Coronary Angioplasty *versus* CABG: Review of Randomized

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Abstract

We carried out a review that included results of randomized trials that made a comparison between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). The 25 selected trials involved 12,305 patients, 11,103 of whom were from studies in patients with multi-vessel disease and 1,212 were from studies in patients with single lesion of the left anterior descending (LAD). In the studies of multi-vessel disease patients, the PCI showed a trend towards lower early mortality (1.2% *versus* 2%) and lower incidence of stroke: 0.7% *versus* 1.65%. There was no difference in the intermediate mortality (3.8% *versus* 3.8%). There was a trend towards the superiority of CABG in late mortality (10.5% *versus* 9.6%). The difference was exclusively due to "balloon era" studies, with a trend towards an inversion in the "stent era" (9.6% *versus* 9.9%). In studies of single lesion of LAD, there was no significant difference in any endpoint. The aggregation of results from nine studies that assessed late mortality in diabetic patients showed a difference in favor of surgery (21.3% *versus* 15.9%). Two studies that evaluated main coronary artery disease did not show a significant difference in mortality at one year (3.9% *versus* 4.7%). The incidence of repeat revascularization was consistently higher in PCI, despite the progressive improvement in results in the stent era.

Introduction

Both the percutaneous coronary intervention (angioplasty or PCI) and the coronary artery bypass grafting (surgery or CABG) are well accepted alternative treatments for coronary insufficiency. A large number of randomized controlled trials comparing the two procedures were published[1-44].

In light of these studies, there seems to be slight superiority of surgery over angioplasty in the ability to reduce anginal symptoms, and a significant difference in the ability to avoid new revascularization procedures. There seems to be no difference with respect to the occurrence of myocardial infarction with development of Q wave. There are still some doubts about the differences in outcomes in terms of mortality in the short term and in the long term, the difference in mortality in diabetics, as well as the difference in risk of cerebrovascular accident (CVA) and the capacity of drug-eluting stents to eliminate the differences regarding the need for repeat revascularization.

The aim of this study was to carry out a review, by adding the results of randomized controlled trials that compared percutaneous transluminal coronary angioplasty with coronary artery bypass surgery.

Keywords

Angioplasty, transluminal, percutaneous coronary; coronary artery bypass; myocardial revascularization; meta-analysis.

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Methods

Selection and characteristics of the studies

In the MEDLINE and CHOCHRANE database, we investigated randomized trials that compared percutaneous transluminal coronary angioplasty with coronary artery bypass surgery, published between January 1986 and March 2010. The month of January, 1986, was chosen as the start date because angioplasty started to establish itself as a therapeutic method in the mid 1980s.

In the investigation of databases, the following terms were used: angioplasty transluminal percutaneous coronary, coronary artery bypass surgery, coronary stents and randomized controlled trial. After the initial survey, which also considered references to review papers on the subject and meta-analyses, we used the following criteria to include studies in the review: to be randomized, to compare CABG with PCI, to have a follow-up of at least six months and to have been published in international journals rated as Qualis A or B by CAPES (Coordination for the Improvement of Higher Education Personnel of the Brazilian Ministry of Education). Papers resulting from observational studies (records) were not considered. We identified a total of 26 randomized studies that met the requirements: RITA[1,2], ERACI[3,4], EAST[5-7], GABI[8,9], CABRI[10,11], TOULOUSE[12], BARI[13-16], MASSI[17,18], LAUSANNE[19,20], ERACI II[21,22], MASS II[23-25], AWESOME[26,27], OCTOSTENT[28], LEIPZIG[29], SIMA[30,31], Drenth et al[32], SOS[33,34], ARTS[35,36], LEMANS[37], SYNTAX[38], MYOPROTECT[39], Hong et al[40], Kim et al[41], Cisowski et al[42], AMIST[43] and CÁRDia[44].

The trials were classified in two types of study: studies in isolated lesions of proximal left anterior descending coronary artery and studies in multivessel disease. All trials that included patients with two-vessel disease, triple-vessel disease or left

left main coronary artery, even if they also included single-vessel disease patients, were classified as multi-vessel disease. Complex anatomy was an exclusion criterion in all studies, except SYNTAX. Main coronary artery was usually also an exclusion criterion, except for ERACI II, SYNTAX and LEMANS. Prior CABG was an exclusion criterion in all studies, except for AWESOME. This study differed from the others because it involved patients at high surgical risk, and because it presented a mean ejection fraction that was significantly below normal. In spite of that, it was not excluded from review, since the indication for CABG for the types of patients included in it has been increasingly common in cardiology. MYOPROTECT was excluded from the review because it had extremely high early mortality (more than three standard deviations above the mean), both for PCI and CABG, and because it had tested a special form of percutaneous intervention, using retrograde perfusion.

