

Robot-assisted nephrectomy

QUESTIONS TO BE ADDRESSED:

1. In patients with renal cancer, is robot-assisted nephrectomy or robot-assisted nephron-sparing surgery clinically effective compared to open or laparoscopic nephrectomy or nephron-sparing surgery?
2. In patients with renal cancer, is robot-assisted nephrectomy or robot-assisted nephron-sparing surgery cost effective compared to open or laparoscopic nephrectomy or nephron-sparing surgery?
3. What is the relationship between hospital surgical volume and outcomes in robot-assisted nephrectomy or nephron-sparing surgery?
4. What is the relationship between surgeon/operator experience of robot-assisted nephrectomy or nephron-sparing surgery and outcomes?

SUMMARY

- **Background:** Nephrectomy is the removal of the whole or part of a kidney, usually performed to treat cancer.
- There are three types of nephrectomy:
 - A partial nephrectomy involves removal of part of the kidney and is used to treat small accessible tumours which have not metastasised. It is sometimes called nephron-sparing surgery.
 - A simple nephrectomy involves the removal of the whole kidney and its ureter. It is mainly used to treat benign renal disease.
 - A radical nephrectomy involves removal of the whole kidney, the ureter, the adrenal gland, local lymph nodes and surrounding tissue. It is used to treat renal cancer confined to the kidney but unsuitable for partial nephrectomy, and sometimes for more advanced renal cancer.
- Nephrectomy can be carried out in three ways:
 - In an open nephrectomy, the kidney is removed through a large incision. The procedure is carried out under direct vision.
 - In a laparoscopic nephrectomy, the surgeon inserts a laparoscope and other surgical instruments through small incisions in the abdominal wall, and uses them to remove the kidney.
 - More recently, surgeons have performed robot-assisted laparoscopic nephrectomy, a variant on the laparoscopic approach.

- **Clinical effectiveness:** We found no randomised trials. The available unrandomised studies are potentially confounded, particularly by tumour size, and provide evidence of only limited reliability.
- A well-conducted systematic review comparing robot-assisted and open nephrectomy reported that estimated blood loss was less and inpatient stay was shorter with the robot-assisted procedure, though the robot-assisted operations took longer to perform. There were fewer complications after robot-assisted procedures.
- This review reported no significant differences in rates of peri-operative transfusion, conversion of partial to radical nephrectomy, ischaemia time, change in glomerular filtration rate and positive surgical margins.
- There are fewer studies comparing robot-assisted and conventional laparoscopic partial nephrectomy. A well-conducted systematic review found no differences with respect to operating times, estimated blood loss, rates of conversion to an open procedure, positive surgical margins or length of hospital stay. The robot-assisted procedures had significantly shorter warm ischaemia times¹ than the conventional laparoscopic group.
- A single recent study published since this systematic review also found that robot-assisted procedures were shorter. It also reported shorter warm ischaemia time with robot assistance. The hospital readmission rate was lower after robotic-assisted surgery, as was the need for secondary procedures. Laparoscopically removed tumours had positive margins significantly more often. The combination of warm ischaemia time of less than 25 minutes, negative surgical margins and no perioperative complications was more frequent with robot-assisted surgery than with laparoscopic nephrectomy.
- A small prospective unrandomised study comparing robot-assisted radical nephrectomy with conventional laparoscopic radical nephrectomy reported that operative time was longer with the robot-assisted procedure.
- We found no evidence that robot-assisted nephrectomy was associated with lower mortality or serious morbidity, lower recurrence risk, longer survival or any durable patient advantage from the use of the robot.
- **Safety:** Complications of nephrectomy include bleeding, infection and organ injury. There are some indications that robot-assisted nephrectomy has lower rates of some complications than other techniques, but this was not reported consistently.

¹ Warm ischaemia time is the period during which the renal artery is clamped to provide the surgeon with a blood-free operative field. The longer it lasts, the greater the risk of renal damage.

- **Cost effectiveness:** We found a systematic review of cost drivers from open, laparoscopic and robot-assisted partial nephrectomy, and two other cost studies.
- Even with optimistic assumptions about levels of robot use, robot-assisted nephrectomy is more expensive than conventional alternatives. This is largely because of the cost of buying and maintaining the machine, but also because of differences in the cost of consumables. Shorter operations and lengths of inpatient stay are not enough to offset this.
- **Volume outcome relationships:** We found no evidence about the relationship between hospital surgical volume and clinical outcome.
- We found only limited evidence about the relationship between surgeon experience and clinical outcome. It was not robust enough to support any conclusions.

1 Context

1.1 Introduction

Nephrectomy is the removal of the whole or part of a kidney, usually performed to treat cancer. Robot-assisted nephrectomy is a newer technique for carrying out the procedure which may have advantages to the patient.

1.2 Existing national policies and guidance

We found no national guidance on robot-assisted nephrectomy.

2 Epidemiology

Nephrectomy is the removal of the whole or part of a kidney.

