Reply to the Letter to the Editor

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Neuza Lopes*, Felipe S. Paulitsch, Whady Hueb
Heart Institute of University of São Paulo, Brazil

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Keywords: Angioplasty; CABG; Medical treatment

We are very pleased by the interest shown in our paper Impact of number of vessels disease on outcome of patients with stable coronary artery disease: 5-year follow-up of medical, angioplasty and bypass surgery study [1] by these distinguished authors [2]. We further analyzed our data as suggested:

First question: When PCI was compared to CABG, new revascularization procedure was performed in 29.4% on PCI vs 2.4% on CABG group (p < 0.01) and 23.3% on PCI vs 3.4% CABG (p < 0.01) in 2VD and 3VD, respectively. Indeed, the need of further revascularization increases health cost at the same survival benefits, as we have shown previously [2].

Second question: To rule out the selection bias, we found no statistical difference among the main characteristics (gender, age, hypertension, diabetes, smoking, previous MI, cholesterol, HDL, LDL, triglycerides levels, and positive treadmill test) stratified by groups (SVD, 2VD and 3VD) in each of the allocated treatment. So, there was a balance of the traditional risk factors among groups.

Third question: We compared the number of patients alive (A) vs cardiac related (CRD) vs non-cardiac related death (NCRD) on SVD (200, 9, 5), 2VD (222, 21, 10) and 3VD (294, 44, 20). We found higher cardiac related deaths on 3VD group (p = 0.004). However, we would like to highlight that the higher risk for death found in 3VD patients was adjusted for age and other comorbid variables, and consequently, the 3VD itself in an independent risk for death. When the 3VD group was stratified by treatment allocation, no statistical differences were noted among PCI (A = 101, CRD = 15, NCRD = 4), CABG (A = 96, CRD = 12, NCRD = 10), and MT (A = 97, CRD = 17, NCRD = 6) (p = 0.43). The main cause of death in PCI and MT was cardiac related, while in CABG group, cardiac and non-cardiac causes were balanced.

Finally, around 80% of our patients were under lipid lowering drugs and the values achieved after 60 months follow-up regarding cholesterol (PCI = 209[46], CABG = 213[46], MT = 212[47], p = 0.52) LDL (PCI = 131[40], CABG = 136[38], MT = 136[39], p = 0.31), HDL (PCI = 43[11], CABG = 43[11], MT = 42[10], p = 0.29), and triglycerides (PCI = 173[93], CABG = 162[91], MT = 186[162], p = 0.35) were balanced respectively, without being statistically different among treatment groups. We would like to stress that along the period of study follow-up, the lipid targets were different than currently used. Thus, we cannot make any conclusion based on the benefits of lipid treatment, since the values were similar and above the expected target. Thank you, indeed the correct cholesterol unit is mg/dl.

References


Letter to the Editor

Clinical impact of heparin-bonded circuits: when a meta-analysis does not clear out the clouds

Marco Ranucci*
Department of Anesthesia and Intensive Care, IRCCS Policlinico S. Donato, Via Morandi 30, San Donato Milanese, Milan 20097, Italy

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Keywords: Heparin-bonded circuits; Clinical impact

We read with interest the systematic review and meta-analysis of Mangoush and co-workers [1] recently published in the European Journal of Cardiothoracic Surgery, addressing the clinical impact of heparin-bonded circuits (HBCs) on clinical outcome following cardiac operations. The authors retrieved 41 randomized control trials (RCTs) and could demonstrate that patients treated with HBCs experienced a better outcome, namely in terms of reduced incidence of allogeneic blood product transfusions and re-sternotomy. Within the exclusion criteria, the authors considered the use of auto-transfusion techniques to manage postoperative bleeding. Of course it is in the right of the authors to decide which criteria should be applied to include RCTs in their meta-analysis. However, the reason for excluding studies

* Corresponding author. Address: Av. Dr. Eneas de Carvalho Aguiar #44, Cerqueira Cesar, São Paulo, SP 05403-000, Brazil. Tel.: +55 11 3069 5032; fax: +55 11 3069 5188. E-mail address: mass@incor.usp.br (N. Lopes).

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* Corresponding author. Address: Av. Dr. Eneas de Carvalho Aguiar #44, Cerqueira Cesar, São Paulo, SP 05403-000, Brazil. Tel.: +55 11 3069 5032; fax: +55 11 3069 5188. E-mail address: mass@incor.usp.br (N. Lopes).

