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Chapter 17

Endoscopy in Renal Cancer Organ Preservation Treatments

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Additional information is available at the end of the chapter

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Abstract

This chapter traces the shift in treatment of localised renal cancer from major open surgery to endoscopic (ie laparoscopy) techniques. It also details the shift in treatment intent for localised Renal cancer toward Organ preservation. With advancement in technology and experience, the principles of endoscopic surgery have been adapted to treat renal malignancy with minimum complications and with maximal preservation of Renal function so much so that endoscopic techniques are seen as the "gold standard" by many. The chapter details these minimally invasive techniques of laparoscopic and Robotic partial nephrectomy and compares and contrasts both Oncological and Functional outcomes from both.

Keywords: Renal Cancer, Prostate cancer, Minimally invasive Surgery, Focal therapy, Partial Nephrectomy

1. Introduction

Urology is rapidly becoming a speciality where operative treatment of disease is primarily endoscopically administered The two last bastions of open surgical procedures in urology were reconstruction and radical surgical treatment of malignancy. In uro-oncology and in intra-abdominal reconstructive procedures such as Pelvi-Ureteric Junction (PUJ) obstruction, minimally invasive techniques are rapidly becoming the norm and indeed the debate is about which endoscopic technique results in the best outcomes [1]. From being the standard, open techniques are now limited to the worst locally advanced malignancies or revision recon-

structive procedures. This review will chart the course of endoscopy in the treatment of localised RCC and especially in the era where organ preservation techniques have become paramount.

2. From open to Laparoscopic Radical Nephrectomy (LRN)

Perhaps the area which best illustrates this shift in emphasis in uro-oncology from open procedures to endoscopy is the treatment of localised Renal Cell Cancer. Robson et al. demonstrated improved survival established using open Radical Nephrectomy (all tissue within Gerotas fascia and ipsilateral adrenal and nodal tissue), and the technique became the gold standard treatment for localised renal cell cancer (T1–T2, see table 1 [2]. For about two decades, this remained the case, but there were concerns regarding complication rates and increased patient dissatisfaction, especially with flank incisions. An illustrative example of the latter is Chatterjee's work from 2004, which showed a 50% dissatisfaction rating vis-à-vis flank bulging and approximately 25% with ongoing wound pain [3].

In the early 1990's, the first laparoscopic procedures on the kidney were performed [4]. As experience with the technique grew and with favourable reports, it became the preferred choice. By mid to late 2000s, laparoscopic nephrectomy was the new gold standard after numerous studies demonstrated equivalent oncological outcomes in addition to enhanced patient experience. An example is the case-controlled study of Dunn et al. wherein equivalent short-term oncological outcomes were demonstrated in a comparative study of open and laparoscopic nephrectomy.

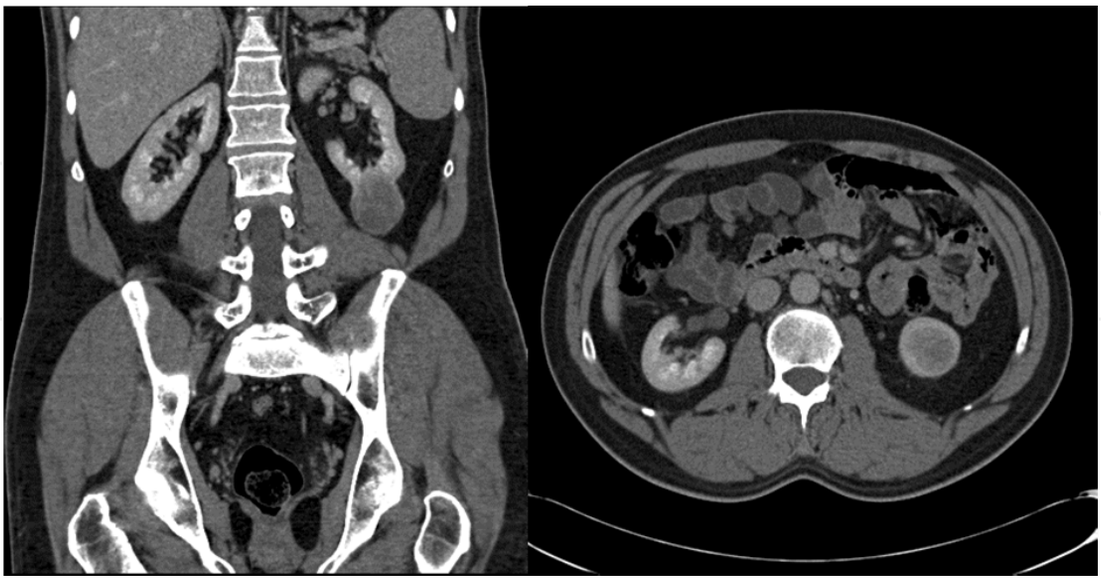

Figure 1. Two slices from a CT series to show a lesion treatable by partial nephrectomy (PN). This is a predominantly exophytic and polar lesion but it does cross the lower sinus line and probably involves the collecting system, thus making it a more complicated lesion than at first appearance.

