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Society for Maternal-Fetal Medicine Consult Series #66: Prepregnancy evaluation and pregnancy management of patients with solid organ transplants

Society for Maternal-Fetal Medicine (SMFM); Roxanna A. Irani, MD, PhD; Lisa A. Coscia, RN, BSN, CCTC; Eugene Chang, MD; and Justin R. Lappen, MD; SMFM Publications Committee

The rate of solid organ transplant in reproductive-aged patients has increased in the past 3 decades. Concurrently, the range of medical immunosuppressive agents has increased, making it safer for reproductive-aged individuals who have received transplants to attempt and continue a pregnancy. In this Consult, we review the general considerations and contemporary approach to medical and obstetrical management of pregnant solid organ transplant recipients, discuss the perinatal outcomes and incidence of graft rejection specific to the most common types of organ transplants, and provide management recommendations based on the available evidence. The following are Society for Maternal-Fetal Medicine recommendations: (1) we recommend that all solid organ transplant recipients capable of pregnancy be offered prepregnancy counseling as part of the pretransplant evaluation and before any posttransplant pregnancy (Best Practice); (2) we recommend deferring pregnancy for at least 1 year (except for lung transplant recipients in which case a 2-year deferral is recommended) following solid organ transplant or any episode of acute cellular rejection (GRADE 1B); (3) we recommend that solid organ transplant recipients have stable allograft function and optimal control of chronic medical comorbidities before attempting pregnancy (GRADE 1B); (4) we recommend that solid organ transplant recipients of reproductive age use highly effective contraception when on mycophenolate or other immunosuppressive agents with known teratogenic risk (GRADE 1A); (5) we recommend that solid organ transplant recipients contemplating pregnancy transition to an appropriate immunosuppressive regimen before attempting pregnancy to establish stable medication dosing and allograft function (GRADE 1C); (6) we recommend close monitoring of serum drug levels during pregnancy and the postpartum period to guide immunosuppressive therapy dosing (GRADE 1C); (7) we recommend that solid organ transplant recipients who are pregnant or contemplating pregnancy receive all indicated vaccinations before and during pregnancy (GRADE 1C); (8) given the risk of fetal and neonatal sequelae secondary to cytomegalovirus infection in pregnancy, we suggest that solid organ transplant recipients ideally complete any indicated antiviral prophylaxis or treatment before pursuing pregnancy (GRADE 2B); (9) we recommend daily low-dose aspirin prophylaxis to reduce the risk for preeclampsia in pregnant solid organ transplant recipients and to reduce the risk for renal allograft failure in renal transplant recipients (GRADE 1C); (10) as for all pregnant people, we recommend that pregnant solid organ transplant recipients have access to mental health specialists and receive screening for depression during pregnancy and the postpartum period (Best Practice); (11) because of the increased incidence of fetal growth restriction and common coexisting medical morbidities, we recommend serial assessment of fetal growth every 4 to 6 weeks throughout gestation after the anatomic survey (GRADE 1C); (12) we suggest antenatal surveillance from 32 weeks of gestation unless other fetal or maternal factors are identified in which case initiation of surveillance at an earlier gestational age is indicated (GRADE 2C); (13) we recommend that renal function be assessed before pregnancy or in early pregnancy in all solid organ transplant recipients (kidney and non-kidney) (GRADE 1C); (14) we suggest individualized delivery timing for pregnant solid organ transplant recipients and to consider delivery at between 37+0/7 and 39+6/7 weeks of gestation; in the absence of other indications, we suggest delivery by 39+6/7 weeks gestation for pregnant solid organ transplant recipients (GRADE 2B); (15) given that a trial of labor is associated with a high success rate and lower neonatal morbidity without increasing maternal morbidity or compromising graft survival, we recommend that cesarean delivery be reserved for medical obstetrical indications in solid organ transplant recipients (GRADE 1C); (16) we recommend that blood pressure targets in pregnant renal transplant recipients with chronic hypertension follow guidelines for nonpregnant recipients with a target blood pressure of $\leq$130/80 mm Hg (GRADE 1C); (17) we recommend monthly urine cultures to screen for asymptomatic bacteriuria with treatment if positive to protect the graft in pregnant renal transplant recipients (GRADE 1C); (18) we recommend that pregnancies in pancreas-kidney transplant recipients be managed in a similar way as those of renal transplant recipients alone (GRADE 1C); (19) we recommend characterizing the underlying condition that led to liver transplantation and assessing baseline renal function in pregnant liver transplant recipients. (GRADE 1C); (20) because of the cardiovascular demand of pregnancy and the unique physiological implications of cardiac transplantation, we recommend that pregnant heart transplant recipients receive multidisciplinary care with cardiology, cardiac and/or obstetrical anesthesiology, and maternal-fetal medicine specialists (Best Practice); and (21) we recommend careful delivery planning to minimize hemodynamic stress (including considering operative vaginal delivery to minimize Valsalva) and suggest continuous intrapartum or intraoperative electrocardiographic monitoring for heart transplant recipients (GRADE 1C).

Key words: allograft function, cellular rejection, immunosuppressive therapy, pregnancy outcomes, solid organ transplant

Introduction

Patients with chronic end-organ dysfunction, such as end-stage liver and kidney disease, often experience secondary amenorrhea and infertility.[1,2] However, within a year of successful transplant, most patients have restoration of their menstrual cycles and ovulate more regularly. In addition, according to the United States Organ Procurement and Transplantation Network, the rate of solid organ transplant among reproductive-aged patients has increased in the past 3 decades.[3] In 2022 in the United States, approximately 16,000 women underwent organ transplant, 35% of whom were of reproductive age.[4]

Previously, it was thought that patients with transplants should not become pregnant because the risks, especially for hypertensive disorders of pregnancy and graft loss, were too high. As the range of medical immunosuppressive agents has increased, it has become safer for reproductive-aged individuals who have received transplants to attempt and continue a pregnancy. Pregnancy in solid organ transplant recipients is no longer considered an absolute contraindication, although it is not without risk. Patients with transplants should have a thorough and detailed evaluation and counseling about the risks related to pregnancy to make informed decisions and have their wishes regarding childbearing supported. This should include encouragement for pregnancy when appropriate and support and access to abortion services when the patient deems the risks or consequences of pregnancy too great to continue.

These facts underscore the importance of prepregnancy counseling and contraception management, which should be introduced during the pretransplant evaluation and followed through the posttransplant process.[5,6] Careful antepartum monitoring by a knowledgeable interdisciplinary team of maternal-fetal medicine subspecialists, transplant experts, and adequate social support services is recommended. The purpose of this Consult is to review the general considerations and contemporary approach to medical and obstetrical management of pregnant recipients of solid organ transplants, to discuss the perinatal outcomes and incidence of graft rejection specific to the most common types of organ transplants, and to provide management recommendations based on the available evidence.

Data sources for posttransplant pregnancy outcomes: the Transplant Pregnancy Registry International

The Transplant Pregnancy Registry International (TPRI), formerly the National Transplantation Pregnancy Registry (NTPR), was established in 1991 to study pregnancy outcomes after transplantation. The TPRI is one of the largest repositories of pregnancy outcomes in recipients of solid organ transplants worldwide and has amassed outcome data for more than 3500 pregnancies.[7] The TPRI contacts subjects every 2 years to assess the health of the patient, their children, and their allograft. Although the TPRI and registry data have improved the understanding of pregnancy outcomes after solid organ transplantation, few prospective studies have been published.

General considerations for pregnancy planning for patients who have undergone solid organ transplant

What is the role of prepregnancy counseling for patients contemplating pregnancy after solid organ transplant?

As recommended by the American Society of Transplantation consensus conference on reproductive issues and transplantation, counseling regarding pregnancy-associated risks should be introduced during the pretransplant evaluation and should be continued throughout posttransplant care.[8] This counseling should involve a discussion of fetal and maternal risks and pregnancy outcomes after transplant, including the risk of obstetrical complications and the impact of pregnancy on allograft function. The recommended timing of pregnancy after transplantation should be discussed, and contraceptive counseling and management are recommended to facilitate appropriate pregnancy timing and reduce the risks of adverse pregnancy outcomes or rejection, which are increased when pregnancy occurs within the first year after transplantation.[9] Prepregnancy and pregnancy management recommendations should be specific to the solid organ that a patient has received, and tailored guidelines for kidney, liver, heart, and lung transplant recipients have been published.[10–12] Patients with transplants who are pregnant or considering pregnancy should undergo multidisciplinary evaluation with transplant surgery, organ-specific medical subspecialists (such as nephrology, hepatology, and cardiology), and maternal-fetal medicine subspecialists. A suggested approach to the baseline assessment before pregnancy is outlined in Box. **We recommend that all individuals with a solid organ transplant who are capable of pregnancy be offered prepregnancy counseling as part of the pretransplant evaluation and before any posttransplant pregnancy (Best Practice).**

What is the recommended timing of pregnancy after solid organ transplantation?

