REVIEW ARTICLE

Important Aspects of Organ-Preserving Surgery for Renal Tumors

Indications, New Standards, and Oncological Outcomes

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SUMMARY

Introduction: Organ-preserving surgery for renal tumors has become more common over the past two decades. At first, part of the kidney, rather than all of it, was resected only if there was an absolute indication for doing so, i.e., if the tumor was located in an anatomically or functionally solitary kidney or if renal failure was already present. Now that favorable oncological outcomes have been demonstrated, renal tumors are increasingly often removed with only partial resection of renal tissue even when the indications are less stringent, including when the other kidney is healthy.

Methods: The indications for, and oncological outcomes of, partial renal resection are presented and discussed on the basis of a selective literature search of Medline as well as the guidelines of the European Association of Urologists (EAU).

Results and Conclusions: The EAU, in its new guidelines for renal cell carcinoma, recommends partial renal resection as the standard treatment for tumors less than 4 cm in size that are wholly contained within one kidney when the other kidney is healthy. This practice yields comparable outcomes to those of nephrectomy, with tumor-specific five-year survival rates exceeding 90%. In major urological centers, partial resection is favored even for tumors larger than 4 cm, as long as they are in a favorable location. Nonetheless, the estimated rate of nephrectomy for tumors less than 4 cm in size currently remains very high in Germany, as it does in American studies, even though the organ-preserving resection of such small tumors usually results in cure.

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Radical nephrectomy, first described by Robson in 1969, was for many years the standard treatment of operable renal tumors. The procedure involves the complete removal of the tumor-bearing kidney within Gerota's fascia, including the ipsilateral adrenal gland (1).

For patients at very high risk of renal insufficiency because of an anatomically or functionally single kidney, those with already existing renal insufficiency, and those with bilateral renal tumors (imperative surgical indications), organ-preserving surgery has increasingly become the new gold standard of treatment, as it keeps such patients off dialysis (2). The advantages of this procedure are

- low complication rates (7% to 11%),
- excellent local tumor control (local recurrence in less than 5% of cases), and
- oncological long-term results that are comparable to those of traditional radical nephrectomy when performed on patients with tumors that are in a comparable stage (tumor-specific 5-year-survival rates between 80% and 95%).

For these reasons, the organ-preserving operation has become established as an alternative to radical nephrectomy, not just in the situations listed above, but also for patients with small unilateral tumors and a second healthy kidney (elective indication). It has rapidly gained wide acceptance in recent years.

Moreover, because small, asymptomatic tumors are being detected ever more often owing to the progressive improvement of imaging techniques such as ultrasonography, computerized tomography, and magnetic resonance imaging, the last 20 years have seen the introduction of risk-adapted treatment for patients with such tumors (3, 4, 5). Partial nephrectomy has therefore been included in the current guidelines of the European Association of Urology as a standard treatment of stage pT1a renal tumors (those that are locally restricted to the kidney and measure less than 4 cm in diameter). Thus, partial nephrectomy has replaced classic nephrectomy for this indication (6).

As the current American studies reveal, although partial nephrectomy is increasingly being used as a standard surgical procedure, it is still being performed much less often than it should be, in view of the indications for which it is now accepted. An analysis of data from the American cancer registry (the SEER program—

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Figure 1: Abdominal CT scan revealing a peripheral tumor in the left kidney of maximal diameter 5.4 cm (red circle) and a normal right kidney, illustrating the good resectability of a tumor exceeding 4 cm in size (extended elective indication). From: Becker F et al.: Organ-erhaltende Nierentumorchirurgie. Urologe A 2008; 47: 215–23; [22], with the kind permission of Springer Verlag, Heidelberg, Germany.

"Surveillance, Epidemiology, and End Results") shows that the percentage of partial nephrectomies performed for tumors greater than 7 cm in diameter rose from 4.6% in 1988 to 17.6% in 2001. Nevertheless, in 2000 and 2001, the percentage of partial resections for tumors greater than 2 cm in diameter was still only 42%, and that for tumors between 2 cm and 4 cm in diameter only 20% (7). According to the guidelines, the percentage of partial nephrectomies for tumors less than 4 cm in diameter should actually be near 100%.

