Compensatory Structural and Functional Adaptation After Nephrectomy in Obese Patients According to Waist Circumference

Kyung Hwa Choi, Seung Ryeol Lee, Young Kwon Hong, and Dong Soo Park

OBJECTIVE To investigate whether the postnephrectomy renal adaptation mechanism, focused on functional hyperfiltration as well as structural hypertrophy, was affected by abdominal obesity.

MATERIALS AND METHODS We retrospectively evaluated 358 patients who underwent simple or radical nephrectomy and nephroureterectomy between 2009 and 2013. Patients were classified according to waist circumference (WC), with values >102 cm in men and >88 cm in women considered high (obesity). Functional renal volume (FRV) was measured using computed tomography performed preoperatively and 6 months postoperatively to evaluate the degree of remnant kidney hypertrophy. The degree of hyperfiltration was calculated from the difference between the preoperative and postoperative glomerular filtration rate (GFR)/FRV.

RESULTS The mean preoperative GFR, FRV, and GFR/FRV were 72.1 mL/min/1.73 m^2, 282.8 cm^3, and 0.25 mL/min/1.73 m^2/cm^3, respectively. The percent GFR reduction was significantly greater in the high WC group (high, 25.9% vs normal, 16.0%, $P = .036$), although the degree of hypertrophic volume in the remnant kidney showed no difference. The change in GFR/FRV was statistically lower in the high WC group (high, 25.7% vs normal, 40.2%, $P = .009$). The factors associated with postoperative increased GFR/FRV were low preoperative GFR, proteinuria, high predictive preserved functional parenchymal volume ratio, absence of hypertension, increased levels of high-density lipoprotein cholesterol, and normal WC (all $P < .05$).

CONCLUSION Patients with high WC might have a large reduction in postoperative renal function, owing to a lower degree of functional hyperfiltration. UROLOGY ■■: ■■–■■, 2017. © 2017 Elsevier Inc.

Long-term stability of renal function is important in patients undergoing nephrectomy because it is directly associated with adverse renal and cardiovascular morbidities.[1] Therefore, prediction of renal function and evaluation of the factors affecting postnephrectomy renal function are important for patient counseling and preventing chronic kidney disease after nephrectomy.

After nephrectomy, glomerular filtration rate (GFR) of the remaining kidney has been reported to recover up to 60%-80% of the preoperative level,[2-4] and the recovery of renal function has been shown to be low in obese patients, elderly patients, and patients with low preoperative GFR.[2,4,5] The effects of age and preoperative renal function on postoperative renal recovery are well known. Postnephrectomy GFR recovery has been reported to be 11%-15% lower in old patients than in young patients,[5] and patients with a preoperative GFR of <60 mL/min/1.73 m^2 have been reported to have a low decline in GFR after nephrectomy, owing to a large compensatory hyperfiltration capacity.[2]

Obesity is accompanied by metabolic syndrome (MS) components, such as hypertension, hyperglycemia, and hyperlipidemia,[6] and it is known to influence the reduction in renal function.[7] However, human studies on the effect of obesity on postoperative renal function have mainly investigated obesity as a predictor of GFR changes.[5,8] There have been no studies on the renal compensational mechanism focused on obesity in humans.

According to animal experiments, GFR compensation occurs after nephrectomy; this is associated with significant hypertrophy of the tubules and glomeruli, and an increase in the single nephron GFR (SNGFR, functional hyperfiltration).[9,10] Recent human studies have evaluated structural hypertrophy through renal parenchymal

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volumetry[2,11,12] and functional hyperfiltration using the concept of GFR/FRV (functional renal volume), which represents the SNGFR.[2,11]

In the present study, we investigated the postnephrectomy renal adaptation mechanism focused on functional hyperfiltration as well as structural hypertrophy in patients with abdominal obesity and presented the different compensation mechanisms in obese patients.

