Cross-Sectional Investigations of Pre- and Post-Operative Renal Global Function and Renal Parenchymal Volumetry in Both Partial and Radical Nephrectomy Utilizing Film-Based Technology

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Abstract
Objectives: To investigate pre- and post-operative renal global function and renal parenchymal volume (RPV) in both partial nephrectomy (PN) and radical nephrectomy (RN) utilizing film-based technology. Patients and Methods: The patient cohort consisted of 81 and 82 cases with T1 tumors (≤ 7 cm) treated by PN and RN, respectively. Renal global function was assessed using the estimated glomerular filtration rate (eGFR), and RPV was measured using a Synapse Vincent volumetric analyzer which creates a reconstructed image from a computed tomography scan. Renal global function and RPV were evaluated pre-operatively and 6 months post-operatively. Results: The percent eGFR decline of PN cases was significantly reduced compared with RN cases (p < 0.0001). Post-operative RPV of the contralateral side was significantly increased compared with pre-operative RPV (p < 0.0001) in RN cases. The percent change of the contralateral side RPV was slightly increased in RN compared with PN cases (p = 0.1881). A strong positive correlation was noted between post-operative eGFR and post-operative total RPV (r = 0.69, p < 0.0001), and a strong negative correlation was noted between percent eGFR decline and post-operative total RPV (r = -0.63, p < 0.0001). Conclusions: Prominent compensatory renal hypertrophy occurred within 6 months after RN. Post-operative renal functional outcome was closely correlated with the post-operative total RPV. In addition to RPV, further studies to unravel post-operative renal function from multifactorial aspects including surgical factors and intrinsic medical disease should be performed in the future.

Introduction
Radical nephrectomy (RN) has served as the most reliable treatment for renal masses for decades. The traditional surgical procedure consists of the removal of the entire kidney including Gerota’s fascia, regional lymph nodes, and the adrenal gland. Post-RN renal global func-
tional deterioration is inevitable as the result of complete loss of the disease-side renal unit including the non-neoplastic renal parenchyma. Given that the post-RN percentage for estimated glomerular filtration rate (eGFR) decline was previously reported as approximately 30% [1–3], the majority of cases treated by RN are categorized as chronic kidney disease (CKD) post-operatively. The negative impact on renal function and the association with CKD was previously demonstrated in a large patient cohort [4]. When compared with the high incidence of post-operative CKD in RN, partial nephrectomy (PN) is an ideal surgical procedure that can reduce the probability of post-operative renal insufficiency. The American Urological Association guidelines advocate that PN is currently considered the treatment of choice for most clinical T1 renal masses, even in those with a normal contralateral kidney [5].

In both RN and PN, post-operative renal global function is a crucial outcome in addition to oncological control. The residual renal parenchymal volume (RPV) may correlates with post-operative renal global function not only in RN but also in PN. For example, compensatory renal hypertrophy (CRH) of the contralateral side plays an essential role in post-RN renal function, whereas post-operative late eGFR primarily depends upon preserved functional RPV in PN [6, 7]. Compared with prominent CRH in neonates and children [8, 9], CRH in adults is modest. Moreover, factors affecting on this phenomenon are multifactorial in the adult population, and details, particularly in PN, are very limited.

In the present study, we investigated post-operative changes of RPV in cases with T1 tumors treated by RN and PN, focusing on CRH of the contralateral side using a high-speed 3-dimensional image analysis system (SYNAPSE VINCENT, Fujifilm Corp, Tokyo, Japan) in a cross-sectional manner. We also analyzed the association between post-operative RPV and renal global functional outcome in both types of surgery.