The most common indication for nephrectomy is a malignant or, less commonly, benign tumour. Kidneys are also removed for other reasons such as trauma, hydronephrosis, chronic infection, polycystic kidney disease, shrunken kidney, hypertension or renal calculus.

For people with a renal tumour apparently confined to the kidney, surgery is usually the only potentially curative approach. Other treatments may be tried for non-neoplastic disease, but if a kidney is irreversibly damaged then its removal may be necessary.

There are three types of nephrectomy:

- A *partial nephrectomy* involves removal of part of the kidney and is used to treat small accessible tumours which have not metastasised. This procedure leaves functioning kidney tissue behind, which is advantageous to the patient, and is sometimes called

nephron-sparing surgery. It is becoming more common, partly because of the rising frequency of small tumours discovered incidentally by radiologists.

- A *simple nephrectomy* involves the removal of the whole kidney and its ureter. It is mainly used to treat benign renal disease.
- A *radical nephrectomy* involves removal of the whole kidney, the ureter, the adrenal gland, local lymph nodes and surrounding tissue. It is used to treat renal cancer confined to the kidney but unsuitable for partial nephrectomy, or to treat more advanced renal cancer.

For public consultation

3 The intervention

Nephrectomy can be carried out in different ways.

- In an *open* nephrectomy, the kidney is removed through a large incision in the side of the body, in the front of the abdomen or in the back. The procedure is carried out under direct vision.
- In a *laparoscopic* nephrectomy, the surgeon inserts a laparoscope and other surgical instruments through three or four small incisions (port sites) in the abdominal wall. The surgeon detaches the kidney and ties the blood vessels. The intact kidney is enclosed in a bag and either removed whole through an incision or broken into pieces and removed through one of the port sites.

A variant on this, hand-assisted laparoscopic nephrectomy, allows the surgeon to place one hand in the abdomen while maintaining the pneumoperitoneum required for laparoscopy. A small incision is made, just large enough for the surgeon's hand, and an airtight sleeve is used to form a seal around the incision. At the end of the procedure, the intact kidney can be removed through the same incision.

- More recently, surgeons have performed *robot-assisted laparoscopic* nephrectomy, a variant on the laparoscopic approach. Once the instruments are inserted, the surgeon sits apart from the patient, viewing the operative field in three dimensions via the laparoscope and manipulating the instruments remotely. The equipment provides three-dimensional vision and robot-assisted control of the instruments, allowing for scaling of movement, increased precision and tremor damping. It differs from conventional laparoscopic nephrectomy, which only has two-dimensional vision and offers fewer degrees of freedom for instrument movement. Differences in perspective and tactile feedback mean that robot-assisted procedures require different skills from the operator.

4 Findings

4.1 Evidence of effectiveness

In June 2014, we searched for evidence about the clinical and cost effectiveness of robot-assisted nephrectomy in comparison with open or conventional laparoscopic total or partial nephrectomy. We included the term "nephron-sparing surgery" in the search strategy, which is in Section 9.

We found three recent systematic reviews of controlled studies, each focussed on different questions. One compared robot-assisted and conventional laparoscopic partial nephrectomy[1], and the second compared robot-assisted and open partial nephrectomy[2]. The third, slightly earlier, systematic review included studies of all types of surgical management of localised renal cancer, including radical nephrectomy which the other reviews did not cover.[3]

We also searched for relevant studies published since the search dates of these reviews. To exclude smaller studies at greater risk of bias, we included only those with more than one hundred participants. We also searched for studies of the relationships of surgeon experience and hospital volume with patient outcomes.

Robot-assisted partial nephrectomy versus open partial nephrectomy

Wu et al published a systematic review and meta-analysis of studies comparing robot-assisted and open partial nephrectomy (search date October 2013).[2] They found eight eligible studies reporting results in 3418 people, 757 for robot-assisted nephrectomy and 2661 for the open procedure.

Wu et al included one prospective non-randomised observational comparison, six retrospective non-randomised contemporary comparisons and one retrospective study using historical controls. None of the studies were randomised or blinded, and allocation was usually at the discretion of the surgeon.

To investigate possible confounding, Wu et al compared the two sets of studies for the number of participants, age, gender, body mass index, laterality, tumour size and malignant/benign pathology ratio. Significant differences were found only for gender (more male participants in the robot-assisted studies, odds ratio (OR) 0.78, 95% CI 0.62 to 0.99, $P=0.04$) and tumour size, which was larger for the open group (weighted mean difference (WMD) -0.74cm , 95% confidence interval [CI] -1.11 to -0.37 , $p<0.0001$). Smaller tumours are sometimes thought more suitable for robot-assisted surgery, so the difference on tumour size is probably because of selection bias.

Complications were more common after open nephrectomy (Table 1). Also, there was a significantly shorter post-operative hospital stay and less estimated blood loss in the robot-assisted group. Robot-assisted procedures took significantly longer. There were no significant differences in intraoperative complication rates. There were also no significant differences in rates of peri-operative transfusion, conversion of partial to radical nephrectomy, ischaemia time, change in glomerular filtration rate and positive surgical margins.