MATERIALS AND METHODS

Patients

The present study was approved by our institutional review board (IRB No. 2016-04-035). The study enrolled 358 patients who underwent radical or simple nephrectomy or nephroureterectomy at our institution between 2009 and 2013. Patients who were followed up with regular Modification of Diet in Renal Disease GFR evaluation and computed tomography (CT) were included. Patients with an abnormal contralateral kidney having a pathologic condition or those with previous surgery, bilateral kidney tumor, hydronephrosis, or preoperative GFR <30 mL/min/1.73 m^2 were excluded. Clinical data were retrospectively collected from medical records. Abdominal obesity was defined as a waist circumference (WC) >102 cm in men and <88 cm in women, according to the National Cholesterol Education Program's Adult Treatment Panel III clinical identification of MS (Supplementary Table S1).[13] Additionally, according to this panel, MS was diagnosed.

Volume Measurement

For kidney volume measurements, preoperative and 6-month postoperative CT images of 5-mm thickness obtained with a 16 or 64 multidetector helical CT system (Siemens, Erlangen, Germany) were used. FRV was measured with Rapidia (Infinitt, Seoul, Republic of Korea) with a tissue segmentation tool, as described previously.[14] FRV was defined as normally enhanced renal parenchymal area, excluding the area of a tumor, vessel, or urinary calyceal system in the venous phase on CT. The final volume was calculated as the mean of 2 results assessed by 3 urologists. Both the interobserver and intraobserver variabilities were <1%, and the intra-class correlation was 0.993 (95% confidence interval, 0.989-0.996). WC was measured by drawing a circle around the skin border at the level of the iliac crest in preoperative CT images.

GFR/FRV was calculated as GFR per FRV at the same observation time point. Because we wanted to predict the preoperative factors related to postoperative GFR, we calculated the "predicted preserved FRV ratio" as preoperative contralateral FRV per preoperative overall FRV, and this preoperative calculated ratio can represent the FRV preservation rate immediately after surgery.

Statistical Analysis

Variables were compared by using Student *t* test and chi-square test. Volume and functional changes were investigated using the analysis of variance test. To determine the factors associated with an increase in postoperative GFR/FRV and the postoperative GFR, univariate and multivariate linear regression analyses were performed. All statistical analyses were performed using PASW statistics 23 software (SPSS, Inc., Chicago, IL). A *P* value <.05 was considered statistically significant.

RESULTS

Different Clinical Features Between Obese Patients and Nonobese Patients

The patient characteristics are presented in Supplementary Table S2. The mean age was 54.2 years, and 26.3% of the patients exhibited MS. The mean preoperative GFR and FRV were 72.1 mL/min/1.73 m^2 and 282.8 cm^3, respectively, and the mean postoperative GFR and FRV were 58.8 mL/min/1.73 m^2 and 168.7 cm^3, respectively. Table 1

Table 1. Perioperative and postoperative differences according to WC

Characteristics	Normal WC (n = 256)	High WC (n = 102)	*P* Value
Age (y)	53.4 ± 17.0	56.1 ± 15.1	.165
Male/Female, (n, %)	176/80 (68.8%/31.3%)	50/52 (49.0%/51.0%)	<.001
Metabolic syndrome, (n, %)	50 (19.5%)	44 (43.1%)	<.001
Hypertension, (n, %)	73 (28.5%)	43 (42.2%)	.010
Hyperglycemia, (n, %)	75 (29.3%)	34 (33.3%)	.266
Hypertryglyceridemia, (n, %)	78 (30.5%)	42 (41.2%)	.036
Reduced levels of HDL-C, (n, %)	128 (50.0%)	60 (58.8%)	.082
Preoperative			
MDRD GFR (mL/min/1.73 m^2)	76.6 ± 33.0	60.8 ± 28.0	<.001
Proteinuria	35 (13.7%)	24 (23.5%)	.025
FRV (cm^3)	292.0 ± 79.5	259.7 ± 53.8	.014
Contralateral kidney volume (cm^3)	161.8 ± 35.7	137.4 ± 47.5	<.001
Predicted preserved FRV ratio	0.56 ± 0.23	0.52 ± 0.17	.018
GFR/FRV (mL/min/1.73 m^2/cm^3)	0.26 ± 0.13	0.23 ± 0.09	.003
Postoperative (6 mo)			
MDRD GFR (mL/min/1.73 m^2)	64.3 ± 34.7	45.0 ± 20.5	<.001
Proteinuria	39 (15.2%)	46 (45.1%)	<.001
FRV (cm^3)	175.0 ± 31.5	153.0 ± 49.8	.002
GFR/FRV (mL/min/1.73 m^2/cm^3)	0.37 ± 0.17	0.29 ± 0.09	.004