However, laparoscopic nephrectomy was associated with more than a 50% reduction in blood loss, analgesic requirement, hospital stay and time to return to normal activities [5]. This low complication rate (eg bleeding rate of 2.8% and transfusion rate of 0.7%) was confirmed by a 2006 meta-analysis. The conversion rate was 2.5% and colonic injury was 1.5% [6]. This difference persists to the present day with Xu et al. showing a significant reduction in Claivan grade 2 complications, a 36% reduction in all complications and a 17% reduction in length of hospital stay [7]. Luo`s study published in 2010 confirmed the long-term oncological equivalence [8].

	Primary lesion
TX	Not assessable
T1a	0–4 cm diameter, limited to kidney
T1b	4–7 cm, limited to kidney
T2a	7–10 cm, limited to kidney
T2b	> 10 cm, limited to kidney.
T3a	Renal vein or segmental branch invasion Peri-renal / Renal sinus invasion confined to gerotas fascia
T3b	Invasion of IVC below diaphragm
T3c	Invasion of IVC above diaphragm Direct IVC wall invasion
T4	Invasion beyond Gerotas fascia Direct invasion of Ipsilateral Adrenal
	Regional Nodes
NX	Not assessed
N0	None
N1	Single node involved
N2	> single node involved
	Metastatic disease
M0	None
M1	Present

Table 1. TNM staging of Renal Cell Cancer (2009) – EAU Guidelines [9]

3. Organ preservation

As laparoscopic nephrectomy was becoming more widely practiced, two separate trends conspired against this endoscopic technique. The first was a stage migration of renal masses

(i.e. presumed cancers) downward, which coincided with an increased incidence secondary to incidentally imaging (US and CT) detected lesions [10-11]. Allied to this was the increased identification of benign pathology in nephrectomy specimens performed for these small masses, which approached 20% in some series.

The second was an increasing realisation that the adverse effect of radical nephrectomy on renal function may result in reduced survival because of an association with cardiac mortality. Go et al. published a sentinel paper in the NEJM, which followed 120,295 adults over five years. Increased mortality, increased risk of vascular and cardiac disease and hospitalisations were significantly more common in those with chronic renal impairment (e GFR < 60 ml/min/ 1.73 m2) [12]. It was well documented that radical nephrectomy was associated with the development of renal failure. In 2006, Huang et al. demonstrated a reduction in the probability of developing new renal failure from 65% to 20% by the use of Nephron sparing Surgery (NSS) [13].

Studies like the above lead to an increasing search for alternatives to RN for T1a (< 4 cm) and T1b RCC (< 7 cm). NSS was the most extensively researched and in time has become a gold standard, especially for T1a lesions. It also led to the introduction of ablative technologies such as cryotherapy, HIFU (High-Intensity Focused Ultrasound) and RFA (Radio Frequency Ablation).

Partial Nephrectomy (table 2-3)

The aim of partial nephrectomy is the complete removal of the detected lesion with a margin of normal tissue of as little as 1 mm and as little damage to the remaining renal tissue as possible. Confirmation of a negative margin often requires frozen section analysis of the specimen. The initial indications for partial nephrectomy were tumours in a solitary kidney, multiple/ bilateral tumors or patients with poor renal function (table 3).

T stage	Recommendation
T 1a	Partial Nephrectomy (PN) is the preferred option
T 1b	Radical Nephrectomy (RN) or PN
T2	Radical Nephrectomy Partial Nephrectomy is associated with greater chance of local failure

Table 2. Accepted indications for PN

Absolute	**Lesions in a single Kidney** **Bilateral synchronous lesions** **T1a lesions with low PADUA scores (see page 6)**
Relative	T1b /T2 lesions with a normal contra-lateral Kidney but significant potential of future renal failure due to comorbidities Hereditary RCC
Elective	T1/ T2 lesion; other kidney normal, no "reno-toxic" comorbidity

Table 3. EAU guidelines for surgical treatment of localised Renal Cell Cancer (RCC) [9]

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Traditionally, this involved dissection of the renal pedicle and subsequent clamping of the renal artery (± renal vein). This results in reduced blood loss and a reduced tissue tension, which makes dissection easier and improves visualisation. The perirenal fat is removed from the relevant area apart from directly over the lesion. The lesion is excised and the collecting system repaired. The kidney is then repaired and when done so satisfactorily, the clamp is removed.