This article summarizes the current indications, preoperative diagnostic evaluation, and operative techniques for partial nephrectomy, as well as its alternatives. To this end, a selective literature search was performed for current articles on the subject. This article incorporates the EAU guidelines as well as a retrospective analysis of the renal tumor database at the authors' own institution.

Indications for partial nephrectomy according to the EAU guidelines

Imperative indications for the procedure

Partial nephrectomy is considered to be imperatively indicated when there would be a danger of renal insufficiency with a need for dialysis if the tumor-bearing kidney were to be entirely removed. This is the case in patients with bilateral renal tumors, a functionally or anatomically single kidney, or pre-existing, compensated renal insufficiency. In such cases, an absolute indication is said to exist.

Relative indications for the procedure

Partial nephrectomy is relatively indicated when the risk of postoperative renal insufficiency after nephrectomy is higher than usual. Examples of such situations include

- pre-existing nephrolithiasis,
- chronic pyelonephritis,
- renal artery stenosis,
- vesicouretero(-renal) reflux, as well as
- systemic diseases such as diabetes mellitus or arterial hypertension, with incipient functional damage to the kidney (8).

Elective indications for the procedure

In view of its good results, which are comparable to those of total nephrectomy—similar survival rates (tumor-specific 5-year survival rates from 80% to 95%) with nearly identical complication rates (7% to 11%) and a practically negligible rate of local recurrence (less than 5%)—the current EAU guidelines for renal cell carcinoma designate partial nephrectomy as a standard treatment of renal tumors less than 4 cm in diameter (i.e., stage pT1a tumors), when the contralateral kidney is normal (6, 9).

Extended elective indications

In recent years, a number of groups have reported favorable oncological results (tumor-specific 5-year survival above 90%) after partial nephrectomy for selected tumors of diameter greater than 4 cm that were considered to be technically resectable without undue difficulty and in a favorable location for surgery (peripheral site in the kidney, "pedunculated" tumor on a small base). Thus, organ-preserving renal tumor excision should be considered in such cases as well (figure 1). Such procedures, however, should only be performed in experienced centers (6, 10, 11).

Preoperative diagnostic evaluation and surgical techniques

Despite the increasing rate of incidental discovery of small, asymptomatic renal tumors (with a worldwide incidence rising by about 2% each year [6]), the preoperative diagnostic evaluation still must include a physical examination, a detailed history, and the appropriate laboratory tests. The results of blood tests rarely change the nature of the treatment offered, yet they often provide valuable information so that the patient can be prepared optimally for surgery (e.g., serum creatinine, hemoglobin, and a basic coagulation profile).

Radiological imaging of the chest is essential and may already yield evidence of thoracic metastases. There is some debate at present over whether a computerized tomogram of the chest must be obtained or whether a conventional chest x-ray is already adequately sensitive (6, 12). In any case, the most important part of the preoperative diagnostic evaluation consists of radiological studies such as ultrasonography (for early diagnosis), computerized tomography, and magnetic resonance imaging of the abdomen. These studies provide ideally complete information about the size, localization, and invasiveness of the tumor and enable the exclusion of metastases. Furthermore, they can also sensitively detect extrarenal growth, venous invasion, adrenal involvement, and lymph node enlargement, and they

enable assessment of the structure and function of the opposite kidney (13, 14).

The choice of the approach (open lumbar, open transperitoneal, laparoscopic transperitoneal, or retroperitoneoscopic) and of the surgical technique (warm, cold, without ischemia, or ex vivo partial resection) depends not just on the clinical situation and the surgical indications, but also on the operative training and experience of the surgical center. The important thing is not the precise method used, but rather the postoperative result obtained. The method with which the team has the most experience is the safest method and should be preferred. Nonetheless, in cases where partial resection seems to be possible and an indication for it exists, yet local expertise is lacking, the patient should be referred to an experienced center rather than undergo a nephrectomy and thereby lose valuable renal function.

