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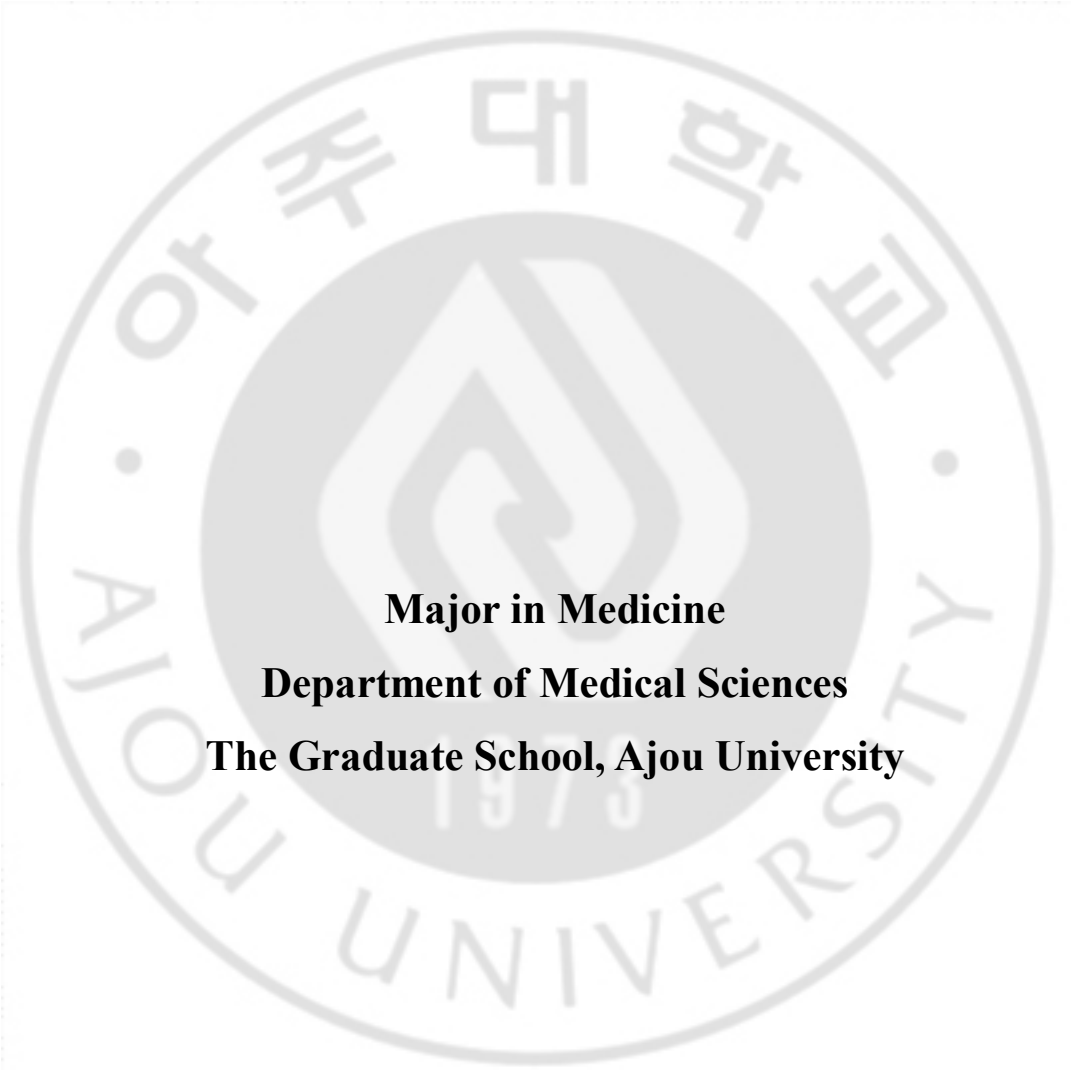
Comparative Analysis of Radiologically Measured Size and True Size of Renal Tumors

