TURKISH JOURNAL OF UROLOGY Turk J Urol 2017; 43(1): 42–7 • DOI: 10.5152/tud.2016.33667

UROONCOLOGY

Original Article

Trends of partial and radical nephrectomy in managing small renal masses

Küçük böbrek kitlelerinin yönetiminde parsiyel ve radikal nefrektomi uygulama eğilimleri

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ABSTRACT

Objective: Use of partial nephrectomy (PN) for renal tumors appears to have relatively lower incidence rates in Jordan. We sought to characterize its trend at King Hussein Cancer Center for the last 10 years.

Material and methods: A retrospective review of our renal cell cancer data was performed. We identified 169 patients who had undergone surgery for renal tumors measuring ≤7 cm between 2005 and 2015. We characterized tumor size, pathology, type of surgery and clinical outcomes. Factors associated with the use of PN were evaluated using univariable and multivariable logistic regression models.

Results: Of the 169 patients, 34 (20%) and 135 (80%) had undergone partial and radical nephrectomy (RN) respectively for tumors ≤7 cm in diameter. Total number of 48 patients with tumors of ≤4 cm in diameter had undergone either PN (n=19; 40%) or RN (n=29; 60%). The frequency of PN procedures steadily increased over the years from 6% in 2005-2008, to 32% in 2013-2015, contrary to RN which was less frequently applied 94% in 2005-2008, and 68% in 2013-2015. In multivariable analysis, delayed surgery (p=0.01) and smaller tumor size (p=0.0005) were significant independent predictors of PN. During follow- up period, incidence of metastasis was lower in PN versus RN (13% and 32%, respectively, p=0.043). Local recurrence rates were not significantly different between PN (6.9%) and RN (7.2%) (p=0.99). The mean tumor sizes for patients who had undergone PN and RN were 4.1 and 5.5 cm respectively, (p<0.0001). The mean follow- up period for PN was 20 months, and for RN 33 months, (p=0.0225).

Conclusion: Partial nephrectomy for small renal tumors is relatively less frequently applied in Jordan, however an increase in its use has been observed over the years. Our data showed lower rates of distant metastasis and similar rates of local recurrence in favor of PN.

Keywords: Current guidelines; partial nephrectomy; renal cell carcinoma; trends.

ÖZ

Amaç: Ürdün'de böbrek tümörleri için parsiyel nefrektominin (PN) düşük oranda uygulandığı görünmektedir. Son 10 yılda Kral Hüseyin Kanser Merkezindeki eğilimi tanımlamaya çalıştık.

Gereç ve yöntemler: Renal hücreli kanser verilerimiz geriye dönük olarak gözden geçirildi. 2005 ile 2015 yılları arasında ≤7 cm olan tümörleri için ameliyat olmuş 169 hasta incelendi. Tümör büyüklüğü, patolojisi, cerrahinin türü ve klinik sonuçları tanımlandı. Tek ve çok değişkenli lojistik regresyon analiz modelleri kullanarak parsiyel nefrektomi ile ilişkili faktörler değerlendirildi.

Bulgular: Yüz altmış dokuz hastanın 34'üne (%20) PN ve 135'ine (%80) RN ameliyatı uygulanmıştır. Tümör çapı ≤4 cm olan 48 hastanın 19'u (%40) PN ve 29'u (%60) RN ameliyatı olmuştur. PN uygulama sıklığı yıllar boyu sürekli artmış, 2005-2008 arası %6'dan 2013-2015 arası %32'ye yükselmiştir. Buna karşın RN uygulama sıklığı ise 2005-2008'de %94'ten 2013-15 döneminde %68'e düşmüştür. Çok değişkenli analizde, cerrahide gecikme (p=0,01) ve daha küçük tümör büyüklüğü (p=0,0005) PN'nin önemli bağımsız belirteçleri idi. İzlem boyunca, PN'de metastaz insidansı daha düşüktü (PN: %13 ve RN: %32; p=0,043). PN ve RN arasında lokal nüks oranları anlamlı derecede farklı değildi (PN: %6,9 ve RN: %7,2; (p=0,99). PN veya RN geçirmiş hastalarda ortalama tümör büyüklükleri sırasıyla 4,1 ve 5,5 cm idi (p<0,0001). Ortalama izlem süreleri PN ve RN için sırasıyla 20 ve 33 ay idi (p=0,0225).

