Donor-Recipient Body Weight Mismatch May Affect Glomerular Basement Membrane Thinning in Electron Microscopic Examination of 1-Hour Renal Allograft Biopsy Specimens

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ABSTRACT

Background. Although an association between body weight mismatch and impaired graft function has been reported, few histologic studies have evaluated this issue, especially using electric microscopic analysis. During routine observations, we have noted a thin glomerular basement membrane (GBM) in the 1-hour biopsy specimen in cases with an overweight recipient and a lightweight donor. Therefore, we hypothesized that donor-recipient body weight mismatch affects the GBM thickness in the 1-hour biopsy specimen. The aim of the present study was to clarify the effect of donor-recipient body weight mismatch on the GBM thickness of the 1-hour biopsy specimen measured using electron microscopy.

Methods. We used an electron microscope to measure the GBM thickness of specimens at 1-hour post-transplantation (n = 24) and at 1 year post-transplantation (n = 17). The GBM thickness of cases with donor-recipient body weight mismatch was compared with those without mismatch. In accordance with a previous study, we defined a donor/recipient body weight ratio of less than 0.9 as donor-recipient body weight mismatch and a ratio of more than 0.9 as no mismatch.

Results. At 1-hour post-transplantation, the mean GBM was significantly thinner in the mismatch group than in the nonmismatch group. However, at 1-year post-transplantation, the mean GBM thickness did not significantly differ between the 2 groups.

Conclusions. The GBM thickness at 1-hour post-transplantation is thinner in cases with donor-recipient body weight mismatch than in cases without mismatch. This implies that donor-recipient body weight mismatch may have to be considered when assessing donor-derived thin GBM disease using the 1-hour biopsy specimen.

THE 1-HOUR biopsy specimen after kidney transplantation provides important information regarding the presence of donor-derived kidney lesions. However, the thickness of the glomerular basement membrane (GBM) in the 1-hour biopsy specimen on electron microscopy (EM) is not yet fully understood.

In our institution, 1-hour biopsy specimens are routinely obtained to detect donor-derived graft lesions. During this routine examination, we have sometimes noted the presence of a thin GBM in the 1-hour biopsy specimen in cases

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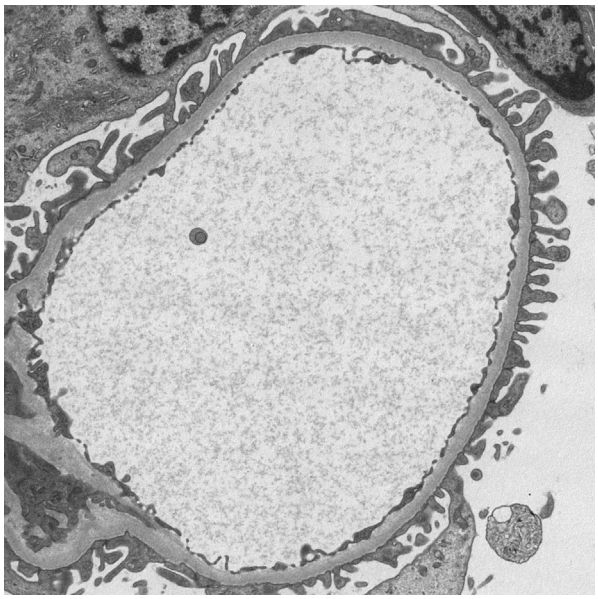

Fig 1. Representative image of the thin basement membrane of a glomerular capillary in a case of donor-recipient body weight mismatch. EM measurements of GBM thickness were made at 3 specified points along each of 10 randomly selected noncollapsing glomerular capillaries to determine the average GBM thickness. In this glomerular capillary, GBM thickness at 3 specified points was 251.0 nm, 286.2 nm, and 299.3 nm, respectively.

involving an overweight recipient and a lightweight donor. In some of these mismatch cases with a thin GBM in the 1-hour biopsy specimen, there is little clinical evidence and/or family history to suggest thin GBM disease in the donor. Therefore, we hypothesized that donor-recipient body weight mismatch results in a thin GBM in the 1-hour biopsy specimen. The long-term renal prognosis of donors with thin GBM disease has not been fully elucidated, and donor adaptation for thin GBM disease is still controversial [1,2]. Thus, it is necessary to accurately diagnose donor-derived thin GBM lesions from baseline biopsy specimens. A previous study reported that a low donor/recipient body weight ratio or size mismatch may contribute to inferior long-term renal allograft survival [3,4]. However, histological analysis of the biopsy specimens has rarely been reported, especially analysis using EM.

The aim of the present study was to analyze the EM findings of biopsy specimens obtained 1 hour after kidney transplantation and to assess the effect of donor-recipient body weight mismatch on the GBM thickness.

