Discussion

Dr Richard G. Ohye (Ann Arbor, Mich). Congratulations, Dr Caputo and colleagues, for completing this trial.

I have 2 questions. As background, I think, the majority of us either do use or would feel very comfortable using normothermia in these straightforward operations with short or limited bypass times. What is the applicability to other cases that are more complex or that have longer bypass times? How may your data be applicable to neonates and more complex operations?

What was the reason for excluding neonates? Do you think that there is anything unique in their anatomy or physiology that may make these data applicable or not applicable?

Similarly, for more complex operations with longer bypass times, did you look at interactions between with bypass time and your outcomes that may show a greater or lesser effect at longer bypass times? It is those more complex operations in which these data may be more applicable.

My second question relates to your graphs, which consistently show a suggestion of a benefit for normothermia, although not statistically significant. Are you willing to speculate that normothermia might not only be worse, but might be beneficial compared with moderate hypothermia?

Dr Caputo. The reason we excluded neonates to start with was that, as in many other units, we were using hypothermia routinely, and to start the trial, we decided that for neonates we were not comfortable using normothermia.

The trial actually is still ongoing, because the second part of this trial will look at clinical outcomes, and the sample size for that is around 300 patients. For that we are excluding only patients who require hypothermic circulatory arrest. For example, we are now doing switches with normothermia for sure.

In terms of the effect of CPB time on these markers, we did not look specifically at the relationship and it is probably worthwhile doing that.

Dr Ohye. Are you willing to commit that normothermia may actually be beneficial compared with hypothermia?

Dr Caputo. Personally, I feel much more comfortable with normothermia, because I really believe that cooling and rewarming are actually detrimental for several organs, and I think the kidney is one of them.

Dr Constantine Mavroudis (Cleveland, Ohio). I wonder about the rate of myocardial rewarming during cardioplegic arrest during normothermic CPB caused by collateral flow or organ proximity to the heart. Do you plan to use myocardial temperature measurements in the future? In addition, in retrospect, did you notice with your normothermic group that the cardioplegia administration did not last as long as determined by immersgence of electrical activity? Was there evidence of myocardial dysfunction after the operation? I think most people would use hypothermia not only for flow reasons but also to protect against myocardial rewarming. What are your thoughts about these issues?

Dr Caputo. Yes, we did look at the heart, and this was actually published a couple years ago. When we looked at markers of ischemia–reperfusion injury and reoxygenation injury in these 2 groups, we noticed that the normothermic group had less, for example, troponin I or 8–isoprostane release. Again, we do not believe that there are detrimental effects on the heart. On the contrary, in terms of reoxygenation injury, we might believe that normothermic CPB was beneficial.

In the same study we did evaluate the inflammatory response of the 2 techniques, and there was no difference. I am pretty confident that normothermia is safe for the heart. In fact, there is now evidence from groups in Paris using warm plegia, even though these are retrospective analyses, but they achieve quite good outcomes.
Second, was this study adequately powered and are we sure this is not just a statistical type II error, since you found no difference in many of your outcome measures?

Dr Caputo. We did not use modified ultrafiltration in these patients because they were not neonates. Normally we tend to use modified ultrafiltration in patients weighing below 5 kg, so they did not receive ultrafiltration. Also, we measured the hematocrit of all these patients.

Dr Karamlou. Thus even if you were not using modified ultrafiltration, what was the perfusion strategy in terms of using filtration during the bypass times?

Dr Caputo. These patients specifically were not subjected to filtration during bypass, and the hematocrit was the same at all the time points for the 2 groups. We did measure the hematocrit levels.

Also, the renal function was actually in the urine, so the main markers are expression of the glomerular damage and tubular damage in the urine according to the glomerular filtration rate. That is the reason we looked at the ratio between the markers and the creatinine in the urine.

Please remind me of the second question.

Dr Karamlou. The second question was about power.

Dr Caputo. Yes, the power for these markers was based on our previous experience, and the sample size calculation was done on the area under the curve of these markers previously measured in similar studies. Thirty patients for each group was power enough to detect a difference there.

Dr Mark H. D. Danton (Glasgow, United Kingdom). Did you have any patients who were cyanotic in this group? One could consider that if there were cyanotic patients with hypothermia, the collateral flow may be increased as the systemic vasoconstriction takes place with hypothermia. Therefore, you may have a difference, you may have better perfusion to the kidneys and the end organs with normothermic bypass with cyanotic patients.

Dr Caputo. Yes, this is possible. Unfortunately, in this series, there are very few cyanotic patients. The reason is that this was clashing with another trial in which we were particularly studying cyanotic patients and reoxygenation injuries. So unfortunately, I cannot answer that question, but it is something we will look at in the future, specifically targeting cyanotic patients.

Dr Emile A. Bacha (New York, NY). What was the temperature of your cardioplegia?

Dr Caputo. It was cold blood cardioplegia in this series, so 4°C.

Dr Bacha. At 4°C?

Dr Caputo. Yes, standard.

Dr Bacha. What kind of flows were you running?

Dr Caputo. These patients were at 2.5 L.

Dr Bacha. I assume the same flows in both groups.

Dr Caputo. Yes.