The Change of the Split Renal Function Before and After a Nephrectomy Using Tc-Mercaptoacetyltriglycine (MAG3)

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The Change of the Split Renal Function Before and After a Nephrectomy Using Tc-Mercaptoacetyltriglycine (MAG3)

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Abstract
Objective: We examined the change in the renal function in the normal side kidney before and after a nephrectomy, by means of a newly developed diuretic renography technique utilizing Tc 99m-mercaptoacetyltriglycine (MAG3).

Materials and methods: Forty patients who underwent a nephrectomy were evaluated using MAG3 diuretic renography. We measured the effective renal plasma flow (ERPF) and Tmax time before and after a nephrectomy. The effects of the patient age and the preoperative ERPF of ill side kidney on the post operative ERPF were then assessed statistically.

Results: The ERPF increased by an average of 44.8 ml/min at 2 weeks after a nephrectomy, but it decreased by an average of 24.3 ml/min at 3 months after a nephrectomy. The Tmax time decreased by an average of 0.58 min at 2 weeks, but thereafter increased by an average of 0.58 min at 3 months after a nephrectomy. The correlation coefficient between the rate of increase in the ERPF and the patient age was 0.197.

Conclusions: The rise of renal function in terms of ERPF and the Tmax time was observed at 2 weeks post-nephrectomy. However, this effect disappeared at 3 months post-nephrectomy. These data demonstrated that the rise in the renal function of the normal-side kidney in such patients was only temporary.

Key words: MAG3, nephrectomy, split renal function

INTRODUCTION

For the treatment of localized carcinomas of the upper urinary tract (ex. renal cell carcinoma, renal pelvis or ureter tumors), a radical nephrectomy or a total nephroureterectomy is commonly performed. In the residual healthy-side kidney of such nephrectomized patients, renal hypertrophy is often observed. Johnson et al1) and the other investigators have shown that a unilateral nephrectomy may subsequently cause an increase in the glomerular filtration rate in the remnant kidney2). Moreover, the functional growth in the residual kidneys has also been reported regarding the serum creatinine level or the 24 hour creatinine clearance level.

A radionuclide renal study is the only method that provides information on both renal structure and function. Technetium 99m-mercaptoacetyltriglycine (MAG3) was introduced by Fritz berg et al4). The bio-
logical properties of MAG3 are somewhat different from those of radio-hippurate. MAG3 is known to act as an effective renal plasma flow radio-agent. Moreover, MAG3 can be used to evaluate such urological disease as renovascular hypertension\(^5\)\(^7\), hydronephrosis\(^8\)\(^14\), renal transplant\(^15\)\(^19\), renal tumor with partial nephrectomy\(^20\)\(^21\) and child's renal disease\(^22\)\(^23\). MAG3 is mainly secreted in uriniferous tubules and it reflects the effective renal plasma flow (ERPF). MAG3 has been shown to be an effective treatment in patients with an impaired renal function. The use of nuclear imaging appears to be advantageous, because it is non-invasive and can be repeated several times. MAG3 can provide objective data and the individual renal function can be evaluated.

We examined the changes in the healthy-side renal function before and after a nephrectomy for urothelial carcinoma using MAG3 nuclear imaging.

**MATERIALS AND METHODS**

Forty patients (24 males and 16 females) with urothelial carcinoma underwent a nephrectomy (either a radical nephrectomy or a total nephroureterectomy) at Kyushu University Hospital from June 1998 through August 2000. The patients were examined by \(^{99m}\)Tc-MAG3 nuclear imaging both before and after a nephrectomy. The patient ages ranged from 33 to 84 years old (a mean of 60.8). Using the MAG3 nuclear imaging system, the ERPF and Tmax (the time of maximum concentration) were evaluated in the individual kidneys before and after a nephrectomy. A total 40 patients showed complete MAG3 measurements at two points; namely pre nephrectomy and 2 weeks after nephrectomy. Among the 40 patients, 22 patients showed complete MAG3 measurements at three points; pre nephrectomy, 2 weeks and 3 months after nephrectomy. Among the 40 patients, 30 cases showed the healthy-side kidney to have a normal function.

