a New York Times article describing our work. Dr Anthony Atala has a much better claim to this milestone achievement.

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Reply to the Editor:

We thank Dr Macchiarini for commenting on our editorial published in the *Journal*, and we acknowledge his team's motivation and efforts to advance tracheal replacement.

In his response to our editorial, Paolo Macchiarini refers to several publications, thus undoubtedly convincing many readers of his views. However, in not one of these articles have mortality rates been published. Furthermore, we cannot follow his suggestion to rely on an unpublished article to obtain this information. Nor indeed can we refer to its content, although we have been in a position to read it. However, the unfortunate results after some of the treatments with "bioengineered" tracheas

have reached investigative journalists of *Science*¹ and other media.^{2,3}

More important, the purpose of our editorial was to inform the scientific community that regeneration of a viable trachea resulting from applying bone marrow cells to a decellularized or a synthetic scaffold in the absence of any blood supply is based on hope and belief and not on scientific evidence. None of the publications that Macchiarini cites in his response provide scientific evidence for his claims. We therefore strongly warn against further unethical human experimentation. The ongoing clinical trials will show whether or not this warning was justified.

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MODIFIABLE RISK FACTORS FOR ACUTE KIDNEY INJURY AFTER CORONARY ARTERY BYPASS GRAFTING

To the Editor:

We read with interest the recent article by Ng and colleagues¹ that identified modifiable risk factors for acute kidney injury (AKI) after coronary artery bypass grafting (CABG) in an Asian population. They showed that preoperative anemia and intraoperative lowest hematocrit were potentially modifiable risk factors independently associated with

postoperative AKI. In the design of this study, however, some important data regarding patient perioperative management, such as intraoperative hemodynamic changes, fluid volume, and use of vasoactive medicines, were evidently missing. It has been shown that intraoperative systolic blood pressure decrease relative to baseline is independently associated with postoperative AKI in patients undergoing CABG.² Furthermore, the combination of intraoperative hemodilution anemia and hypotension can synergistically act to increase the risk of AKI after cardiac surgery.³ Campbell and associates⁴ have demonstrated that fluid volume before cardiopulmonary bypass can contribute significantly to intraoperative hemodilution anemia and that restricting fluid volume before cardiopulmonary bypass can attenuate intraoperative hemodilution anemia and decrease the need for transfusion in patients undergoing CABG. In addition, perioperative inotropes, vasopressors, antiarrhythmics, and diuretics may also influence development of AKI after cardiac surgery. We therefore argue that optimizing perioperative management, such as intraoperative avoidance of excess fluid volume, hypotension, and renal arterial vasoconstrictive drugs, should be importantly modifiable factors in decreasing the occurrence of postoperative AKI in patients undergoing CABG. We believe that the results of this study would have been more informative had these factors been taken into account.

Ng and colleagues¹ did not mention the specific timing of postoperative creatinine measurements. It was also unclear whether continuous creatinine measurements were performed. It is therefore difficult to determine whether the cases of AKI reported in this study were due to intraoperative or postoperative factors. Although serum creatinine lags behind acute changes in renal function, AKI (defined by serum creatinine >10 mmol/L greater than normal values)

caused by intraoperative factors can be often detected between 1 and 3 days after surgery. Thereafter, the AKI is more likely to be attributable to postoperative factors, such as hemodynamic instability, anemia, transfusion, and so on. Westenbrink and coworkers⁵ have found that postoperative anemia is common after CABG, frequently persists for months, and is associated with impaired postoperative outcomes. We therefore emphasize that efforts to avoid the modifiable risk factors for AKI should be continued in the postoperative period to prevent new AKI or aggravation of existing kidney injury by postoperative factors, especially for patients who are at high risk for AKI.

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Reply to the Editor:

We thank Xue and colleagues for their interest in our publication, in which we showed the potential modifiable risk factors of acute kidney injury (AKI) after coronary artery bypass grafting.¹

The focus of this study was on studying the effects of 3 known modifiable risk factors, the lowest hematocrit during cardiopulmonary bypass (CPB), preoperative anemia, and intraoperative red blood cell transfusion, on postoperative AKI in our Asian patient population with smaller average body sized. As such, we did not look in this study specifically at the effects of intraoperative hemodynamic changes and their potentiation of hemodilutional anemia to result in postoperative AKI. The intraoperative systolic blood pressure was typically maintained within a tight range of 100 to 130 mm Hg, however, it is likely that a greater decrease in systolic blood pressure would be present in hypertensive patients. We also showed a history of hypertension to be an independent risk factor for AKI,¹ albeit an unmodifiable factor.

We are cognizant that liberal pre-CPB crystalloid infusion may result in hemodilution, especially for patients with smaller body size. Although the pre-CPB crystalloid infusion volume was not recorded, it was standard practice to give no more than 1000 mL of crystalloid before CPB.

The influences on AKI of perioperative medications, such as diuretics, inotropes, statins and antiarrhythmics, were studied. Of these, only loop diuretics were significantly associated with AKI in the univariate analysis presented in our article.¹ None of the medications were independently associated with AKI in the multivariate analysis.

In our study, postoperative creatinine measurements were done routinely in the intensive care unit in accordance

with institutional protocol. Continuous creatinine measurements were not done. The peak serum creatinine was the highest creatinine value obtained within the first 3 postoperative days and was used to calculate against the preoperative serum creatinine to determine whether a patient had postoperative AKI. AKI was defined according to the Acute Kidney Injury Network (AKIN) stage 1 criteria in this study.

To compare postoperative AKI incidence with other study cohorts, we had to use a uniform and standard classification of AKI. Numerous articles have used either the RIFLE (Risk, Injury, Failure, Loss of function, and End-stage renal disease) or AKIN criteria to define AKI. We chose the AKIN criteria because they account for smaller changes in serum creatinine, which is shown to be associated with adverse outcomes such as mortality.² Moreover, the AKIN criteria use a shorter time frame of 48 hours to assess renal function than the RIFLE criteria, which has a 7-day window period for AKI diagnosis.³

We found that not only was postoperative anemia associated with postoperative AKI, it was independently associated with the persistence of AKI up until hospital discharge (unpublished data). We therefore agree that strategies to improve postoperative anemia can reduce the persistence of AKI and prevent the subsequent development of chronic kidney disease in cardiac surgical patients.

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