On-Pump versus Off-Pump Coronary-Artery Bypass Surgery: a Meta-Analysis

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Abstract

There are controversies about the possible benefits of off-pump coronary artery bypass grafting (OPCABG) compared to on-pump coronary artery bypass grafting (ONCABG). For a better perspective on this important issue, we performed a meta-analysis of randomized controlled trials, comparing the two techniques.

The objective of this study was to verify which technique applied in Coronary Artery Bypass Surgery, OPCABG or ONCABG, provides better results through a meta-analysis of published randomized trials comparing the two techniques.

We carried out a computer-based literature search in PubMed, Embase, B-on and Science Direct from March 2009 to January 2010. The studies covered were recovered according to predetermined criteria. A systematic review of randomized clinical trials was performed in order to evaluate the differences between the two revascularization techniques (OPCABG versus ONCABG) regarding mortality and morbidity. Selected studies did not include patients at high risk and long-term longitudinal evaluations.

The meta-analysis focused on nine randomized clinical trials, corresponding to a total of 75,086 patients, and compared OPCABG to ONCABG. Regarding mortality, a reduction of 18% in the risk of cardiovascular mortality (OR: 0.82, 95%CI: 0.70 to 0.98, p = 0.03) and 27% in the risk of stroke postoperatively (OR: 0.73, 95%CI: 0.63 to 0.85, p = 0.0001) were observed, both in favor of OPCABG. Concerning the occurrence of complications associated with the procedure, no significant differences were found between the two surgical techniques, particularly with regard to the occurrence of kidney complications (OR: 0.97, 95%CI: 0.84-1.14, p = 0, 74) and sepsis (OR 0.98, 95%CI: 0.64-1.51, p = 0.93, respectively).

Off-pump CABG significantly reduces the occurrence of major cardiovascular events (mortality and CVA) compared to on-pump CABG surgery.

Keywords

Coronary artery bypass; off pump; myocardial revascularization; intraoperative complications; meta-analysis.

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Introduction

Cardiopulmonary bypass (CPB) as a support method in cardiac surgery is, from the historical point of view, relatively new. Among the several procedures of myocardial revascularization surgery (CABG), only the method of Vineberg[1] showed promising results, and it was performed without knowledge of the anatomy of coronary arteries[1]. Later, Rene Favaloro was the pioneer of the CABG surgery using the saphenous vein, using CPB and cardiac arrest[2]. The familiarity of surgeons with the CPB circuit and the development of strategies for myocardial protection has led to the carrying out of CABG procedures using this technique[3].

One of the most important trends of the 90s was the search for methods that would allow a reduction of the trauma that accompanies the CABG procedures with CPB. The first such initiative was the rediscovery of the CABG procedures without CPB, initially described by Kolesov[4-6] in 1967, but made popular only in the second to last decade by Benetti[4,7] in Argentina and Buffolo in Brazil[4,8].

Currently, off-pump (OPCABG) CABG has acquired its own identity; however, despite evidence of the feasibility and safety of this technique, conventional on-pump CABG (ONCABG) is still used by most surgeons[4].

Cardiovascular diseases are the ninth leading cause of mortality[9], and coronary heart disease (CHD) the fourth leading cause of years of life lost, making it an important public health problem[10].

Today, several therapeutic options are available in the context of ischemic heart disease. Regarding surgical options, several techniques have been developed, but controversies remain regarding the benefits of the different available types[11].

ONCABG surgery remains a reference in this context; however, important limitations are acknowledged in this technique. In the last two decades, in spite of a dramatic increase in patient risk factors, morbidity and postoperative complications have decreased significantly. These improvements are attributed to systematic advances in surgical techniques, anesthetic techniques and myocardial protection strategies[11,12]. Nevertheless, neurologic complications remain a risk for patients undergoing CPB. Currently, the use of this method is still recognized as a leading cause of complex organic systemic inflammatory response (OSIR), which greatly contributes to several adverse effects in the postoperative period, namely, kidney, pulmonary or neurological complications and bleeding episodes, among other[13,14].

