**Name of Journal:** *World Journal of Transplantation*

**Manuscript NO:** 47697

**Manuscript Type:** EDITORIAL

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

Blazel JW *et al*. Outpatient management of DGF

Justin W Blazel, Jennifer A Turk, Brenda L Muth, Sandesh Parajuli

**Justin W Blazel, Jennifer A Turk, Brenda L Muth, Sandesh Parajuli**, Division of Nephrology, Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI 53705, United States

**ORCID number:** Justin W Blazel (0000-0002-9020-460X); Jennifer A Turk (0000-0003-2534-6932); Brenda L Muth (0000-0002-0175-6825); Sandesh Parajuli (0000-0003-1667-7465).

**Author contributions:** Blazel JB designed and prepared the manuscript; Turk JA edited the manuscript; Muth BL designed and edited the manuscript; Parajuli S concept, designed and edited manuscript.

**Conflict-of-interest** **statement:** The authors have no conflict of interest to declare.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Manuscript source:** Invited manuscript

**Corresponding author: Sandesh Parajuli, MBBS, MD, Assistant Professor,** Division of Nephrology, Department of Medicine, University of Wisconsin School of Medicine and Public Health, UW Medical Foundation Centennial Building 4175, 1685 Highland Avenue, Madison, WI 53705, United States. [sparajuli@medicine.wisc.edu](mailto:sparajuli@medicine.wisc.edu)

**Telephone:** +1-608-2650152

**Received:** March 21, 2019

**Peer-review started:** March 24, 2019

**First decision:** June 7, 2019

**Revised:** July 13, 2019

**Accepted:** August 6, 2019

**Article in press:**

**Published online:**

**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

**© The Author(s) 2019.** Published by Baishideng Publishing Group Inc. All rights reserved.

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

Blazel JW, Turk JA, Muth BL, Parajuli S. Blessing and a curse of outpatient management of delayed graft function. *World J Transplant* 2019; In press

**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[1]. It is more commonly seen after deceased donor kidney transplantation with an estimated incidence of 30%[1,2].

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[3]. 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[4,5]. Longer CIT, over 20 h, is also associated with a higher incidence of DGF[6]. There is a higher risk of developing DGF following DCD kidney transplantation due to the presence of warm ischemia and reduced perfusion during procurement[7].

DGF is a costly complication and often leads to prolonged hospitalization. DGF recovery is most often seen within 7 to 10 d[8], 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[9]. 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[3,10,11]. 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, urine analysis, 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[12]. 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[13].

To assess the impact of this clinic on outpatient DGF management, Muth *et al*[14] 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[14]. 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[14]. 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 multidiscplinary 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. Center with a high volume of DGF may benefit from establishing a DGF clinic.

**REFERENCES**

1 **Siedlecki A**, Irish W, Brennan DC. Delayed graft function in the kidney transplant. *Am J Transplant* 2011; **11**: 2279-2296 [PMID: 21929642 DOI: 10.1111/j.1600-6143.2011.03754.x]

2 **Mannon RB**. Delayed Graft Function: The AKI of Kidney Transplantation. *Nephron* 2018; **140**: 94-98 [PMID: 30007955 DOI: 10.1159/000491558]

3 **Ojo AO**, Wolfe RA, Held PJ, Port FK, Schmouder RL. Delayed graft function: risk factors and implications for renal allograft survival. *Transplantation* 1997; **63**: 968-974 [PMID: 9112349 DOI: 10.1097/00007890-199704150-00011]

4 **Gupta A**, Chen G, Kaplan B. KDPI and donor selection. *Am J Transplant* 2014; **14**: 2444-2445 [PMID: 25155434 DOI: 10.1111/ajt.12930]

5 **Zens TJ**, Danobeitia JS, Leverson G, Chlebeck PJ, Zitur LJ, Redfield RR, D'Alessandro AM, Odorico S, Kaufman DB, Fernandez LA. The impact of kidney donor profile index on delayed graft function and transplant outcomes: A single-center analysis. *Clin Transplant* 2018; **32**: e13190 [PMID: 29314286 DOI: 10.1111/ctr.13190]

6 **Sert I**, Colak H, Tugmen C, Dogan SM, Karaca C. The effect of cold ischemia time on delayed graft function and acute rejection in kidney transplantation. *Saudi J Kidney Dis Transpl* 2014; **25**: 960-966 [PMID: 25193891 DOI: 10.4103/1319-2442.139865]

7 **Singh RP**, Farney AC, Rogers J, Zuckerman J, Reeves-Daniel A, Hartmann E, Iskandar S, Adams P, Stratta RJ. Kidney transplantation from donation after cardiac death donors: lack of impact of delayed graft function on post-transplant outcomes. *Clin Transplant* 2011; **25**: 255-264 [PMID: 20331689 DOI: 10.1111/j.1399-0012.2010.01241.x]

8 **Lim WH**, Johnson DW, Teixeira-Pinto A, Wong G. Association Between Duration of Delayed Graft Function, Acute Rejection, and Allograft Outcome After Deceased Donor Kidney Transplantation. *Transplantation* 2019; **103**: 412-419 [PMID: 29762458 DOI: 10.1097/TP.0000000000002275]

9 **Harhay M**, Lin E, Pai A, Harhay MO, Huverserian A, Mussell A, Abt P, Levine M, Bloom R, Shea JA, Troxel AB, Reese PP. Early rehospitalization after kidney transplantation: assessing preventability and prognosis. *Am J Transplant* 2013; **13**: 3164-3172 [PMID: 24165498 DOI: 10.1111/ajt.12513]

10 **Ravindra KV**, Sanoff S, Vikraman D, Zaaroura A, Nanavati A, Sudan D, Irish W. Lymphocyte depletion and risk of acute rejection in renal transplant recipients at increased risk for delayed graft function. *Am J Transplant* 2019; **19**: 781-789 [PMID: 30171800 DOI: 10.1111/ajt.15102]

11 **Patel SJ**, Duhart BT Jr, Krauss AG, Moore LW, Egidi MF, Amiri HS, Gaber LW, Gaber AO. Risk factors and consequences of delayed graft function in deceased donor renal transplant patients receiving antithymocyte globulin induction. *Transplantation* 2008; **86**: 313-320 [PMID: 18645496 DOI: 10.1097/TP.0b013e31817ef190]

12 **Parajuli S**, Reville PK, Ellis TM, Djamali A, Mandelbrot DA. Utility of protocol kidney biopsies for de novo donor-specific antibodies. *Am J Transplant* 2017; **17**: 3210-3218 [PMID: 28805293 DOI: 10.1111/ajt.14466]

13 **Salcido-Ochoa F**, Allen JC Jr. Biomarkers and a tailored approach for immune monitoring in kidney transplantation. *World J Transplant* 2017; **7**: 276-284 [PMID: 29312857 DOI: 10.5500/wjt.v7.i6.276]

14 **Muth BL**, Astor BC, Turk J, Mohamed M, Parajuli S, Kaufman DB, Mandelbrot DA, Djamali A. Outpatient Management of Delayed Graft Function Is Associated With Reduced Length of Stay Without an Increase in Adverse Events. *Am J Transplant* 2016; **16**: 1604-1611 [PMID: 26700736 DOI: 10.1111/ajt.13689]

**P-Reviewer:** Salcido-Ochoa F **S-Editor:** Dou Y **L-Editor: E-Editor:**

**Specialty type:** Transplantation

**Country of origin:** United States

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0