International Journal of Cardiology 116 (2007) 383–388

International Journal of Cardiology

www.elsevier.com/locate/ijcard

A comparison of percutaneous coronary intervention and surgical revascularization after fibrinolysis for acute myocardial infarction. Insights from the InTIME-2 trial

José C. Nicolau *, J.A. Marin-Neto [b], Roberto R. Giraldez [a], Valdir Golin [c], Álvaro Rabelo Jr. [d], José A.F. Ramires [a]
On behalf of the InTIME-2 investigators

[a] *Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil*
[b] *University of São Paulo, Ribeirão Preto Medical School, Ribeirão Preto, Brazil*
[c] *Santa Casa de São Paulo Medical School, São Paulo, Brazil*
[d] *Federal University of Bahia Medical School, Salvador, Brazil*

Received 23 December 2005; received in revised form 28 February 2006; accepted 24 March 2006
Available online 17 October 2006

Abstract

Background: A substantial proportion of patients treated with fibrinolytics for acute myocardial infarction (AMI) is subsequently submitted to surgical or percutaneous revascularization procedures during the same hospitalization. However, data comparing these procedures are scarce in the literature. The purpose of this study was to analyze the outcomes of a population with AMI who, during the in-hospital phase, received fibrinolytic therapy followed by coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI).
Methods: The study population included 3532 patients submitted to CABG ($N=574$) or PCI ($N=2958$), out of 15,114 patients studied in the InTIME-2 trial. Among patients treated with PCI there were no differences between those who received stents or isolated balloon angioplasty, so that their data were pooled for analysis.
Results: CABG and PCI groups were compared regarding all-cause mortality (at 30 days and one year post-AMI) and non-fatal events (reinfarction, need of additional post-discharge revascularization and re-hospitalization for an ischemic event) within 30 days after MI. There was no significant difference in mortality rates between the groups – both unadjusted and adjusted – at 30 days and one year post-MI. The unadjusted 30-day rates of combined fatal and non-fatal events were 10.3% for the CABG group, and 15.3% for the PCI group (odds-ratio 0.64, $P=0.0017$), but the adjusted odds-ratio for the combined endpoint only achieved borderline significance ($P=0.048$).
Conclusion: Mortality rates for CABG and PCI were similar up to one year after AMI, but CABG tends to carry a better event-free survival in the first 30 days.

Keywords: Acute myocardial infarction; Fibrinolysis; Coronary artery bypass graft; Percutaneous coronary intervention

1. Introduction

The role of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) was analyzed in stable coronary artery disease patients [1–5]. Despite variable patient population and entry criteria among these trials, both invasive treatment techniques consistently yield similar rates of early and late hard events, i.e., death and non-fatal acute myocardial infarction (AMI), with higher reintervention rates for the PCI groups.

Not uncommonly, revascularization procedures are required in the early period after an acute coronary syndrome, specially for patients who are risk-stratified by coronary angiography [6,7]. However, there are no data in

* Corresponding author. Aureliano Coutinho, 355-14 andar, São Paulo 01224-020, Brazil. Tel.: +55 11 30695058/5196; fax: +55 11 30883809.
E-mail address: corjnicolau@incor.usp.br (J.C. Nicolau).

0167-5273/$ - see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijcard.2006.03.062

the literature comparing early treatment with CABG or PCI specifically in patients with acute ST-elevation AMI who have received fibrinolytic treatment. Therefore, the aim of this study was to evaluate the outcome of a population included in the multicenter, international, InTIME-2 study [8], and submitted to CABG or PCI during the in-hospital phase post-AMI.

2. Materials and methods

Details of the InTIME-2 study protocol were published elsewhere [8]. In summary, 15,114 patients with ST-elevation AMI within 6 h of symptom onset, without contraindications for fibrinolytic treatment and in the absence of cardiogenic shock, were included in the study and treated with lanoteplase or alteplase in a double-blind 2:1 randomization. ASA was indicated for all patients as adjuvant therapy. The primary objective of the trial was to demonstrate that lanoteplase was as effective as or superior to alteplase in reducing all-cause mortality at 30 days of follow-up.

During the in-hospital phase, 5674 (37.5%) patients were submitted to coronary angiography, 574 (3.8%) to surgical myocardial revascularization (CABG group), and 2958 (19.6%) received percutaneous coronary intervention (PCI group). In this group 2017 (68.2%) patients underwent bare-metal stent implantation, the remaining being treated with isolated balloon dilatation. Because there were no differences in mortality, non-fatal events or event-free survival between patients with stenting and isolated balloon angioplasty, both subgroups were pooled for the comparisons between PCI and CABG.