Materials and Methods

Patients
We retrospectively collected detailed clinicopathological data from 230 patients with ipsilateral renal tumors who underwent PN or RN between October 2005 and August 2014 at Tottori University Hospital and affiliated hospitals. Among these patients, 163 patients with T1 tumors (≤ 7 cm) were extracted for the study. In total, 81 and 82 patients were treated by PN and RN, respectively. The ischemic method was employed in all cases of PN. The study was approved by an appropriately constituted ethics committee at Tottori University Hospital.
Post-Operative Renal Global Functional Evaluation

Patient eGFR was calculated using the following equation: eGFR = 194 × serum creatinine \(^{-1.094}\) × age \(^{-0.287}\) (for female × 0.739) [10]. This formula is currently recommended by the Japanese Society of Nephrology. The percent eGFR decline was defined as follows: (pre-operative eGFR – post-operative eGFR) / pre-operative eGFR × 100%. The examinations of eGFR was performed within 3 months pre-operatively and 6 months post-operatively.

Renal Parenchymal Volumetry

Renal parenchymal volumetry as assessed by computed tomography (CT) scan was performed using the volume analyzer SYNAPSE VINCENT (Fujifilm). In the cases treated by PN for pre-operative renal parenchymal volumetry of diseased side, volumetry was performed using the constructed renal image after determining the tumor area (fig. 1). The percent change of RPV was defined as follows: (post-operative RPV – pre-operative RPV) / pre-operative RPV × 100%. CT scans were performed within 3 months pre-operatively and 6 months post-operatively.

Statistical Analyses

Post-operative renal global functional decline between PN and RN cases was analyzed using unpaired Student’s t-tests. Comparisons of RPV (diseased, contralateral and bilateral sides) between pre- and post-operative periods were analyzed using paired Student’s t-tests. The percent change of contralateral side RPV between PN and RN cases was analyzed using unpaired Student’s t-tests. The correlation between post-operative eGFR and post-operative total RPV as well as post-operative eGFR decline and post-operative total RPV were analyzed using Pearson’s product moment correlation coefficient. P < 0.05 was considered to be statistically significant.

Table 1. Patient backgrounds of T1 cases treated by PN and RN

| Variables | Value (mean ± SD / n) | p |
|-----------|-----------------------|---|
| Age, year | 64.0 ± 13.3 65.4 ± 14.1 | 0.519 |
| Gender | | 0.7008 |
| Male | 53 | 53 |
| Female | 28 | 29 |
| BMI, kg/m\(^2\) | 24.0 ± 3.4 23.5 ± 3.1 | 0.3901 |
| ECOG PS | | 0.2144 |
| 0 | 48 | 58 |
| 1 | 32 | 24 |
| 2 | 1 | 0 |
| Age-adjusted CCE: median (range) | 4 (2–8) 3 (0 – 7) | 0.1245 |
| ASA score | | 0.2792 |
| Class I | 11 | 20 |
| Class II | 65 | 55 |
| Class III | 4 | 6 |
| Class IV | 1 | 1 |
| Pre-operative eGFR, ml/min/1.73m\(^2\) | 76.2 ± 18.5 75.8 ± 15.1 | 0.8828 |
| Post-operative eGFR, ml/min/1.73m\(^2\) | 67.2 ± 17.2 51.2 ± 11.5 | <0.0001 |
| Diseased side | | 0.4817 |
| Right | 42 | 38 |
| Left | 39 | 44 |
| Tumor diameter, cm | 2.4 ± 0.8 4.0 ± 1.5 | <0.0001 |
| Tumor volume, ml | 9.1 ± 8.1 26.1 ± 25.8 | <0.0001 |
| Surgical type | | <0.0001 |
| Open | 39 | 33 |
| Laparoscopic | 20 | 49 |
| Robotic | 22 | 0 |
| Ischemic method | | |
| Warm | 40 | N/A |
| Cold | 41 | N/A |
| Ischemic time, min | 26.9 ± 14.5 | N/A |
| Pathology | | 0.0223 |
| Benign | 5 | 0 |
| Malignant | 76 | 82 |
| Surgical margin | | 0.1522 |
| Negative | 79 | 82 |
| Positive | 2 | 0 |
| Fuhrman grade | | 0.3966 |
| 1 | 27 | 35 |
| 2 | 51 | 43 |
| 3 | 3 | 4 |
| 4 | 0 | 0 |
| Cell type | | 0.1355 |
| Clear cell | 55 | 51 |
| Chromophobe | 18 | 14 |
| Papillary | 6 | 7 |
| Cystic | 2 | 5 |
| Sarcomatoid | 0 | 5 |

BMI = Body mass index; CCI = Charlson comorbidity index.