By

Kook Bin Lee



Major in Medicine

Department of Medical Sciences

The Graduate School, Ajou University

아주대학교
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Comparative Analysis of Radiologically Measured Size and True Size of Renal Tumors

By

Kook Bin Lee

A Dissertation Submitted to the Graduate School of Ajou University in Partial Fulfillment of the Requirements for the Degree of Master of Medicine

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August, 2013

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- Abstract -

Comparative Analysis of Radiologically Measured Size and True Size of Renal Tumors

Purpose: We evaluated the effects of different tumor conditions on discrepancy between radiologically measured size and true size of renal tumors**.**

Materials and Methods: The data from 238 patients who underwent radical or partial nephrectomy for a renal tumor at our institution were reviewed. Radiologic tumor size defined as the largest diameter on a CT scan was compared to pathologic tumor size defined as the largest diameter on gross pathologic examination**.**

Results: There was no significant difference between the mean radiologic and pathologic size for all tumors ($p=0.078$). When stratified according to radiologic size range, mean radiologic size was significantly larger than mean pathologic size for tumors <4 cm ($p=0.001$), but there was no significant difference between them for tumors 4-7 cm, and >7 cm. When classified according to histologic subtype, mean radiologic size was significantly larger than pathologic size only in clear cell renal cell carcinoma ($p=0.005$). When classified according to tumor location, mean radiologic size was larger than pathologic size in endophytic tumors ($p=0.050$), but not in exophytic tumors. When endophytic tumors were stratified according to radiologic size range, there was a significant difference between the radiologic and pathologic size for tumors <4 cm ($p<0.001$) and 4-7 cm ($p=0.007$), but not for tumors >7 cm.

Conclusions: Radiologic tumor size seems to correlate well with pathologic tumor size. However, there was a tendency to overestimate tumor size in smaller tumors. Endophytic renal tumors are more likely to have size overestimated by CT scan than exophytic tumors.

Key Words: Kidney; Neoplasms; Pathology; Radiology

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I. INTRODUCTION

Elective nephron-sparing surgery for small renal masses (tumor size <4cm, T1a) has been accepted as an oncologically safe alternative with limited complications in the presence of a healthy contralateral kidney (Zini et al, 2009). The benefit of nephron-sparing surgery for small renal masses includes the preservation of renal function, with equal or better survival compared to radical nephrectomy (Zini et al, 2009; Thompson et al, 2008). Recently, the incidence of renal cancer including renal cell carcinoma (RCC) has been increasing around the world, which can be accounted for by increasing exposure to risk factors and increasing diagnosis of incidental tumors by improved imaging technology (Mathew A, et al, 2002). Parallel to the increase in incidentally discovered renal tumors, the size of tumors has become smaller (choi et al, 2011; Jayson et al, 1998).

Renal tumor size is important for the selection of treatment modality and prognosis. Previous studies have shown that the prognosis of RCC is dependent on the pathologic size of the tumor, especially for patients with tumors confined to the kidney (Beldetrun et al, 1999; Fergany et al, 2000). However, treatment decision, including the feasibility of nephron-sparing surgery, can only be made based on the radiologic size of tumor. Consequently, it is important to define the relationship between radiologic and pathologic size of renal tumor. Previous studies that examined the size difference between radiology and pathology have yielded conflicting results (Herr et al, 2000; Irani et al, 2001; Yaycioglu et al, 2002; Schlomer et al, 2006; Kanofsky et al, 2006; Choi et al, 2010; Mistry et al, 2008; Kurta et al, 2009; Lee et al, 2010). In many of these studies, smaller tumor size and clear cell pathology were predictive of overestimated tumor size by radiology. And to the best of our knowledge, the study comparing the radiologic and pathologic tumor size according to tumor location is limited, and we could find only one report (Lee et al, 2010). Therefore, in this study we examined the effects of different tumor conditions including tumor location (endophytic or exophytic) on discrepancy between radiologically measured size and true size of renal tumors.

