8 Open Partial Nephrectomy

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Abbreviations

BHD	Birt–Hogg–Dubé syndrome
HRPC	Hereditary papillary renal carcinoma
NSS	Nephron-sparing surgery
OPN	Open partial nephrectomy
OS	Overall survival
PFS	Progression-free survival
PN	Partial nephrectomy
RN	Radical nephrectomy
SRM	Small renal mass
VHL	Von Hippel–Lindau

Key Messages

- The three main goals of open partial nephrectomy (OPN) are complete removal of tumour, preservation of renal function and minimal perioperative complications.
- Standardization of the surgical technique of open partial nephrectomy along with excellent oncological outcomes and reduced morbidity has contributed to its growing application around the world.
- Preoperative and multidisciplinary care with nephrologist helps optimize renal function after partial nephrectomy.
- To minimize renal injury, small tumours can be dissected without ischaemia using manual compression by the assistant.
- OPN usually employs a flank, thoracoabdominal or subcostal incision, but a dorsal lumbotomy may also be used.

8.1 Introduction

Over the last three decades, renal cell cancer is increasingly being diagnosed at a much earlier stage than in the past [1]. This owes primarily to the widespread use of ultrasound and CT. Technological improvements in imaging

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and its easy availability have led to the increasing identification of small renal mass (SRM). It is defined as an enhancing renal tumour <4 cm in the largest dimension on imaging [2]. It has been estimated that at least 48–66% of RCC diagnoses occur as a result of cross-sectional imaging in otherwise asymptomatic patients [3]. T1a RCC has become an increasingly prevalent clinical scenario for urologic surgeons, and it has become imperative to use less invasive means of management for these masses. Nephron-sparing approaches, particularly partial nephrectomy (PN), have become increasingly popular. Although it can be performed laparoscopically and by robot-assisted PN, the greatest experience remains in open partial nephrectomy.

In the initial years, it was performed for patients with absolute indications such as bilateral RCC, RCC in a solitary kidney or RCC in the setting of pre-existing kidney disease [4]. However, lately it is being employed at tertiary-care centres for the management of localized renal tumours. Nephron-sparing surgery (NSS) is also valuable in cases of unilateral multifocal RCC and bilateral renal tumours. They are typically seen in various hereditary forms of RCC, like Von Hippel–Lindau (VHL), hereditary papillary renal carcinoma (HRPC) and Birt–Hogg–Dubé (BHD) syndromes. Bilateral and multifocal renal cancers are challenging clinical scenarios. Management strategies include concomitant bilateral PN and staged PN with either the more complex side done first or the less complex side done first. There are pros and cons of these approaches.

PN is classically done for T1a or selected patients with T1b RCC; however, several series report on the successful use of PN for tumours larger than 7 cm or with renal vein thrombus [5]. Alanee et al. reviewed contemporary series on data of 359 patients undergoing PN for T2+ RCC [6]. Median tumour size was 7.5–8.7 cm, and tumour histology was mainly clear cell. Technique was mainly open, the reported median ischaemia time was 29–45 min, and median operative time was 170–221 min. Positive margin rates were 0–31%. With a median follow-up of between 13 and 70 months, a 5-year progression-free survival (PFS) was 71–92.5%, and a 5-year overall survival (OS) was 66–94.5%. This led to a conclusion that the ability to preserve parenchyma, not tumour size, should be the main determinant of the feasibility of PN [7]. Radical nephrectomy (RN) however continued to be standard surgical approach for most renal tumours outside specialized centres. This was partly due to associated complications and concern for oncological outcomes. Most commonly encountered complications are haemorrhage, urinary fistula formation, ureteral obstruction, acute renal insufficiency and infection [8]. Van Poppel et al. compared PN (n = 2 68) and RN (n = 273) together with a limited lymph node dissection in a prospective, multicentre, phase 3 trial [9]. It was noted that PN for small, easily resectable, incidentally discovered RCC in the presence of a normal contralateral kidney can be performed safely with slightly higher complication rates than RN. Subsequent analysis of the data for oncological outcomes showed 10-year OS rates of 81.1% for RN and 75.7% for PN. With a hazard ratio (HR) of 1.50 (95% confidence interval [CI], 1.03–2.16), the test for non-inferiority is not significant ($p = 0.77$), and the test for superiority is significant ($p = 0.03$) [10]. There is considerable evidence that PN reduces the risk of chronic kidney disease (CKD) compared with RN [7]. When compared with RN, PN always provides better renal functional outcomes in similar patients [11].

