의학석사 학위논문

Effect of Post-transplant Glycemic Control on Long-term Clinical Outcomes in Kidney Transplant Recipients

-A Multicenter Cohort Study in Korea-

신장이식 환자에서 이식 후 혈당조절이 장기적 예후에 미치는 영향

-다기관 코호트 연구-

2014 년 10 월

서울대학교 대학원

임상의과학과

신 나 라

A thesis of the Degree of Master

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October 2014

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지도교수 김 연 수

이 논문을 의학석사 학위논문으로 제출함

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(-A Multicenter Cohort Study in Korea-)

by

Nara Shin

A thesis submitted to the Department of Clinical Medical Sciences in partial fulfillment of the requirements for the Degree of Master of Clinical Medical Science at Seoul National University College of Medicine

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Approved by Thesis Committee:

Professor _____Chairman

Professor _____Vice chairman

Professor _____

ABSTRACT

Introduction Diabetic nephropathy is the leading cause of end stage renal disease (ESRD). The number of kidney transplantations due to diabetic nephropathy is increasing and there is debate on glycemic control after kidney transplantation. In this study, I used a multi-center database to determine the relationship between post-transplant glycemic control and the outcomes of kidney transplantation in patients with diabetic nephropathy.

Methods: I conducted a retrospective chart review of kidney transplant recipients(KTRs) with diabetic nephropathy from three tertiary hospitals to analyze the association between post-transplant glycemic control and the clinical outcomes of graft failure, including patient death and biopsy-proven acute rejection (BPAR). Among 3,538 KTRs, a total of 476 patients received kidney transplantation because of diabetic nephropathy. I assessed time-averaged glucose level and hemoglobin A1c (HbA1c) for 36 months after kidney transplantation.

Results: Mean time-averaged glucose and HbA1c levels were

147 ± 46 mg/dl and 7.7 ± 1.5 %, respectively. The highest quartile of baseline glucose was related to poor graft outcomes and the 3rd quartile of time-averaged HbA1c was associated with significantly better graft outcomes than the 1st, 2nd or 4th quartiles. On the other hand, time averaged glucose levels were not significantly related to graft outcomes. There were no significant differences in the risk of BPAR across the 4 quartiles of glucose and HbA1c.

Conclusions: Strict glycemic control post-transplantation is not necessary for successful outcomes but poor glycemic control is associated with poor graft outcomes. There was no significant relationship between post-transplant glycemic control and BPAR.

Keywords: diabetic nephropathy, kidney transplantation, glycemic control, outcomes, graft failure, acute rejection

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LIST OF ABBREVIATIONS

HbA1c, hemoglobin A1c

ESRD, end-stage renal disease

HR, hazard ratio

SD, standard deviation

BPAR, biopsy-proven acute rejection

KTR, kidney transplantation recipient

INTRODUCTION

Diabetic nephropathy is the leading cause of end stage renal disease (ESRD). In the United States Renal Data System (USRDS) 2013 annual report, diabetes was the most common cause of ESRD at nearly 50% of total incident dialysis (1). According to the 2013 ESRD Registry in Korea, the incidence rate of diabetes in ESRD is 48.0%. There are three choices for renal replacement therapy (RRT): hemodialysis, peritoneal dialysis and kidney transplantation. Hemodialysis is the most common RRT modality, however, the rate of kidney transplantation is on the rise. Moreover, when compared to hemodialysis, kidney transplantation in patients with diabetic nephropathy is associated with better outcomes in terms of both mortality and cardiovascular complications such as coronary artery diseases and peripheral vascular events(2). In the United States, the prevalence of diabetic nephropathy in kidney transplantation patients was 27.6% in 2002 and 28.9% in 2012; diabetic nephropathy was the main cause of primary renal disease (3).

Poor glycemic control in diabetic patients without nephropathy

is a well-known risk factor for cardiovascular(4) and all-cause mortality (5). Also, compared to other causes of primary renal disease, diabetic nephropathy is associated with poor outcomes in terms of cardiovascular complications and mortality in patients with ESRD (6). Although successful kidney transplantation decreases cardiovascular morbidity and mortality compared to chronic dialysis therapy, diabetes is still a risk factor for poor outcomes among kidney transplant recipients (KTRs) (7, 8).

The American Society of Transplantation (ATC) published guidelines for the care of KTR in 2009. They recommended targeting HbA1c around 7.0-7.5% and avoiding HbA1c $\leq$ 6.0%, especially if hypoglycemic reactions are common in the patient(9). In the general diabetic populations, it is recommended to target HbA1c < 7.0% and less stringent HbA1c targeting (<8%) is recommended in the advanced diabetic population with complications such as microvascular or macrovascular disease(10). Diabetic nephropathy is an advanced microvascular complication; optimizing glycemic control is needed to slow the progression of nephropathy. But glycemic control in KTRs is still up for debate. In a randomized

control trial (RCT) of glycemic control in a cohort of type I diabetic KTRs, the standard treatment group showed a more than twofold increase in mesangial matrix expansion (an indicator of diabetic nephropathy) compared with an optimized treatment control group. However, the optimized group showed a higher incidence of severe hypoglycemic episodes than the standard treatment group(11). Recently, one study revealed that poor pre-transplant glycemic control is associated with decreased post-transplant survival (12). In this study, pre-transplant time-averaged HbA1c ≥ 8% appeared to be associated with higher all-cause and cardiovascular mortality, but not with post-transplant graft outcomes or delayed graft failure. Moreover, this study showed no evidence to recommend intensive glycemic control after kidney transplantation. Wiesbauer et al. reported that maximum glucose levels but not HbA1c predicted survival in diabetic patients who underwent kidney transplants (13). Ramirez et al. evaluated the association between preoperative and chronic glycemic control and clinical outcomes such as graft rejection, infection and hospital admission after kidney transplantation (14). Their results showed that in the first 12 months after kidney

transplantation, perioperative or chronic glycemic control was not associated with post-transplant outcomes. As such, it seems that near normal glycemic targets are not necessary for managing hyperglycemic after kidney transplantation; the effect of post-transplant glycemic control on long-term clinical outcomes was not clearly determined.