Assessed endpoints

The endpoints of interest were: mortality, stroke and repeat revascularization. Mortality was divided into early, intermediate and late. Early mortality was defined as the percentage of deaths occurring within 30 days after the procedure, added to pre-procedure deaths[2,8,33,35,38]. Early mortality was provided by 23 studies. In the two in which it was not given[35,38], it could be estimated by the survival curves[35,38] and then it was placed in the tables, but it was not included in the calculation of the total of events (since they referred to numbers that were not actually published). The intermediate mortality was defined as the percentage of deaths reported up to a maximum period of 2.5 years after the procedure. In 19 studies, the mortality of 1 year was reported. In 2 studies, the mortality of 6 months[40,42] was reported. In one study, the mortality of 1.5 year was reported[21] and in 2 studies, the mortality of 2.5 years was reported[1,19]. This represented an average follow-up of 1.1 year. Late mortality was defined as mortality reported as having occurred 2.6 years or more after the procedure. It was provided in 18 studies. In 12 studies, the mortality of 5 years was reported; in two, the mortality of 3 years[4,26]; in two, of years[32,11]; in one, of 6.5 years[1], in one, of 7.5 years[28]; and in one, of 10 years[31]. This represented an average follow-up of 4.9 years. The incidence of stroke was reported in 20 studies. In 19 studies, strokes that occurred within 30 days after the procedure were considered and, in one study, the strokes that occurred up to one year after the procedure were considered. The incidence of repeat revascularization took into account the results of the first publication, usually one year after the procedure, a period when the need for further angioplasties is more frequent. In 19 cases, the results of one year were considered and, in one case, the results of 6 months[40]. Based on the data reported, we calculated the incidence of repeat revascularization by an alternative procedure: surgery in patients of the PCI group and angioplasty in patients of the CABG group.

Data collection and summary of results

The results reported in each study were collected by two researchers and the incidence of events (deaths and stroke) was placed in an Excel spreadsheet. Data from studies of patients with multi-vessel disease were grouped as if they referred to a single study. The same was done with data from studies in patients with single-vessel disease. This seemed to be justifiable for the following reasons: a) the assessed endpoints (mortality and stroke) are well-defined variables; b) all studies, whether in multi-vessel disease patients, or in single-vessel disease patients, had one element in common: patients were referred to revascularization, which could be carried out either by PCI or by CABG; c) despite the progress in interventional cardiology, there is no definitive evidence that stents have reduced the mortality or incidence of stroke when compared with PCI with balloon.

The results in diabetics, reported in nine studies, as well as those of patients with left main coronary artery disease, reported in two studies, were evaluated separately. The results of studies of the balloon era and stent era were also evaluated. The comparison between studies, both individually and in all of the results, was also made by means of a "relative risk index," which took into account the event-free survival. This index was obtained by dividing the percentage of event-free patients from the angioplasty group by the percentage of event-free patients from the surgery group event. Neither the odds ratio nor the conventional relative risk (of event occurrence) were chosen as a source a comparison between the studies, due to the existence of a significant number of trials where the number of endpoints was zero.

Results

Out of the 25 studies, nine belonged to the balloon era[1-20], 15 to the stent era, and one to an intermediate period (AWESOME)[21-44]. This last one was classified as a study from the stent era. Nine studies assessed only patients with single proximal lesion of the anterior descending coronary. In studies classified as multi-vessel disease, 11 evaluated patients with two-vessel or three-vessel disease; one evaluated an obstruction of the main coronary artery (LEMANS); one assessed patients with triple-vessel disease or main coronary artery disease (SYNTAX); three included patients with single-vessel, two-vessel or three-vessel disease (ARTS, RITA and OCTOSTENT). In most studies, cardiopulmonary bypass (CPB) was used in the surgery. Three studies in patients with multi-vessel disease (ARTS, SYNTAX and SOS) also used off-pump surgery in selected patients, according to local practice. In OCTOSTENT, only off-pump surgery was used. In three of the nine studies of single proximal obstruction of the anterior descending artery, the surgery was performed with CPB and median sternotomy (MASS I, LAUSANNE and SIMA). In the others, off-pump CABG was performed using left lateral thoracotomy (Drenth et al[32], Leipzig, Hong et al[40], Kim et al[41], Cisowski et al[42] and AMIST). Main coronary artery disease was an exclusion criterion in 22 studies. The main coronary artery disease was present in ERAC II (5% of patients), in SYNTAX (39% of patients), and in LEMANS (100% of patients). Only four studies (SYNTAX, LEMANS, CARDia and Hong et al[41]) used drug-eluting stents. One study evaluated only diabetics (CÁRDia).

The 25 studies involved 12,305 patients, 11,103 of whom belonged to studies in patients with multi-vessel disease and 1,212 to studies in a single lesion of the left anterior descending artery. In the 16 studies in patients with multi-vessel disease,

the two-vessel disease was predominant in the balloon era and the three-vessel disease or main coronary artery disease was predominant in the stent era. In all the studies with patients with multi-vessel disease, over 50% of patients had three-vessel disease or main coronary artery disease and more than 50% had proximal obstruction of the left anterior descending coronary artery (in studies that reported this information). Decreased ejection fraction was almost always absent in studies with a single lesion of LAD coronary artery. In the studies in patients with multi-vessel disease, it was decreased in 18% of the patients (not considering CABRI and AWESOME, which did not report this information). The average patient age was 62 years and 77% were male. The mean age tended to be higher in studies with patients with multi-vessel disease than in single lesion of LAD coronary artery. The mean age was also higher in stent era than in the balloon era. Diabetes mellitus was present in 20% of patients. The vast majority of patients were symptomatic (unstable, stable angina or previous infarction). Unstable angina was present at a frequency that ranged from 0% (MASS studies) to 92% (ERAC II study).

