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The Role of Nephron-Sparing Surgery (NSS) for Renal Tumours >4 cm

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1. Introduction

For many years, radical nephrectomy (RN) has been the gold standard treatment for renal tumours. However, at present the available evidence supports elective nephron-sparing surgery (NSS) as the standard surgical treatment for renal cortical tumours ≤4 cm (clinical stage T1a). Furthermore, an increasing body of evidence demonstrates that even a minor loss of renal function can increase cardiovascular morbidity and consequently reduce life expectancy (Go et al., 2004). Thus, surgeons have the responsibility to preserve as much renal parenchyma as possible.

International guidelines at present recommend NSS for small renal tumours up to 4 cm. However, the role of NSS for larger renal tumours (stage T1b: 4.1 – 7 cm, stage T2: >7 cm) remains controversial. During the last couple of years, data has emerged which demonstrates that NSS can be safely performed with acceptable complication rates compared to RN (Van Poppel et al., 2010). The advantage of NSS lies in avoiding the development of end-stage renal disease and the need for haemodialysis, while maintaining quality of life (Lesage et al., 2007).

The size of the tumour is no longer considered to be a limiting factor for NSS and some now advocate NSS whenever possible and feasible (Becker et al., 2009).

2. Open partial nephrectomy

2.1 Oncologic control

2.1.1 Positive Surgical Margins (PSM): Incidence, clinical relevance

NSS aims to preserve renal function without lacking its primary goal: eradicate the tumour. One of the challenges of NSS is to achieve negative surgical margins (NSM). It means that there are no cancer cells seen at the outer edge of the resection piece. This is marked with ink.

In general, the incidence of PSM in T1b tumours is between 0 % (Patel et al., 2009) and 16.7% (Lee et al., 2010). Lee showed that the difference in recurrence rate for patients with PSM compared to NSM was not significant.

Coffin et al (Coffin et al., 2011) found that an imperative indication for NSS had an impact on PSM rates (p=0.03). However, he also noticed that the median tumour size was significantly larger in the imperative indication group, compared to the elective indication group (p=0.03).

Publication	TNM	Single vs multi-institution	n=	PSM %
Roos pT1b (J Urol 2010)	pT1b	Single	73	7.6 *
Coffin (2011)	all sizes	Single	155	9.7
Joniau (2008)	pT1b	Single	67	5.8
Porpiglia (2010) World J Urol	pT1b	Multi	63	6.5
Porpiglia (2010) BJU	pT1b	Single	33	0
Patel (2009)	pT1b	Single	15	0
Coffin (2011)	all sizes	Single	155	9.7

* There were 12/158 Positive frozen section, therefore a RN was performed.

Table 1. PSM rates.

Nevertheless, he noticed that tumour size was not a significant predictor of recurrence, while multifocality was associated with recurrence. These findings demonstrate that the clinical impact of PSM is not as important as previously thought. To evaluate the impact of PSM, Bensalah et al. (Bensalah et al., 2010) collected 111 cases with PSM from an international multicentre database. Tumours were stage T1, T2 or T3 without nodal invasion or distant metastasis. He compared those with a population of 664 patients who had NSM at resection: groups were matched for age, indication, tumour size and grade. With comparable follow up (PSM 37 versus NSM 35.4 months), the recurrence rate was higher in PSM group than NSM group (10.1% versus 2.2%). However, Overall Survival (OS) and cancer specific survival (CSS) were not significantly different. He also compared 101 PSM with 102 NSM matched for surgical indication (elective versus imperative), tumour size and Fuhrman grade and also found a higher rate of tumour recurrence (10.9% vs. 2.9%), however OS and CSS were again similar.

Russo (Russo 2010) commented the study of Bensalah (Bensalah 2010): in his experience he has more PSM for small renal tumours than for larger, particularly when they are endophytic.

Yossepowitch (Yossepowitch et al., 2008) analysed a cohort of 1344 patients who had undergone partial nephrectomy: there were 77 cases of PSM. Surprisingly, the larger the tumour, the lower the incidence of PSM was. He could not show an association between PSM and a higher risk of recurrence or metastatic progression.

These observations suggest that the presence of PSM is a risk factor for recurrence but does not impact on OS and CSS. These facts also argue for a closer follow up in the first post-operative years.

Most patients with PSM will not experience local recurrence (Van Poppel et al., 2007). Positive margins detected at frozen section or at final histology should not be considered an indication for RN.

2.1.2 Overall survival, cancer-specific survival, progression free survival

We reviewed 98 patients operated at our institution between 1997 and 2009 for a renal tumour larger than 4 cm. All patients underwent an open partial nephrectomy. Mean diameter was 5.32 cm. At final histopathology, three quarters of the tumours were malignant and 2.7% were staged pT3a. 53.4% of the renal cell cancers (RCC) showed a low grade (Furhman grade 1-2) versus 46.6% high grade (Furhman grade 3-4). The 5–year OS and CSS rates were 77.9% and 98%, respectively. We observed 5 local reccurences (5.1%) and 7 metastatic recurrences (7.1%). (Joniau et al., 2011)