The objective of this study was to examine the association between post-transplant glycemic control and long-term clinical outcomes of transplantation (graft survival and graft rejection). I hypothesize that poor glycemic control after kidney transplantation is associated with post-transplant graft survival and rejection.

MATERIALS AND METHODS

1. Patients

I performed a multicenter cohort study including patients admitted to three tertiary hospitals: Seoul National University Hospital, Asan Medical Center University of Ulsan College of Medicine, and Kyungpook National University Hospital. A total of 3,538 adult KTRs aged ≥18 years who underwent transplantation between 1997 and 2011 were included in this study. The present study was performed in accordance with the ethical standards of the Helsinki Declaration and was approved by each hospital's institutional review board.

2. Data collection

Patient characteristics were collected from a review of medical records. Transplant-related variables included age; gender; body mass index; primary cause of kidney failure; dialysis modality and duration; type of immunosuppressant; and history of pre-transplant hypertension, ischemic heart disease, and cerebrovascular disease. Pre-transplantation laboratory values

for glucose, HbA1c and hemoglobin were obtained, and every 3months follow up for glucose and HbA1c values were obtained. In addition, donor-related variables, including age and donor type were reviewed.

3. Outcomes

The primary endpoint was graft failure in transplant recipients. Graft failure was defined as composite of graft dysfunction that necessitated new renal replacement therapy after transplantation or patient death, which included death with functioning graft. The secondary outcome was a biopsy-proven acute rejection (BPAR) defined as a clinically meaningful acute rejection proven by kidney biopsy. Acute rejection episodes which were revealed in a protocol biopsy but not treated were not included.

4. Statistical analysis

To investigate the effect of glycemic control on the outcomes, a comparison of outcomes among 4 quartiles of glucose and HbA1c was performed. Continuous variables were reported as means and standard deviations, and categorical variables were

presented as frequencies with percentages. Continuous variables such as recipient and donor age and dialysis duration were compared using one-way ANOVA; categorical variables, such as proportion of comorbidities, cause of ESRD, and previous RRT modality, were compared using the Chi-square or Fisher exact test. The significance threshold for all analysis was set at $p < 0.05$. The independent risk factors for graft and patient survival were analyzed using multivariate Cox proportional hazard regression models. Appropriate covariates that were statistically significant in the univariate Cox proportional hazard regression analysis were included. All the variables were analyzed using the IBM SPSS software package (version 20.0; Armonk, NY, USA).

RESULTS

Baseline Patient Characteristics

During the study period, 3,538 patients underwent kidney transplantation. The number of kidney transplants has increased each year and the proportion of kidney transplantation due to diabetic nephropathy has also increased (Figure 1). Among 3,538 KTRs, a total of 476 patients received kidney transplantation because of diabetic nephropathy. Clinical, demographic and laboratory characteristics of patients are summarized in Table 1.

Data was collected for patients with diabetic nephropathy from time of transplant to 36 months follow up. Of the 476 patients included in the data analysis, the majority were male (66.9%) and mean age at time of transplantation was 50 ± 10.2 years. In addition, 43.3% of patients received living-related transplants, 32.3% living-unrelated transplants, and 24.4% deceased-donor transplants. The mean HbA1c before transplantation was 7.5 ± 1.7 % and the mean random glucose level was 194 ± 113 mg/dl.

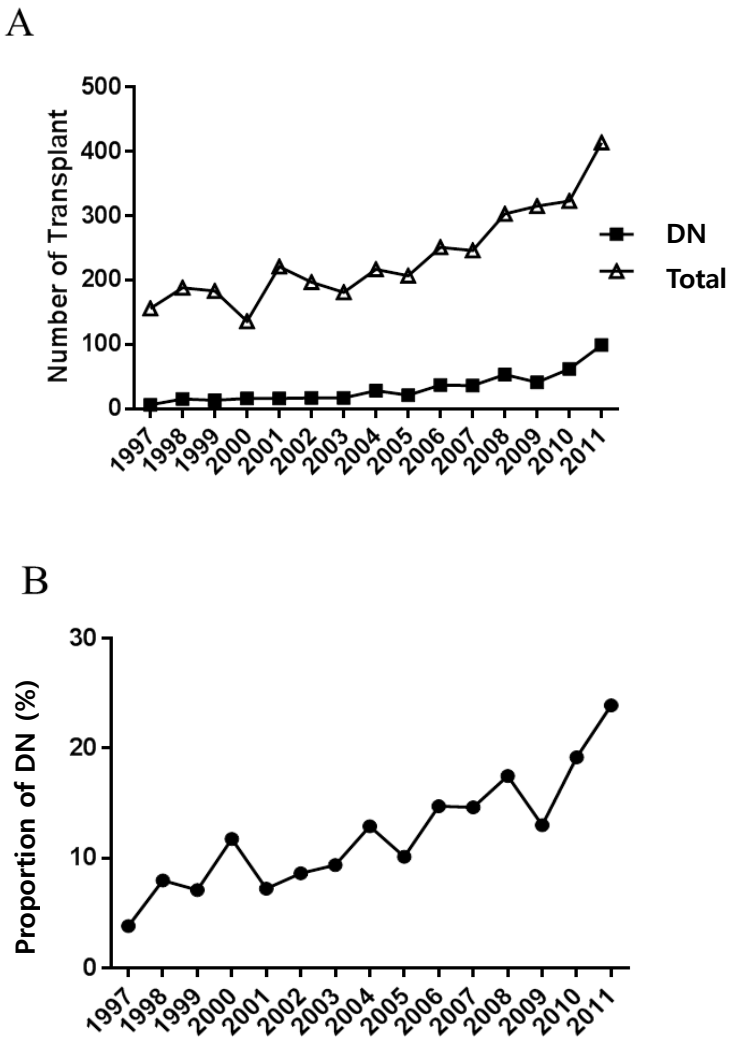


Figure 1. Number (A) and proportion (B) of patients with diabetic nephropathy among total kidney transplantations from 1997 to 2011 in three hospitals (SNUH, AMC and KUH). DN: diabetic nephropathy

