[Original article]

Estimated functional renal parenchymal volume predicts the split renal function following renal surgery

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Abstract

Purpose: The change in functional renal volume (FRV) has an absolute influence on renal function after nephrectomy (Nx) or nephron sparing surgery (NSS). In this study, we prospectively examined whether the postoperative renal function following Nx and NSS could be accurately predicted, and assessed the reproducibility of our newly developed 3-D image reconstruction system to measure the functional renal volume (FRV). **Methods:** We enrolled 98 patients who underwent Nx and 41 patients who underwent NSS from April 2006 to September 2009 to predict postoperative FRV and renal function. FRV was measured before and after (1 month and 1 year) renal surgery. The postoperative estimated glomerular filtration rate (eGFR) was predicted from the preoperative eGFR calculated from the serum creatinine (sCr) level and the ratio of the postoperative/preoperative FRV. To assess the reproducibility and accuracy of our newly developed 3-dimensional (3-D) image reconstruction system, FRV was measured by 5 examiners using images obtained by CT (5 cases) and MRI (5 cases). **Results:** Significant correlation was found both for FRV and renal function between the predictive values and the actually measured values at 1 month and 1year after surgery, not only in the Nx group, but also the NSS group. The accuracy and reproducibility could be confirmed both with CT and MRI studies. **Conclusions:** The postoperative FRV and renal function could be predicted preoperatively using a 3-D image reconstructive system, preoperative routine diagnostic imaging, and preoperative sCr level.

Key words: Renal function, renal volume, nephrectomy, nephron-sparing surgery, 3-D image reconstruction

Introduction

The number of patients undergoing partial nephrectomy as nephron-sparing surgery (NSS) for the treatment of small renal cell carcinoma (RCC) has recently increased since the outcomes of NSS are quite favorable, similar to those of conventional radical nephrectomy (Nx), particularly in patients with RCC of 4.0 cm or less in diameter.[1,2] However, most of the patients who undergo conventional NSS usually need temporary intraoperative ischemia of the ipsilateral kidney despite being indicated for NSS both with open and laparoscopic approaches. Previous studies confirmed that the preserved parenchymal volume was the primary determinant of renal function after NSS.[3, 4] On the other hand, to preserve as much renal function as possible, we have employed non-ischemic partial nephrectomy using a microwave tissue coagulator (MTC).[5] We have previously reported that the postoperative renal function could be predicted preoperatively based on 3-dimensional (3-D) image reconstruction software, routine diagnostic imaging (e.g., CT scan and MRI), and serum creatinine (sCr) level.[6]

In the present study, we prospectively examined whether the postoperative renal function following Nx and NSS could be accurately predicted, and prospectively assessed the reproducibility of our newly developed 3-D image reconstruction system to measure the functional renal volume (FRV).

Materials and Methods

Software and procedures for volumetric measurement

The newly developed 3-D image reconstruction software (MU1128, not commercially available) can use any images stored as Digital Imaging and Communications in Medicine (DICOM) files. Enhanced CT scans and MRI images were input into the computer program. We used the dynamic image of the arterial phase to determine the functional renal parenchyma. For each diagnostic image, the renal parenchyma was traced by erasing the other neighboring organs, fat tissue, muscle, and the collecting system, which are of no interest, by computer mouse operation. The traced outlines of the renal parenchyma in all the images were collected to automatically reconstruct a 3-D image. The functional FRV was estimated by integral calculation software. In NSS cases, the tumor, marginal tissue coagulated by MTC, and renal cyst were also calculated separately, and their volumes were subtracted from the total renal parenchymal volume. We defined "marginal tissue" as 10 mm from the renal tumor because the area coagulated with a microwave tissue coagulator is approximately 5mm in width. The preoperative 3-D image of a patient who underwent NSS and postoperative imaging at 1 month after surgery are shown in Figure 1. (Fig.1-a, 1-b) The purple colored area indicates the FRV. The renal tumor and urinary tract (renal pelvis, renal calyx and ureter) were colored brown and yellow, respectively.

