initiation of heparin anticoagulation before treatment with factor concentrates in bleeding patients under ECC is controversial, because the effect of heparin is antithrombin dependent. We recommend the close monitoring and substitution of antithrombin in conditions with an ongoing activation of the hemostatic system. Although there is no evidence from the literature yet, inhibitor levels (in particular antithrombin) should be kept within the normal range before administration of factor concentrates to attenuate the procoagulant response, possibly resulting in thromboembolic complications.

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Is there an evidence in favor of off-pump coronary artery bypass?

To the Editor:

We read with interest the report of Mack and colleagues¹ that shows "improved outcome in coronary artery bypass grafting with beating-heart techniques." In the era of evidence-based medicine and megatrials, class A level evidence will remain the standard tool that forces change of direction of currently applied surgical procedures, including coronary artery bypass grafting. We concede that in the absence of major prospective randomized trials^{2,3} retrospective studies such as this may contribute enough evidence to sway the balance in favor of or against off-pump coronary artery bypass grafting (OPCAB).

However, we wish to highlight two issues that could have a significant impact on the conclusions derived from the study. First, at one point the authors claimed that the conversion rate was 2.9% and stated that "these patients were analyzed with the on-pump group." Later, however, they reported a conversion rate of 1.6% and suggested that the analysis was performed on an intent-to-treat basis (that conversions were analyzed with the OPCAB group). These conflicting statements require further clarification. Second, the need for a subgroup analysis of the cases converted from OPCAB to an on-pump procedure cannot be overemphasized. This analysis may provide the answer to a number of important questions regarding OPCAB, such as indications, timing, predictors, and, more importantly, the outcome of conversion in terms of mortality and morbidity.

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Short esophagi and a long career

To the Editor:

Professor J. Leigh Collis, a prominent surgeon, made several contributions to the development of the thoracic and cardiac surgery. However, he was immortalized and known worldwide for his work on gastropasty, originally published in this Journal 46 years ago.¹

I contacted by letter the then-90-year-old Professor Collis, asking for data to be used in an article concerning the history of esophageal surgery. I was honored with a concerned and pleasant reply. After our last contact, however, I received the grievous notice that Professor Collis had died on February 4, 2003.

It is fitting to pay homage to this singular character in the history of the esophageal surgery in the same *Journal* that immortalized him.

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Problems with complication rate analysis

To the Editor:

In a recent issue of this Journal, Grunkemeier and Wu¹ analyzed complication rates after bileaflet valve implantation by means of pooled data and regression anal-

ysis. Their criticism regarding inappropriate comparison of complication rates for different valve prostheses is more than justified. They approached the problem as a meta-analysis, although the exact criteria and methodology were not well documented.

Valid comparison of results with different heart valve substitutes is restricted to controlled, randomized studies. If randomized studies are not available, results of nonrandomized studies may be used to answer clinical questions. However, one should be extremely careful not to misuse and misinterpret the data analyzed. The article to which we are responding is a potential example of misuse and misinterpretation of data taken from the literature, including the data set of my own group.² The article has at least four major shortcomings: (1) inconsistent use of linearized rates, (2) inclusion violations, (3) inadequate reflection of follow-up techniques, and (4) publication bias.

First, in terms of inconsistent use of linearized rates, for their analysis Grunkemeier and Wu¹ appear to have included the early postoperative follow-up period in the linearized complication rates per patient year. However, it is not clear whether this rule was consistently applied. This can lead to misleading results because of the elevated and nonlinear rates for both bleeding and thromboembolic complications in the early postoperative period.³

Second, the study exhibits severe violations of its own inclusion criteria. For well-considered reasons, the study results published by our group and included in the regression analysis were explicitly not based on the American Association for Thoracic Surgery and Society of Thoracic Surgeons guidelines for reporting valve-related morbidity and mortality. Instead, we used a modified Karnofsky scale, which does not correspond to these guidelines. This scale, adapted by us to the special requirements for the long-term follow-up after valve replacement, allowed grading of reported complications^{2,4} and reporting of minor bleeding complications. Lack of differentiation between the two reporting systems resulted in severe violation of study inclusion criteria.

Third, a major problem when analyzing pooled data is invalid reporting of complications as a result of inappropriate follow-up techniques.⁵ The guidelines for re-

porting morbidity and mortality used in the data sets selected by Grunkemeier and Wu require reporting of *all* complications occurring during follow-up. The completeness of reporting is directly related to the follow-up strategies, such as the time intervals between consecutive follow-up examinations and how the data are gathered.⁵ Reliable follow-up data that include information on transient and reversible events are most effectively collected with regular follow-up visits to a specialized outpatient clinic or by on-line documentation, a strategy first used by my group.² Indeed, studies have shown that when, parallel to the regular follow-up in the outpatient department, the same patients were sent questionnaires at 6-, 18-, and 36-month intervals, about half of the events that were transient or reversible had been forgotten and therefore were not mentioned on the 18- and 36-month questionnaires.^{5,6} Incomplete data reporting may be illustrated further by the following. Of the 21 studies giving full information with regard to bleeding and thromboembolism, 4 reported linearized rates after aortic valve implantation below the background incidence for the combined end point of thromboembolism plus bleeding, indicating that proper follow-up techniques were lacking because not even the background incidence of such complications in the age-adapted general population was detected.