FRV, functional renal volume; GFR, glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; MDRD, Modification of Diet in Renal Disease; WC, waist circumference.
Data are presented as mean ± SD or number (%).

presents comparisons between the normal WC group and high WC group. Among the components of MS, hypertension and hypertriglyceridemia were significantly more common in the high WC group than in the normal WC group (42.2% vs 28.5% and 41.2% vs 30.5%, respectively, both $P < .05$). However, other components of MS, such as hyperglycemia and reduced levels of high-density lipoprotein cholesterol, were not significantly different between the groups. The preoperative GFR was significantly lower in the high WC group than in the normal WC group (60.8 mL/min/1.73 m^2 vs 76.6 mL/min/1.73 m^2, $P < .001$). Proteinuria was more common in the high WC group than in the normal WC group (23.5% vs 13.7%, $P = .025$). Additionally, the preoperative FRV and contralateral kidney volume were lower in the high WC group than in the normal WC group (259.7 cm^3 vs 292.0 cm^3, $P = .014$, and 137.4 cm^3 vs 161.8 cm^3, $P < .001$, respectively). Moreover, the preoperative predicted preserved FRV ratio and GFR/FRV were significantly lower in the high WC group than in the normal WC group (0.52 vs 0.56, $P = .018$, and 0.23 mL/min/1.73 m^2/cm^3 vs 0.26 mL/min/1.73 m^2/cm^3, $P = .003$, respectively). The postoperative GFR, FRV, and GFR/FRV were significantly lower in the high WC group than in the normal WC group (45.0 mL/min/1.73 m^2 vs 64.3 mL/min/1.73 m^2, $P < .001$; 153.0 cm^3 vs 175.0 cm^3, $P = .002$; and 0.29 mL/min/1.73 m^2/cm^3 vs 0.37 mL/min/1.73 m^2/cm^3, $P = .004$, respectively).

Different Compensational Adaptation After Nephrectomy in Obese Patients

The decrease in GFR after surgery was higher in the high WC group than in the normal WC group (25.9% vs 16.0%, $P = .036$, Fig. 1A). Comparison of postoperative changes in each group showed that the remnant kidney volume increased by 11.4% in the high WC group and 8.1% in the normal WC group, and the difference was not significant ($P = .675$, Fig. 1B). Overall, GFR/FRV showed a 36.4% increase 6 months after surgery, and groupwise assessment showed that the GFR/FRV increase was significantly lower in the high WC group than in the normal WC group (25.7% vs 40.2%, $P = .009$, Fig. 1C).

Predictors of Postoperative Increase in GFR/FRV and GFR at 6 Months Postoperatively

Multivariate analysis revealed that the low preoperative GFR ($P = .005$), proteinuria ($P < .001$), the high predicted preserved FRV ratio ($P = .043$), absence of hypertension ($P = .003$), increased levels of high-density lipoprotein cholesterol ($P = .044$), and a normal WC ($P = .025$) could significantly predict a postoperative increase in GFR/FRV (Table 2). Additionally, multivariate analysis revealed that young age ($P < .001$), the high preoperative GFR ($P < .001$), absence of proteinuria ($P = .042$), the high predicted preserved FRV ratio ($P < .001$), absence of hypertension ($P = .002$), and a normal WC ($P = .003$)

Table 2. Multiple linear regression analysis for factors associated with postoperative increase in GFR/FRV and postoperative 6-month MDRD GFR