In the InTIME-2 study there was no protocol-mandated indication or contraindication for coronary angiography and subsequent PCI or CABG, so that these procedures were always left at the discretion of the investigator.

The impact of CABG and PCI treatments was compared regarding all-cause mortality (30 days and one year follow-up) and non-fatal events (reinfarction, post-discharge revascularization and re-hospitalization for an ischemic event as reported by the investigators) within 30 days after AMI (only this time frame was available for non-fatal events). Reinfarction was defined per protocol as follows:

(A) If ≤18 h after the onset of the index AMI: recurrent chest pain at rest accompanied by new or recurrent ST segment elevation of ≥0.1 mV in any contiguous leads; chest pain and/or ST segment elevation must last ≥30 min.
(B) If >18 h after the onset of the index myocardial infarction: new ischemic chest pain at rest lasting ≥30 min associated with:
  1. Re-elevation in serum CK to >2 times the upper limit of normal. If measured prior to the CK returning to within the normal limits after the index infarction:
    a. A rise ≥50% above the lowest recovery CK level associated with the index infarction, or
    b. A rise ≥50% above the CK level from the sample drawn at the onset of new symptoms.
  2. Appearance of new, abnormal Q waves (≤30 ms) in any contiguous leads (not showing ST segment elevation on the qualifying ECG) or new LBBB on an ECG obtained >18 h after the index event.
(C) After interventional coronary revascularization: CK greater than 3 times the upper limit of normal and at least 50% greater than the previous value or new Q waves in 2 or more contiguous leads.
(D) After surgical revascularization: CK greater than 5 times the upper limit of normal and at least 50% greater than the previous value or new Q waves in 2 or more contiguous leads.

2.1. Statistical analysis

For the comparison between categorical variables the Chi-square test was utilized. Continuous variables were compared by the Student's *t*-test. Kaplan–Meier estimate curves were constructed for all-cause mortality, freedom of

Table 1
Baseline characteristics

	CABG (*N*=574)	PCI (*N*=2958)	*p*-value	95% CI for difference
Age	62.8±9.7	58.9±11.4	<0.0001	−4.9 to −2.9
Gender (male)	78.8%	77.8%	0.601	−2.7 to 4.7
White	93.2%	94.7%	0.145	−3.5 to 0.5
USA	33.5%	21.8%	<0.001	7.9 to 15.5
Time from symptom onset to fibrinolytic (h)	2.91±1.4 Median=2.67	2.88±1.4 Median=2.62	0.5885	−0.16 to 0.09
Time from symptom onset to PCI or CABG (days)	10.7±6.2 Median=9	6.5±6.2 Median=5	<0.0001	3.66 to 4.8
Prior MI	25.5%	14.0%	<0.001	8.2 to 14.8
Prior lytic	7.4%	5.2%	0.037	0.2 to 4.2
Hx diabetes	16.3%	13.8%	0.113	−0.6 to 5.6
Hx angina	24.4%	17.1%	<0.001	3.8 to 10.8
Hx CHF	2.5%	1.4%	0.070	−0.1 to 2.2
Hx hypertension	37.9%	31.5%	0.003	2.2 to 10.6
Prior PCI	6.9%	8.3%	0.245	−3.8 to 1.0
Prior CABG	3.5%	3.5%	0.972	−0.016 to 0.016
SBP	140.3±22.1	139.2±21.7	0.288	−3.0 to 0.89
DBP	81.9±14.5	81.6±14.1	0.740	−1.5 to 1.06
Heart rate	75.9±18.0	74.6±17.4	0.090	−2.9 to 0.21
Weight (kg)	79.4±13.9	79.8±14.8	0.519	−0.88 to 1.75
Height (cm)	171.0±9.1	171.1±9.1	0.805	−0.74 to 0.95
Anterior MI	42.7%	38.2%	0.043	0.1 to 8.9
Killip 2–4	8.1%	8.4%	0.801	−0.028 to 0.022

All *p*-values are Chi-squared or Student's *t*-test; CABG=coronary artery bypass graft; PCI=percutaneous coronary intervention; USA=patients treated in USA vs. other countries; MI=myocardial infarction; Hx=history; CHF=congestive heart failure; SBP=systolic blood pressure; DBP=diastolic blood pressure.