Results

Comparison of Patient Backgrounds between PN and RN

The backgrounds of all patients are summarized in table 1. In comparisons of backgrounds between PN and RN, significant differences were noted in pre-operative eGFR, tumor diameter, tumor volume, surgical type and pathology (benign or malignant) between the 2 groups. Post-operative eGFR was significantly increased in PN compared with RN. Tumor diameter and volume were significantly reduced in PN compared with RN. Surgical type significantly shifted towards robot-assisted surgery in PN compared with RN. Pathology significantly shifted towards benign in PN compared with RN.

Comparison of Post-Operative Renal Global Functional Decline between PN and RN Cases

The mean and standard deviation (SD) values of percent eGFR decline in PN cases were 11.8 and 8.9, respectively. The mean and SD values of percent eGFR decline in RN cases were 32.3 and 9.1, respectively. The percent eGFR decline of PN cases was significantly reduced compared with RN cases (p < 0.0001).

Comparisons of RPV between Pre- and Post-Operative Periods in Cases Treated by PN and RN

The mean (SD) pre-operative RPV of contralateral, diseased side, and bilateral sides in PN cases were 161.5 (40.0), 159.7 (44.8) and 321.1 (80.0) ml, respectively. The mean (SD) post-operative RPV of contralateral, diseased side and bilateral sides in PN cases were 166.3 (41.8), 131.7 (42.6) and 298.0 (76.0) ml, respectively.

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Post-operative RPV of diseased and bilateral sides both significantly decreased, whereas that of the contralateral side had a tendency to increase compared with pre-operative RPV (fig. 2A). On the other hand, the mean (SD) pre- and post-operative RPV of contralateral side in RN cases was 165.4 (37.0) and 176.2 (43.0) ml, respectively. Post-operative RPV of contralateral side was significantly increased compared with pre-operative RPV (fig. 2B).

**Comparisons of Percent Change of Contralateral Side RPV between PN and RN Cases**

The mean (SD) percent change of contralateral side RPV in PN and RN cases was 3.99 (14.7) and 6.98 (14.1), respectively. The percent change of contralateral side RPV was slightly increased in RN cases compared with PN cases (p = 0.1881). Namely, post-operative contralateral side CRH was slightly prominent in RN cases compared with PN cases.

**Correlation between Post-Operative Renal Global Function and Post-Operative Total RPV**

To elucidate the correlation between post-operative renal global functional outcome and post-operative total RPV in renal surgery, both groups of PN and RN cases were combined. The correlation between post-operative eGFR and post-operative total RPV and the correlation between post-operative eGFR decline and post-operative total RPV were analyzed. A strong positive correlation was noted between post-operative eGFR and post-operative total RPV (r = 0.69, p < 0.0001) (fig. 3), and a strong negative correlation was noted between percent eGFR decline and post-operative total RPV (r = -0.63, p < 0.0001) (fig. 4).

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**Fig. 2.** Comparisons of RPV between pre- and post-operative periods in cases treated by PN (A) and RN (B) are presented. White and black bars indicate pre- and post-operative RPV, respectively. Longitudinal lines at the top of each bar indicate SD.
Currently, two surgical therapeutic approaches are available for renal tumors: RN, and nephron-sparing surgery known as PN. Oncological outcome and post-operative renal function are critical follow-up factors after both types of renal surgery. In our patient cohort, the percent eGFR decline of PN cases was significantly reduced compared with RN cases. Our results are consistent with the universal consensus that PN is beneficial for patients with small renal masses in terms of improved renal function [5]. Considering post-operative renal function in re-

**Discussion**

Currently, 2 surgical therapeutic approaches are available for renal tumors: RN, and nephron-sparing surgery known as PN. Oncological outcome and post-operative renal function are critical follow-up factors after both types of renal surgery. In our patient cohort, the percent eGFR decline of PN cases was significantly reduced compared with RN cases. Our results are consistent with the universal consensus that PN is beneficial for patients with small renal masses in terms of improved renal function [5]. Considering post-operative renal function in re-

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![Graph 1](image1.png)  
**Fig. 3.** The scatter plots and linear correlation between post-operative eGFR and post-operative total RPV are presented. A strong positive correlation was noted between post-operative eGFR and post-operative total RPV ($r = 0.69, p < 0.0001$).