Prediction of postoperative renal function

The sCr level was measured before surgery and at 1 month and 1 year after surgery. The estimated glomerular filtration rate (eGFR) was calculated from the sCr and age using the following equation: eGFR (mL/min/1.73m^2) = 194 × sCr $^{-1.094}$ × Age $^{-}$

$^{0.287}$ × 0.739 (if female). This equation has been revised for the Japanese population by the Japanese Society of Nephrology from the original equation of the Modification of Diet in Renal Disease (MDRD) Study. [7] The preoperative and postoperative FRVs were calculated using the 3-D image reconstruction software. The predicted postoperative eGFR was calculated from the preoperative eGFR using the following equation: predicted postoperative eGFR = preoperative eGFR × (estimated postoperative FRV / estimated preoperative total FRV)

Comparison between the actual and predictive values of the postoperative FRV and renal function

We enrolled 98 patients (53 males and 45 females) who underwent Nx and 41 patients (30 males and 11 females) who underwent NSS at Nara Medical University Hospital in this prospective study from April 2006 to September 2009. We employed non-ischemic NSS using a microwave tissue coagulator without clamping the renal artery. The patient background is shown in Table 1. The mean age in the Nx and NSS groups was 60.7 and 61.6 years, respectively. The Nx Group included 57 cases of renal cell carcinoma, 31 cases of donor nephrectomy, 9 cases of nephroureterectomy, and 1 case of oncocytoma. On the other hand, the NSS group included 40 cases of renal cell carcinoma and 1 case of angiomyolipoma. The mean maximum diameter of the renal tumor and the mean tumor volume in the Nx group were 6.5 cm and 122.5 mL, respectively. On the other hand, the mean maximum diameter of the renal tumor and the mean tumor volume in the NSS group were 2.6 cm and 9.8 mL, respectively.

The preoperative images and postoperative images as well as the sCr levels at 1 month and 1 year after surgery were obtained to calculate the FRV and eGFR.

Spearman's rank correlation test was used to examine the significance of the correlations between the predictive and actually measured postoperative FRV and eGFR. Wilcoxon's signed rank test was used to determine the differences between the predictive and actually measured postoperative FRV and eGFR. The preoperative and postoperative sCr levels were compared by Wilcoxon's signed rank test. All statistical analyses were carried out using SPSS 17.0J (SPSS Inc., Chicago, IL, USA). Statistical significance was considered as $P < 0.05$ in all statistical tests.

The institutional reviewer board approved this prospective study, and informed consent was obtained from all patients after explaining the aim and methods of this study.

Reproducibility and accuracy of volumetric measurement

To assess the reproducibility and accuracy of measuring FRV, 5 volunteers participated as examiners in this study. The 5 volunteers consisted of 2 medical engineers, 2 company workers and 1 clerical staff. To obtain a learning curve, each volunteer experienced 10 cases to measure FRV. After that, each volunteer started measurement of the FRV on the enhanced CT and MRI images of 5 cases each. All examiners repeated the FRV measurement of the same images 5 times. One-way analysis of variance (ANOVA) was used to assess the reproducibility and accuracy among the results of the 5 repeated measurements and among the results of the 5 examiners.

Results

Prediction of FRV and postoperative renal function in the Nx group

There was a significant correlation between the mean predictive FRV and the actually measured FRV at 1 month after surgery (Spearman's ρ = 0.96; $p < 0.001$), while the mean actually measured FRV showed a significant increase of 8.4% compared with the mean predictive FRV at 1 month after surgery (p < 0.001). In 75 of the total 98 patients in the Nx group, the mean predictive FRV and actually measured FRV at 1 year after surgery were 160. and 174.6 cm^3, respectively. There was a significant correlation between the mean predictive FRV and the actually measured FRV at 1 year after surgery (Spearman's ρ = 0.96; $p < 0.001$), while the mean actually measured FRV showed a significant increase of 9.0% compared with the mean predictive FRV at 1 year after surgery (p < 0.001). There were also no significant differences in the mean actually measured FRV values between 1 month and 1 year after surgery. （Table 2）

The mean predictive eGFR significantly correlated with the actual eGFR at 1 month after surgery (Spearman's ρ = 0.79; $p < 0.001$). Among all 98 patients in the Nx group, the mean eGFR at 1 year after surgery could be calculated in 85 patients. The mean predictive eGFR at 1 year after surgery significantly correlated with the actual eGFR at 1 year after surgery (Spearman's ρ = 0.79; $p < 0.001$). The mean eGFR at 1 month and 1 year after surgery were significantly greater（19% and 23.4%） than those predicted preoperatively ($p < 0.001$) (Table 3).