Roos and Brenner (Roos et al., 2010) compared 73 patients who had undergone elective NSS for T1b or greater tumours with a pair-matched cohort of 100 radical nephrectomies: the OS rates were comparable for NSS vs. RN. The 5, 10 and 15-year CSS rates after NSS (95%, 91% and 82%, respectively) were comparable with RN (97%, 95 and 88%, respectively).The 5, 10 and 15-year PFS rate after NSS (89%, 85% and 76%, respectively) were similar to RN (92%, 89% and 77%, respectively). In a retrospective study by Antonelli (Antonelli et al., 2008), there was no significant difference in progression and survival rates between NSS and RN both for tumours ≤ 4 cm as for those >4 cm. Interestingly, even when not significant, the group of patients with the larger tumours treated with radical surgery experienced a progression rate which was double compared to those who underwent NSS. In the same study, when operated by NSS, the patients with a T1a tumours had a higher risk of local recurrence in the operated kidney, as well as in the contralateral kidney. T1b tumours showed a higher risk of metastatic and local recurrence. Cytonuclear grading was correlated with higher risk of recurrence in tumours larger than 4 cm. However, even in large tumours with high cytonuclear grade, the type of surgery had no significant influence on oncologic outcomes: nor on progression rate nor on disease free survival rate at 5 years.

Nemr (Nemr et al., 2007) described similar oncologic outcomes for NSS and RN in T1b renal tumours: Mean follow up was 45 months and there was no significant difference in recurrence free survival with 100% for PN vs. 89.3% for RN.

Margulis (Margulis et al., 2007) retrospectively compared RN (576) with NSS (34) for tumours >4 cm: recurrence occurred in 4 patients (12%) who underwent NSS vs. 164 patients (28.9%) who underwent RN at a median follow-up of 24.2 and 13.2 months, respectively. 5-year RFS was higher for NSS but CSS was similar. 27% of NSS were performed for elective indications; the remainders had solitary kidneys (29%) or chronic kidney disease (CKD) (44%). The indication does not seem to impact 5-year RFS and CSS. However, this was a retrospective comparison of a small group of NSS versus a large group of RN cases, with a selection bias resulting in an imbalance for smaller tumour size and more pT3a in the NSS group compared to the RN group.

Coffin et al (Coffin et al., 2011) tried to determine the impact of an imperative indication for NSS on the oncologic outcomes. The study counted 155 patients who underwent NSS: 96 elective indications and 59 imperative indications. 62.7% (37 patients) with imperative indications were staged pT1B or higher versus 22% (22 patients) with elective indications. NSS was applied whenever possible: the usual limitations were tumour size and location. Imperative cases were associated with lower 5- and 10-year OS rates. Tumour size was also a significant prognostic factor for 5- and 10-year Overall Survival.

Becker (Becker et al., 2006) evaluated the oncologic outcomes of NSS in tumours larger than 4 cm with mean follow up of 6.2 years. There were 10% of deaths but none was cancer related. The Cancer specific survival was 100% after 5, 10 and 15 years. Of the 69 patients, 5.8% experienced disease recurrence. 5-, 10- and 15-year overall survival rates were 94.9%, 86.7% and 86.7%, respectively.

In carefully selected patients with tumours >4 cm, NSS appears to obtain equivalent oncologic outcomes compared to those achieved with RN. Although higher morbidity rates were seen after NSS, the complication type and severity were acceptable.

Publication	TNM	Single vs multi-institution	n=	DFS 5 years %	Local Reccurence %	Distant Metastase %	Median FU months	mean diam cm
Margulis (2007)	pT2-pT3b	single	34	82	0	12	62.1	5.2
Antonelli (2008)	pT1b	Single	52	93	1.9	5.3	54.3	4.8
Roos (J Urol 2010)	pT1b	Single	73	95	1.3	9.6	55.2	5.0
Coffin (2011)	all sizes	Single	155	81.8	*	*	95	3.7
Coffin (2011)	pT1b	Single	59	74	*	*	95	?
Joniau (2008)	pT1b	Single	67	84	4	6	40.2	4.5
Patard (2004)	pT1b	multi	65	93.8	3.6	7.1	51	5.3
Becker (2006)	pT1b	Single	69	100	5.8	5.8	70	5.3
Leibovitch (2004)	pT1b	Single	91	98	5.4	4.4	64	4.9
Hafez (1999)			175	86	0.8	?	47	

Table 2. Oncologic outcomes.

2.2 Complications

2.2.1 Complication rates of NNS vs. RN

Haemorrhage is the most common intra-operative complication (1.2 -4.5%). Post-operative complications are urinary fistula formation (1.4-17%), acute renal failure (0.7-26%), post-operative bleeding (0-4.5%), wound infection (1.2-5.9%), perinephric abscess (0.6-3.2%), chronic renal insufficiency (3.2-12%) and urinary retention (Lesage et al., 2007). Non-urological complications include pulmonary and cardiac complications, and also delirium.

We have recently published results of an uncontrolled and retrospective study of 67 patients who underwent NSS for T1b RCC at our institution. A rate of 3% of post-operative haemorrhage requiring embolization was observed, and none developed a urinary fistula. Four patients (6%) had positive resection margins; none of these developed tumour recurrence. After a median (range) follow-up of 40.1 (1-98.3) months, 10 patients (15%) had died, of whom only one death was related to NSS (postoperative hypovolemic shock). The recurrence rate was 10%: 3 patients (4%) developed a local recurrence and 4 (6%) loco-regional or distant disease but all of these patients were alive at last follow-up (Joniau et al., 2009).

In our recently updated series of 98 open partial nephrectomies for cT1b tumours, two patients died in the peri-operative period, but both had extensive cardiac histories. We encountered 7 post-operative acute kidney haemorrhages: of those, 3 required a reoperation, 2 were embolized and 2 were treated conservatively. There was one urinary fistula which was successfully managed by placing a double–J stent. Thus, major complication rate (Dindo score ≥3) was 9.2%.

