Symposium

Robotic assisted kidney transplantation

Pranjal Modi, Bipinchandra Pal, Jayesh Modi, Suresh Kumar, Akshay Sood[1], Mani Menon[1]

Department of Urology and Transplantation Surgery, Smt. G. R. Doshi and Smt. K. M. Mehta Institute of Kidney Diseases and Research Centre, Dr. H. L. Trivedi Institute of Transplantation Sciences, Asarwa, Ahmedabad, Gujarat, [1]Henry Ford Hospital, Detroit, Michigan, USA

ABSTRACT

Kidney transplantation is the standard of care for patients with end stage renal disease. While open surgery remains the gold standard, minimally invasive surgery has recently been introduced for the recipient undergoing kidney transplantation. We review the evolution of techniques of minimally invasive surgery for kidney transplantation with specific emphasis on technical aspects of robotic assisted kidney transplantation.

Key words: da Vinci surgical system, kidney recipient, laparoscopy, robotic assistance

INTRODUCTION

Alex Carrel received the Nobel Prize for achieving perfection in the technique of vascular anastomosis and performing autoplastic and homoplastic transplantation of the kidney and thyroid gland in 1912.[1] The vessel suturing technique demonstrated by him relied upon a triangulation approach in which three retaining stitches located at equidistant points converted the round opening into a triangular one and did not produce stenosis. This spectacular innovation gave a reliable method of vascular anastomosis, which is the basis of a technically successful transplantation. The first successful kidney allograft transplantation in human from a living donor was performed by Joseph Murray in 1954 for which he received the Nobel Prize in 1990.[2] The success of transplantation of human kidney allograft resulted in the subsequent development of other solid organ transplantation like heart, lung, liver, etc. In the ensuing 40 years, several developments in immunology and pharmacology of transplantation occurred; however, the development of technical aspects of surgery was limited. With the development of laparoscopic living donor nephrectomy in 1995 and subsequent introduction of robotic assisted surgery in 1999, progressive development occurred in the surgery of kidney transplantation. This article will review the development of minimally invasive surgery for kidney transplantation, especially robotic assisted kidney transplantation (RAKT).

For correspondence: Dr. Pranjal Modi,
Smt. G. R. Doshi and Smt. K. M. Mehta Institute of Kidney Diseases and Research Centre, Dr. H. L. Trivedi Institute of Transplantation Sciences, Civil Hospital Campus, Asarwa, Ahmedabad - 380 016, Gujarat, India.
E-mail: dr_pranjal@yahoo.com

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MATERIALS AND METHODS

A non-systemic review of the literature was performed using the National Library of Medicine database (PubMed) using the terms: Robotic, kidney, transplantation. A total of 130 articles were found between December 1992 and January 2014; 17 articles were relevant. Additional searches were made using key words: Minimally invasive, kidney transplantation. Of a total 315 articles, 17 relevant articles were reviewed. Of 19 articles, five were unique to the new search. In addition, articles found during cross references were reviewed. A few older articles were cited for historical purposes.

Minimally invasive surgery for kidney recipient

Traditionally, kidney transplantation is carried out through an incision in the lower abdomen. The length of the wound varies depending on surgeon's preference and the habitus of the patient. In general, obese recipients require larger incisions. Similarly, in children, compared to body size, larger incisions are placed for kidney transplantation.

Several risk factors for wound related morbidity are known in general surgery; e.g., obesity, diabetes mellitus, smoking, etc. Transplant patients have additional risk factors like use of immunosuppressants.

In general, larger wounds are associated with more wound related morbidity in terms of more pain, longer convalescence and postoperative recovery, and poor cosmesis. To minimize wound related morbidity renal transplantation using a small incision were performed.[3,4] However, significant retraction of the muscles is required for access to the iliac vessels, which might lead to hematoma and bruising of muscles leading to more pain. Compression of femoral nerve by retractors can lead to injury. In addition, vascular anastomosis is challenging through the small incision. Open kidney transplantation through a small incision is thus not practiced widely.