Unfortunately, clamping is associated with ischaemia, which led to techniques to reduce the effects of ischaemia, and the concept of hypothermia following preconditioning prior to clamping with mannitol was introduced. The purported effect of mannitol is as promoter of renal vasodilation, thus promoting blood flow. It also prevents cast formation and decreases post-ischaemic swelling [14]. Hypothermia aims to get the renal core temperature to 15–20^{0}C and is achieved by cooling with ice slush for 10–15 minutes post clamping. This slows metabolism down to minimise the effects of ischaemia.

Initially this was thought to be possible only using open techniques, which meant a reduction in laparoscopic renal cancer procedures, although this tended to be mainly driven by academic centres. With time, the use of PN spread and Kim et al. using a US nationwide dataset showed the percentage of small renal masses treated by RN fell from 85% to 75% in the period from 2002 until 2008 [15].

The initial studies confirmed that OPN produces equivalent oncological outcomes compared to RN. Lau et al. showed equal cancer-specific survivals for both groups and metastatic disease in less than 5% of both RN and OPN groups in the case-controlled study of 164 patients in each group [16]. Similarly, Tan et al. showed excellent long-term cancer-specific survival again comparable to RN. Using the SEER database, they compared outcomes for 1925 PN against 5213 RN and showed similar RCC mortality from both PN (1.9%) and RN (4.3%) [17].

A significant proportion of the early debate in OPN focused on the question of the determinants of local recurrence and the potential effect on survival. One such risk is a positive surgical margin and Yossepowitch estimated that to happen in 2–8% of OPN [18]. Thankfully, this does not appear to have a survival impact, judging by the review of Van Popell and Joniou [19]. They have suggested that a 1 mm clear margin is enough to prevent local recurrence. An alternative technique practiced by some is lesional enucleation. This would be expected to be associated with greater local failure, but from the study of Minnervi et al., this would appear not to be the case [20]. Similarly, good oncological outcomes are achieved where PN is performed for lesions up to 7 cm [21].

Much of the early work on partial nephrectomy was done by the Cleveland Clinic group, especially by Novick and Gill. Some of their initial work confirmed the hypothesis that LRN was associated with significantly worse renal function (as measured by serum creatinine) at follow up albeit with reduced peri-operative complications in terms of bleeding, analgesia requirement and hospital stay. However, the two groups were not well matched as the LN group were significantly older, of greater comorbidity (as judged by ASA score) and had larger masses [22]. By the time Lesage`s review paper came out in 2007, the gap had narrowed and the complication rates were not significantly different, although there was a trend towards

greater complications in the OPN groups. Importantly, the significantly increased risk of renal failure with RN compared to PN was confirmed [23]. Up to 22% of LRN patients had insufficiency at 10 years compared to at most 11.6% of the OPN group [16].

There are three factors, which contribute to renal function loss post any renal surgical intervention. These are pre-operative renal function (including comorbidity affecting renal function), the volume of excised/ damaged renal tissue and any intraoperative surgical ischaemia (be this warm or cold ischaemia). Of these, it is the ischaemia time which is the only variable open to surgical control. Warm ischaemia time (WIT) is defined as the length of time the blood supply is cut off or reduced at body temperature. Essentially, this equates to clamping time. Cold ischaemia time (CIT) is the time between when a tissue is cooled, has its blood supply reduced or cut off and is then re-warmed to body temperature [24].

It was because of the absolute centrality of clamping (and therefore a resultant ischaemic insult) to PN that the pendulum swung back to open surgery. This was the case even in centres that were pioneers in the field of PN and laparoscopic urology. IS Gill in an editorial in December 2012 stated of his time working with Dr. Novick at the Cleveland Clinic that *"never did we even discuss the possibility of doing major PN surgery without clamping the main renal artery" [25].*

As experience with PN grew and it became clear that PN was associated with superior functional and equivalent oncological outcomes, research shifted to focus on what if any was the limit of WIT and on methods to reduce ischaemic time. It is worth noting the primary tasks, which have to be completed during this time. These are removal of the lesion with a negative margin. The second is the repair of any collecting system injury, which may be checked by intravenous administration of indigo carmine and thirdly, the closure of the kidney using continuous sutures and adjunct measures. As can be imagined, the more complicated the lesion (larger, centrally placed or single kidney), the longer each step took, and hence, a greater potential for ischaemic injury.