Most of the variables meta-analysed by Wu showed little heterogeneity. It was significant for four variables, all continuously distributed: ischaemia time, post-operative hospital stay, blood loss and operative time. This heterogeneity is however probably not a threat to Wu et al's conclusions: the results for ischaemia time were not significant, all seven of the studies showed significantly shorter hospital stay with the robot-assisted procedure, five of six showed lower blood loss and five of six showed longer operative times. Wu et al's review is generally reliable. The most serious threat to the results' validity is the confounding effect of the differences in tumour size between the two sets of studies, which might explain the differences in blood-loss and complication rates. Wu et al included a funnel plot of complication rates against study size which indicated a low risk of publication bias.

Robot-assisted partial nephrectomy versus conventional laparoscopic partial nephrectomy

Zhang et al published a systematic review and meta-analysis of randomised and non-randomised controlled studies comparing robot-assisted partial nephrectomy and conventional laparoscopic partial nephrectomy (search date January 2013).[1] They found seven eligible studies, but the studies were much smaller than those reported by Wu et al, with only three having more than one hundred participants. There were only 766 participants in total. All the studies were retrospective observational comparisons published since 2009.

To investigate possible confounding, Zhang et al compared the two sets of studies for age, gender, malignant pathology, tumour size, or laterality; they reported no significant differences.

There were no differences between the two groups with respect to operating times, estimated blood loss, rates of conversion to an open procedure, positive surgical margins, complications or length of hospital stay. The robot-assisted procedures had significantly shorter warm ischaemia times than the conventional laparoscopic group, potentially important because shorter warm ischaemia times are associated with better post-operative renal function.[5]

There was significant heterogeneity among the results for operating time, warm ischaemia time and estimated blood loss. This suggests that the participants or the intervention were not similar enough in the included studies to make meta-analysis secure, and means that these results should be treated with caution.

As a sensitivity test, the authors then removed one study with only 13 participants in order to reduce heterogeneity. This made no difference to the results of meta-analysis nor to which results were affected by heterogeneity.

Zhang et al found fewer and smaller studies than Wu et al, and correspondingly had less statistical power and wide confidence intervals. The one significant result, warm ischaemic time, showed significant heterogeneity. That said, six of the seven studies reported shorter warm ischaemic time with the robot-assisted procedure, indicating that the heterogeneity is not a threat to the results of meta-analysis in this case.

Few strong conclusions can be drawn from this review. All but one of the results was not significant, and many had wide confidence intervals consistent with a large range of possible outcomes.

Table 1: Evidence on robot-assisted versus open and conventional laparoscopic nephrectomy

Study	Patients	Intervention	Comparator	Results*	Comment
Wu et al [2]	Eight studies including a total of 3418 patients with renal tumours. Six were single centre studies. Recruitment was from 2005 to 2010.	Robot-assisted partial nephrectomy (RPN) (757)	Open partial nephrectomy (OPM) (2661)	<p>Complication rate: RPN 19.3%, OPN 29.5%, OR 0.53, 95% CI 0.42 to 0.67, $p < 0.00001$.</p> <p>Peri-operative transfusion rate: OR 0.81, 95% CI 0.54 to 1.23, $P = 0.32$.</p> <p>Conversion rate of RPN to OPN or LPN: 1.4%. Conversion to radical nephrectomy: RPN 0.7%, OPN 0.6%, OR 1.66, 95% CI 0.37 to 7.40, $P = 0.50$.</p> <p>Warm ischaemia time: weighted mean difference (WMD) 1.21 mins, 95% CI -0.97 to 3.39, $P = 0.20$.</p> <p>Estimated change in glomerular filtration rate: WMD -3.30 ml/min, 95% CI -8.37 to 1.77, $P = 0.20$.</p> <p>Post-operative hospital stay: WMD -2.78 days, 95%CI -3.36 to -1.92, $p < 0.00001$. Estimated blood loss: WMD -107 ml, 95%CI -176 to -37.3, $P = 0.003$. Operation time: WMD 40.9 mins, 95% CI 14.4 to 67.4, $P =$</p>	<p>Sound systematic review with appropriate checks for publication bias.</p> <p>Potentially confounded by differences in tumour size.</p>

				0.002. Positive surgical margins: OR 0.78, 95% CI 0.39 to 1.57, P= 0.49.	
Zhang et al [1]	Seven studies including a total of 766 patients with renal tumours. Three of the studies were conducted in the USA, two in Korea, one in France and one in Turkey. They were published between 2009 and 2012.	Robot-assisted partial nephrectomy (RPN) (425)	Laparoscopic partial nephrectomy (LPN) (341)	Operating times: WMD -4 mins, 95% CI -28.3 to 20.3, P = 0.75. Estimated blood loss: WMD -10.8mls, 95% CI -76.73 to 55.21, P = 0.75. Conversion to open procedure: OR 0.77, 95% CI 0.35 to 1.69, P = 0.52. Positive surgical margins: OR 1.25, 95% CI 0.53 to 2.96, P = 0.61. Complications: OR 0.78, 95% CI 0.50 to 1.21, P = 0.27. Length of hospital stay: WMD -0.16 days, 95% CI -0.44 to 0.12, P = 0.27. Warm ischaemia times: WMD -3.65 mins, 95% CI -6.46 to -0.83, P = 0.01.	Fewer safeguards against bias than Wu et al.
Khalifeh et al [4]	A single-surgeon retrospective series of 500 partial nephrectomies carried out for tumours between 2002 and 2012.	Robot-assisted partial nephrectomy (RPN) (261)	Laparoscopic partial nephrectomy (LPN) (231)	Pre-operative morbidity: Charlson comorbidity index RPN 3.75, LPN 1.26, P < 0.001. Tumour complexity: RENAL score RPN 5.98, LPN 7.2, P < 0.001.	The senior author declared a financial interest and/or other relationship with Intuitive