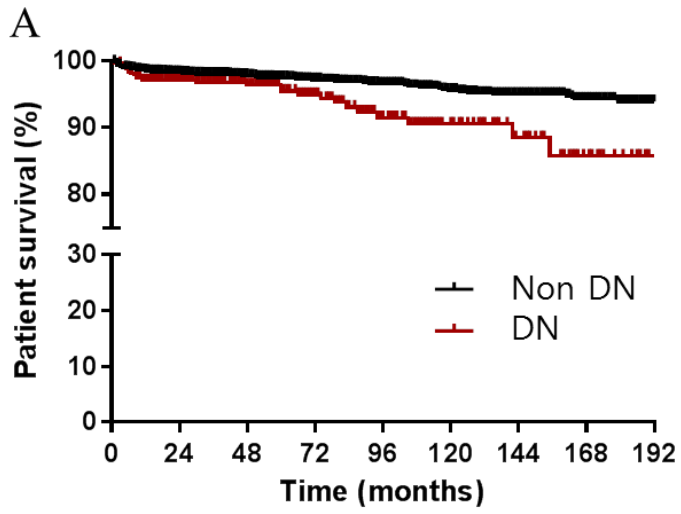
Table 1. Baseline characteristics by quartiles of time-averaged HbA1c levels

	All patients	Quartile of time-averaged HbA1c				*P*
		Q1	Q2	Q3	Q4	
N	476	110	96	114	100	
Age (year, min-max)	50 (±10.2)	47.1 (±11.3)	51.6 (±9.2)	50.8 (±10.0)	50.0 (±9.3)	0.007
Gender (Male, %)	66.9	63.6	77.1	63.2	65.0	0.116
BMI (kg/m^2)	23.4 (±3.2)	22.5 (±2.8)	24.0 (±2.9)	23.4 (±3.0)	23.8 (±3.8)	0.005
Co-morbidity (%)						
Hypertension	89.5	83.6	93.8	93.9	87.0	0.031
Ischemic heart disease	15.0	7.3	22.9	14.9	16.0	0.019
Cerebrovascular disease	5.0	2.7	6.3	7.9	3.0	0.225
Donor factors						
Donor age (y)	40.5 (±13.9)	39.7 (±14.2)	41.1 (±14.2)	41.3 (±12.9)	39.6 (±13.2)	0.717
Gender (Male, %)	55.9	59.3	60.8	54.5	49.4	0.458
Donor type (%)						0.003
Living related	43.3	33.7	42.6	54.0	41.8	
Living unrelated	32.3	30.8	27.7	31.0	39.8	
Deceased donor	24.4	35.6	29.8	15.0	18.4	
Duration of dialysis (months)	28.0	32.6	27.5	27.6	24.0	0.366
Dialysis modality (%)						0.873
Preemptive	14.0	12.5	12.5	14.9	16.0	
Hemodialysis	68.8	71.2	68.8	70.2	65.0	
Peritoneal dialysis	15.0	12.5	16.7	13.2	18.0	
Mixed (HD+PD)	2.2	3.8	2.1	1.8	1.0	
Immunosuppressant						
Calcineurin inhibitor (%)	99.5	100	100	100	97.6	0.073
Antimetabolite (%)	96.3	96.7	97.6	96.1	94.9	0.829
Baseline laboratory finding						
HbA1c (%)	7.5 (±1.7)	6.6 (±1.4)	6.9 (±1.2)	7.7(±1.3)	8.8 (±2.1)	<0.001
Glucose (mg/dl)	194 (±113)	171 (±98)	100 (±11)	131 (±12)	114 (±6)	0.005

Albumin (g/dl)	3.4 (±0.6)	3.6 (±0.6)	3.4 (±0.6)	3.4 (±0.6)	6.4 (±0.6)	0.144
Hemoglobin (mg/dl)	10.7 (±1.5)	10.7 (±1.5)	10.6 (±1.8)	10.5 (±1.6)	10.3 (±1.9)	0.369

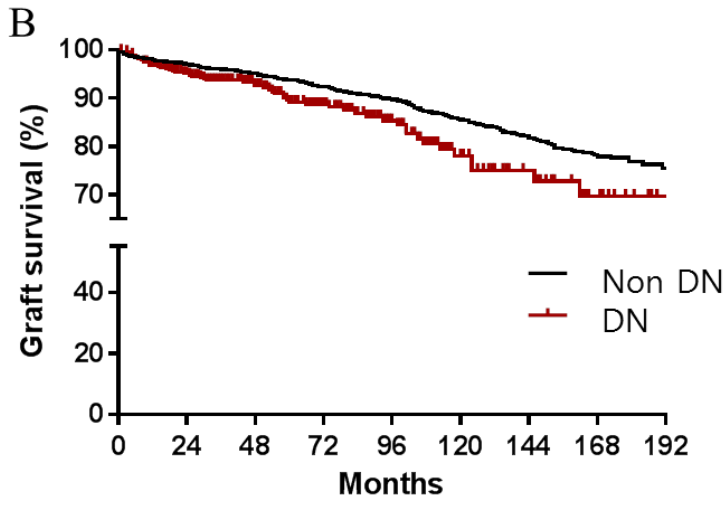
Comparison of Post-transplant Outcomes between Diabetic Nephropathy and Non-diabetic Nephropathy

During the follow-up period, 60 graft failures (12.6%) and 30 deaths (6.3%) occurred in patients with diabetic nephropathy, compared to 354 graft failures (11.6%) and 117 deaths (3.8%) in patients with non-diabetic nephropathy. Post-transplant patient survival of KTRs with diabetic nephropathy was poorer than that of KTRs with non-diabetic nephropathy ($p < 0.001$; Figure 2A). The survival rate of diabetic nephropathy and non-diabetic nephropathy was 97.0% and 98.5% at 1 year follow up, and 95.4% and 97.5% at 5 years. In addition, graft survival of KTRs with diabetic nephropathy was inferior to graft survival of non-diabetic nephropathy ($p < 0.001$; Figure 2B). The graft survival rate of diabetic nephropathy versus non-diabetic nephropathy was 96.8% and 98.0% respectively at 1 year, and 89.2%, respectively, and 93.8% at 5 years.