Table 2
Pre-admission and index hospitalization medication

	CABG (N=574)	PCI (N=2958)	p-value	95% CI for difference
Pre-admission				
Beta-blockers	23.1%	17.0%	<0.001	2.7 to 9.5
Ca^+ channel blockers	21.7%	16.3%	0.002	2.0 to 8.8
Nitrates	21.3%	12.4%	<0.001	5.8 to 12
Antiarrhythmics	0.9%	1.1%	0.608	−1.1 to 0.7
Diuretics	11.2%	8.3%	0.027	0.4 to 5.4
ACE-I/AII antagonists	15.4%	12.8%	0.093	−0.4 to 5.6
Cardiac glycoside and/or other inotropes	1.4%	1.3%	0.879	−0.9 to 1.1
Oral anticoagulants	1.1%	0.5%	0.093	−0.1 to 1.3
Aspirin	31.6%	20.8%	<0.001	7.1 to 14.5
Antiplatelet therapy other than ASA	0.9%	1.0%	0.811	−1.0 to 0.8
GP 2b/3a inhibitor	0.2%	0.03%	0.195	−0.1 to 0.4
Hypolipidaemic therapy	15.7%	12.5%	0.032	0.2 to 6.2
Between admission and discharge/day 7 (whichever was sooner)				
TPA	37.1%	34.2%	0.177	−1.4 to 7.2
Beta-blockers	85.4%	85.0%	0.792	−2.8 to 3.6
Ca^+ channel blockers	22.5%	15.1%	<0.001	4.1 to 10.7
Nitrates	95.8%	91.5%	<0.001	1.9 to 6.7
Antiarrhythmics	21.6%	17.2%	0.014	1.0 to 7.8
Diuretics	48.1%	24.3%	<0.001	19.8 to 27.8
ACE-I/AII antagonists	54.0%	54.2%	0.925	−0.047 to 0.043
Cardiac glycoside and/or other inotropes	29.8%	10.2%	<0.001	16.6 to 22.6
Oral anticoagulants	6.2%	3.9%	0.012	0.5 to 4.1
Antiplatelet therapy other than ASA	14.0%	51.2%	<0.001	−41.6 to −32.8
GP 2b/3a inhibitor	0.9%	15.1%	<0.001	−17.2 to −11.2
Hypolipidaemic therapy	36.5%	38.5%	0.357	−6.3 to 2.3

All p-values are Chi-squared; Ca^+=calcium; ACE-I=angiotensin converting enzyme inhibitor; AII=angiotensin II AT1 receptor; ASA=acetyl salicylic acid; GP 2b/3a=glycoprotein 2b/3a.

non-fatal events, and event-free survival, and the log-rank test was used for the comparison between the groups. A stepwise logistic regression analysis was developed, with all significant variables (Tables 1 and 2) included in the model. The 11 most powerful variables obtained were used for adjustment analysis between CABG and PCI: age, treatment in USA, pre-admission use of nitrates and ASA, time to CABG/PCI, in-hospital use of antiarrythmics, cardiac glycosides, oral anticoagulants, antiplatelets other than ASA, glycoprotein IIb/IIIa inhibitors, and diuretics. The Cox proportional hazards regression was applied for the one year adjusted mortality analysis. The confidence interval was set at 95% and differences were considered significant when $p<0.05$ (two-tailed).

3. Results

Table 1 shows baseline population characteristics for the CABG and PCI groups. Patients in the CABG group were older and had a higher prevalence of prior MI, history of angina pectoris and arterial hypertension, anterior MI location on the ECG, and previous fibrinolytic treatment.