Laparoscopic kidney transplantation was introduced recently. The first case report was published in 2010.[5] The authors used a 7 cm incision at the right iliac fossa to place the kidney in the abdomen. A pouch of peritoneum was created to place the kidney in an extra-peritoneal location. Modi *et al.* described the feasibility and safety of laparoscopic kidney transplantation when kidney was procured from a deceased donor.[6] A suprapubic incision was made to place the kidney in the abdomen. Using Carrel's patch, wide arterial anastomosis was carried out. Comparing outcomes with open kidney transplantation using the contralateral kidney procured from the same deceased donor, the authors found longer operative anastomosis time and overall operative time in laparoscopic kidney transplant group compared to open kidney transplant group. However, at the end of 1-month and 1-year, there was no statistical difference in estimated glomerular filtration rate (eGFR) in either group. Clearly, these reports have demonstrated the feasibility of laparoscopic kidney transplantation.[7]

Transplantation of en-bloc renal allograft is usually used when kidneys are procured from pediatric deceased donor. Laparoscopic en-bloc kidney transplantation has been described for kidneys procured from a 70-year-old nonheart beating deceased donors with excellent 1-year outcome.[8] The allograft was introduced through a 5 cm incision and subsequently, infra-renal vena cava and aorta were anastomosed to external iliac vein and artery, respectively.

Modi *et al.* have subsequently demonstrated effectiveness of laparoscopic kidney transplantation when the kidney was procured by retroperitoneoscopic living donor nephrectomy.[9] The anastomosis time was longer in the laparoscopic group compared to the open surgery group. eGFR at 1-month was lower in the laparoscopic group than in the open group. However, eGFR in both groups was equivalent at the end of 3-month and, graft and patient survival at the end of 1-year was comparable. Two grafts were lost in laparoscopic kidney transplantation group due to torsion of the graft and the authors suggested fixing the kidney in the retroperitoneum by means of a peritoneal flap. No graft was lost due to torsion subsequent to this additional step. Besides reduced requirement of analgesic drugs, there was no incidence of perigraft collection in the laparoscopic group. Till date, this is the largest and only series consisting of more than five patients on laparoscopic kidney transplantation.

He *et al.* demonstrated the feasibility of laparoscopic orthotopic kidney transplantation in the pig model.[10,11] Indications of orthotopic kidney transplantation are previously used iliac fossae, thrombosis of the iliac vein or severe atheromatosis of the iliac vessels. At present, no literature is available for laparoscopic orthotopic kidney transplantation in humans. However, this animal model not only validated orthotopic kidney transplantation, the authors also demonstrated the feasibility of end-to-end arterial and venous anastomosis.

RAKT through transperitoneal approach: Initial experience in United States and Europe

The first RAKT was performed in France.[12] The recipient was undergoing a second transplant using a kidney procured from a deceased donor. The first graft had been transplanted through an open surgery. For RAKT in the left iliac fossa, the patient was placed in supine position with legs spread and flexed to allow rolling in the surgical cart. The assistant standing on the left side of the patient made an incision in the left lower quadrant and placed the self-retaining retractor after retraction of peritoneum. During the remaining part of the procedure the assistant surgeon's role was to perform hemostasis, placing the vascular clamps and maintaining traction on the running sutures placed by the robot. Besides a camera arm, two other instrument arms were used for arteriotomy, venotomy, vascular anastomosis and ureteroneocystostomy. A 5–0 polypropylene running suture was used for vascular anastomosis and 6–0 polydioxanone suture for ureteroneocystostomy. Vascular anastomosis was performed in 57 min and immediate graft function was achieved.

This case report clearly demonstrated that handling of fine suture material during vascular anastomosis and ureteric reimplantation by da vinci surgical system: Intuitive Surgical, Synnyvale, CA, USA. Nothing for Pott's scissors. was feasible. Articulated tip Pott's scissors cut tissues with ease in various directions without spatial restriction of movements. The entire procedure was performed through a standard open surgery incision. Several limitations were described for this procedure. First, due to lack of haptic feedback, force applied on the suture was not known and the assistant surgeon was requiredto follow the suture. Second, the arms of the robot obscured the operative field leading to limited vision and access to the assistant surgeon. Third, the cost of the operative procedure was very high. Fourth, the operative time was greater than standard open kidney transplantation.

Despite the early success of this operative procedure, enthusiasm for RAKT was not much and further development did not occur until 2009. In January 2009, robotic kidney transplant was performed at Saint Barnabas Medical Center through a two inch incision.[13] Unfortunately, this report was not published in a medical journal, but the technique was demonstrated by Dr. Geffner at the '5th International Conference: Living donor abdominal organ transplantation: State of the art' (June 25–26, 2010 in Florence, Italy). Dr. Geffner placed the kidney graft extra-peritoneally through an incision in the iliac fossa along the line of conventional kidney transplant and robotic assisted vascular anastomosis and ureteral reimplantation were carried out transperitoneally. At the end of the procedure, the graft lay in the retroperitoneum.

