

Review Article,

Left Main Disease PCI vs CABG: A Brief Review of Important Literature

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Introduction:

Left main coronary artery (LMCA) disease is defined as > 50% narrowing of vessel diameter; it is the disease of significant morbidity and mortality because it supplies 75% of the left ventricle, so any insult to the left main can lead to severe LV dysfunction, sudden cardiac arrest and arrhythmia. The incidence of left main disease in patients undergoing coronary angiography is 4-6%. The untreated left main disease has mortality around 20% at 1 year [1,2]. Initially, the procedure of choice for the significant left main disease was coronary artery by-pass surgery (CABG), as medical therapy carries a high mortality rate as compared to CABG (36.5% vs 16.0%). Nevertheless, with the advancement in percutaneous intervention (PCI), there is a growing interest and passion in the percutaneous intervention of LMCA [3].

European [4] and American [5] guidelines recommend CABG (class I) as the treatment method of choice for LMCA in patients with all anatomical complexities. Current European treatment guidelines give PCI class I along with CABG if SYNTAX score < 22, class IIa if between 23-32, and class III (Harm) if SYNTAX > 33. Current US guidelines currently gives class IIa recommendation for PCI if syntax score is low, class IIb for a score between 23-32 and similar to European guideline's class III (Harm) for SYNTAX score > 33. We reviewed the major landmark trials that compare PCI vs CBAG as a treatment option for left main disease along with important meta-analysis

Keywords: Coronary artery bypass surgery, left main coronary artery disease, target lesion revascularization, major adverse cardiac event

Review of important Trials and meta-analysis:

The earliest outcome data regarding left man intervention dated back to CASS trial that was done between 1974 to 1979. It includes approximately 1400 patients with left main coronary artery stenosis. Results of this study showed CABG is better than medical therapy for treatment of left main coronary artery stenosis [6]. In Initial trials like PRECOMBAT and SYNTAX, PCI vs CABG was compared in era of first-generation drug-eluting stents. Among initial trials that used 1st generation drug-eluting stent (DES), SYNTAX trial was one of the most important

trial. Total 1800 patients enrolled in SYNTAX trial and were randomized to PCI and received 1st generation stent (Paclitaxel or sirolimus drug eluting stent) versus CABG. Out of those 1800 patients, 705 patients had a left main disease. In the SYNTAX Trial participants were divided into three separate groups depending upon the anatomical score known as the SYNTAX score. Low complexity group has a score of <22 Intermediate 22-32 and the high anatomical complexity has scored of more than 32. One year result of the SYNTAX trial showed PCI was inferior to bypass surgery for the composite

primary endpoint of death, MI and stroke (17.8 in PCI vs 12.1 in CABG). A detailed review of the data by experts showed a lot of those differences between two groups were due to high target lesion revascularization (TLR) rate in the PCI group, especially in patients with high SYNTAX Score > 33 significant differences between the incidence of death, CVA and MI observed between CABG and PCI (12.6% vs 28.2%). In groups with low SYNTAX score, a difference of death, CVA or MI was significantly less (14.8% vs 17.5%). But in contrast even in the subgroup with low syntax score < 22, target vessel revascularizations rate (TLR) was much higher in PCI group. The SYNTAX trial did not accomplish the primary endpoint of non-inferiority of PCI as compared to CABG [7]. Meanwhile, stent technology continues to improve and with the arrival of newer (2nd) generation Drug-Eluting Stent (DES) and its proven efficacy compared to 1st generation drug-eluting stent new trials were designed out and one of the most important trial among those is the EXCEL trial. 10-year follow-up data of SYNTAX trial was published that sure not a big difference in term of all-cause death/mortality between 2 groups (26.7% vs 26.1%) [8].