				<p>Operative time: RPN 170 mins, LPN 192 mins, $P < 0.01$. Warm ischaemic time: RPN 17.9 mins, LPN 25.2 mins, $P < 0.001$. Intraoperative complications: RPN 2.6%, LPN 5.6%, $P < 0.001$. Postoperative complications: RPN 25%, LPN 32%, $P = 0.004$. Positive surgical margins RPN 2.9%, LPN 5.6%, $P < 0.001$.</p> <p>Readmission rate: RPN 0%, LPN 3.5%, $P = 0.002$. Secondary procedures: RPN 0.07%, LPN 2.6%, $P = 0.034$.</p> <p>Trifecta** rate: RPN 58.7%, LPN 31.6%, $P < 0.001$.</p>	<p>Surgical, a leading manufacturer of surgical robots.</p> <p>Trifecta is an arbitrarily defined measure without a clear link to patient outcome.</p>
MacLennan et al [3]	One unrandomised comparison of robot-assisted and conventional laparoscopic radical nephrectomy, New Delhi, 2006 and 2007.	Robot-assisted radical nephrectomy (RRN) (15)	Laparoscopic radical nephrectomy (LRN) (15)	<p>Operating time: RRN 221mins, LRN 175 mins, 95% CI 21.83 to 69.57, $P = 0.001$. Estimated blood loss: RRN 210ml, LRN 195 ml, 95% CI -4.66 to 35.26, $P=0.13$. Blood transfusion: RRN 3%, LRN 2%, 95% CI -0.78 to 0.26, $P = 0.50$.</p> <p>The mean analgesic requirement, hospital stay and convalescence were similar in</p>	<p>A small and low-powered study.</p> <p>Participants in the two appeared similar but the limited numbers make the extent of confounding</p>

				two groups ($P > 0.05$). There were no local, port-site or distal recurrences in either group.	hard to gauge.
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* Negative values indicate better outcomes from robot-assisted procedures.

** A combination of warm ischaemia time less than 25 minutes, negative surgical margins and no perioperative complications.

For public consultation



We found one study with more than a hundred participants published too recently for inclusion in Zhang et al's review. Khalifeh et al reported a single surgeon's results from 500 consecutive patients treated at a hospital in Ohio with partial nephrectomy between March 2002 and February 2012 [4] It is not clear how patients were assigned to procedures. The surgeon's practice shifted from laparoscopic to robot-assisted surgery in 2007 and 2008. Those treated with the robot-assisted procedure had significantly more morbidity and larger, more complex and surgically challenging tumours than those who had conventional laparoscopic surgery.

The robot-assisted procedures were shorter, with lower warm ischaemia time and fewer intraoperative and postoperative complications. The hospital readmission rate was lower after robot-assisted surgery, as was the need for secondary procedures. Laparoscopically removed tumours had positive margins significantly more often.

Khalifeh et al used the concept of trifecta to summarise a good surgical result. They defined it as a combination of warm ischaemia time less than 25 minutes, negative surgical margins and no perioperative complications. The trifecta rate was higher with robot-assisted surgery than with laparoscopic nephrectomy; multivariate analysis revealed that the choice of surgical technique was the only statistically significant predictor of achieving the trifecta.

Robot-assisted radical nephrectomy versus open or conventional laparoscopic radical nephrectomy

We found one systematic review of all modes of interventional treatment for localised renal cancer (search date January 2012).[3] MacLennan et al's review had an earlier search date than either Wu et al or Zhang et al, which is why we used those as evidence about partial nephrectomy above. However, MacLennan et al is the most recent review that we found which included studies of robot-assisted, open and conventional laparoscopic radical nephrectomy.

MacLennan et al included one prospective but unrandomised study comparing robot-assisted radical nephrectomy with conventional laparoscopic radical nephrectomy by Hemal et al.[8] This was a study of fifteen people who received robot-assisted radical nephrectomy and were compared with a contemporary group who underwent conventional laparoscopic radical nephrectomy. All participants had the same surgeon. The only significant difference reported was in operation time, which was 46 minutes longer with the robot-assisted procedure. There were no significant differences in estimated blood loss, blood transfusion rate, specimen weight, analgesic requirement, duration of hospital stay and convalescence and recurrence.