The first full RAKT was reported by Giulianotti *et al*. from Chicago.[14] The indication for RAKT was morbid obesity since higher body mass index (BMI) in kidney transplant recipients is associated with increased risk of surgical site infections which negatively impact graft survival. Subsequently, the authors performed 28 more cases in obese recipients (BMI 42.6 ± 7.8 kg/m^2) by a similar technique and reported satisfactory outcomes.[15-17] Authors positioned the patient in the left lateral decubitus position, exposing the right flank. A 7-cm paraumbilical incision was made, and a hand access device (Lap Disc, Ethicon, Cincinnati, OH) was inserted, through which a 12-mm assistant port was placed. Three trocars were used for robotic arms. The camera port was placed at the left lower quadrant, slightly towards the left side of midline, and two 7-mm robotic trocars were inserted in the suprapubic region and in the right flank. dVSS was docked into position from the patient's right side. Following vascular bed preparation, the graft was placed through a periumbilical incision. Plastic bulldog clamps and 5-0 expanded polytetrafluoroethylene (Gore-Tex CV-6, W. L. Gore & Associates, Flagstaff, AZ, USA) was used for vascular anastomosis. The robot was repositioned for ureteroneocystostomy; the robotic arms were reattached and rotated in a counter clockwise direction. 6-0 polydiaxone (PDS II, ethicon, USA) was used for ureteroneocystostomy over a double J stent. The authors left the renal allograft in the peritoneal cavity and needed to perform laparoscopy for renal biopsy when it was required.[15]

Several observations were made in these studies. First, improvement in creatinine clearance was slower in RAKT than comparable patients in open kidney transplantation in the immediate perioperative period. However, at the end of 6-month, eGFR was similar in both groups. These findings are similar to what have been shown for laparoscopic kidney transplantation.[9] In this series of RAKT in obese patients, there was no difference in cold ischemia time and warm ischemia time between the open surgery group and robotic surgery group. The probable mechanism of delayed improvement in creatinine clearance is the impact of pneumoperitoneum, reducing renal allograft perfusion. The ideal rewarming time (time from taking the kidney out of the ice-box till opening of vascular clamps) is unknown. However, it should be as short as possible and preferably less than 60 min. In this report, 28.6% of patients in the open transplant group developed surgical site wound infection versus 3.6% patients in robotic transplant group ($P = 0.02$). Four patients in the open group required re-admission for surgical site wound infection. However, the mean total hospital days over 6-month follow-up was not statistically different. Hospital costs for transplant admission and total hospital costs over the 6-month following transplant were significantly higher in the robotic group. The final graft placement in this series was intra-peritoneal. The potential complications of this are torsion of allograft and para-transplant hernia. Fixation of the graft is required to avoid torsion. The authors placed the graft in the pelvic cavity and hence biopsy in the follow-up period is difficult. They required separate laparoscopy under anesthesia for renal biopsy, an additional operative procedure and hospitalization. One case required exploration of graft through right iliac fossa incision for renal biopsy. Though biopsy is considered a separate procedure, the need for a peri-operative invasive procedure should be considered a complication, possibly Clavien Grade 3b. Clearly, extra-peritoneal graft placement is required for future biopsy in patients undergoing RAKT. There was no difference in the number of acute cellular or antibody mediated rejections in the two groups. The authors did not discuss pain scores and requirement of analgesic medication.

The first RAKT in Europe was performed by Boggi *et al*.[18] in a female patient with a past history of open surgery for hysterectomy The patient was positioned supine, with the right flank slightly elevated. The table was tilted 25° to the left, further elevating the right flank, and 15° in Trendelenburg's position. A 7-cm suprapubic incision was made along the previous Pfannenstiel incision where a hand access device was inserted (Lap Disc, Ethicon spa, Pomezia, Italy). Through a 12-mm port, placed within the lap disk, pneumoperitoneum was created. The port for endoscope was placed slightly to the left of midline, below the level of the umbilicus. One 8-mm port was placed in the right pararectal line 5 cm below the costal margin, and another 12-mm assistant port was placed at the left pararectal line halfway between the incision and camera port. The dVSS was placed on the patient's right side, and a 0° telescope was used. The distal robotic arm was docked through a port placed within the suprapubic lap disc.

The cecum was mobilized, exposing the common iliac vessels. Laparoscopic bulldog clamps and the graft were introduced into the abdomen through the Pfannenstiel incision.

