

# 7 Years Experience of Living Donor Kidney Transplantation in Indonesia: A Retrospective Cohort Study

**Maruhum Bonar H. Marbun, Endang Susalit, Vidhia Umami**

Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

**Corresponding Author:**

Vidhia Umami, MD. Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital. Jl. Diponegoro 71, Jakarta 10430, Indonesia. email: vidhiaumami@yahoo.com.

## ABSTRAK

**Latar belakang:** transplantasi ginjal di Indonesia sedang berkembang pesat pada beberapa tahun terakhir, namun data mengenai karakteristik dan kesintasan transplan belum tersedia. Di Indonesia, hanya donor hidup yang diperbolehkan, namun pencarian donor ini seringkali sulit. Penelitian ini bertujuan untuk mendapatkan angka kesintasan graft dan pasien, mendeskripsikan karakteristik resipien dan donor serta proses rekrutmen dan evaluasi dari transplantasi ginjal di Indonesia. **Metode:** studi dengan desain kohort retrospektif pada semua donor dan resipien di RSUPN Dr. Cipto Mangunkusumo (RSCM) Januari 2011 – Mei 2017. Hanya resipien pada Januari 2011 hingga Mei 2014 yang diikutsertakan dalam analisis kesintasan graft dan pasien 1 dan 3 tahun, datanya kemudian dideskripsikan menggunakan kurva Kaplan-Meier. **Hasil:** dari 492 data transplantasi ginjal didapatkan median usia donor 30 (17-66) tahun, 25,1% diantaranya terkait hubungan saudara; rerata usia resipien  $47 \pm 13.18$  tahun. Sebanyak 138 resipien diteliti lebih lanjut, lalu didapatkan kesintasan 1 tahun death-censored graft, all-cause graft, dan pasien sebesar 92%, 82,6 %, dan 87%. Kesintasan 3 tahun death-censored graft, all-cause graft, dan pasien sebesar 90,6%, 76,1% and 79,7%. Kurva Kaplan-Meier menunjukkan laju mortalitas tertinggi tampak pada bulan-bulan awal. **Kesimpulan:** angka kesintasan 1 tahun graft dan pasien adalah 92% dan 87%, sementara kesintasan 3 tahun graft dan pasien adalah 90,6% dan 79,7%. Hanya sebagian kecil donor yang terkait keluarga. Rekrutmen dan evaluasi donor hidup masih merupakan tantangan besar di Indonesia.

**Kata kunci:** evaluasi donor, kesintasan graft, kesintasan pasien, penyakit ginjal kronis, transplantasi organ.

## ABSTRACT

**Background:** kidney transplantation has been developing rapidly in Indonesia in recent years, yet data on transplants' characteristics and survival is still unavailable. In Indonesia, only living donors are permitted. Living donor are advantageous, but challenging to recruit. This study aimed to establish the graft and patient survival rates and to describe the characteristics of recipient and donor as well as the process of donor recruitment and evaluation of kidney transplantation in Indonesia. **Methods:** the study was a retrospective cohort on all donors and kidney transplant recipients at Cipto Mangunkusumo Hospital (CMH) from January 2011 to May 2017. Only recipients from January 2011 to May 2014 were included to establish the 1-year and 3-year graft and patient survival; which were described using Kaplan-Meier method. **Results:** data from 492 kidney transplant procedures were obtained (donor median age, 30 (17 – 66) years; 25.1% were family-related. Recipients mean age, 47 (SD 13.18 years). Data from total of 138 kidney transplant recipients were further analyzed. The 1-year death-censored graft survival, all-cause graft survival and patient survival were 92 %, 82.6 % and 87%. The

3-year death-censored graft survival, all-cause graft survival and patient survival were 90.6%, 76.1% and 79.7%. Kaplan-Meier's curve showed the highest mortality rates occurred in the early months. **Conclusion:** the 1-year graft and patient survival rate were 92% and 87%. The 3-year graft and patient survival rate were 90.6% and 79.7%. Only small percentage of donor were family-related. Living donor recruitment and evaluation are still a big challenge in Indonesia.