The results of studies in multi-vessel disease patients are presented in table 1 and in figures 1 to 3. Early mortality was lower with PCI in most studies. The aggregation of results was favorable to angioplasty. (1.2 *versus* 2%: $p = 0.034$). But when we include the estimated results of ARTS and SYNTAX, the differences were less significant (1.3% *versus* 1.7%). The studies that contributed most to the worst result of the surgery were ERACI, AWESOME and ERACI II, which included a substantial number of acute patients.

With regard to the intermediate mortality, the results were identical (3.8 *versus* 3.8%). In the late mortality, there was a trend towards a better outcome of surgery (10.5% *versus* 9.6%: $p = 0.07$). This difference was exclusively due to "balloon era" studies, with a trend towards an inversion in the "stent era" (9.6% *versus* 9.9%). Only one study of the stent era showed lower mortality with surgery (SOS), due to a higher cancer mortality in the PCI group. Figure 2 shows marked heterogeneity of results with a tendency to superiority of surgery in the balloon era, and of angioplasty in the stent era.

The incidence of stroke was higher with surgery (0.7% *versus* 1.65%: $p < 0.001$), with virtually all studies in patients with multi-vessel disease showing improved outcome with angioplasty (Fig. 3).

The data of studies in single lesion of LAD coronary artery are shown in table 2. In the aggregation of results, there was no significant different in any endpoint: 0.5% *versus* 0.9%, for early mortality; 1.1% *versus* 2.4%, for intermediate mortality; 6.7% *versus* 5.5% for late mortality; and 0.4% *versus* 0.5% for stroke.

The data regarding the need for further revascularization are shown in table 3 and figure 4. The superiority of surgery over angioplasty was consistent in 23 of 24 studies. However, there has been gradual improvement in the results of PCI. In studies of multi-vessel disease patients, the incidence of repeat revascularization in the PCI group dropped from 49% in EAST and 44% in BARI to around 11% in SYNTAX and in CÁRDia. In patients with single lesions of LAD coronary artery, it dropped from 39.9% in MASS I to less than 10% in recent studies of the stent era. Figure 4 shows that the relative risk of new revascularization by means of an alternative procedure (surgery for patients undergoing PCI and angioplasty for patients undergoing CABG) showed a clear tendency to equalization of outcomes in the stent era.

Nine studies reported late mortality in the diabetic subgroup. Six showed a trend in favor of surgery (CABRI, EAST, BARI, MASS II, ARTS and SOS), one was neutral (ERACI II) and two showed a trend in favor of angioplasty (RITA and AWESOME). By aggregating the results of these studies, the late mortality was 21.3% in the intervention group and 15.9% in the surgery group.

Two studies have mentioned the results of mortality at one year in unprotected main coronary artery disease (Table 4). In SYNTAX, the mortality was 4.2% in the PCI group *versus* 4.4% in the CABG group. There was a trend towards lower mortality with angioplasty in patients with low or intermediate SYNTAX score, and a tendency towards higher mortality with CABG in patients with high SYNTAX score. In LEMANS, the mortality was 2% in the PCI group *versus* 8% in the CABG group. When the results of the two trials were aggregated, there was no significant difference (3.9% *versus* 4.7%). When we added the results of LEMANS (in which most of the patients did not show high angiographic complexity) to those of the subgroups of patients with low or intermediate SYNTAX score, it was possible to notice a trend clearly in favor of angioplasty (1.1% *versus* 5.6%).

Discussion

Several reviews[45], meta-analyses of randomized trials[46-48], and a major collaborative study[49] were published comparing PCI with CABG. The main difference of this review is the number of studies and patients evaluated. This was due to the fact that we considered tracks of occurrence and not rigidly fixed moments. Furthermore, there was the addition of recent studies that used drug-eluting stents[39,45] and involved a large numbers of patients.

The trend towards higher early mortality found in surgical patients is in line with the Registries of the New York State[50], which showed that hospital mortality with surgery is more than two times higher than that of patients who underwent angioplasty (0.68% *versus* 1.75%). It is worth remembering that the worst outcome of the surgery was due to studies of the balloon era and, in the stent era, due to the ERACI II and AWESOME studies, which involved a substantial number of acute patients or patients at a high surgical risk. In addition, there has been significant improvement in surgical outcomes in more recent clinical trials[34,35,38]. With respect to the intermediate mortality, the data from this study are highly consistent and are in line with what has been published until now: no difference at one year between angioplasty and surgery. There was also no significant difference in late mortality, particularly in the stent era, which was also suggested in a recent systematic review, but this is at odds with an older meta-analysis[46]. This meta-analysis showed a progressive trend in favor of surgery as the comparison was delayed. There is a possible explanation for this discrepancy: when we compared angioplasty with surgery in such meta-analysis,

Table 1 - Mortality and stroke. Studies involving patients with multi-vessel disease

