ROBOTIC-ASSISTED KIDNEY TRANSPLANTATION: A REVIEW

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ABSTRACT

Objective: To discuss about kidney transplantation (KT), primarily on robotic-assisted kidney transplantation (RAKT) and to present the current updates on RAKT techniques performed by different centres worldwide. Material & methods: We searched and compiled various literatures on RAKT, focussing on different techniques used to perform the procedure. All the references cited in this review are indexed in PubMed or Scopus. Results: Since the first successful kidney allograft transplantation in human was performed in 1954, KT has become the preferred treatment modality for patients with endstage renal disease (ESRD) seeking a more definitive outcome and better quality of life. Over the years, newer techniques of KT have been introduced, including minimally-invasive laparoscopic KT. However, laparoscopic KT has its own limitations, which include loss of hand-eye coordination and poor ergonomics for the surgeon. RAKT offers the same benefits as laparoscopic KT without its limitations. There are several transplantation centres worldwide performing RAKT regularly. The differences in RAKT technique between these centres are regarding patient's position during surgery, location of incision for graft placement, use of regional hypothermia, and techniques of graft placement and ureteric reimplantation. Conclusion: The invention of RAKT as a minimally-invasive KT technique has enabled surgeon to perform surgeries when the operative field is deep and narrow and when fine dissection and microsuturing are required.

Key words: Kidney transplantation, robotic-assisted kidney transplantation, end-stage renal disease.

ABSTRAK

Tujuan: Untuk memaparkan mengenai transplantasi ginjal, terutama robotic-assisted kidney transplantation (RAKT) dan untuk menjabarkan perkembangan terkini pada teknik RAKT yang digunakan oleh beberapa pusat transplantasi ginjal di dunia. Bahan & cara: Penulis melakukan pencarian dan kompilasi terhadap literatur mengenai RAKT, dengan fokus pada teknik RAKT. Semua referensi yang digunakan pada tinjauan ini terindeks di PubMed atau Scopus. Hasil: Sejak operasi transplantasi ginjal pertama yang sukses dilakukan pada manusia di tahun 1954, tindakan ini menjadi metode tatalaksana pilihan untuk pasien penyakit ginjal tahap akhir (PGTA) dengan luaran yang lebih definitif dan kualitas hidup yang lebih baik. Dalam perkembangannya, teknik baru dalam transplantasi ginjal telah diperkenalkan, salah satunya tehnik laparoskopi yang merupakan tindakan invasi minimal. Namun demikian, transplantasi ginjal laparoskopi juga memiliki kekurangan, yaitu hilangnya koordinasi tangan-mata dan ergonomi yang buruk bagi operator. RAKT menawarkan keunggulan yang sama dengan teknik laparoskopi dan menghilangkan kekurangan teknik ini. Saat ini terdapat beberapa pusat transplantasi ginjal di dunia yang telah menggunakan metode RAKT secara rutin. Perbedaan pada teknik RAKT antara pusat transplantasi ginjal tersebut terletak pada posisi pasien saat operasi, lokasi insisi untuk penempatan cangkuk, penggunaan hipotermia regional, dan teknik untuk penempatan cangkuk serta reimplantasi ureter. Simpulan: RAKT sebagai teknik transplantasi ginjal invasi minimal sangat berguna terutama pada lapangan operasi yang dalam dan sempit serta untuk melakukan penjahitan mikro.

Kata kunci: Transplantasi ginjal, robotic-assisted kidney transplantation, penyakit ginjal tahap akhir.

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INTRODUCTION

Chronic kidney disease (CKD) is defined as a decreased kidney function, characterized by glomerular filtration rate (GFR) of <60 mL/min per

1.73 m², and/or based on the presence of kidney damage, manifested as albuminuria, for 3 months or more. It is now a worldwide public health problem with increasing incidence and prevalence.¹ Since GFR plays a central role in the pathophysiology of

this disease, CKD is classified into five stages based on the level of GFR: stage 1 (GFR ≥ 90 mL/ min per 1.73 m²), stage 2 (GFR 60-89 mL/min per 1.73 m²), stage 3 (GFR 30-59 mL/min per 1.73 m²), stage 4 (GFR 15-29 mL/min per 1.73 m²), and stage 5 (GFR <15 mL/min per 1.73 m²). Stage 5 CKD is regarded as the most serious outcome of chronic kidney disease and symptoms are usually caused by complications of reduced kidney function. These include fluid retention due to extracellular volume overload, anemia, disturbances of bone and mineral metabolism, dyslipidemia and protein energy malnutrition. This condition is associated with high morbidity and mortality. When symptoms are advanced, renal replacement therapy (RRT)-dialysis or transplantation-are needed to substitute the function of the failing kidneys. Patients with stage 5 CKD receiving RRT are considered as suffering from ESRD. For patients with ESRD, KT is the preferred treatment with more definitive outcome, i.e. longer survival and better quality of life.²

