



# The Correlation Between Total Ischemic Time with Length of Hospitalization in Kidney Transplantation: A Single Centre Report

Eriawan Agung Nugroho<sup>1)</sup>, Muhamad Azwin Kamar<sup>2)</sup> and Dila Junita<sup>2)</sup>

<sup>1)</sup>Division of Urology, Dr Kariadi General Hospital/Medical Faculty Diponegoro University, Semarang Indonesia

<sup>2)</sup>Department of Surgery, Dr Kariadi General Hospital/Medical Faculty Diponegoro University, Semarang Indonesia

Email: [eriawanspu@gmail.com](mailto:eriawanspu@gmail.com)

**Abstract** - Kidney transplantation is recognized as an advanced modern therapeutic modality for patients with end stage renal failure. Cold ischemic time (CIT) has been found as an important independent risk factor for delayed graft function (DGF) in kidney transplantation. Recent studies suggested that prolonged warm ischemic time (WIT) may decrease graft's survival in living kidney transplantation donor. The study is aimed to evaluate the total ischemic time during recipient surgery and accessed its contribution for hospitalization time in kidney transplantation patients. This is an observational, cross sectional study. The data was collected from medical record of patient who underwent kidney transplantation from January 2014 until December 2018 at Kariadi General Hospital Semarang. There were 28 patients, 18 were male and 10 were female. Total ischemic time was compared with length of hospitalization. Data was analyzed with Spearman test in SPSS version 23. The study showed that total ischemic time was significantly correlated with hospitalization time ( $p < 0.001$ ). However, donor's age did not affect prolonged total ischemic time with  $p = 0.673$ , which is not significant (significant if  $p < 0.05$ ). In conclusion, total ischemic time has a significant correlation with hospitalization time. In contrary, no significant correlation between donor's age and prolonged total ischemic time.

**Keywords** — Total Ischemic Time, Length of Hospitalization, Kidney Transplantation

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## I. INTRODUCTION

Kidney transplantation is recognized as an advance modern therapeutic that provides high-quality life for patients with end-stage renal disease (ESRD), in more than 80 countries (Jha *et al.*, 2013; Garcia *et al.*, 2012). From 1965 to 1980, survival patients increased to 90% and transplant survival increase from less than 50% in one year to at least 60% after the first donor kidney transplant died, based on immune suppression with azathioprine and prednisolone (Kyles, 2017).

In the past two decades, cold ischemic time (CIT) was found as an important independent risk factor for delayed graft function (DGF). DGF is also related to the patient postoperative survival. These data were associated with longer hospitalization and the use additional resources in dialysis (Kim *et al.*, 2009). The latest information showed that warm ischemic time (WIT) can decrease graft survival in kidney transplants living donors.

The aim of this study was to evaluate the total ischemic time during the recipient's surgery and accessed its

contribution for length of hospitalization, and also to evaluate additional factors related to length of stay in kidney transplantation patients.

## II. MATERIAL AND METHOD

This is an observational, cross sectional study. The data was collected from medical record of patient who underwent kidney transplantation from January 2014 until December 2018 at Kariadi General Hospital Semarang.

The subject of this study were all patients who underwent kidney transplantation that recorded in medical record from January 2014 until December 2018. Exclusion criteria was patients who cancel underwent the kidney transplantation.

The extracted data was included recipient's age, gender, body mass index (BMI), body weight, calculated panel reactive antibody (cPRA), incompatibility of human leukocyte antigen (HLA), relation to the donor, surgery date, length of stay, comorbid factors (diabetes mellitus, hypertension, heart disease, stroke, depression, tuberculosis,

chronic gastritis and others), left Ventricle ejection fraction (LVEF), blood laboratory (hemoglobin, leukocytes, platelets, urea, creatinine , Na, K, Cl), culture (blood, urine, drainage fluid), the number of arteries and veins in the donor.

Total ischemic time (in hours) is defined as the time of disruption of the renal artery or aortic clamp, until the time of release of clamps at the renal artery in the recipient. The total ischemic time was recorded and evaluate whether it affected the length of stay. Data was analysed with *Spearman test* in SPSS version 23 (significant if  $p < 0.05$ ).