Study and nr. of patients	Early mortality		Intermediate mortality		Late mortality		Stroke	
	Angioplasty	Surgery	Angioplasty	Surgery	Angioplasty	Surgery	Angioplasty	Surgery
RITA (1,011)	0.8%	1.6%	3.1%	3.6%	7.6%	9%	0.2%	1%
ERACI I (127)	1.5%	4.5%	4.6%	4.6%	9.2%	4.6%	1%	3%
EAST (392)	1%	1%	7.1%	6.2%	12.5%	9.2%	0.5%	1.5%
GABI (359)	1.6%	4.5	2.2%	4.5%	7.3%	6.3%	0%	1%
CABRI (1,054)	1.3%	1.9	3.4%	2.2%	10.9%	7.3%	NA	NA
BARI (1,829)	1%	1.3%	4%	4%	13.7%	10.7%	0.2%	0.8%
TOULOSE (151)	1.3%	1.3%	2.7%	2.3%	13.3%	10.4%	NA	NA
AWESOME (454)	3.2%	5.2%	6%	10%	16%	18%	1%	1.5%
ERACI II (450)	0.9%	5.7%	3.1%	7.5%	7.1%	11%	1%	1.5%
MASS II (408)	2.4	2.5	4.5%	4%	12.8 %	15.5 %	1%	3%
SOS (998)	0.8%	0.2%	5%	2%	8.1%	4.3%	1%	2%
ARTS (1,205)	1.5*	1.0*	2.5%	2.8%%	8%	7.6%	1.5%	2.1%
OCTOSTENT (280)	0%	1.4%	0%	2.8%	8.7%	13.4%	0%	0%
SINTAX (1,800)	1.9*	0.9*	4.4%	3.5%	ND	ND	0.6%	2.2%
LE MANS (105)	0%	4%	2%	8%	ND	ND	0%	4%
CÁRDIA (510)	NA	NA	3.2%	3.2%	ND	ND	0.4%	2.8%
Total of patients	3,809**	3,799**	5,570	5,533	4,315	4,280	4,753	4,741
Total of events	45**	77**	219	222	459	425	34	78

*Early mortality - % of deaths within 30 days after the procedure. Intermediate mortality - % of deaths within 2.5 years after the procedure; Late mortality - mortality within 2.6 years or more after the procedure. Studies in bold are from the "stent era". The other ones are from the "balloon era". The underlined ones used drug-eluting stents. * - data estimated on the basis of curves of survival and deaths before the procedure and not considered in the aggregation of results. ND - not defined.*