The patients were studied after ingesting 250mL of water 30 minutes before the renogram. The 200 to 500 MBq of MAG3 was then injected at time zero. The radioactivity was then measured using a gamma camera (Multispect, Siemens, Germany) with a low-energy, all-purpose collimator integrated with an Icon computer system. The region of interest was imaged over both kidneys, and the background was measured as a crescent inferolateral to each kidney. The activity of the scanned areas was measured between 30 and 90 seconds after the injection of the radiopharmaceutical and the differential renal function was determined before the isotopes appeared in the renal pelvis as a ratio of the counts on the ill side compared with the counts on the normal side. The patients were scanned for a total of 25 to 40 minutes. Subsequently, the time radioactivity curves were generated by computer, and Tmax was calculated. The clearance curves were then evaluated by computer.

**Fig. 1** The transition in the ERPF in the healthy side kidney, before a nephrectomy and at two weeks after a nephrectomy.
A statistical analysis was performed based on the signed rank test for paired data in Figures 1 to 4. The Spearman rank correlation procedure was used to determine the correlation coefficients and their P values. AP value of 0.05 or less was used as a definition of significance.

RESULTS

We investigated the ERPF and Tmax before and after a nephrectomy in forty patients. As shown in Fig. 1 and Fig. 2, the ERPF showed a significant upregulation of 44.8 ml/min from 325.8 to 370.6 (p=0.036) and Tmax time showed a significant shortening of -0.58 minute from 4.61 to 4.03 (p=0.034), respectively. The ERPF and Tmax at 3 months after a nephrectomy were obtained in 22 of 40 patients. The ERPF at 2 weeks, however, significantly decreased at 3 months after a nephrectomy, from 370.6 to 346.3 (p=0.004, Fig. 3). Furthermore, we could also examine the Tmax in 22 patients at 2 weeks and three months after a nephrectomy. The Tmax increased from 3.4 to 3.98 minutes, but the difference was not significant (p=0.106, Fig. 4).

We next investigated the correlation between the preoperative ERPF in the ill side kidney and the rate of increase in the ERPF at 2 weeks postoperatively in the normal side kidney in 30 patients. As a result, no significant correlation was observed between them (r=0.076, p=0.69, Fig. 5). Furthermore, no significant correlation was seen between the increasing rate in the ERPF at 2 weeks after a nephrectomy and the patient age (r=0.197, p=0.40, Fig. 6).

DISCUSSION

In the treatment of renal cell carcinoma, renal pelvic tumors or ureter tumors, a
A correlation was observed between the ERPF before a nephrectomy on the ill side kidney and the rate of increase in the ERPF at 2 weeks postoperatively in the healthy side kidney.

A correlation was observed between the patient age and the rate of increase in the ERPF at 2 weeks after a nephrectomy in the healthy side kidney was.

surgical extirpation of the kidney (either a radical nephrectomy or a total nephroureterectomy) is commonly performed. In such nephrectomized patients, postoperative imaging studies such as CT often show hypertrophy in the residual normal side kidney. Furthermore, the change of the renal function in nephrectomized patients has also been reported in terms of a change in the serum creatinine level or creatinine clearance. However, there have so far been few reports showing renal hypertrophy using nuclear medicine techniques. Therefore, we used MAG3, and examined the transition of the normal side kidney function before and after a nephrectomy in 40 patients. The advantages of nuclear medicine techniques are that 1) the split renal functions can be analyzed preoperatively and quantitatively, 2) the pre and post renal functions can be compared at different times, and 3) morphological changes in the residual kidney can also be analyzed. The parenchyma parameters of scintigraphy were determined by plasma clearance methods like ERPF, the glomerular filtration rate (GFR), and the renal transit time such as parenchyma mean transit time (Tmax, T1/2). In this study, we used 99mTc-MAG3 as the nuclear material. In comparison to 131I-OIH, the biological properties of 99mTc-MAG3 seem to be inferior, but the physical properties for external imaging are superior. 99mTc-MAG3 has less radiation than 131I-OIH. Therefore, regarding MAG3, the dosage of more quantity can be given to patients, and better images can be provided than with 131I-OIH. In addition, the clinical availability of an instant kit is better than 131I-OIH. The image quality with 99mTc-MAG3 is higher than that with DTPA in the presence of decreased renal function. Therefore, a renal study with MAG3 is considered to be the diagnostic modality of choice. Furthermore, MAG3 has less radiation exposure than 131I-OIH. MAG3 has a lower extraction coefficient (55%) due to its low secretion and high protein binding. Moreover, its high protein binding keeps it in the blood for longer and finally, the excretion rates of MAG3 and OIH are similar. A disadvantage of MAG3 is its high protein binding, which is a limiting factor when estimating ERPF.