The early animal and clinical studies suggested that 20 minutes of WIT and 120 min of CIT was the safe threshold above which irreversible renal damage was done [26]. This was not universally accepted and others argued that a WIT of up to 30 minutes was acceptable [27]. An elegant combined functional (MAG 3nuclear scan) and anatomical study (CT) from Japan would appear to suggest that the ideal time is around 25 minutes. In this study, Funahashi et al. used functional data from a MAG 3 study to show a net 25% drop in uptake at one week and more crucially that this drop had not recovered by six months. Importantly, the decreased uptake was globally seen and not limited to or concentrated on the operated site [28]. Becker et al. detail an excellent review on the topic of renal ischaemia in partial nephrectomy, which is worth reading as it details the pathophysiology, etc. Basically, the insult comes from a reperfusion injury brought on by free radical release, which, in turn, were formed by adenosine triphosphate breakdown due to vascular endothelial damage. It would also appear that, given that modern OPN is associated with WIT usually below 30 minutes, that there may be no benefit from cold ischaemia or indeed from mannitol. Where used, cold ischaemia is delivered using surface ice slush usually but can also be delivered using a retrogradely placed ureteric catheter or rarely by direct canulation of the renal artery [27].

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Given this benchmark WIT of 20–25 minutes, it became crucial that techniques were developed to minimise WIT. The techniques considered were early unclamping, selective clamping or in select cases, control of the artery and vein with manual clamping of the hilum if necessary. This led to an upsurge in laparoscopic partial nephrectomy as the biggest fear amongst those offering LPN was to what extent the prolonged WIT of the early LPN experience had on renal outcomes. In a laparoscopic partial nephrectomy, there are three key steps. The first is lesion excision followed by accurate closure of the tumour bed and collecting system using two layers of interrupted sutures and thirdly, closure of the renal parenchyma. It is the latter that takes most time. Early unclamping is removal of the clamp once the lesion is excised and any repair required to the collecting system is finished. Any bleeding from the tumour bed can be controlled with separate sutures at that time. Nguyen and Gill dropped their WIT from a mean of 31.9 minutes to 13.9 minutes by this simple measure in a series of 100 consecutive LPN. There were more complications in the early unclamping group but this did not reach significance [29]. Similarly, a group from Europe in a cohort of 40 LPN demonstrated an equally impressive reduction in WIT from a mean of 27.2 minutes (± 5) to 13.7 (± 4), where two continuous sutures were used to close the tumour bed before unclamping and 10.3 (± 1.2), where one suture was used. In this study, there were no differences in blood loss, operative time or the need for transfusion between the control and early unclamping groups. Interestingly, the one major urinary leak happened in the control group and unfortunately required nephrectomy for management. The two vascular complications were also in the control group [30].

Selective arterial clamping (with laparoscopic bulldogs) appears to be more commonly studied in the minimally invasive PN series, especially in the robotic partial nephrectomy literature (RPN). The aim is to clamp the second-, third- or fourth-level branches within the renal sinus so that the area of ischaemia is limited to the renal mass only if possible or failing this that the area rendered ischaemic is a small as possible. It requires quite a sophisticated approach, which starts with 3D rendering of the kidney, its tumour and especially, its blood supply. The cross-sectional imaging used for this mapping is most commonly CT but can also be MRI. One- to three-mm slices are taken and processed using software, which provides the 3D reconstruction. The arterial and venous trees can then be mapped from the main artery and vein right up to the lesion. The level of the planned clamping is decided at this time and does not change unless due to unavoidable intraoperative reasons such as unexpected vessels. These images are thus available for review in theatre or in the case of robotic PN can be displayed on the operator's viewscreen.