Objectives of Open Partial Nephrectomy

The three main goals of OPN are:

1. Complete removal of tumour
2. Preservation of renal function
3. Minimal perioperative complications

The ideal oncological outcome for extirpative surgery is a negative surgical margin. In PN the competing key objective is to preserve renal function as much as possible. This makes PN a technically demanding procedure. Positive surgical margin in PN is defined as no cancer cells in the inked specimen [12]. Recently, Buffi and colleagues proposed a simple classification system to identify patients with the optimal outcomes after PN procedures [13]. They combined the three main goals of PN, i.e. the negative surgical margin, <20 min warm ischaemia and minimal complications; the authors abbreviated this as an MIC. The background of the MIC system was as follows: According to this system, the goal of PN is achieved when (1) the surgical margins are negative, (2) the warm ischaemia time (WIT) is <20 min and (3) no major complications (grades 3–4 according to Clavien classification) are observed.

8.1.1 Oncological Outcomes

The standardization of the surgical technique of PN along with excellent oncological outcomes and reduced morbidity has contributed to the more frequent use of PN in many centres around the world. Oncologic results are similar to those found after RN, with better preservation of renal function [14]. Once the safety and efficacy of the procedure was established, there was the phase of expanding indications. It is classically performed in patients with multiple small RCC, bilateral RCC, RCC in patients with compromised renal function mostly in patients with T1a cancer. In select patients, even localized RCC larger than T1a can be treated with elective PN, providing good long-term outcomes [15]. For T1b RCC the data is limited, and recommendations are based on some series with carefully selected peripheral lesions. In a series of 69 carefully selected patients with >T1a peripherally located tumours, Becker noted that 55 (79.7%) had clear-cell pathology, the mean pathologic tumour size was 5.3 cm (range, 4.1–10 cm) and less than 6% experienced disease recurrence at a median follow-up of 5.8 years [15].

8.1.2 Functional Outcome

The second important goal of performing a good-quality PN is to preserve renal function. Evaluation of functional outcome however is not straightforward. The timing and method of functional assessment are less well defined in the literature. Functional impairment of the ipsilateral renal unit is multifactorial. Comorbid conditions (patient-related factors) and surgical factors (warm ischaemia time) are both important. The impact of latter is relatively straightforward and assessed by WIT. A safe WIT range is between 20 and 30 min [16]. Therefore, having a WIT <20 min can be considered a good clinical cut-off value [17]. The remnant renal parenchyma after PN is another significant predictor of postoperative renal function [18].

Yoo et al. [19] studied robot-assisted PN using warm ischaemia or OPN using cold ischaemia (CI). The authors noted that OPN was superior to robot-assisted PN in patients with a small renal mass and ischaemia time ≥25 min. However, robot-assisted procedure yielded renal functional outcomes comparable to those of open partial when ischaemia time was <25 min.

There is compelling evidence in support that even when preoperative risk factors for renal insufficiency are controlled, patients undergoing open RN are at a greater risk of chronic renal insufficiency than a similar cohort of patients undergoing PN, without compromising the oncological outcome [20]. Huang and colleagues demonstrated that the 3-year probability of absence of new-onset of glomerular filtration rates (<60 mL/min per 1.73 m^2) in a cohort of 662 patients who underwent radical/partial nephrectomy for a solitary renal tumour was 80% (95% confidence interval [CI], 73–85) after PN and 35% (95% CI, 28–43; $p < 0.0001$) after RN [8]. The authors observed that RN is an independent risk factor for new-onset kidney dysfunction.

