DELAYED GRAFT FUNCTION FOLLOWING LAPAROSCOPIC LIVE DONOR NEPHRECTOMY: A MULTIVARIATE ANALYSIS

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ABSTRACT

Objective: *This study was performed to define and investigate the incidence, risk factors, and clinical characteristics of delayed graft function (DGF) in laparoscopic live donor nephrectomy (LDN).* ***Material & methods:*** *We retrospectively analyzed the medical records of donor and recipient from our first 100 cases of laparoscopic LDN in Cipto Mangunkusumo General Hospital Jakarta, from November 2011 to February 2014. The criteria used to define DGF were the requirement for dialysis in postoperative week 1 and/or serum creatinine greater than 2.5 mg/dl at postoperative day 7. Patients who did not match any of these criteria were define as having normal renal allograft function.* ***Results:*** *The overall prevalence of DGF was 14%. Recipients body mass index, cold ischemia time, vascular anastomosis time, and total ischemia time were higher among the delayed graft function group, but no risk factors for DGF were significantly associated after multivariate analysis.* ***Conclusion:*** *The incidence of DGF in our study was in the range of that observed in previous studies. The factors that previously reported and believed as risk factors of DGF in laparoscopic LDN were not significantly associated with the development of DGF in our study.*

Keywords: *Delayed graft function, laparoscopic, live donor, nephrectomy.*

ABSTRAK

Tujuan: *Penelitian ini dilakukan untuk menentukan dan mengetahui kejadian, faktor risiko, dan karakteristik klinis delayed graft function (DGF) pada laparoscopik live donor nephrectomy (LDN).* ***Bahan & cara:*** *Kami menganalisis secara retrospektif rekam medis 100 kasus donor dan resipien transplantasi ginjal perdana yang dilakukan nefrektomi donor hidup secara laparoskopi di RSUPN Cipto Mangunkusumo Jakarta, dari November 2011 sampai Februari 2014. Kriteria yang digunakan untuk menentukan DGF adalah dilakukannya dialisis dalam minggu pertama pasca operasi dan/atau serum kreatinin lebih dari 2.5 mg/dl pada hari ke-7 pasca operasi. Pasien yang tidak memenuhi kriteria tersebut dianggap memiliki fungsi ginjal allograft yang normal.* ***Hasil:*** *Prevalensi DGF pada penelitian ini adalah 14%. Indeks massa tubuh resipien, cold ischemic time, lama anastomosis pembuluh darah, dan total waktu iskemia lebih tinggi pada kelompok DGF namun tidak ada faktor risiko yang signifikan terkait dengan DGF setelah dilakukan uji multivariat.* ***Simpulan:*** *Insiden DGF pada penelitian kami berada pada rentang yang dilaporkan oleh studi-studi sebelumnya. Faktor-faktor yang sebelumnya dilaporkan dan diyakini sebagai faktor risiko DGF pada nefrektomi donor hidup secara laparoskopi tidak terbukti pada penelitian kami.*

Kata kunci: *Delayed graft function, laparoskopi, donor hidup, nefrektomi.*

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INTRODUCTION

Delayed graft function (DGF) is usually defined as the need for dialysis within a week after renal transplantation.[1] Various definitions of DGF are used in the literature without a uniformly accepted technique to identify DGF.[2] The impact on graft survival of DGF is still controversial.[3] Some literatures report reduced long-term survival, whereas others have observed no relation between DGF and long-term impaired graft function.[3]

Delayed graft function commonly observed in deceased-donor renal transplantation, owing to the prolonged cold ischemia time.[1] However, many

published studies have investigated DGF in live donor nephrectomy (LDN) and the risk factors for DGF in LDN have not been established.[1]

Since the introduction of laparoscopic LDN in the mid~1990s, the procedure has been refined and adopted at several centers.[4] There are many advantages and limitations regarding laparoscopic LDN. The major advantage of this technique is decreased donor morbidity.[5] The advantages including less pain, shorter hospital stay, more rapid return to normal activities and improved cosmesis.[4,5] The limitations including a potentially longer operating time, longer warm ischemic time, and dependence on the learning curve of the surgeon.[4] The DGF after laparoscopic LDN affects 2-30% of recipients.[4-13] The risk factors for DGF in laparoscopic LDN have not been established.