![Graph 2](image2.png)  
**Fig. 4.** The scatter plots and linear correlation between post-operative eGFR decline and post-operative total RPV are presented. A strong negative correlation was noted between percent eGFR decline and post-operative total RPV ($r = -0.63, p < 0.0001$).
nal surgery, post-operative CRH of the contralateral side is a well-known influential factor in RN. Although the renal functional outcome of the diseased side kidney plays a vital role in post-operative renal global function, CRH of the contralateral side also indicates post-operative renal global function in PN. In our cases treated by PN, post-operative RPV of the contralateral side slightly increased compared with pre-operative RPV. A few studies demonstrate CRH of the contralateral side in a PN patient cohort [11, 12]. Kim et al. [12] demonstrated that the tumor and resected parenchymal volume were independent predictive factors of CRH after robot-assisted PN. Large tumors (> 7 cm) were significantly associated with CRH in a mixed cohort of RN and PN [13]. The resected parenchymal volume was also significantly associated with CRH in a mixed cohort of RN and PN [14]. In our cases treated by RN, prominent CRH was of great statistical significance. In the case without intrinsic medical disease that affected renal function, it is predicted that the nephron volume correlates with renal function. Considerable RPV should dictate favorable renal function. In our combined cases of PN and RN, a strong positive correlation between post-operative eGFR and post-operative total RPV was demonstrated. Moreover, a strong negative correlation between percent eGFR decline and post-operative total RPV was demonstrated. These findings strongly suggested that post-operative RPV dictates post-operative renal global functional outcome.

In addition to post-operative RPV, various factors affect post-operative renal global function in renal surgery. Ischemic time from renal arterial clamping is currently considered as the most important surgical factor in PN [15]. Additionally, baseline pre-operative renal function and patient comorbidities are also critical in PN [16, 17]. Similarly, patient intrinsic factors, such as baseline renal function and patient comorbidities, affect post-operative renal functional outcomes in RN. Patient intrinsic factors that affect renal function may be explored by the histopathological analysis of normal renal parenchyma. Bijol et al. [18] demonstrated the presence of pathological arteriosclerosis and diabetes mellitus as frequent findings in nephrectomized normal renal parenchyma in a cohort of 110 consecutive renal tumor patients. Based on the hypothesis that the histopathological environment is identical between the diseased and contralateral sides, the significant association between the extent of global glomerulosclerosis and post-operative renal functional outcome was demonstrated in the RN patient cohort [19]. The elucidation of the relationships among renal function, intrinsic medical disease, RPV and histopathology of normal renal parenchyma should be a future task for the interpretation of post-operative renal functional outcome in renal surgery.

Our study has certain limitations. First, the comparison of RPV was performed between 2 time frames based on the methodology used for a cross-sectional investigation. Longitudinal investigation with long-term, post-operative follow-up is necessary to evaluate the duration for the completion of CRH of the contralateral side. Second, although the volumetric software was easy to use, and we have confidence in our results, some inter-observer variability might exist in the measured volumes. Third, the retrospective nature and the small sample size of patients was an additional limitation.

Conclusions

Prominent CRH occurred 6 months after RN. PN was significantly more beneficial than RN in terms of post-operative renal global functional change. Post-operative renal functional outcome was closely correlated with the post-operative total RPV. However, multiple factors are thought to affect post-operative renal function in renal surgery. Further exploration from multifactorial aspects, including surgical factors and intrinsic medical disease, should be performed to elucidate post-operative renal functional outcome in renal surgery.
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