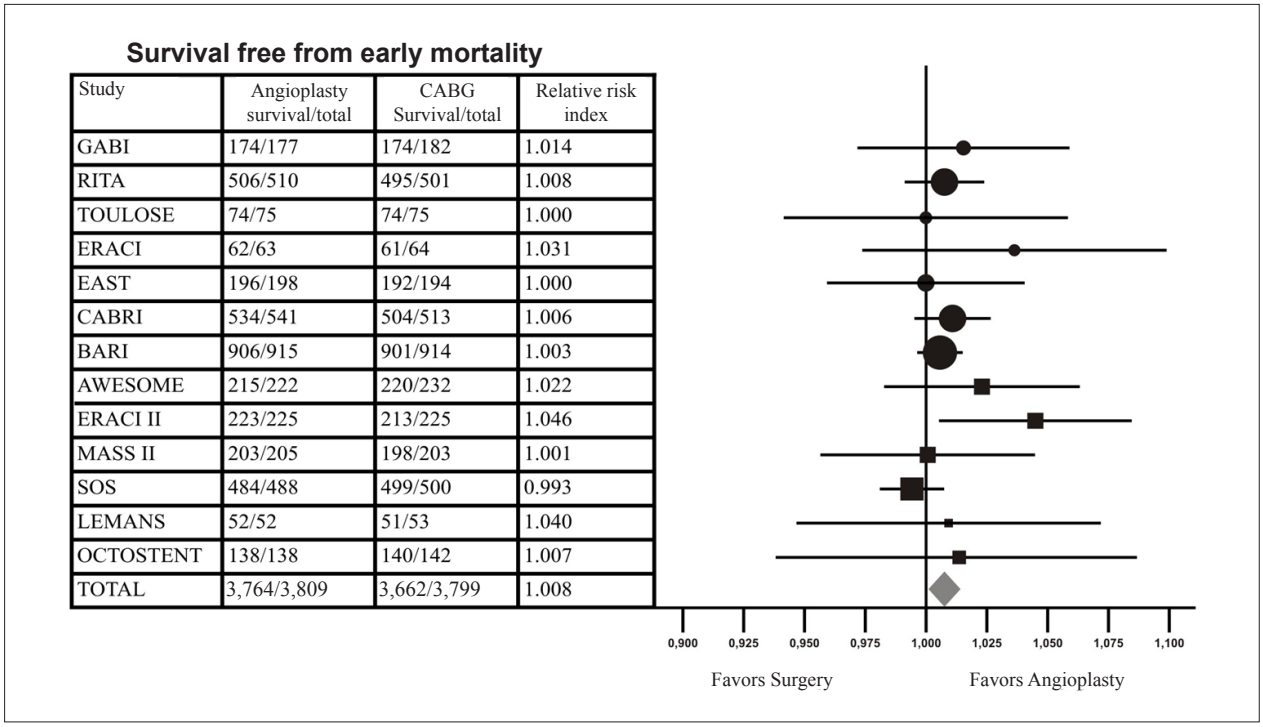

Figure 1 - *Studies in patients with multi-vessel disease. Graphical representation of the "relative risk index" of early mortality. Values above 1 favor angioplasty and values below 1 favor surgery. Circles represent studies of the balloon era. Squares represent studies of the stent era. The diamond represents the total of results. The size of the circles and squares is directly proportional to the number of patients in the study and the bar size is inversely proportional. When the bar does not cross the midline, there was statistical difference between the results.*

Survival free from late mortality

Study	Angioplasty survival/total	CABG Survival/total	Relative risk index
GABI	164/177	157/168	0,989
ERACI I	57/63	61/64	0,992
RITA	483/510	474/501	1,015
TOULOSE	66/76	68/76	0,967
BARI	790/915	816/914	0,966
EAST	153/174	161/177	0,963
CABRI	484/541	482/513	0,971
AWESOME	130/165	125/162	1,020
ERACI II	209/225	200/225	1,043
MASS II	172/205	171/203	1,028
ARTS	542/590	538/584	0,995
SOS	444/484	467/488	0,960
OCTOSTENT	126/138	119/142	1,059
TOTAL	3,856/4,315	3,855/4,280	0,992

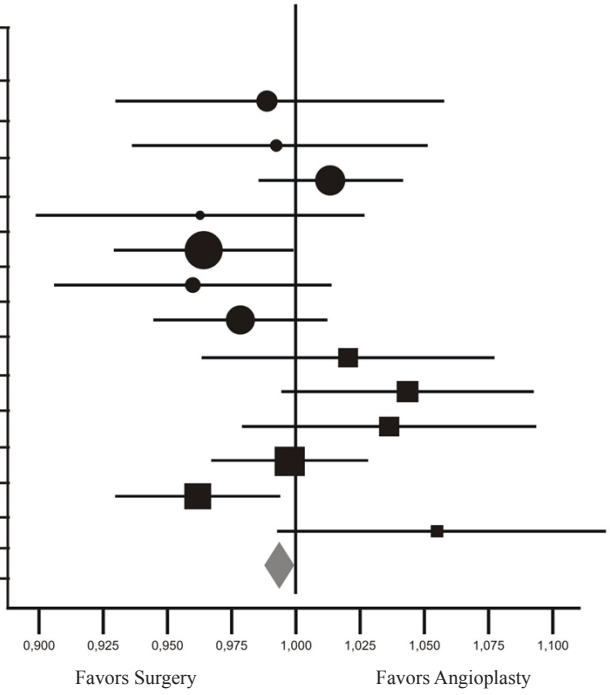

Figure 2 - Studies in patients with multi-vessel disease. Graphical representation of the "relative risk index" of late mortality. Values above 1 favor angioplasty and values below 1 favor surgery. Circles represent studies of the balloon era. Squares represent studies of the stent era. The diamond represents the total of results. The size of the circles and squares is directly proportional to the number of patients in the study and the bar size is inversely proportional. When the bar does not go cross the midline, there was statistical difference between the results.

Survival free from stroke

Study	Angioplasty survival/total	CABG Survival/total	Relative risk index
RITA	505/510	486/501	1,008
ERACI	62/63	60/62	1,020
EAST	197/198	191/194	1,010
GABI	182/182	177/178	1,010
BARI	913/915	907/914	1,006
AWESOME	220/222	229/232	1,005
ERACI II	225/225	223/225	1,005
MASS II	182/182	175/177	1,021
SOS	483/488	490/500	1,010
ARTS	591/600	593/605	1,006
SINTAX	894/900	880/900	1,023
OCTOSTENT	138/138	138/138	1,000
LE MANS	52/52	51/53	1,040
CARDIA	256/255	254/247	1,025
TOTAL	4,729/4,753	4,663/4,741	1,010

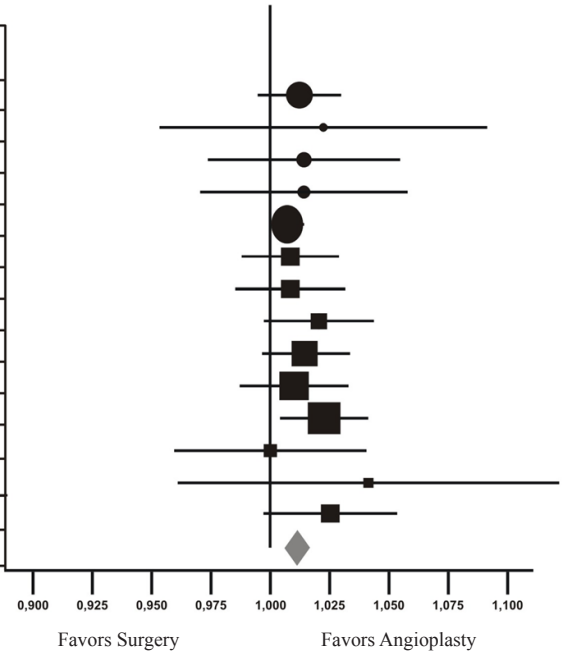

Figure 3 - Studies in patients with multi-vessel disease. Graphical representation of the "relative risk index" of stroke. Values above 1 favor angioplasty and values below 1 favor surgery. Circles represent studies of the balloon era. Squares represent studies of the stent era. The diamond represents the total of results. The size of the circles and squares is directly proportional to the number of patients in the study and the bar size is inversely proportional. When the bar does not cross the midline, there was statistical difference between the results.