OBJECTIVE

The present study was performed to define and investigate the incidence, risk factors, and clinical characteristics of DGF in laparoscopic LDN. To assess DGF we used the criteria as mention on previous study.[2]

MATERIAL & METHODS

We retrospectively reviewed donor and recipient medical records from our first 100 cases of laparoscopic LDNs performed in Cipto Mangunkusumo General Hospital Jakarta, from November 2011 to February 2014.

All donors underwent routine preoperative evaluation, including three-dimensional computed tomography and renal angiography. The rationale for donor kidney selection for laparoscopic LDN was identical to the standard principles used for open LDN. When the kidneys were equal, the left kidney was selected to take advantage of the longer left renal vein. However, if the left renal vascular anatomy was unfavorable compared with that of the right or if a right renal parenchymal lesion was identified, the right kidney was selected.[4]

All the kidneys were harvested laparoscopic transperitoneally. The donor placed in a modified lateral decubitus position, 4-port trocars were introduced transperitoneally. The abdomen was insufflated. The colon was mobilized and displaced medially. The White Line of Toldt and Gerota's fascia were opened and the renal pedicle was identified. Branches of the adrenal, gonadal and lumbar veins were clipped and divided. Intravenous fluid, mannitol and furosemide were given as required to help prevent pneumoperitoneum pressure induced oliguria. Before renal artery ligation, 5000 U of heparin were given intravenously. The renal vessels were controlled individually using clips for ligation. Care was taken to maintain adequate periureteral tissue to preserve ureteral vascularity, maximize renal vessel length, ensure adequate diuresis from the transected ureter before vascular ligation. The kidney was hand-extracted through muscle splitting Pfannensteil incision and flushed perfusion were performed immediately with Custodiol® solution and stored on ice. Recipient surgery was performed through a Gibson incision, with creation of end to side vascular anastomoses from donor's renal vessels to recipient's external iliac vessels and extravesical Lich-Gregoir ureteroneocystostomy guided by JJ-stent was also performed. We minimized the use of any nephrotoxic drugs during the perioperative period. Cefoperazone is the standard antibiotic we used for wound prophylaxis.

The criteria used to classify DGF were the requirement for dialysis in postoperative week 1 and/or serum creatinine greater than 2.5 mg/dl at postoperative day 7. Patients who did not match any of these criteria classified as having normal renal graft function. Body mass index (BMI) was calculated by weight in kilograms per height in square meters. The warm ischemia time was defined as the time from renal artery occlusion to kidney perfusion. The cold ischemia time was defined as the time from kidney perfusion to the start of revascularization. The vascular anastomosis time was defined as the time to anastomose the donor vessels into their respective recipient vessels.[4] The total ischemia time was defined as the sum of the warm ischemia, cold ischemia, and vascular anastomosis times.

Continuous numerical data, expressed as mean + standard deviation, were analyze using the unpaired t-test and Mann-Whitney test. Categorical data were analyze using the Fisher's exact test. Multivariate logistic regression model were used to identify significant risk factors associated with DGF. A p value of < 0.05 was considered as statistically significant. All statistical analyses were performed using SPSS version 16.0 for Windows.

Ethics Committee approval from Faculty of Medicine, Universitas Indonesia was obtained.

RESULTS

Of a total of 100 patients enrolled in this study 86 were classified as having normal renal graft function. There were 14 patients who qualified with the criteria of DGF category. The overall prevalence of DGF in this study was 14%.

The demographic comparisons for donors and recipients are listed in table 1. Mean recipients BMI was higher in DGF group compared with those in normal renal graft function group (27.2 ± 6.3 kgs/m^2 versus 22.1 ± 2.6 kgs/m^2; p = 0.077). However, there was no significant difference between these 2 groups. None of the other variables were found to be the risk factors for DGF. Table 2 presents the comparison of preoperative factors between normal renal graft function and DGF groups of recipients. None of them showed significant differences. Table 3 showed the comparison of intraoperative factors between normal renal graft function and DGF groups of recipients. None of them showed significant differences also.

Table 1. Demographic comparisons for donors and recipients.