**Keywords:** chronic kidney diseases, donor evaluation, graft survival, organ transplantation, patient survival.

## INTRODUCTION

The definitive treatment for end-stage renal disease (ESRD) is renal replacement therapy, which consists of hemodialysis, peritoneal dialysis, and kidney transplant.<sup>1</sup> Kidney transplant is one of the best choices in renal replacement therapy because it can improve long-term survival and quality of life patients' compared with dialysis.<sup>2</sup>

In developed countries, kidney transplant has become the primary choice of therapy for patients with ESRD.<sup>3</sup> In the United States, in 2013, there have been 17,600 kidney transplants.<sup>4</sup> In Indonesia, kidney transplantation is growing rapidly in these few years, particularly in some well-known healthcare centers such as Cipto Mangunkusumo Hospital (CMH). In the last 7 years, there have been 500 kidney transplantations in CMH.<sup>4</sup>

All kidney transplantations carried out in Indonesia were from living donors.<sup>1</sup> It is considered that living-donor kidney transplantation offers better result than cadaveric donor. The main reasons for these advantages are that living donors are selected carefully from healthy individuals and the organs are not exposed to haemodynamic instability, sepsis, or nephrotoxic agents, as are those of cadaveric donors during brain death. Despite some advantages of living donors, the number of donors, especially family related ones are limited and it has become a problem for countries which only permit living donors. Furthermore, the 1-year survival rate of post-transplant patients in various countries was quite high, but the survival rate decreased in the next several years.<sup>5</sup> Adekoya et al<sup>2</sup> reported that there was a decrease in graft survival rate from 80.4% in the first year to 67.7% in 3 years after transplantation. Similar decrease also occurred in patient survival rate. It declined from 91.9% in the first year to 82.1% in 3 years after transplantation.

Hashiani et al<sup>6</sup> conducted a study following transplant patients for 10 years and concluded that the trend of survival rate also decreased. In the study, the one year graft survival was 96.6% and decreased to 93.7% within 3 years. The number of survival of the graft tends to decrease at the 5<sup>th</sup>, 7<sup>th</sup> and 10<sup>th</sup> year, respectively to 88.9%, 87.1%, and 85.5%. Although it was considered that graft and patient survival rate will decrease every year, the difference in the percentage of graft and patient survival in each country is different.

The aim of this study is to establish the characteristics of recipient and donor of kidney transplantation in CMH and the process of donor recruitment and evaluation of kidney transplantation in Indonesia. In addition, this study also aimed to determine the 1-year and 3-year survival rate in CMH. This study is expected to be a reference to develop and improve the success rate of kidney transplantation in Indonesia through better management and to initiate the establishment of government organization for kidney transplantation.

## METHODS

This was a retrospective cohort study which were obtained from patients' medical record at Cipto Mangunkusumo Hospital from 2011 to 2017. The subjects of this study were 492 patients who had transplantation from 2011 to May 2017, with consecutive sampling technique. All transplantation patients aged more than 16 years old were included.

To establish the 1-year and 3-year survival rate, only recipients from January 2011 to May 2014 were included. The precise time of transplant was considered as "initial event". The time of irreversible rejection of transplant in which patient needs dialysis and/or the time when patients die within 1 year and 3 years were considered as the "end-point event". All patients

who were lost to follow up were censored. Kaplan - Meier method were used to determine the survival rate. Collected data were processed using SPSS version 17.0, manufactured by IBM. The basic characteristics and clinical research subjects was presented in tabular form. This study had been approved by ethical committee of Faculty of Medicine, Universitas Indonesia and Cipto Mangunkusumo General Hospital.

## RESULTS

In general, there were 492 kidney transplantation procedures performed at Cipto Mangunkusumo GHospital from January 2011 to May 2017. For about 9 patients under 16 years and 9 patients whose data were not found in the medical record were excluded. For survival data analysis, there were 30 censored patients and 108 patients who were observed within 3 years after transplantation (**Figure 1**).