Table 2 - Mortality and stroke: studies in single proximal lesion of the left anterior descending (LAD) coronary artery

Study and nr. of patients	Early mortality		Intermediate mortality		Late mortality		Stroke	
	Angioplasty	Surgery	Angioplasty	Surgery	Angioplasty	Surgery	Angioplasty	Surgery
MASS I (142)	0%	0%	1.4%	1.4%	8.8%	2.9%	0%	0%
LAUSANNE* (134)	0%	0%	1.5%	0%	9.7%	3.3%	ND	ND
SIMA* (135)	1.6%	0%	1.6%	3.2%	8%	6.4%	1.6%	0%
DRENTH (105)	0%	4%	0%	4%	0%	6%	2%	0%
CISOWSKI (100)	0%	0%	0%	0%	ND	ND	0%	0%
KIM (100)	0%	0%	4%	4%	ND	ND	ND	ND
LEIPZIG (220)	0%	1.9%	0%	1.9%	10%	12%	0%	1%
AMIST (100)	0%	0%	0%	4%	ND	ND	ND	ND
HONG (189)**	1.7%	1.5%	1.7%	4.3%	ND	ND	0%	1.4%
Total of patients	632	580	632	580	348	348	465	413
Total of events	3	5	7	12	23	19	2	2

Early mortality - % of deaths within 30 days after the procedure; Intermediate mortality - % of deaths up to 2.5 years after the procedure; Late mortality - % of mortality within 2.6 years or more after the procedure. Studies in bold are from the "stent era". The other ones are from the "balloon era". The underlined ones used drug-eluting stents. ND - not defined.

Table 3 - Studies of main coronary artery disease. Mortality in subgroups of SYNTAX and in LEMANS

Study	Number of patients	Angioplasty mortality	Surgery mortality	Significance (p)
SYNTAX - low risk	221	0.9%	3%	0.150
SYNTAX -intermediate risk	195	1%	6.7%	0.054
SYNTAX - high risk	285	9.7%	4.1%	0.060
LE MANS	105	2%	8%	0.370
Low risk SYNTAX + intermediate risk SYNTAX + LEMANS	521	1.1%	5.6%	0.045
Total (SYNTAX+LEMANS)	810	3.9%	4.7%	0.410

Mortality at one year in main coronary artery disease. Subgroups of SYNTAX study and LEMANS study. The results of the SYNTAX subgroups were obtained from: Serruys P. Syntax primary end points TCT; October 14, 2008; Washington DC, being recently published[54].

the later the assessment was carried out, the more "balloon era" studies were included, in which there was a tendency to the superiority of surgery. In this review, in which a more significant number of "stent era" studies were included, the late superiority of surgical results tended to decrease.

It is also possible to note the similarity of results in studies of single proximal lesion of LAD coronary artery, even with a trend toward the superiority of angioplasty in the stent era, at least in terms of early and intermediate mortality. This makes PCI, since it is less invasive, the preferred form of revascularization in patients with single proximal lesion of LAD coronary artery, unless the anatomy is clearly inadequate. The possibility that less invasive surgical techniques may improve surgical outcomes is not corroborated in this review. A separate analysis of data from tables 2 and 4 suggests that the best results of surgery were precisely in studies using conventional techniques, that is, median sternotomy and surgery with CPB (SIMA, LAUSANNE and MASS I), and the worst ones in those that used minimally invasive techniques.

The trend towards a higher incidence of stroke in the surgical group had been suggested previously[48], and it had reached statistical significance in SYNTAX. The superiority of angioplasty in this review is unquestionable, since it groups a larger number of patients and it adds the results of SYNTAX and CÁRDia. One interesting fact was that we found no difference in the incidence of stroke in studies with patients with single lesions of LAD coronary artery, nor in OCTOSTENT, which used off-pump surgery. Besides the less intense manipulation of the aorta and the almost exclusive use of mammary artery, we could suggest, as an explanation for such fact, a lower degree of atherosclerosis in these patients.