The other surrogate markers for functional impairment are proteinuria and serum creatinine of >2 mg/dL. The Mayo Clinic experience using a matched comparison of PN and RN has shown a higher risk for proteinuria (defined as a protein-to-osmolality ratio of 0.12 or higher) and chronic renal insufficiency (defined as serum creatinine >2.0 mg/dL) after RN (risk ratio, 3.7; 95% confidence interval [CI], 1.2–11.2; $p = 0.01$) [21].

8.2 Technical Considerations

8.2.1 Indications

In order to standardize description of renal tumours, several nephrometry systems are described [22]. The two most commonly applied systems include the RENAL and PADUA nephrometry systems. They characterize anatomical features in terms of tumour radius, endophytic component, proximity to sinus fat/collecting system and location (anterior/posterior aspect and location relative to polar lines) [23]. The centrality index is the ratio of the distance between the tumour and renal centre over the tumour radius [24]. The RENAL [25] described in 2009 is perhaps the most commonly employed system and is associated with perioperative functional outcome of warm ischaemia time and estimated blood loss [26]. More recently Hsieh and colleagues [27] have described a mathematical model to determine the contact surface area of the tumour. They concluded that the contact surface area determination is a novel, reproducible, open-source and software-independent method of describing the complexity of renal tumours. It correlates with estimated blood loss and operative time and also had a better predictive value for changes in postoperative kidney compared with RENAL score.

8.2.2 Renal Ischaemia

Current evidence indicates that the use of a single cut-off for duration of ischaemia time as a dichotomous value for renal function outcomes during partial nephrectomy is flawed [28]. Current evidence has shown that patients with two kidneys undergoing nephron-sparing surgery can tolerate ischaemia times of more than 30 min without a clinically significant decline in renal function. However, every minute counts, and it is preferable to keep ischaemia time to as short as possible until clear cut-off is defined.

Small polar tumours can be resected without ischaemia; manual compression of the renal parenchyma by the assistant suffices (Fig. 8.1). Various kidney clamps have been described, but may not have any added advantage over manual compression [29]. For more complex tumours, it is preferable to have a dry field. The upper limit for warm ischaemia time is controversial; however, it should not exceed 30 min. Clamping of vessels during partial nephrectomy facilitates surgery by decreasing blood loss and improving visibility facilitating both tumour removal and renorrhaphy. Every attempt is made to limit the warm ischaemia time during partial nephrectomy. Various modifications of local parenchymal compression like manual compression, Kaufmann clamp, etc. have been described [30]. Trehan [31] in a recent meta-analysis of data from contemporary off-clamp and vessel compression series noted that off-clamp PN may be associated with improved long-term renal outcome when compared to on-clamp PN, but no difference was seen in peri- and postoperative variables, surgical complications and oncological outcomes.

Selective arterial clamping is another useful technique to reduce ischaemia and avoid reperfusion injury during partial nephrectomy [32]. This could be further improved by administering dye, commonly indocyanine green (ICG) which is injected intravenously and can be identified throughout the vascular system in less than 1 min. However, cost (requires a near-infrared camera) and debatable long-term benefit limit its use. For complex partial nephrectomy, the kidney may be cooled after clamping and the tolerable (cold) ischaemia time is significantly longer. The administration of an osmotic diuretic such as mannitol before (and after) clamping the renal vessels is often used to reduce reperfusion injury after renal ischaemia. There is, however, lack of credible data supporting the use of mannitol in the context of OPN [33]. There is controversy concerning current indications as well as optimal temperature for cold ischaemia. The two major urological association guidelines (AUA and EAU) suggest the use of hypothermia when an