Coffin (Coffin et al., 2011) encountered a higher complication rate in NSS compared to RN. Total complication rate was 37.7% (of 69 patients) versus 24.5%, respectively. Rates of pulmonary complications and delirium were comparable in both techniques (9.4% versus 9.6% and 3.1% versus 1.1%, respectively) while cardiac complications were more frequent after RN (20.2% versus 1.5% after NSS). Urinary fistula rate was 5.8%. Transfusion rate was higher in NSS (23.2%) versus RN (13.8%). Spleen damage was not encountered during NSS but occurred three times during RN. Contrary to most studies, NSS did not require surgical revision but one patient was re-operated after a RN. (Roos et al., 2010)

Publication	Approach	Single vs multi-institution	N =	C %	SR %	RN %	CR %	I %	II %	IIIa %	IIIb %	IV %	V
Porpiglia (2010)	Lap	multi	41	7.3	7.3	2.4	26	4.8	7.3	7.3	7.3		0
*Porpiglia (2010)	Lap	one	33	0	6	3	27	9	3	9	6		0
Becker (2006)	open	one	69	-			13			10	3		0
Patel (2009)	Robot	one	15	0	6		26.6	0	6.6	13.2	0	6.6	0
Joniau (2011)	open	one	98	-	3	0	27,5	8.16	11.2	0	5.1	2	1

C= Conversion
SR = Surgical Revision
RN = Radical Nephrectomy
CR = Complication rate
I, II, III, IV, V = Complication rate according to the Dindo-Clavien classification

Table 3. Complication Rate.

NSS has a higher rate of complications, however this remains acceptable. Most complications can be managed in a conservative or minimally invasive fashion and therefore in none of the reports, an impact on the length of hospital stay or the hospital costs was found.

2.2.2 Risk factors for complications

2.2.2.1 Imperative indications

Is there an impact of imperative indications for NSS on peri-operative complications? In a study by Cofin, no significant difference was seen between elective and imperative indications regarding operating time, but the elective group had better surgical outcomes: less blood loss and better control of post-operative creatinin level (Coffin 2011). For oncologic outcomes, Antonelli (Antonelli et al., 2008) found a lower recurrence rate and a higher disease free survival rate at 5 years in elective indications compared with imperative indications.

2.2.2.2 Elderly

Being older than 65 years does not seem to be a significant prognostic factor for having surgical as well as medical complications after partial nephrectomy. The difference was statistically significant for cardiac complications only (Roos et al., 2010).

2.3 Renal function

2.3.1 Renal function deterioration after NSS vs. RN

Acute reduction in functional renal mass leads the remnant glomeruli to maintain the renal function by several mechanisms: adaptive glomerular hypertrophy, hyperperfusion, hypertension and hyperfiltration. These phenomena result in proteinuria.

NSS aims to achieve two goals: a complete excision of the tumour but at the same time guarantee an optimal preservation of renal function. With less excision of healthy renal tissue with NSS, we can expect less glomerulosclerosis and renal failure (Van Poppel et al., 2003). Therefore, NSS seems to be the best way to prevent Chronic Kidney Disease (CKD).

In one of our studies on OPN for T1b renal tumours (Joniau et al., 2009), 10% of patients developed de novo renal insufficiency. Six of those seven patients had imperative indication. Serum creatinin levels dropped significantly in imperative indication, while this was not seen in elective and relative indications.

In our last study of 98 open partial nephrectomies for T1b, estimated Glomerular Filtration Rate (eGFR) deteriorated postoperatively on average by 1.74 ml/min/1.73m².

10.2% of patients developed CKD post-operatively, but 20.4% patients had an improved CKD stage after surgery.

In his study, Roos (Roos & Brenner, 2010) also observed a significant difference in eGFR at last follow up and in e GFR difference (calculated as e GFR preoperative – eGFR at last follow up). After NSS, 14.5% of patients (10) had reached an eGRF < 60ml/min/1.73m² versus 44.7% (42) after RN.

In a retrospective study (Lane et al., 2010) Lane studied 2402 patients with a normal preoperative kidney function (serum creatinin less or equal to 1.4 mg/dl) and compared: 1833 PN versus 569 RN. Tumour stage was pT1b or more in 31% of PN and 64% of RN. NSS even - with a warm ischemia time of longer than 31 minutes - demonstrated better renal outcomes, however patients in the RN group were older, had more co-morbidities and were affected by larger and more aggressive tumours.

A solitary kidney is not a contra-indication for NSS. Lee (Lee 2010) reports 38 patients with solitary kidney who underwent partial nephrectomy: 53. 1% of them had a tumour larger than 4 cm and 76.3 % had post operatively a GFR more than 30 ml/min/1.73m². He noticed an acceptable complication rate: 7.9% Clavien I, 18.4% for Clavien II and 5.3% Clavien III. One patient required immediate post-operative haemodialysis and another one long term haemodialysis for a mean follow up of 20 months.

Partial nephrectomy offers minimal reduction of renal function, but on the other hand unfortunately exposes the patient to higher peri-operative risk.

2.3.2 Surgical aspects influencing renal function preservation

For small tumours, clamping the renal artery is sometimes not necessary. Resection without clamping can provide adequate oncologic surgery with a lower peri-operative complication rate and limited renal function deterioration. In the case of larger renal tumours, surgery requires in most cases an interruption of renal blood flow through pedicle clamping.