The differences in results between the randomized studies, when evaluated in a meta-analysis or review such as this one, and the data registries, such as New York one[50], deserve to be addressed. Registries, unlike the meta-analyses, showed almost uniformly higher mortality of angioplasty in subgroups classically regarded as surgical (3 vessels, 2-3 vessels with obstruction of the proximal LAD coronary artery, poor ventricular function). However, registries showed selection bias that even the best statistical techniques can not eliminate. The possibility that has been classically raised is that the absence of differences in mortality in randomized trials is due to a predominance of two-vessel disease over three-vessel disease, and the small number of patients with poor ventricular function or proximal

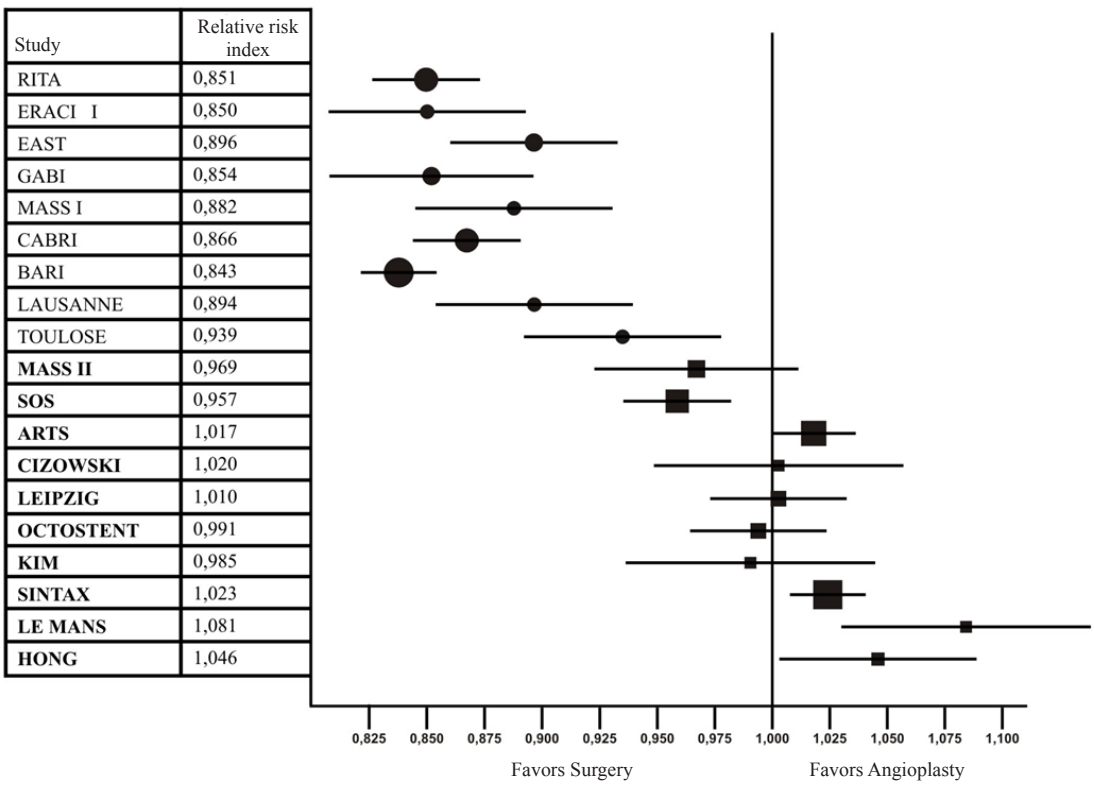

Figure 4 - *Studies in patients with multi-vessel disease. Graphical representation of the "relative risk index" of survival for new revascularization by alternative procedure (surgery to patients undergoing angioplasty and angioplasty for patients undergoing surgery). Values above 1 favor angioplasty and values below 1 favor surgery. Circles represent studies of the balloon era. Squares represent studies of the stent era. The size of the circles and squares is directly proportional to the number of patients in the study and the bar size is inversely proportional. PCI - percutaneous coronary intervention, CABG - surgery.*

obstruction of LAD coronary artery[51,52] does not seem to be valid today, for the following reasons: a) most patients with multi-vessel disease, as defined in this review, consisted of patients with three-vessel disease or obstruction of left main coronary artery, especially in the stent era; b) there was a trend in favor of angioplasty in studies involving patients with single proximal lesion of LAD coronary artery; c) more than 50% of multi-vessel disease patients had obstruction of the proximal LAD coronary artery and about 18% had poor ventricular function, a number that is not insignificant; d) several studies suggest that conditions such as triple-vessel disease, poor ventricular function (in non-diabetics) and the obstruction of proximal LAD coronary artery do not compromise the results of PCI, compared with surgery[14,22,23,49].

In the comparison between the balloon era and stent era, it is worth highlighting the improvement in the late mortality results of angioplasty in the stent era, despite the greater complexity of patients. The hypothesis for this improvement would be the progress in the interventional technique, making it possible to handle, in a more complete and secure way, the obstructions, as well as the progress in clinical treatment, due to the more liberal use of lipid-lowering agents and antiplatelet agents. The worse surgical results in early studies of the stent era, particularly in relation to early mortality, can be attributed to the severity of the patients' conditions, and mainly to ERACI II and AWESOME studies. Considering the results of recent studies, including those estimated by the survival curves, the surprising fact is that the operative mortality is extremely low, below 1%[34,35,38]. At first glance, the decrease in surgical mortality in recent studies could be explained by the improvement in postoperative care and surgical techniques, including the use of off-pump surgery in selected patients. An alternative explanation could be that the majority of patients with high risk unstable angina, in the past, often treated by surgery, are now being referred to angioplasty.