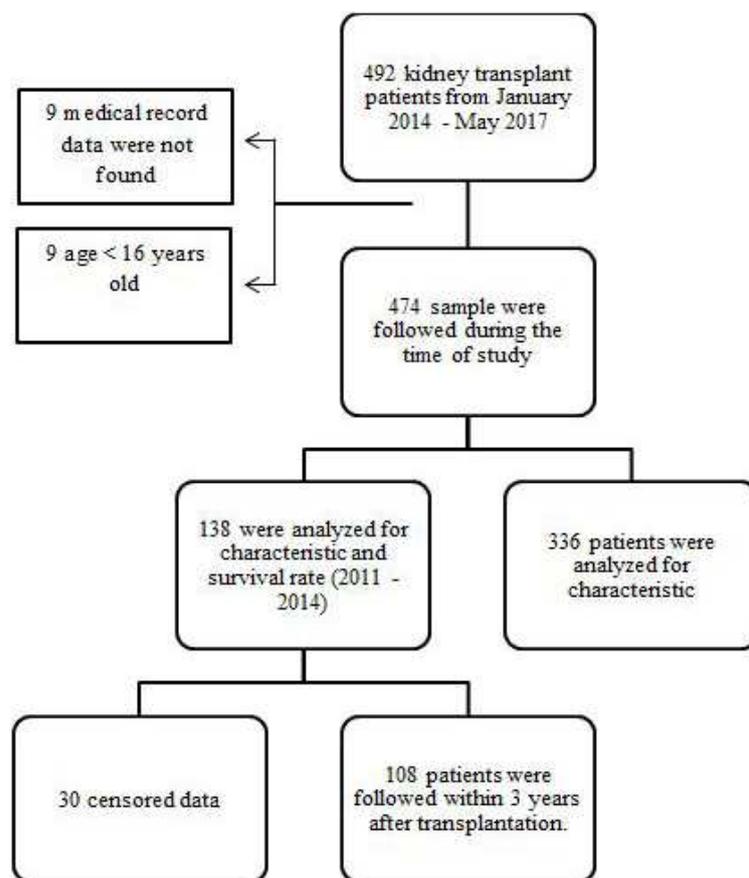
All recipients received kidneys from living donors. A total of 335 recipients (70.7%) and

317 donors (66.9%) were male. The mean age of transplant recipients was 47 (13.18) years old and the median age of donor at transplantation time was 30 years old (17 - 66 years).

There were 13 patients (2.7%) who had pre-emptive transplantation. There were 16 patients (3.4%) who had undergone peritoneal dialysis before transplantation, while the rest had undergone hemodialysis. The most frequent cross-match results were 20-30% (52.1%) and there were 57 patients (12.0%) that have cross-match results of >30-40%. First-degree family relationships with recipients (older siblings, siblings, parents, or children) were only found in 119 patients (25.1%).

### Graft and Patient Survival in 1 Year After Transplantation

Graft survival was defined as the percentage of the functioning graft. In the analysis, graft survival was divided into two definitions, that was death censored graft survival where patients who died with a functioning graft were



**Figure 1.** Research subjects surveillance

**Table 1.** Characteristics of kidney transplant patients from January 2011 – May 2017

Characteristics (N=474)	Value
Recipient age (years), mean (SD)	47 (13.18)
Donor age (years), median (range)	30 (17 – 66)
Recipient sex, n (%)	
- Male	335 (70.7)
- Female	139 (29.3)
Donor sex, n (%)	
- Male	317 (66.9)
- Female	157 (33.1)
Dialysis type, n (%)	
- Hemodialysis	445 (93.9)
- Peritoneal Dialysis	16 (3.4)
- Pre-emptive transplantation	13 (2.7)
Cross-matching, n (%)	
- 0 – 10 %	4 (0.8)
- 10 – 20 %	69 (14.6)
- 20 – 30 %	247 (52.1)
- > 30 – 40 %	57 (12.0)
- Data is not available	97 (20.5)
Recipient-donor relationship, n (%)	
- Related	119 (25.1)
- Not related	355 (74.9)

considered to have a functioning graft and all-caused graft survival where patients who died with functioning graft were considered to have a failed graft. Patient survival was defined as the percentage of patients who still alive in 1 year or 3 years after transplantation.

In the first year after transplantation, 11 of 138 patients (8%) experienced graft failure, therefore the 1-year death censored graft survival rate was 92%. Five of them died and six patients were still alive within 1 year after transplantation. Two patients died after the first year and 4 patients underwent hemodialysis again. In this study, there were 13 patients who died with a functioning graft, thus the all-cause graft survival rate was 82,6%. Furthermore, eighteen patients died within 1 year after transplantation, so the 1- year patient survival rate was 87%.