Clamping is necessary to resect the tumour in a bloodless field, to minimise intra-operative blood loss, to contribute to a better vision during dissection and to facilitate renorraphy. Ischemia induces endothelial lesions which lead via multi-inflammatory response to vasoconstriction and vasospasms and thus ischemia. The low renal blood flow induces renal cell lesions and subsequent release of angiotensin II and eicosanoids. During ischemia, there is a failure of oxidative phosphorylation and depletion in adenosine triphosphate (ATP). It causes cellular swelling by passive diffusion of water into cells. Cell swelling prevents reperfusion when unclamping (no reflow phenomenon) and ATP degradation produces free radicals which cause further cell damage (reperfusion injury).

2.3.2.1 Impact of clamping time

For warm ischemia, maximal clamping time to preserve renal function was previously thought to be less than 31 minutes. Later it was suggested to try to limit warm ischemia time to less than 20 minutes (Becker et al., 2009). But Thompson goes further and states that "every minute counts". In his retrospective study, he analysed 362 patients with solitary kidneys and demonstrated that 25 minutes is the best cut-off for clamping time to make the distinction of patients at risk for acute renal failure, a GFR < 15ml /min per 1.73 m^2 and new-onset stage IV chronic kidney disease during follow up. Each additional minute increased this risk. The same cut off for irreversible renal damage was found in a prospective study (Funahashi 2009).

Thus we should consider 20-25 minutes to be the best cut-off to avoid adverse renal consequences, keeping in mind the shorter the clamping time the better. We should not forget that even with extended ischemia, partial nephrectomy still offers better renal function outcomes compared to RN (Lane et al., 2010).

2.3.2.2 Impact of clamping technique

Regarding clamping technique, Coffin did not observed a difference in postoperative renal function between mechanical and digital clamping of the pedicle.

There is no consensus for type of clamping: arterial or "en bloc" arterial and venous clamping. It is also not known whether intermittent clamping is better than continuous.

2.3.2.3 Cooling

Kidney cooling prior to clamping can prevent cell damage. The optimal temperature to achieve this seems to be 15°C (Becker 2009).

When ischemia time is estimated to be probably more than 25 minutes, cold ischemia is a good option. The principle is to cool the kidney with ice slush for 10 minutes, after which the hilum should be clamped. Nevertheless, also cold ischemia time must be limited to the minimum. A maximum of 35 minutes has been proposed by several authors (Thompson et al 2007).

2.3.2.4 Pharmacologic strategies

In order to reduce the impact of ischemia, it is advised to provide preoperative hydration to facilitate renal perfusion and stimulate urine production. Therefore, furosemide administered intra-operatively is useful. Intravenous mannitol at a dose of 1 ml/kg has also been proven to be beneficial for optimal reperfusion (Becker et al., 2006). Weizer and his

Fig. 1. Cooling.

team use the following schema: 12,5 g mannitol are administered ten minutes before resection and the same additional dose is given at removal of the clamp (Weizer et al., 2011). The use of an angiotensin-converting enzyme inhibitor such as enalapril has also been proposed. This should theoretically prevent vasospasm and induce vasodilatation. To prevent thrombosis, administration of heparin intravenously has been proposed but its benefit has not been proved.

Other important points are to maintain a normal blood pressure and hemodynamic stability in the peri-operative and postoperative period.

3. Alternative surgical techniques

3.1 Simple enucleation

3.1.1 Definition, surgical technique

Urologic surgeons are increasingly proposing careful, pure enucleation consisting of an incision of the renal parenchyma within a few millimetres of the tumour, followed by a blunt dissection following a plane between the pseudo-capsule and the healthy renal parenchyma, thereby minimizing loss of nephrons.

Fig. 2. Enucleation.

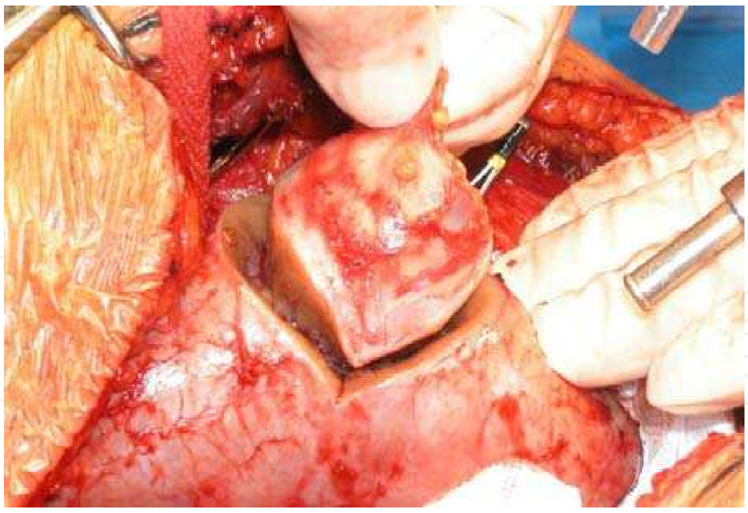

Fig. 3. Wedge Resection.

3.1.2 Simple enucleation versus standard partial nephrectomy

3.1.2.1 Positive surgical margin rate

Minervini (Minervini et al., 2011) retrospectively analysed 1519 patients operated for renal cell carcinoma to determine the impact of simple enucleation on oncologic outcomes: 982 underwent a standard partial nephrectomy versus simple enucleation in 537 cases. 25.9% of patients belonging to the standard partial nephrectomy group versus 21.3% of patients in the simple enucleation group had a renal cell carcinoma larger than 4 cm. PSM rate was significantly lower in the simple enucleation group (0.2%) versus the standard partial nephrectomy group (3.4%) ($p<0.001$).

