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INVITED COMMENTARY

Pregnancy after heart transplant: not for the faint of heart

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Solid organ transplantation has evolved significantly in the last 50 years. When heart transplantation began, patient survival was scarcely past a year [1], and the question of pregnancy for female heart transplant patients was not a significant consideration. Now, since the era of cyclosporine and conventional triple-drug therapy it is important to anticipate that women of childbearing age may desire to become pregnant. As the survival post-transplant for heart patients is an average of 10–12 years (with some surviving 20 years), this is not an unreasonable notion [2].

One of the major issues is the risk of teratogenicity as transplant recipients are usually on a combination of immunosuppressive agents, and almost all are considered to have teratogenic potential. As no one site has a large number of female post-transplant patients, particularly with pregnancies, registries have been developed to combine data across centers. The largest registry is the National Transplantation Pregnancy Registry, which carefully tracks outcomes of transplanted mothers and their offspring [3,4]. There is general consensus that mycophenolate mofetil is teratogenic, particularly in the first trimester and its use is associated with an increased risk of miscarriage as well as birth defects [5,6]. Calcineurin inhibitors seem to be reasonably well tolerated although it is possible that they contribute to the increased risk of maternal hypertension and pre-eclampsia.

Dagher and colleagues from the Montreal Heart Institute add to the current literature with a province-wide analysis of pregnancies in heart transplant patients in Quebec, Canada [7]. Similar to other authors, they found that pregnancy itself was safe for the mother at least during gestation, with uncommon rejection, and no deaths, but a slight worsening of renal function, which was related to higher calcineurin doses later in the pregnancy. They also noted higher incidence of preterm delivery and pre-eclampsia as compared with the Canadian incidence of this complication. Importantly, they reported on planned pregnancies (PP) versus unplanned pregnancies (UPP), which has not been performed in prior studies of heart transplant patients. They identified that UPP had a worse outcome than PP, which may be due to mycophenolate mofetil, use of statin drugs, or the fact that the UPP were in patients who smoked tobacco, used illicit drugs, or both. It is likely that the unplanned status was a marker of overall noncompliance with care, as the patients were instructed to discuss plans for pregnancy to allow a concerted approach to management, prior to conception, and through delivery.

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Another important aspect of care is the immunosuppressive regimen to use for a patient with pregnancy. As noted, mycophenolate mofetil should be avoided and could be switched for azathioprine. However, half of the patients in this study were on tacrolimus monotherapy, which was continued following delivery. Our group has reported on the utility of tacrolimus monotherapy [8], and we have had two patients with three deliveries while maintained on such a regimen. Clearly, this approach is most appropriate for selected patients who have not experienced significant rejection and are compliant with single-agent therapy. Tacrolimus monotherapy has been extensively studied in liver transplantation as well, where it appears to be a reasonable choice [9].

The authors note 'Of the 18 pregnancies, 72.2% were live births (UPP = 60% vs. PP = 87.5%, P = NS). Elective and spontaneous abortions occurred in 27.8% (UPP = 40% vs. PP = 12.5%, P = NS), between 5–7 gestational weeks'. While statistical significance is not met, due to small numbers of patients and gestations, clearly even in PP with compliant patients the risk of untoward outcomes is significant. We do not know which heart transplant recipients had heritable conditions which may have predisposed to fetal loss. Moreover, as women of childbearing age are less likely to have ischemic cardiomyopathy, it is likely that there may be a genetic basis for some of the 'dilated cardiomyopathies' in these patients. Considering genetic counseling and the possibility of offspring having a similar cardiomyopathy must be considered.

The study also highlights one of the other sad realities of cardiac transplantation, which is the finite lifespan of the transplant recipient. Three of the eight patients who had a child died within a mean of 3.9 years (2.6–5.4 years) following the birth. The children were 5.8 (2.6–11.8) years old at the time of their mother's death. Ultimately, deciding to have a child is the choice of the parents, but reports such as Dagher *et al.* provide data to facilitate rational decisions. The 'fairy tale' of life happily ever after following a heart transplant is exceedingly rare, and while some patients live many years following transplant, they are the minority. Certainly, those patients who are exceedingly compliant and partner with their physicians and care team are most likely to enjoy a long life, and perhaps be deemed suitable candidates for re-transplantation if the eventual need arises.

In summary, 50 years after its inception, heart transplantation has saved many lives and allowed patients with a terminal illness to have many more years of life. The desire to have children is unquestioned, but the path forward is fraught with peril. We are fortunate that we have increasing data to allow patients and their families to make choices guided by evidence rather than emotion alone.

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