No. at risk

DMN	473	375	255	171	104	66	41	23	5
Others	3039	2672	2119	1647	1226	915	610	350	96



DMN	471	366	248	163	98	56	34	20	4
Others	3025	2641	2067	1573	1155	836	538	296	84

Figure 2. Patient survival (A) and graft survival (B) for kidney transplant patients.

Post-transplant Glycemic Control and Risks of Graft Failure

The median follow up duration for patients with diabetic nephropathy was 49.9 months. The changes in fasting glucose levels and HbA1c every 6 months were shown in Figure 3. Each post-transplant HbA1c was higher than baseline but within the range of 7-8% (baseline HbA1c = 7.5±1.7 vs. time-averaged HbA1c = 7.7±1.5, $p < 0.001$). Post-transplant glucose levels were lower than baseline levels, in the range of 120-160. The mean time-averaged glucose levels and HbA1c at 36 months were 147 ± 46 mg/dl and 7.7 ± 1.5%, respectively.

The highest quartile of time-averaged glucose level predicted poor graft survival in the Kaplan Meier survival analysis model ($p = 0.014$; Figure 4A). In addition, the 3rd quartile of time-averaged HbA1c showed good graft survival compared to the other quartiles in the Kaplan Meier survival anlaysis model ($p = 0.006$; Figure 4B).

Next, I performed a Cox regression analysis. Figure 5 shows the unadjusted and adjusted graft failure hazard ratios (HRs) for the quartile groups based on baseline glucose, baseline HbA1c, time-averaged glucose, and time-averaged HbA1c. In

the unadjusted model and in the model adjusted only for age and gender, the highest quartile (Q4) of baseline glucose showed low HR for graft failure(in the unadjusted model– HR 0.362, 95% CI 0.142–0.926, p=0.034; in the model 1– HR 0.366, 95% CI 0.143–0.938, p=0.036), but in the model adjusted for age, gender, comorbidities, age of donor, donor type, baseline hemoglobin and BPAR, there was no significant association (HR 0.410, 95% CI 0.155–1.081, p=0.071) (Figure 5A). Using time–averaged glucose level as a modifier, highest quartile of time–averaged glucose showed high HR for graft failure in unadjusted model (HR 2.331, 95% CI 1.141–4.759, p=0.020), the model adjusting for age and gender (HR 2.475, 95% CI 1.209–5.066, p=0.013), and the model adjusting for age, gender, comorbidities, age of donor, donor type, baseline hemoglobin and BPAR (HR 2.194, 95% CI 1.048–4.594, p=0.037) (Figure 5B).

HbA1c, an index of glycemic control, was used for analyze the effect of post–transplant glycemic control on graft failure. In Cox regression analysis, baseline HbA1c was not significantly associated with graft failure (Figure 5C). However, in the analysis using time–averaged HbA1c quartiles, the 1st (HR 6.46,

95% CI 1.82-22.9, p=0.004), 2nd (HR 4.61, 95% CI 1.29-16.38, p=0.024) and 4th quartiles (HR 7.89, 95% CI 2.28-27.30, p=0.001) were related to poor graft outcomes compared with the 3rd quartile (7.6-8.6%), after adjusting age, gender, comorbidities, donor age, donor type, baseline hemoglobin and BPAR (Figure 5D).

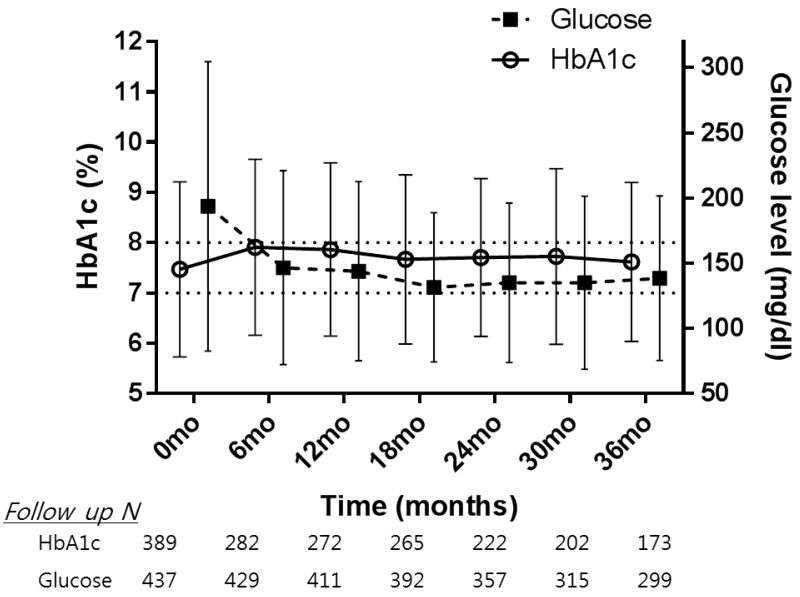


Figure 3. Transition of post-transplant glycemic control by serum glucose level and HbA1c