Suitability for RPN/LPN and the extent of possible complications can be predicted using a variety of nephromotory scoring systems. One of the more commonly used is the Pre-operative Aspects And Dimensions Used for Anatomical (PADUA) system (table 4). It uses six characteristics to classify each lesion. These are relationship to the sinus line, location relative to renal border, relationship to renal sinus, collecting system involvement, the depth of penetration and the lesion size. The minimal score is 6 and the maximal score is 14. Not only can it be used to predict complexity (and thus suitability for PN) but it also correlates with complications. On this basis, lesions can be assigned to one of three groups, Low (6–7), intermediate (8–9) and

Anatomical feature	Scores 1	Scores 2	Scores 3
Sinus line	Entirely polar Crosses line < 50% Crosses > 50%	Between sinus lines	
Location vs. rim	Lateral border Endophytic near lateral border	Medial Border Endophytic near medial border	
Sinus located at lesion	None	Present	
Collecting system involvement	Not involved Dislocated i.e. compressed	Involved	
Depth of penetration into kidney	> 50% Exophytic	< 50% Exophytic	Endophytic
Size of lesion	< 4 cm	4–7 cm	> 7 cm

Table 4. PADUA score

high (>10) risk. Complications are significantly more likely to occur if the score is above 8. Using a baseline score of 6–7 as a comparator, those with a score of 8–9 had a 14-fold increased risk of complications and this increased to a 30-fold increased risk for score > 10 [31].

Shao et al. reported their experience of laparoscopic selective clamping in 125 patients over a two-year period and with 18 months of follow up. Visual clamping of the tumour vessel(s) was achieved in over 90% of cases, with the remainder requiring main artery clamping. The number of vessels clamped was totally dependent on tumour characteristics and this in turn predicted loss of renal function. Clamping of two or more vessels significantly increased the risk of bleeding and reduction in eGFR. Interestingly, they showed that posterior tumours were more likely to require 2 or more vessels clamped. This is slightly surprising given their approach to the kidney is retroperitoneal. Other factors predictive of multiple vessel clamping were size > 3 cm, endophytic lesions or lesions which were < 50% exophytic and lesions which involved both surfaces. Multiple vessel clamping in turn increases renal parenchymal tissue loss and thus renal function [32].

IS Gill is one of the "founding fathers" of PN and has been heavily involved in laparoscopic and robotic renal surgery. He has detailed his experience of LPN and his progression from full clamping through early unclamping, through selective clamping and finally to what he calls "zero ischaemia" [33-34]. This is the ultimate in selective clamping and entails clamping only the lesional vessel. As mentioned above, the preoperative lesional mapping is extremely important and this group uses 2–3 mm slices through the kidney and its vasculature. For their robotic work, the reconstructed images are displayed on the operating surgeons console. Putting this simply, the operating surgeon has a roadmap in front of them as they operate. Not only do they isolate the renal artery and its segmental branches but depending on tumour position, they can dissect third- and fourth-order branches. In addition to the highly detailed roadmap, the visual magnification from the use of MIS and the extra dexterity in tissue

http://dx.doi.org/10.5772/60543

manipulation from using robotic instruments, this group uses two other adjunct techniques to minimise bleeding and clamping. The first was hypotensive anaesthesia. The second is to quantify the ischaemic area using either laparoscopic colour flow doppler ultrasound or more recently, intravenous indocyanine green [34-35].

Hypotensive anaesthesia involved controlled pharmacological lowering of systemic blood pressure. The aim is to avoid vasoconstriction of the arterial tree, thus maintaining perfusion in the setting of low pressure. Initially, the patient is given a mannitol solution followed by preloading with crystalloid. The required MAP of 60 mmHg is reached at the time at which the operator is dissecting the deep part of the lesion. It is achieved using a nitroglycerine infusion and isoflurane inhalation with heart rate support from a short-acting beta blocker. On removal of the lesion, the pressure is reversed. The advantage is that blood loss is minimised by reduced pressure while maintaining tissue oxygenation and thus preventing an ischaemic cascade. The disadvantage is that hypotension may trigger other end-organ failure and result in significant comorbidity. In their later experience, this group no longer used this technique. This is due to a combination of concern regarding the possibility of ischaemic complications such as myocardial infarction or cerebrovascular accidents and improved lesional vascular dissection helped in part by the adjunct technique described below [34-35].

Gill's group now uses indocyanine green as an adjunct to confirm devascularisation. This is used in conjunction with near-infrared fluorescence, which shows a black and white image with perfused areas being bright green. This group place the lesional vascular bulldog clamp. They then intravenously inject 7.5 mg of indocyanine green, switch to near infrared and confirm uptake by visualisation of the renal artery by its being outlined in green following which they visualise the lesion. If it is dark, then super-selective dissection has been successful; if not, they either search for an accessory vessel or convert the procedure to a standard clamped PN [35].

In their pilot study of 34 patients, some 80% underwent zero-ischaemia RPN. Most of the failures were due to persistent fluorescence, indicating accessory vessels. When paired with a cohort of “standard” clamped RPNs, the only differences were a longer operating time and better renal function in the zero-ischaemia group. None of the patients studied had a positive margin [35].