The superiority of CABG over PCI with respect to the incidence of new revascularization is widely recognized. However, there is an inexorable source of bias in this comparison. PCI does not compromise future revascularizations, whether they are a new angioplasty or first surgery, but the same does not happen with CABG. The latter often precludes future angioplasties and significantly increases the risk in case of new surgical revascularization. In this work, despite the clear superiority of surgery, it is possible

Table 4 - New revascularization and new revascularization by alternative procedure

Study and nr. of patients	Transluminal coronary angioplasty			Coronary artery bypass grafting		
	New revascularization by angioplasty	New revascularization by surgery (NRAP)	Total of new revascularizations	New revascularization by angioplasty (NRAP)	New revascularization by surgery	Total of new revascularizations
ERACI I (127)	14.5%	17.7%	32.2%	3.2%	0%	3.2%
EAST (392)	27%	22%	49%	13%	1%	14%
MASS I (142)	29.1%	11.8%	39.9%	0%	0%	0%
RITA (1,011)	12%	15%	27%	2%	2%	4%
GABI (359)	23%	18%	41%	4%	0%	4%
CABRI (1,054)	20.8%	15.7%	36.5%	2.7%	0.8%	3.5%
BARI (1,829)	22%	22%	44%	6.7%	0.7%	7.4%
LAUSANNE (134)	11.8%	13.2%	25%	3%	0%	3%
MASS II (454)	8.8%	3.5%	12.3%	0.5%	0%	4%
AWESOME (454)	ND	ND	11%	ND	ND	4%
ERACI II (450)	ND	ND	15.5%	ND	ND	4.5%
SOS (998)	11%	9%	20%	5%	1%	6%
OCTOSTENT (280)	7.2%	2.9	10.1%	2.1%	0%	2.1%
CISOWSKI *(100)	6%	0%	6%	2%	0%	2%
ARTS (1,205)	15.7%	6.7%	22.4%	8.3%	1.2%	9.5%
LEIPZIG (220)	22.7	3.6	26.1	4.5	0	4.5
KIM* (100)	12%	2%	14%	0%	2%	2%
DRENTH* (105)	ND	ND	8%	ND	ND	3%
AMIST (100)	ND	ND	4%	ND	ND	0%
SINTAX (1,800)	11.4%	2.8%	14.2%	4.7%	1.3%	6%
LE MANS (105)	26.9%	2%	28.9%	9.4%	0%	9.4%
CÁRDIA (510)	ND	ND	11.8%	ND	ND	2%
HONG* (180)	1.7%	0%	1.7%	4.4%	1.5%	5.9%

Studies in bold are from the stent era. The other ones are from the balloon era. The underlined ones used drug-eluting stents. Numbers in bold represent: NRAP - new revascularization by alternative procedure: surgery in patients of the angioplasty group and angioplasty in patients from the surgery group. ND - not defined.

to notice the progressive improvement of angioplasty in the stent era, culminating in excellent results with the use of drug-eluting stents. This improvement is particularly striking when we consider only the risk of new revascularization by alternative procedures, in which there was a tendency to equalization of outcomes in the stent era.

Until recently, the unprotected main coronary artery disease was a definite indication for surgery. Since surgery has proven to be beneficial for the reduction in mortality and due to the catastrophic nature of an acute occlusion during percutaneous intervention, surgery has been classified as the preferred indication for main coronary artery lesion in the guidelines, with angioplasty being characterized for a long time as type-III indication and only recently as a type IIb[53]. The results of SYNTAX and LEMANS, as well as the trend towards the superiority of angioplasty in patients with SYNTAX score below 33[54], point to the need for a better classification of percutaneous coronary intervention in a main coronary artery disease, provided that the patients' anatomy is good for the intervention.

In general, surgery is the preferred indication for diabetic patients with multi-vessel disease. The evidence against angioplasty in diabetic patients comes from the balloon era, based on occasional findings of the BARI study. Its researchers evaluated a subgroup of 343 diabetic patients and found a late mortality of 34.5% for intervention with balloon and 19.4% for surgery ($p = 0.03$). Thus, surgery is the preferred indication, in the guidelines, for diabetes in patients with multi-vessel disease, with angioplasty in such patients being classified as IIb.

In this study, which included the mortality rate in 4 years of CABRI and in 5 years of ARTS and SOS, the aggregation of results was favorable to surgery, with a tendency to statistical significance. This trend towards superiority is likely to be related simply to the complexity degree of the lesions, not being valid for all diabetics. In particular, it would not apply to patients with unstable angina (ERACI study II), patients at high surgical risk (AWESOME study) and patients that undergo vein grafting procedures more frequently (RITA study). Moreover, none of these nine studies used drug-eluting stents. SYNTAX and CÁRDia, the first studies that compared drug-eluting stents

with surgery in diabetic patients, showed no difference in mortality at one year. However, since they are initial results, a definitive answer must wait for the late results of these studies, as well as for those of the FREEDOM study.

Conclusion

The data from this review confirm the current trend towards considering the complexity of the lesions and not the number or type of vessels involved, or even the poor ventricular function, as the main factor for choosing between the revascularization procedures.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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