Over the last ten years there has been an increasing interest in performing CABG without CPB, or off-pump CABG (OPCABG), stimulated by the recognition of the harmful effects of CPB[12-18]. In this sense, the OPCABG has gained some acceptance and has become a widely performed procedure in an attempt to reduce morbidity and neurological injury related to ONCABG from[12,19-25].

In contrast, according to some authors, the OPCABG involves risk of intraoperative hemodynamic instability and incomplete revascularization, thereby increasing mortality and morbidity in the long term[26-31]. However, the real clinical impact of this alternative surgical technique remains limited by the scarcity of studies comparing the two methods[26-31]. According to Gerola et al[32], there are no statistically significant differences in mortality and morbidity rates in low-risk patients.

On the other hand, some studies have documented important effects of OPCABG, although the available evidence is not sufficient to define the possible relevance of this technique in clinical practice; thereby, the controversy remains on the real benefits of its use[23-37].

Thus, we carried out a meta-analysis of randomized controlled trials comparing the ONCABG to OPCABG, to assess the relative benefits in terms of mortality, morbidity and complications inherent in the procedures.

Methods

Research

We carried out a literature search using the search engines PubMed, Embase, B-on and Science Direct, looking for articles that contained the combinations of the words: coronary artery bypass grafting, on-pump versus off-pump, Complications, morbidity, mortality, cardiopulmonary bypass, myocardial revascularization, CPB versus off-pump, complications, morbidity, mortality, cardiopulmonary bypass. The research began in March 2009 and ended in January 2010.

Inclusion Criteria

We analyzed the titles and abstracts of the articles and included in the review all those that reported CABG in the context of on-pump and off-pump surgeries. We only considered studies with adult patients undergoing CABG with and without CPB. Research with animals were excluded from this review, as well as studies written in other languages rather than English, Spanish or Portuguese.

Data extraction

The selection criteria of the methods described were applied to 94 studies identified in literature search in the aforementioned search engines. Based on a review by two independent observers, which concealed the identity of the authors, the articles were accepted or not.

In a first phase, the titles and abstracts of 94 studies were analyzed to determine potential eligibility for further evaluation. Thus, all studies that met the following criteria were selected: prospective randomized study comparing on-pump and off-pump CABG. In this first phase, it was observed that 32 studies were duplicates, 6 had combined procedures, 11 studies were not randomized, 6 had no OPCABG group and did not contain ONCABG group, leaving only 34 studies.

In a second phase, the 34 selected studies were evaluated in more details, showing that 19 contained insufficient data, 4 did not meet the inclusion criteria, and two were still ongoing. Thus, nine studies remained, which showed characteristics potentially suitable for inclusion in the meta-analysis. The following endpoints were obtained from these articles: mortality, cerebrovascular accident (CVA), kidney complications and septicemia.

Statistical Analysis

The data were analyzed using the Statistical Review Manager Version 5.0 (Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2008) using fixed effect and random effect models. Heterogeneity was assessed by Q test and complemented with I^2, which indicates the proportion of variability between studies, providing a measure of heterogeneity[38-40].

The results were assessed as dichotomous variables, for which the *odds ratio* (OR) and 95% confidence intervals (95%CI) were calculated[41]. The criterion for statistical significance was a p value ≤ 0.05 for a confidence interval of 95%.

Results

Selected studies

The inclusion criteria were applied to the 94 studies assessed, but only nine articles were selected and evaluated in details. These were all published studies, of which clinical characteristics are shown in Table 1[42-50].

Meta-analysis

Mortality

Mortality was reported in seven studies (23,163 patients, Figure 1)[42,44-48,50] and according to the analysis, it was significantly lower in off-pump group (OR = 0.82, 95%CI: 0.70 – 0.98, p = 0.03), with heterogeneity regarding the overall effect in the sample (Chi^2 = 24.51, p = 0.0004). The OR represents a 18% reduction in the mortality risk in favor of the OPCABG surgical technique and must be considered with care in the context of the heterogeneity among the studies mentioned above.