3.1.2.2 Cancer-specific survival rate

For tumours smaller than 4 cm, pure enucleation provides long-term cancer-specific survival rates similar to RN and is not associated with a greater risk of local recurrence compared to partial nephrectomy (Carini 2006). Minervini (Minervini 2011) compared standard partial nephrectomy with simple enucleation: he could not find any significant difference between those 2 techniques after adjusting for cancer-specific survival probabilities: age at surgery (younger or older than 65 years), tumour stage (pT1a, pT1b or pT3a) and Fuhrman nuclear grades (1-2 versus 3). Patients who underwent a simple enucleation and had a Fuhrman nuclear grade 4 showed a significantly worse cancer-specific survival compared to patients who were treated with standard partial nephrectomy.

In another publication (Carini et al., 2006), Carini and Minervini reviewed 71 simple enucleations for renal cell carcinoma with diameter 4 to 7 cm. Median follow up was 74 months. There was no peri-operative mortality and no major complications requiring reintervention. Oncologic outcomes were acceptable: 5- and 8-year cancer-specific survival rates were 85.1% and 81.6%, respectively. Tumour stage had an impact on cancer-specific survival: 5-year cancer-specific survival rate was 95.1% for tumours of 4 cm, 83.3% for stage pT1b and 58.3% for stage pT3a tumours. He reported 10 patients (14.1%) with progressive disease but only 4.2% with local recurrence.

Simple enucleation can be performed for tumours larger than 4 cm. Long-term outcomes are comparable to standard NSS.

3.2 Laparoscopic partial nephrectomy

Laparoscopic partial nephrectomy (LPN) offers the benefits of a minimal invasive approach together with the benefits of preserving renal function.

3.2.1 Surgical aspects

3.2.1.1 Transperitoneal versus retroperitoneal approach

62% of the tumours were operated transperitoneally in the study of Patel (Patel et al., 2010). Porpiglia (Popiglia et al., 2010) observed a higher rate of the transperitoneal approach for tumors larger than 4 cm, with no higher rate of conversion to open surgery.

3.2.1.2 Resection technique

Most surgeons performing laparoscopic NSS prefer an enucleo- resection: excision of the tumour with a thin layer peritumoral healthy parenchyma (Porpiglia et al., 2010). In several studies, a laparoscopic ultrasound probe was used to identify the lesion intraoperatively (Porpiglia et al., 2010; Patel et al., 2010), even when it concerned large renal tumours (> 4 cm).

3.2.1.3 Impact of clamping technique and time on renal function

In all the centres of the study by Porpiglia, the renal artery was clamped alone (Porpiglia et al., 2010).

Patel described clamping of both, the artery and the vein in case of large, endophytic and central tumors. On the other hand, the artery alone is clamped for small, peripheral or cortical tumors (Patel et al., 2010).

To prevent vascular injury, bulldog clamps are preferred to a Satinsky clamp, even though the true benefit of this approach remains to be proven (Weizer et al., 2011). Some surgeons use vessel loops with a hem-o–lock as clamp in order to prevent pedicle lesions.

To prevent renal function loss, Shao (Shao et al, 2011) proposed another technique consisting in selective clamping of the feeding segmental renal artery. This technique demands a larger dissection to expose 2-3 arterial branches for selective clamping. The demarcation line of the parenchymal ischemia is observed to ensure the resection area is clamped. In case the ischemic area does not encompass the tumour, multiple segmental arteries are clamped. Patients with tumours larger than 4 cm were included if their resection was estimated feasible. There were 11 cT1b tumours operated: respectively 5 operated with main renal artery clamping and 6 with selective clamping. Of, the latter group, half of them had to be converted to main renal artery clamping. There was a significant increase in operative time, blood loss and warm ischemia time in the selective clamping. 3 months post-operatively, GFR was estimated with a camera-based method measuring the renal uptake of technetium 99m diethylenetriamine-pentaacetic acid. The GFR reduction of the affected side was significantly less with selective clamping. Half of the tumours larger than 3.5 cm tumours required clamping of 2 or more segmental arteries. Complication rate was acceptable. This technique seems not really appropriate for large tumours given the high conversion rate.

A critique to the laparoscopic approach remains that ischemia time is usually longer than in open procedure. In a European survey (Porpiglia et al., 2010), mean warm ischemia time was 25.7 minutes with a range 15-46 minutes. Cooling techniques in laparoscopy are time consuming. Clamping usually lasts from the beginning of the resection to the end of parenchymal suture. In order to reduce warm ischemia time, Nguyen (Nguyen et al., 2008) proposed to remove the clamp after the first layer of parenchymal suture. The remaining renorrhaphy is thus performed in the revascularized kidney. This technique decreases warm ischemia time by over 50%. There was a trend towards improved outcomes: less overall complications (16% vs. 22%), less postoperative renal haemorrhage (2% vs. 4%) and a decreased re-intervention rate (6% vs. 16%). However, those differences were not statistically significant. No patient had a positive resection margin, required open conversion or showed renal dysfunction.

3.2.1.4 Impact of parenchymal suture on renal function

The goal of efficient renorraphy is to reduce warm ischemia time. The type of suture (running of interrupted) is not correlated with longer warm ischemia time.