Partial resection can be performed either without clamping of the vascular pedicle (i.e., without ischemia) or under ischemic conditions, with or without hypothermic perfusion (so-called cold and warm ischemia, respectively). Alternatively, when the tumor is multilocular or the preoperative studies suggest that technical difficulties can be expected in resection or reconstruction (common situations when partial nephrectomy is imperatively indicated), the entire kidney can be removed and an ex vivo resection can be performed under hypothermic conditions on a separate, sterile operating table. Afterward, the kidney can be autotransplanted into the patient's contralateral iliac fossa, just as in a conventional renal transplantation procedure (15, 16).

The duration of surgery under ischemia is an important predictor of the postoperative functioning of the kidney that is operated on. A healthy kidney tolerates ischemia for no longer than 30 minutes. This is the maximum time allowable for the removal of the tumor and for the surgical maneuvers in the tumor bed that must be performed immediately thereafter (*figures 2a, 2b*) (17).

Laparoscopic partial nephrectomy should only be performed in centers that do the procedure often and have adequate experience with it. Particularly during the ischemic phase of the operation, it is essential that the tumor should be resected and the resection bed cared for (with suture of its blood vessels, tubular system, and parenchyma) both quickly and safely, in order to optimize postoperative renal function. An analysis of multiple published studies comparing laparoscopic with open partial nephrectomy has shown that the former is associated with less blood loss and with shorter times of hospitalization and recuperation. The disadvantages of laparoscopic partial nephrectomy are the longer ischemia time and the higher rate of complications, above all intraoperative hemorrhage. The oncological and functional results in the two groups are similar (8).

The following alternative treatments are still experimental and should only be performed in patients judged to be inoperable:

- Minimally invasive and ablative techniques such as cryoablation, radiofrequency ablation, and HIFU (high intensity focused ultrasound) treatment

Figure 2: (a) A 6 cm tumor at the lower pole of the kidney, seen upon exposure of the kidney (red arrows, tumor; dotted line, border between normal renal parenchyma and tumor). The peritumoral fat is left attached to the specimen. (b) The resection bed after the tumor has been completely removed up to healthy tissue and vascular sutures have been laid in the resection bed.

- The so-called surveillance strategy (continued follow-up at close intervals without surgery).

For all of these methods, there is still a lack of prospective, long-term oncological data (6, 18).

Results

Complication rates

The reported complication rates after partial nephrectomy range from 4% to 30%. There is an important difference between patients operated on for elective and imperative indications: Perioperative complications are more frequent in the latter. The following are special problems that can occur after partial nephrectomy:

TABLE

The 5-year survival rates (5-YSR), recurrence rates, and local recurrence rates after partial nephrectomy for renal cell carcinoma with imperative, elective, and extended elective indications, as exemplified by the Homburg patient collective

	Tumor-specific 5-YSR (%)	Recurrence rate (%)	Local recurrence rate (%)
Group A (imperative, n = 175)	94.8	18.4	4.4
Group B (elective, n = 311)	97.8	5.5	1.2
Group C (extended elective, n = 69)	100	5.8	0

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- Urinary fistula (after the tubular system is opened)
- Postoperative renal insufficiency
- The need for dialysis (because of renal failure due to excessively prolonged ischemia or renal injury through clamping of the renal vessels).

Other problems, such as splenic injury, infections/abscesses, and intra- or postoperative hemorrhage, possibly leading to a need for emergency reoperation or to perioperative mortality, are counted among general surgical complications (17). The complication rate (as well as the hospitalization cost) of partial nephrectomy has been shown to be about as low as that of total nephrectomy (10% versus 3.3%, $p = 0.2$) (19).

Survival rates

Lane and Novick have written a current review of the oncological results reported in the larger published studies. Tumor-specific 5-year survival rates of 89% to 98% were achieved. As a result of patient selection,

lower survival rates were found in studies in which most patients had undergone partial nephrectomy for imperative indications (8). As already mentioned above, such patients have more frequent complications than electively operated ones.

In a recent study of 381 patients who had undergone partial nephrectomy for elective indications, a very high 10-year survival rate of 97% was achieved (20). Retrospective comparative studies of the survival rates after elective partial nephrectomy and total nephrectomy in comparable patient groups have revealed no significant differences between the two procedures with respect to survival (9, 17).