	Univariate			Multivariate		
Factor	β	(95% CI)	*P* Value	β	(95% CI)	*P* Value
Postoperative increase in GFR/FRV						
Age (y)	−0.001	−0.002 to 0.001	.530	−0.001	−0.003 to 0.001	.187
Female	−0.034	−0.083 to 0.014	.162			
Preoperative MDRD GFR (mL/min/1.73 m^2)	−0.002	−0.003 to −0.001	.003	−0.001	−0.002 to −0.001	.005
Proteinuria	0.092	0.031-0.154	.003	0.112	0.052-0.171	<.001
Predicted preserved FRV ratio	0.148	−0.010 to 0.307	.067	0.167	0.005-0.329	.043
Hypertension (y/n)	−0.069	−0.114 to −0.023	.004	−0.069	−0.114 to −0.024	.003
Hyperglycemia (y/n)	−0.051	−0.104 to 0.002	.057			
Hypertryglyceridemia (y/n)	−0.043	−0.090 to 0.004	.075			
Reduced levels of HDL-C (y/n)	−0.051	−0.097 to −0.004	.032	−0.045	−0.090 to −0.001	.044
High waist circumference (y/n)	−0.055	−0.107 to −0.004	.036	−0.055	−0.107 to −0.004	.025
Metabolic syndrome (y/n)	−0.019	−0.070 to 0.031	.455			
Postoperative 6-month MDRD GFR						
Age (y)	−1.115	−1.285 to −0.946	<.001	−0.298	−0.445 to −0.151	<.001
Female	10.839	3.926-17.752	.002	1.724	−2.083 to 5.532	.373
Preoperative MDRD GFR (mL/min/1.73 m^2)	0.762	0.721-0.804	<.001	0.662	0.605-0.719	<.001
Proteinuria	−14.071	−22.939 to −5.203	.002	−4.869	−9.568 to −0.170	.042
Predicted preserved FRV ratio	0.647	0.473-0.821	<.001	32.037	19.201-44.872	<.001
Hypertension (y/n)	−8.765	−15.928 to −1.602	.017	−5.668	−9.300 to −2.035	.002
Hyperglycemia (y/n)	−8.096	−15.391 to −0.801	.030	0.324	−3.561 to 4.209	.870
Hypertryglyceridemia (y/n)	−6.164	−13.265 to 0.937	.089			
Reduced levels of HDL-C (y/n)	−2.822	−9.583 to 3.939	.412			
High waist circumference (y/n)	−19.232	−26.446 to −12.018	<.001	−6.179	−10.181 to −2.177	.003
Metabolic syndrome (y/n)	−7.339	−14.954 to 0.277	.059			

Abbreviations as in Table 1.
Data are presented as mean ± SD or number (%).