	Outcome		P-Value
	Normal renal graft function	Delayed graft function	
% Number	86	14	-
Mean donor age ± SD	32.4 ± 9.8	33.0 ± 5.2	0.358*
Mean recipient age ± SD	48.2 ± 14.3	46.2 ± 16.5	0.632†
Mean donor BMI ± SD	23.8 ± 4.1	23.5 ± 4.3	0.762*
Mean recipient BMI ± SD	22.1 ±2.6	27.2 ± 6.3	0.077†
% Donor to recipient gender			
Male to female	16.3	14.3	1.000‡
Female to male	26.7	21.4	1.000‡
% Unrelated donor	72.1	85.7	0.346‡

* Mann-Whitney test † Unpaired t-test ‡ Fisher's exact test

Table 2. Comparison of preoperative factors between normal renal graft function and DGF groups of recipients.

	Outcome		P-Value
	Normal renal graft function	Delayed graft function	
Mean mmHg systole ± SD	140.6 ± 21.3	132.9 ± 30.9	0.272*
Mean mmHg diastole ± SD	85.1 ± 10.4	84.3 ± 17.2	0.450*
Mean hemoglobin ± SD	10.1 ± 1.8	10.1 ± 1.5	0.951†
Mean hematocrit ± SD	30.4 ± 5.6	30.5 ± 4.7	0.974†
Mean leucocyte ± SD	7804.8 ± 2939	7813.3 ± 2379	0.689*
Mean thrombocyte ± SD	219.5 ± 90.1	209.4 ± 44.4	0.840*
Mean serum ureum ± SD	76.7 ± 31.4	90.6 ± 41.8	0.307*
Mean serum creatinine ± SD	7.9 ± 3.2	7.8 ± 2.8	0.863*
Mean months dialysis duration ± SD	15.3 ± 20.1	29.2 ± 53.1	0.422*

* Mann-Whitney test † Unpaired t-test

Table 3. Comparison of intraoperative factors between normal renal graft function and DGF groups.

	Outcome		P-Value
	Normal renal graft function	Delayed graft function	
Mean mins donor operation ± SD	172.4 ± 37.9	185.7 ± 55	0.411*
Mean ml blood loss ± SD	259.7 ± 266.2	271.4 ± 160.2	0.318*
Numbers right/left kidney	20/66	0/14	0.066‡
% Multiple vessels	17.8	27.3	0.693‡

* Mann-Whitney test ‡ Fisher's exact test

Table 4. Comparison of ischemia times between normal renal graft function and DGF groups

	Outcome		P-Value
	Normal renal graft function	Delayed graft function	
Mean secs warm ischemia ± SD	365.1 ± 184.4	431.5 ± 238.5	0.286*
Mean mins cold ischemia ± SD	27.6 ± 12.1	31.7 ± 12.2	0.090*
Mean mins vascular anastomosis ± SD	44.8 ± 8.4	53.3 ± 10.2	0.001†
Mean mins total ischemia ± SD	78.2 ± 18	91.7 ± 21.1	0.017*

Bold indicates significance * Mann-Whitney test † Unpaired t-test

Table 5. Analysis of factors associated with postoperative DGF.

Variables	Univariate Analysis P-Value	Multivariate Analysis	
		OR (95% CI)	P-Value
Recipients BMI	.077	0.87 (0.62 -1.20)	0.388
Cold ischemia time	.090	0.93 (0.61 -1.44)	0.757
Vascular anastomosis time	.001	0.77 (0.45 -1.32)	0.346
Total ischemia time	.017	1.09 (0.70 -1.70)	0.689

The comparison of ischemia times between normal renal graft function and DGF groups are shown in table 4. The normal renal graft function group had shorter time of vascular anastomosis than did those of DGF group (44.8 ± 8.4 minutes versus 53.3 ± 10.2 minutes; p = 0.001); correspondingly, the total ischemia time was significantly shorter in the normal renal graft function group (78.2 ± 18 minutes versus 91.7 ± 21.1 minutes; p = 0.017). However, when these variables were fitted into a multivariate model, no difference remained significant (Table 5).