Cerebral-vascular Accident (CVA)

The incidence of CVA was reported in five studies (64,713 patients, Figure 2)[42,43,45,47,48]. The analysis showed that this incidence was significantly lower in the OPCABG group and that there was no heterogeneity, i.e., the studies were homogeneous with respect to the overall effect in the sample (Chi^2 = 3.86, p = 0.43). The meta-analysis showed a

Table 1 – Clinical characteristics of the selected studies

Study (year)	Country	N of patients involved (off-pump vs. on-pump CABG)	Patients' characteristics
BRONW[42] (2006)	USA	2.300 (1.000/1.300)	Small size of the blocked artery (< 1.25 mm); intramyocardial and posterior location of the vessel; multiple stenoses and poor quality of vessels; presence of multiple comorbidities; age ≥ 75 years, in combination with COPD; kidney failure; cerebral and peripheral vascular disease.
HANNAN[43] (2007)	USA	49.830 (13.899/35.941)	--------
MACK[44] (2004)	USA	7.376 (3.688/3.688)	--------
MIZUTANI[45] (2007)	Japan	228 (114/114)	--------
MUNERETTO[46] (2003)	Italy	176 (88/88)	Patients' exclusion criteria were ≥ 75 years of age; presence of COPD; renal dysfunction; symptomatic carotid disease; peripheral arterial disease; severe atherosclerotic disease of the ascending aorta; history of CVA.
PALMER[47] (2007)	USA	1,251 (654/597)	--------
PUSKAS[48] (2008)	USA	12,812 (5,667/7,145)	Emergency patients were included. Patients' mean age was 63 years. Exclusion criteria were concomitant surgery (valvular or aortic pathology) and emergency procedures. The inclusion criteria of patients were ≥ 80 years of age, ventricular dysfunction, kidney failure, COPD, reoperation.
STRAKA[49] (2004)	Czech Republic	388 (204/184)	
YOKOYAMA[50] (2000)	USA	725 (242/483)	

CVA – cerebrovascular accident; COPD - chronic obstructive pulmonary disease; CABG - Coronary-artery bypass grafting

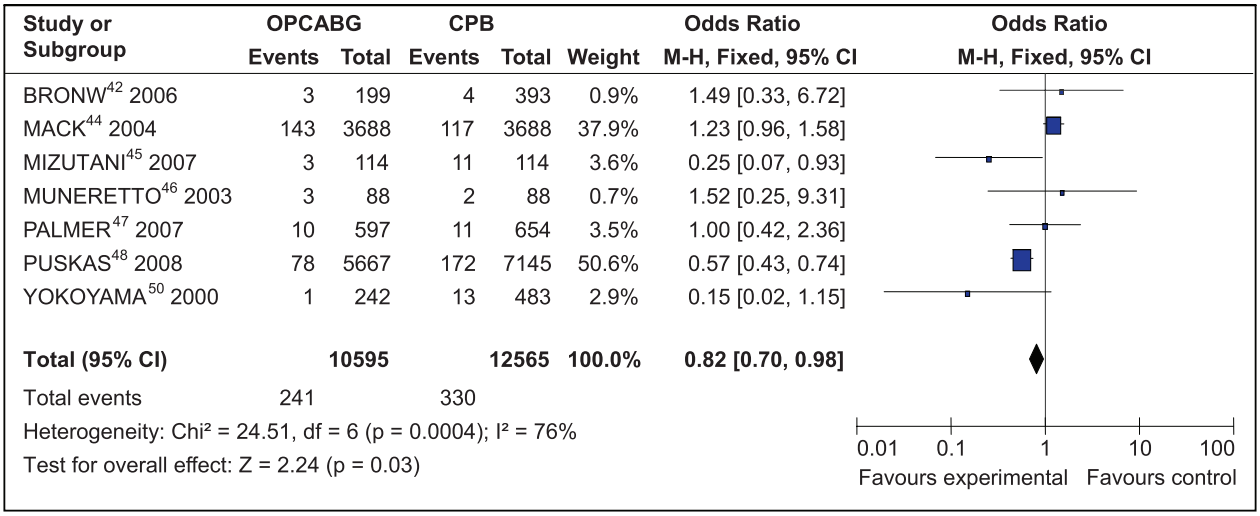

Figure 1 - *Forest plot for comparative analysis of mortality.*

significant difference in CVA risk, with an OR of 0.73 (95%CI: 0.63 to 0.85, p = 0.0001), indicating a 27% reduction in risk of postoperative CVA in favor of OPCABG.