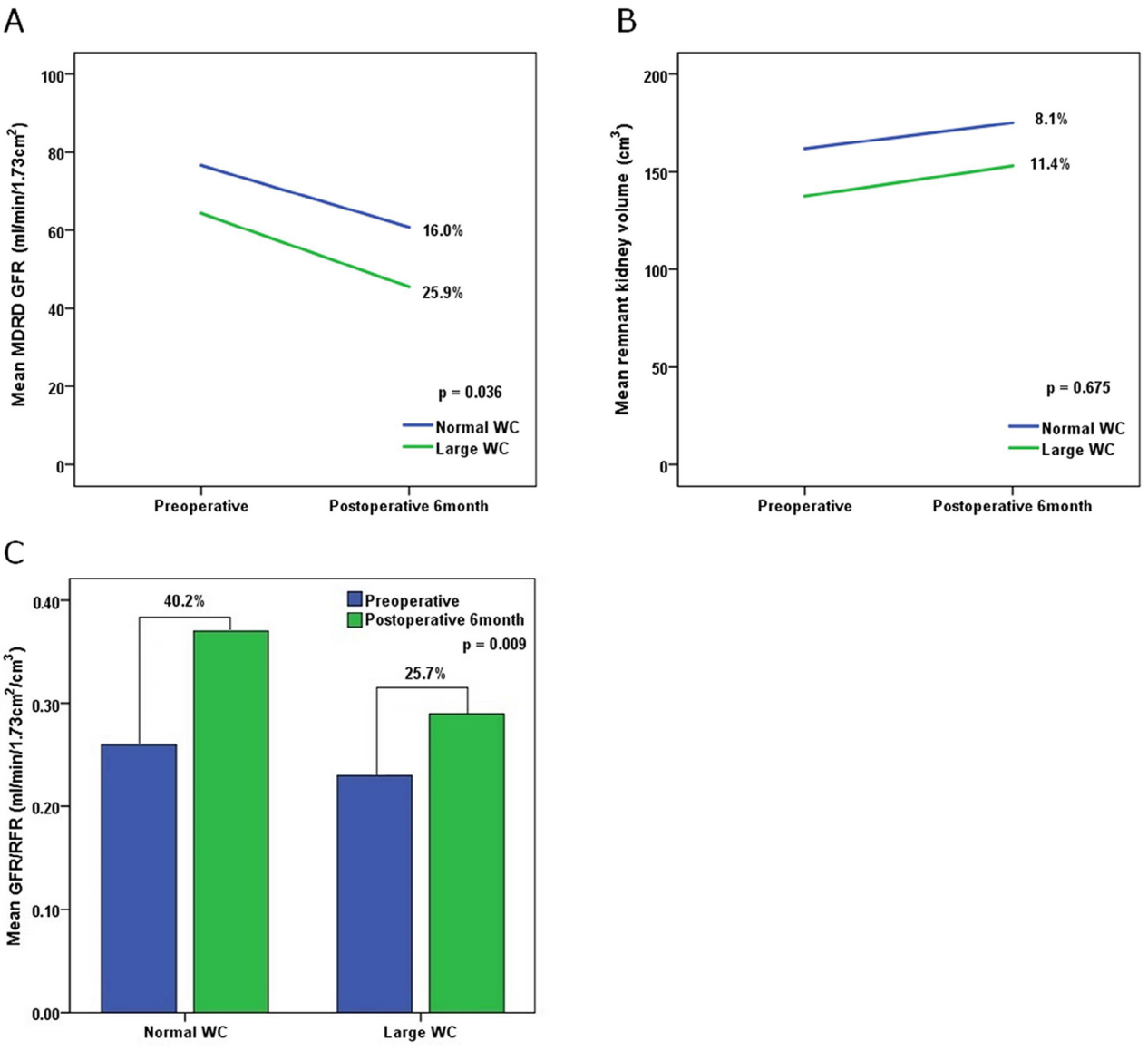

Figure 1. Perioperative changes of GFR, remnant kidney volume, and GFR/FRV. **(A)** Preoperative GFR and postoperative reduction in GFR according to WC. **(B)** Preoperative FRV of the remnant kidney and degree of postoperative hypertrophy according to WC. **(C)** Postoperative increase in GFR/FRV according to WC. FRV, functional renal volume; GFR, glomerular filtration rate; WC, waist circumference. (Color version available online.)

could significantly predict the postoperative GFR (Table 2). Sex was a predictive factor for postoperative GFR only in univariate analysis and not in multivariate analysis.

DISCUSSION

Abdominal obesity is one of the MS components[13,15] and is associated with medical comorbidities.[16,17] Obesity and MS are likely to be accompanied by chronic histological changes, such as glomerulosclerosis.[6] Our finding that preoperative renal function and renal volume were significantly lower in obese patients than in normal patients might be related with comorbidities and histological changes, which result in aggravation of nephron deficiency and renal volume decrease.[1,18] Thus, nephrectomy in patients with obesity or MS might be associated with subsequent delayed recovery of renal function.[7] Old age, low preoperative renal function, hypertension, obesity, and preserved FRV have been reported to be predictors of kidney dysfunction after nephrectomy[15,19]; these findings are consistent with our results. Yoon et al reported that obesity is the most significant factor for predicting delayed kidney function recovery after nephrectomy,[15] and preoperative histological change and combined hypertension in obese patients have been shown to lead to perioperative acute kidney injury.[16] Compensational adaptation after nephrectomy could be explained by both structural hypertrophy and functional glomerular hyperfiltration.[2,11] However, postoperative compensatory adaptation in obese patient has not been examined previously. Therefore, we evaluated glomerular

hyperfiltration as well as compensatory hypertrophy in obese patients who underwent uninephrectomy.

In our study, the renal function decrease 6 months after nephrectomy was over 25% in the high WC group and was 16% in the normal WC group. Additionally, the increase in proteinuria was over 21.6% in the high WC group and was 1.5% in the normal WC group. A previous study reported that obese patients showed an increased prevalence of renal insufficiency and that 30% and 60% of obese patients showed chronic renal failure and proteinuria 10 years after nephrectomy.[20] On the other hand, in another previous study, healthy living kidney donors showed a reduction in the GFR of 12.5% and a small increase in 24-hour proteinuria.[21] In another study, postoperative renal functional reserve capacity was absent in obese donors and obesity had a higher impact on the loss of renal reserve capacity in young patients.[8] Our findings of a large decrease in GFR after nephrectomy among patients with high WC are supported by these previous reports.