Recurrence rates

The rate of recurrence of renal tumors after partial nephrectomy is about as low as that after total nephrectomy in comparable clinical situations (tumor stage and size, patient age and sex). Recurrence rates of 2% to 17% have been reported. The rate of local recurrence after partial nephrectomy ranges from 0% to 10%. The opponents of partial nephrectomy have long pointed to the supposedly greater risk of local recurrence, yet the current data tend to weaken this argument. When the studies that have been compared to one another are more closely examined one by one, it emerges that the studies in which a large percentage of patients underwent partial nephrectomy for imperative indications had, on average, the highest rates of progression and local recurrence (8, 17).

The authors' experience

From 1975 to 2005, the authors operated on a total of 2627 patients with renal tumors, of whom 486 (18.5%) underwent partial nephrectomy. The low rate of partial nephrectomy was due to the large percentage of tumors that were in advanced stages or had already metastasized at the time of surgery (nearly 50% of all cases), as well as to the fact that partial resection has only become an established urological technique in the past 10 to 15 years. At present, in our institution (University Clinics of the Saarland), favorably situated tumors are almost always operated on with organ-preserving intent. 175 of these 486 patients (36%) underwent partial nephrectomy

Comparison of survival rates after elective partial nephrectomy and total nephrectomy ($p < 0.05$). The patient groups were matched pairwise for important clinical parameters.
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FIGURE 3

for imperative indications (group A), while the remaining 311 (64%) underwent it for elective indications (group B). In 69 patients undergoing the procedure electively, the tumor was greater than 4 cm in diameter (extended elective indication, group C). The tumor-specific survival rates and (local) recurrence rates are listed in the *table*. A direct comparison of survival rates after elective partial resection versus tumor nephrectomy (performed by matched-pair analysis, in which pairs of patients were matched for age, sex, tumor stage, grade, and size, and tumor entity) revealed a significant advantage for elective partial resection: The 5-year survival rates were 92.7% after tumor nephrectomy and 97.8% after elective partial resection, $p < 0.05$ (*figure 3*). The evident survival advantage certainly reflects selection bias favoring the group that underwent partial resection. This demonstrates not only that suitable patients must be filtered out for each method of treatment, but also that such operations do not inherently confer a higher risk when performed in experienced hands, and that they will certainly be more widely performed in years to come (9, 11).

Conclusions

Organ-preserving partial nephrectomy is an oncologically safe surgical technique. It is the only appropriate method of treatment for patients with imperative indications. For another group of patients, those with tumors less than 4 cm in size and a normal contralateral kidney, elective partial nephrectomy is accepted as a standard treatment by the current EAU guidelines. This is justified on the basis of favorable long-term oncological data on large patient collectives, with outcomes comparable to those of total nephrectomy in equivalent clinical situations. The complication rates and hospitalization costs of partial and total nephrectomy are comparably low, yet the patients' quality of life is higher after partial nephrectomy (20). Nonetheless, despite this evident paradigm shift, too many patients with small tumors restricted to the kidney are still being overtreated with total nephrectomy.

Extended elective partial nephrectomy is now regularly performed in urological centers for the treatment of favorably situated peripheral tumors measuring more than 4 cm in diameter, whenever this seems to be both technically feasible and reasonable from the oncological point of view.

Conflict of interest statement

The authors declare that they have no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors.

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Key messages

- Organ-preserving partial nephrectomy has now become a standard treatment for solitary renal tumors less than 4 cm in size, when the other kidney is normal.
- Organ preservation can also be attempted when a solitary renal tumor that is larger than 4 cm in diameter is favorably situated.
- Overall tumor-specific 5-year survival rates above 90% have been achieved after partial nephrectomy for renal cell carcinoma.
- Compared to total nephrectomy, partial nephrectomy has similarly low rates of complications and recurrences. The probability of a local recurrence is below 10%.
- Organ preservation should be attempted more often in patients with locally restricted renal tumors. This technique spares both renal function and the patient's quality of life.

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