Kidney Complications

Kidney complications were reported in five studies (59,410 patients, Figure 3)[43-45,47,50] and the analysis showed there was heterogeneity regarding the overall effect in the sample ($Chi^2 = 10.01$, p = 0.04). The meta-analysis showed no significant difference in kidney complications, indicating an OR of 0.97 (95%CI: 0.84 - 1.14, p = 0.74).

Septicemia

Septicemia was reported in three studies (58,457 patients, Figure 4)[43,44,47], which, according to the analysis, were homogeneous with respect to the overall effect in the sample ($Chi^2 = 3.09$, p = 0.21). The meta-analysis showed no significant difference in septicemia (OR = 0.98, 95%CI: 0.64 -1.51, p = 0.93).

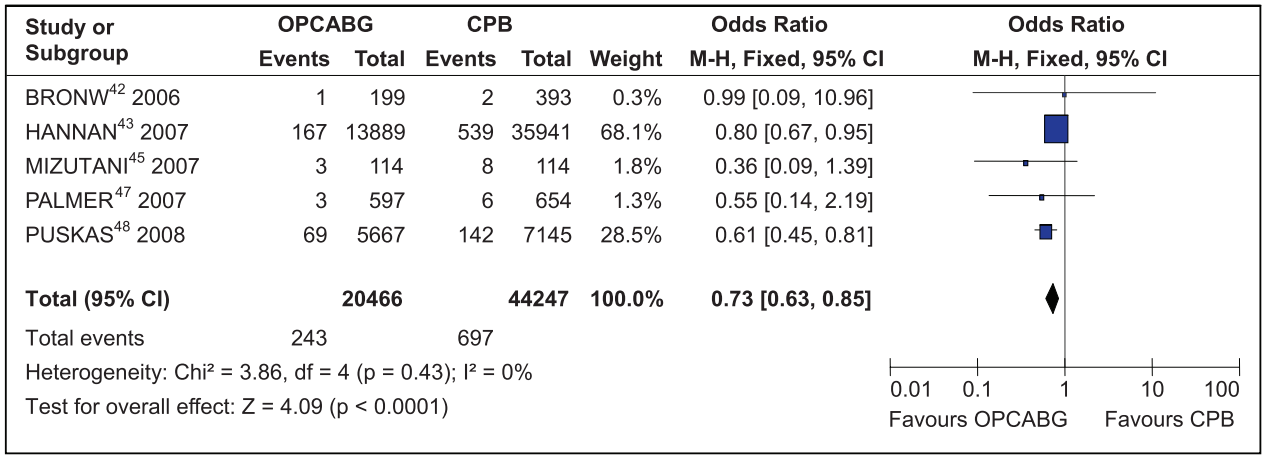

Figure 2 - *Forest plot for comparative analysis of cerebrovascular accident.*

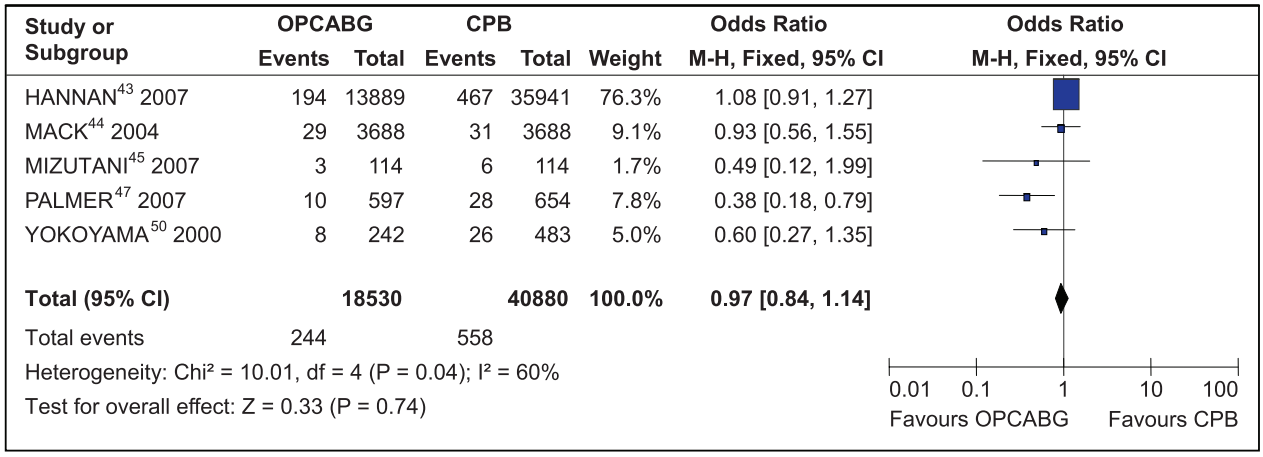

Figure 3 - *Forest plot for comparative analysis of renal complications.*

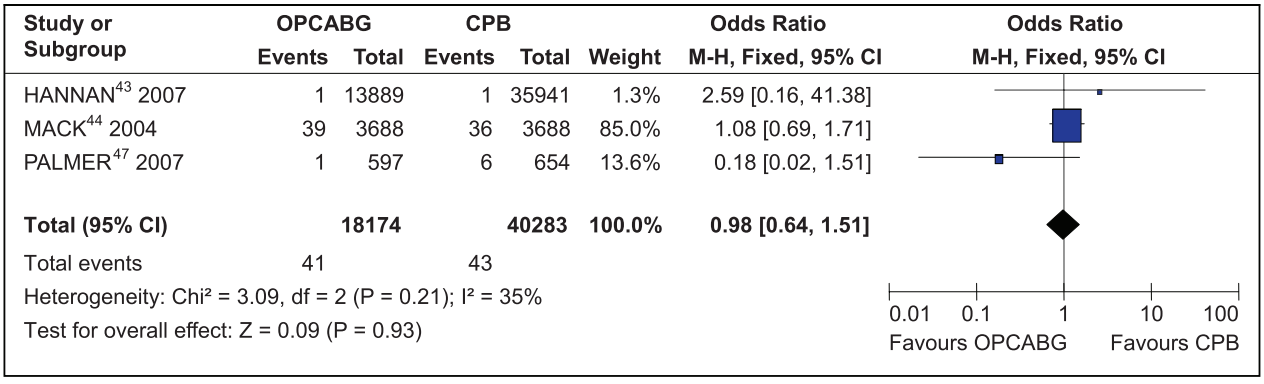

Figure 4 - *Forest plot for comparative analysis of septicemia.*

Discussion

The OPCABG is an important surgical technique in the present context, although its use and dissemination in clinical practice still lack scientific support, regardless of any improvements made over the past years in order to reduce mortality and morbidity in the postoperative period attributable to the surgery[51-54]. However, due to difficulties in conducting prospective randomized trials in this area and therefore the small number of recorded patients, the statistical

power of available studies is relatively low. Moreover, one must consider the low incidence of mortality and morbidity in patients undergoing myocardial revascularization[55].

In recent years, several studies have been published, but the number of available randomized clinical trials is also limited[56-58]. Thus, with regard to key endpoints (death and CVA), only randomized studies with large samples can conclusively demonstrate differences in outcomes between treatment groups of low-risk patients[54]. On the other hand, the studies series tend to exclude higher-risk patients, perhaps the most likely to benefit from the OPCABG technique, and therefore, doubts remain about the safety of this technique in this context[51,56-58].