Sonuç: Ürdün'de küçük böbrek tümörleri için PN düşük oranda uygulanmakla birlikte yıllar içinde bu oranlarda artış gözlenmiştir. Verilerimiz PN lehine daha düşük oranlarda uzak metastaz ve benzer oranlarda lokal nüks olduğunu göstermiştir.

Anahtar Kelimeler: Güncel kılavuzlar; parsiyel nefrektomi; renal hücreli kanser; eğilimler.

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Submitted: 05.04.2016

Accepted: 15.06.2016

Available Online Date: 06.01.2017

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Available online at www.turkishjournalofurology.com

Introduction

In 2009, the American Urological Association (AUA) published evidence-based practice guidelines for the management of clinical T1a renal masses as a guide for clinicians to consider partial nephrectomy (PN) to be the reference standard for T1a renal masses.[1] Since then PN has been widely accepted as the standard of care for renal tumors 4 cm or less in diameter (T1a), with strong evidence supporting its use in tumors up to 7 cm (T1b) in carefully selected patients.[2-4]

Partial nephrectomy has been well supported in the literature due to its ability to preserve renal function with an overall lower incidence of chronic kidney disease[5,6], and a significant trend towards less frequent receipt of dialysis services, dialysis access surgery, or renal transplantation[7], when compared to radical nephrectomy (RN). These benefits are not limited to renal function but also involve overall mortality, as it has been shown that in patients younger than 65 years, radical nephrectomy was significantly associated with death from any cause compared with PN.[8]

Multiple studies have showed that PN is still underutilized in the United States[9,10] and around the world. We sought to examine the patterns of PN utilization in managing small renal masses in King Hussein Cancer Center- a tertiary referral center in Jordan- and to further characterize possible predictors for PN use.

Material and methods

After institutional review board (IRB) approval, we reviewed our nephrectomy data base for cases between 2005, and 2015. We identified 477 patients who had either radical or PN for renal tumors. Renal cell carcinoma (RCC) with size >7 cm, Wilms tumor, neuroblastoma and patients with nodal or distant metastasis at surgery were excluded from analysis, and 169 patients with a renal tumor of ≤7 cm in diameter were identified.

Descriptive analysis was performed for a comparison between PN and RN, and for all categorical factors using *chi*- square or Fisher's exact test. A logistic regression model was adopted to evaluate the impact of various factors as independent predictors of PN use, and a significance criterion of $p \leq 0.05$ was used in the analysis. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Hundred and sixty-nine patients had undergone either partial (n=34; 20%) or RN (n=135; 80%) for tumors of ≤7 cm in diameter. The most common histological type was clear- cell renal carcinoma 65%, and grade 2 was the most common Fuhrman grade detected in 60% of the cases (Tables 1, 2).

Table 3 depicts clinical features by operation type. We divided the study duration into 3 periods: 2005-2008, 2009-2012 and 2013-2015. A trend toward an increased use of PN as years pass was found and the majority of them have been performed within time intervals of 2009-2012 (44%), and 2013-2015 (47%) (p=0.003). Increased use of PN compared to RN was observed from 2005-2008 (6%) to 2013-2015 (32%). While RN use declined from 94% to 68% during the same time intervals (Figures 1-3). Surgery type was stratified by tumor size. Patients who had tumors of ≤4 or >4 cm in diameter had undergone either PN (40 vs. 13%) or RN (60 vs. 87%).

Forty-five patients who developed metastasis, had undergone either PN (9%) or mostly (91%) RN (p=0.043). There was no significant difference in local recurrence rates between PN and RN (p=0.99). Of the 44 patients that died only 6.8% underwent PN vs 93.2% who had RN (p=0.012).

As shown in Table 4, the average age at surgery for both operation types was 53.5 years, while the median tumor sizes, and follow- up periods for patients who had undergone PN, and RN were 4 vs. 6 cm (p<0.0001) and 19.7 vs 33.5 months, respectively (p=0.0225). No significant change was observed in the serum creatinine levels between the two groups. Twenty patients who had chronic renal failure had undergone either RN (n=16;80%) or PN (n=4; 20%)

Logistic regression analysis was performed to identify the predictors of procedure type (Table 5). Delayed surgery and smaller tumor size were significant predictors, with OR of 6.7 (p=0.019) and 6 (p=0.0005) on multivariable analysis, respectively. Younger age had OR of 3.13 (p=0.08). Gender was not a significant predictor.