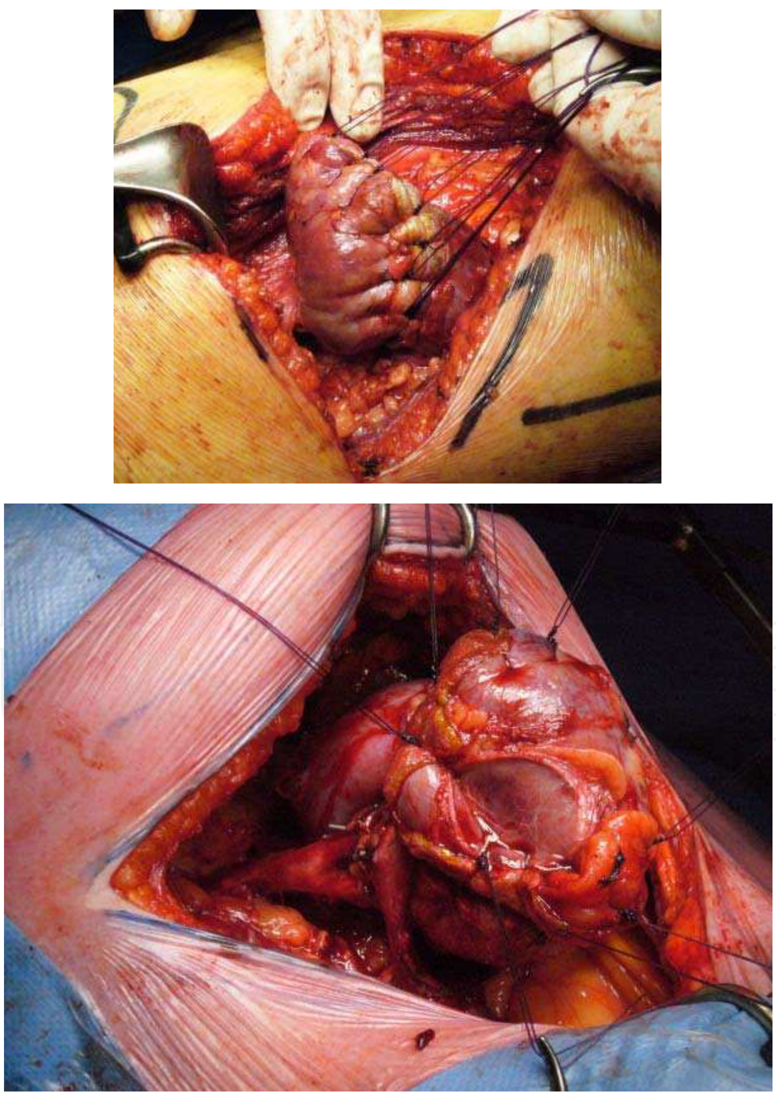

Fig. 4-5. Examples of interrupted suture in open surgery.

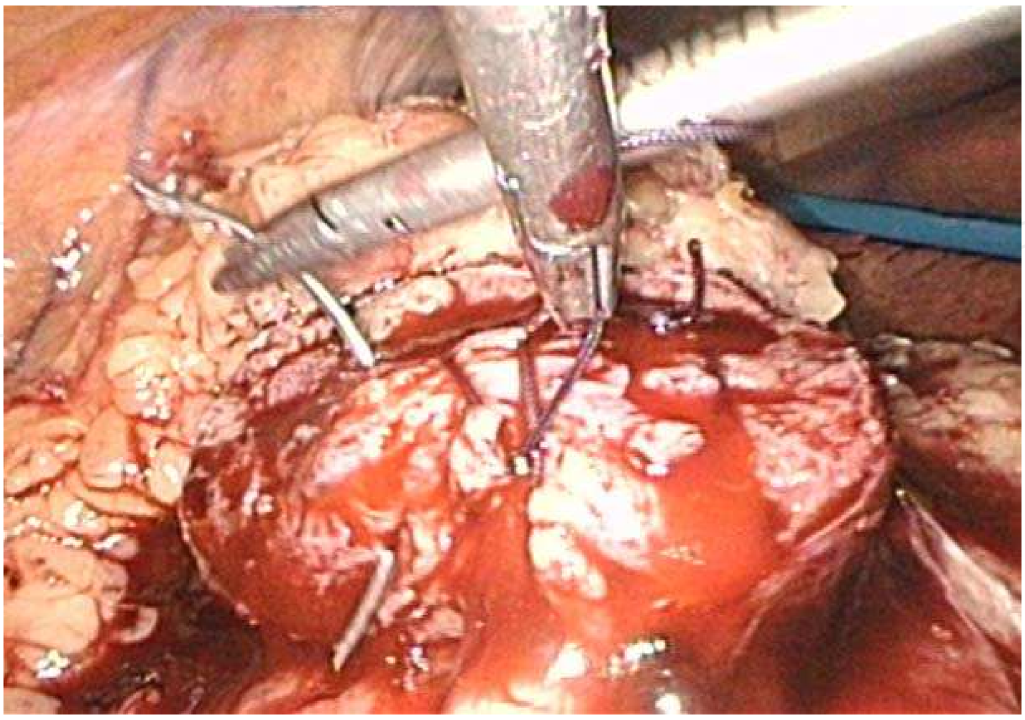

Fig. 6. Laparoscopic running suture.

Likewise, the use of haemostatic sealant had no significant impact on warm ischemia time (Porpiglia et al., 2010).