### III. RESULT AND DISCUSSION

The data was collected from medical record of patients who underwent kidney transplantation from January 2014 until December 2018 at Kariadi General Hospital Semarang. The total respondents were 28 patients, 18 were male and 10 were female.

Spearman’s test was used to evaluate the correlation between total ischemic time and length of hospitalization. Table 1 shows that there is a significant correlation between total ischemic time and length of hospitalization, with  $r = 0.961$  (positive and significant).

Table 1. Correlation between length of hospitalization and total ischemia time

Variable	p <sup>¶</sup>	r	Result
Length of Hospitalization Total Ischemic Time	<0.00	0.96	Significant, positive, Very strong

¶ Spearman’s correlation

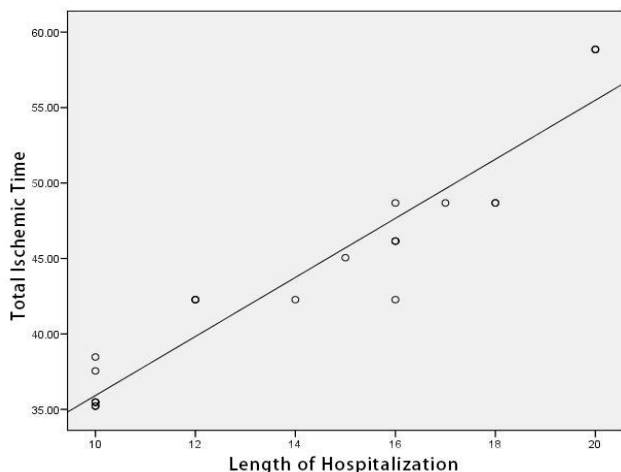


Figure 1. This chart shows the correlation between length of hospitalization and total ischemic time

Patient’s age is used as an additional variable that evaluated in this study. Table 2 shows that correlation between the age and total ischemic time with  $r=-0.09$  with an insignificant impression (significant if  $p < 0.05$ ).

Table 2. Correlation between age and total ischemia time

Variable	p <sup>¶</sup>	r	Result
Age Total ischemic	0.67	-0.09	Not significant

¶ Spearman’s correlation

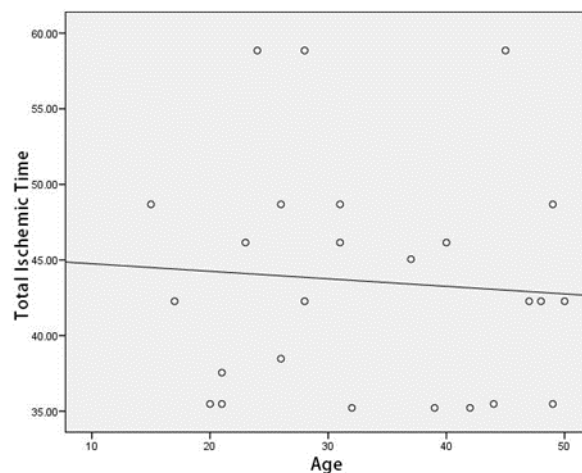


Figure 2. This chart shows the correlation between patients age and total ischemia time

Normality test for total ischemic time based on gender was normal in female group (*shapiro-wilk test*) and in male group showed a normal data distribution based on Mann Whitney test ( $p=0.60$ , statistically significant).

Table 3. Normality test based on gender

Gender	Total Ischemic		p <sup>£</sup>
	Mean ± SD	Median (min – max)	
Male	42.66 ± 6.60	42.27 (35.22 – 58.85)	0.04
Female	45.98 ± 9.76	45.05 (35.22 – 58.85)	0.20*

\* Normal ( $p > 0.05$ ); £ *Shapiro-wilk*

#### Total Ischemic Time related to Length of Hospitalization

Total ischemic time is defined as the time of the donor renal artery interruption or aortic clamp, until the time of release the clamp on the renal artery in the recipient (in hours). Total ischemic time is a combination of cold ischemic ime (CIT) and warm ischemic time (WIT) (Wong *et al.*, 2017). Many studies have shown that CIT is an independent risk factor of delayed graft function (DGF) (Van *et al.*, 2011; Kayler and Srinivas, 2011), the longer CIT is associated with increase of DGF and longer length of stay which consequently increase the cost of transplantation (Serrano, 2019). CIT triggers a dangerous effect cascade that strengthen by blood reperfusion. These injuries cause an immune and inflammation response that potential to produce DGF, alloimmune reactivity and progressive pathological changes (Ponticelli, 2015).