At our center, mostly partial and RN cases were performed using open surgical techniques. But a similar trend towards the increased use of laparoscopy is being observed, with 25% of PN and 35% of RN cases were performed laparoscopically.

Our average warm ischemia time was 13 minutes, and we used mannitol infusion (12.5 gr/200 mL of normal saline) for renoprotection. In two of our patients with purely exophytic tumors and with significant underlying CKD, resection of the tumor without renal artery occlusion was done.

Discussion

Widespread use of cross-sectional imaging has led to a down-migration in the size of diagnosed renal masses. Strong evidence is supporting the use of PN as the standard of care for T1a (≤4 cm) tumors.[1] A trend towards an increase in the use of PN has been expected which was reflected by our data with the bulk

Turk J Urol 2017; 43(1): 42-7
DOI:10.5152/tud.2016.33667

(87%) of PN operations being done after the release of guidelines in 2009. However, RN is still being overused. Indeed, most of the patients (87%) who had tumors 4-7 cm in diameter, and a significant number of patients (60%) with tumors ≤4 cm in size had undergone RN.

Our results have indicated that PN use has increased from 7% during 2005-2008, to 32% in 2013-2015, while use of RN has declined from 94% to 68% during the same time intervals.(Figures 1-3). A similar trend has been observed in other countries. Liss et al.[9] reported an increase in the prevalence of PN from 29% in the years prior to guideline release to 35% in the years following guideline release with an adjusted odds ratio (OR) of 1.24 (p=0.049) in the USA.

There are serious potential consequences to overusing RN in patients with small renal masses. Recent observations clearly demonstrated a significantly increased risk of chronic kidney disease (CKD) in patients treated with RN as opposed to PN.[5,6] Huang et al.[5] reported 3-year probability of freedom from new onset of GFR lower than 60 mL/min/ 1.73 m^2 was 80% after PN and 35% after RN (p<0.0001). In our study 80% of the patients with new onset post-operative renal failure had undergone RN.

Table 1. Histopathological characteristics of the tumors detected in the study population

Type	Number	%
Clear cell	111	65
Chromophobe	18	10
Papillary	17	10
Translocation	7	4
Oncocytoma	4	2
Others	12	9
Total	169	

Table 2. Histologic grades of the resected tumors

Grade	Number	%
1	8	5.8
2	83	60.1
3	36	26.1
4	11	8.0
Total	138	

Table 3. Clinical features by treatment type in 169 patients treated surgically between 2005 and 2015

Parametres	Value	Total	PN	RN	p
Year n=169	2005-2008	54 (32.0%)	3 (5.6%)	51 (94.4%)	0.003
	2009-2012	65 (38.5%)	15 (23.1%)	50 (76.9%)	
	2013-2015	50 (29.6%)	16 (32.0%)	34 (68.0%)	
Gender	F	50 (29.6%)	7 (20.6%)	43 (31.9%)	0.198
	M	119 (70.4%)	27 (79.4%)	92 (68.1%)	
Tumor size (cm) (n=170)	Size<=4	48 (28.2%)	19 (39.6%)	29 (60.4%)	<0.0001
	Size >4	122 (71.8%)	16 (13.1%)	106 (86.9%)	
Health Status (n=169)	Lost to follow up	14	4	10	0.012
	Alive	111 (71.6%)	27 (24.3%)	84 (75.7%)	
	Dead	44 (28.4%)	3 (6.8%)	41 (93.2%)	
Recurrence (n=154)	Lost follow up	14	4	10	0.99
	Yes	11 (7.1%)	2 (6.9%)	9 (7.2%)	
	No	143 (92.9%)	27 (93.1%)	116 (92.8%)	
Metastasis (n=155)	Lost to follow- up	14	4	10	0.043
	Yes	45 (29.0%)	4 (13.3%)	41 (32.8%)	
	No	110 (71.0%)	26 (86.7%)	84 (67.2%)	