MATERIALS AND METHODS

There were 42 cases of kidney transplantation performed in our institution from January to December 2011. We analyzed the EM findings of the biopsy specimens obtained at 1 hour and 1 year post-transplantation. We excluded 14 pediatric cases, 2 cadaver transplantation cases, and 2 cases in which the 1-hour biopsy specimens were not analyzed by EM; thus, a total of 24 cases were included. The 1-year biopsy analysis included 17 of these 24 cases; the excluded cases were 4 that did not undergo EM analysis of 1-year biopsy specimens and 3 that received insulin treatment.

We used EM analysis to determine the average GBM thickness of the 1-hour and 1-year biopsy specimens. EM measurements of GBM thickness were made at 3 specified points along each of 10 randomly selected noncollapsing glomerular capillaries to determine the average GBM thickness in accordance with the method used in a previous study [5] (Fig 1). We defined a donor/recipient body weight ratio of less than 0.9 as donor-recipient body weight mismatch and a ratio of more than 0.9 as no mismatch in accordance with previous studies [3,6]. For EM performed in our hospital, kidney tissue was fixed in glutaraldehyde and embedded in epoxy resin, semi-thin sections were stained by toluidine blue, and the most appropriate section of tissue containing the glomerulus was cut into ultra-thin sections.

All statistical data were analyzed with SPSS software version 23.0 for Windows (IBM Japan, Tokyo, Japan), and P value of $< .05$ was considered to indicate statistically significant differences. We compared variables using the χ^2 test, Fisher's exact test, Student t test, the Mann-Whitney U test, paired t test, and Wilcoxon signed-ranks test. All data are presented as mean ± standard deviation or

Table 1. Clinical Background of Donor and Recipient at Kidney Transplantation

	Mismatch Group (n = 8)	Nonmismatch Group (n = 16)	*P* Value
Male/female of donor (n)	0/8	10/6	<.01
Male/female of recipient (n)	7/1	5/11	.014
Recipient age at transplantation (years)	51.0 ± 12.3	41.4 ± 12.1	.081
Donor age at transplantation (years)	54.3 ± 9.2	52.8 ± 12.0	.77
BMI (kg/m^2) of recipient	23.3 ± 2.2	19.9 ± 4.1	<.01
BMI (kg/m^2) of donor	20.3 ± 3.1	23.5 ± 3.1	<.01
Body weight of recipient (kg)	66.1 ± 6.7	50.3 ± 11.6	<.01
Body weight of donor (kg)	51.1 ± 6.4	64.5 ± 12.7	.011
Body height of recipient (cm)	168.6 ± 5.9	158.5 ± 9.2	.014
Body height of donor (cm)	159.0 ± 6.4	165.1 ± 7.8	.072
WIT (minutes)	3.4 ± 0.7	3.6 ± 1.1	.697
TIT (minutes)	71.9 ± 21.0	78.1 ± 40.4	.951

Abbreviations: BMI, body mass index; TIT, total ischemic time; WIT, warm ischemic time.

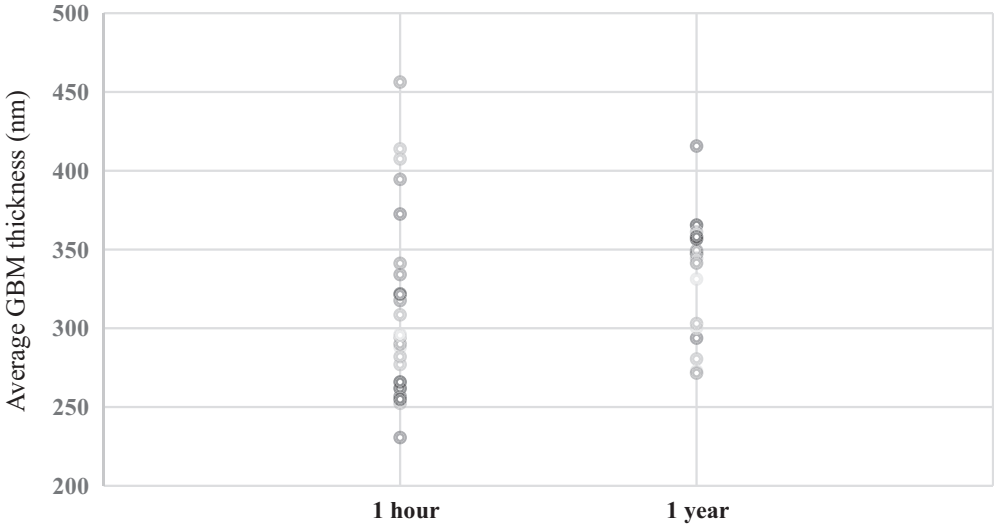

Fig 2. Average glomerular basement membrane (GBM) thickness in the 1-hour biopsy specimens (n = 24) and in the 1-year biopsy specimens (n = 17).

the number (%). Our study was approved by the Ethics Committee of Toho University, Omori Hospital (approval number M18132).