In the Nx group, the mean sCr levels before and at 1 month and 1 year after surgery were 0.77, 1.18, and 1.17 mg/dL, respectively. The mean sCr levels at 1month and 1year after surgery showed a significant increase compared with the preoperative sCr level ($p < 0.001$). There were no significant differences in the mean sCr levels between 1 month and 1 year after surgery.

Prediction of FRV and postoperative renal function in the NSS group

The mean predictive FRV and actually measured FRV at 1 month after NSS were 275.9 cm^3 and 274.5 cm^3, respectively. There was a significant correlation between the mean predictive FRV and the mean actually measured FRV (Spearman's $\rho = 0.99$; $p < 0.001$), and there were no significant differences. In 30 of the total number of 41 patients, a significant correlation was also seen between the mean predictive FRV and the actually measured FRV at 1 year after surgery (Spearman's $\rho = 0.98$; $p < 0.001$). The mean actually measured FRV at 1 year after surgery was significantly larger (1.3%) than the mean predictive FRV (292.4 cm^3 vs. 296.1 cm^3; p = 0.037) (Table 2).

The mean predictive eGFR significantly correlated with those at 1 month and 1 year after surgery (Spearman's $\rho = 0.89, 0.79$; $p < 0.001$). The mean eGFR values at 1 month and 1 year after surgery were significantly smaller (8.6%) than those predicted preoperatively ($p < 0.001$) (Table 3).

In the NSS group, the mean sCr levels before and at 1 month and 1 year after surgery were 0.89, 0.99, and 0.95 mg/dL, respectively. The mean sCr levels at 1 month and 1 year after surgery showed a significant increase compared with the preoperative value ($p < 0.001$, $p = 0.001$), but there were no significant differences in the sCr levels between 1 month and 1 year after surgery.

Correlation between actually measured surgical loss of FRV and predictive surgical loss of FRV (Fig.2)

In the Nx group, the mean predictive and actually measured surgical loss of RPV at 1 month after surgery were 147.2 cm^3 ±5.0 (SD) and 133.8 cm^3 ±35.0 (SD), respectively. A significant correlation between the predictive and actually measured surgical loss of FRV was observed ($R^2 = 0.883$, $p < 0.001$).

On the other hand, in the NSS group the mean predictive and actually measured surgical loss of FRV at 1 month after surgery were 8.2 cm^3±4.5 (SD) and 9.6 cm^3 ±9.1 (SD), respectively. There was a weak correlation between the predictive and actually measured surgical loss of FRV that was significant ($R^2 = 0.154$, $p < 0.001$).

Reproducibility and accuracy

One-way ANOVA did not show significant inter-examiner differences in calculation of the FRV among the 5 examiners both for CT scans and MRI images (Table 4). There were also no significant differences between the five repeated FRV measurements among the 5 examiners. In other words, both reproducibility and accuracy of volume measurement were confirmed for CT as well as MRI studies.

Discussion

The postoperative renal function should be taken into consideration in terms of deterioration of quality of life and life-threatening problems, not only in patients who undergo Nx, but also in patients who undergo NSS. Previous studies concluded that the postoperative renal function in patients who underwent Nx or donor nephrectomy was well-preserved. [8-10] On the other hand, Lau *et al.* reported that the postoperative renal function was better preserved in patients who underwent NSS than in patients who underwent Nx.[2] Clark *et al.* reported that patients treated with NSS showed significantly less deterioration of the overall renal function compared to those treated with Nx.[11] The oncological therapeutic outcomes of NSS are considered very similar to those of Nx in patients with small RCC. [12-15] Indeed, Kunzel *et al.* reported that renal parenchymal volume measured by preoperative CT was independently associated with the development of chronic kidney disease in patients undergoing renal tumor surgery. If the non-bearing kidney constituted ≥ 50% of the total bilateral preoperative renal parenchymal volume, then the risk of developing chronic kidney disease decreased.[16] The number of patients undergoing NSS will therefore increase even more in the future to preserve the postoperative renal function.