According to the United States Renal Data System (USRDS), there were 117.162 new cases of ESRD reported by the end of 2013 with 363 per million/year incidence rate.³ Perkumpulan Nefrologi Indonesia (PERNEFRI) reported in 2011 that there were 12.780 ESRD patients in Indonesia.4 With increasing number of ESRD patients, the need for RRT also increases. At the end of 2013 alone, there were 661.648 prevalent dialysis and transplant patients receiving treatment for ESRD, a 3.5% increase from 2012.3 Between 1998 and 2007, the annual number of KTs performed in the United States (US) grew by 31%, from 12.318 transplants in 1998 to 16.119 transplants in 2007. At the end of 2006, 103.312 patients had a functioning kidney transplant compared with 64.779 in 1998, showing an increase of 59%.5 Abundant research, trials and modifications of surgical techniques regarding RRT, especially KT, in recent years contribute to the decrease of overall mortality rates among patients, with steeper declines in more recent years. USRDS shows that, among KT recipients, the mortality rate fell by 12% from 1996 to 2003 and by 28% from 2004 to 2013.³

OBJECTIVE

To discuss about kidney transplantation (KT), primarily on robotic-assisted kidney transplantation (RAKT) and to present the current updates on RAKT techniques performed by different centres worldwide.

MATERIAL & METHODS

We performed literature searches to identify case reports, case series, case control, and cohort studies on the application of robotic surgical device in kidney transplantation. The databases PubMed, Embase, Scopus, and ScienceDirect were used with the search terms 'kidney transplantation', 'da Vinci surgical system', and 'robotic-assisted kidney transplantation' to identify all the relevant studies.

RESULTS

Joseph Murray performed the first successful kidney allograft transplantation in human from an identical-twin living donor in 1954. Nowadays, although open surgery remains the gold standard in KT, minimally-invasive approach has recently been introduced for the recipient of KT.6 Rosales et al reported in 2009 of a patient undergoing successful laparoscopic KT.7 This case report shows that KT can be performed laparoscopically. However, it does not demonstrate that laparoscopic KT can be duplicated widely. Laparoscopy is not regularly used in surgeries requiring multiple vascular anastomosis because of several factors. Loss of hand-eye coordination; use of long instruments, which amplifies surgeon's tremor; and poor ergonomics, which only leads to fatigue are the main reasons why it is uncommon to perform multiple vascular anastomosis using laparoscopic technique. The invention of minimally-invasive, surgical robots, such as the daVinciTM surgical system (dVss) (Intuitive Surgical®, Sunnyvale, CA, USA) has filled the niche for difficult surgeries to be performed more easily, particularly when the operative field is deep and narrow and when fine dissection and microsuturing are required, such as in KT. Since the first case of RAKT was reported in France and published in 2001, the application of robotic technology in minimally-invasive KT by several centers worldwide has shown promising results for its regular usage in the future.6

Therefore, the aim of this review is to evaluate the benefits and limitations of RAKT as well as to explain the techniques of RAKT used in several centers worldwide.

The dVss is a computer-assisted electromechanical device, which acts as a remote telepresence manipulator controlled by a surgeon. Although the dVss has many models based on its indications for use and capabilities, fundamentally it consists of an ergonomically designed console where the surgeon sits while performing the surgery, a patient-side cart where the patient is positioned during surgery and consists of three to four robotic arms that carry out the surgeon's commands, a 3D high-definition (HD) vision system and image processing equipment, and articulated EndoWrist® instruments (Figure 1).

The dVss provides the operating surgeon with 3D HD view and up to 10-15 times magnification with immerse view of the surgical

field, which supports hand-eye coordination. It employs Endowrist®, with seven degrees of freedom and a range of motion far greater than the human hand, minimizing surgeon's tremor. The dVss is also capable of tracking the surgeon's movements 1.300 times/s, providing for tremor filtration and scaled motion (Figure 2).