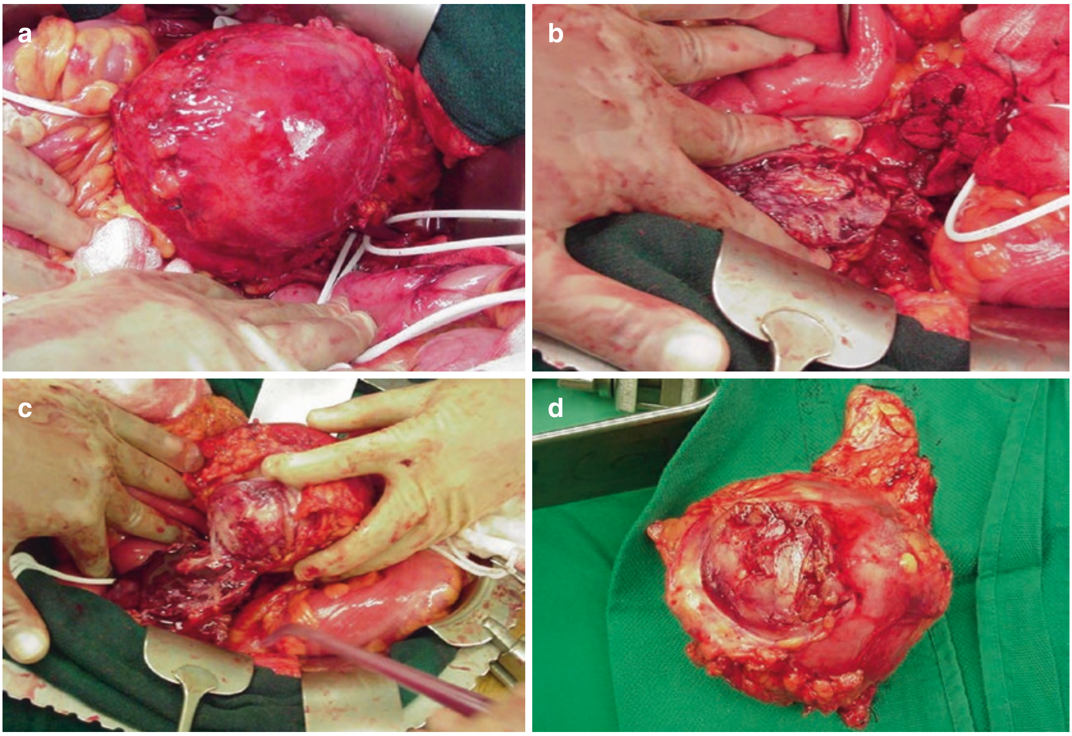

Fig. 8.1 T1b, clear-cell carcinoma of the kidney, operated via abdominal incision. (**a**) Kidney completely mobilized and vessel loos applied without clamping the vessels. (**b**) Tumour dissection along with perirenal fat and (**c**) tumour bed; haemostasis secured using manual compression only. (**d**) Specimen, see attached perirenal fat

ischaemia time (>30 min) is expected [34]. Cold ischaemia (CI) should also be kept as short as possible, ideally within 35 min. The CI technique used includes in situ cold arterial perfusion, the use of ice slush around the kidney, retrograde calyceal perfusion using cold saline or ex situ cold arterial perfusion with autotransplantation depending on preoperative findings, surgical technique (open, laparoscopic or robotic) and institutional experience [15]. In an interesting work reporting a multicentre study of 660 patients treated with warm ($n = 360$) or cold ($n = 300$) ischemic conditions in patients with a solitary kidney, authors noted that in spite of longer ischaemia during PN with cold ischaemia (median, 45 min) than with warm ischaemia (median, 22 min), the decrease in postoperative GFR (21% vs. 22%) and follow-up GFR (10% vs. 9%) was observed, confirming a protective effect of hypothermia [35].