CT-based kidney volume measurement is an objective and reproducible tool for assessing renal parenchymal volume,[3,14,22] and kidney volume has been found to correlate well with the number of functioning nephrons.[23] Compensational hypertrophy is an adaptive mechanism for nephron loss and consequential functional loss, and renal hypertrophy after nephrectomy is mainly associated with significant hypertrophy of tubules.[9,10] In previous studies with rats that underwent uninephrectomy, the volume, diameter, and length of the proximal convoluted tubule increased by 96%, 17%, and 35%, respectively, while these parameters of the distal tubule increased by 25%, 12%, and 17%, respectively.[9,10] In recent human studies, compensational hypertrophy of the remnant kidney was 17%-30%, and the rate of hypertrophy was higher in donor nephrectomy cases than in radical nephrectomy cases.[2,3,24] Generally, compensational hypertrophy after nephron loss is mainly influenced by preserved parenchymal volume[22,25]; however, limited data are available on whether obesity influences compensational hypertrophy after nephrectomy. Age, medical conditions, such as hypertension, and preoperative impaired renal function status were not found to be associated with the degree of hypertrophy after nephrectomy; however, the relationship between obesity and hypertrophy has been controversial.[2,24] In our study, compensational hypertrophy was significant in both the normal and high WC groups; however, the degree of hypertrophy was not different according to the WC status. These results indicate that structural hypertrophic adaptation is not the primary event that leads to a different functional GFR recovery course in patients with high WC.

Functional glomerular adaptation after nephrectomy has been reported to occur over the entire recovery period.[9,26] As a result of adaptation, the SNGFR increases and offsets the overall GFR decrease after functional volume loss. The mechanism of functional compensation has 2 phases. In the early phase, afferent arteriolar resistance reduction and transforming growth factor-β reactivity increase, owing to functional volume loss, resulting in an increase in fluid absorption in isolated proximal tubule segments within 24 hours of nephrectomy in both animals and humans.[26,27] Therefore, the SNGFR increases for solute handling before hypertrophy occurs. In the chronic phase, an increase in the reabsorptive load stimulates structural hypertrophy in both the proximal and distal tubules, which has been mentioned previously.[9,10] Salehmoghaddam et al found that the mitochondrial volume, but not the density, is increased in the hypertrophic proximal tubule.[28] This indicates that the activity of the Na^+/K^+/ATPase pump, which generates the main driving force for proximal tubule solute transport, is increased. Subsequently, passive Starling forces and the glomerulotubular balance mechanism of the loop of Henle and distal tubule result in the final SNGFR increase.[9] Therefore, functional hyperfiltration and structural hypertrophy occur simultaneously, and one condition can trigger the other.

As there are many difficulties in the measurement of the SNGFR in humans, the concept of GFR/FRV, which clinically indicates the SNGFR, is being increasingly used.[2,11,12] In GFR/FRV studies using CT volumetry, GFR/FRV increase was associated with age, hypertension, diabetes mellitus, body mass index, and preoperative GFR.[2,11] The data indicated that postoperative GFR/FRV is lower in obese patients than in nonobese patients, and this is consistent with our findings. However, no study about GFR/FRV that focused on obese patients has been performed. Our data showed that the preoperative GFR and degree of compensational hyperfiltration were lower in obese patients than in nonobese patients. Additionally, obesity as well as preoperative renal function, the predictive preserved functional parenchymal volume ratio, hypertension, and hyperglycemia were related to the degree of hyperfiltration after nephrectomy, and these findings are almost consistent with those of a previous study.[2] However, we noted that structural hypertrophy was not different between the 2 groups. This indicates that obesity affects the degree of hyperfiltration, and the low degree of compensational hyperfiltration in obese patients results in a smaller degree of final GFR increase after nephrectomy when compared with the degree in normal patients.

