

What about current guidelines for coronary revascularization 2018 ESC/EACTS for stable angina?

Part I. Stable angina

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Current medical practice is based on evidence-based medicine. The clinical guidelines have this purpose to regulate both medical and surgical treatment. Coronary heart disease is the leading cause of death worldwide. Despite a series of absolute indications for revascularization, there are still some situations where the decision-making process is hard to select. We present herein the most notable aspects, highlights when deciding about the stable coronary artery disease.

Key words: Cardiac Surgery; Clinical guidelines; Coronary artery bypass grafting; Coronary revascularization; Evidence-based medicine.

La práctica médica actual está soportada en la medicina basada en evidencia. Las guías clínicas tienen este propósito para regular el tratamiento médico y quirúrgico. La enfermedad coronaria es la principal causa de muerte en todo el mundo. A pesar de una serie de indicaciones absolutas para la revascularización coronaria, todavía hay algunas situaciones en las que el proceso de toma de decisiones es difícil de seleccionar. Presentamos aquí los aspectos más notables, destaca al decidir sobre la enfermedad arterial coronaria estable.

Palabras clave: Cirugía cardíaca; Guías clínicas; Revascularización coronaria; Medicina basada en evidencia.

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Coronary artery bypass grafting is the most popular operations in cardiac surgery all over the world. According to data coming from the World Health Organization, in 2016 more than half of the 56.9 million deaths all across the globe were linked to the 10 main mortality causes. Ischemic coronary artery disease and stroke are the two leading causes inducing around 15.2 million deaths. No changes have been noted for the last 15 years [1]. Data from the Organization for Economic Co-operation and Development (OECD) ischemic heart disease and stroke caused more than one-fifth of all deaths in EU in 2013 [2]. In addition, the representative mean for the European Union for coronary revascularization procedures was 258 per 100,000 habitants [2]. The ratio for percutaneous coronary interventions:coronary artery bypass surgery was 3.29 in the European Union in 2007 [3]. Over the years, in 2014, angioplasty accounts for 84% of all coronary revascularization procedures [2].

The Heart team compounded by at least one interventional cardiologist, one cardiac surgeon, the patient's clinical cardiologist has laid the practical foundation for optimal strategies in cases with stable complex coronary disease [3].

Given the fact that nowadays a national database is missing in Mexico, it is nearly impossible to get our own practical guidelines for coronary revascularization by ourselves. In this context, our decision-making process is largely based upon the 2018 ESC/EACTS guidelines on myocardial revascularization, being the most recent and current ones worldwide [4]. At the same time, the lessons learned over the years have made so clear for undeniable progress of the CABG over the medical treatment under very specific situations (**Table 1**).

In accordance with the forgoing, we will discuss herein in this paper the current indications for each and every condition for stable angina in coronary artery disease.

SYNTAX TRIAL

Taking into consideration a large part of the current guidelines for myocardial revascularization is based upon the Syntax trial, it is more than necessary to get into a bit more detail in respect thereof.

The Syntax trial was especially designed to prove the non-inferiority of the PCI over the CABG using the Taxus first generation stents according to Major Adverse Cardiac and Cerebrovascular Events (MACCE) [5]. It was conceived as a randomized trial with nested registries for PCI as well as CABG for multivessel disease (3VD) and left main (LM) coronary artery disease (isolated or in association with 1, 2 or 3

Table 1. Indications for coronary revascularization

INDICATION	CLASS of RECOMMENDATION	LEVEL of EVIDENCE
LM coronary artery stenosis > 50%	I	A
LAD proximal stenosis > 50%	I	A
2 or 3 vessels with stenosis > 50%, LVEF ≤ 35%	I	A
Significant coronary artery lesion 1) incapacitant angina 2) inadequate medical response	I	A
Large LV area: 1) > 10% LF(by functional test) 2) anormal FFR (< 0.75)	I	B
The only functional artery with stenosis > 50%	I	C

LAD: Left anterior descending, LM: Left main, LVEF: Left ventricle ejection fraction, FFR: Fractional flow reserve

VD) with especial attention for cases with complex coronary disease. The primary clinical end point was freedom from MACCE through 1 year after procedure.

After assigned 1,800 patients (897 patients for CABG, and 903 for PCI) with three-vessel or left main coronary artery disease to undergo CABG or PCI (in a 1:1 ratio) were allocated. At 12 months of the event, when gathering all cause-death, stroke, and myocardial infarction there were no statistically significant difference between both groups (CABG:7.5%, PCI: 7.6%; $p=0.86$). When comparing the stroke rate, for CABG: 2.2%, for PCI: 0.6% ($p=0.003$). Now, when including the phenomenon called “repeat revascularization”, the weighting is towards in favor of surgery (CABG: 5.9%, PCI: 13.7%; $p<0.001$). Consequently, if this last phenomenon is incorporated as part of the MACCE, the balance is tipped in favor of surgery again (CABG: 12.1%, PCI: 17.8%; $p=0.001$). Hence, after 1 year of follow-up, the SYNTAX trial failed to prove the non-inferiority from PCI over the CABG [6].

