

SYNTAX From the Evidence to the Disobedience

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DOI: 10.5935/1678-9741.20130023

The results between coronary artery bypass grafting and myocardial coronary angioplasty has been the subject of controversy since the year 1979, when percutaneous technique was introduced by Andreas Grüntzig [1].

Since then, numerous randomized and multicenter studies were performed including: ERACI, EAST, GABI, CABRI, MASS, BARI, SIMA, LAUSANNE, RITA, TOULOUSE [2]. All studies have shown superiority of surgical revascularization versus percutaneous treatment, which consisted of substrate for abandoning balloon angioplasty and the emergence of a new era with stents.

In this second phase, the results of angioplasty and stenting procedures are again compared, new studies were undertaken including: AWESOME, ARTS, SOS, ERACI, MASS, among others. Overall, the results in the first year were similar in both groups, but in 5 years, the reoperations in the stent group were higher due to multiple restenosis, which reaffirmed the surgical revascularization was the best option for this group of patients.

With the emergence of drugs stents, new studies comparing surgery and the new generation of stents became necessary, now using chemicals to prevent restenosis.

All prospective randomized studies were criticized, because they included only 5% of randomized susceptible patients. Research had serious distortions to include few patients with 3-vessel injury and critical injury of anterior proximal descending artery. These studies also excluded patients with left main coronary artery lesion [2].

The results presented in the short- and medium-term have brought a lot of confusion because they were from a sample of only 5% of the cases, by assuming that in the real world results would be similar to clinical trials.

The Synergy Between PCI with Taxus and cardiac surgery (SYNTAX) study, when looking more realistic approach proposed to compare surgical outcomes with new-generation percutaneous techniques including patients with 3-vessel lesions, trunk lesions or both. The study was designed as a prospective randomized controlled trial of more complex cases in which surgical or percutaneous treatment would be accepted by surgeons and hemodynamicists.

The aim of this study was to demonstrate the non-inferiority of surgical versus percutaneous treatment, outcomes of interest to all participants of this scientific study.

85 sites were selected, with 62 European and 23 from U.S. Patients with arteries smaller than 1.5 mm or obstructions below 50% were not included in the study [3].

It was established that the sponsors would collect data and perform biostatistics assessment, and the writing and publication of the results would be provided by the researchers. The study was approved by the Research Ethics Committees of all participating hospitals. The study sponsor was Boston Scientific Corp., with a cost of \$ 50 million.

The patients who were initially considered for the study were 3,075 cases, 1,275 were rejected for entry in the register of randomization by the complexity of the lesions. Of these, 1077 were directly surgically treated and only 198 were selected for stent procedure. The inclusion of this large number of patients was due to the rejection of interventional hemodynamicists to treat these patients with stents.

Of the patients accepted for randomization, 897 underwent surgery and 903 underwent angioplasty with TAXUS stent.

We assessed 29 clinical variables with homogeneous groups differed only on 5 parameters: hypertriglyceridemia, duration of hospital stay, duration of the procedure and the waiting time, which was higher for the surgical group.

Complete myocardial revascularization was higher for the surgery group.

Of the randomized patients, 25.6% had diabetes in the stent group versus 24.6% in the surgery group. The average score of the SYNTAX score, which assesses the complexity of coronary artery disease, was 28.4% for the stent group versus 19.1% for the surgical group, without statistical significance.

The SYNTAX score assessed calcified lesions, total occlusions, arterial tortuosity and vessels smaller than 2.5 mm, etc..

In patients undergoing CABG, there were 3.2 anastomoses per patient, and complete revascularization with arterial grafts was achieved in 18.9% of the cases. An arterial graft in 97.3% of the cases and double mammary was used in 27.6%. Isolated vein graft was used only in 2.6% of patients (Table 1).

In the percutaneous treatment group, the mean was 4.2 stents per patient.

Annually, the results of 1,275 patients were assessed demonstrating a significant difference in both groups, with an incidence of stroke (4.2% (stent) versus 2.5% (surgery)), increased mortality (7.3 and 2.5%, respectively), higher need for percutaneous treatment in stent group compared with the surgical group (12 and 3%, respectively). It was proved that the surgical

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revascularization had better results in at least one third of the initial population of SYNTAX.

The resolutions of the SYNTAX study was first published in 2009 [4], (Table 2) and showed the following conclusions: “The SYNTAX trial was designed to compare surgical or percutaneous revascularization in patients with 3-vessel lesions, trunk lesions or both. For the first objective of death or serious adverse events, the non-inferiority was not demonstrated by the results of percutaneous treatment. Surgical treatment proved superior and should remain the treatment of choice for these patients”.

In the following years, data at 2, 3 and 4 years were assessed, showing that the differences observed initially at the end of the first year, were heightened in the following years (Table 3), for the first time has shown a reduction in mortality and myocardial infarction for the surgical group. At 4 years, significant differences disappear with respect to stroke among both study groups [5,6].

However, in patients with SYNTAX score <22, the stent is as safe as surgical revascularization [7].

Surprisingly, the SYNTAX study in patients with isolated left main coronary artery disease showed no significant differences between surgery and angioplasty [8].

