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## Blessing and a curse of outpatient management of delayed graft function

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### Abstract

Delayed graft function (DGF) is a common complication occurring most often after deceased donor kidney transplant with several donor characteristics as well as immunologic factors that lead to its development post-transplant. These patients require dialysis and close kidney function monitoring until sufficient allograft function is achieved. This has resulted in limited options for DGF management, either prolonged hospitalization until graft function improves to the point where dialysis is no longer needed or discharge back to their home dialysis unit with periodic follow up in the transplant clinic. DGF is associated with a higher risk for acute rejection, premature graft failure, and 30-d readmission; therefore, these patients need close monitoring, immunosuppression management, and prompt allograft biopsy if prolonged DGF is observed. This may not occur if these patients are discharged back to their home dialysis unit. To address this issue, the University of Wisconsin-Madison created a clinic in 2011 specialized in outpatient DGF management. This clinic was able to successfully reduce hospital length of stay without an increase in 30-d readmission, graft loss, and patient death.

**Key words:** Delayed graft function; Kidney transplantation; Immunosuppression; Acute rejection; Kidney donor profile index; Kidney donor risk index; Dialysis

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**Core tip:** Delayed graft function (DGF), traditionally defined as needing dialysis within seven days following kidney transplant, occurs most often after deceased donor kidney transplantation. Both donor characteristics, as well as immunologic factors, influence the development of DGF. Historically, outpatient management has been difficult, often leading to increased length of stay (LOS), however, the DGF clinic at University of Wisconsin - Madison which was established in 2011 has shown that it is possible to

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provide high-quality outpatient DGF management without increasing LOS, 30-d readmission, or acute rejection rates.

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## APPROACH TO MANAGING DELAYED GRAFT FUNCTION

Delayed graft function (DGF) is most often defined as the need for dialysis within the first seven days following kidney transplantation. However, this definition is subject to center level variation<sup>[1]</sup>. It is more commonly seen after deceased donor kidney transplantation with an estimated incidence of 30%<sup>[1,2]</sup>.

Certain factors are associated with the development of DGF including the cause of donor death, donor age, kidney donor profile index (KDPI), cold ischemia time (CIT), and higher serum creatinine at the time of death<sup>[3]</sup>. KDPI is a numerical measure of overall kidney quality in deceased donor (DD) kidneys. It is derived by first calculating kidney donor risk index (KDRI) which incorporates several donor characteristics including age, height, weight, cause of death, history of diabetes, history of hypertension, ethnicity, Hepatitis C status, serum creatinine, and donation after circulatory death (DCD) status. Lower KDRI and KDPI scores are associated with increased donor quality and expected longevity whereas higher scores (> 85%) are associated with increased risk for DGF as well as decreased graft survival and longevity<sup>[4,5]</sup>. Longer CIT, over 20 h, is also associated with a higher incidence of DGF<sup>[6]</sup>. There is a higher risk of developing DGF following DCD kidney transplantation due to the presence of warm ischemia and reduced perfusion during procurement<sup>[7]</sup>.

DGF is a costly complication and often leads to prolonged hospitalization. DGF recovery is most often seen within 7 to 10 d<sup>[8]</sup>, however, it can take up to three to four weeks for DGF to completely resolve to the point where dialysis is no longer needed. Managing DGF poses a unique challenge for health care providers who are tasked with reducing hospital stay while at the same time ensuring these patients are receiving close monitoring of kidney function. Traditionally DGF management has been limited to either prolonged length of stay (LOS) until allograft recovery has been achieved or discharge back to their home dialysis center with regular follow up in the clinic. These patients are often medically complex with fluctuating volume status, so care must be taken to prevent inappropriate dialysis during DGF recovery. They are at high risk for readmission within the first 30 d after transplantation<sup>[9]</sup>. Those with DGF are also at higher risk for acute rejection which can lead to premature graft failure and is associated with decreased 1, 3, and 5-year graft survival<sup>[3,10,11]</sup>. Therefore, not only is optimizing immunosuppression critical but prompt diagnosis with renal allograft biopsy, if prolonged DGF is observed, is also important. These opportunities may be missed if patients are not followed closely in the transplant clinic.

Because outpatient DGF management has been challenging due to the need for ongoing dialysis and close monitoring of kidney function, the transplant clinic is the ideal setting for DGF follow-up. However, this can be difficult for patients and family members who do not reside near the transplant center. In order to address this need for consistent outpatient DGF management, the University of Wisconsin Hospital created an outpatient clinic in July 2011 which specializes in DGF management. This multidisciplinary clinic consists of transplant nephrology physicians, experienced advanced practice providers (APPs) specialized in kidney transplantation, social workers, and pharmacists. DGF discharge planning frequently is initiated upon consultation to transplant nephrology when DGF is suspected. These patients are then either discharged home (if local) or to a nearby hotel with a support person along with a scheduled clinic visit within 1-3 d of discharge. Majority of these patients are required to follow up in the DGF clinic 3 d per week. Each clinic visit day begins with labs which are usually completed in the outpatient labs at the hospital. These include complete metabolic panel, complete blood count, should be urinalysis, urine protein-creatinine ratio, beta-2-microglobulin, tacrolimus drug level. Patients then proceed to the clinic where height, weight, and vital signs are obtained. They then undergo assessment and physical exam by either an APP or physician. If dialysis is deemed

necessary, an appointment is then scheduled for dialysis in the hospital inpatient dialysis unit that same day. Prior to leaving clinic, a follow-up appointment is scheduled and a new medication list is provided to the patient. DGF clinic follow up continues until adequate graft function is achieved. During dialysis, all patients go through the same standard isolation precaution of contact or airborne isolation or no isolation. If no improvement in graft function is noted within 7 to 14 d after transplantation, a kidney transplant biopsy is scheduled. Donor-specific antibodies (DSA) are monitored on all patients at the time of a kidney biopsy. Also, DSA are monitored on all patients, based on the immunological risk as described previously<sup>[12]</sup>. In the near future, we are also planning to monitor DGF and perform biopsy based on the new biomarkers, along with the banking of the tissue, serum and urine sample<sup>[13]</sup>.

To assess the impact of this clinic on outpatient DGF management, Muth *et al*<sup>[14]</sup> conducted a retrospective review of 697 DD performed from July 2009 to July 2014. Patients were divided into three groups, no DGF, and DGF before and after implementation of the DGF clinic. Baseline characteristics of the three groups were similar. They compared LOS, 30-d readmission, acute rejection, and patient/graft survival. What they found was a significant decrease in LOS post-DGF clinic compared pre-DGF clinic<sup>[14]</sup>. DGF clinic patients were less likely to develop acute rejection, while 30-d readmission, graft loss and patient death did not differ significantly between pre and post-DGF clinic<sup>[14]</sup>. These findings suggest outpatient DGF management can successfully reduce LOS without increasing adverse outcomes or compromising patient care. To achieve this, we needed a dedicated multidisciplinary team as well as a motivated patient with their support person to navigate DGF, because often times, the patient is overwhelmed due to the frequent nature of clinic visits as well as being away from home. In summary, our experience with intensive multidisciplinary outpatient management of DGF has been effective in closely monitoring and supporting patients in their DGF recovery, and limiting adverse events. Based on our experience, we recommend a transplant center to weigh the cost-benefit of this complex patient. Centers with a high volume of DGF may benefit from establishing a DGF clinic.

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