#### Graft and Patient Survival in 3 Years After Transplantation

Within 3 years after transplantation, 13 of 138 patients (9.4%) had graft failure, therefore the 3-year death censored graft survival rate was

90.6%. Eight of them died within 3 years after transplantation. Five patients were alive until the end of study, four of them were required to undergo hemodialysis again and one patient had another transplantation.

In this study, there were 20 patients who died with a functioning graft until the third year after transplantation. Therefore, all-cause graft survival rate was 76.1%.

Twenty eight patients of 138 recipients died within the first 3 years, thus the 3-year patient survival rate was 79.7 %. Among 28 patients, eight were preceded by graft failure, while 20 (71,5%) patient's death were caused by other causes (death with functioning graft), such as irreversible sepsis or cardiovascular events, either acute myocardial infraction, pulmonary embolism, stroke, or cardiogenic shock.

The results of graft and patient survival both in the first 3 years and at the end of the study can be seen in **Table 2**.

**Table 2.** Graft and patient survival rate in 1 year and 3 years after transplantation

	1-year	3-year
Death censored graft survival	92.0%	90.6%
All-cause graft survival	82.6%	76.1%
Patient survival	87.0%	79.7%

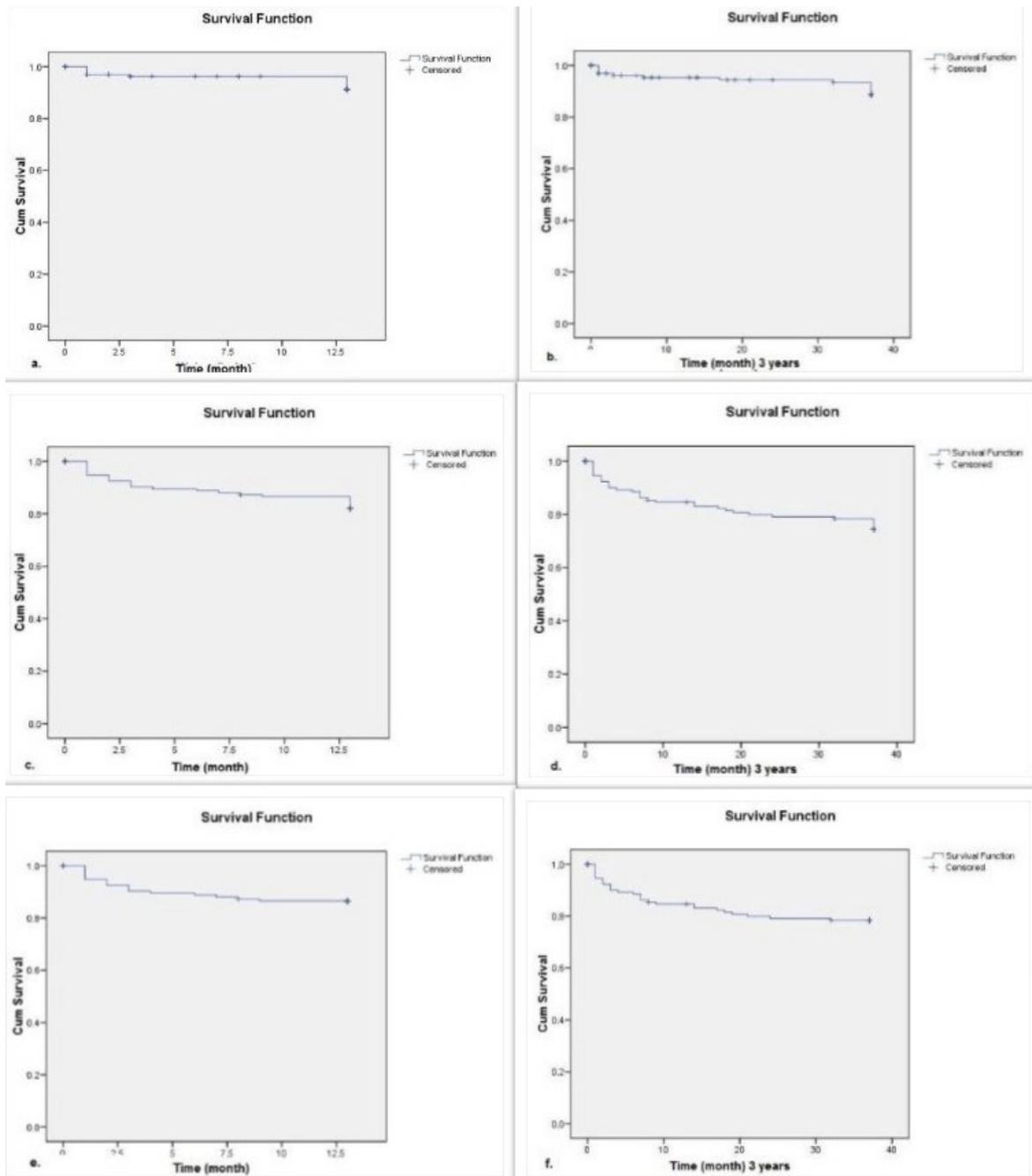
#### Kaplan-Meier Survival Curve

The graft and patient survival rate in 1 year and 3 years after transplantation are illustrated by the Kaplan-Meier curve, as shown in the **Figure 2**.

#### DISCUSSION

There was a decrease in survival rate in the first 3 years compared to the first year, from 92% to 90.6% for graft survival and from 87% to 79.7% for patient survival.<sup>1</sup> The same pattern also occurred in the United States and it showed the same results in Indonesia. In the United States in 2012 the 1-year graft survival with living donors was 97% and the 5-year graft survival was 85%.<sup>4</sup>

Some researches in Asia reported various results, but there were similar trend of declining survival rates in the following years. Data from Thailand national registry reported that the



**Figure 2.** Kaplan-Meier curve. a: 1-year death censored graft survival; b: 3-year death censored graft survival; c: 1-year all-cause graft survival; d: 3-year all-cause graft survival; e: 1-year patient survival, f: 3-year patient survival

1-year survival of patients with living donors from 2009-2013 was 99.0% and this number decreased in the 5-year survival to 95.8%.<sup>7</sup> Likewise, the 1 year graft survival with living donors from 2009-2013 decreased from 97.8% to 91.6%. From the Malaysian national registry until 2014, the survival of 1-year graft survival with living donors was 93% and decreased to