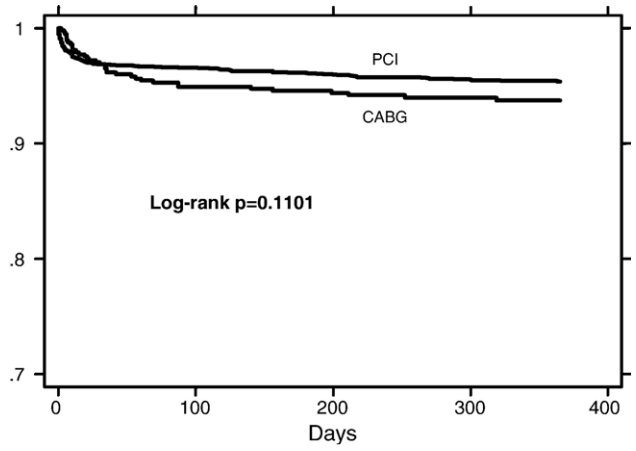

Fig. 1. Kaplan–Meier survival estimates to one year by in-hospital coronary artery bypass surgery (CABG) or percutaneous coronary intervention (PCI). Adjusted model: HR CABG vs. PCI=0.79, P=0.326. Variables included in the model were age, USA-treatment, time do CABG/PCI, pre-admission nitrates, pre-admission ASA; in-hospital antiarrythmics, cardiac glycosides, oral anticoagulants, antiplatelet other than ASA, GP 2b/3a inhibitor, and diuretics.

They were also more often treated in the USA, and showed a longer time between the symptom onset and the revascularization treatment.

Table 2 shows pre-admission and index hospitalization therapeutic regimens. In relation to pre-admission therapy, groups were significantly different regarding the use of beta-blockers, calcium channel blockers, nitrates, diuretics, aspirin and hypolipidemic drugs. Relatively to medication utilized during hospital stay, differences occurred for calcium channel blockers, nitrates, antiarrythmics, diuretics, cardiac glycoside and/or other inotropic agents, oral anticoagulants, antiplatelets other than aspirin, and glycoprotein IIb/IIIa inhibitors.

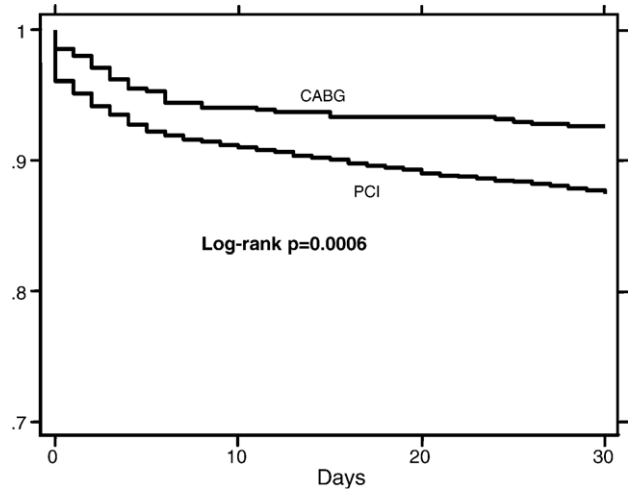

Fig. 2. Kaplan–Meier free of non-fatal events estimates to 30 days by in-hospital coronary artery bypass surgery (CABG) or percutaneous coronary intervention (PCI). Endpoints reinfarction, post-discharge revascularization, re-hospitalization for ischemic event; only pts alive at day 30 included.

Table 3
Multivariable adjusted odds-ratios for CABG vs. PCI

	OR (95% CI)	*p*-value
30-day fatal events	0.61 (0.30 to 1.22)	0.161
30-day non-fatal events	0.74 (0.51 to 1.08)	0.126
30-day fatal or non-fatal events	0.71 (0.50 to 0.99)	0.048

Variables included in the adjusted model: age, USA-treatment, time do CABG/PCI, pre-admission nitrates, pre-admission ASA; in-hospital anti-arrythmics, cardiac glycosides, oral anticoagulants, antiplatelet other than ASA, GP 2b/3a inhibitor, and diuretics.

When comparing stented vs. non-stented patients in the PCI group, data were similar: 30-day mortality 3.1% and 3.1%, respectively ($P=0.95$); one year mortality 4.4% and 4.7% ($P=0.77$); 30-day non-fatal events 13.2% and 11.1% ($P=0.11$); 30-day fatal or non-fatal events 15.9% and 13.8% ($P=0.14$).

Fig. 1 displays the Kaplan–Meier one year-survival estimates for the CABG and PCI groups. Both non-adjusted and adjusted results were similar in the two groups. The mortality rates for 30 days were identical (3.1% in each group), and the adjusted model (CABG vs. PCI) showed an odds-ratio=0.61 ($P=0.161$). For one year, the mortality rates were 6.1% for CABG and 4.5% for PCI (hazard-ratio=1.35, $P=0.11$), and the adjusted hazard-ratio CABG vs. PCI was 0.79 ($P=0.326$).