At a longer follow-up for 5 years, the same results were reaffirmed and strengthened yet again. For myocardial infarction, an overly broad difference was obtained while comparing both groups (CABG: 3.8% vs PCI: 9.7%; $p<0.001$). Repeat revascularization was more frequent for PCI group at 60 months after allocation (CABG: 13.7% vs PCI: 37.9%; $p<0.001$). MACCE (including repeat revascularization) was in favor of surgery (CABG: 26.9% vs PCI: 37.3%; $p<0.001$). The only issue in favor of PCI was for stroke (CABG: 3.7% vs PCI: 2.4%; $p=0.09$).

Concerning all of the above, a landmark finding could be stated out as final result. Once again, the SYNTAX trial failed to demonstrate the non-inferiority of the PCI over the CABG at 5-year follow-up [7]. In fact, cardiac death due to myocardial infarction was 10-fold higher after PCI than CABG in high-risk group [8].

SYNTAX SCORE

The SYNTAX score has been a very useful tool derived from the SYNTAX trial according to the morphology of the coronary lesions and the possible complications for treatment coming from this morphology. In such a way that in an attempt to find out some utility in favor of PCI, the universe of patients was divided *post hoc* according to the SYNTAX score and risk for complications in terciles: Low risk score (0-22), intermediate risk score (23-32), and high-risk score (≥ 33). It is worth highlighting this split was not initially contemplated [7].

For the first tercile (low score, 0-22), 275 patients for CABG and 299 for PCI (total, 574) were collected. At 5-year follow-up, MACCE was for CABG: 28.6% vs PCI: 32.1%; $P=0.43$). None of the separate issues were statistically significant in this group, including repeat revascularization and myocardial infarction ($p=0.06$ and $p=0.11$, respectively). Therefore, PCI with non-inferiority over CABG was found useful [7].

For the second tercile (intermediate score, 23-32), 300 cases for CABG and 310 for PCI (total, 610) were allocated. Overall comparison was MACCE at 5-years, for CABG: 25.8% vs PCI: 36%; $p=0.008$. Myocardial infarction and repeat revascularization both were statistically significant, the two of them with $p<0.001$). As a consequence, no recommendation for using PCI instead of CABG in this special group was found [7].

For the third tercile (high score, ≥ 33), 315 cases for CABG and 290 for PCI, (total, 605) were captured. All issues (including myocardial infarction and repeat revascularization) but stroke was in favor of CABG. At 5-years for MACCE, the overall effect was for CABG: 26.8% vs PCI: 44%; $p<0.001$. All these efforts clearly demonstrate once more the importance attached to SYNTAX score in choosing CABG instead of PCI in this pool of patients with high-risk score [7].

In view of all this above, it is very easy to understand that

Table 2. Indications for coronary revascularization in stable angina for one or two vessels

INDICATION	CABG		PCI	
	COR	LOE	COR	LOE
ONE VESSEL				
LAD WITHOUT proximal stenosis	IIb	C	I	A
LAD WITH proximal stenosis	I	A	I	A
TWO VESSELS				
LAD WITHOUT proximal stenosis	IIb	C	I	B
LAD WITH proximal stenosis	I	B	I	C

CABG: Coronary artery bypass grafting, COR: Class of recommendation, LAD: Left anterior descending, LOE: Level of evidence, PCI: Percutaneous coronary intervention.

the only possibility for PCI in multivessel disease (3VD) as well as left main coronary artery disease is in cases with low score (0-22). In other words, a clear advantage for CABG in both the intermediate and high SYNTAX score groups with multivessel disease and left main disease was clearly evident [8].

ONE VESSEL DISEASE

Recommendations from 2018 ESC/EACTS guidelines for myocardial revascularization for one vessel are very specific. If no proximal lesion in left anterior descending (LAD) coronary artery, PCI is widely preferred (IA) (Class of Recommendation I, Level of Evidence A) On the contrary, if proximal lesion in the LAD, CABG or PCI is exactly the same (IA). (Table 2).

TWO VESSELS

For this group, if no proximal lesion in left anterior descending (LAD) coronary artery is present, PCI is preferred (IB). If proximal lesion present in LAD, CABG (IB) has a slight advantage over PCI (IC) (Table 2).

LEFT MAIN CORONARY ARTERY

Low SYNTAX score (0-22) is the only chance suitable for PCI in LM stenosis. For intermediate (23-32) as well as high score (≥ 33) groups, CABG is the sole amenable option with IA indication (Table 3).

Another meta-analysis comparing CABG vs PCI for LM stenosis showed that for subgroup of 3VD, the p value was very in favor of CABG ($p < 0.001$) [9].