DISCUSSION

Laparoscopic LDN is an advanced procedure. However, it requires the integrity of renal parenchyma, renal vessels and ureter remain unharmed. In addition, the warm ischemia time must be kept short to maximize graft function postoperatively. Previous report documented no deleterious effects on immediate graft function with the laparoscopic LDN compared to the traditional open procedure.[12]

DGF is the term used to describe the failure of the transplanted kidney to function immediately after transplantation due to ischemia-reperfusion and immunological injury. It can be considered a form of acute kidney injury post-transplantation and is an important complication of kidney transplantation. DGF complicates post-transplant management, increases morbidity, prolongs patient hospitalization, and increases health care costs.[2] In addition to the well-known complications of acute kidney injury and dialysis, DGF predisposes the graft to both acute and chronic rejection, and increases the risk of chronic allograft nephropathy and premature graft loss.[2] The risk factors known to be associated with DGF can be divided into immunologic and nonimmunologic variables.[1]

Previous studies have already reported the rate of DGF after laparoscopic LDN. It affects 2-30% of recipients.[4-13] Recent study showed that the rate of DGF after laparoscopic LDN was 14%. This founding is between the range of previous studies.

Several studies have investigated risk factors for DGF in LDN in the terms of demographic and preoperative factors with various results. Sharma et al showed that donor age was significantly higher and diastolic blood pressure was significantly lower in the DGF group.[14] Kwon et al reported that recipient-donor body weight ratio was significantly higher in the DGF group.[15] Senel et al reported that the recipient-donor body weight ratio and donor age were significantly higher in the DGF group.[16] Abreu et al reported that recipient age and female donor kidneys into male recipients were significantly higher in the DGF group compare with non-DGF group.[5] In contrast, a study conducted by Park et al reported that none of the variables mentioned above had a significant differences.[1] Our study found that none of the variables had a significant differences also.

Previous study showed that donors and recipients body mass index did not have significant

differences between DGF and non-DGF groups.[5] Our study had a similar result with previous study. We found that donor and recipients body mass index did not significantly different between DGF and non-DGF groups. Park et al reported that there was no significantly different in the dialysis duration before transplantation between DGF group and non-DGF group.[1] This study had a similar finding with previous study. Mange et al cited that preemptive transplantation of kidneys from living donors without the previous initiation of dialysis is associated with longer allograft survival than transplantation performed after the initiation of dialysis.[17]

Mean donor operation time had reported by several studies, which had the range of 200 to 306 minutes.[5-7,10,18-21] Mean donor operation time on this study were 172.4 minutes in the non-DGF group and 185.7 minutes in DGF group. Our mean donor operation time was faster than previous studies. Abreu et al reported that there was no significantly different on the mean donor operation time between DGF and non-DGF groups.[5] Our study had a similar finding with previous study. Mean blood loss during operation had already reported by many studies, which had the range of 100 to 266 mililiters.[5-7,10,18,21,22] Mean blood loss in this study were 259.7 ml in the non-DGF group and 271.4 ml in the DGF group. We had a slightly more blood loss in the DGF group compared with previous studies. Abreu et al reported that there was no significantly different on the mean blood loss between DGF and non-DGF groups.[5] Our study showed similar finding with previous study.

Cooper et al reported that complex vascular anatomy is not a contraindication to laparoscopic LDN. Recipients with allograft with more than 2 arteries experience longer warm and cold ischemia times, greater incidence of DGF, and greater propensity for ureteral complications. They found that the rate of DGF among single, dual, and multiple arteries were not significantly different.[9] Sharma et al and Abreu et al showed that there was no significantly different in multiple arteries between DGF and non-DGF groups.[5,14] We found a similar finding with previous literatures.

The length of warm ischemia time had been reported with the range of 2.3 to 6.6 minutes.[5,7,18-20] Our study showed slightly longer warm ischemia times in the DGF group. Sharma et al and Abreu et al reported that there was no significantly different in the length of warm ischemia time between DGF and non-DGF groups.[5,14] In recent study, we found it similar with previous studies. Abreu et al found that there were significantly different in the length of cold ischemia time and total ischemia time between DGF and non-DGF groups.[5] In contrast, Park et al showed that no significant differences found in total ischemia time between DGF and non-DGF groups.[1] Our study had a similar finding with the study conducted by Abreu et al, we found that there was significantly different in the total ischemia time between DGF and non-DGF groups. In this study also showed that the length of vascular anastomosis time was significantly different between DGF and non-DGF groups. However, the multivariate model revealed that none of these variables were significantly associated as the risk factors of DGF.

CONCLUSION

The incidence of DGF in our study was in the range of that observed in previous studies. The factors that previously reported and believed as risk factors of DGF in laparoscopic LDN were not significantly associated with the development of DGF in our study, although they had significant value in the univariate analysis.

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