The composite incidence of non-fatal events (reinfarction, repeat revascularization, re-hospitalization for ischemic events) up to 30 days post-AMI was significantly lower for the CABG group (7.4%), relatively to the PCI group (12.5%, $P=0.0006$) — Fig. 2 and Table 3. However, when adjusted models were used, the incidence of non-fatal events was comparable in the two groups ($P=0.126$) — Table 3. The incidences of each variable, for CABG and PCI groups, were as follows: reinfarction 6.20% and 9.56% ($P=0.015$); repeat revascularization 0.72% and 1.54% ($P=0.14$); re-hospitalization 0.48% and 2.9% ($P=0.011$).

The composite incidence of non-fatal events and death was significantly lower in the CABG group (10.3%) relative to the PCI group (15.3%, $P=0.0017$) as seen in Fig. 3. The adjusted models (Table 3) showed a borderline significant smaller incidence of events in the CABG group, when taking into account the combination of fatal and non-fatal events ($P=0.048$).

4. Discussion

In patients with inducible ischemia after fibrinolytic treatment for ST-elevation AMI, revascularization procedures (CABG or PCI) are potentially more beneficial than the conservative approach [9]. However, previous reports on the results of surgery performed early after myocardial infarction or unstable angina, consistently showed a higher risk associated to the procedure [10–12]. On the other hand, although rescue PCI after failed pharmacological fibrinolysis and routine invasive strategy soon after AMI appear to be reasonable measures on the basis of more recent trials [13,14], most of such patients have multivessel coronary disease, so that PCI may not be the best revascularization procedure in this population. Thus, in early post-AMI, the issue on selection of the most appropriate form of revascularization is not settled.

To the best of our knowledge, this is the first study comparing CABG with PCI in patients treated with fibrinolytics for AMI. Because this is a post-hoc analysis of data, as expected, the two groups had markedly distinct baseline characteristics. Of note, patients selected for CABG had a higher risk profile for complications, as indicated by their older age or the presence of previous myocardial infarction and angina. Despite these baseline differences, mortality rates were similar following both revascularization procedures. Also, similarly to what has been found in patients with stable angina or non-ST-elevation acute coronary syndromes [1,5,15,16], an apparent benefit of CABG in our study was restricted to reduction in non-fatal cardiac events — reinfarction, and hospital readmission for acute ischemia. Moreover, the differences between the groups, regarding isolated non-fatal events, did not reach statistical significance when adjusted models were applied. Furthermore, the probability of event-free survival at 30 days showed only a borderline significant difference favoring CABG, with a *p*-value=0.048. Thus, overall, our results show that both CABG and PCI performed well in patients requiring revascularization procedures soon after fibrinolysis for AMI.

It is possible to speculate about the possible mechanisms for the trend observed in this study toward some advantages of CABG over PCI in selected patients early after fibrinolysis. Recent studies have shown that there is a systemic inflammatory and prothrombotic status associated with acute coronary syndromes, leading to simultaneous unstabilization of multiple atherosclerotic plaques [17–19]. Also, angiography and other methods demonstrate that

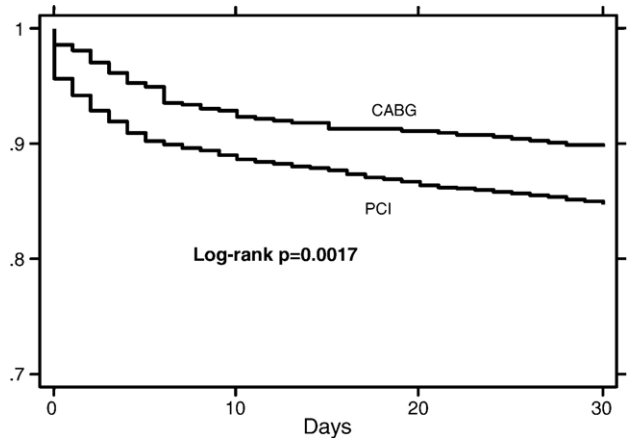

Fig. 3. Kaplan–Meier event-free survival estimates to 30 days by in-hospital coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI). Endpoints death, reinfarction, post-discharge revascularization, re-hospitalization for ischemic event.