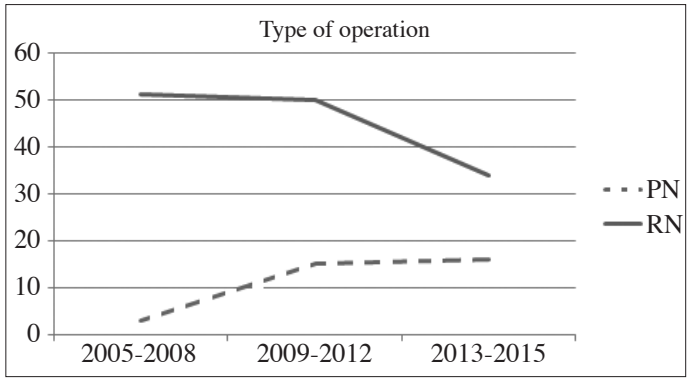


Figure 1. The number of patients and their corresponding surgery type (RN vs. PN) were plotted against three study periods 2005-2008, 2009-2012 and 2013-2015
PN: partial nephrectomy; RN: radical nephrectomy

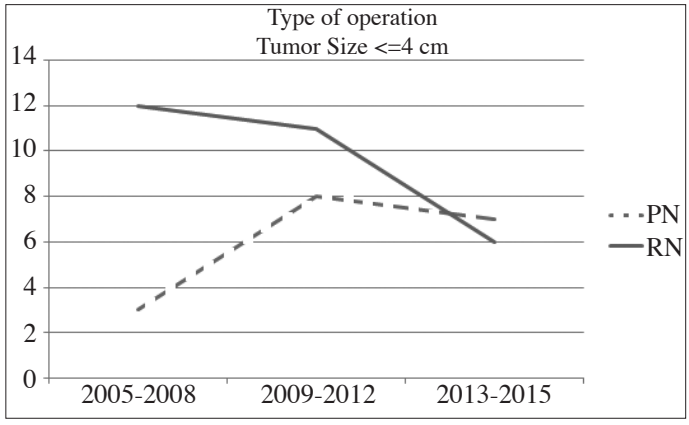


Figure 2. The number of patients and their corresponding surgery type (RN vs. PN) for tumors <=4 cm were plotted against three study periods 2005-2008, 2009-2012 and 2013-2015
PN: partial nephrectomy; RN: radical nephrectomy

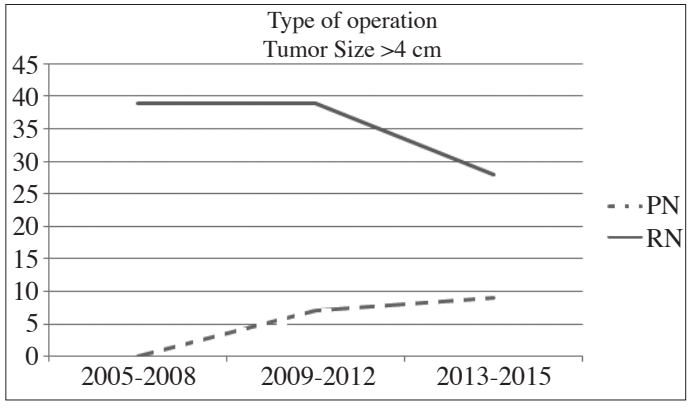


Figure 3. The number of patients and their corresponding surgery type (RN vs. PN) for tumors > 4 cm were plotted against three study periods 2005-2008, 2009-2012 and 2013-2015
PN: partial nephrectomy; RN: radical nephrectomy

Radical nephrectomy is associated with a reduction in overall survival and an increase in non-cancer related deaths.[8,11] Zini et al.[11] reported that RN was associated with absolute increase in overall (4.9%) and non-cancer related mortality (4.6%) at 5 years after surgery (p=0.001). Similarly, Thompson et al.[8] reported an increase of death from any cause in patients 65 years or younger with a relative risk of 2 (p=0.02). Our results were congruent with previously reported data (PN 6.8% vs. RN 93.2% of overall deaths) (p=0.012).

Radical nephrectomy can still be preferred by some urologists, as PN cases had more procedure- related complications compared to RN (9% vs. 3%, respectively, p=0.0001) due to complications of urinary leak and subsequently higher re-intervention rate (2.5% vs. 0.6%, p=0.02).[12] However, the majority of these complications were of minor degree, and the authors concluded that overall, PN is not associated with greater number of complications relative to RN.