8.2.3 Cell Saver

The kidney is a highly vascular organ, and at any given time, nearly 15% of the effective circulatory volume passes through the kidney. The blood loss during surgery for renal cell carcinoma (RCC) can be significant. Perioperative transfusion rates for partial nephrectomy may be up to 14.8% [36]. Notably, perioperative blood transfusion is an independent risk factor for decreased cancer-specific and overall survival in patients with RCC [37]. Using the Cell Saver system, which involves collection of blood lost during surgery with subsequent autotransfusion of the patient's own cells, has the potential to decrease transfusion requirement during partial nephrectomy. Lyon et al. [38] assessed if Cell Saver transfusion during open partial nephrectomy was associated with inferior outcomes with short-term follow-up, and they found that none of the patients developed metastatic disease. It is one of the first series assessing the safety of Cell Saver during partial open nephrectomy. The data do not support the theory that intraoperative autotransfusion can lead to the rapid development of systemic metastases, and in fact we found no differences in clinical outcome between patients who did and patients who did not receive a Cell Saver transfusion. There are limitations in this retrospective work, and further work is needed to definitively determine whether the use of a Cell Saver system can mitigate the known risks associated with allogenic blood transfusion in patients with RCC.

8.2.4 Access

The standard approach for OPN employs a flank, thoracoabdominal or subcostal incision, based on the surgeon's preference and the anatomy of the mass [39]. The most commonly employed is the flank approach, particularly through the 11th rib supracostal incision. An alternative surgical approach that has been seldom explored for PN is dorsal lumbotomy. In a recent report by Tennyson et al. [40], it was noted to be associated with shorter operative times, shorter hospital stay, lower postoperative narcotic requirements and complication rates comparable. It is important to mobilize the whole kidney, so that other smaller lesions can also be identified. It is important that the prerenal fat overlying the tumour is left intact, as capsular invasion is a common finding. The renal hilum is dissected to allow application of a vascular clamp, even if no arterial clamping is envisaged. Palpation of hilar lymph nodes and para-aortic (left-sided tumours) and paracaval (right-sided cancer) should be done and any suspicious node removed and sent for frozen section.

8.2.5 Drain, Stent and Renorrhaphy

In cases of OPN, Godoy et al. suggested that drain placement might not be necessary in carefully selected patients with superficial tumours that could be removed without opening of the collecting system or after its certain closure when removing a more endophytic mass [41]. In a recent randomized trial, Kriegmair et al. [42] noted that drain placement during open partial nephrectomy can safely be omitted, even in cases with violation of the collecting system. Stents are rarely required except when there is a significant breach of the collecting system. Furthermore, dye injected through the ureter can be used to confirm complete and watertight closure of the collecting system. In case of doubt, a stent may be left in place for a few weeks. Renorrhaphy provides additional haemostasis; specific capillary bleeders should be secured and the collecting system closed. Various materials are used to bridge the renal defect; however, perirenal fat is a readily available, cheap and reliable option. The defect is closed with interrupted 3/0 Vicryl preferably on a Surgicel™ bolster to prevent sutures from cutting through the soft parenchyma. Postoperative measures are important and assessment of patients following PN. About one-fifth have acute kidney injury following PN, in a solitary kidney. However, in majority of cases, it is self-limiting and only 1% require dialysis [43].

Conclusions

Preservation of renal function without compromising the oncological outcome should be the most important goal in the decision-making process. Preoperative evaluation of several parameters, such as control of hypertension, active surveillance to detect early proteinuria and multidisciplinary care with nephrologist, helps optimize renal function after PN. Although duration of ischaemia is the surrogate marker of renal function following PN, the remaining parenchyma is an important predictor.

PN is a technically demanding procedure; however, the advantage over radical nephrectomy for T1a in terms of renal function preservation and prevention of CKD is a valid reason for using PN in most favourably located cancers. The incidence of local recurrence and even enucleation and overall and recurrence-free survival is comparable to RN. The dissection is done in Gerota's fascia; however, peri-tumoural fat is left intact. Arterial clamping when done should limit the WIT to 20 min. In most cases of peripheral small tumours, manual and local compression suffices.

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