Hemal et al was a small study with wide confidence intervals, and lacked power to detect anything but very large differences. The longer duration of robot-assisted procedures is unexpected, but may reflect lack of surgeon experience.

MacLennan found no other studies comparing robot-assisted and conventional laparoscopic radical nephrectomy, and no studies comparing robot-assisted and open radical nephrectomy.

We found no relevant studies comparing robot-assisted and conventional laparoscopic radical or open radical nephrectomy published since MacLennan et al's search date.

For public consultation

4.2 Trials in progress

We searched clinicaltrials.gov but found no trials of robot-assisted nephrectomy in progress.

4.3 Evidence of cost effectiveness

We found a systematic review of cost drivers from open, laparoscopic and robot-assisted partial nephrectomy (search date not stated, but undertaken during 2010 – the review included references from 2010 and was published in 2011).[9] Mir et al included in their meta-analysis all studies of one of the three forms of radical nephrectomy used for cancer which reported operating times and lengths of inpatient stay. They excluded studies published before 2000 (because of possible subsequent changes in surgical technique), case series for robot-assisted procedures with fewer than twenty participants (because the surgeon might be inadequately experienced) and length of stay from non-US studies (because of “cultural differences in determining timing of discharge” – the authors were from Texas).

Mir et al also obtained cost data from the University of Texas Southwestern Medical Center. These data included the costs of purchase (US\$1.5m, £882,000) and annual maintenance (\$150,000, £88,200) costs of the robot. The authors assumed it would be used for 300 procedures annually for seven years and then scrapped, adding \$364,285 (£214,000) to hospital costs, or \$1214 (£715) per case. Other costs included \$772 (£454) per hour for the operating room and \$508 (£300) per day for a general ward bed.

Mir et al found the weighted average duration of each procedure to be 188 minutes for robot-assisted, 200 minutes for laparoscopic and 193 minutes for open nephrectomy, and lengths of inpatient stay were 2.6, 3.2 and 5.9 days respectively. Based on these data, Mir et al concluded that the laparoscopic procedure was the lowest cost procedure at \$10,311 (£6070). Open partial nephrectomy cost \$11,427 (£6750) and robot-assisted partial nephrectomy \$11,962 (£7040). The high equipment costs of the robot-assisted procedure were not fully offset by shorter operating times and inpatient stay.

Sensitivity analysis indicated that the robot-assisted operation would remain more expensive even if performed as an outpatient procedure.

Mir et al’s analysis suggests that the robot-assisted approach to partial nephrectomy is the most expensive. The following issues need to be considered in assessing their results:

- The study reflects costs at one hospital in the United States. Costs in the NHS will be different from those that they reported.
- Sample sizes were small: pharmacy and laboratory costs were based on fourteen laparoscopy and sixteen open surgical patients.

- The authors did not take into account the incidence and cost of complications. However, the systematic reviews do not suggest these are materially higher with conventional laparoscopic partial nephrectomy than with robot-assisted partial nephrectomy.
- The surgeons whose results Mir et al used in their analysis may achieve better results than average. If the duration of robot-assisted operations and inpatient stays is longer for less experienced and accomplished surgeons, that approach will be even more expensive.
- There may be allocation bias between the patients receiving the different procedures.
- Achieving 300 robot-assisted procedures per year may be ambitious. This is about 1.2 procedures per normal working day; it is unclear how many hospitals could generate that level of demand, especially if robot-assisted procedures are more costly than conventional alternatives.

Mir et al's rationale was that "it is unlikely that a robot can be used for many more cases" and that this assumption "reduces the bias with respect to low utilization of the robot". Arguably, the assumption introduces an opposite bias. The authors did not explore the effect of lower utilisation on costs. Indeed, their sensitivity analysis was intended only to find ways to "improve the cost effectiveness of the procedure".

Laydner et al reported costs of open, laparoscopic and robot-assisted partial nephrectomy at the Cleveland Clinic in Ohio.[10] They analysed the hospital records of 325 patients treated by four surgeons in 2009 and 2010. They found that, even ignoring the robot's purchase cost, the robot-assisted procedure's median cost was higher than the laparoscopic one (\$10,556 vs \$9924, £6210 vs £5840), because of higher costs for instruments and supplies; open partial nephrectomy's median cost was \$10,237 (£6020). Although these differences were not statistically significant, they are consistent with other evidence and plausible. Assuming a \$1.65m purchase cost for the robot, an eight-year life and 300 cases per year adds \$670 (£390) to the cost of the robot-assisted procedure, widening its cost disadvantage versus the laparoscopic alternative.

The design of Laydner et al's study is similar to Mir et al's and affected by many of the same factors. It does however corroborate the finding that shorter procedures and inpatient stays do not offset more expensive equipment.

The final cost study was also from the United States. Castle et al compared costs in 173 consecutive patients treated for small renal masses at a hospital in Miami between 2008 and 2011.[11] The study's authors included follow-up costs. The robot was costed at \$1.5m (£880,000) to purchase and \$150,000 (£88,000) for annual maintenance, and was assumed to be used for 250 cases a year.