II. MATERIALS AND METHODS

We retrospectively identified 238 consecutive patients who underwent radical or partial nephrectomy for a renal tumor suspicious for malignancy at our institution between May 2002 and February 2011. All patients underwent a contrast-enhanced CT scan before surgery. Radiographically, the tumor diameter was measured at supero-inferior, antero-posterior, and left to right axes on a contrast-enhanced CT scan, and the largest of these three diameters was taken as representing the radiologic size of the tumor. The pathologic tumor size was taken as the largest diameter of the tumor on gross examination before formalin fixation.

Patients' demographic data were collected from the medical records. The histologic subtypes of tumor were categorized as clear cell RCC, papillary RCC, chromophobe RCC, unclassified RCC, oncocytoma, angiomyolipoma, and other benign tumor. In case of RCC, the final pathologic staging was done according to the 2009 TNM staging system.

Preoperative CT scan was reviewed to categorize the tumor location. The tumor was arbitrarily classified as exophytic if more than 50% of the mass was extending off the natural surface of the kidney, and as endophytic if less than 50% of the mass was extending off the natural surface of the kidney

The mean values of the radiologic and pathologic size and the differences were calculated. The two measurements were compared using paired Student's t-tests with SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Values of $p<0.05$ were considered to be statistically significant in all of the analyses.

III. RESULTS

The mean age of the total 238 patients included in this study was 54.8 years (range, 28-81 years). The patients included 167 (70.2%) men and 71 (29.8%) women. Of the 238 tumors, 225 (94.5%) were RCC and 13 (5.5%) were benign tumors. Demographic data as well as pathologic data including the histologic subtypes of RCC, T stage, and tumor location are shown in Table 1.

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Table 1. Clinicopathologic characteristics of 238 patients who underwent radical or partial nephrectomy

Characteristics	No. of patients (%)
Total patients	238
Age (y)	54.8 (range, 28-81)
Gender	
Male	167 (70.2)
Female	71 (29.8)
Types of surgery	
Radical nephrectomy	222 (93.3)
Partial nephrectomy	16 (6.7)
Histology	
Clear cell RCC	194 (81.5)
Papillary RCC	15 (6.3)
Chromophobe RCC	14 (5.9)
Unclassified RCC	2 (0.8)
Oncocytoma	6 (2.5)
Angiomyolipoma	5 (2.1)
Other benign tumor	2 (0.8)
Tumor stage	
T1a	91 (38.2)
T1b	65 (27.3)
T2	16 (6.7)
T3a	22 (9.2)
T3b	30 (12.6)
T3c	1 (0.4)
T4	0 (0)
Tumor location	
Endophytic	160 (67.2)
Exophytic	78 (32.8)

RCC, renal cell carcinoma.

The mean radiologic and pathologic size for all tumors was 5.01±2.74 cm and 4.92±2.83 cm, respectively, and the difference was not statistically significant (p=0.078). Table 2 shows a comparison of the radiologic and pathologic tumor size categorized into radiologic size of less than 4 cm, 4 to 7 cm, and larger than 7 cm. There was no statistically significant difference between the radiologic and pathologic size for tumors 4 to 7 cm (p=0.389), and larger than 7 cm (p=0.941). However, for tumors less than 4 cm, mean radiologic size was significantly larger by 0.16 cm than mean pathologic size (p=0.001).

Table 2. Difference between radiologic and pathologic tumor size according to radiologic size range

Radiologic size range (cm)	No. of patients	Radiologic tumor size (cm)	Pathologic tumor size (cm)	Difference (cm)	p-value
<4	101	2.82±0.73	2.66±0.83	0.16±0.46	0.001
4 to 7	93	5.22±0.88	5.14±1.12	0.07±0.79	0.389
>7	44	9.63±2.31	9.61±2.29	0.02±1.47	0.941
Total	238	5.01±2.74	4.92±2.83	0.10±0.85	0.078

Values are presented as mean±standard deviation.