multiple coronary artery sites have unstable features, sometimes making it difficult to pinpoint the actual lesion triggering the acute event [17]. Therefore, in this setting, a broader revascularization, as provided by CABG, may be especially beneficial in such patients. Since the time to the procedure was longer for CABG than for PCI, it is possible that relatively more interventional procedures have been undertaken in emergency settings and that surgery could have been carried out under more stable conditions. Finally, the difference in non-fatal events was largely driven by a lesser incidence of reinfarction in the CABG group. However, in our analysis the total number of reinfarctions occurring throughout the period from the index AMI to 30 days was considered in the group comparisons, not the incidence of such events after each procedure. Since the definition of reinfarction based on elevation of serum markers of necrosis varied between the two groups, this difference may have influenced the results. Nevertheless, it is relevant to point out that although less frequent because of a higher threshold, the increase of serum levels of myocardial necrosis markers may be prognostically worse after surgery than following PCI [20,21].

The suggestion that surgery performed at least equally well to PCI in selected patients referred for revascularization early after MI is both clinically relevant and reassuring in the context. Thus, randomized trials comparing CABG and PCI have not enrolled patients with complex forms of coronary disease such as left main disease and refractory post-MI angina [13–15,21,22]. Moreover, in these studies very often cardiologists, interventionists and surgeons have difficulty reaching final consensus in terms of equal treat ability. As a result, a relatively small percentage of screened patients is actually selected for these trials. This stresses the importance of database analyses, like the one developed in this study, where a large population, non-selected on the basis of which revascularization procedure could be carried out, and including patients with complex lesions and clinical settings, was enrolled.

Our results are also reassuring because new developments in both, PCI and CABG, are continuously being implemented. In special, drug-eluting stents, decreasing the incidence of reestenosis and necessity of reintervention in comparison with bare-metal stents [23,24], is expected to improve the outcome of patients undergoing PCI after AMI.

4.1. Limitations of the study

This study is a post-hoc analysis which suffers from inherent limitations. First, as in all similar studies, the population enrolled in the InTIME-2 trial represents a highly selected population of patients with acute myocardial infarction. Second, the analysis carried out refers to nonrandomized data for both groups, thus preventing a completely unbiased assessment of treatment effects. As seen, CABG and PCI groups were not alike at baseline, and the number of patients included in each group was distinct. Moreover, variables as the extent of the coronary artery disease and left ventricular ejection fraction, that could have a major impact in the adjusted models if different among the groups, were not captured in our databank. Although differences in age, presence of previous MI and time to the procedure, among others, were adjusted by multivariable analyses, such statistical procedures are of limited value. However, other reports strengthen the importance of such nonrandomized studies, suggesting that observational investigations often (but not always) yield results that mirror those of randomized trials [25,26].

Another limitation to this study was that non-fatal events were reported for a brief period of time (30 days) that might not represent long-term results. However, the long-term outcome may also be improved when surgery is performed after myocardial infarction instead of PCI [27]. Moreover, most of clinical events post-AMI occur in the first 30 days of follow-up [28]. Finally, it is important to stress that the results of this study should not be generalized to any country in particular, and to the current practice of both PCI and surgery, since both procedures have experienced considerable technical improvement recently; nevertheless, as in the main paper, the results hereby analyzed reflect the average practice worldwide.

In conclusion, mortality rates for CABG and PCI were similar up to one year after AMI, and the 30-day incidence of non-fatal events showed a trend in favor of CABG in this population. A possible benefit associated with CABG is likely to be due to more complete revascularization achieved with surgery and to the population characteristics, which resulted in more stable patients after AMI being treated with CABG.

Acknowledgment

The authors are indebted to Elliott Antman MD, for his support in the development of the manuscript, to Michael Gibson, MD, MS and Sabina A. Murphy, MPH, for their help in the statistical analysis, and Pedro A. Lemos, MD, for his suggestions on the paper.

References

[1] Hamm CW, Reimers J, Ischinger T, Rupprecht HJ, Berger J, Bleifeld W. A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI). N Engl J Med 1994;331:1037–43.

[2] Hueb WA, Bellotti G, de Oliveira SA, et al. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995;26:1600–5.

[3] Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. N Engl J Med 1996;335:217–25.