In this study, we demonstrated the reproducibility and accuracy of calculating FRV both with CT and MRI images. To assess the reproducibility and accuracy of measuring FRV, 5 volunteers (2 medical engineers, 2 company workers and 1 clerical staff) participated as examiners in this study. We specifically did not choose urologists or radiologists to confirm the usability of the software. To obtain a learning curve, each volunteer experienced 10 cases to measure FRV. We used dynamic images in the arterial phase to determine the functional renal parenchyma. The poorly enhanced portion of the renal parenchyma was excluded from FRV. In the Nx group, FRV significantly increased with 8.4% at 1 month after surgery. This compensatory increase in FRV was maintained at 1 year after surgery. Correspondingly, eGFR significantly increased by 19.2% at 1 month after surgery, and the actually calculated eGFR at 1 year after surgery showed a significant increase of 23.4% compared with the predictive eGFR. Funahashi *et al.* reported the changes in the contralateral renal parenchymal volume at 1 week and 6 months after unilateral nephrectomy in a similar way as our study. [17] The FRV at 6 months after surgery showed a significant increase of 8.9%, and this result was comparable to the present study.

In the NSS group of our study, the change in FRV was small at 1 month and 1 year after surgery, while the actually measured FRV at 1 year after surgery showed a slight but significant increase ($p = 0.037$). The correlation between the predictive and actual FRV loss in the NSS group was significant but not strong ($P<0.001$, $R^2 =0.154$, Figure2). On the other hand, the eGFR at 1 month and 1 year after surgery showed a significant decrease compared with the predictive eGFR ($P < 0.001$). The reason why the actually calculated postoperative eGFR was significantly lower than the predictive eGFR is unknown, even though the actually measured postoperative FRV was significantly greater than the predictive FRV. It is expected that the tumor location (exophytic vs. medially located) affects the decrease in the postoperative renal function, even though the loss of FRV is similar for the two locations. Preoperative background and intraoperative factors also affect the renal function after surgery. It is also conceivable that the thermal effect on normal renal tissue near the tumor may affect the postoperative renal function. We examined the preoperative and intraoperative predictive parameters to induce a significant decrease in the postoperative eGFR compared with the predictive eGFR by age, body mass index, sCr, FRV, tumor volume, operation time, and estimated blood loss using logistic regression analysis (data not shown). At 1 month after surgery, the operation time was a significant predictor (odds ratio: 6.233, 95% confidence interval: 1.396-27.841, $p = 0.017$), and estimated blood loss was also a significant predictor (odds ratio: 10.899, 95% confidence interval: 1.140-103.977, $p = 0.038$). These results suggest that the burden of surgery affected the postoperative renal function in the NSS group. On the other hand, compensatory hypertrophy was seen in the Nx group. Consequently, the postoperative renal function at 1 month and 1 year after surgery was significantly higher than the predictive renal function in the Nx group.

Tests like renography using radioisotopes are common to test the split renal function. However, radioisotope examination is expensive and time-consuming. The present software used for 3-D image reconstruction can calculate the volume more simply and rapidly, and all kinds of diagnostic images saved in the DICOM file are available for 3-D image reconstruction. Figure 2 demonstrates that there was a weak yet significant correlation between eGFR and FRV, not only in the NX group, but also in the NSS group. This indicates that each FRV does not represent the absolute figure of renal function. Comparison of FRV between individual patients also has little meaning due to patient-to-patient variations. On the other hand, there was strong evidence that the change in FRV after surgery significantly correlated with the change in renal function both in the Nx and the NSS groups.

Our results demonstrated the reproducibility and accuracy of volumetric measurement using this software. Although the number of patients was small and the follow-up period was short in some cases in this prospective study, the postoperative FRV and renal function could be predicted preoperatively by the present 3-D image reconstruction software, preoperative routine diagnostic imaging, and sCr level. In the near future, we will show longer-term and larger-scale results of the prediction of postoperative renal function following renal parenchymal surgery as well as the results of comparison between the current reconstruction study and radioisotope examination.

Conclusion

Postoperative FRV and renal function could be predicted preoperatively in our series of patients undergoing Nx or NSS using a 3-D image reconstruction system including our computer software, preoperative routine diagnostic imaging, and preoperative sCr level.

Acknowledgment

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Figure captions

Fig.1 Three-dimensional reconstruction images (1-a: preoperative, and

1-b: 1 month after partial nephrectomy)

The purple color indicates FRV.

Renal tumor and urinary tract renal pelvis, renal calyx and ureter） are colored brown and yellow, respectively.

White arrows indicate the surgical site.

Fig.2 The correlation between predictive FRV loss and actual FRV loss

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