the location of left main disease (ostial and shaft vs. bifurcation), the coexistence of multivessel disease and the SYNTAX score. Non distal ULMCA stenosis, isolated or associated with 1-vessel disease, is considered a class II a indication. Distal ULMCA stenosis, isolated or associated with one-vessel disease, is considered a class IIb indication. When ULMCA stenosis is associated with multivessel disease, the SYNTAX score becomes the discriminating factor. In fact, in patients with SYNTAX score<33, PCI of ULMCA stenosis has a class IIb recommendation, while in those with SYNTAX score "33 a class III indication.

Further evidence is therefore needed before PCI of ULMCA stenosis can become standard clinical practice in patients who are otherwise good surgical candidates. Most of the evidence, in fact, comes from observational registries. Although consistent in reporting similar hard clinical end points between PCI and CABG, randomized and observational studies performed so far should be interpreted with caution. Similarly, the results of the SYNTAX trial should also be considered hypothesis generating due to the fact that the non-inferiority hypothesis between PCI and CABG was not demonstrated. All these issues will be addressed in the EXCEL trial, which is a randomized trial in which more than 2,000 patients with ULMCA stenosis and a SYNTAX score<33 are being assigned to either CABG or PCI. The primary end point of the study is the occurrence of death, MI or stroke at a median follow- up of 3 years. Major secondary end points are death, MI, stroke or unplanned revascularization. Both end points are powered for sequential non inferiority and superiority testing. Another point is the access site. It is associated with bleeding events, while bleeding itself has been associated with an increased risk of death and ischaemic events [18]. TRA is shown to reduce major vascular access site complications and major bleeding [19]. In our observations TRA was used in 151(89%) of patients, TUA in 10(6%) TFA in 9(5%), using 5F and 6F guiding catheters. Drug-eluting stents were used in 131(77%) of patients treated with standard medications regiment. GP IIB/IIIA inhibitors were administrated only in 7(4%) patients. All procedures were achieved with TIMI 3 flow. Ten patients (6%) died during in hospital stay and there was no additional deaths during 6 months follow up period. Nine deaths (5%) were cardiac and one (1,7%) was dye severe gastric bleeding.

5. Conclusions

Trans-radial stenting of unprotected left main disease in symptomatic patients is feasible and safe when performed by experienced high-volume operators.

Selection, evaluation of the patient as well as the planning of the procedure is crucial. The EXCEL trial will hopefully address many unresolved issues and will better clarify the value of PCI for the treatment of ULMCA stenosis.

6. References

1. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ *et al*. ACC/AHA 2004 Guidelines update for coronary artery bypass graft surgery. Circulation 2004; 110:1168–1176.
2. 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; 45:351–6.
3. Kim YH, Park SW, Hong MK *et al*. Comparison of simple and complex stenting

techniques in the treatment of unprotected left main coronary artery bifurcation stenosis. Am J Cardiol 2006; 97:1597–601.

4. Valgimigli M, Malagutti P, Rodriguez GG *et al*. Single vessel versus bifurcation stenting for the treatment of distal left main coronary artery disease in the drug eluting stenting era: clinical and angiographic insights into the Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital (RESEARCH) and Taxus-Stent Evaluated at Rotterdam Cardiology Hospital (T-SEARCH) registries. Am Heart J 2006; 152:896–902.
5. Park SJ, Lee CW, Kim YH, Lee JH, Hong MK, Kim JJ *et al*. Technical feasibility, safety, and clinical outcome of stenting of unprotected left main coronary artery bifurcation narrowing. Am J Cardiol 2002; 90:374–8.
6. Mehilli J, Kastrati A, Byrne R *et al*. for the ISAR-LEFT MAIN (Intracoronary Stenting and Angiographic Results: Drug-Eluting Stents for Unprotected Coronary Left Main Lesions) Study Investigators. Paclitaxel- versus sirolimus-eluting stents for unprotected left main coronary artery disease. J Am Coll Cardiol 2009; 53:1760–8.
7. Palmerini T, Marzocchi A, Tamburino C *et al*. Impact of bifurcation technique on 2 year clinical outcomes in 773 patients with distal unprotected left main coronary artery stenosis treated with drug-eluting stents. Circ Cardiovasc Interv 2008; 1:185–92.
8. Mohr FW, Morice MC, Kappetein AP, Feldman TE, Ståhle E, Colombo A *et al*. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial.
9. ACC/AHA 2009 Focused Updates for STEMI and PCI. Circulation 2009; 120:2271-2306.
10. SYNTAX score II: a useful tool to decide type of revascularization therapy, Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A *et al*. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. Lancet 2013; 381:639-50.
11. Stone GW. Motivation, Objective and Implication of EXCEL Study. Presented at Transcatheter Therapeutics Asia Pacific; April 28, 2010; Seoul, South Korea.
12. Alaide C, Valeria M, Azeem L, Francesco M, Alfonso I, Matteo M. 5-Year Outcomes Following Percutaneous Coronary Intervention With Drug- Eluting Stent Implantation Versus Coronary Artery Bypass Graft for Unprotected Left Main Coronary Artery Lesions: The Milan Experience. J Am Coll Cardiol Intv 2010; 3(6):595-601.
13. Garg S, Stone GW, Kappetein AP, Sabik JF, Simonton C, Serruys PW. Clinical and angiographic risk assessment in patients with left main stem lesions. J Am Coll Cardiol Int 2010; 3:891–901.
14. Min SY, Park DW, Yun SC *et al*. Major predictors of long-term clinical outcomes after coronary revascularization in patients with unprotected left main coronary disease: analysis from the MAINCOMPARE study. Circ Cardiovasc Interv 2010; 3:127–33.
15. King SB III, Smith SC Jr, Hirshfeld JW Jr *et al*. 2007 focused update of the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines: 2007 writing group to review new evidence and update the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention, writing on behalf of the 2005 writing committee. Circulation 2008; 117:261–295.
16. Smith SC Jr, Dove JT, Jacobs AK *et al*. ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines)-executive summary: A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) endorsed by the Society for Cardiac Angiography and

Interventions. Circulation 2001; 103:3019–3041.

17. Smith SC Jr, Feldman TE, Hirshfeld JW Jr *et al*. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ SCAI Writing Committee to update 2001 guidelines for percutaneous coronary intervention). Circulation 2006; 113:e166–e286.
18. Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KAA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation 2006; 114:774–782.
19. Jolly SS, Yusuf S, Cairns J, Niemela K, Xavier D, Widimsky P. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet 2011; 377:1409–1420.