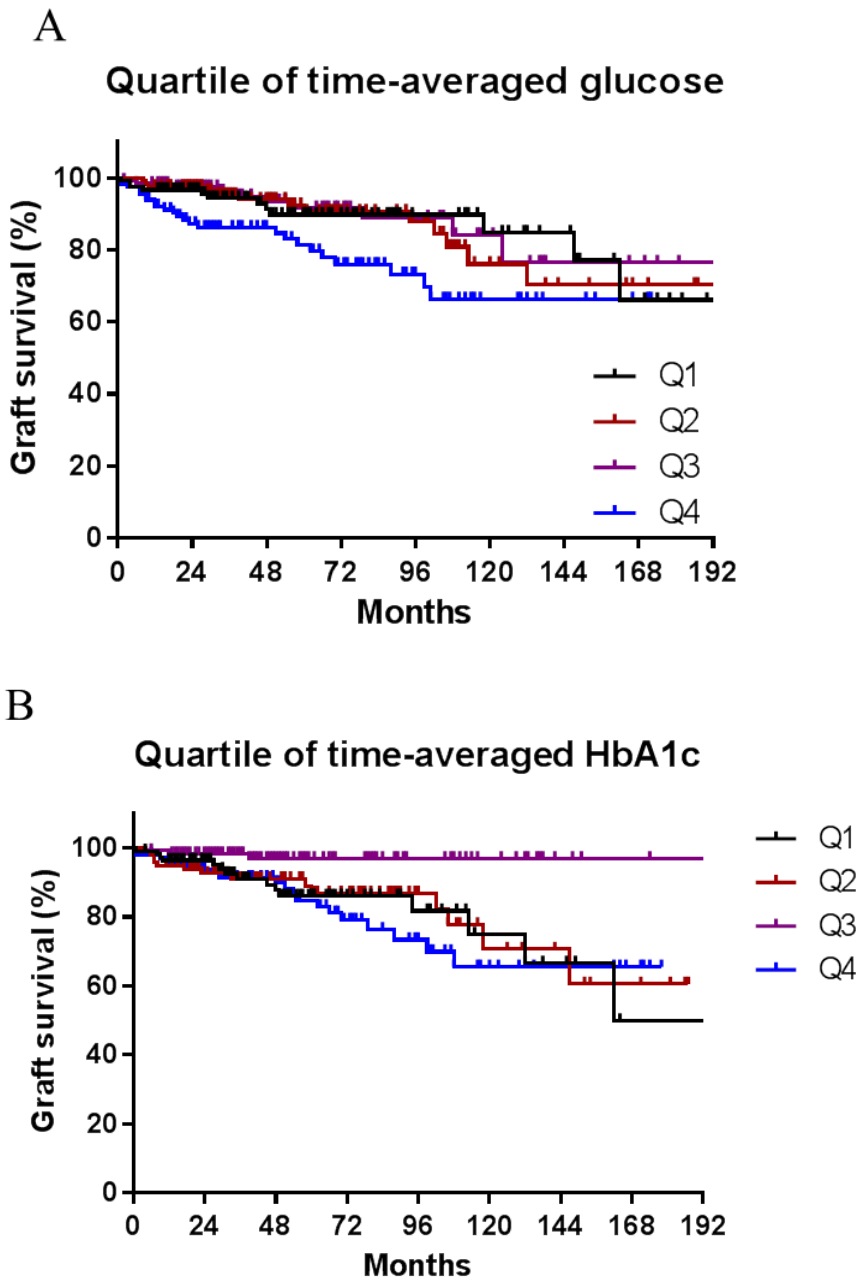
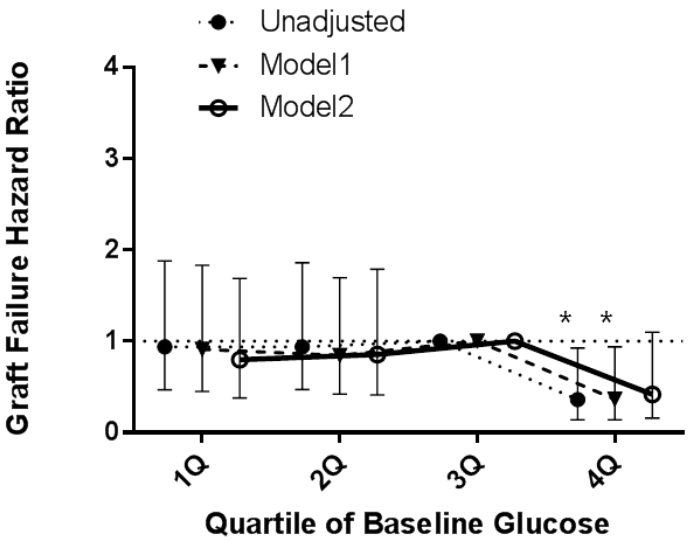


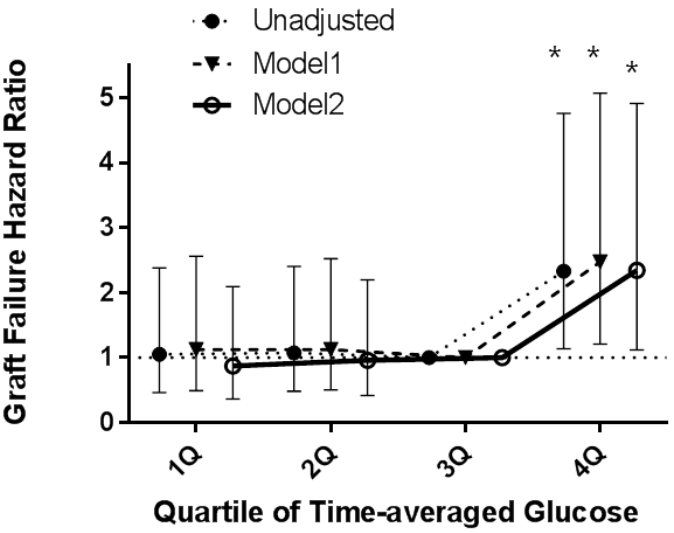
Figure 4. Kaplan-Meier estimates according to quartiles of glucose and HbA1c. Graft survival included graft failure and patient death with functioning graft.