Median costs were \$17,018 (£10,000) for open partial nephrectomy, \$20,314 (£11,900) for robot-assisted laparoscopic partial nephrectomy, \$13,965 (£8200) for laparoscopic radiofrequency ablation and \$6,475 (£3800) for computer tomography-guided

radiofrequency ablation. The type of surgical approach remained a significant predictor of cost after multivariate linear adjustment. The comparison with radiofrequency ablation is not relevant to larger tumours, but this paper also indicates that robot-assisted procedures are the most expensive approach to treatment.

Castle et al's study also corroborates the cost disadvantage of robot-assisted partial nephrectomy. It too is affected by inherent methodological limitations, but nevertheless the broad findings are likely to be relevant to the NHS.

4.4 Hospital surgical volume and outcomes in robot-assisted nephrectomy

We found no evidence on this question.

4.5 Surgeon/operator experience and outcomes in robot-assisted nephrectomy

We found no papers reporting exclusively on the relationship between the experience of the surgeon and the outcomes from robot-assisted nephrectomy.

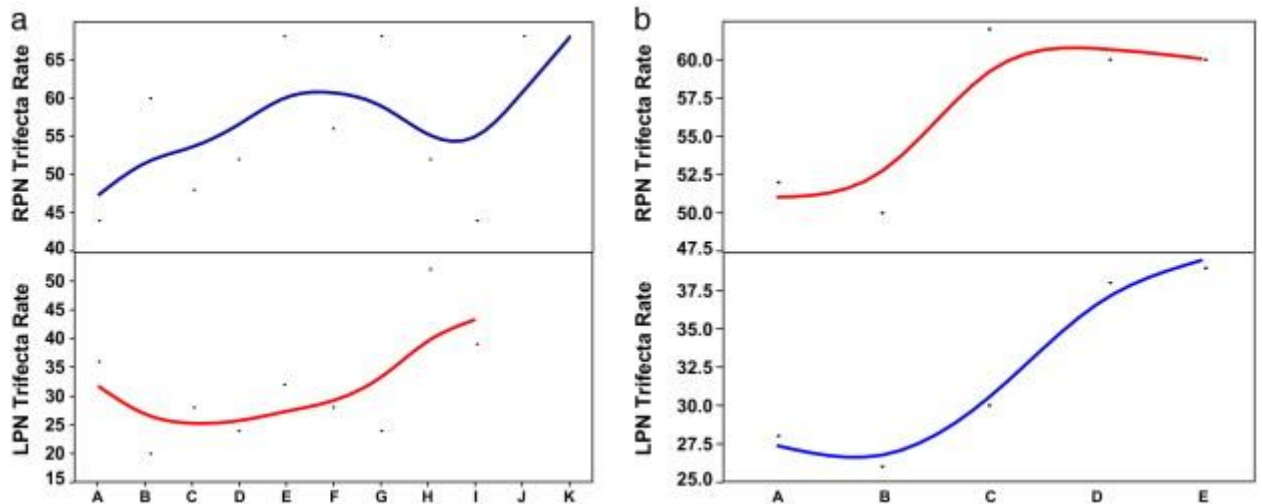
However, Khalifeh et al reported a single surgeon's results over ten years, during which his practice changed from conventional laparoscopic partial nephrectomy to the robot-assisted procedure (see above).[4] The authors reported the proportion of patients in whom the surgeon achieved a trifecta (warm ischaemia time less than 25 minutes, negative surgical margins and no perioperative complications). The authors grouped cases into groups of 25 and 50 for each procedure based on when the procedures were performed and calculated rates of trifecta for each group (Figure 1).

Khalifeh et al describe Figure 1 as showing "a steep increase in the [robot-assisted nephrectomy] trifecta rate, which plateaued at 60% after the first 50 cases. The [laparoscopic partial nephrectomy] trifecta rate improved gradually after the first 100 cases and plateaued later at almost 40%".

The data are certainly open to other interpretations: it is not clear how the line was drawn on the graphs, and the authors did not statistically analyse their results, for example as an interrupted time-series. Whether the data are presented in groups of 25 (left of Figure 1) or of 50 (right of Figure 1) markedly influences the shape of the line, indicating the sensitivity of the results to arbitrary elements of the authors' approach to analysis. There are only a limited number of datapoints, and the graph does not show a clear point of inflexion, especially when the false zero of the graph is taken into account.

In any case, the relationship between experience and outcomes of a single surgeon may not be generalisable.

Figure 1: Trifecta rates after robot-assisted and conventional laparoscopic partial nephrectomy



Trifecta defined as warm ischaemia less than 25 minutes, negative surgical margins and no intraoperative or postoperative complications.

a: 11 groups (A to K) of 25 cases each. b: 5 groups (A to E) of 50 cases each.

Note false zero on vertical axis.

Source: Khalifeh et al [4]

4.6 Safety

Differences in rates of complications, including include bleeding, infection and organ injury, were reported in some of the systematic reviews noted above. There are some indications that robot-assisted nephrectomy has lower rates of some complications that other techniques, but this was not reported consistently.

