Response to Letter Regarding Article, “Donor Pretreatment With Hypertonic Saline Attenuates Primary Allograft Dysfunction: A Pilot Study in a Porcine Model”

We thank Drs Deutsch and Kaczmarek for their careful review of our article.1 As they note, we observed enhanced ventricular recovery in addition to preserved coronary artery vasomotor function with donor pretreatment with hypertonic saline in a porcine heart transplant model. They postulate that a mechanism to explain our positive results is the prevention of intracellular Ca2+ accumulation induced by extracellular hypernatremia. Furthermore, they present the results of 2 retrospective studies2,3 that examined the correlation between donor serum sodium levels immediately before organ procurement and primary graft failure and note that the lowest incidence of primary graft failure occurred with the most severely hypernatremic donors, although this did not reach statistical significance.

Although we did not specifically measure intracellular Ca2+ levels in our study, we agree with Deutsch and Kaczmarek’s suggestion that the prevention of intracellular Ca2+ accumulation likely contributes to the improved preservation of ventricular function that we observed in our study. In our article, we cited work by Kusuoka and associates4 that demonstrated improved myocardial function after reperfusion with a hypernatremic solution. However, it is important to note that we did not induce hypernatremia in our recipient animals, nor did we reperfuse with hypernatremic blood. Our study only examined the effect of hypernatremia induced in the donor prior to organ procurement. As we discussed in our article, high extracellular sodium concentrations result in the hyperpolarization of the plasma membrane, leading to a forward mode of the Na+/Ca2+ exchange channel, which prevents accumulation of Ca2+ accumulation. The reduction of cytoplasmic Ca2+ levels, as the work by Harada and associates5 suggests, preserves Ca2+ responsiveness of the myocardial contractile elements. Thus, we believe that hypernatremia in the donor before organ procurement not only directly prevents the accumulation of Ca2+, primarily during the ischemic period, but also and perhaps more importantly primes the myocardial contractile elements to have a preserved Ca2+ responsiveness during reperfusion. Furthermore, we believe that this is only 1 of many mechanisms that may be involved in mediating the beneficial effects of hypertonic saline observed in our study.

The retrospective studies that Deutsch and Kaczmarek cite,2,3 and particularly their multicenter experience,2 provide some reassurance that donor hypernatremia in and of itself does not negatively correlate with primary cardiac allograft failure. However, given that they did not demonstrate a statistically significant difference in primary graft failure among the 4 quartiles of patients in their study, we would caution against suggesting that hypernatremia is protective against primary graft failure on the basis of their retrospective observations. Furthermore, correlation between donor hypernatremia and a reduced incidence of primary graft failure does not necessarily imply a causative effect of hypernatremia. Organ donor brain death is associated with many pathophysiological events other than hypernatremia, some of which may directly correlate with hypernatremia. Our study in a porcine non–brain-dead organ donor model suggests a direct protective effect of hypertonic saline–induced hypernatremia on posttransplantation myocardial function; however, we cannot exclude the possibility that the potentially protective effect of hypernatremia that occurs after brain death may be modified by other events that occur during brain death. Clearly, as Deutsch and Kaczmarek suggest, clinical studies investigating the posttransplantation effect of donor hypertonic saline administration are required to determine whether this simple strategy confers clinically relevant benefits.

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Disclosures
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