A



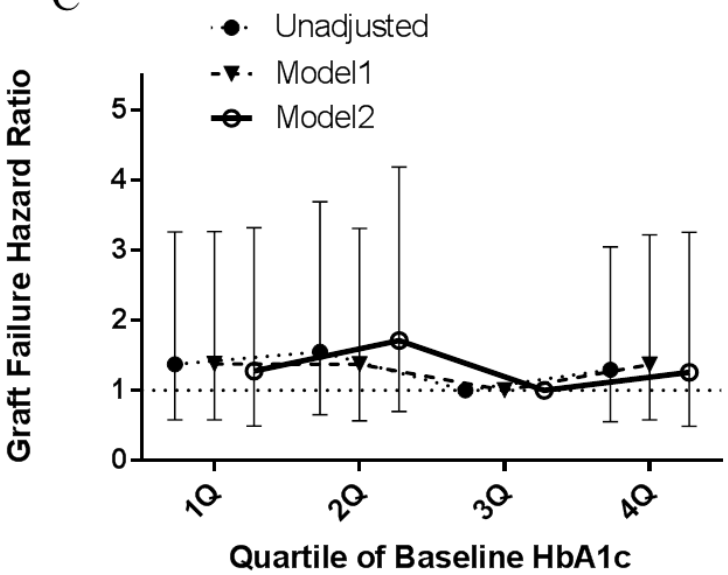
Min-max	42-114	115-161	162-247	248-862
Mean±SD	90±16	138±12	199±26	345±106

B



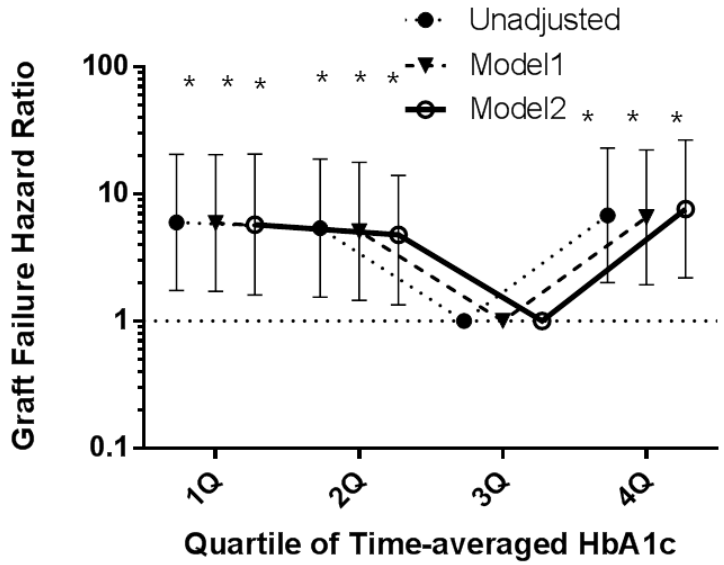
Min-max	21-115	116-137	138-170	172-363
Mean±SD	100±13	126±6.1	154±9.9	208±40

C



Min-max	4.8-6.3	6.4-7.0	7.1-8.4	8.5-15.2
Mean±SD	5.7±0.43	6.7±0.19	7.6±0.40	9.9±1.4

D



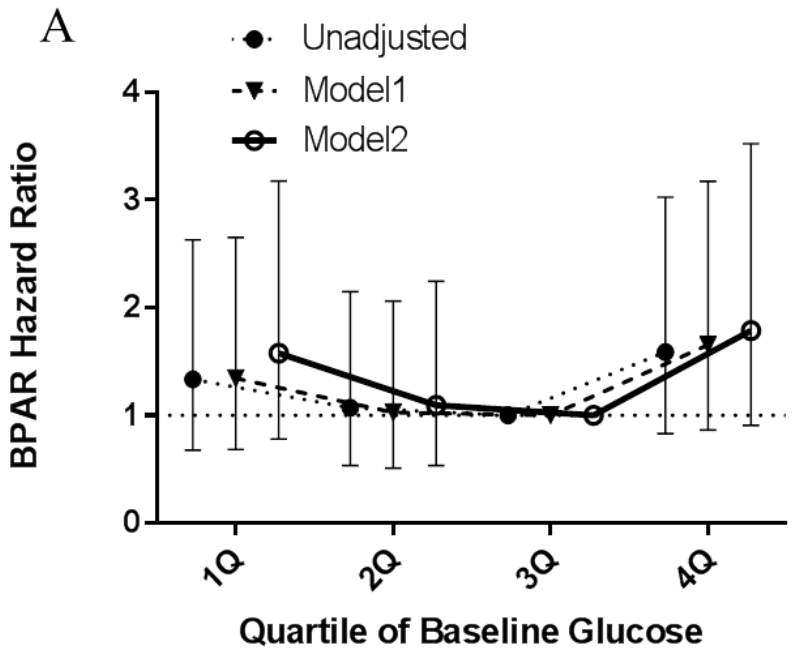
Min-max	4.7-6.7	6.8-7.5	7.6-8.6	8.7-15.2
Mean±SD	6.1±0.5	7.1±0.2	8.1±0.3	9.7±1.2

* <0.05
** <0.001

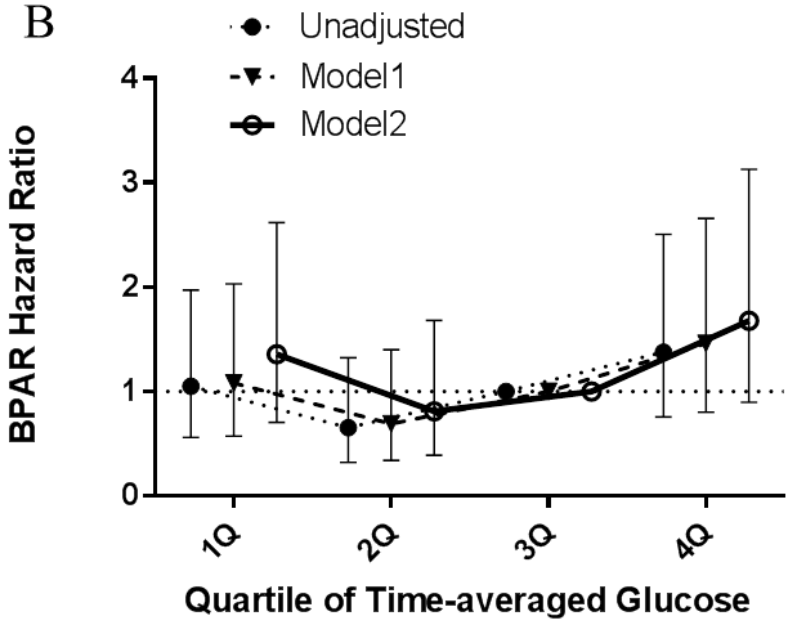
Figure 5. HRs of graft failure by serum glucose using standard Cox proportional hazards regression (A) and a time-averaged model (B). HRs of graft failure by HbA1c using standard Cox proportional hazards regression (C) and a time-averaged model (D). Model 1 is adjusted for age and gender. Model 2 is adjusted for age, gender, comorbidities (hypertension, ischemic heart disease), donor age, donor type, baseline hemoglobin level, and BPAR.