Reserve capacity is the ability to induce hyperfiltration of the total kidney volume, and it is assessed as the increase in GFR during pharmacological stimulation with low-dose dopamine, amino acids, and both. This rise in GFR is mediated by a rise in renal blood flow as well as altered glomerular pressure. A previous study reported that reserve capacity, which can indirectly represent the SNGFR, was low in obese patients who underwent nephrectomy.[8] Additionally, the study assessed GFR before and after donation and found that the reserve capacity was low in older and obese donors after donation.[8] These findings indicate that hemodynamic changes differ between obese patients and nonobese patients after nephrectomy, although the FRV was not considered. Glomerular hyperfiltration in obese patients does not increase as much as that in normal patients, possibly because of the underlying hyperfiltration

status and medical comorbidities in obese patients. Obesity-related glomerulopathy is characterized by elevated GFR, increased renal plasma flow, and glomerulomegaly with or without glomerulosclerosis.[29] This hyperfiltration-induced glomerulopathy reinitiates a cascade of hyperfiltration by increasing arterial pressure and intraglomerular pressure.[30] Therefore, there is little room for the additive hyperfiltration compensation to adapt to renal volume loss after nephrectomy, because the kidneys of obese patients are already maximally using this pathway to maintain baseline adaptation and have a hyperfiltration reserve. Obesity-related comorbidities could also cause low functional compensation after nephrectomy in obese patients. Our data showed that hypertension and hyperglycemia are significantly associated with obesity. A previous study demonstrated that hypertension, diabetes mellitus, and chronic kidney disease are related with an increase in GFR/FRV above the mean value.[2] Additionally, high prevalence of chronic histological changes in MS patients[6] could weaken the compensational hyperfiltration capacity. For these reasons, the results of compensational adaptation are somewhat different between obese patients and nonobese patients. In summary, the degree of compensational hyperfiltration was lower in obese patients than in nonobese patients, whereas the degree of structural hypertrophy was similar between the patient groups. These were associated with the small degree of overall GFR increase in obese patients after nephrectomy.

In our study, sex was not a predictive factor for the 6-month GFR. However, in subgroup multivariate analysis, we found that in the male group, the 6-month GFR was low in old and obese patients (both $P = .001$, data not shown). This result is consistent with that in a previous report,[5] suggesting that old obese male patients should be closely followed up after surgery.

The present study has some limitations. The study had a retrospective design and included a nonhomogenous sample with various types of nephrectomies. Additionally, we had to use the calculated GFR because of the lack of true measured GFR (exp. iohexol, isotopes) results in our retrospective data. Selective bias may be present as cases that were regularly followed up with CT were selected for CT-based volume measurement. Additionally, measurement errors might be present in the volume and WC measurements. We intend to continue our investigation on a large scale to obtain prospective long-term follow-up data with a large number of patients.

CONCLUSION

We found that compensatory adaptation after nephrectomy involves not only hypertrophy but also functional hyperfiltration in obese patients. Additionally, during compensatory adaptation, functional hyperfiltration might be more crucial than structural hypertrophy for determining postnephrectomy renal function recovery in high WC patients.