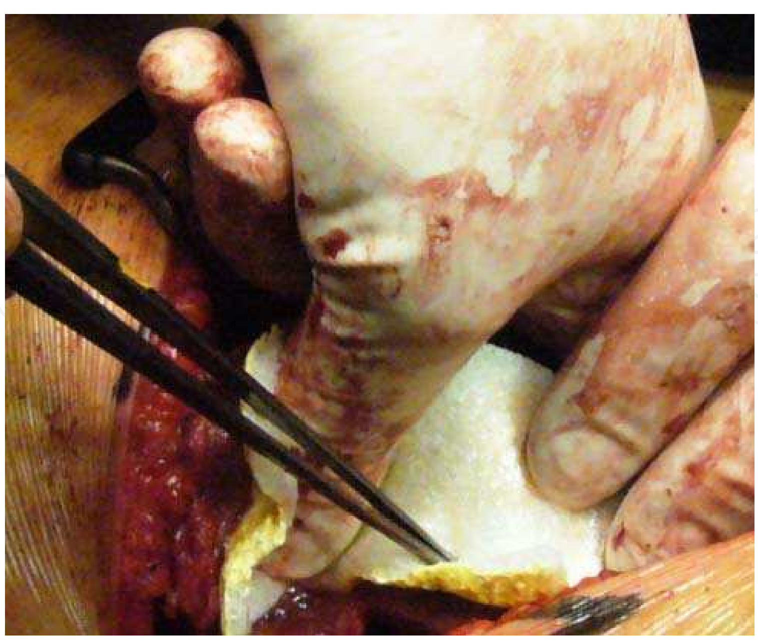

Fig. 7. Hemostatic sealant application.

Fig. 8. Tumor bed after hemostatic sealant application.

3.2.2 Complications: Open versus Laparoscopy

Open NSS is well established in T1a tumours and is becoming increasingly accepted in T1b tumours. In the last few years, a tendency to apply a laparoscopic approach for T1a renal tumours has been observed. In some centres this is already the standard of care. Indeed, in experienced hands, the laparoscopic approach achieves intermediate-term oncological and renal function outcomes comparable to open surgery.

In a multicenter study (Porpiglia et al., 2010), 63 patients underwent a laparoscopic partial nephrectomy by enucleo-resection with intraoperative ultrasound. The conversion rate was 7.3%: always for bleeding but without requiring RN. Postoperative complication rate was 26%: acute hemorrhage, urinary fistula, fever, chyluria and retroperitoneal hematoma. Acute hemorrhage was the most frequent (9.7%). Half of them were treated with embolization, the other half with reoperation. One patient required a RN. Urinary fistulas (4.4%) required a double J placement and one patient necessitated a re-operation. 6.5% of patients had PSM. There was no correlation between PSM status and tumour size or location.

3.2.3 Impact of tumour size

3.2.3.1 Impact of tumour size on peri-operative and post-operative complications

Porpiglia (Porpiglia et al., 2010) reviewed 100 consecutive laparoscopic partial nephrectomies. A third of these procedures concerned tumours larger than 4 cm. Intraoperatively, the latter required more often a transperitoneal approach and pelvicalyceal repair. Also, warm ischemia time was longer and they were associated with greater blood loss, however no significant bleeding or conversion occurred. Complication rates were similar in the small versus large tumour groups respectively: fever (6% vs. 3%), acute hemorrhage (4.5% vs. 15.1%, p=0.06), retroperitoneal hematoma (1.5% vs. 6%). One case of pneumonia was seen in the small tumour group and one urinary fistula in large tumours group.

The sole significant risk factor for overall complications was the cortico-medullar location of the tumour (Porpiglia et al., 2010).

3.2.3.2 Impact of tumour size on renal function

In the same study of Porpiglia (Porpiglia et al., 2010), small and large tumours groups had comparable preoperative serum creatinin and estimated GFR. On the 5th post-operative day, elevation of serum creatinin level was not significantly higher in the large tumour group, but deterioration of eGFR was statistically significant ($p > 0.004$).

The size of the tumour had no significant impact on the warm ischemia time (Porpiglia et al., 2010).

In large tumours, they recorded 4 cases (12%) with CKD progression, but these could not be explained by a longer warm ischemia time.

3.2.3.3 Impact of tumour size on oncologic outcome

Comparable to Russo in open partial nephrectomy, Porpiglia (Porpiglia et al., 2010) had a higher PSM rate in small tumours. Thus it appears that, as seen in open NSS, tumour size does not impact on PSM risk in the laparoscopic approach.

3.3 Robot-assisted laparoscopic partial nephrectomy

Laparoscopy causes less morbidity than a flank incision. Robotic assistance is useful for suturing and tying (Weizer et al., 2011). This technique combines the minimally invasive approach of laparoscopy with the freedom of movement and dexterity acquired with the robot. Preliminary results with robotic NSS are comparable to results obtained with LPN (Van Poppel, 2010). With similar oncologic outcomes, the robotic approach seems to have a shorter learning curve compared to laparoscopic approach. It offers other benefits: lower intra-operative blood loss, reduced hospital stay and shorter warm ischemia time (Benway et al., 2010).