Table 3 shows a comparison of the radiologic and pathologic size according to histologic subtype. Mean radiologic tumor size was significantly larger than pathologic size only in clear cell RCC (p=0.005).

Table 3. Difference between radiologic and pathologic tumor size according to histologic subtype

Histologic subtype	No. of patients	Radiologic tumor size (cm)	Pathologic tumor size (cm)	Difference (cm)	p-value
Clear cell RCC	194	5.06±2.62	4.88±2.67	0.18±0.86	0.005
Non-clear cell RCC	31	5.11±3.64	5.40±3.87	-0.29±0.81	0.057
Benign	13	4.09±2.01	4.24±2.21	-0.15±0.39	0.193
Total	238	5.01±2.74	4.92±2.83	0.10±0.85	0.078

Values are presented as mean±standard deviation. RCC, renal cell carcinoma.

Table 4 shows a comparison of the radiologic and pathologic size according to tumor location. Mean radiologic tumor size was larger than pathologic size in endophytic tumors with equivocal statistical significance (p=0.050), but not in exophytic tumors (p=0.902). When endophytic tumors were categorized into radiologic size of less than 4 cm, 4 to 7 cm, and larger than 7 cm, there was a statistically significant difference between the radiologic and pathologic size for tumors less than 4 cm (p<0.001) and 4 to 7 cm (p=0.007), but not for tumors larger than 7 cm (p=0.615) (Table 5).

Table 4. Difference between radiologic and pathologic tumor size according to tumor location

Tumor location	No. of patients	Radiologic tumor size (cm)	Pathologic tumor size (cm)	Difference (cm)	p-value
Endophytic	160	5.03±3.04	4.89±3.15	0.14±0.90	0.050
Exophytic	78	4.98±2.01	4.97±2.02	0.01±0.75	0.902

Values are presented as mean±standard deviation.

Table 5. Difference between radiologic and pathologic tumor size according to radiologic size range in endophytic tumors

Radiologic size range (cm)	No. of patients	Radiologic tumor size (cm)	Pathologic tumor size (cm)	Difference (cm)	p-value
<4	74	2.69±0.74	2.52±0.81	0.17±0.37	<0.001
4 to 7	51	5.20±0.91	4.90±1.05	0.29±0.75	0.007
>7	35	9.75±2.45	9.89±2.37	-0.14±1.59	0.615
Total	160	5.03±3.04	4.89±3.15	0.14±0.90	0.050

Values are presented as mean±standard deviation.

IV. DISCUSSION

Increasing popularity of nephron-sparing surgery and other forms of ablative therapy for small renal masses have led to the necessity of creating valid tumor size criteria for selecting appropriate patients. In this respect, the adequacy of the 1997 TNM staging system was challenged by many and evidence was presented that tumor size cut-off of 4 or 4.5 cm had better prognostic value after radical nephrectomy than 7 cm (Igarashi et al, 2001; Zisman et al, 2001). Moreover, in a large series of 798 patients, Crispen et al. (Crispen et al, 2008) have shown that each 1 cm increment in tumor size from below 1 cm to 7 cm was associated with decreased long-term outcome following partial nephrectomy, stressing the importance of tumor size in comparing outcome following ablative and observational therapy. However, all these results were based on survival analysis of patients stratified by pathologic tumor size, and not radiologic tumor size, when the latter is the actual guide to the treatment selection. For this reason, to define the relationship between radiologic and pathologic size is important for localized renal tumors.