RESULTS

Clinical Background Characteristics of the Donors and Recipients

Table 1 summarizes the clinical background characteristics of the donors and recipients at the time of kidney transplantation. There were no significant differences between the mismatch group and the nonmismatch group in the sex prevalence of donors and recipients, recipient age at transplantation, donor age at transplantation, body height of donor, warm ischemic time, and total ischemic time. Body mass index, body weight, and body height of recipients were significantly higher in the mismatch than without mismatch. Body mass index and the body weight of donors were significantly lower in the mismatch than without mismatch. Cases with familial history of thin GBM disease and with persistent isolated hematuria were not found in the mismatch group.

Glomerular Basement Membrane Thicknesses in the 1-Hour Versus 1-Year Biopsy Specimens and Glomerular Basement Membrane Thicknesses in the 1-Hour and 1-Year Biopsy Specimens of the Mismatch Versus Nonmismatch Groups

Figure 2 shows the average GBM thicknesses in the 1-hour biopsy specimens (n = 24) and the 1-year biopsy specimens (n = 17). Figure 3 shows the average GBM thicknesses in

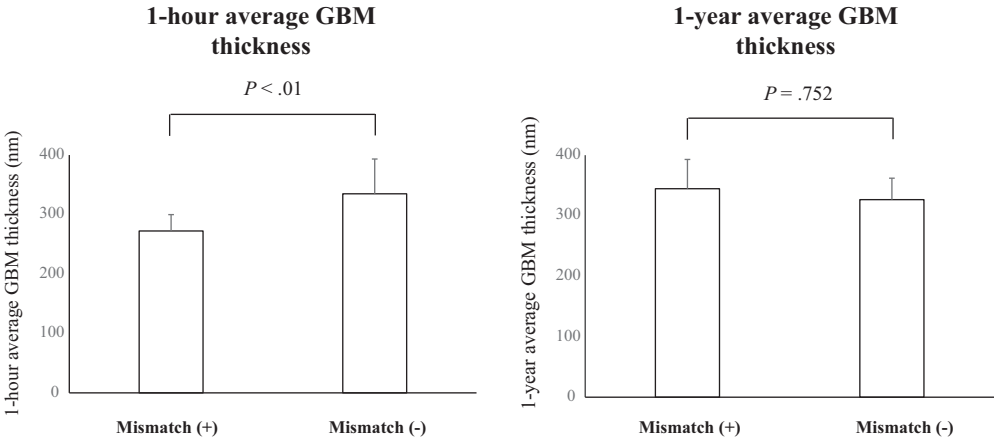

Fig 3. Average glomerular basement membrane (GBM) thicknesses in the 1-hour and 1-year biopsy specimens of the donor-recipient body weight mismatch group and the nonmismatch group. In the 1-hour biopsy specimens, the mean GBM thickness was significantly thinner in the mismatch group than in the nonmismatch group; however, in the 1-year biopsy specimens, the mean GBM thickness did not significantly differ between the 2 groups.