Lesser number of metastases were observed in patients who had undergone PN (9%) relative to RN (91%). This phenomenon might be partly explained by the fact that patients who had undergone RN had larger tumor sizes compared to PN patients, We also did not find significant differences as for local recurrence rates between the two groups (PN, 6.9% and RN, 7.2%) (p=0.99).

Table 5 demonstrates univariable, and multivariable analysis of various suspected predictors of PN use. As expected, delayed surgery and smaller tumor size were independent predictors (p=0.0119 and 0.0005 respectively). Younger age was a potential factor (p=0.08), and this should be addressed when deciding on the type of operation. Use of renoprotective PN should be encouraged in older patients on account of their greater number of comorbidities and their declining GFR among these patients who are also in desperate need of preserving their renal function.

Our results are similar to what has been shown in other studies[7,13], but contrary to theirs, in our experience, gender was not a significant predictor in the decision to perform PN.

There are some limitations to our study. Our data reflect the experience at King Hussein Cancer Center, a tertiary referral center, and we suspect that the rates of PN are in fact lower in other hospitals. Individualized surgeon specific experience might have accounted for the observed trends. Tumor location might have been a factor in choosing RN over PN, and we tried to account for this variable in our analysis. R.E.N.A.L nephrometry score has been effectively utilized to predict the amenability of renal masses to PN[14], with its scoring system ranging from 1-12 points accounting for the tumor complexity, taking in consideration multiple factors to characterize the mass location. We were

Turk J Urol 2017; 43(1): 42–7
DOI:10.5152/tud.2016.33667

Table 4. The mean (± SD) and median (min-max) values of several clinical features in the study population

Parametres	Surgery type	Mean (95% CI)	Median (Min, Max)	p
Tumor size (cm) (n=170)	PN	4.1 (3.6, 4.6)	4.0 (1.1, 7.0)	<0.0001
	RN	5.5 (5.3, 5.8)	6.0 (1.7, 7.0)	
Length of follow up (months)	PN	19.7 (11.1, 28.4)	6.0 (1.0, 120)	0.0225
	RN	33.5 (28.7, 38.3)	23.0 (1.0, 121)	
Age at the time of surgery (years)	PN	53.5 (50.3, 56.7)	52.0 (34.0, 79.0)	0.8010
	RN	53.9 (51.3, 56.4)	54.0 (13.0, 81.0)	
Serum Cr (mg/dL) before the operation	PN	1.2 (0.8, 1.5)	0.9 (0.6, 7.7)	0.56
	RN	1.0 (1.0, 1.1)	1.0 (0.5, 2.7)	
Serum Cr (mg/dL) after the operation	PN	1.7 (1.0, 2.3)	1.0 (0.4, 10.3)	0.88
	RN	1.6 (1.4, 1.8)	1.3 (0.3, 7.3)	

PN: partial nephrectomy; RN: radical nephrectomy

Table 5. Univariable and multivariable logistic regression models for PN vs RN rates according to population characteristics

	Odds Ratio Estimates							
	Univariable				Multivariable			
Effect	Odds ratio	95% Wald Confidence limits		p	Odds ratio	95% Wald Confidence limits		p
2009-2012 vs 2005-2008	3.018	0.766	11.89	0.1142	3.929	0.883	17.489	0.0725
2013-2015 vs 2005-2008	4.665	1.219	17.854	0.0245	6.762	1.525	29.983	0.0119
Size<=4 vs Size>4 cm	5.089	2.056	12.595	0.0004	6.071	2.209	16.685	0.0005
Age<=62 vs Size>62 years	2.462	0.78	7.767	0.1243	3.133	0.864	11.364	0.0824
M vs F	1.891	0.652	5.485	0.2411	1.975	0.611	6.382	0.2556

not able to acquire the preoperative CT scan images for all of our patients, one reason being, that a number of them who came from other neighboring countries had been lost to follow- up.