Although the optimal timing of conception after solid organ transplant remains uncertain, the American Society of Transplantation consensus report recommends deferring pregnancy for at least 1 year following solid organ transplant.[8] Several cohort studies in solid organ transplant recipients support delaying pregnancy for 1 year after transplant to achieve stable graft function and to improve obstetrical and transplant outcomes. A study from the United Kingdom demonstrated a higher rate of acute cellular rejection in patients with liver transplants who became pregnant within 1 year when compared with those who

Corresponding author: Society for Maternal-Fetal Medicine (SMFM) Publications Committee. pubs@smfm.org

BOX

Baseline evaluation before pregnancy in individuals with a solid organ transplant

- Multidisciplinary consultation with transplant surgery, organ-specific medical subspecialists (nephrology, hepatology, cardiology), maternal-fetal medicine, and other medical subspecialists based on individual patient requirements and risk assessment
- Posttransplant history to identify pertinent clinical events in preceding year, including episodes of acute rejection or potentially fetotoxic infections
- Comprehensive medical history, elucidating medical comorbidities and indication for solid organ transplant
- Evaluation of medications including maintenance immunosuppressive regimen to assess stability and identify teratogenic risk
- Assessment of vaccination status with provision of indicated vaccinations
- Blood pressure and vital sign assessment and complete physical examination
- Baseline laboratory evaluation and assessment of allograft function (complete metabolic panel, complete blood count, hemoglobin A1c, urine protein/creatinine ratio, echocardiography, EKG)
- Type and screen because of risk for posttransplant red blood cell alloimmunization
- Evaluation of psychosocial status and involvement of psychological and social support services if needed

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became pregnant beyond 1 year of transplant (46% vs 11%; $P=.001$).[13] In addition to cohort studies, meta-analyses have demonstrated improved maternal and neonatal outcomes and a decreased incidence of obstetrical complications (including preterm birth, low birthweight, and hypertensive disorders of pregnancy) among individuals with a liver or kidney transplant when pregnancy was deferred for at least 1 year following transplant.[14,15] Although there are no published reports studying transplant-to-pregnancy intervals and obstetrical outcomes among heart transplant recipients, the International Society for Heart and Lung Transplantation recommends waiting at least a year from transplant to pregnancy.[11] Notably, given the increased incidence of graft rejection with long-term graft dysfunction and obstetrical complications among individuals with a lung transplant when compared with other solid organ transplant recipients, those with lung transplants are typically counseled to defer pregnancy for 2 years after transplant.[12,16]

In addition to transplant-to-pregnancy interval, other favorable clinical factors should be considered in guiding the timing of pregnancy following solid organ transplant, including no evidence of graft rejection in the past year; adequate, stable transplant function (eg, serum creatinine <1.5 mg/dL, no or minimal proteinuria, stable electrocardiogram [EKG] or echocardiogram); and no acute infections that might impact the fetus (eg, cytomegalovirus [CMV]). Other mitigating circumstances should be taken into consideration, including etiology of the original disease leading to transplant; chronic graft dysfunction; maternal age; medical comorbidities including hypertension, diabetes, and obesity; native kidney function for nonkidney solid organ transplant recipients; inherited diseases and other genetic considerations; and viral status. Prepregnancy allograft function is the critical factor that should guide counseling for solid organ transplant recipients who are contemplating pregnancy. Recipients should be advised of the potential for increased postpartum graft loss when the serum analytes or other biomarkers of adequate transplant function (eg, serum creatinine) are elevated before pregnancy.[8,11,17-20] **We recommend deferring pregnancy for at least 1 year (except for individuals with a lung transplant in which case deferral for 2 years is recommended) following solid organ transplant or any episode of acute cellular rejection (GRADE 1B). We recommend that individuals with a solid organ transplant have stable allograft function and optimal control of chronic medical comorbidities before attempting pregnancy (GRADE 1B).**

How should immunosuppressive therapy be managed before pregnancy and during pregnancy and lactation for solid organ transplant recipients?

Immunosuppression is vital to the health of the transplanted organ and the patient and must be continued throughout pregnancy to maintain adequate graft function and prevent rejection. Mainstay immunosuppressive therapy includes calcineurin inhibitors (cyclosporine, tacrolimus), antiproliferative agents (mycophenolate mofetil, azathioprine, sirolimus), and corticosteroids.[21] For kidney recipients, the most common regimens at discharge are tacrolimus and mycophenolate with or without oral prednisone.[22] Although all immunosuppressive therapies have maternal and fetal risks, multiple agents are considered safe to use during pregnancy and lactation. Commonly used immunosuppressive agents in individuals with a solid organ transplant, including implications for pregnancy and lactation, are listed in Table 1. This table does not include medications used to treat acute rejection episodes and those used in the immediate postoperative period to prevent rejection because their use around pregnancy is uncommon.[23]

Because most transplant recipients will leave the hospital on a mycophenolate regimen, pregnancy planning is particularly important because mycophenolate is a known teratogen. Exposure to mycophenolate increases the risk of embryopathy and early pregnancy loss and decreases the rate of live birth when compared to pregnancies without exposure.[24-29] Transplant recipients of reproductive age should be counseled regarding the use of effective, long-term contraception to prevent pregnancy while taking mycophenolate products. In addition, mycophenolate

TABLE 1
Common immunosuppressive therapies and considerations for pregnancy and lactation[21]

Agent or class	Mechanism of action	Adverse effects	Use in pregnancy	Use in lactation
Mycophenolate mofetil and mycophenolic acid products (MPA)[24-29]	- Inhibitor of purine synthesis through inosine-5'-monophosphate dehydrogenase, which inhibits T-cell and B-cell proliferation	- First trimester spontaneous abortion (up to 50%) - Teratogenicity • Facial malformations (cleft lip/palate, micrognathia, hypertelorism, absent/abnormal external/middle ear, coloboma, microphthalmos • Digit malformations (brachydactyly, polydactyly, syndactyly) • Cardiac abnormalities (atrial and ventricular septal defects) • Esophageal atresia • CNS malformations (neural tube defects)	- Contraindicated - Discontinue 6 wk prior to pregnancy (long half-life 18—24 h)	- Generally discouraged, minimal data
Corticosteroids[30-33]	- Multiple immunosuppressive effects mediated through gene transcription - Reduce inflammatory cytokine secretion - Inhibit activity of leukocytes, macrophages, T-cells	- Limited and conflicting data on risk of oral clefs - Limited fetal exposure due to metabolism by 11b-hydroxysteroid dehydrogenase - Dose-dependent steroid-related side effects including: glucose intolerance/gestational diabetes, hypertension, adrenal suppression, Cushingoid features, peptic ulcer disease, poor wound healing - Associated with PPROM and FGR	- Low risk	- Compatible
Azathioprine[34-36]	- Prodrug converted to 6-mercaptopurine, inhibits purine synthesis and blocks DNA replication - Inhibits T-cell and B-cell proliferation	- Existing data do not demonstrate increased risk of teratogenicity - Association with preterm birth and FGR	- Low risk	- Compatible
Calcineurin inhibitors • Cyclosporine[37] • Tacrolimus[38]	- Inhibit production and release of interleukin II - Inhibit T-cell activation	- Existing data do not demonstrate increased risk of teratogenicity - Association with preterm birth and FGR - Dose-related adverse effects include hypertension, hyperglycemia, acute kidney injury, electrolyte abnormalities, peripheral neuropathy, seizures - Levels affected by concurrent use of CYP450 inhibitors and inducers - Substantial alterations in drug levels in pregnancy (highly bound to albumin/erythrocytes)	- Low risk	- Compatible
T- and B-cell inhibitors • Sirolimus/Everolimus[39-41]	- Forms complex that inhibits intracellular protein kinase important to cell cycle progression - Inhibits T-cell activation and proliferation in response to cytokine stimulation, inhibits antibody production	- Limited conflicting data with some reports demonstrating increased risk for congenital malformations	- Not recommended - Discontinue 12 wk before pregnancy (long half-life, 57—63 h)	- Limited data, individualize
Selective T-cell inhibitor • Belatacept[42,43]	- Selective T-cell co-stimulation inhibitor, blocking interaction between T-cell and antigen presenting cells	- Limited data in pregnancy	- Limited data, individualize	- Limited data, individualize

CNS, central nervous system; *FGR*, fetal growth restriction; *PPROM*, preterm premature rupture of membranes.

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should be discontinued at least 6 weeks before pregnancy because of the long half-life of the metabolites.[19,44,45] **We recommend that reproductive-aged individuals with a solid organ transplant use highly effective contraception when on mycophenolate or other immunosuppressive agents with a known teratogenic risk (GRADE 1A).** Before a planned pregnancy, most experts recommend transitioning from mycophenolate to azathioprine, which has an appropriate safety profile in pregnancy. Compared with mycophenolate, pregnancies with exposure to azathioprine, calcineurin inhibitors, and low-dose corticosteroids have not demonstrated an increase in birth defects or miscarriages and these medications are generally considered safe during pregnancy.[23] **We recommend that an individual with solid organ transplant who is contemplating pregnancy transition to an appropriate immunosuppressive regimen before attempting pregnancy to establish stable medication dosing and allograft function. (GRADE 1C).**

During pregnancy, numerous physiological changes impact the pharmacokinetic and pharmacodynamic properties of medications, including immunosuppressive therapies.[46] These physiological changes (increased plasma volume and volume of distribution, changes in protein binding, increased hepatic activity of cytochrome P450 proteins, delayed gastric emptying with slower bowel transit, and increased estimated glomerular filtration rate [eGFR]) often lead to subtherapeutic immunosuppressive drug levels, and dose increases of 20% to 25% are common over the course of pregnancy.[47] Given that subtherapeutic immunosuppression increases the risk for allograft rejection, close monitoring of serum levels is recommended during pregnancy to guide immunosuppressive therapy dosing. An otherwise stable transplant recipient on immunosuppressive medications such as cyclosporine and tacrolimus should have serum levels assessed at minimum every 4 weeks throughout pregnancy, every 1 to 2 weeks after 32 weeks of gestation in preparation for delivery, and then within 1 week postpartum. However, the timing of serum drug monitoring can be individualized, and more frequent serum monitoring may be required in those with a history of nonadherence to therapy or subtherapeutic drug levels. Postpartum doses are often immediately lowered because of the restoration of renal function and drug metabolism even if the recipient chooses to breastfeed.[48] **We recommend close monitoring of serum drug levels during pregnancy and the postpartum period to guide immunosuppressive therapy dosing (GRADE 1C).**

In general, patients should not discontinue their maintenance immunosuppression while lactating. Breastfeeding should be encouraged for all patients who are stable on a regimen of calcineurin inhibitors, azathioprine, or corticosteroids.[49] For these medications, there is negligible neonatal exposure from breastmilk, which has been found to be less than the exposure in utero to the same medications.[50] Should a patient require mycophenolate postpartum, breastfeeding is generally discouraged although limited reports have demonstrated no adverse effects in breastfed infants exposed to this medication.[49,51,52] The TPRI has reported information on 6 patients who breastfed 7 infants up to 14 months while taking mycophenolate. There were no reported adverse reactions.[49] Given the limited but reassuring data, we support shared decision-making to address lactation in patients requiring mycophenolate. There are limited lactation data on the T- and B-cell inhibitors, so their continued use while breastfeeding is cautioned.