The dVss is not, however, without limitations. Compared to open and laparoscopic surgery, the dVss charges bigger expenses and needs larger



Figure 1. The da Vinci™ surgical system device Image courtesy of: ©[2016] Intuitive Surgical, Inc.

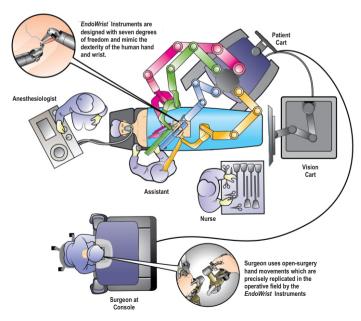


Figure 2. Illustration of operating room schematic using the da Vinci™ surgical system Image courtesy of: ©[2016] Intuitive Surgical, Inc.

Table 1. Benefits and Limitations of RAKT.

Benefits Limitations

Surgical precision and varied range of movements Shorter learning curve Preferred KT technique for obese patients Lower risk of wound complications Relatively more expensive than open or conventional laparoscopic KT Demands for bigger resources Absence of tactile feedback

consumption of resources such as space and the availability of skilled technical staff. Furthermore, surgeons performing any invasive procedure with dVss are also completely devoid of tactile feedback (Table 1).

The application of robotic surgical system, such as the dVss, in KT is a refinement from minimally-invasive laparoscopic approach, RAKT overcomes the limitations and drawbacks of laparoscopy surgery while still maintaining its benefits.¹¹ In laparoscopic surgery, the surgeon only receives two-dimensional view of a threedimensional operative field and limited range of movement, thus providing limited precision.12 Moreover, loss of hand-eye coordination, use of long instruments and poor ergonomics only pose as nuisances to the surgeon. On the contrary, the dVss has the advantages of three-dimensional vision with adjustable magnification and articulated Endowrist® instruments with a greater range of movement compared to the human hand, thus allowing ease of suturing and an unparalleled level of operative precision.6

The use of laparoscopic approach in surgery is also significantly associated with a learning curve. The learning curve of a skilled open surgeon to master laparoscopic radical prostatectomy is estimated at 80-100 cases yet for the same group to master robotic laparoscopic radical prostatectomy, the learning curve is predicted at 8-12 cases. Unfortunately, no publication yet is found on the comparison between the estimated learning curve of an experienced open surgeon to master KT with laparoscopic approach and the learning curve of the equal group to achieve proficiency in performing RAKT.

ESRD patients with obesity (body mass index [BMI] $\geq 30 \text{ kg/m}^2$) often find difficulty to be cleared for KT. Although this group of ESRD patients is often overlooked, they comprise 20 - 50% of all ESRD patients that are on dialysis. According to Segev et al, ESRD patients with

BMI >40 kg/m² listed for KT have significantly longer wait times for the procedure compared to patients with BMI <25 kg/m². Higher BMIs in kidney transplant recipients are positively correlated with risk of surgical site infection (SSI), which will eventually impact graft survival. Increased risk of SSI towards ESRD patients with obesity accompanied by the expectation of some centers to give obese patients time to lose weight are the main reasons why a number of transplant centers in the US are reluctant to list obese patients for transplantation.¹⁷ Unfortunately, many these obese patients also have other comorbidities, such as diabetes and hypertension. Patients with diabetes and/or hypertension who are on dialysis have a high mortality rate. According to USRDS, the 5-year mortality rates for diabetes and hypertension patients who are on dialysis are 75% and 70%, respectively. A study by Lynch et al in 2009 reported that obese patients undergoing KT that did not develop SSI had the same kidney transplant success rate as patients without obesity.18

The development of RAKT fills the niche for a lower-SSI-risk KT procedure for ESRD patients with obesity. This minimally-invasive, robotic technique avoids any incision in the infection prone lower quadrants of the abdomen. In addition, there is also less direct contact between the operator and the patient, which would further reduce the risk of developing SSI. Oberholzer et al conducted a study from June to December 2009 investigating the suitability of RAKT for obese patients. In this study, they compared intraoperative and postoperative outcomes between 28 obese patients undergoing RAKTs and 28 control patients undergoing standard open KT. They found that there were similar intraoperative outcomes between the two groups regarding warm and cold ischemia times and volume of blood loss. Furthermore, there were no need for intraoperative blood transfusion and no intra-operative vascular complication among the RAKT group, while there were one patient needing

intraoperative blood transfusion and two patients suffering from intraoperative vascular complications from the control group. These results, however, were not significantly different.¹⁹

Oberholzer et al, also analyzed 6-month post-operative outcomes between the two study groups. It was found that among the robotic group, there was 0 case of wound infection while there were eight patients from the open-surgery group suffering from incisional-superficial SSI (p=0.004). Additionally, total follow-up months were also reduced significantly among the RAKT group, in which the mean follow-up months were 12.0 while for the control group, the mean follow-up months were 35.7 (p<0.001).