Table 1. Characteristics of the surgical group on SYNTAX group

Revascularization using arterial grafts	18.90%
At least one internal mammary	97.30%
Double internal mammary	27.60%
Mammary + saphenous	78.10%
Use of radial artery	14.10%
Only venous grafts	2.60%
Grafts per patient	2.8 +/- 0.7%
Distal anastomoses per patient	3.2 +/- 0.9%

15.0 of surgeries were performed without cardiopulmonary bypass

Table 2. Results on the follow-up year of the SYNTAX trial

	Stent TAXUS	coronary artery bypass grafting	P
Total mortality	4.30%	3.50%	0.37
Acute myocardial infarction	4.80%	3.20%	0.11
Stent occlusion/thrombosis	3.30%	3.40%	0.89
ACVA	0.60%	2.20%	0.003
Death by ACVA or myocardial infarction	10.10%	10.30%	0.96
New revascularization	16.10%	3.90%	0.0025

ACVA: acute cerebrovascular accident

Table 3. 4-years clinical results of the SYNTAX trial

	Surgery (%)	Stent (%)	P
Major events	2.3	33.5	< 0.001
Death/MI/ACVA	14.6	18	0.07
All cause mortality	8.8	11.7	0.048
Death from cardiac causes	4.3	7.6	0.04
ACVA	3.7	2.3	0.06
Infarction	3.8	8.3	< 0.001
New revascularization	11.9	23	< 0.001

ACVA: acute cerebrovascular accident

This observation led to the study Evolution of Xience Prime versus coronary artery surgery in left main revascularization (EXCEL), which has already begun with the planned inclusion of 2,500 patients. The design of this study is very unfavorable for surgery because patients with complex coronary artery disease and previous surgical revascularization were included. The differences between the two alternative revascularization will be difficult to prove in 3 years.

In February 2013, the 5-year results of the SYNTAX study have been published in Lancet [9] showing significant differences in favor of surgery when patients present intermediate to high SYNTAX score (Tables 4 and 5).

In all published studies of SYNTAX, comparing percutaneous coronary intervention with surgery, some thoughts have been extracted:

1. The need to classify each patient with the SYNTAX score, prior to making the decision of which therapy is the most recommended for that patient.

2. The treatment of choice for patients with medium and high SYNTAX score should be surgical, reserving for low-risk patients the stent treatment, which remains a safe alternative.

3. In 65% of all patients with left main coronary artery disease (SYNTAX > 32) and in 79% of patients with 3 vessel disease (SYNTAX > 22), coronary artery bypass surgery has advantages for three years, which is maintained at 5 years.

Table 4. 5-years results of SYNTAX trial on three-vessels disease

	Surgery(%)	Stent(%)	P
Number of patients	549	546	
Death	9.2 (-5.4%)	14.6	0.006
Cardiac death	4 (-5.2%)	9.2	0.001
AMI	3.3 (-7.3%)	10.6	0.001
ACVA	3.4 (+0.6%)	3	0.66
Death + cardiac death + myocardial infarction	14 (-8%)	22	0.001
New coronary revascularization	12.6 (-12,8%)	25.4	0.001

ACVA: acute cerebrovascular accident, AMI: infarction

If we assess the SYNTAX score, there was no significant differences between both groups of patients at low risk score (<23), but significant differences was found on the intermediate risk (23-32)

Table 5. 5-years results of SYNTAX trial on left trunk disease

	Surgery(%)	Stent(%)	P
Number of patients	348	357	
Death	14.6 (+1.8%)	12.8	0.53
Cardiac death	7.2 (-1.4%)	8.6	0.46
AMI	4.8 (-3.4%)	8.2	0.1
ACVA	4.3 (+2.8%)	1.5	0.03
Death + cardiac death + myocardial infarction	20.8 (+1.8%)	19	0.57
New coronary revascularization	15.5 (-11.2%)	26.7	0.001

ACVA: acute cerebrovascular accident, AMI: acute myocardial infarction.

If we assess the SYNTAX score, there was no significant differences between both groups of patients at low and medium risk, but significant differences was found on the high score (<32), where the surgery has better results than the stent

4. Developing the concept of “core-team”, multidisciplinary group comprising clinical cardiologist, hemodynamicist, the surgeon and the patient, which ultimately will make the best decision for him.

5. The examination of the coronary anatomy must be assessed by the team in all patients, to decide in daily practice what is the best therapeutic option for him and not just discuss in conferences and different publications which ideal behavior for each subgroup of patients.

The new clinical practice guidelines for myocardial revascularization show philosophical and ethical change in the treatment of coronary artery disease and recommend the surgical treatment as the best choice for left main coronary artery disease and 3-vessel involvement with anterior proximal descending artery. The ad hoc coronary angiography is indicated only in patients with unstable angina, in other cases, the patient must have enough time to choose his treatment of choice, advised by team work [10,11].

Current scientific evidence, the publications of the new guidelines of the European Society of Cardiology, Hemodynamics and Surgery, and the various prospective randomized multicenter studies indicate that surgical revascularization is the preferred option for patients with complex coronary lesions, diabetics, trunk lesions and multivessel ostial lesions of the left anterior descending [12-15]. In day to day, however, it is recommended to avoid sternotomy and subject the patient to percutaneous treatment, often leaving scientific evidence-based medicine, perhaps we are faced with an extra ethical issue [16].

Despite scientific evidence available in randomized trials, meta-analyses and guidelines that confirm that coronary artery bypass surgery is better, patients are still undergoing percutaneous treatment.

We wonder what is the ethical and economic cost of not indicating the right therapy for each patient.

Cardiovascular surgeons and scientific societies must enforce and defend the implementation of the new guidelines for coronary revascularization and the evidence in favor of surgery at 5 years demonstrated in the SYNTAX study [17].

Professionals must persuade hospital management bodies and insurers, that patients requiring coronary revascularization should be assessed, discussed between cardiologists and surgeons, indicating the more correct therapy for each patient.

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