Some studies have examined the relationship between radiologic and pathologic size of renal tumor, with conflicting results. In 50 patients undergoing partial nephrectomy, Herr (Herr et al, 2000) prospectively compared the tumor size as assessed on a CT scan with the actual tumor size, and showed that radiologic tumor size was 0.63 cm larger than pathologic tumor size. He concluded that, because renal artery occlusion results in shrinkage of the entire kidney, a similar decrease in tumor size might occur. From his observation, he suggested that partial nephrectomy could be attempted more often in patients with borderline tumor size. Irani et al. (Irani et al, 2001) retrospectively reviewed 100 patients with renal tumors who had undergone radical nephrectomy and also found the average radiologic tumor size was significantly larger than pathologic tumor size (7 cm vs. 6 cm, $p=0.005$). Yaycioglu et al. (Yaycioglu et al, 2002) retrospectively reviewed 291 patients who underwent radical or partial nephrectomy and found the difference between radiologic and pathologic size was not significant ($p=0.1679$). However, estimated blood loss of less than 700 ml, localized tumors, and clear cell RCC were associated with significantly larger radiologic size than the pathologic size. They also warned that many additional features may lead to imprecise

radiologic tumor measurement. Schlomer et al. (Schlomer et al, 2006) retrospectively identified 126 patients who underwent radical or partial nephrectomy within 60 days of CT scanning and found that the radiologic and pathologic size for all tumors was not significantly different (4.5 vs. 4.1 cm, p=0.35). However, in pathologic T1a tumors, the radiologic size was significantly larger than the pathologic size (p=0.009), and the difference was significant for tumors 4 to 5 cm (p=0.025). Kanofsky et al. (Kanofsky et al, 2006) retrospectively studied 236 renal cancers and found that tumor size reduction due to loss of blood flow to the tumor had an impact on discordant radiologic and pathologic renal tumor size. In this study, the most frequent downstaging was observed for clear cell RCC compared with chromophobe or papillary type. Choi et al. (Choi et al, 2010) also found a large difference of greater than 0.45 cm between radiologic and pathologic renal tumor size, but only in pT1a, pT1b and clear cell RCC, but not in pT2 tumors.

In a more recent study, Mistry et al. (Mistry et al, 2008) showed that there was no statistically significant difference between radiologic and pathologic size of renal tumor. In a retrospective analysis of 521 patients, Kurta et al. (Kurta et al, 2009) found a statistically significant difference between the radiologic size (4.79 cm) and pathologic size (4.69 cm) (p=0.02). However, the overall difference was only 1 mm, suggesting that CT scan provides an accurate method of tumor size estimation. Lee et al. (Lee et al, 2010) retrospectively reviewed 467 patients who received radical or partial nephrectomy, and found that overall difference between radiologic and pathologic size was not significant, except for tumors in the 4 to 5 cm range and clear cell RCC. However, that difference was minimal and judged to be clinically insignificant.

Parallel to the results of more recent studies, our study also showed only insignificant overall difference between radiologic and pathologic size (5.01 cm vs. 4.92 cm, p=0.078). The difference was significant only for tumors of less than 4 cm and clear cell RCC. Contrary to the previous assumptions that vascular occlusion results in significant tumor shrinkage, more recent observations show that this effect might induce only insignificant degree of tumor shrinkage. Development of imaging techniques with better definition of tumor boundary might have contributed to more precise estimation of true tumor size by CT scan. Interestingly, the difference between the radiologic and pathologic size in our study became more significant when endophytic tumors were taken separately. This result was in contrast

with that of Lee et al. (Lee et al, 2010), which was the only study prior to ours to investigate radiologic and pathologic size difference by tumor location. Their study showed no significant tumor size difference regardless of whether the tumor was endophytic or exophytic. Despite better imaging technique, small and well enhancing conventional RCC embedded in the renal cortex might still be a diagnostic challenge and might have resulted in size overestimation of endophytic tumors. However, this needs to be validated by further studies.

This study had several limitations. It was a retrospective, single institution study, and the size of the study population was small. The tumor diameter measured in three axes on a CT scan may be inaccurate for the measurement of radiologic size, because the longest dimension may be diagonal to the three axes. There may be the variability in the scanning techniques and not all patients were examined using the same CT scanner.