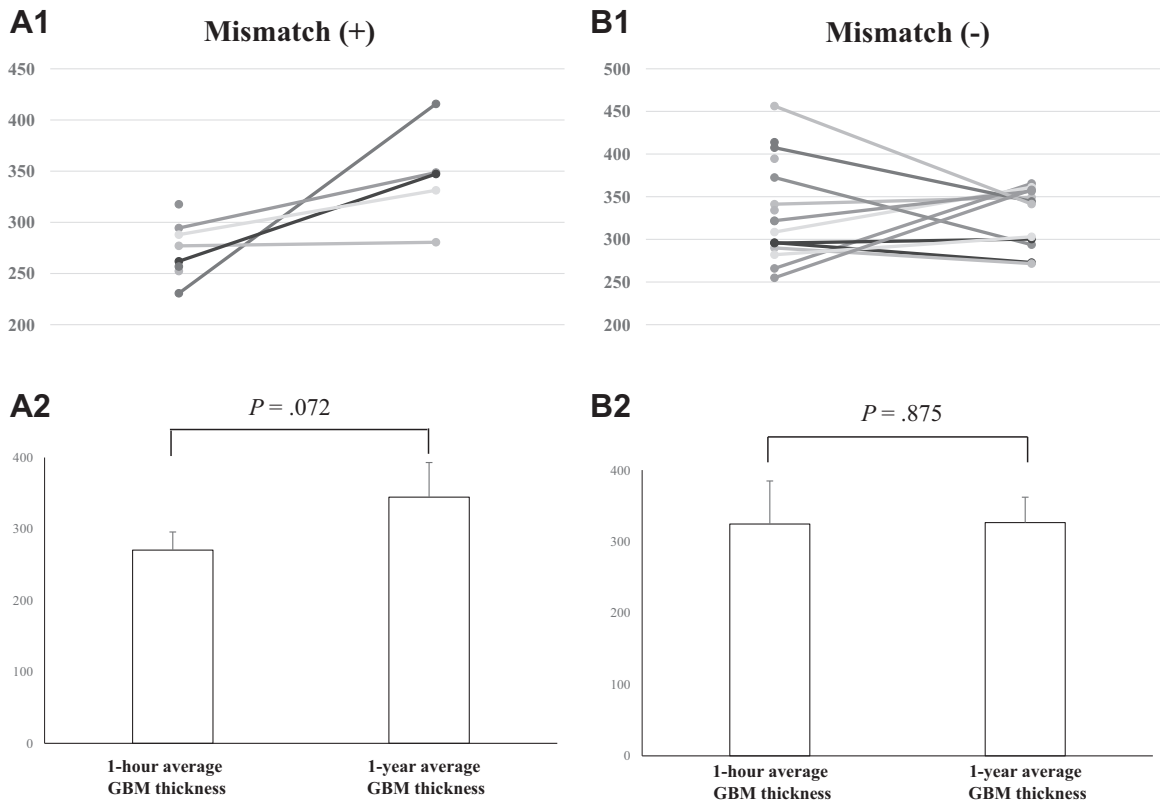

Fig 4. Changes in glomerular basement membrane (GBM) thickness between biopsy specimens obtained at 1 hour and 1 year after kidney transplantation in the donor-recipient body weight mismatch group and the nonmismatch group. In the mismatch group, the GBM thickness of the 1-year biopsy specimens tended to be thicker than that of 1-hour biopsy specimens. In the nonmismatch group, the GBM thickness of the 1-year biopsy specimens did not differ from that of the 1-hour biopsy specimens.

the 1-hour and 1-year biopsy specimens of the mismatch and nonmismatch groups. In the 1-hour biopsy specimens, the mean GBM thickness was significantly thinner in the mismatch group than in the nonmismatch group; however, in the 1-year biopsy specimens, the mean GBM thickness did not significantly differ between the 2 groups.

Changes in GBM Thickness Between the 1-Hour and 1-Year Biopsy Specimens in the Mismatch and Nonmismatch Groups

Figure 4 shows the changes in GBM thickness between the specimens obtained at 1 hour and 1 year post-transplantation in the mismatch and nonmismatch groups. In the mismatch group, the GBM tended to be thicker at 1 year post-transplantation than at 1 hour post-transplantation. In the nonmismatch group, the GBM thickness at 1 year post-transplantation did not differ from that at 1 hour post-transplantation.

DISCUSSION

In the present study, the average GBM thickness of the 1-hour biopsy specimens was thinner in the donor-recipient body weight mismatch group than in the nonmismatch group. In contrast, the average GBM thickness of the 1-year biopsy specimens did not differ between the mismatch and nonmismatch groups.

The observation of GBM thinning in a 1-hour biopsy specimen is usually considered to indicate a donor-derived lesion. The long-term renal prognosis of donors with thin GBM disease has not been fully elucidated, and donor adaptation for thin GBM disease is still controversial [1,2]. Thus, the accuracy of the diagnosis of donor-derived thin GBM lesions via the analysis of baseline biopsy specimens is an important clinical issue. Our study implied that donor-recipient body weight mismatch may have to be considered when assessing donor-derived thin GBM disease based on the 1-hour biopsy specimen.

In our study, the average GBM thickness of the 1-hour biopsy specimen was thinner in the donor-recipient body weight mismatch group than in the nonmismatch group. A previous study reported that the hemodynamic autoregulation system of the kidney graft deteriorates because of denervation [7]. Therefore, we speculate that the stretching of the GBM may be caused by the acute entry of the blood flow from the relatively large recipient into the denervated

kidney graft from the relatively small donor in cases of donor-recipient body weight mismatch. However, it is presumed that the extended GBM subsequently returns to its original state by autoregulation via the myogenic response and the effects of angiotensin II. Thus, the average GBM thickness of the 1-year biopsy specimens did not differ between the mismatch and nonmismatch groups.

The main limitation of the present study was that we did not evaluate the 0-hour biopsy specimens. This was because a 0-hour biopsy is not routinely performed in our institution. Further studies are required to analyze the difference in GBM thickness between the 0-hour and 1-hour biopsy specimens, especially in the cases with donor-recipient body weight mismatch.

CONCLUSIONS

The average GBM thickness of the 1-hour biopsy specimens was thinner in the donor-recipient body weight mismatch group than in the nonmismatch group. The present findings imply that donor-recipient body weight mismatch may have to be considered when using the 1-hour biopsy specimen to diagnose donor-derived thin GBM disease.

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