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.

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doi:10.1016/j.ejcts.2008.06.017

Reply to the Letter to the Editor

Reply to Ranucci

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Received 10 June 2008; accepted 11 June 2008

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],
which was excluded due to the use of postoperative blood transfusion. In the Baufreton et al. study there was no mention of postoperative autotransfusion and there was no indication that these patients came from another study population. There was no reference to the Wildervuur study in their manuscript. This might be explained by the fact that both studies were accepted at different journals at the same time with only 2 days difference.

The conclusion Ranucci reached is not valid as it was based on simple analysis, as he described, and this defeats the object of systemic meta-analysis. Heterogeneity is a major problem in a systematic review and it can result in a wrong conclusion, therefore excluding a group of studies might be important to avoid such a problem. Poor reporting of surgical RCT is a known problem, which might lead to some mistakes and confusion when reporting systematic reviews.

References


Letter to the Editor

Technique for combined application of fibrin sealant and bioabsorbable felt against alveolar air leakage

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Received 11 April 2008; accepted 2 June 2008

Keywords: Alveolar air leakage; Fibrin sealant; Polyglycolic acid (PGA) felt; Adhesion

We read the article by Itano titled ‘The optimal technique for combined application of fibrin sealant and bioabsorbable felt against alveolar air leakage’ with great interest [1]. Air leaks are frequently observed after pulmonary resection, while some air leaks can be avoided with careful surgical techniques. Therefore, the development of methods that enable an airtight closure of the lung parenchyma during pulmonary surgery is of importance. The ideal tissue adhesive should have an outstanding safety profile, be easily manipulated, and be approveable by regulatory agencies. Furthermore, the ideal tissue adhesive should be flexible enough to respond to contraction and relaxation during respiration. Fibrin glue, various other biological sealants, and synthetic sealants have been applied for intraoperative air leak and have been reported by many investigators. Fibrin based sealants have generally failed to show significant improvement. Fibrin glue can be easily absorbed and is frequently applied as an air leak sealant, immediate closure often does not occur, and in many cases postoperative recurrences can occur due to poor tissue-bonding strength. Therefore, the most effective technique may be the combined application of fibrin sealant and synthetic bioabsorbable sheet to control alveolar air leakage. However, it has been previously observed that the implantation of nearly all polymer materials, such as polyglycolic acid (PGA), polylactic acid, and polylactic-co-glycolic acid causes a non-specific inflammatory response. It has been observed that there is a negative effect of the acidic environment that is created by polymer degradation. It is believed that acidic pH is created at the sealing site [2,3]. As a result, the implanted PGA felt lead to pleural adhesion. We experienced the postoperative pneumothorax recurrence that performed the combined application of fibrin sealant and PGA felt for air leak 3 months ago. In our case, pleural adhesion existed in the areas of implanted PGA. Histological examination revealed chronic inflammation and thick pleura.

Thoracic re-interventions become the standard management practice in an increasing number of patients with lung diseases. We think that it is desirable for pleural adhesion not to happen. Therefore Itano’s technique may be suitable for selective patients.

References