Venotomy and arteriotomy were carried out using a Pott's scissors. Renal vessels were anastomosed to the external iliac vessels using 6/0 expanded polytetrafluoroethylene running sutures. Ureteric reimplantation was done through the suprapubic incision using open surgical technique. Before closure of the Pfannenstiel incision, the graft was covered by cecum and pelvic peritoneum thus retroperitonealizing it. The warm ischemia time was 51 min and immediate graft function was noted on release of vascular clamps. One day after transplant, the patient was ambulant and started orally. Pain was minimal, and no analgesia was required after 48 h.

The problems encountered during laparoscopic and RAKT are (1) intra-operative cooling of the kidney is not practical, (2) kidney may slide on the smooth surface of the peritoneum during the operative procedure, leading to traction on the suture line and (3) re-docking of the robot is required after placement of kidney into the abdomen. Re-docking takes a few minutes time which add to the warm ischemia time.

Regional hypothermia and robotic assisted kidney transplantation

Menon *et al.* from Detroit collaborated with Ahlawat in Gurgaon, and Modi in Ahmedabad in establishing two kidney transplant programs in India. In this phase-wise, systematic study, the initial experiment was carried out in human cadavers and subsequently in clinical practice (Phase 0 and 1).[19] The robot was docked between the split-legs of the patient in a lithotomy position. The kidney was inserted into the abdomen of the recipient through a midline umbilical. A Gel-point port was used to seal the mid-line incision. The gel point was also used to introduce a vascular punch for arteriotomy, ice-slush and the graft. The rewarming time was 51.4 ± 9.1 (35–61) min and intra-corporeal graft temperature at the time of opening the clamps was 22.5 ± 4.2°C (16.4–27.8). In this small series of seven patients, one required exploration for high hemorrhagic drain output (Clavien complication Grade 3b).[18] It was secondary to an anti-platelet agent and not from the anastomosis. Subsequently, a total of thirty-nine RAKT were performed with 100% graft survival at 3-month.[20] In the phase 2a study, it was shown that surgeons having experience of robotic surgery adopt easier to RAKT and outcome are better than for a surgeon who has extensive experience of open kidney transplantation, but is a novice for robotic surgery.[21] Importantly, regional hypothermia did not protect the graft when anastomosis time was longer and delayed graft function was observed in one patient.

Several observations can bemade from this study. First the Trendelenberg position is familiar to urologists performing robotic radical prostatectomy and cystectomy and hence easy for them to adopt it. Second, ice slush was used to create regional hypothermia. The authors demonstrated that kidney temperature rises quickly despite placing ice slush around it. This clearly demonstrates that surgeon experience in robotic surgery is needed to complete the anastomosis before the kidney achieves body temperature and surgeons with limited experience of robotic suturing may take more time to perform the anastomosis and regional hypothermia may not protect the kidney from rewarming. The overall body temperature is also expected to decrease with exposure of the peritoneal cavity to ice slush. However, short- and long-term effects of regional and systemic hypothermia are currently not known. Third, no change of patient position or re-docking of the robot was required for ureteric reimplantation. Furthermore, the authors used barbed sutures for ureteric reimplantation, which potentially reduced operative time.

A comparison of all three techniques is given in Table 1.

Retroperitoneal approach and robotic kidney transplantation

RAKT in the retroperitoneum was described by Tsai *et al.* in 10 patients.[22] The kidney was placed in the retroperitoneum through an open incision (7.7 ± 1.04 cm) in the iliac fossa. Dissection was carried out till the exposure of the iliac vessels from the umbilical level to the urinary bladder. The robot was docked from behind the patient's back and the assistant surgeon stood between the two legs of the patient. The table was tilted 15° to the left side for right iliac fossa transplantation. Two working ports were placed at the umbilicus and in the anterior axillary line. The anterior abdominal wall was lifted up 3 cm by dVSS robotic arm ports. The kidney was placed in the wound after controlling the iliac vessels and the wound was left open. Vascular anastomosis was carried out by the robot and the robot was undocked. The console surgeon scrubbed to perform ureteric reimplantation by the open method.

This method is similar to one described in year 2002.[12] It eliminates adverse effects of pneumoperitoneum on the renal allograft. The major advantage of this procedure is no violation of the peritoneal cavity and the graft can be placed extra-peritoneally. Any delayed vascular or urinary leak can be managed extra-peritoneally. However, several small incisions are made for port placement very close to the main wound which may add to post-operative pain. The robotic arms are also likely to collide with each other.