A very interesting by-product of the use of indocyanine green as a marker of devascularisation is that it appears to be poorly absorbed by RCC. Of 10 tumours, seven RCC appears were hypo-perfused, suggesting that this marker may have a further part to play in PN.

The previous ten paragraphs have described some of the techniques and strategies used by those at the cutting edge of partial nephrectomy to marry the enhanced patient experience of MIS with the improved functional outcomes from partial nephrectomy. These trail blazers describe a trifecta for minimally invasive PN of negative surgical margins, minimal loss of renal function and no urological complications. The question to be asked is can similar results be delivered by others.

The more widespread uptake of LPN started when the trail blazing units started to publish their experience. Initially, the lesions treated were the Anterior, polar and exophytic lesions,

which scored a 6–7 using a PADUA system [31]. As experience was gained, units started doing more complicated lesions, while at the same time, experienced open surgeons with some laparoscopy skills began using robotic techniques. To this end, it can be difficult to compare OPN to LPN/ RPN as the number of centres publishing outcome data from LPN/RPN is very small. Amongst others to do such a comparative review was Van Poppel in a publication in 2010 [36]. This review looked at the published data at that time and as such was mainly, but not exclusively, from trail blazing units. The review has multiple tables which, for illustrative purposes, we have, somewhat crudely, condensed into two. The first (Table 5) attempts to summarise the oncological comparison. As would be expected, the mean follow-up is shorter and the mean lesion size is smaller for the LPN group. That said, the immediate (positive margins, local recurrence) oncological measure would appear to be equivalent. The intermediate performance comparator (% 5 year CSS – Cancer Specific Survival) would also suggest LPN provides an equivalent outcome.

	OPN	LPN
# Patients per quoted study	51–75	34–430
Mean size lesion (cm)	2.5–5.5	2.9–3.6
% Positive surgical margin	0– 5	0–2.9
% local recurrence	0–5.9	0–2.4
% 5 year CSS	89–98	91–100
% 10 year CSS	76–97	
Mean FU (months)	35–120	15–68

Table 5. Comparison of oncological outcomes of OPN (open partial nephrectomy) and LPN (laparoscopic partial nephrectomy) – modified from Van Poppel [36]

In partial nephrectomy, preservation of renal function and lack of urological complications are equally as important as excellent oncological outcomes. The second of the two tables (Table 6) summarises these outcomes from that Van Poppel publication. Some explanation of the table layout is required. The quoted studies had varying number of patients and hence the wide bands of reported complications. In an attempt to put each complication into context, the cumulative columns were constructed. Thus it can be seen that the operative and functional complications of LPN are equivalent to OPN [36].

One of the concerns expressed about the widespread expansion of LPN/RPN was that WIT times would increase as less experienced surgeons would prioritise tumour excision and renal repair. The accepted optimal WIT has been established at 20-30 minutes [26-28]. However it would appear from the "zero-ischaemia" work quoted above that each minute of WIT increases tissue loss [34-35]. One of the criticisms of MIS is the length of time it takes to become proficiently skilled in the procedure, the so-called learning curve. This is a controversial topic. One definition quoted is the number of cases to achieve a WIT of < 20 minutes. For robotic PN, Mottrie et al. put this at as little as 30–40 cases and based it on a single surgeon experience

http://dx.doi.org/10.5772/60543

	OPN		LPN	
	Range	**Cumulative**	**Range**	**Cumulative**
# Patients per quoted study	59–1029	2756	49–507	1679
% Overall complications	4.1–38.6	587 (21%)	9–33	337 (20%)
% Haemorrhage	0–7.5	88 (3%)	1.5 - 9.5	82 (5%)
% Urine leak	0.7–17.4	109 (4%)	1.4–10.6	57 (3%)
% sepsis	0 - 2.7	13 (0.4%)	0–2.5	11 (0.7%)
% Renal Failure	0–12.7	38 (1.4%)	0–2	12 (0.7%)

Table 6. Comparison of complications of OPN and LPN again modified from Van Poppel [36]

where the mean time for WIT in a group of 10 patients was less than 20 minutes. The caveat to this is that this group had significant robotic experience. However, the editorial comment accompanying their paper appeared incredulous that such a number could be quoted. The author of this editorial had > 400 LPNs under his belt. In LPN, the same debate seems to be taking place [37].