Although the use of PN for small renal tumors has a relatively lower incidence in Jordan, an increase in its utilization has been observed over the years. Our data have shown lower rates of distant metastasis favouring PN, and nearly similar rates of local recurrence marginally in favor of partial nephrectomy.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of King Hussein Cancer Center.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.AD; Design - I.AS; Supervision - A.AD; Resources - S.G., I.A., K.A.; Materials - S.G., N.Q.; Data Collection and/or Processing - I.AS., S.G., I.A., K.A., N.Q.; Analysis and/or Interpretation - I.AS.; Literature Search - I.AS., S.G., I.A.; Writing Manuscript - I.AS., A.AD., K.A., S.G., I.A.; Critical Review - I.AS., A.AD.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Komite Onayı: Bu çalışma için etik komite onayı Kral Hussein Kanser Merkezi'nden alınmıştır.

Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - A.AD; Tasarım - I.AS; Denetleme - A.AD; Kaynaklar - S.G., I.A., K.A.; Malzemeler - S.G., N.Q.; Veri Toplanması ve/veya İşlemesi - I.AS., S.G., I.A., K.A., N.Q.; Analiz ve/veya Yorum - I.AS.; Literatür Taraması - I.AS., S.G., I.A.; Yazıyı Yazan - I.AS., A.AD., K.A., S.G., I.A.; Eleştirel İnceleme - I.AS., A.AD.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

References

1. Campbell SC, Novick AC, Belldegrun A, Blute ML, Chow GK, Derweesh IH, et al. Guideline for management of the clinical T1 renal mass. J Urol 2009;182:1271-9. [CrossRef]
2. Patard JJ, Shvarts O, Lam JS, Pantuck AJ, Kim HL, Ficarra V, et al. Safety and efficacy of partial nephrectomy for all T1 tumors based on an international multicenter experience. J Urol 2004;171:2181-5, quiz 435. [CrossRef]
3. Becker F, Siemer S, Humke U, Hack M, Ziegler M, Stockle M. Elective nephron sparing surgery should become standard treatment for small unilateral renal cell carcinoma: Long-term survival data of 216 patients. Eur Urol 2006;49:308-13. [CrossRef]
4. Leibovich BC, Blute M, Cheville JC, Lohse CM, Weaver AL, Zincke H. Nephron sparing surgery for appropriately selected renal cell carcinoma between 4 and 7 cm results in outcome similar to radical nephrectomy. J Urol 2004;171:1066-70. [CrossRef]
5. Huang WC, Levey AS, Serio AM, Snyder M, Vickers AJ, Raj GV, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. Lancet Oncol 2006;7:735-40. [CrossRef]
6. Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. Mayo Clin Proc 2000;75:1236-42. [CrossRef]
7. Miller DC, Schonlau M, Litwin MS, Lai J, Saigal CS. Renal and cardiovascular morbidity after partial or radical nephrectomy. Cancer 2008;112:511-20. [CrossRef]
8. Thompson RH, Boorjian SA, Lohse CM, Leibovich BC, Kwon ED, Cheville JC, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. J Urol 2008;179:468-73. [CrossRef]
9. Liss MA, Wang S, Palazzi K, Jabaji R, Patel N, Lee HJ, et al. Evaluation of national trends in the utilization of partial nephrectomy in relation to the publication of the American Urologic Association guidelines for the management of clinical T1 renal masses. BMC Urol 2014;14:101. [CrossRef]
10. Baillargeon-Gagne S, Jeldres C, Lughezzani G, Sun M, Isbarn H, Capitanio U, et al. A comparative population-based analysis of the rate of partial vs radical nephrectomy for clinically localized renal cell carcinoma. BJU Int 2010;105:359-64. [CrossRef]
11. Zini L, Perrotte P, Capitanio U, Jeldres C, Shariat SF, Antebi E, et al. Radical versus partial nephrectomy: effect on overall and noncancer mortality. Cancer 2009;115:1465-71. [CrossRef]
12. Stephenson AJ, Hakimi AA, Snyder ME, Russo P. Complications of radical and partial nephrectomy in a large contemporary cohort. J Urol 2004;171:130-4. [CrossRef]
13. Miller DC, Hollingsworth JM, Hafez KS, Daignault S, Hollenbeck BK. Partial nephrectomy for small renal masses: an emerging quality of care concern? J Urol 2006;175:853-8. [CrossRef]
14. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol 2009;182:844-53. [CrossRef]