Post-transplant Glycemic Control and Risk of BPAR

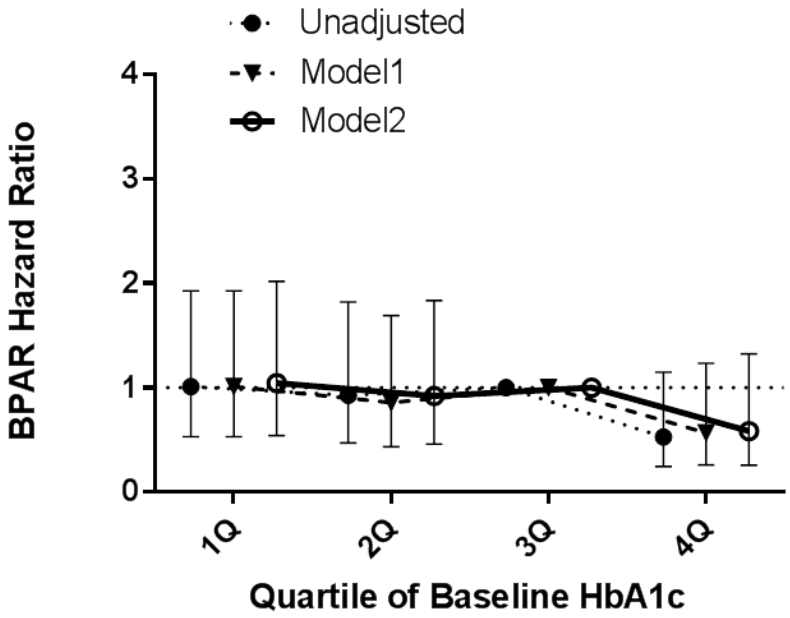
During the follow up period, episodes of BPAR were confirmed in 81 patients (17.0%) with diabetic nephropathy. There was no significant relationship between BPAR and baseline/time-averaged glucose or between BPAR and HbA1c levels (Figure 6).



B


Unadjusted
Model1
Model2
BPAR Hazard Ratio
4
3
2
1
0
1Q
2Q
3Q
4Q
Quartile of Time-averaged Glucose

C


Unadjusted
Model1
Model2
BPAR Hazard Ratio
4
3
2
1
0
1Q
2Q
3Q
4Q
Quartile of Baseline HbA1c

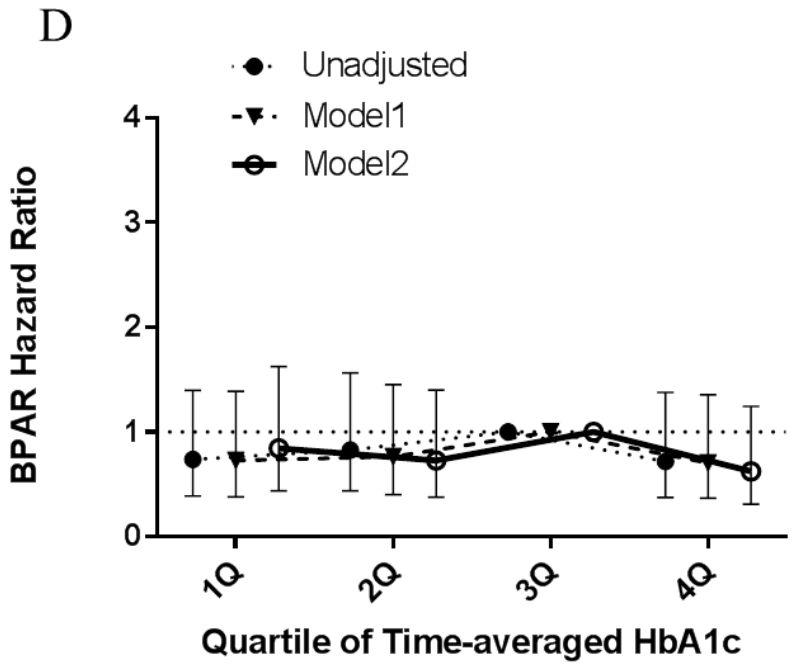


Figure 6. HRs of BPAR by serum glucose using standard Cox proportional hazards regression (A) and a time-averaged model (B). HRs of BPAR by HbA1c using standard Cox proportional hazards regression (C) and a time-averaged model (D). Model 1 is adjusted for age and gender. Model 2 is adjusted for age, gender, comorbidities (hypertension, ischemic heart disease), donor age, donor type and baseline hemoglobin level.

DISCUSSION

This multicenter retrospective cohort study reports the clinical outcomes of kidney transplantation in diabetic nephropathy and its relationship with post-transplant glycemic control. Graft and medical outcomes after kidney transplantation for diabetic nephropathy were poor compared to outcomes for patients with non-diabetic nephropathy. In addition, post-transplant glycemic control, assessed by time-averaged glucose levels and HbA1c, affected graft survival. The time-averaged HbA1c group with 7.6-8.6% showed the best graft outcome. However, pre-transplant glycemic control was not associated with graft survival. Our results suggest that post-transplant glycemic control could be more important than pre-transplant glycemic control for long-term graft outcomes. Acute rejection was not associated with pre- or post-transplant glycemic control.