What is the approach to vaccinations for patients who have undergone solid organ transplant?

Given that vaccine responses are attenuated after transplantation because of immunosuppressive therapy, many transplant programs have adopted a systematic approach to pretransplant vaccination because this strategy optimizes protection against vaccine-preventable infection.[53] All patients with a solid organ transplant should be vaccinated against hepatitis A and B, pneumococcal disease, tetanus diphtheria pertussis (TDaP), polio, seasonal inactivated influenza and *Haemophilus influenzae* type B (Hib), human papillomavirus, measles-mumps-rubella, *Neisseria meningitides*, varicella-zoster virus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[54-56] The live-attenuated vaccines (nasal influenza, measles-mumps-rubella, oral polio, and varicella-zoster) are recommended before transplant but not afterward and are also avoided in pregnancy. Hepatitis A and B, seasonal influenza, pneumococcal, meningococcal, and SARS-CoV-2 vaccinations are safe during any trimester of pregnancy. The TDaP vaccine should be recommended between 27 and 36 weeks of gestation for neonatal protection. Although evidence supporting a serology-based approach to screening and revaccination of pregnant transplant recipients is limited, a strategy of universal screening to determine hepatitis B surface antibody status with vaccination of susceptible individuals in pregnancy may be cost effective.[57] **We recommend that individuals with a solid organ transplant who are pregnant or contemplating pregnancy receive all indicated vaccinations before and during pregnancy (GRADE 1C).**

What are infectious considerations for solid organ transplant recipients who ae planning pregnancy?

Because solid organ transplant recipients receive chronic immunosuppressive therapy, infectious disease screening is an important component of routine pretransplant care to identify and treat active infection before transplant and to guide the prevention and treatment of posttransplant infection.[58] This evaluation includes exposure and vaccination history, as well as serologic testing. Patients who become pregnant within the first year following a transplant are at the highest risk for developing infection or reactivation of latent infection, which may lead to perinatal transmission. In patients who are pregnant or planning pregnancy following solid organ transplant, the results of any transplant-related infectious disease screening and treatment should be evaluated

and should guide individualized counseling regarding maternal or fetal risks in pregnancy. Routine repeat screening is not recommended, and pregnant individuals with a solid organ transplant should receive standard prenatal infectious disease screening as a part of routine obstetrical care.

CMV is the most commonly diagnosed opportunistic infection among individuals with a solid organ transplant. Therefore, solid organ recipients and donors are screened for a history of CMV infection before a transplant.[59] Because of medical immunosuppression, transplant patients are at high risk for primary and nonprimary CMV infections, particularly in the first year following transplantation[60] Given that CMV is an important cause of morbidity and mortality following a solid organ transplant, consensus guidelines support antiviral prophylaxis or preemptive treatment for 3 to 6 months following a transplant.[59] If patients are also pregnant during a primary and, to a lesser extent, nonprimary CMV infection, then there is risk for vertical transmission and fetal sequelae (hearing loss, microcephaly, development delay, and perinatal morbidity).[61,62] Using ganciclovir, foscarnet, or cidofovir for the treatment of severe, end-organ CMV disease in immunocompromised patients has not demonstrated decreased perinatal transmission or improved outcomes, and there are limited data on the fetal risk.[44,63] High-quality data to guide the optimal duration and frequency of CMV monitoring and the timing of pregnancy after CMV infection are lacking. **Given the risk of fetal and neonatal sequelae secondary to CMV infection in pregnancy, we suggest that solid organ transplant recipients ideally complete any indicated antiviral prophylaxis or treatment before pursuing pregnancy (GRADE 2B).**

Most cohort analyses showed that the rates of neonatal infections in transplant recipients were not increased when compared with the general obstetrical population and that follow-up reports of the infants delivered to pregnant patients on immunosuppressive therapy are favorable overall.[64-66] In contrast, one study compared hospitalizations and antibiotic treatment in the first year of life between children of Danish kidney recipients exposed to maintenance immunosuppression in utero (n=124) and unexposed children (n=1231).[67] The authors found that the offspring of individuals with a kidney transplant had an increased risk for hospitalization for the treatment of infection during the first year of life when compared with nonexposed children, especially if they were delivered prematurely or had a low birthweight when compared with the unexposed cohort. The TPRI plans to conduct a long-term follow-up study of the children born to individuals with a solid organ transplant who were exposed to maintenance immunosuppressive therapy during pregnancy.

What long-term health risks does pregnancy hold for patients who have undergone solid organ transplant?

Transplant recipients have a decreased life expectancy because of higher risks of cancer, cardiovascular disease, and infection. There is variation in the life expectancy by organ transplanted. Recent United States data reflect that the 5-year posttransplant survival rates for females after kidney transplant is 79.5%, whereas for heart-lung recipients it is 59.0%.[16,68] However, based on several studies comparing transplant recipients who became pregnant with those who were never pregnant, long-term survival does not seem to be impacted by pregnancy as an independent risk factor.[17,69-71]

What is the risk of pregnancy to the allograft?

Pregnancy is associated with substantial physiological changes in cardiovascular (increased cardiac output, expanded blood volume, decreased systemic vascular resistance), renal (50% increase in GFR and reduction in serum creatinine), and hepatic function (decreased serum albumin and increased clotting factor production), which may impact graft function in individuals with a solid organ transplant. Notably, when individuals with a solid organ transplant become pregnant with stable graft function, the transplanted organ is more likely to maintain function throughout pregnancy with minimal adverse effects. However, if a person becomes pregnant with signs of chronic rejection or other markers of transplant dysfunction, further deterioration or graft loss is more likely to occur. Meta-analyses and large center reports have not demonstrated overall increases in graft loss or rejection during pregnancy.[14,15,72] Importantly, there should be a low threshold to investigate any deviation from baseline function with further laboratory tests or diagnostic imaging. In addition, in the setting of acute rejection, the risks of continuation of pregnancy should be balanced with the need to treat acute rejection (because treatment options are limited), and early delivery or even termination of pregnancy should be considered in the management of these patients as appropriate. Further discussion of organ-specific risks and considerations related to acute rejection are discussed below.

General approach to obstetrical management for individuals with a solid organ transplant

What are the fetal and maternal risks of pregnancy among individuals with a solid organ transplant?

The pregnancy-associated risks in transplant recipients by solid organ type are depicted in Tables 2 to 4 and the Figure with a comparison to the background rates of outcomes in the general obstetrical population when appropriate. The following sections provide additional details on the pertinent fetal and maternal outcomes that are increased in pregnant individuals with a solid organ transplant.

Hypertensive disorders

The rates of hypertension and preeclampsia among individuals with a solid organ transplant are significantly higher than the background prevalence of chronic hypertension (1.9%) and preeclampsia (6.5%) in the general

TABLE 2
Pregnancy outcomes among individuals with a solid organ transplant [7]

Organ	Recipients/pregnancies/ outcomes[a] (n/n/n)	Ectopic	IUFD	Elective Termination	Miscarriage	Live birth
Kidney	1251/2233/2318	1%	2%	4%	19%	75%
Liver	363/716/734	1%	1%	3%	23%	72%
Kidney-pancreas	71/131/139	1%	0%	4%	27%	68%
Heart	110/187/192	1%	1%	4%	26%	68%
Lung	41/54/56	2%	0%	9%	27%	63%

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IUFD, intrauterine fetal demise.

[a] Includes multifetal gestations (twins and triplets).

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obstetrical population (Table 3, Figure).[7,73,74] In recent meta-analyses of pregnant individuals with a liver transplant, the pooled incidences of any hypertensive disorders and preeclampsia were 18.2% and 12.8%, respectively.[75] However, publications by the TPRI and earlier meta-analyses of pregnant individuals with a liver transplant reported rates of hypertension and preeclampsia as high as 27.2% and 21.0%, respectively. Chronic hypertension is common after cardiac transplantation and is reported in 39% to 46% of pregnancies in individuals with a heart transplant.[15] Several large cohort analyses showed an increased incidence of preeclampsia in pregnancies in individuals with a heart transplant ranging from 11.8% to 27%, which may contribute to cardiac dysfunction, poor fetal and neonatal outcomes, and decreased long-term maternal survival postpartum.[7,17,70,76]

Notably, up to 50% to 80% of individuals with a kidney transplant have preexisting hypertension.[77] Therefore, it is not surprising that the most common obstetrical complications among individuals with a renal transplant are related to hypertensive disorders of pregnancy. Two large meta-analyses and other large cohort series of pregnancy outcomes in kidney recipients showed an overall incidence of preeclampsia of 21% to 29%.[14,78] This rate is consistent with the overall rate from the TPRI of 29% in kidney recipients and is approximately 6-fold higher than in the general obstetrical population.[14,78-81] The increased prevalence of hypertensive disorders of pregnancy may contribute to the risk of maternal and perinatal morbidity and mortality secondary to the sequelae of severe hypertension, fetal growth restriction, and medically indicated preterm birth. Although nonsteroidal anti-inflammatory drugs (NSAIDs) are typically avoided in individuals with kidney transplants, a retrospective study of 830 patients with a renal transplant who received low-dose aspirin (100 mg/day) demonstrated improved renal allograft function and allograft survival and no negative impact on kidney function.[82] A meta-analysis of 9 studies in which varying doses of aspirin were compared with no treatment similarly found a reduced risk fo allograft failure.[83] Therefore, the benefit of

TABLE 3
Maternal factors across individuals with a solid organ transplant[7]

Organ	Recipients/ pregnancies/ outcomes[a] (n/n/n)	Mean transplant to conception interval (y)	Unplanned pregnancy	Drug treated hypertension	Preeclampsia[b]	Insulin treated diabetes	Allograft rejection during pregnancy	Adequate graft function at last TPRI follow-up
Kidney	1251/2233/2318	5.4	30%	48%	29%	8%	3%	67%
Liver	363/716/734	8.9	36%	21%	21%	8%	5%	80%
Kidney-pancreas	71/131/139	4.4	36%	50%	34%	2%	5%	48%
Heart	110/187/192	7.7	37%	48%	27%	8%	8%	61%
Lung	41/54/56	4.1	54%	59%	15%	30%	13%	66%

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[a] Includes multifetal gestations (twins and triplets); [b] Collected from live births only.