In terms of surgical wound scar, since RAKT is a minimally-invasive procedure that does not need wide, gaping incision to be made during surgery, patients would have lower risk of developing visible surgical scar compared to if they undergo open surgery. This result, however, is not exclusive to RAKT as it is also observable in patients undergoing non-robotic, laparoscopic KT.¹¹

One of the biggest pitfalls of RAKT, as in other robotic surgeries, is bigger financial expenses. Robotic surgical systems, such as the dVss, have high fixed costs, with prices ranging from \$0.6 million to \$2.5 million for each unit based on the type. As mentioned above, there is also a learning curve in which surgeons must perform a number of procedures to become adept in using the robotic surgical system. Furthermore, in addition to regular sumable, single-use, robotic instruments/ accessories needed to prevent technical failure during usage, the system also require the use of additional concostly maintenance by specifically-trained technician with prices ranging from \$700 to \$3.200 per procedure. Nonetheless, like other computer-driven technologies, capital and maintenance costs are predicted to drop over time when the number of robotic devices and patient cases increase. Furthermore, since the patent of "remote center-of-motion robot for surgery" (US patent number: 5397323; issue date: 14 March 1995) has already expired on 30 October 2012, other companies now have a chance to propose and produce alternative robotic surgical systems.11

One of the differences between open and robotic surgery is that in robotic surgery, the surgeon works from a console and rely on the assistant to carry out some tasks that could not be performed by the device alone. The outcomes of surgery are

critically dependent on the competence of the whole surgical team. Therefore, it is important to train not only the operating surgeons but also the operating room nursing staffs and anesthesia staffs on the differences between this mode of surgery and open or conventional laparoscopic surgery. Without the support of the whole surgery team, surgeons will meet difficulties in communicating their intentions regarding the surgery, which will carry a high risk towards the patients. Moreover, there is no device or technology that is impervious to technical malfunction. Although the dVss is designed to avoid this issue with its system redundancy features, in which it can sustain recoverable faults, specialist technical staff must be employed on daily basis to deal with any technical issue that may happen before or during the surgery.9

Lack of tactile feedback has also become a drawback of the dVss. Logically, it could lead to an increased risk of unintentional tissue injury, such as infirm suture knot. However, up to now, no association is found between robotically performed surgery and higher clinical complication rates compared to open or laparoscopic surgery. This issue can also be overcome by using an expanded polytetrafluoroethylene suture that is more resistant to grasp and less likely to brake.

Hoznek et al performed the first ever RAKT. The surgery took place in France and was reported in 2001. The patient was a 26-year old male with ESRD due to focal segmental glomerulosclerosis and had already been on hemodialysis for 11 years. He underwent a transplant using a kidney procured from a deceased donor. The surgery, however, was more of an open surgery performed with the aid of a robotic surgical system rather than a pure RAKT. The patient was placed in supine position under general anesthesia with the legs spread and flexed to allow rolling into the surgical cart at the time of anastomosis. The assistant surgeon at the left side of the patient made an incision in the left lower quadrant of the abdomen and placed a self-retaining retractor after peritoneum was dissected. During the remaining part of the procedure the assistant surgeon role was to perform hemostasis using electrocautery. placing the vascular clamps and maintaining traction on the running sutures.²⁰

The first case of pure RAKT surgery was performed by Giulianotti et al from the University of Illinois, Chicago and was reported in 2010. The patient was an obese (BMI 41 kg/m²), 29-year old Caucasian woman with ESRD secondary to conge-