[4] Carrie D, Elbaz M, Puel J, et al. Five-year outcome after coronary angioplasty versus bypass surgery in multivessel coronary artery

disease: results from the French Monocentric Study. Circulation 1997;96:II-6.
[5] Henderson RA, Pocock SJ, Clayton TC, et al. Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy. J Am Coll Cardiol 2003;42:1161–70.
[6] Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001;344:1879–87.
[7] Lagerqvist B, Husted S, Kontny F, et al. A long-term perspective on the protective effects of an early invasive strategy in unstable coronary artery disease: two-year follow-up of the FRISC-II invasive study. J Am Coll Cardiol 2002;40:1902–14.
[8] Intravenous NPA for the treatment of infarcting myocardium early; Intime-II, a double-blind comparison of single-bolus lanoteplase vs accelerated alteplase for the treatment of patients with acute myocardial infarction. Eur Heart J 2000;21:2005–13.
[9] Madsen JK, Grande P, Saunamaki K, et al. Danish multicenter randomized study of invasive versus conservative treatment in patients with inducible ischemia after thrombolysis in acute myocardial infarction (DANAMI). DANish trial in Acute Myocardial Infarction. Circulation 1997;96:748–55.
[10] Gardner TJ, Stuart RS, Greene PS, Baumgartner WA. The risk of coronary bypass surgery for patients with postinfarction angina. Circulation 1989;79:I79–80.
[11] Kouchoukos NT, Murphy S, Philpott T, Pelate C, Marshall Jr WG. Coronary artery bypass grafting for postinfarction angina pectoris. Circulation 1989;79:I68–72.
[12] Fremes SE, Goldman BS, Weisel RD, et al. Recent preoperative myocardial infarction increases the risk of surgery for unstable angina. J Card Surg 1991;6:2–12.
[13] Fernandez-Aviles F, Alonso JJ, Castro-Beiras A, et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. Lancet 2004;364:1045–53.
[14] Schomig A, Ndrepepa G, Mehilli J, et al. A randomized trial of coronary stenting versus balloon angioplasty as a rescue intervention after failed thrombolysis in patients with acute myocardial infarction. J Am Coll Cardiol 2004;44:2073–9.
[15] de Feyter PJ, Serruys PW, Unger F, et al. Bypass surgery versus stenting for the treatment of multivessel disease in patients with unstable angina compared with stable angina. Circulation 2002;105:2367–72.
[16] Buffon A, Biasucci LM, Liuzzo G, D'Onofrio G, Crea F, Maseri A. Widespread coronary inflammation in unstable angina. N Engl J Med 2002;347:5–12.
[17] Goldstein JA, Demetriou D, Grines CL, Pica M, Shoukfeh M, O'Neill WW. Multiple complex coronary plaques in patients with acute myocardial infarction. N Engl J Med 2000;343:915–22.
[18] Buffon A, Biasucci LM, Liuzzo G, D'Onofrio G, Crea F, Maseri A. Widespread coronary inflammation in unstable angina. N Engl J Med 2002;347:5–12.
[19] Zairis MN, Papadaki OA, Manousakis SJ, et al. C-reactive protein and multiple complex coronary artery plaques in patients with primary unstable angina. Atherosclerosis 2002;164:355–9.
[20] Costa MA, Carere RG, Lichtenstein SV, et al. Incidence, predictors, and significance of abnormal cardiac enzyme rise in patients treated with bypass surgery in the arterial revascularization therapies study (ARTS). Circulation 2001;104:2689–93.
[21] Serruys PW, Unger F, Sousa JE, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344:1117–24.
[22] Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. Lancet 2002;360:965–70.
[23] Saia F, Lemos PA, Lee CH, et al. Sirolimus-eluting stent implantation in ST-elevation acute myocardial infarction: a clinical and angiographic study. Circulation 2003;108:1927–9.
[24] Lemos PA, Saia F, Hofma SH, et al. Short- and long-term clinical benefit of sirolimus-eluting stents compared to conventional bare stents for patients with acute myocardial infarction. J Am Coll Cardiol 2004;43:704–8.
[25] Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. N Engl J Med 2000;342:1878–86.
[26] Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med 2000;342:1887–92.
[27] Nicolau JC, Oliveira, Martinez E, et al. Comparison between coronary artery bypass surgery and percutaneous coronary intervention performed in the acute phase of myocardial infarction, in the long-term follow-up. J Am Coll Cardiol 2002;9:306B.
[28] Pitt B, White H, Nicolau J, et al. Eplerenone reduces mortality 30 days after randomization following acute myocardial infarction in patients with left ventricular systolic dysfunction and heart failure. J Am Coll Cardiol 2005;46:425–31.