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TABLE 4
Live birth outcomes across individuals with a solid organ transplant[7]

Organ	Recipients/ pregnancies/ outcomes[a] (n/n/n)	Live births, n (%)	Mean gestational age at delivery (wk)	Late-preterm delivery[b] (wk)	Mean birthweight (g)	Low birthweight	Neonatal deaths	Cesarean delivery
Kidney	1251/2233/2318	1735 (75)	35.8	37%	2555	42%	1%	51%
Liver	363/716/734	528 (72)	36.7	26%	2772	28%	1%	43%
Kidney-pancreas	71/131/139	94 (68)	34.1	51%	2142	62%	1%	70%
Heart	110/187/192	131 (68)	36.2	32%	2595	37%	0	45%
Lung	41/54/56	35 (63)	34.0	34%	2192	66%	9%	47%

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[a] Includes multifetal gestations (twins and triplets); [b] Delivery between 32 weeks 0 days to 36 weeks 6 days of gestation.

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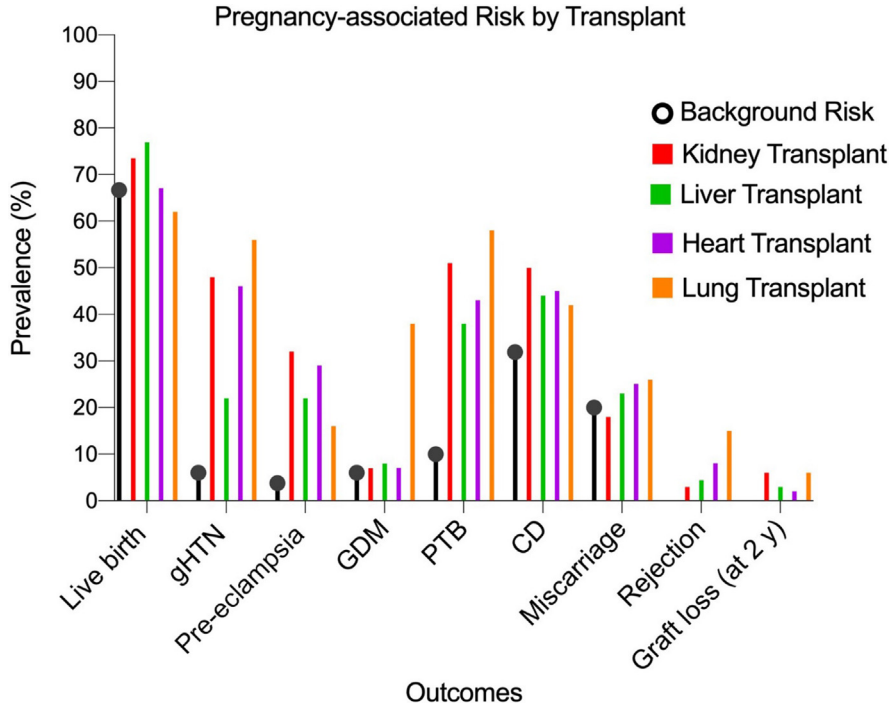
preeclampsia risk reduction exceeds the risk of using low-dose aspirin in individuals with a renal transplant. **We recommend daily low-dose aspirin prophylaxis to reduce the risk for preeclampsia in pregnant individuals with a solid organ transplant and to reduce the risk of renal allograft failure in renal transplant recipients (GRADE 1C).**[84,85]

Although preeclampsia is a known risk factor for future end-stage renal disease, in a multicenter international cohort of pregnancies after kidney transplantation, there was a transient drop in GFR with preeclampsia. However, this was not associated with a higher rate of long-term renal dysfunction or allograft loss.[86,87] Thus, expectant

FIGURE
Pregnancy outcomes and morbidity in solid organ transplant recipients[74]



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CD, cesarean delivery; *GDM*, gestational diabetes mellitus; *gHTN*, gestational hypertension; *PTB*, preterm birth.

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management of preeclampsia without severe features before term is appropriate.[87] There is, however, a lack of long-term data on the effects of preeclampsia on renal function in patients with a transplant, which limits guidance for those patients with severe preeclampsia.[88] In patients with early-onset severe preeclampsia, we suggest maintaining a lower threshold for delivery given the potential impact of severe preeclampsia on long-term allograft function.

Finally, acute rejection in individuals with a renal transplant can present with sudden worsening of hypertension, elevated serum creatinine, and increased proteinuria. These clinical features of acute renal allograft rejection may mirror preeclampsia, posing a diagnostic dilemma with important clinical implications. A recent case-control registry study demonstrated that pregnant individuals with a renal transplant complicated by acute allograft rejection more frequently presented with elevations in serum creatinine (73% vs 14%; $P<.001$), whereas preeclampsia was associated with significant increases in proteinuria from baseline ($P=.029$).[89] In a patient with a renal transplant with clinical findings suggestive of preeclampsia, prompt interdisciplinary assessment is critical to distinguish acute rejection from preeclampsia and to guide management decisions. Increased creatinine without worsening proteinuria should raise suspicion for rejection and, when appropriate, prompt kidney biopsy.[89]

Preterm birth, fetal growth restriction, and low birthweight

In general, the fetal outcomes among pregnant individuals with a solid organ transplant are favorable; however, fetal complications, including preterm birth, fetal growth restriction, and low birthweight, occur more frequently in this population than in the general obstetrical population and likely reflect complications related to hypertension (Tables 2 and 4, Figure).[7,14,15,78] Despite advances in immunosuppressive medical management and laboratory surveillance, preterm delivery continues to be extremely common in individuals with a solid organ transplant. Data from several cohort analyses showed a preterm birth rate among individuals with a kidney transplant of 37% to 52% with a mean gestational age at delivery of approximately 35 weeks of gestation.[7,18,78] A recent meta-analysis of 6712 pregnancies in 4174 individuals with a kidney transplant showed a preterm birth rate of 43.1% with a mean gestational age at delivery of 34.9 weeks.[78] Similarly, the rate of preterm birth is increased among individuals with a liver transplant with meta-analyses and cohort studies reporting rates of preterm birth ranging from 27% to 40% and a pooled gestational age at delivery of 36.7 weeks of gestation.[15,72,90-93] As reported for other individuals with a solid organ transplant, there is an increased incidence of preterm birth after a cardiac transplant with the rates in cohort studies ranging from 41% to 53.8%. The overall data suggest that the reported rates of preterm birth in individuals with a solid organ transplant are 4-fold higher than the background rate of preterm birth in the United States.[94] Although most studies in individuals with a solid organ transplant do not delineate the exact indications for preterm delivery (medically indicated or spontaneous preterm delivery), most authors postulate that medically indicated deliveries, particularly those related to hypertensive disorders, represent the most common etiology.

Individuals with a solid organ transplant also have increased risks for fetal growth restriction and low birthweight neonates when compared with the general obstetrical population.[95] The rate of fetal growth restriction in pregnant individuals with a renal transplant ranges from 20% to 30%, which is 2- to 3-fold higher than that in the general obstetrical population.[95-97] Several meta-analyses showed a mean birthweight of 2470 to 2555 g for neonates of individuals with a renal transplant, and the rate of low birthweight neonates among individuals with a liver transplant ranges from 28% to 41%.[7,18,78] Similarly, an increased incidence of low birthweight is consistently reported for the infants born to recipients of a cardiac transplant.[76] Given that prematurity and low birthweight are associated with increased risks for childhood morbidity and mortality and future cardiovascular disease, neurodevelopmental abnormalities, and other chronic health conditions, counseling regarding the short- and long-term risks of prematurity and fetal growth abnormalities should be discussed with individuals with a solid organ transplant during the pretransplant and prepregnancy periods and during the pregnancy.

Stillbirth and neonatal death

Overall, the pregnancy outcomes in individuals with a solid organ transplant are favorable with live birth rates and miscarriage rates similar to those in the general population (Tables 2 and 4).[7,15,91,92,98] However, published data demonstrate an increased risk for perinatal mortality in pregnancies after solid organ transplant. The rate of stillbirth among individuals with a solid organ transplant ranges from 1% to 5%, which is significantly higher than the background rate of approximately 6 per 1000 live births in the general obstetrical population.[7,14,78,99-101] In addition, the reported rates of neonatal mortality in some populations of recipients of a solid organ transplant are elevated above the background risk. For example, the rate of neonatal death among individuals with a kidney transplant ranges from 1.0% to 3.8% and may be as high as 9% among individuals with a lung transplant when compared with the national United States average of 0.4%.[7,78,102] Conversely, data on individuals with a liver or cardiac transplant have not demonstrated a substantially increased risk for neonatal death.[7,17,70,76,93] However, in the cardiac transplant population, this finding may reflect the small number of pregnancy outcomes published. Although the etiology of the increased risk for stillbirth and neonatal death in pregnancies of individuals with a solid organ transplant has not been definitively elucidated, the risk likely reflects the increased

risks related to preterm birth and prematurity, underlying maternal medical comorbidities (including disease flares of the underlying conditions that led to transplant), or pregnancy complications such as hypertensive disorders.