Moreover, one must consider the existence of studies that effectively show a reduction in mortality and morbidity in the operative and post-operative period of OPCABG when compared to ONCABG. However, the generalization of results can be questioned due to the subtle external validity of the studies[26,51,57,58]. In addition to the existing controversy, some studies also advocate that patients undergoing OPCABG have increased risk of postoperatively bypass occlusion. Thus, one discusses the durability of revascularization supported by this technique, although it has been recognized that the risk of obstruction in the first year is low and the two procedures can overlap[58,59].

Aiming to contribute to the clarification of key issues that have polarized the discussion of this topic, several meta-analysis have been carried out, using data available in the scientific literature, with the main objective of providing additional statistical support to clarify the status of OPCABG[54-57] compared to ONCABG. The present study is an attempt to provide further clarification. In this sense, the results indicate a clinical advantage toward OPCABG, indicating an 18% reduction in the mortality risk (OR 0.82, 95%CI: 0.70 - 0.98, p = 0.03) and a 27% reduction the risk of postoperative CVA (OR 0.73, 95%CI: 0.63 - 0.85, p = 0.0001). Regarding the occurrence of postoperative complications, namely, sepsis and kidney complications, no statistically significant differences were found, although most of the included studies suggested a greater impact of ONCABG on the kidney. This aspect is expressed in the results obtained in the meta-analysis (OR 0.97, 95%CI: 0.84 - 1.14, p = 0.74), outlining a trend suggestive of lower risk of complications associated with OPCABG[29,57,60-62].

Other evidence relevant to this problem, previously addressed in other studies, concern the need for transfusion, length of hospital stay and cost of surgery. In this sense, the currently available evidence indicates that OPCABG is characterized by reduced need for blood transfusion, shortest length of stay and therefore, lower hospital costs[45,46,48-50,55-57,63].

These aspects have been supported by a recent meta-analysis[54], which has shown that the OPCABG is less expensive compared to ONCABG. Moreover, another study[64] showed that the costs of patients submitted to OPCABG were significantly lower when compared to ONCABG (OPCABG 6,515 ± 926 € *vs*. ONCABG 9,872 ± 1,299 €, p <0.0001). This difference is mainly due to decreased postoperative complications and reduced stay in intensive care unit. However, one should consider that patients submitted to OPCABG requiring transition to ONCABG, have a higher risk of postoperative mortality and multiple organ failure, compared to patients submitted initially to ONCABG surgery[43,65]. This reinforces the need to select the right patients for the surgical technique that best suits the individual clinical profile.

Limitations

The studies included in this meta-analysis were published between 2002 and 2007 and therefore may not reflect practical realities that are non-representative of more current surgical and anesthetic practices. While they overall favor the OPCABG, the results should be interpreted with some caution, as four of the nine studies did not contain information concerning the clinical characteristics of patients included in the study.

Although this meta-analysis outlines the current situation, it also serves to highlight some of the questions that remain to be clarified. The most notable is the lack of long-term clinical research, as well as the lack of research in high-risk patients, which makes it difficult to place the OPCABG technique in terms of clinical significance in patients at high surgical risk[57].

Conclusion

The ONCABG, of the two surgical techniques studied, is the oldest and most widely used in current clinical practice; technological and surgical advances have allowed this procedure to present very low mortality and morbidity, with excellent results. On the other hand, the OPCABG, which is a newer technique, has comparative advantages, as it has excellent results, but with potentially smaller rates of mortality, morbidity and complications as well as lower costs.

These aspects have been well illustrated in this meta-analysis of randomized trials, showing that the OPCABG technique is associated with lower mortality rates and lower risk of CVA. However, this apparent clinical superiority of OPCABG compared to ONCABG surgery still needs to be demonstrated in particular clinical contexts. Both techniques are evolving and have advantages and disadvantages in certain subgroups of patients[65], and risks and benefits of both approaches need to be considered, so that the choice of strategy for the patient will maximize the long-term benefit and minimize short-term risk[55,58].

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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