In EXCEL trial initially, 2900 patients with left main disease and a SYNTAX score < 32 were enrolled. Out of 2900 patients, roughly 1800 patients qualified for intervention. The major inclusion criteria in EXCEL trial was unprotected left main disease with 70 % stenosis. Patients with stenosis of >50-70 % required to have non-invasive evidence of LM ischemia or IVUS MLA < 6.0 mm or FFR < 0.80. Primary endpoints include death, Stroke, or MI at three years. The incidence of death, stroke and MI in the PCI group was 15.4% vs 14.7% in the CABG group. The secondary endpoint includes Death, stroke or MI at 30 days that was 4.9% in the PCI group and 7.9% in the CABG group. One other secondary endpoint was ischemia-driven revascularization at three years that was 23.1% in the PCI group and 19.1% in the CABG group. In adjudicated outcomes at 3 years there was not a big difference between definite cardiovascular death between two groups. (3.7% vs 3.4%). Non-cardiovascular death was higher in the PCI group (3.9% vs 2.3%). Ischemia-driven revascularization was 12.6 % in the PCI group and 7.5 % in the CABG group. In terms of angina relief, there was no difference between the two groups. Stroke incidence was slightly higher in CABG group as

compared to PCI (2.9% vs 2.3%). As a conclusion EXCEL trial showed that treatment of left main coronary artery disease patients with low or intermediate SYNTAX score and use of 2nd Generation cobalt-chromium everolimus drug-eluting stent showed similar rates of primary endpoint of, stroke, death or MI at 3 years with less adverse events within 30 days compared to CABG. In 2019, five-year outcome data was published of EXCEL trial. Five-year data showed higher incidence of death, stroke or MI in PCI group vs CABG group (22.0% vs 19.2%) as compared to three years follow up data, but there was the very minor difference between 2 groups in term of definitive cardiovascular death (5.0% vs 4.5%). The incidence of stroke was higher in CABG group while the incidence of revascularization was higher in PCI group (16.9% vs 10.0%) [9].

NOBEL trial is also an important trial consisting of 1200 patients. Mean syntax score was 22 and 15% of the trial population was diabetic. NOBEL trial showed PCI is associated with more mortality as compared to CABG (12% vs 9%). PCI group also has more revascularization rate (16% VS 10%), and CABG group actually has lesser stroke incidence as compared to PCI (2% vs 5%) unlike EXCEL trial [10].

PRECOMBAT trial was also an initial trial regarding comparison of PCI versus CABG in left main. Total trial population was 600 patients with a mean SYNTAX score of 25. This trial also did not show any differences in mortality between CABG versus PCI, but the PCI group did show increased rate of revascularization (16% vs 8%).[11]

Meta-analysis:

In one meta-analysis comparing 11 trials with 11,518 patients with multivessel disease including Left main showed, all-cause mortality in PCI vs CABG group was not different 10.7% vs 10.5% in patients with left main disease. This meta-analysis did show patients who have diabetes and multivessel disease benefitted with CABG.[12]. A recently published meta-analysis in a European heart journal that includes all the four important trials of left main coronary artery Intervention showed no difference in all-cause mortality between PCI versus CABG.[13]

Conclusion:

The choice of CABG vs PCI as a treatment for the

significant left main disease remains a hard time discussion. Both are quite different approaches with different long and short-term benefits. In the case of PCI, the advantages are, it is less invasive, and has fewer peri-procedural complications such as stroke MI, atrial fibrillation, bleeding, and acute kidney injury. In comparison CABG has long-term advantages. It is more durable, there are less adverse events after 30 days, particularly the need repeat revascularization. In the lack of clear and homogenous information, our patients need a lot of help to navigate this challenging decision.

Reference:

- [1] Ragosta M, Dee S, Sarembock IJ, Lipson LC, Gimple LW, Powers ER. Prevalence of unfavorable angiographic characteristics for percutaneous intervention in patients with unprotected left main coronary artery disease. *Catheter Cardiovasc Interv.* 2006 Sep;68(3):357-62. doi: 10.1002/ccd.20709. PMID: 16892431.
- [2] Conley MJ, Ely RL, Kisslo J, Lee KL, McNeer JF, Rosati RA. The prognostic spectrum of left main stenosis. *Circulation.* 1978 May;57(5):947-52. doi: 10.1161/01.cir.57.5.947. PMID: 639216.
- [3] Harris PJ, Harrell FE, Jr, Lee KL, et al. Survival in medically treated coronary artery disease. *Circulation* 1979; 60:1259-69. 10.1161/01.CIR.60.6.1259
- [4] Corrigendum to: 2018 ESC/EACTS Guidelines on Myocardial Revascularization.” *European Heart Journal*, vol. 40, no. 37, Oct. 2019, pp. 3096–3096. *Silverchair*,
- [5] Hillis, L. David, et al. “2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery.” *Journal of the American College of Cardiology*, vol. 58, no. 24, Dec. 2011, pp. e123–210. *jacc.org (Atypon)*, <https://doi.org/10.1016/j.jacc.2011.08.009>.
- [6] Coronary artery surgery study (CASS): a randomized trial of coronary artery bypass surgery. Survival data. *Circulation.* 1983 Nov;68(5):939-50. doi: 10.1161/01.cir.68.5.939. PMID: 6137292.
- [7] Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009; 360:961-72. 10.1056/NEJMoa0804626
- [8] Thuijs, Daniel J. F. M., et al. “Percutaneous Coronary Intervention versus Coronary Artery Bypass Grafting in Patients with Three-Vessel or Left Main Coronary Artery Disease: 10-Year Follow-up of the Multicentre Randomized Controlled SYNTAX Trial.” *The Lancet*, vol. 394, no. 10206, Oct. 2019, pp. 1325–34. DOI.org (Crossref), [https://doi.org/10.1016/S0140-6736\(19\)31997-X](https://doi.org/10.1016/S0140-6736(19)31997-X).
- [9] Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice MC, Puskas J, Kandzari DE, Karpaliotis D, Brown WM 3rd, Lembo NJ, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogáts G, Mansour S, Noiseux N, Sabaté M, Pomar J, Hickey M, Gershlick A, Buszman PE, Bochenek A, Schampaert E, Pagé P, Modolo R, Gregson J, Simonton CA, Mehran R, Kosmidou I, Généreux P, Crowley A, Dressler O, Serruys PW; EXCEL Trial Investigators. Five-Year Outcomes after PCI or CABG for Left Main Coronary Disease. *N Engl J Med.* 2019 Nov 7;381(19):1820-1830. doi: 10.1056/NEJMoa1909406. Epub 2019 Sep 28. Erratum in: *N Engl J Med.* 2020 Mar 12;382(11):1078. PMID: 31562798.
- [10] Mäkikallio, Timo, et al. “Percutaneous Coronary Angioplasty versus Coronary Artery Bypass Grafting in Treatment of

Unprotected Left Main Stenosis (NOBLE):
A Prospective, Randomised, Open-Label,
Non-Inferiority Trial.” *The Lancet*, vol. 388,
no. 10061, Dec. 2016, pp. 2743–52.
DOI.org (Crossref),
[https://doi.org/10.1016/S0140-6736\(16\)32052-9](https://doi.org/10.1016/S0140-6736(16)32052-9).

- [11] Park, Seung-Jung, et al. “Randomized Trial of Stents versus Bypass Surgery for Left Main Coronary Artery Disease.” *New England Journal of Medicine*, vol. 364, no. 18, May 2011, pp. 1718–27. DOI.org (Crossref),
<https://doi.org/10.1056/NEJMoa1100452>.
- [12] Head SJ, Milojevic M, Daemen J, Ahn JM, Boersma E, Christiansen EH, Domanski MJ, Farkouh ME, Flather M, Fuster V, Hlatky MA, Holm NR, Hueb WA, Kamalesh M, Kim YH, Mäkikallio T, Mohr FW, Papageorgiou G, Park SJ, Rodriguez AE, Sabik JF 3rd, Stables RH, Stone GW, Serruys PW, Kappetein AP. Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. *Lancet*. 2018 Mar 10;391(10124):939-948. doi: 10.1016/S0140-6736(18)30423-9. Epub 2018 Feb 23. Erratum in: *Lancet*. 2018 Aug 11;392(10146):476. PMID: 29478841
- [13] Ahmad Y, Howard JP, Arnold AD, Cook CM, Prasad M, Ali ZA, Parikh MA, Kosmidou I, Francis DP, Moses JW, et al. Mortality after drug-eluting stents vs. coronary artery bypass grafting for left main coronary artery disease: a meta-analysis of randomized controlled trials. **Eur Heart J**. 2020. DOI:
<https://doi.org/10.1093/eurheartj/ehaa135>.
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