Psychological considerations

Patients who have undergone a transplant are often acutely aware of their overall health and graft status, contributing to increased rates of anxiety and depression.[103] Depression is associated with an increase in the risk for posttransplant mortality.[104] Pregnancy can contribute to increased anxiety about their health and potential loss of graft function. Psychosocial support should be offered early and often throughout a pregnancy so that patients have a framework of support during the antepartum and postpartum periods. An interdisciplinary approach that includes mental health specialists is an important consideration in the contemporary management of these complex patients. In addition, given the baseline prevalence of anxiety and depression, solid organ transplant recipients are likely at an increased risk for postpartum depression, and early screening for postpartum depression is recommended.[105] **As for all pregnant people, we recommend that pregnant individuals with a solid organ transplant have access to mental health specialists and receive screening for depression during pregnancy and the postpartum period (Best Practice).**

What is the recommended approach to antenatal fetal surveillance for individuals with a solid organ transplant during pregnancy?

Given the increased risks for obstetrical complications, such as hypertensive disorders of pregnancy, fetal growth restriction, and stillbirth, pregnancy after a solid organ transplant requires close maternal and fetal surveillance. Data to guide an evidence-based approach to antenatal surveillance in pregnant individuals with a solid organ transplant are lacking; however, we suggest that the following considerations should be integrated into the approach for this high-risk obstetrical population. Given the high incidence of early pregnancy loss, preterm delivery, and fetal growth disorders, early and accurate pregnancy dating is crucial and dating ultrasonography is recommended.

Counseling regarding perinatal genetic risks and options for aneuploidy screening should be provided to all individuals with a solid organ transplant during pregnancy.[106] Cell-free fetal DNA screening in this population is controversial given the potential for interference from the allograft because sex discordance between organ donors and recipients could theoretically impact fetal sex chromosome analysis. An approach to screening for the common autosomal trisomies (trisomy 21, 13, and 18) without sex chromosome evaluation should be considered when using cell-free fetal DNA screening in pregnant individuals with a transplant. There is no contraindication to amniocentesis and chorionic villus sampling for these patients because of medical immunosuppression, and this procedure can be offered as clinically indicated and appropriate. Given the potential to enter pregnancy while on teratogenic medications, the requirement for immunosuppressive polypharmacy during organogenesis and the potential for perinatal infections such as CMV, a detailed fetal anatomic survey (level II) is recommended for all individuals with a solid organ transplant and fetal echocardiography should be considered. **Because of the increased incidence of fetal growth restriction and common coexisting medical morbidities,[95,96] we recommend serial assessment of fetal growth every 4 to 6 weeks throughout gestation after the anatomic survey (GRADE 1C).**[107] Unless fetal growth restriction is suspected or diagnosed, there is no evidence to support routine fetal umbilical artery or middle cerebral artery Doppler evaluation. **Lastly, we suggest antenatal surveillance beginning at 32 weeks of gestation unless other fetal or maternal factors are identified in which case initiation of surveillance at an earlier gestational age is indicated[107] (GRADE 2C).** An individualized approach should be developed based on relevant fetal and maternal considerations for each individual with a solid organ transplant.

How should allograft function be monitored during pregnancy?

Allograft function should be assessed at the time of the prepregnancy consultation to help guide counseling, upon diagnosis of a confirmed intrauterine pregnancy, and every 4 to 8 weeks throughout pregnancy. A suggested approach to graft function assessment by transplanted organ is displayed in Table 5. More frequent surveillance may be required should immunosuppressive dosages be subtherapeutic. Any symptoms or clinical suspicion of acute cellular rejection also warrants immediate laboratory assessment and possible imaging (with or without biopsy) for evaluation of the allograft in consultation with the other members of the patient's multidisciplinary team. Lastly, baseline renal dysfunction in individuals with a nonkidney solid organ transplant is associated with an increased risk for adverse obstetrical outcomes, including hypertensive disorders of pregnancy and preterm birth.[91] **Therefore, we recommend that renal function be assessed before pregnancy or in early pregnancy in all individuals with a solid-organ transplant (kidney and nonkidney transplant cases) (GRADE 1C).**

How should delivery be managed for individuals with a solid organ transplant?

Timing of delivery

Evidence-based recommendations guiding the timing of delivery in pregnant individuals with a solid organ transplant are lacking, and as for most transplant types, more than half of the patients are delivered preterm or early term. Delivery

TABLE 5
Assessment of graft function in transplanted organs during pregnancy

Transplanted organ	Graft function assessment	Findings of allograft dysfunction
Kidney	• Serum creatinine, GFR, and urine protein/creatinine ratio or 24-h urine protein collection	• With normal graft function, serum creatinine should be <1.5 mg/dL and proteinuria should be <500 mg/24 h. • Allograft dysfunction presentation may clinically mirror preeclampsia and demonstrate increasing creatinine and proteinuria
Liver	• Liver enzymes (AST, ALT, GGT) • Liver function tests (PT/INR, aPTT, bilirubin)	• Liver enzymes and tests of liver function should be < 1.5 times the upper limit of normal
Heart	• EKG • Echocardiogram • Chest X-ray[a] • Cardiac catheterization[a] • Gold standard to evaluate rejection is endomyocardial biopsy[a]	• Chronic allograft rejection typically presents as accelerated coronary artery disease; patients may present with arrhythmias, decompensated heart failure, myocardial infarction (often silent due to cardiac denervation)
Lung and heart/lung	In addition to heart recommendations above: • SpO_2 monitoring (at each office visit) • Pulmonary function testing (PFT) • Chest X-ray • Arterial blood gas • Chest CT[b] • Bronchoscopy[b]	• Often present with upper respiratory infection symptoms; chest X-ray demonstrates perihilar infiltration or graft opacification • Chronic rejection indicated by bronchiolitis obliterans • PFT with obstructive defect (decreased FEV_1) • Increased A-a gradient

ALT, alanine transaminase; *aPTT*, activated partial thromboplastin time; *AST*, aspartate aminotransferase; *CT*, computed tomography; *EKG*, electrocardiogram; *FEV_1*, forced expiratory volume; *GFR*, glomerular filtration rate; *GGT*, gamma-glutamyl transferase; *PT/INR*, prothrombin time/international normalized ratio; *SpO_2*, oxygen saturation.

[a] Chest X-ray, cardiac catheterization, and/or endomyocardial biopsy are recommended for baseline assessment before pregnancy or possibly in early pregnancy and are not typically repeated unless clinically indicated; [b] Chest CT and bronchoscopy may be considered as part of the baseline clinical assessment of graph function but are not routinely repeated in pregnancy unless clinically indicated.

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at 39 weeks of gestation may be appropriate in a stable individuals with a solid organ transplant without other fetal or maternal indications for delivery. However, because of the increased prevalence of underlying medical comorbidities and the risk for hypertensive disorders of pregnancy,[14,15,78,108] individuals with a solid organ transplant may benefit from early term delivery to reduce the risk for adverse fetal and maternal outcomes with expectancy. **We suggest individualized delivery timing in pregnant individuals with a solid organ transplant with consideration of delivery between 37+0/7 and 39+6/7 weeks of gestation. In the absence of other indications, we suggest delivery by 39+6/7 weeks of gestation in pregnant individuals with a solid organ transplant (GRADE 2B).**

Route of delivery

Expert consensus supports a trial of labor in individuals with a solid organ transplant with cesarean delivery reserved for obstetrical medical indications.[8] Despite this recommendation, there continues to be a high incidence (approximately 50%) of cesarean delivery among individuals with a transplant across all transplant types (Table 4, Figure). Although data to guide recommendations regarding route of delivery are sparse, a recent registry-based retrospective cohort study by Yin and colleagues provides important information to guide care decisions.[109] In their study of 1865 pregnant individuals with a kidney (n=1435) or liver (n=430) transplant, a trial of labor was not associated with an increased risk for adverse maternal or neonatal outcomes, and the rate of successful vaginal delivery among patients attempting a trial of labor was approximately 70%. Furthermore, in individuals with a kidney transplant, a trial of labor was associated with a decreased rate of composite neonatal morbidity when compared with a scheduled cesarean delivery. This finding was independent of whether the trial of labor ended in a successful vaginal delivery (trial of labor with vaginal delivery: adjusted odds ratio [aOR], 0.63; 95% confidence interval [CI], 0.24–0.53; trial of labor with cesarean delivery: aOR, 0.52; 95% CI, 0.32–0.82). For individuals with a liver transplant, a trial of labor with successful vaginal delivery was also associated with a decreased likelihood of neonatal morbidity. Importantly, the risk for allograft loss within 2 years after delivery was not associated with the mode of delivery. These concepts should guide practitioners when forming a delivery plan with individuals with a transplant because surgical delivery is not without risk. Immunocompromised individuals are at increased risk for postoperative complications, surgical site infection, and potentially delayed or impaired wound healing. **Given that a trial of labor is associated with a high success rate and lower neonatal morbidity without increasing maternal morbidity or compromising graft survival, we recommend that**

cesarean delivery be reserved for obstetrical medical indications in individuals with a solid organ transplant (GRADE 1C).

Other delivery considerations: medications, anesthesia, and surgical

Medication and anesthetic considerations are integral to delivery planning for pregnant individuals with a solid organ transplant. Intravenous stress dose steroids may be indicated at delivery if a patient is on chronic corticosteroids. In addition, the discontinuation of maintenance immunosuppression is not recommended during the antepartum or intrapartum periods. Postpartum, immunosuppressive medications may be adjusted (usually lowered) because of the immediate shift in volume of distribution. Establishing the immediate postpartum medical regimen in consultation with the other subspecialties before delivery is important, and the patient's desire to breastfeed should be considered in medication decisions.