A significant up regulation of the renal function of residual normal side could be observed at 2 weeks after a nephrectomy
regarding the ERPF and Tmax. However, it returned to preoperative levels at 3 months after surgery (Figs. 1-4). These results seem to show that the functional upregulation was transient.

The acceleration of the renal function after a nephrectomy has been reported to not necessarily take place in the case of elderly patients. In an examination of the donors in living-related kidney transplantation, the rate of glomerular filtration was reported to be elevated within 24 hours postoperatively and reach 70-80% of the preoperative level by 7 months post-operatively\(^2\). However, this change may not necessarily apply to elderly donors. It is possible that the postoperative acceleration of the renal function was transient because most of our cases were also comparatively elderly patients. An elderly person often has glomerulosclerosis. In such patients, the renal blood flow and GFR tend to decrease tremendously while the systemic blood pressure is usually elevated. The mechanism involved may be related to the hyperfiltration of the surviving nephron, and it can also be induced experimentally by renal mass reduction\(^3\).

In order to clarify the factors which caused postoperative upregulation of the kidney, we investigated the influence of the patient age on the increase in the ERPF. However, no correlation between the age and an increase in ERPF was observed in this study.

The degree of renal dysfunction in the ill-side kidney and the period of its low function may affect the compensatory hypertrophy of the normal side kidney. In our study, the ERPF of the ill side kidney before a nephrectomy did not significantly affect the rate of increase in ERPF of the normal side kidney.

Many important questions remain regarding the compensation mechanism of the renal function. Hypertrophy of the remaining kidney following a uninephrectomy may thus be related to an increase in the renal insulin growth factor-1 content\(^3\), epidermal growth factor or hepatocyte growth factor, which is also known as kidney reproduction factor\(^3\). The elucidation of the role that these factors play in kidney reproduction is eagerly awaited.

At present, the MAG clearance is thus considered to be a highly promising factor to quantitatively assess the split renal functions at different times; even though it is still unknown whether or not the MAG clearance itself is useful for assessing the renal function.

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Tc-MAG3を用いた腎摘除術前後における健側腎機能の推移

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Tc-MAG3を用いて、腎摘除術前後における健側腎機能の推移を検討した。【対象と方法】
対象は当科にて腎摘除を行い、術後前にTc-MAG3を用いたrenographyを行った40名。
renographyでは、effective renal plasma flow（ERPF）とTmax timeを評価項目としていた。また、健側腎ERPFの増加率については、
健側腎機能に影響を与えると考えられる患者年齢・患側腎のERPFと相関がないか検討した。【結果】健側腎のERPFは、術後2週目には44.8ml/min有意に増加し、Tmax timeも0.58分有意に短縮した。しかし、術後3ヶ月目には、術後2週目と比較しERPFは24.3ml/min有意に減少し、Tmax timeも有意ではなかった。また、健側腎における術後2週目のERPF増加率と対象の患者年齢・患側腎の機能と相関がないか検討したが、
相関はなかった。【結論】腎摘除術前後における健側腎機能の機能亢進は一過性であった。また、患者年齢や患側腎のERPFは、健側腎の機能亢進を起こす患者側の因子ではなかった。