Reply to the Editor:

In their letter, Koster and coworkers refer to our recent articles on a comprehensive blood-sparing approach in pediatric cardiac surgery and the effects of this approach on blood transfusion incidence and on potential effects of blood transfusion on postoperative morbidity.^{1,2} They propose a pair of simple but plausible mechanisms to explain how morbidity may contribute to the need for blood transfusion, rather than vice versa. The first is based on the well-known vasodilatory effect of analgesia. We fully agree that the resulting volume treatment could induce hemodilution to such an extent that it would contribute to the need for blood transfusion. In counterpoint to the suggestion of Koster and coworkers, however, this effect already occurs in all infants during surgery, and infants are transferred to the intensive care unit with balanced volume status, as assessed by central venous pressure and transesophageal echocardiography. During the early postoperative period, analgesia is continued for all infants, regardless of whether they are mechanically ventilated, although possibly to a lesser depth when they are not. We therefore do not believe that mechanical ventilation exerts a major effect on postoperative transfusion incidence through the suggested mechanism.

Second, Koster and coworkers suggest that increased diagnostic blood sampling during mechanical ventilation may accumulate to blood loss volumes sufficiently large to contribute to the need for transfusion. To substantiate this hypothesis, they estimate the total blood loss in the different groups of transfused and not transfused infants on the basis of a fixed sampling scheme with blood gas analyses at 2-hour intervals during mechanical ventilation. We fully agree that diagnostic blood sampling may accumulate to sample volumes that contribute to the need for blood

transfusion, especially in smaller infants. We recognized this when designing our comprehensive blood-sparing approach and therefore included reduction of diagnostic blood sampling as a major measure, as stated previously. To avoid frequent blood sampling in the postoperative period, measurements of end-expiratory P_{CO_2} and of arterial oxygen saturation by pulse oximetry are used to monitor the efficiencies of ventilation and gas exchange. Blood gas analyses are performed only occasionally to confirm the data from noninvasive monitoring and to obtain additional information on acid-base status and other parameters, such as lactate or electrolyte concentrations. The table presented in the letter of Koster and coworkers thus does not reflect the practice in our intensive care unit, and the actual blood sampling volumes are considerably smaller. In addition, most postoperative blood transfusions occur during the early postoperative period, before differences in ventilation time have induced major differences in blood loss as a result of the cumulative blood loss by blood sampling.

We are grateful to Koster and coworkers for pointing out the impact that frequent diagnostic blood sampling may have on hemodilution and the need for blood transfusion in small infants. We also agree that diagnostic blood sampling is increased during mechanical ventilation; however, it is not increased to the extent suggested by Koster and coworkers and also not to an extent that would have a dominant effect on the correlation between blood transfusion and duration of ventilation.

Finally, Koster and coworkers asked why age was not included as confounder in the multivariate analyses. It is correct that age is closely associated with both the rate of transfusion and postoperative morbidity. As stated in the statistics sections of both our previous articles,^{1,2} we included body weight rather than age in the multivariate

analyses. The strong collinearity between age and body weight precludes inclusion of both parameters in such analyses, and we decided to include body weight because of its slightly stronger association with transfusion incidence in the univariate analysis. Nevertheless, inclusion of age instead of body weight produces very similar results in the multivariate analyses.

In a more general context, the remarks of Koster and coworkers point to a major problem of retrospective analyses of clinical data, as in our recent study: statistics can help us to demonstrate correlations between clinical parameters, but they cannot tell us what is cause and what is effect. This question can only be approached by carefully analyzing the putative mechanisms that may lie behind such statistical associations. In the case of the correlation between blood transfusion and clinical outcome, we face an additional statistical problem: the same clinical parameters that determine the need for transfusion also determine clinical outcome. These are namely body weight (or age), the complexity of the underlying disease, and the resulting complexity of surgery. As discussed previously, the resulting group assignment bias may not be sufficiently addressed by conventional multivariate analyses as performed in our study.² We would like to use this occasion to thank the reviewers of the *Journal* for stimulating us to perform additional analyses in subgroups of infants formed according to risk scores, so that group assignment bias would have less effect. These analyses confirmed our results.

In conclusion, we thank Koster and coworkers for pointing out some mechanisms through which morbidity may affect the rate of blood transfusion. Nevertheless, we remain convinced that the relationship goes both ways: morbidity determines the need for blood transfusion, and transfusion in turn

contributes to postoperative morbidity after surgery for congenital heart disease. Quantification of either effect, however, remains a challenge.

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CARDIAC MAGNETIC RESONANCE IMAGING FOR ASSESSMENT OF AORTIC VALVE MORPHOLOGY

To the Editor:

We noted with interest the findings of Malaisrie and colleagues,¹ who reported in the August 2012 issue of the *Journal* that cardiac magnetic resonance imaging (CMRI) was superior to 2-dimensional transthoracic echocardiography (TTE) in determining the presence of a bicuspid aortic valve.

At our institution, we compared the accuracies of CMRI and TTE in the

TABLE 1. Accuracy of 2-dimensional transthoracic echocardiography versus cardiac magnetic resonance imaging in the identification of aortic valve morphology

Classification	TTE findings	CMRI findings	Surgical findings
Tricuspid valve	24 (66%)	27 (75%)	26 (72%)
Bicuspid valve	6 (17%)	8 (22%)	10 (28%)
Nondiagnostic	6 (17%)	1 (3%)	

Data are presented as number and percentage of patients. TTE, Transthoracic echocardiography; CMRI, cardiac magnetic resonance imaging.

identification of aortic valve morphology by comparing both with pathologic examination at the time of surgery as the criterion standard for diagnosis. Thirty-six subjects with severe aortic stenosis underwent both TTE and CMRI before aortic valve replacement. Valve assessment was classified as tricuspid valve, bicuspid valve, or nondiagnostic. The findings are outlined in Table 1.

CMRI was superior to TTE for identification of valve morphology, with a diagnostic, concordance of 94% versus 78% with TTE (κ for CMRI 0.85, $P < .001$; κ for TTE 0.45, $P = .007$). More specifically, test sensitivity for bicuspid aortic valve morphology was 80% with CMRI and just 60% with TTE. The accuracy of TTE morphologic assessment may be influenced by the severity of aortic valve calcification (moderate 87%; severe 70%), although this difference did not reach statistical significance ($P = .24$).

The correct identification of valve morphology has important clinical implications, in particular with regard to the associated aortopathy with bicuspid aortic valve disease, because operative intervention on the ascending aorta is recommended at a smaller threshold than with atherosclerotic disease.²

CMRI enables a comprehensive assessment of the valve, left ventricle, and aorta in patients with aortic stenosis, although routine clinical application for this purpose is not yet available because of the limitations of cost and availability of scanner time, in addition to standard contraindications for CMRI (rapid uncontrolled arrhythmia, metallic

implants, permanent pacemaker, claustrophobia). The alternative to CMRI is transesophageal echocardiography, which can accurately define aortic valve morphology³; however, this procedure is semi-invasive, requires intravenous sedation, and may present difficulties in complete evaluation of the thoracic aorta.⁴

Our findings replicate those of Malaisrie and colleagues,¹ and we propose that in selected individuals with aortic stenosis and dilated ascending aortas, CMRI increases the diagnostic certainty of anatomic assessment, thereby improving risk stratification and assisting with decisions regarding the timing of surgical intervention.

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