References

1. Fong D, Denton KM, Moritz KM, et al. Compensatory responses to nephron deficiency: adaptive or maladaptive? *Nephrology (Carlton)*. 2014;19:119-128.
2. Choi DK, Jung SB, Park BH, et al. Compensatory structural and functional adaptation after radical nephrectomy for renal cell carcinoma according to preoperative stage of chronic kidney disease. *J Urol*. 2015;194:910-915.
3. Jeon HG, Gong IH, Hwang JH, et al. Prognostic significance of preoperative kidney volume for predicting renal function in renal cell carcinoma patients receiving a radical or partial nephrectomy. *BJU Int*. 2012;109:1468-1473.
4. Mueller TF, Luyckx VA. The natural history of residual renal function in transplant donors. *J Am Soc Nephrol*. 2012;23:1462-1466.
5. Mjoen G, Oyen O, Midtvedt K, et al. Age, gender, and body mass index are associated with renal function after kidney donation. *Clin Transplant*. 2011;25:E579-E583.
6. Alexander MP, Patel TV, Farag YM, et al. Kidney pathological changes in metabolic syndrome: a cross-sectional study. *Am J Kidney Dis*. 2009;53:751-759.
7. Ohashi Y, Thomas G, Nurko S, et al. Association of metabolic syndrome with kidney function and histology in living kidney donors. *Am J Transplant*. 2013;13:2342-2351.
8. Rook M, Bosma RJ, van Son WJ, et al. Nephrectomy elicits impact of age and BMI on renal hemodynamics: lower postdonation reserve capacity in older or overweight kidney donors. *Am J Transplant*. 2008;8:2077-2085.
9. Skorecki K. *Brenner & Rector's The Kidney [electronic resource]*. Philadelphia, PA: Elsevier/Saunders; 2016.
10. Hayslett JP, Kashgarian M, Epstein FH. Functional correlates of compensatory renal hypertrophy. *J Clin Invest*. 1968;47:774-799.
11. Hosokawa Y, Tanaka N, Mibu H, et al. Follow-up study of unilateral renal function after nephrectomy assessed by glomerular filtration rate per functional renal volume. *World J Surg Oncol*. 2014;12:59.
12. Takagi T, Mir MC, Campbell RA, et al. Predictors of precision of excision and reconstruction in partial nephrectomy. *J Urol*. 2014;192:30-35.
13. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation*. 2002;106:3143-3421.
14. Gong IH, Hwang J, Choi DK, et al. Relationship among total kidney volume, renal function and age. *J Urol*. 2012;187:344-349.
15. Yoon YE, Choi KH, Lee KS, et al. Impact of metabolic syndrome on postdonation renal function in living kidney donors. *Transplant Proc*. 2015;47:290-294.
16. Suneja M, Kumar AB. Obesity and perioperative acute kidney injury: a focused review. *J Crit Care*. 2014;29:694-696.
17. Martin Rodriguez E, Guillen Grima F, Martí A, et al. Comorbidity associated with obesity in a large population: the APNA study. *Obes Res Clin Pract*. 2015;9:435-447.
18. Henegar JR, Bigler SA, Henegar LK, et al. Functional and structural changes in the kidney in the early stages of obesity. *J Am Soc Nephrol*. 2001;12:1211-1217.
19. Isotani S, Shimoyama H, Yokota I, et al. Novel prediction model of renal function after nephrectomy from automated renal volumetry with preoperative multidetector computed tomography (MDCT). *Clin Exp Nephrol*. 2015;19:974-981.
20. Praga M, Hernández E, Herrero JC, et al. Influence of obesity on the appearance of proteinuria and renal insufficiency after unilateral nephrectomy. *Kidney Int*. 2000;58:2111-2118.
21. Garg AX, Muirhead N, Knoll G, et al. Proteinuria and reduced kidney function in living kidney donors: a systematic review, meta-analysis, and meta-regression. *Kidney Int*. 2006;70:1801-1810.
22. Choi KH, Yoon YE, Kim KH, et al. Contralateral kidney volume change as a consequence of ipsilateral parenchymal atrophy pro-

motes overall renal function recovery after partial nephrectomy. *Int Urol Nephrol*. 2015;47:25-32.
23. Nyengaard JR, Bendtsen TF. Glomerular number and size in relation to age, kidney weight, and body surface in normal man. *Anat Rec*. 1992;232:194-201.
24. Taner T, Iqbal CW, Textor SC, et al. Compensatory hypertrophy of the remaining kidney in medically complex living kidney donors over the long term. *Transplantation*. 2015;99:555-559.
25. Simmons MN, Hillyer SP, Lee BH, et al. Functional recovery after partial nephrectomy: effects of volume loss and ischemic injury. *J Urol*. 2012;187:1667-1673.
26. Tabei K, Levenson DJ, Brenner BM. Early enhancement of fluid transport in rabbit proximal straight tubules after loss of contralateral renal excretory function. *J Clin Invest*. 1983;72:871-881.
27. Kamper AL, Holstein Rathlou NH, Strandgaard S, et al. Glomerular filtration rate and segmental tubular function in the early phase after transplantation/uninephrectomy in recipients and their living-related kidney donors. *Clin Sci*. 1994;87:519-523.
28. Salehmoghaddam S, Bradley T, Mikhail N, et al. Hypertrophy of basolateral Na-K pump activity in the proximal tubule of the remnant kidney. *Lab Invest*. 1985;53:443-452.
29. Goumenos DS, Kawar B, El Nahas M, et al. Early histological changes in the kidney of people with morbid obesity. *Nephrol Dial Transplant*. 2009;24:3732-3738.
30. Brenner BM, Lawler EV, Mackenzie HS. The hyperfiltration theory: a paradigm shift in nephrology. *Kidney Int*. 1996;49:1774-1777.

APPENDIX

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.urology.2017.02.022.