Table 3. Indications for coronary revascularization in stable angina for left main coronary artery stenosis

INDICATION	CABG		PCI	
	COR	LOE	COR	LOE
LEFT MAIN CORONARY ARTERY				
LM with LOW Syntax score (0-22)	I	A	I	A
LM with INTERMEDIATE Syntax score (22-32)	I	A	IIa	A
LM with HIGH Syntax score (≥ 33)	I	A	III	B

CABG: Coronary artery bypass grafting, COR: Class of recommendation, LM: Left main coronary artery, LOE: Level of evidence, PCI: Percutaneous coronary intervention.

Table 4. Indications for coronary revascularization in stable angina for multivessel disease

INDICATION	CABG		PCI	
	COR	LOE	COR	LOE
THREE VESSELS without DIABETES MELLITUS				
LOW Syntax score (0-22)	I	A	I	A
INTERMEDIATE or HIGH Syntax score (> 22)	I	A	III	A
THREE VESSELS with DIABETES MELLITUS				
LOW Syntax score (0-22)	I	A	IIb	A
INTERMEDIATE or HIGH Syntax score (> 22)	I	A	III	A

CABG: Coronary artery bypass grafting, COR: Class of recommendation, LOE: Level of evidence, PCI: Percutaneous coronary intervention.

In addition to this above, we should always bear in mind that in LM stenosis, up to 80% of cases show distal disease, which is more amenable to be treated by CABG. At the same time, 80% of them have multivessel (3VD) disease [10].

MULTIVESSEL DISEASE

Up to 40% of patients undergoing CABG have diabetes mellitus [11]. The vast majority of diabetic patients with 3VD have coronary arteries with small diameter, which makes their prognosis difficult [12]. It contributes to explain why CABG

is better than PCI in 3VD diabetic patients [13]. The FREEDOM trial compared elective revascularization with CSBG vs PCI in 1,900 patients with 3VD diabetes mellitus without LM coronary stenosis at 5-years follow-up. For myocardial infarction was for CABG: 6.0% vs PCI: 13.9% (p<0.001). In relation with the insulin-dependence there was no difference between insulin-dependents and non-insulin-dependents [13].

In a more general view, CABG is the most appropriate management for diabetic patients when coronary revascularization is indicated [14]. What is the concrete evidence tilting in favor of CABG instead of PCI for coronary revasculariza-

Table 5. Indications for coronary revascularization in stable angina for chronic heart failure an LVEF ≤ 35%

INDICATION	COR	LOE
Multivessel disease with acceptable surgical risk= CABG	I	B
1 or 2 vessels = PCI	IIa	C
3 vessels = PCI	IIa	C

CABG: Coronary artery bypass grafting, COR: Class of recommendation, LOE: Level of evidence, PCI: Percutaneous coronary intervention.

Table 6. SUMMARY OF INDICATIONS FOR CORONARY REVASCLARIZATION IN STABLE ANGINA

EXTENT OF LESION	CABG		PCI	
	COR	LOE	COR	LOE
ONE VESSEL				
LAD PROXIMAL STENOSIS	I	A	I	A
TWO VESSELS				
LAD PROXIMAL STENOSIS	I	B		
LEFT MAIN				
LOW SYNTAX score (0-22)	I	A	I	A
INTERMEDIATE SYNTAX score (23-32)	I	A		
HIGH SYNTAX score (≥ 33)	I	A	III	B
MULTIVESSEL WITHOUT DIABETES				
LOW SYNTAX score (0-22)	I	A	I	A
INTERMEDIATE or HIGH SYNTAX score (≥ 23)	I	A	III	A
MULTIVESSEL WITH DIABETES				
LOW SYNTAX score (0-22)	I	A		
INTERMEDIATE or HIGH SYNTAX score (≥ 23)	I	A	III	A

CABG: Coronary artery bypass grafting, COR: Class of recommendation, LOE: Level of evidence, PCI: Percutaneous coronary intervention.

tion in diabetic patients with 3VD? First, in the SYNTAX trial, while no statistical difference for MACCE between PCI and CABG at 5 years, repeat revascularization was higher in PCI than CABG (HR=2.01; 95% CI: 1.04 to 3.08; p<0.001) [15]. Second, the BEST trial, freedom from death, myocardi-

al revascularization or repeat revascularization was better for CABG than PCI (19% vs 9.1%; p=0.007) [16]. More broadly, there was a higher incidence of MACCE in PCI patients with low, intermediate, and high SYNTAX score compared with those who underwent CABG (36.6% vs. 25.9%, p = 0.02;

43.9% vs. 26.8%, $p < 0.001$; 48.7% vs. 29.7%, $p = 0.003$, respectively) [17].

Now therefore, in consideration of the aforementioned, the available evidence favors the use of CABG as a modality of choice for the revascularization of patients with diabetes and multivessel disease (Table 4).

CHRONIC HEART FAILURE AND LOW LEFT VENTRICLE EJECTION FRACTION ($\leq 35\%$).

For patients with coronary artery disease and severe systolic dysfunction, CABG is mandatory over PCI, regardless the number of target vessels, with an acceptable surgical risk (IA indication) [18-20] (Table 5).

To sum up, all summarized indications including IA, IB indications while excluding all those containing II, III and level of C are shown in Table 6.

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