Laboratory training for *ex vivo* kidney transplantation

Following the emergence of several case reports and early series there is increasing interest in performing RAKT. In an *ex vivo* model, 10 euthanized pig kidneys were used for learning vascular anastomosis.[23] The authors noted that with each kidney transplanted, there was an improvement in the time taken to satisfactory completion of anastomosis, reduction in number of anastomotic leaks, reduction in the number of "wasted" moves and improvement in surgical finesse.

Robotic assisted kidney and pancreas transplantation

Boggi *et al.* performed the first robotic assisted pancreas transplant.[24,25] The first patient received a pancreas after

Table 1: Varying techniques of RAKT

Variable	Giulianotti and Oberholzer *et al.*[14-16]	Boggi *et al.*[18]	Menon *et al.*[19-21]
Patient's position	Left lateral decubitus	Left lateral tilt of patient and table with 15° Trendelenburg	Supine with lithotomy and steep Trendelenburg position
Docking of robot	Right side of patient	Right side of patient	Between two legs
Incision for graft placement	Paraumbilical vertical	Suprapubic horizontal	Paraumbilical vertical
Use of hand assisted device	Yes	Yes	Yes
Placement of camera port	Left lower quadrant, slightly left to midline	Left to the midline below the level of umbilicus	Through gel-point placed at paraumbilical incision
Graft placement	Transperitoneal	Initially transperitoneal shifted to extra-peritoneal for final position	Initially transperitoneal shifted to extra-peritoneal for final position
Selection of patient group	Obese	Non-obese	Non-obese
Use of regional hypothermia	No	No	About 300cc ice-slush
Ureteric reimplantation	Re-docking of robot	Open surgery	No re-docking of robot was required
Creatinine clearance following RAKT versus open surgery	Initial slow clearance; no difference at 3 months	-	Similar clearance from day one onwards in hands of experienced robotic surgeon, slow initial clearance in hands of surgeon less experience for robotic surgery

RAKT = Robot assisted kidney transplantation

kidney transplant, the second a simultaneous pancreas-kidney transplant (simultaneous kidney-pancreas [SKP]), and the third a pancreas transplant alone. In case of SKP, both organs were transplanted in the ipsilateral iliac fossa. A 7-cm midline incision above the umbilicus was used for placing the organs into the abdomen and performing Roux-en-Y duodenojejunostomy. It took 11 h for the SKP. No patient had complications during or after surgery. The major advantage of this procedure is to reduce the size of incision in the patient having Type-1 diabetes mellitus. Outcomes are excellent and encourage multi-institutional trials.[26]

This case series of three patients has opened up a new avenue for robotic assisted multi-organ transplantation. Vascular anastomosis with great vessels in the retroperitoneuml is feasible and safe during robotic assisted transplantation. A planned incision of 7-cm in the upper abdomen is used not only for placing the organs in the abdomen but also to perform bowel anastomosis. Robotic assisted Roux-en-Y operation is described, but in this case series, where an incision is inevitable, the open procedure is quicker and easier than robotic surgery.

SUMMARY

Minimally invasive surgery including small incision open kidney transplantation, laparoscopic and RAKT are feasible. The da Vinci robotic surgical system has the advantages of three-dimension vision, control of the camera by surgeon, articulated wristed instruments with 7° of movements leading to ease of suturing, and it tracks surgeon's movements 1300 times/s. This eliminates human tremor - an essential requirement for performinga good vascular anastomosis. The initial experience in a group of highly selected patients has demonstrated benefit of RAKT in obese recipients. Both the transperitoneal and extra-peritoneal approach to kidney transplantation are feasible. Anastomosis time is likely to improve with an increase in experience of the surgeon. Regional hypothermia, in a short series, has demonstrated benefit in improving early graft function for surgeons experienced in robotic surgery but not for robotic naïve surgeons. Several technical evaluations are likely since different surgeons used various techniques. Multi-organ transplantation including SKP transplantation through a small incision and robot assistance is technically feasible, and initial results are excellent.

CONCLUSION

Robotic assisted kidney transplantation is an emerging modality of minimally invasive surgery and several surgeons are trying to perform it different ways. Despite the enthusiasm for RAKT, the current high cost is the most prohibitive factor for its widespread use. Larger studies and long-term follow-up of recipients are required to determine the effectiveness of RAKT.

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