In this analysis, I could show that post-transplant serum glucose levels decrease and HbA1c levels increase during 36 months follow up (Figure 3) compared to baseline levels. Kidney KTRs take steroids and immunosuppressant agents, which increase postprandial glucose levels and postprandial

glucose levels could affect increase of HbA1c levels. But most KTRs examine their blood tests before a meal because of monitoring drug levels, for this reason, their glucose level could decrease, which represent the fasting glucose levels.

In figure 5A, the highest quartile of baseline glucose levels tends to better graft survival than other quartiles. When I analyze the relationship of quartiles of baseline glucose and time-averaged HbA1c by chi-square test, among 113 patients in the 3rd qaurtile of time-averaged HbA1c, 40 patients were belongs to the highest quartile of baseline glucose levels, and 23, 18, and 32 patients were belong to 1st, 2nd, and 3rd quartiles, respectively . There is significant correlation between the quartiles of baseline glucose and time-averaged HbA1c (Pearsone Chi-square test, p=0.029).

The relationship between post-transplant glycemic control and clinical outcomes after kidney transplantation in clinical studies is controversial. Hyperglycemia is associated with ischemic reperfusion injury in animal models (15). Also, in human kidney transplantation, hyperglycemia reportedly increases ischemic injury (16) and mesangial matrix expansion (11). Wiesbauer et al. reported that maximal glucose levels

were associated with mortality (13). Hermayer et al. conducted a RCT with patients who underwent kidney transplantation, randomized to either the intensive group with i.v. insulin or the standard treatment group with s.c. insulin (17). However, results suggested that contrary to what was expected, the intensive glycemic control after kidney transplant increased risk for rejection episodes and hypoglycemic events.

Glycemic control in kidney transplantation is challenging. Most patients could undergo hyperglycemia after kidney transplantation due to corticosteroid and immunosuppressive agents. In particular diabetic nephropathy patients who underwent kidney transplantation had difficulty controlling their diabetes because of complications, such as autonomic neuropathy. Therefore, the American Society of Transplantation (ATC) recommends targeting HbA1c 7.0−7.5% and avoiding targeting HbA1c ≤6.0% (9).

In this study, strict glycemic control as well as poor glycemic control were related to poor graft outcomes, which supports the ATC recommendations for glycemic control. I suggest that HbA1c is more important parameter than glucose to survey for

post-transplant glycemic control because, unlike glucose, it is associated with graft outcome.

Our study has some limitations. First, as with all retrospective studies, our data cannot be interpreted causally. Second, the data for glucose levels could contain both fasting and random glucose levels because I cannot recognize whether the blood samples were collected before or after a meal. Third, I classified the laboratory findings into quartiles using cutoffs suggested by the data, rather than by the clinical literature. Furthermore, I had no information regarding diabetes medications, and whether patients were taking oral agents or insulin. This may be a confound as Wiesbauer et al. suggested that diet and oral medications seem to be superior to subcutaneous insulin obtaining optimal glycemic control (13). Also the number of patient deaths and graft failures was small, which may have reduced the power in our analyses.

However, to our knowledge, this study represents the largest cohort study of Asian kidney transplantation to date, using multicenter cohort data. Furthermore, I used both glucose levels and HbA1c as indices of glycemic control. By measuring time-averaged glucose and HbA1c, I was able to reduce

observed variability over time and examine overall trends in the association between glycemic control and survival. However, these methods may mask significant changes in laboratory parameters that are important to survival.

In conclusion, our study suggests that strict glycemic control is not necessary for managing hyperglycemia after kidney transplantation, but that poor glycemic control is also associated with poor graft outcomes. However, there was no significant relationship between glycemic control and BPAR. As a parameter of glycemic control after kidney transplantation, HbA1c may be superior to glucose because it may predict graft outcomes.

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국문 초록

서론: 당뇨병성 신증은 말기신부전의 가장 많은 원인 질환이며, 이로 인한 신장 이식은 증가하는 추세이다. 신장 이식 후 혈당 조절은 아직 논쟁이 있다. 본 연구는 당뇨병성 신증으로 신장 이식을 시행한 환자에서 이식 후 혈당조절과 장기적인 임상 결과와의 관계를 규명하고자 하는데 목적이 있다.

방법: 국내 3 차 병원 세 곳에서 신장 이식을 시행한 환자의 의무기록을 후향적으로 분석하였다. 1997 년부터 2011 년까지 신장 이식을 받은 3,538 병의 환자 중, 476 명이 당뇨병성 신증으로 신장 이식을 시행하였다. 이 환자에서 이식 후 혈당조절과 사망을 포함한 이식 실패와의 연관성을 분석하였다. 이식 후 36 개월 동안 시행한 시간평균(time-average) 혈당 수치와 당화혈색소(hemoglobin A1c)를 분석하였다.

결과: 시간평균 혈당과 당화혈색소의 평균은 각각 140± 45.7 mg/dl, 7.7 ± 1.48 % 였다. 이식 전 혈당 수치를 4 분위로 나누었을 때, 4 번째 사분위 그룹은 높은 이식 실패 위험도를 보였다. 시간평균 당화혈색소의 3 번째 사분위 그룹(7.6-8.6%)은 다른 그룹에 비하여 이식 신 실패 위험이 가장 낮았다 (1^{st} quartile HR 6.13, 95% CI 1.73-21.75; 2^{nd} quartile HR 4.29, 95% CI 1.21-15.25; 4^{th} quartile HR 6.96, 95% CI 2.02-23.97;

reference– 3rd quartile). 그러나 시간평균 혈당 수치는 이식 신 실패 위험도와 유의한 차이를 보이지 않았다. 조직검사로 증명된 급성 이식거부반응(biopsy–proven acute rejection)은 혈당조절 인자와 관련이 없었다.

결론: 신장 이식 후 엄격한 혈당조절이 필요하지는 않지만, 잘 조절되지 않은 혈당은 이식 신 실패 위험과 관련성이 높다.

주요어 : 당뇨병성 신증, 신장 이식, 혈당 조절, 이식 신 실패, 급성 거부 반응

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