4.7 Summary of Section 4

The evidence about robot-assisted nephrectomy is not robust. The absence of randomised trials creates a substantial risk of hidden confounding. Also, many of the available studies have been carried out by particularly expert surgeons whose results may not be achievable in less skilled hands.

The key comparison is with conventional laparoscopic partial nephrectomy, which is the standard operation for renal cancer because it preserves useful renal function. Taken together, the evidence suggests that robot-assisted nephrectomy takes less time to perform and leads to earlier discharge. Warm ischaemic time is also a little shorter, and complications less common. All these findings are consistent with the expected benefits of robot-assisted nephrectomy.

There is less evidence comparing robot-assisted radical nephrectomy with the open alternative, and a lack of statistical power. Few strong conclusions are possible.

A consistent finding is that robot-assisted procedures are more expensive, largely because of the cost of buying and maintaining the machine, but also because of differences in the cost of consumables. These are not fully offset by earlier discharge.

We found no evidence that robot-assisted nephrectomy was associated with lower mortality or serious morbidity, lower recurrence risk, longer survival or any durable patient advantage from the use of the robot.

5 Cost and activity

No information was available on this.

6 Equity issues

No ethical issues were identified.

7 Discussion and conclusions

1. *In patients with renal cancer, is robot-assisted nephrectomy or nephron-sparing surgery clinically effective compared to open or laparoscopic nephrectomy or nephron-sparing surgery?*

Probably. In the short-term, robot-assisted nephrectomy appears at least as clinically effective as alternative procedures. There is no evidence about patient-orientated and longer-term outcomes. However, the evidence is subject to confounding.

Laparoscopic partial nephrectomy has become the standard treatment for renal cancers which can be resected without a radical procedure. It preserves valuable renal function and is both better for patients and cheaper than open surgery.

However, laparoscopic partial nephrectomy is a technically difficult procedure. One of the attractions of robot-assisted nephrectomy is that surgeons can, at least in theory, carry out an operation of a similar, or even better, technical quality more easily and comfortably. There is also evidence that it is quicker to perform, and quicker to recover from, than a conventional laparoscopic nephrectomy. The shorter period of ischaemia may improve long-term renal function, though the difference is less than two minutes on average and so probably has limited impact.

Compared with conventional laparoscopic partial nephrectomy, robot-assisted partial nephrectomy has only so far been shown to offer limited procedural advantages. We found no evidence of substantial material benefit for patients, such as lower recurrence risk or longer survival. This is perhaps not surprising. Advocates of robot-

assisted partial nephrectomy generally do not claim it will have better long-term oncological results; the intention is rather to carry out the same procedure more easily.

For public consultation

- 2. In patients with renal cancer, is robot-assisted nephrectomy or nephron-sparing surgery cost effective compared to open or laparoscopic nephrectomy or nephron-sparing surgery?*

Probably not. Robot-assisted nephrectomy is more expensive than alternatives, but does not offer any substantial offsetting impact on quality or duration of life for patients.

The equipment needed to carry out robot-assisted surgery is costly to buy and maintain, and consumable and disposable accessories are also more expensive. Because of this, cost evaluations from the United States consistently show the robot-assisted nephrectomy to be more expensive than conventional laparoscopic partial nephrectomy – the savings from shorter duration operations and admissions are more than negated by the equipment costs.

We found no cost-utility analysis to evaluate whether the procedure's limited patient benefits are worth its higher costs. This is far from self-evident; until it has been shown, the case for robot-assisted nephrectomy is incomplete.

- 3. What is the relationship between hospital surgical volume and outcomes in robot-assisted nephrectomy or nephron-sparing surgery?*

We do not know. We found no evidence on this question.

- 4. What is the relationship between surgeon/operator experience of robot-assisted nephrectomy or nephron-sparing surgery and outcomes?*

We do not know. The limited evidence that we found on this question was not robust enough to support any conclusions.