Warm ischemia time is defined as the period starting from organ withdrawal from ice storage and ending with initiation of graft reperfusion, depending on the time of renal vessel anastomosis. A prolonged WIT not only has a detrimental effect on renal allograft outcome immediately after transplantation, but also effects long-term graft function (Heylen *et al.*, 2015; Tennankore *et al.*, 2016). Prolonged WIT is also associated with longer time of hospitalization after transplantation (Marzouk *et al.*, 2013) and long-term graft survival disruption after donations from living donor (Hellegering *et al.*, 2012) and also deceased donor (Weissenbacher *et al.*, 2015) on a kidney transplant.

Prolonged ischemia can cause an increased risk of delayed graft function (DGF), reduce allograft function at 12 months after transplantation and increase the risk of overall graft loss and death. In previous studies, it was found that exposure to increased total ischemic time associated with various graft results could be detrimental to kidney transplant recipients (Wong *et al.*, 2017). However, these observations were inconsistent but could be predicted based on donor age and donor death pathways. We can't conclude and correlate with our research because in those studies used deceased donor. In our analysis with *Spearman test*, there was significant result between the prolonged total ischemic time resulted in longer length of hospitalizations.

Another study showed that the total ischemic time of 36.9 minutes has a mean length of stay 11 days (10-14 days) (Supit *et al.*, 2019), this is in line with our finding which showed that the increase of total ischemic time associated longer time of hospitalization. Another research with a larger sample size of 7452 patients stated that recipients with a total ischemic time of > 14 hours increased the risk the delayed graft function (DGF) compared to groups with a total ischemic time of < 14 hours (Akkinia *et al.*, 2009). Delayed Graft Function is a condition where recipients need dialysis > 7 days (Kim *et al.*, 2009; Akkinia *et al.*, 2009; Chang *et al.*, 2007) after the transplant procedure, so DGF is associated with an increase in patient length of stay (Marzouk *et al.*, 2013; Yarlagaadda *et al.*, 2008).

#### Donor's Age related to Total Ischemic Time

The kidneys of older donors and with comorbidities currently give important contribution. Unlike kidney of younger donors, older kidneys are far more susceptible to the effects of prolonged cold ischemia time and subsequent ischemic reperfusion injury, as result of intense inflammatory response which can further endanger this vulnerable donor graft (Wong *et al.*, 2017). Older kidneys also have fewer functional reserves, therefore this intense initial inflammatory response can accelerate damage to these kidneys (Kementrian Kesehatan RI, 2007). In contrary, to the calculation of our research analysis, age was not proven to affect the extension of total ischemic time. The age factor of the donor does not cause long periods of operation when freeing the renal artery, renal vein, or ureter, or even making the total time of ischemia long, and does not affect the length of stay in hospitalization (Kementrian Kesehatan RI, 2007).

In a study where the average age of donors was 46.1 (24-64) years, the mean total ischemia was 36.9 hours (Supit *et al.*, 2019). In another cohort study, there were two groups based on cold ischemic time (CIT), the group with CIT < 14 hours has a donor age of 43 years with a mean Total Ischemia Time of 10.0 hours. Groups with CIT > 14 hours had a mean age of 42.5 years with a mean total ischemic time of 17.7 hours (Chang *et al.*, 2007). This shows that the age of donors did not have a significant effect on ischemic time in line with our study.

#### IV. CONCLUSIONS

In this study, we found a significant correlation between total ischemic time and the length of hospitalization after

surgery in kidney transplant patients. There was no significant correlation between the age of the donor and length of stay.

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