Finally, some of the studies included in the analysis represent atypical situations. One example is the series published by Baudet,⁷ who had patients during the first postoperative year on antiplatelet medication only. This series contributed 23 of the 82 valve thromboses (28%, 0.29%/patient-y) of the St Jude Medical data pool, compared with an average of 0.13%/patient-y for all other series. One must not include such an experimental series in the analysis of pooled data, because it can lead to arbitrary and unreliable conclusions.

To conclude, there are three messages that may come from the article that I criticize here. First, we need refined criteria for reporting morbidity and mortality after valve replacement. Cerebral events of unknown etiology should no longer be counted as thromboembolism, because most such patients have cerebral bleeding, not embolism, when cerebral computed tomographic scans are performed. Simple counting of complications is inappropriate,

because the vast majority of bleeding complications documented during appropriate follow-up have neither a prognostic impact nor do they influence quality of life. Reporting of morbidity should go along with grading the severity of the respective complications, as suggested earlier.²

Second, for each study it must be clear which patients have been included. For consecutive patients not only the postoperative survivors should be considered but all patients who underwent surgery (intent-to-treat analysis). An inept surgeon with a high intraoperative mortality would in effect eliminate many patients who would have to be considered at high risk for postoperative complications.

Third, in the era of evidence-based medicine the cardiovascular community should develop guidelines for the follow-up of patients. A careless cardiologist unwilling or unable to document potential complications because of inappropriate follow-up techniques will end up with the best results (and the combination of an inept surgeon and a careless cardiologist will always produce the best results). That may be the true impact of this article. With regard to follow-up, the message should be that it is the careful follow-up documentation of all complications that ensures the quality of the study. Sophisticated statistical techniques, no matter how elegant, cannot make up for deficiencies in this area.

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Reply to the Editor:

We thank Dr Horstkotte for his comments on our article comparing two heart valves by means of reports from the literature. In describing the limitations of such comparisons, he gives us another opportunity to stress the main purpose of our report, which was to point out precisely these limitations.

Dr Horstkotte found four "shortcomings" and agreed with three "messages" in our article. The shortcomings were (1) inconsistent use of linearized rates, (2) inclusion violation, (3) inadequate reflection of follow-up techniques, and (4) publication bias.

We attempted to include only late events in the linearized event rates. Most reports used in our study considered late events only, but some used both early and late events and some were unclear on this point. We tried to separate those that used late events from those that used both and attempted classify those that were unclear from other clues in the published reports, but we found this extremely difficult. We finally decided to use the results as published, and we specified this in the Clinical Material section.

We selected only articles that claimed to adhere to the American Association for Thoracic Surgery and Society of Thoracic Surgeons guidelines for reporting,^{1,2} as did Horstkotte and colleagues' 1993 article,³ which said, "Prosthetic valve related and anticoagulant-related complications were reported according to the current guidelines for reporting morbidity and mortality after valve replacement surgery."¹ In addition they used another set of definitions that included minor bleeding events, but we used only the major bleeding events, as recommended by the American Association

for Thoracic Surgery and Society of Thoracic Surgeons.² We did not include their 1994 article⁴ in our analysis.

We agree that the completeness of reporting complications is directly related to the follow-up strategy. We only selected articles with at least 95% follow-up completeness, evaluated the results as a function of follow-up completeness, and emphasized this issue in the Discussion section. However, there is no doubt a wide variation in the use of the word *complete*. A thorough evaluation of this variable should include not just the quantitative (percentage) aspect but also a qualitative description of what is meant. Such meanings can range, for example, from regular office visits with the patient to a phone contact with a widowed spouse long after the patient has died.

We attempted to eliminate articles that did not use universal anticoagulation. We apparently missed the fact that in Baudet and associates' report⁵ 65 patients with aortic replacements and 10 with mitral replacements received aspirin and dipyridamole only for 1 year, and had a higher incidence of thrombosis and embolism, because the article itself presented combined linearized rates. If this article had been eliminated from our study, however, it would have not changed the conclusions. The term *publication bias* refers to the fact that the publication of research studies is nonrandom but depends on the nature and direction of their findings, as described in our Discussion section.

We agree completely with the three "messages" that Dr Horstkotte took from our article—the needs for (1) refined reporting of complications, including grading of severity, (2) consecutive patients, and (3) thorough follow-up techniques—and we again thank him for emphasizing these points. The purpose of our study was to stress the limitations of data collection and definitions, as well as to present refined statistical methods of valve comparison used to deal with variability. The shortcomings that Dr Horstkotte mentioned were exactly what we studied and discussed in the article.

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Safety of bronchoplastic resection after induction therapy for lung cancer

To the Editor:

We read with interest the article by Ohta and colleagues¹ concerning the impact of induction treatment on patients who underwent full sleeve resection. Ohta and colleagues¹ concluded that preoperative therapy did not significantly affect postoperative outcome. The issue of the impact of the neoadjuvant chemotherapy in patients with lung cancer is today an object of debate. It has been demonstrated that right pneumonectomy after induction treatment is associated with a high risk of postoperative complications,² and Rendina and colleagues³ showed that lung-sparing resection could reduce the rate of pneumonectomy and could provide an alternative to a pneumonectomy after induction treatment.

We published in 2002 our experience with 27 patients who underwent induction treatment before lung-sparing resection.⁴ We had similar results, demonstrating that chemotherapy or chemoradiotherapy before surgery did not influence postoperative outcome. In addition, in our experience postoperative radiotherapy done for patients with N2 disease did not influence