IS Gill suggests that it took him about 550 cases to become what he deemed to be proficient [33]. This is from one of the leading laparoscopic and robotic protagonists of PN. On the other hand, Springer et al. in their paper comparing OPN and LPN state that the fact that the two main surgeons had performed over 90 OPN and LPN each helped overcome the learning curve [38].

Their paper is worth summarising, representing as it does the experience of an early adapter of LPN where previously OPN was the procedure of choice. This group compared 140 consecutive LPNs (May 2005–November 2010) to a historic control group of 140 OPN (May 1999–April 2005). Overall, the oncological results, both in terms of positive margins (1.2 % LPN, 1.7 % OPN) and five-year CSS (91% LPN, 88% OPN), were identical and identical to the review by Van Poppel, which is tabulated above [36]. In addition, the functional outcomes were identical with approximately 5% of each group having post-operative complications. Hence, it would appear that the excellent results from LPN performed at centres of excellence are transferrable to the wider urological community.

This may be a moot point because of the rapid expansion in centres offering RAPN. Primarily, this is because robotics offers several significant advantages over "traditional" LPN. These are improved magnification, greater surgeon ergonomic comfort, instruments such as the endoWrist, which give greater degrees of movement facilitating easier dissection and suturing [35-37]. One of the latest meta-analyses on series comparing LPN and RPN is from Zhang et al. They identified seven valuable studies from an initial find of 569 studies on the topic. Unsurprisingly, there was no difference in tumour characteristics nor indeed in any discussed parameter apart from WIT. This was significantly shorter in the RAPN groups. While this is not a new finding, it is not universally found. It does appear to reaffirm the fears about LPN being associated with prolonged WIT. Looking at the tables in a little more detail, it becomes apparent that the series with larger numbers tended to have identical and more acceptable

	RPN		LPN	
	Ranges	**Cumulative**	**Ranges**	**Cumulative**
Numbers in quoted studies	11–220	425	14–102	341
Mean operating time in mins	152.17–233	176.2	117.5–226.5	194.35
Mean WIT mins	14.1–35.3	19.83	17.2–36.4	41.9
Mean blood loss mls	122.4–286.4	239.51	146.3–387.5	232.31
Conversion rate	N = 0–13 (0- 5.9%)	N = 18 4.24%	N = 0–5 (0–15%)	N = 12 3.52%
Positive margins	N = 0–18	N= 22 5.58%	N = 0–7	N = 11 3.49%
Complications	N= 0–45 (0–22%)	N = 69 (17.51%)	N= 0–17 (0–31%)	N = 55 (16.92%)
LOS days	2.51–6.1	4.98	2.7–6.8	4.48

Table 7. Comparison of complications and immediate oncological outcomes of RAPN (Robotic assisted) and LPN (Laparoscopic), modified from Zhang et al. [39] N refers to the total number of patients in the studies quoted

WIT for both RAPN and LPN. If 21 minutes is used as a marker for an acceptable WIT limit, four of the LPN and two of the RAPN trials are well above that limit. This is not discussed in the review but it may represent a learning curve effect or may reflect surgeons switching to the technically less demanding robotic approach [39]. Some evidence, albeit circumstantial, for the latter point is that having access to robotic technology increases the uptake of PN [40].

As can be seen from the preceding tables, it can be difficult to compare the MIS techniques for PN. In an effect to standardise reporting of outcomes, the MIC system was proposed and some groups have reanalysed their data accordingly. The MIC system is based on the trifecta discussed earlier. That is, negative surgical margins, WIT < 20 minutes and no significant complications. MIC is present when all three factors are present. Acceptability in terms of a study is where the global MIC score is > 80%. In their study, Porpiglia et al. showed increasing MIC with increasing experience and that acceptability was achieved after approximately 150 cases of LPN, i.e. the learning curve is 150 cases. The other factor negatively affecting MIC was increasing complexity of cases [41].

The future of endoscopically delivered NSS is secure and judging by recent publications describing MIS PN for increasingly more complex lesions, the focus will shift to which technique will become most practised. The debate is no longer about whether OPN is superior, it is now how about which of the endoscopic techniques will best achieve MIC.

4. Renal ablative therapies

Whilst most groups focused on organ preservation through PN other looked at the role of ablative technologies. The European Association of Urology guidelines suggest ablative

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therapies can be used for High risk patients who are keen to have definitive treatment. Two ablative techniques have entered main stream clinical practice and these are radiofrequency ablation (RFA) which uses heat energy and Cryotherapy (CA) which uses cold energy applied in a heat–thaw cycle to produce cell death. Tissue destruction happens when sufficient energy is applied at a rate equal to the rate thermal energy is removed (i.e. Heat sink). These techniques can be performed under general anaesthesia or sedation and in either an operating theatre (using ultrasound as the image guidance technique) or interventional radiology suite (using CT or MRI). Both require intensive imaging-based follow-up schedules as post-ablative biopsy histology is not very accurate. Failure (persistent contrast enhancement or growth on serial scans) or success (no contrast enhancement, lesion shrinkage) is based on cross-sectional imaging findings [42].