Despite these limitations, we believe that there exists a tendency to overestimate tumor size in smaller tumors and endophytic tumors on a CT scan compared to pathologic size. Large-scale, multicenter, prospective study will be needed to verify these findings.

V. CONCLUSIONS

Renal tumor size measured by contemporary CT scans seems to correlate well with true tumor size. However, the tendency to overestimate tumor size was present in smaller tumors and is still unexplained. Our study showed that endophytic renal tumors are more likely to have size overestimated by CT scan than exophytic tumors. This needs to be verified by further studies.

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– 국문 요약 –

신종양의 영상의학적으로 측정된 크기와 병리학적으로 측정된 실제 크기에 대한 비교 분석

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이국빈
(지도교수: 김세중)

목적: 신종양의 수술적 치료방법 결정에서 중요한 인자 중 하나가 종양의 크기인데, 이전 연구들에서 술 전 영상의학적 크기와 술 후 병리학적 크기 사이에 유의한 차이가 있다는 결과가 보고되었으나 아직 논란의 여지가 있다. 본 연구에서는 신종양으로 부분 혹은 근치적 신절제술을 시행 받은 환자들에서 영상의학적으로 측정된 크기와 병리학적으로 측정된 실제크기사이의 차이에 대한 비교 분석을 하고자 하였다.

대상 및 방법: 2002년 3월부터 2011년 2월까지 신세포암이 의심되어 본원에서 부분 혹은 근치적 신절제술을 시행 받은 환자들 중 본원에서 술 전에 복부전산화단층촬영을 시행하여 분석이 가능하였던 238명 (남자 167명, 여자 71명, 평균연령 54.8세)을 대상으로 하였다. 술 전 영상의학적 크기는 복부전산화단층촬영을 재검토하여 종양의 가장 긴 길이로 정의하였고, 술 후 병리학적 크기는 의무기록을 재검토하여 검체에서 가장 긴 길이로 정의하였다.

결과: 30개월의 전체 238명의 환자 중 신세포암이 225례 (94.5%)였으며, 양성종양은 13례 (5.5%)로 호산성과립세포종 6례 (2.5%), 혈관근육지방종 5례 (2.1%), 고립섬유종양 1례 (0.4%), 혼합형 상피성 간질성 종양 1례 (0.4%)였다. 전체 크기 비교에서는 영상의학적 크기는 5.01±2.74 cm, 병리학적 크기는 4.92±2.83 cm으로 통계학적으로 유의한 차이가 없었다 ($p=0.078$). 임상적 T 병기 기준으로 분류한 결과 T1a 군에서 ($p=0.001$), 조직학적 유형을 기준으로 분류하였을 때 투명세포암에서 영상의학적 크기가 병리학적 크기보다 통계학적으로 크다는 유의한 결과를 보였다 ($p=0.005$), 종양의 신장에서 위치를 기준으로 분류하였을 때 내장성(endophytic) 종양에서 영상의학적 크기가 병리학적 크기보다 통계학적으로 크다는 유의한 결과를 보였느나 ($p=0.050$), 외장성(exophytic) 종양에서는 유의한 차이가 없었다. 내장성 종양을 크기에 따른 분류를 하였을 때 4cm 미만($p<0.001$), 4cm이상 7cm이하($p=0.007$)에서는 영상의학적 크기가 병리학적크기보다 통계적으로 크다는 결과를 보였고, 7cm 초과에서는 통계적으로 유의한 차이가 없었다.

결론: 본 연구 결과 영상의학적으로 측정된 신종양의 크기와 병리학적으로 측정된 실제 크기는 대체적으로 잘 맞는 결과를 보였다. 하지만, 크기가 작을수록 영상의학적 크기가 과평가되는 성향을 보였다. 또한 내장성 종양이 외장성종양보다는 영상의학적으로 과평가되는 성향을 보였다.

핵심어: 신장, 종양, 병리학, 영상의학