Labor analgesia and anesthesia for cesarean delivery in patients with a solid organ transplant with normal allograft function do not differ markedly from obstetrical patients without a transplant; however, additional considerations for parturients with a transplant include drug metabolism and other pharmacologic considerations related to allograft function or drug interactions with immunosuppressive therapy, transfusion implications (red blood cell alloantibodies arising from transplanted organs), and prevention of infection. There are particular anesthetic implications in individuals with a cardiac transplant related to the consequences of the denervated cardiac allograft, which impacts maternal heart rate and stress response, cardiac output (preload dependent), and arrhythmia risk.[110] Furthermore, individuals with a cardiothoracic transplant may have a poor or absent cough reflex and diminished ability to clear secretions leading to an increased aspiration risk and limited ability to protect their airway. Antepartum consultation with obstetrical anesthesiology can guide delivery planning for patients with a solid organ transplant.

Lastly, there may be cases with a pelvic graft (eg, kidney allograft in the iliac fossa) or a native organ in the pelvis or retroperitoneal space (eg, enlarged, native polycystic kidneys left in situ at the time of the original transplant), so appropriate surgical planning should be performed. In these instances, involving the surgical transplant team before delivery is recommended to plan the most appropriate abdominal entry (because of previous surgical entry type or multiple previous surgeries with intraabdominal scarring) and to discuss aberrant anatomic considerations (such as a deviation of the normal ureteral course after reattachment to the pelvic graft). In general, the commonly employed Pfannenstiel incision and low-transverse hysterotomy should not confer increased surgical risks to most allografts, even if pelvic. Although there are case reports of allograft injury at the time of cesarean delivery, contemporary data suggest that the risk for allograft injury is small (<1% in individuals with a renal transplant).[89,111,112]

Organ-specific considerations in pregnancy after solid organ transplant

What issues are most important for each particular organ transplant?

Kidney

The kidney is the most commonly transplanted organ, and the majority of pregnancies in individuals with a solid organ transplant are among those with renal transplants.[7] Therefore, this cohort of patients with a transplant represents the population with the most obstetrical data and experience. Individuals with a kidney transplant can have a successful pregnancy, and a well-functioning allograft should tolerate the physiological renal changes in pregnancy.[113] However, prepregnancy renal function (serum creatinine, eGFR, and proteinuria) is a major factor in both graft and pregnancy outcomes for kidney recipients. Bramham et al[18] found a 6-fold higher likelihood of poor fetal outcomes (fetal death, miscarriage, neonatal death, preterm delivery before 32 weeks of gestation, and congenital anomalies) among women with elevated prepregnancy creatinine levels and high diastolic blood pressure measurements. Another report suggests that the presence of nephrotic range proteinuria increases the risk for spontaneous abortion, fetal growth restriction, and premature delivery in pregnant individuals with a renal transplant.[19] In addition, the TPRI analyzed 984 singleton pregnancies among 695 kidney recipients divided in cohorts by prepregnancy eGFR.[114] Progressively lower prepregnancy eGFR was found to be associated with increased maternal complications, graft loss, and adverse fetal outcomes, especially when eGFR was <30 mL/min/1.73m.[114] As such, the general predictors of poor pregnancy outcomes for these patients include uncontrolled preexisting hypertension, elevated prepregnancy creatinine ≥1.4 mg/dL, nephrotic range proteinuria (>3.5 gm/24 hours), and a history of ≥2 renal transplants.[108]

Chronic hypertension occurs in 80% to 90% of individuals with a renal transplant and has considerable prognostic implications for this transplant population.[115,116] Notably, chronic hypertension negatively impacts renal allograft survival and increases the risk for recipient cardiovascular disease and mortality, particularly among those with poor control.[117,118] Therefore, appropriate blood pressure control following renal transplantation is critical for improving allograft and patient survival. The Kidney Disease: Improving Global Outcomes clinical practice guidelines recommend a blood pressure target of ≤130/80 mm Hg among individuals with hypertension and a renal transplant.[119] Data on blood pressure targets specific to pregnant individuals with a renal transplant are lacking. The Control of Hypertension in Pregnancy[120] and the Treatment for Mild Chronic Hypertension During Pregnancy[121] trials excluded patients with chronic kidney disease. Based on limited evidence, the United Kingdom National Institute of Health and Clinical Excellence clinical guidelines recommend a blood pressure target of ≤140/90 mm Hg for pregnant women with end-organ damage, including chronic

kidney disease.[122] **We recommend that blood pressure targets in pregnant individuals with a renal transplant with chronic hypertension follow guidelines for nonpregnant recipients with a target blood pressure of ≤ 130/80 mm Hg (GRADE 1C).**

In addition to the increased risk for hypertensive disorders of pregnancy, pregnant individuals with a renal transplant have an increased risk for urinary tract infections with rates reported to be as high as 42% in a single-center series.[123] Although urinary tract infections are common in pregnancy because of physiological urinary stasis, medical immunosuppression and the anatomy of the transplanted urinary tract amplifies this risk for pregnant individuals with a renal transplant. Furthermore, there are some reports of increased pyelonephritis in this patient cohort, which is associated with adverse pregnancy outcomes.[19,124] **We recommend monthly urine cultures to screen for asymptomatic bacteriuria with treatment if positive for the protection of the graft in pregnant individuals with a renal transplant (GRADE 1C)**. There is no current evidence to support routine daily suppressive medications in the absence of another indication. If the patient was prescribed daily suppression before pregnancy, this could then be continued with a pregnancy-safe medication.

The risk for allograft rejection in individuals with a kidney transplant does not seem to be impacted by pregnancy. The commonly reported rate of rejection in large cohort studies is between 3% to 9%, which is comparable with the rejection rate outside of pregnancy.[7,18,78] Prompt consultation with nephrology and the kidney transplant team should be undertaken if rejection or failure is suspected so that the appropriate diagnostic testing can be performed with swift therapeutic management. An ultrasound guided renal biopsy may be indicated for definitive histologic diagnosis. Renal biopsy is not contraindicated in pregnancy, although complications including infection, bleeding, or perinephric hematoma (which may require intervention or transfusion) may occur. Several small series have reported that the complication rates of a percutaneous renal biopsy in pregnancy are similar to those in nonpregnant patients; however, a recent meta-analysis comparing 243 antenatal biopsies with 1236 postpartum biopsies demonstrated an increased risk for complications with antenatal biopsy (7% vs 1%; P=.001).[125-128] In general, renal biopsy should be pursued in pregnancy when a histologic diagnosis will change management.[129] Intravenous corticosteroids are the mainstay of treatment for acute cellular rejection and are effective in pregnancy.

Many reports and meta-analyses have demonstrated that pregnancy after a kidney transplant does not impact long-term allograft survival.[14] In a case-control study comparing 120 parous and 120 nulliparous individuals with a kidney transplant by age and year of transplant, duration of transplant, and serum creatinine, Levidiotis et al[130] reported that a first live birth was not associated with decreased patient or allograft survival at 20 years. When comparing pregnancy in kidney recipients with nulliparous transplant controls, the risk of graft failure after pregnancy is primarily related to established poor prognostic factors including hypertension and baseline graft dysfunction (prepregnancy proteinuria and high serum creatinine).[69,130,131] Although the overall rates of graft loss are not increased as a consequence of pregnancy, there are some data to suggest that pregnancy may negatively impact grafts. In a large meta-analysis, Shah et al[90] found a significant change in the prepregnancy vs postpregnancy creatinine levels (1.23±0.16 mg/dL vs 1.37±0.27 mg/dL; P=.007), suggesting an impact of pregnancy on allograft function beyond delivery, but the overall long-term clinical implication of this finding is unclear.[78]

Lastly, for individuals with a renal transplant, judicious use of NSAIDs in the postpartum period is recommended. In a longitudinal cohort study of individuals with a renal transplant, a short course of NSAIDs (<7 days) was associated with an increased risk for acute kidney injury (AKI) (OR, 1.05; 95% CI, 1.02−1.08; P<.001).[132] In addition, the risk for AKI increased with increasing NSAID dose and longer duration of therapy. As such, if NSAIDs are required in this specific transplant population, the lowest effective dose should be used for the shortest duration possible.

Pancreas-kidney

Pancreas-kidney (PK) transplantation is typically performed in patients with diabetes requiring insulin with advanced chronic or end-stage renal disease. In the United States, nearly 90% of pancreas transplants are performed simultaneously with kidney transplants, whereas the remainder are performed as pancreas transplant after kidney transplant or as pancreas transplants alone.[133] Simultaneous PK transplant may confer a mortality benefit when compared with a kidney transplant alone and may decrease recipient morbidity related to improving the sequelae of diabetes, including the risks for cardiovascular disease, hyperlipidemia and atherosclerosis, neuropathy, and retinopathy.[134-136]

Individuals who become pregnant after PK transplant have similar obstetrical outcomes and graft complications as individuals with a kidney transplant alone (Table 3). A TPRI study compared transplant survival after pregnancy in individuals with type 1 diabetes (n=103; PK, n=61; kidney alone [KA], n=42). Pregnancy outcomes in individuals with a PK and KA transplant were similar with high rates of preeclampsia, prematurity, and cesarean delivery. There was a trend toward a higher mean birthweight in KA vs PK pregnancies (2423±842 vs 2127±744 g, respectively; P=.05).[137] Survival analyses showed no significant difference between patients with a KA vs PK transplant (P=.98). Overall, the transplanted pancreas can adapt to the glycemic demands of pregnancy, which is reflected by the low incidence of insulin use during pregnancy (Table 3). Therefore, routine screening for gestational diabetes is indicated. Otherwise, the obstetrical data are limited with a few recent reports of pregnancy after a PK transplant.[138-140] In these

available series, increased rates of hypertension and preeclampsia are reported but with a high likelihood of a successful pregnancy outcome. **We recommend that pregnancies in patients with a pancreas-kidney transplant be managed similar to those of individuals with a renal transplant alone (GRADE 1C).**

One potential consideration unique to individuals with a pancreas transplant involves the location for exocrine drainage of the transplanted pancreas. Historically, bladder exocrine drainage was performed, which causes normal anion gap metabolic acidosis, hyponatremia, and volume depletion and requires chronic sodium bicarbonate supplementation. The current surgical approach in pancreatic transplantation typically involves enteric drainage, which has largely eliminated this metabolic disturbance.[141] As such, an understanding of postsurgical anatomy is relevant to the care of individuals with a PK transplant.