4.1. Cryotherapy Ablation (CA)

Cryotherapy has primarily been delivered laparoscopically. The principle is to deliver sufficient energy using freeze–thaw cycles to cause apoptosis and cell damage by mechanical and vascular means. The initial freeze cycle (using Argon gas) causes ice formation within the extracellular spaces. This acts as an osmotic agent and attracts fluid from the intracellular space. Freezing also causes mechanical cell damage. Thawing (using Helium gas) restores blood flow but damaged cells are released into the vasculature and result in thrombosis. The ideal freeze time appears to be 10 minutes for RCC based on basic science and clinical studies. The ideal tissue temperature is approximately -40^0C. The margin of the iceball should be approx. 0.5 cm beyond the rim of the lesion [42].

Most of the studies on CA for localised RCC have involved a large proportion of small lesions < 3 cm and have at best short- to medium-term follow-up. The majority have performed laparoscopically. The initial oncological results seem encouraging with reported 3- and 5-year CSS equivalent to that of PN AT 98–100% and 92%, respectively. The downside is that there is a significant local failure rate of 10–20%. Aron et al. have 5-year follow-up on a group of 80 patients. Their 5-year CSS is 92% but the local recurrence rate is 14%. The definition of recurrence post CA is radiological because of the difficulty interpreting post CFA biopsy specimens. Exophytic, small (<3 cm) lesions along the lateral rim of the kidney are those with the best outcomes [43].

While CA appears to be an effective therapy, there are very few head-to-head trials comparing it to PN. One such trial was conducted by Tanagho et al., who compared CA to RAPN. This trial used the Clavien classification of complications, which standardises definitions and allows for more accurate reporting. Many criticisms of LCA trials had discussed complication reporting in addition to a more favourable lesional profile. They compared 267 patients treated by CA to 233 RAPN and the groups were matched for all matched characteristics. The immediate complication rate was equal (CA 8.6% vs. RAPN 9.4%). The renal preservation was significantly better for CA, but this was at the cost of a 12.7% local recurrence rate at approx. 40 months versus 0% for RAPN at a mean fu of approximately 22 months. That said, they conclude that CA is an excellent therapy [44].

4.2. Radio Frequency Ablation (RFA)

This is predominantly delivered percutaneously. A probe is advanced under screening into the lesion and heating begun using a high-frequency alternating current. This induces molecular oscillation, which leads to friction and cell death by coagulative necrosis. The temperature at the centre of the lesion lies between 50 and 120 °C depending on the interplay between device and patient factors. Device factors include the probe composition, its surface area, length and duration of use. Patient factors include the position of the lesion vis-à-vis the hilum (i.e. collecting system and major vessels), which can affect the heat sink principle as proximity to a major vessel results in greater heat dissipation, which in turn leads to less thermal injury to the lesion unless more energy is delivered. Depending on the tissue temperature, the destruction can be instantaneous or result in the triggering of an inflammatory cascade [42].

A recent report on 200 RFA in 165 patients is one of the largest to date and is unusual in that most of the treatments were performed under general anaesthesia. This may explain the technical success rate of 98.5% in a group of lesions of mean size 2.9 cm (range 1–5.6). For central lesions, they used cold pyeloperfusion to cool the upper ureter and collecting system via a retrogradely placed ureteric catheter. They also describe hydrodissection to move bowel within 1 cm of an exophytic lesion. This is achieved by the instillation of dextrose solution (i.e. nonconductive).

In terms of oncological outcomes, this group achieved a 97.9% CSS with exophytic and tumours < 3 cm doing best. Nine required retreatment and of those, six were tumour free after a further 1–2 treatments. From a functional outcome, Only 2% of their cohort had long-term renal function loss [45].

5. Conclusion

Open Radical Nephrectomy has gone from being the only therapy available to treat localised RCC to a therapy which is now rarely practised. Indeed, partial nephrectomy seems to be competing with ablative therapies for localised disease. This chapter has attempted to trace that change albeit trying to simplify the often crossing timelines between the various interventions. The place of endoscopy in organ preservation in localised RCC is however secure.

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