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For public consultation

8 References

1. Zhang X, Shen Z, Zhong S, et al. Comparison of peri-operative outcomes of robot-assisted vs laparoscopic partial nephrectomy: a meta-analysis. *BJU International* 2013; 112: 1133-1142.
2. Wu Z, Li M, Lui B, et al. Robotic versus open partial nephrectomy: A systematic review and meta-analysis. *PLoS ONE* 2014; 9: 4.
3. MacLennan S, Imamura M, Lapitan MC, et al. Systematic review of perioperative and quality-of-life outcomes following surgical management of localised renal cancer. *Euro Urol* 2012; 62: 1097-1117.
4. Khalifeh A, Autorino R, Hillyer SP, et al. Comparative outcomes and assessment of trifecta in 500 robotic and laparoscopic partial nephrectomy cases: a single surgeon experience. *J Urol* 2013; 189: 1236-1242.
5. Thompson RH, Lane BR, Lohse CM, et al. Renal function after partial nephrectomy: effect of warm ischemia relative to quantity and quality of preserved kidney. *Urology* 2012; 79: 356-60.
6. Seo IY, Choi H, Boldbaatr Y, et al. Operative outcomes of robotic partial nephrectomy: a comparison with conventional laparoscopic partial nephrectomy. *Kor J Urol* 2011; 52: 279-83.
7. Kural AR, Atug F, Tufek I, Akpınar H. Robot-assisted partial nephrectomy versus laparoscopic partial nephrectomy: comparison of outcomes. *J Endourol* 2009; 23: 1491-7.
8. Hemal AK, Kumar A. A prospective comparison of laparoscopic and robotic radical nephrectomy for T1-2N0M0 renal cell carcinoma. *World J Urol* 2009; 27: 89-94.
9. Mir SA, Cadeddu JA, Sleeper JP, Lotan Y. Cost comparison of robotic, laparoscopic, and open partial nephrectomy. *J Endourol* 2011; 25: 447-453.
10. Laydner H, Isac W, Autorino R, et al. Single institutional cost analysis of 325 robotic, laparoscopic, and open partial nephrectomies. *Urology* 2013; 81: 533-538.
11. Castle S M, Gorbatiy V, Avallone MA, et al. Cost comparison of nephron-sparing treatments for cT1a renal masses. *Urol Oncol* 2013; 31: 1327-1332.

9 Search Strategy

Search date June 2014.

Inclusion criteria for identification of relevant studies

Patients/Population	Intervention	Comparator	Outcomes	Study types
Adults (18 years or over) with renal cancer	Robot-assisted total nephrectomy, partial nephrectomy or nephron sparing surgery (including search terms 'robotics' and 'da Vinci')	Open total or partial nephrectomy or nephron-sparing surgery Laparoscopic total or partial nephrectomy or nephron sparing surgery	Clinical effectiveness Adverse events/complications Mortality Quality of life (including patient self-reported outcome measures) Occupational-related outcomes e.g. backache Length of stay Re-admissions Cost/cost-effectiveness Any	Meta-analyses Systematic reviews Randomised controlled trials Prospective non-randomised clinical study Other clinical study Health economics studies

Search strategy

1. robotics/
2. robot*.ti.
3. (robot* adj5 assist*).ti,ab.
4. (robot* adj5 (surg* or procedure* or operat*)).ti,ab.
5. da vinci.ti,ab.
6. 1 or 2 or 3 or 4 or 5
7. exp Kidney Neoplasms/su [Surgery]
8. kidney/su [Surgery]
9. Nephrectomy/
10. ((kidney* or renal) adj5 (surg* or procedure* or operat*)).ti,ab.

11. (((kidney* or renal) adj5 (cancer* or neoplas* or metasta* or malignan* or tumo?r* or carcinoma*))) and (surg* or procedure* or operat*)).ti,ab.
12. nephrectom*.ti,ab.
13. (kidney* or renal).ti.
14. 7 or 8 or 9 or 10 or 11 or 12 or 13
15. 6 and 14
16. (robot* adj5 (nephrectom* or nephron spar*)).ti,ab.
17. 15 or 16
18. limit 17 to english language
19. limit 18 to "reviews (maximizes specificity)"
20. limit 18 to "therapy (best balance of sensitivity and specificity)"
21. limit 18 to ("economics (best balance of sensitivity and specificity)" or "costs (best balance of sensitivity and specificity)")
22. (outcome* adj3 volume).ti,ab.
23. (surgeon* adj3 volume).ti,ab.
24. ((hospital or institution* or centre* or center*) adj5 volume).ti,ab.
25. (outcome and volume).ti.
26. ((high* or low* or medium*) adj3 volume).ti,ab.
27. (caseload* or case load*).ti,ab.
28. 22 or 23 or 24 or 25 or 26 or 27
29. 18 and 28

1. robotics/
2. robot*.ti.
3. (robot* adj5 assist*).ti,ab.
4. (robot* adj5 (surg* or procedure* or operat*)).ti,ab.
5. da vinci.ti,ab.
6. 1 or 2 or 3 or 4 or 5
7. urologic surgical procedures/ or urologic surgical procedures, male/
8. Urinary Tract/su [Surgery]
9. ((urin* or urolog* or urogenital) adj5 (surg* or procedure* or operat*)).ti,ab.
10. 7 or 8 or 9
11. 6 and 10
12. (robot* adj5 (urin* or urolog* or urogenital)).ti,ab.
13. 11 or 12
14. limit 13 to english language
15. limit 14 to "reviews (maximizes specificity)"
16. limit 14 to "therapy (best balance of sensitivity and specificity)"
17. limit 14 to ("economics (best balance of sensitivity and specificity)" or "costs (best balance of sensitivity and specificity)")
18. (outcome* adj3 volume).ti,ab.
19. (surgeon* adj3 volume).ti,ab.
20. ((hospital or institution* or centre* or center*) adj5 volume).ti,ab.
21. (outcome and volume).ti.
22. ((high* or low* or medium*) adj3 volume).ti,ab.
23. (caseload* or case load*).ti,ab.
24. 18 or 19 or 20 or 21 or 22 or 23

25. 14 and 24

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