Liver

Liver transplantation is typically performed in patients with end-stage liver disease with a variety of etiologies including congenital anatomic abnormalities, infections, metabolic diseases, cirrhosis, malignancy, or other acute or chronic insults. One of the primary challenges following liver transplantation is recurrence of the primary disease that initially cause hepatic injury. Although conditions related to congenital anatomic abnormalities (biliary atresia, hepatic fibrosis, Alagille syndrome) or metabolic disease (Wilsons disease, alpha-1 antitrypsin deficiency) generally do not recur following liver transplantation, other causes of liver disease including hepatitis B and C infection, primary sclerosing cholangitis, autoimmune hepatitis, hemochromatosis, alcoholic liver disease, and hepatocellular carcinoma can recur and are associated with allograft injury and failure. In addition, chronic kidney disease develops in the majority of individuals with a liver transplant and negatively impacts allograft and patient survival.[142] **We recommend characterizing the underlying condition that led to liver transplantation and assessing baseline renal function in pregnant individuals with a liver transplant (GRADE 1C).**

Overall, recipients of a liver transplant tolerate pregnancy better than many other individuals with a solid organ transplant. They have lower incidences of hypertension and preeclampsia than individuals with a kidney, PK, heart, or lung transplant. Their infants tend to be born closer to term and have higher mean gestational ages at delivery and birth weights than the other organ recipients, and they have a lower incidence of maternal hypertensive disease in pregnancy (Tables 2–4, Figure).[75] The American Association for the Study of Liver Diseases (AASLD) has published an extensive document regarding reproductive health and liver disease in general, which includes guidance for individuals with a liver transplant in pregnancy.[10]

Specific to individuals with a liver transplant, pregnancy is associated with an increased risk for intrahepatic cholestasis of pregnancy (ICP). In data from the TPRI, ICP was reported in 7% of pregnant individuals with a liver transplant compared with a background rate of 0.2% to 2% in the general obstetrical population.[7,143,144] Similar to the general obstetrical population, there was considerable variation in the prevalence of ICP among individuals with a liver transplant by geography and ethnicity.[144,145] The postpartum resolution of ICP symptoms in individuals with a liver transplant is similar to those without a transplant. As demonstrated by the TPRI report, pregnant individuals with a liver transplant with ICP did not have persistent cholestatic liver disease or graft complications attributable to ICP.[7] Although the incidence of ICP is increased in this transplant group, assessment of the baseline total bile acids is not routinely indicated. If a pregnant individual with a liver transplant develops symptoms concerning for ICP, obstetrical care providers should then have a low threshold for obtaining laboratory evaluation and initiate ursodeoxycholic acid treatment with fetal surveillance as clinically appropriate.[146]

If prepregnancy graft function is normal, individuals with a liver transplant can maintain adequate transplant function during pregnancy, and there is not an overall increased risk for allograft loss attributable to pregnancy.[13,15,91] In a TPRI analysis of postpartum liver recipients, 16 recipients with graft loss were compared with 145 recipients without graft loss within 5 years of pregnancy. Significant factors that contributed to graft loss included younger age at transplant (44% vs 19%; P=.03), episode of rejection during pregnancy (40% vs 7%; P=.0001), and episode of rejection within 3 months postpartum (47% vs 12%; P=.002). The authors concluded that rejection during pregnancy was the strongest risk factor associated with graft loss within 5 years of pregnancy. Overall, the published rates of acute rejection in pregnant individuals with a liver transplant are similar to the background risk in this transplant population.[147,148] In the TPRI data set, episodes of graft rejection were reported in 4.8% of pregnancies among individuals with a liver transplant.[7] A prospective study from the United Kingdom showed rates of rejection requiring treatment of 7.7% during pregnancy and of 1.4% within the first 3 months postpartum.[92] The variation in the reported rates of rejection in pregnancy likely reflects different definitions, with some studies only including biopsy-proven cases of rejection.

Heart

Since the first reported pregnancy and delivery of a patient after a cardiac transplant in 1988, experience with pregnancies after a cardiac transplantation has grown.[149] Guidelines on the approach to care in pregnant individuals with a cardiac transplant have been published by the International Society for Heart and Lung Transplantation.[11] Although successful pregnancies may be achieved, this population of individuals with a solid organ transplant remains at increased risk of morbidity and mortality.

The transplanted heart generally tolerates the physiological cardiovascular changes of pregnancy, including the increase in cardiac output, blood volume expansion, and the

decrease in systemic vascular resistance, and the available evidence does not suggest that cardiac allografts are negatively impacted by pregnancy.[17,70] However, numerous considerations and consequences for pregnant individuals with a cardiac transplant arise from the denervated cardiac allograft.[110] Because of sympathetic and parasympathetic denervation, transplanted hearts typically have an intrinsic heart rate of 80 to 100 beats/minute, a delayed or blunted stress response, and an increased frequency of arrhythmias. Cardiac allografts are preload dependent with cardiac output maintained by the stroke volume through Starling mechanics. The denervated heart is also vulnerable to accelerated atherosclerosis, and given the lack of afferent innervation, silent myocardial ischemia may occur. **Because of the cardiovascular demand of pregnancy and the unique physiological implications of cardiac transplantation, we recommend that pregnant individuals with a heart transplant receive multidisciplinary care with cardiology, cardiac, and/or obstetrical anesthesiology, and maternal-fetal medicine specialists (Best Practice). We recommend careful delivery planning to minimize hemodynamic stress (including consideration of operative vaginal delivery to minimize Valsalva) and suggest continuous intrapartum or intraoperative electrocardiographic monitoring for individuals with a heart transplant (GRADE 1C).** According to the American Heart Association, individuals with a cardiac transplant do not routinely require subacute bacterial endocarditis prophylactic antibiotics unless there is regurgitation caused by a structurally abnormal valve.[150]

Cardiac function should be thoroughly evaluated before pregnancy to characterize each patient's baseline because pregnancy is best tolerated if the patient is classified as functional New York Heart Association class 1.[17] This evaluation includes an electrocardiogram, echocardiogram, and endomyocardial biopsy and cardiac catheterization if indicated (Table 5). Multidisciplinary care teams may also consider cardiac magnetic resonance imaging during pregnancy planning, which can also be performed safely during pregnancy without contrast. Coronary angiography is also ideally done outside of pregnancy, but if necessary, it can be performed during pregnancy with minimal fetal risk.[151] Should a patient demonstrate high-grade cardiac allograft vasculopathy during the prepregnancy assessment, pregnancy should be deferred.[11]

The underlying etiology of the initial cardiac disease that led to transplantation should be investigated and discussed, because the primary disease process may have pregnancy implications. For example, patients with a pretransplant diagnosis of congenital heart disease have an increased risk for congenital heart disease in their offspring with the magnitude of the risk related to the underlying lesion or any known genetic etiology.[152] As such, fetal echocardiography is recommended for this subgroup of pregnant heart transplant recipients. Although data on patients with a history of peripartum cardiomyopathy that led to cardiac transplant are limited, theoretically, based on the current understanding of the pathogenesis of peripartum cardiomyopathy, these patients may be at risk for recurrence in future pregnancies.[153]

Based on available data, the incidence of acute allograft rejection in individuals with a heart transplant does not seem to be increased during pregnancy. Acute rejection was reported in 9.1% to 11.8% of cases in some series, which is not elevated above the baseline frequency in patients with a heart transplant.[70,76,154] Any worsening of symptoms (chest pain, tachycardia, palpitations, orthopnea, dyspnea at rest or exertion, shortness of breath, lower extremity edema, etc) or declining cardiac function noted in the antepartum period should be evaluated promptly in consultation with cardiology and the patient's surgical transplant team. Many of the symptoms of cardiac decompensation overlap with the symptoms of pregnancy (shortness of breath, fatigue, lower extremity swelling); therefore, patient counseling is key to reporting and not dismissing concerning signs and symptoms of acute cellular rejection.

Although successful pregnancies after a heart transplant can be achieved, pregnancy after cardiac transplant confers substantial risks for morbidity and mortality. Long-term survival is not as favorable as for abdominal transplants, even without a pregnancy, with a 5-year survival of female heart recipients of 76%.[11] Punnoose et al,[76] in one of the largest longitudinal cohort studies of pregnant individuals with a heart transplant (91 patients with 157 pregnancies), reported deaths in 30 of 91 (33%) patients at a mean period of 9.4±6.2 years after pregnancy, with cardiac allograft vasculopathy, cardiac arrest, and rejection leading to graft failure being the most common causes of death (63). D'Souza et al[70] reported maternal deaths in 2 of 16 (12.5%) cases at 10 and 18 months postpartum, reportedly because of medical nonadherence. Dagher et al[17] reported postpartum maternal deaths in 3 of 8 (37.5%) cases that occurred at a mean time of 3.9 years after delivery. However, long-term mortality was similar for individuals with a heart transplant with at least 1 pregnancy and reproductive-aged individuals with a heart transplant without pregnancy exposure (37.5% vs 28.9%; $P=.81$). These authors believe that the maternal long-term survival among individuals with a heart transplant is mostly related to the heart transplant itself and is not affected by pregnancy.

