See Article page 128.

Commentary: Primary graft dysfunction is leaving us curiouser and curiouser

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CENTRAL MESSAGE

PGD after heart transplant is persistent and mysterious. The origins and treatments are not clear and this review summarizes the current state and highlights what we still do not understand.

Despite 50 years of clinical heart transplantation, very little is known about primary graft dysfunction (PGD). Few phenomena bring as much dread, exhaustion, and frustration to normally resilient heart surgeons. The current review by D'Alessandro and colleagues[1] at the Massachusetts General Hospital nicely summarizes our current state. This comprehensive review highlights critical and problematic aspects of PGD. It also reminds us that much work remains to be done on this problem. Although we have a sense for predictors of PGD, we are routinely surprised by seemingly high-quality hearts that fail after implantation. The most important question that remains unanswered is: What exactly is it? The hearts looked great in the donor, why don't they work after implant? Why do some hearts with really long ischemic times or older donors work fine? Current guidelines divide PGD by left and right ventricle with graded severity. However, this definition is largely qualitative and hardly biologic. If it is just ischemia–reperfusion injury, then why haven't we found a pharmaceutical solution? Many of the pathways have been well described for decades. Equally frustrating is the limited treatment options. Essentially all roads lead to temporary extracorporeal circulation, and whereas an elegant solution in the middle of the night, the outcomes remain sobering and poor. The long-term consequences among survivors are even less clear.

PGD occurs in a minority of patients and yet it haunts heart transplantation. Decisions on donors are primarily made with the conscious and unconscious biases surrounding PGD risk. Stable recipients drive teams to avoid using donors for fear of PGD and the moral agony of hurting that patient waiting at home. The current allocation scheme has deprioritized left ventricular assist devices in part due to the outstanding durability of modern devices, but also because heart transplant is not without real risk of death. This pernicious uncertainty grips even the most fearless transplant team.

The current review is in many ways a call to action for our field. First, we need a better system to identify PGD to allow for prognosis and desperately needed management strategies. Biomarkers, lactate kinetics, or even echocardiograph-derived parameters readily available in the operating room would allow early institution of mechanical support. Second, a best practice on how to protect a recovering PGD heart. Similar to protective lung ventilation, cardioprotective support strategies are needed so teams can have better expectations on recovery duration and trajectory. Finally, novel therapeutic programs are needed to mediate the injury and prevent long-term consequences. PGD feels like Alice's trip down the rabbit hole. It's time to end the fall and take a hard stare into the looking glass.

Reference

1. Hull TD, Crowley JC, Villavicencio MA, D'Alessandro DA. Primary graft dysfunction in heart transplantation: how to recognize it, when to institute extracorporeal membrane oxygenation, and outcomes. *J Thorac Cardiovasc Surg Open*. 2021;8:128-33.

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