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where auto-transfusion techniques were employed is unclear. Their decision led to the exclusion of two major RCTs, from Wildevuur and co-workers [2] and McCarthy and co-workers [3], respectively including 805 and 350 patients. Moreover, it is unclear how they could decide in which studies the postoperative auto-transfusion was allowed. As a matter of fact, in one excluded study [2] this technique was clearly mentioned, whereas in the other [3] this is not stated. Conversely, Mangoush and co-workers included in their meta-analysis our study published in 1999 [4]. Actually, our study was focused on high-risk patients, and we applied exactly the same protocol as the previous one [2] focused on low-risk patients, which I co-authored, where postoperative autotransfusion was allowed. Finally, the authors included the study from Baufreton and co-workers [5], being unaware that it was designed as a separate arm of the main study on low-risk patients [2]. By doing this, they included the same patient population coming from two different studies, and again admitted to the meta-analysis another study, which allowed postoperative auto-transfusion.

As a result of these biases, 1155 patients have been excluded by the analysis. Considering that the population included in the meta-analysis accounts for 3434 patients, the exclusion of 25% of the potential total patient population may lead to wrong conclusions.

Strictly looking at the allogeneic blood transfusions, the authors found out that heparin-bonded circuits were associated with a significant decrease in transfusion rate (odds ratio 0.8, 95% confidence interval 0.6–0.9, \( p = 0.004 \)). This result is of course strongly dependent on a single study [4] including 886 patients, that theoretically should have been excluded according to the authors’ criteria.

This outcome analysis can be addressed in a different way. If we simply consider the three major RCTs [2–4], without applying artificial exclusion criteria, we can analyze as many as 2041 patients. Pooling these three studies together, the odds ratio for allogeneic blood transfusions is 0.99 (95% confidence interval 0.83–1.19, \( p = 0.924 \)).

This result denies the protective effect of heparin-bonded circuits in terms of allogeneic blood transfusion rate, and is so far from significant that even including the other 39 RCTs (with a total population of 2548 patients, and a mean number per study of only 65 patients) we are inclined to believe that the results will not change.

References


* Corresponding author. Tel. +39 02 52774320; fax: +39 02 55602262. E-mail address: cardioanestesia@virgilio.it.

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Reply to the Letter to the Editor

Reply to Ranucci

Omar Mangoush*

Department of Cardiothoracic Surgery, Hammersmith Hospital, Imperial College Healthcare NHS Trust, 150 Du Cané Road, London W12 OHS, UK

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Keywords: Heparin-bonded circuit; Cardiopulmonary bypass; Perfusion

I thank Ranucci for his interest and comments [1] about our recently published meta-analysis of the outcome of heparin-bonded circuits [2]. This letter is in response to his comments.

Ranucci asked why we elected to exclude RCT used postoperative autotransfusion? The reason was explained in the last paragraph of the heterogeneity section of our article. If we do not exclude these studies, there will be a big disparity in the blood transfusion between studies used and studies not used by the technique.

He asked, how do we know if RCT used an autotransfusion technique? The manuscripts of all potential studies were scrutinized independently by two authors, and if postoperative autotransfusion was not mentioned, that means the technique was not used. If it was mentioned, but not clear from the manuscript, the author of the manuscript would have been contacted for clarification.

He also claims that the study by McCarthy et al. [3], which was excluded from the analysis, did not state that they have used the autotransfusion technique. This is not true, as this was clearly stated at the end of the result section of that article. They have autotransfused postoperative blood loss in the first 8 h.

Ranucci stated in his letter that in his study [4], which was included in our analysis, he used the same protocol of Wildevuur et al. [5] who used postoperative autotransfusion and therefore we should have not included his study [4]. In Ranucci’s manuscript he did not mention this fact. Therefore, there was no way for us to guess that. Actually, the Wildevuur study was not referred to in his material and methods section at all. He only made reference to this study on two occasions, one at the introduction and one at the comment sections. On both occasions he discussed the result of the study, but made no reference to the protocol in question.

He claims that the study by Baufreton et al, cited as reference number 5 in his letter, which was included in our analysis, was an arm of a bigger study by Wildevuur et al. [5],