88% in 3 years after transplantation. The decline also occurred in 3-year patient survival to 94% from 96% in the first year after transplantation.<sup>8</sup> A study conducted in Iran also stated that there was a decrease in graft survival rates from 1 year to 3 years post transplantation (93.8% to 86.8 %).<sup>9</sup>

Some factors that were suspected to affect

graft and patient survival had been studied previously. Factors from recipients were serum creatinin levels ( $p=0.0001$ ), comorbidity (diabetes mellitus  $p<0.01$ ), and surgical complications ( $RR=5.64$ ).<sup>9-11</sup> Otherwise, there were some factors from donor such as unrelated donor relations ( $P=0.0002$ ).<sup>10</sup> In Indonesia, because all donors are living donors and using the same immunosuppressant protocol, the dominant factors from recipients that may affect survival include comorbidity, infectious disease, and unrelated donors. Age and kidney function both on recipients and donors will certainly affect graft resistance and mortality. Other factors that should be considered are patient compliance after transplantation such as adherence to immunosuppressant drug and healthy lifestyle. In some circumstances, patient compliance may be affected by the problem of unequal drug availability and considerable distance between patient's residence and transplant center.

This is the first study in Indonesia that observed the 7-year experience of kidney transplant in Indonesia. This study is expected to establish the characteristics of kidney transplant in Indonesia. The strength of this study was the study population was from the largest transplantation center that can represent the population of kidney transplant patients in Indonesia. This study used a total sampling technique so that only a few patients were excluded. This study has several weaknesses. This research did not analyze the risk factors of graft and patient survival. This study also did not analyze the cause of death in patients who died. It is expected in the future to do further research to assess the survival at a longer period of time.

## CONCLUSION

The 1-year graft and patient survival rate were 92% and 87%. The 3-year graft and patient survival rate were 90.6% and 79.7%. Only small percentage of donor were family-related. Living donor recruitment and evaluation are still a big challenge in Indonesia.

## ACKNOWLEDGMENTS

The authors wish to thank the donors, recipients, and the organ transplantation team in Cipto Mangunkusumo Hospital for their participation enabled the development of this study.

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