Lung and heart-lung

Pregnancies after lung and lung-heart transplantation are rare, and there are limited data on the obstetrical outcomes. Most of these patients are affected by cystic fibrosis, which is commonly the indication for transplant; therefore, genetic counseling should be offered before or during pregnancy. Given the background rate of allograft rejection and chronic dysfunction in individuals with a lung transplant, patients are often recommended to defer pregnancy for 2 years after a lung transplant to establish stability, which differs from other solid organ recipients.[12,16,155] Baseline pulmonary function testing and optimization of medications and allograft function before pregnancy is especially important for this cohort

Summary of recommendations

	Recommendation	Grade
1	We recommend that all individuals with a solid organ transplant who are capable of pregnancy be offered prepregnancy counseling as part of the pretransplant evaluation and before any posttransplant pregnancy.	Best practice
2	We recommend deferring pregnancy for at least 1 year (except for individuals with a lung transplant in which case deferral for 2 years is recommended) following solid organ transplant or any episode of acute cellular rejection.	1B
3	We recommend that individuals with a solid organ transplant have stable allograft function and optimal control of chronic medical comorbidities before attempting pregnancy.	1B
4	We recommend that reproductive-aged individuals with a solid organ transplant use highly effective contraception when on mycophenolate or other immunosuppressive agents with a known teratogenic risk.	1A
5	We recommend that an individual with a solid organ transplant who is contemplating pregnancy transition to an appropriate immunosuppressive regimen before attempting pregnancy to establish stable medication dosing and allograft function.	1C
6	We recommend close monitoring of serum drug levels during pregnancy and the postpartum period to guide immunosuppressive therapy dosing.	1C
7	We recommend that individuals with a solid organ transplant who are pregnant or contemplating pregnancy receive all indicated vaccinations before and during pregnancy.	1C
8	Given the risk of fetal and neonatal sequelae secondary to CMV infection in pregnancy, we suggest that individuals with a solid organ transplant ideally complete any indicated antiviral prophylaxis or treatment before pursuing pregnancy.	2B
9	We recommend daily low-dose aspirin prophylaxis to reduce the risk for preeclampsia in pregnant individuals with a solid organ transplant and to reduce the risk of renal allograft failure in renal transplant recipients.	1C
10	As for all pregnant people, we recommend that pregnant individuals with a solid organ transplant have access to mental health specialists and receive screening for depression during pregnancy and the postpartum period.	Best Practice
11	Because of the increased incidence of fetal growth restriction and common coexisting medical morbidities, we recommend serial assessment of fetal growth every 4 to 6 weeks throughout gestation after the anatomic survey.	1C
12	We suggest antenatal surveillance beginning at 32 weeks of gestation unless other fetal or maternal factors are identified in which case initiation of surveillance at an earlier gestational age is indicated.	2C
13	We recommend that renal function be assessed before pregnancy or in early pregnancy in all individuals with a solid-organ transplant (kidney and nonkidney).	1C
14	We suggest individualized delivery timing in pregnant individuals with a solid organ transplant with consideration of delivery between 37+0/7 and 39+6/7 weeks of gestation. In the absence of other indications, we suggest delivery by 39+6/7 weeks of gestation in pregnant individuals with a solid organ transplant.	2B
15	Given that a trial of labor is associated with a high success rate and lower neonatal morbidity without increasing maternal morbidity or compromising graft survival, we recommend that cesarean delivery be reserved for obstetrical medical indications in individuals with a solid organ transplant.	1C
16	We recommend that blood pressure targets in pregnant individuals with a renal transplant with chronic hypertension follow guidelines for nonpregnant recipients with a target blood pressure of $\leq$ 130/80 mm Hg.	1C
17	We recommend monthly urine cultures to screen for asymptomatic bacteriuria with treatment if positive for the protection of the graft in pregnant individuals with a renal transplant.	1C
18	We recommend that pregnancies in patients with a pancreas-kidney transplant be managed similar to those of individuals with a renal transplant alone.	1C
19	We recommend characterizing the underlying condition that led to liver transplantation and assessing baseline renal function in pregnant individuals with a liver transplant.	1C
20	Because of the cardiovascular demand of pregnancy and the unique physiological implications of cardiac transplantation, we recommend pregnant individuals with a heart transplant receive multidisciplinary care with cardiology, cardiac and/or obstetrical anesthesiology, and maternal-fetal medicine specialists.	Best Practice
21	We recommend careful delivery planning to minimize hemodynamic stress (including consideration of operative vaginal delivery to minimize Valsalva) and suggest continuous intrapartum or intraoperative electrocardiographic monitoring for individuals with a heart transplant.	1C

CMV, cytomegalovirus.

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Society for Maternal-Fetal Medicine grading system: grading of recommendations assessment, development, and evaluation (GRADE) recommendations[159a]

GRADE of recommendation	Clarity of risk and benefit	Quality of supporting evidence	Implications
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa	Consistent evidence from well-performed, randomized controlled trials, or overwhelming evidence of some other form Further research is unlikely to change confidence in the estimate of benefit and risk	Strong recommendation that can apply to most patients in most circumstances without reservation Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
1B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate	Strong recommendation that applies to most patients Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
1C. Strong recommendation, low-quality evidence	Benefits appear to outweigh risks and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws Any estimate of effect is uncertain	Strong recommendation that applies to most patients Some of the evidence base supporting the recommendation is, however, of low quality
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well-performed randomized controlled trials or overwhelming evidence of some other form Further research is unlikely to change confidence in the estimate of benefit and risk	Weak recommendation; best action may differ depending on circumstances or patients or societal values
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws Any estimate of effect is uncertain	Very weak recommendation, other alternatives may be equally reasonable
Best practice	Recommendation in which either (i) there is an enormous amount of indirect evidence that clearly justifies strong recommendation (direct evidence would be challenging, and inefficient use of time and resources, to bring together and carefully summarize), or (ii) recommendation to the contrary would be unethical		

[a] Adapted from Guyatt et al.[160]

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Guidelines
The content of this document reflects the national and international guidelines related to pregnancy after solid organ transplant

Organization	Title	Year of publication
American Association for the Study of Liver Diseases	Reproductive health and liver disease: Practice guidance by the American Association for the Study of Liver Diseases[10]	2021
American College of Obstetricians and Gynecologists	Committee Opinion No. 736: Optimizing postpartum care[105]	2018
American College of Obstetricians and Gynecologists	Practice Bulletin No. 226: Screening for fetal chromosomal abnormalities[106]	2020
American College of Obstetricians and Gynecologists	Committee Opinion No 828: Indications for outpatient antenatal fetal surveillance[107]	2021
American Heart Association	Prevention of infective endocarditis[150]	2007
American Society of Transplantation	Cytomegalovirus in solid organ transplant recipients[59]	2019
American Society of Transplantation	Reproduction and transplantation: Report on the AST consensus conference on reproductive issues and transplantation[8]	2005
European Best Practice Guidelines Expert Group on Renal Transplantation	European best practice guidelines for renal transplantation[19]	2002
International Liver Transplantation Society	Report of the first international liver transplantation society expert panel consensus conference on renal insufficiency in liver transplantation[142]	2009
International Society of Heart and Lung Transplantation	Guidelines for the care of heart transplant recipients[11]	2010
Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group	KDIGO clinical practice guideline for the care of kidney transplant recipients[119]	2009
National Institute for Health and Care Excellence (NICE)	Hypertension in pregnancy: the NICE guidelines[122]	2011
Society for Maternal-Fetal Medicine	Society for Maternal-Fetal Medicine Consult Series 39: Diagnosis and antenatal management of congenital cytomegalovirus infection[62]	2016

Society for Maternal-Fetal Medicine. Prepregnancy evaluation and pregnancy management after solid organ transplant. Am J Obstet Gynecol 2023.

because of the increased frequency of graft rejection with long-term graft dysfunction, preterm birth, and neonatal mortality when compared with pregnant individuals with abdominal solid organ transplants[7,12,156] (Tables 3 and 4). Data on pregnancy-associated changes in pulmonary allograft function (defined as a 1-year decrease in forced expiratory volume of 5% or more) are conflicting with one single-center series reporting no change and another series reporting significant deterioration after pregnancy (pre-pregnancy, 83.9% predicted; 1 year postpartum, 77.3% predicted; P=.04).[12] Long-term effects of pregnancy on pulmonary allograft function remain inadequately characterized. Pulmonary infection is a common complication in individuals with a lung transplant during pregnancy and the postpartum period, with single-center studies and registry data reporting an overall infection rate of 21% to 23%.[12,156] Close antenatal and postpartum surveillance in this cohort is warranted because of the risk for acute cellular rejection, which is reported to complicate 13% of pregnancies and may lead to increased rates of graft dysfunction in the year following pregnancy.[7]

Emerging recipient groups

Other small groups of organ recipients should be mentioned including those with small bowel, pancreas only, multiple organ, liver-kidney, multivisceral, and the ever-increasing group of uterus-only transplants. In general, these transplants confer many of the same risks as all solid organ transplants; however, additional caution is warranted because of issues related to each individual organ and, in many cases, multiple organ diagnosis to optimize, monitor, and manage. Their obstetrical outcomes have been reported in small numbers only. Although considered an experimental therapy for uterine factor infertility in the United States, reports are growing of livebirths after living and deceased donor uterus transplant.[157,158] Increasing numbers of pregnancies following uterine transplantation are anticipated over the next decade.

Conclusion

Patients who have undergone solid organ transplant can have successful pregnancies, although they are considered to be at high risk for both maternal and fetal adverse outcomes. A multidisciplinary approach to care is recommended, including a specific surgical transplant team, organ-specific medical subspecialists, anesthesiologists, and maternal-fetal medicine subspecialists with expertise in managing these complex patients, in concert with strong psychosocial support. Counseling on pregnancy-associated risks should be introduced during the pretransplant evaluation, and prepregnancy consultation is recommended to facilitate medication optimization, timely administration of vaccinations, and assessment of graft stability before pregnancy. Once pregnancy begins, the patient, fetus, and the allograft should be monitored closely and regularly with serial evaluation and titration of immunosuppressive medications as necessary. Information on how to enroll in a national or international pregnancy and transplant registry should be provided and encouraged to help garner more robust obstetrical outcome data for these increasingly less rare and complex patients.

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process approved by the Society for Maternal-Fetal Medicine (SMFM) Board of Directors. SMFM has neither solicited nor accepted any commercial involvement in the specific content development of this publication.

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  https://doi.org/10.1016/j.ajog.2023.04.022