3.3.1 Surgical aspects

3.3.1.1 Retroperitoneal or transperitoneal approach

The retroperitoneal access has the advantage of reducing the risk of intraperitoneal urine leak, intestinal lesions and future adhesions. Robot-assisted Retroperitoneal Partial Nephrectomy (RRPN) is indicated for posterior, interpolar or lower pole tumours. Morbid obesity and previous intra-abdominal surgery are no contra-indications. One major disadvantage of the retroperitoneal approach is the smaller working space, requiring a good coordination and more help from the assistant. Weizer (Weizer et al., 2011) described 2 conversions in 16 RRPN : one to conventional laparoscopy (difficulty of positioning robot's arms) and one to a transperitoneal approach because of peritoneal perforation. Six complications occurred: musculo-skeletal pain in one, 2 pneumonias, one urinary retention, one urinary fistula, one atrial fibrillation. In this study, all tumours were smaller than 3.5 cm. A retroperitoneal approach does not seem indicated for T1b tumours. The transperitoneal approach is preferred for tumours larger than 4 cm and upper pole tumours.

3.3.2 Complications in Robot assisted laparoscopic partial nephrectomy

The complication rate in a series of 183 Robot-assisted Partial Nephrectomy (RAPN) was 9.8%: 8.2% were major complications and 1.6% minor (Benway et al., 2010).

3.3.3 Impact of tumour size

Patel (Patel et al., 2010) described 71 transperitoneal robotic partial nephrectomies. On preoperative imaging, 15 were larger than 4 cm.

Peri-operatively, warm ischemia time was significantly longer in larger tumours. (p=0.011). He noted no intra-operative complications. The other peri-operative parameters: operative time, need to repair the collecting system, estimated blood loss, elective conversions were not significantly different between the smaller and the larger tumour groups. Post-operative complication rate was similar. There were also no differences in post-operative variables: length of stay and change of haemoglobine. Tumour size between 4 and 7.9 cm was not a risk factor for increased peri- and post-operative complications in patients undergoing robotic partial nephrectomy.

3.3.4 PSM

Benway (Benway et al., 2010) compared 118 LPN and 129 RAPN: the PSM rates were 0.8% and 3.9%, respectively. The PSM rate was higher in RAPN, however this was not significant (p=0.11). Wang (Wang & Bhayani, 2010) reviewed 100 LPN versus 100 RAPN and also noted no significant differences in PSM rate. Benway (Benway et al., 2010), in a review of 183 RAPN, described 3.8% PSM. Gill (Gill et al., 2007) reported a PSM rate of 2.85% in LPN versus 1.26% in open procedures. Kural (Kural et al., 2009) reported no PSM but his study contained only 10 RAPN. On his 71 RAPN, Patel (Patel et al., 2010) had no PSM in 15 tumours larger than 4 cm and 3 PSM on 56 smaller tumours. To our knowledge, no study showed an increased PSM rate in tumours measuring between 4 and 7 cm.

3.3.5 Renal function

Having a tumour larger than 4 cm was not significantly predictive of an increased risk of kidney function loss at the first post- operative day or at 1-3 month follow-up. However, only 9 tumours larger than 4 cm and 28 smaller tumours were included (Patel et al., 2010)

3.3.6 Oncologic outcomes

Robot-assisted partial nephrectomy is still a young technique. Follow up is yet too limited to evaluate recurrence-free survival and cancer-specific survival rates.

4. Conclusion

Our latest study showed excellent surgical feasibility and cancer-specific survival for NSS in T1b RCC (Joniau et al., 2008). Local cancer control was achieved in the large majority of patients, with preservation of renal function in those with elective indications. NSS is at present the gold standard treatment for renal tumours less than 4 cm. Other studies confirmed the feasibility of NSS for tumours of 4 to 7 cm, achieving good oncologic outcomes and preserving kidney function.

The presence of PSM seemed to not have an impact on survival.

Warm ischemia time (WIT) remains a key point. It has to be reduced or avoided as much as possible. If the procedure is suspected to be laborious and WIT lasts more than 25 min, several techniques are useful to help preserve renal function: use of mannitol, cooling …

A laparoscopic approach avoids a painful flank incision but is associated with a longer WIT. Robot assistance joins the minimally invasiveness of the laparoscopic approach with the dexterity of the open NSS. We need longer follow-up before final conclusions can be drawn on oncologic outcomes and renal function preservation of robot-assisted NSS.

In the future, NSS is going to be used for an increasing number of indications. Tumor size does not seems to be a limiting factor anymore. Becker (Becker et al., 2011) already showed the feasibility of NSS even for tumours larger than 7 cm.

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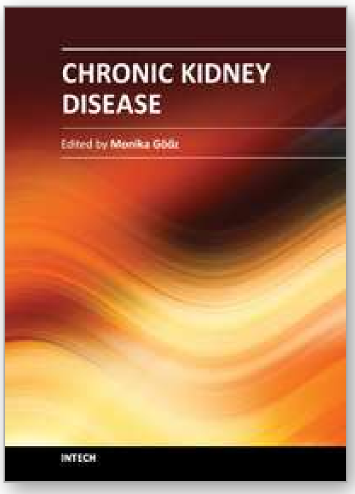

Chronic Kidney Disease
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Chronic kidney disease is an increasing health and economical problem in our world. Obesity and diabetes mellitus, the two most common cause of CKD, are becoming epidemic in our societies. Education on healthy lifestyle and diet is becoming more and more important for reducing the number of type 2 diabetics and patients with hypertension. Education of our patients is also crucial for successful maintenance therapy. There are, however, certain other factors leading to CKD, for instance the genetic predisposition in the case of polycystic kidney disease or type 1 diabetes, where education alone is not enough.