nital posterior urethral valves. The patient was put in general anesthesia and positioned in left lateral decubitus, exposing the right flank. A 7-cm periumbilical incision was made and a hand access device was inserted. Afterwards, four additional trocars were inserted. A 12-mm trocar for the 30° robotic scope was inserted in the left lower quadrant slightly toward the left side of the midline, two 7-mm robotic trocars were inserted in the suprapubic region and the right flank, and a 12-mm port, for the assistant, was inserted between the umbilicus and the trocar placed on the right flank. Then, the dVss was docked into position (from the patient's right side) and integrated to the ports.²¹ After appropriate vascular dissection, the graft was brought into the operative field through the midline incision and appropriately oriented for implantation to the external iliac vessels. The renal vein and artery were sutured end-to-side in a continuous fashion to the external iliac vein and artery, respectively, with 5-0 and 6-0 expanded polytetrafluoroethylene suture. The bladder was distended with saline and methylene blue in order to facilitate its dissection. Following incision of the muscular layers, the bladder was anastomosed to the ureter with running 5-0 polydioxanone suture. After the anastomoses were tested and showed no leak, the kidney was revascularized. Hemostasis was completed, and no significant bleeding was observed. The total operative time was 223 min, with 11 h and 50 min of cold and warm ischemia times, respectively. The kidney functioned immediately.6

In 2013, Oberholzer et al from the same group published a retrospective study of a 6-month follow-up, where 28 obese patients who underwent RAKT were compared to a frequency-matched cohort of 28 obese patients who underwent open KT. The control group had a significantly lower average BMI than the RAKT group (mean \pm SD: 38.1 ± 5.4 kg/m² vs 42.6 ± 7.8 kg/m², respectively; p=0.02). However, the proportion of patients who were obese/morbidly obese was comparable between the two groups. There was no SSI in the robotic group, while 8/28 patients (28.6%) in the control group developed SSIs (p=0.004). The patient and graft survivals between the two groups after a 6-month follow up showed comparable results. ¹⁹

The first full RAKT in Europe was performed by Boggi et al in 2011. The recipient was a 37-year-old woman with lupus nephritis and had already been on dialysis for 32 months. The patient was positioned supine, with the right flank slight-

ly elevated. A 7-cm suprapubic incision was made along the previous Pfannenstiel incision and the hand access device was inserted. The robot was placed on the patient's right side, and a 0° telescope was used. Renal vessels were anastomosed by the robot, although ureteral implantation was done through the suprapubic incision using open surgical technique. Before closure of the Pfannenstiel incision, the graft was covered by the cecum and pelvic peritoneum to keep it in the retroperitoneum. Surgery lasted 154 min, including 51 min of warm ischemia of the graft. Urine production started immediately after graft reperfusion. Renal function remained optimal at the longest follow-up of 3 months.¹¹

In 2014, Menon et al from Vattikuti Urology Institute, Detroit, USA in collaboration with Ahlawat in Gurgaon, India, and Modi in Ahmedabad, India published a prospective study of 50 consecutive patients with a mean BMI of 24.1 kg/m² who underwent RAKTs. Based on their technique, the robot was docked between the split-legs of the patient in a lithotomy position. A GelPOINT® device, a hand-access platform which allow easy introduction of ice slush and the graft was used to seal the midline incision in the periumbilical region. The pelvic bed was cooled to 18-20°C with the introduction of 180-240 ml ice slushvia modified Toomey syringes. A temperature probe was used to continuously monitor renal cooling. The graft was inserted into the abdomen through the GelPOINT® port incision. The vascular anastomosis and the ureteroneocystostomy were performed robotically. The kidney graft was retroperitonealized for the final position.22

Tsai et al from Taiwan also reported their experience with 10 patients from July 2012 to June 2013. The patients' mean BMI was $22.8 \pm 3.5 \text{ kg/m}^2$ (18.9-28.2 kg/m²). Based on their technique, the surgery was performed with a Gibson incision and two working ports. The kidney was placed in the retroperitoneum through the Gibson incision (7.7 ± 1.04 cm) in the iliac fossa. The robot was docked from behind the patient's back, and the assistant surgeon stood between the two legs of the patient. The robotic arms were attached to the robotic ports and set to lift the abdominal wall about 3 cm higher. A 30° endoscope was placed over the Gibson incision. Like Boggi et al, vascular anastomosis was carried out robotically, while ureteral implantation was done in an open fashion. All patients resumed oral intake and ambulation within 24 h post-surgery

Table 2. Varying techniques of RAKT.

Variables	Giulianotti and Oberholzer et al. ^{19,21}	Boggi et al. ¹¹	Menon et al. ²²	Tsai et al. ²³	Breda et al. ²⁴	Doumerc et al. ²⁵
No. of patients	28	1	50	10	1	1
Patient's position	Supine with legs on legrest, table at 20-30° Trendelenburg	Left lateral tilt, table at15° Trendelenburg	Supine with lithotomy, Trendelenburg 15°position	Supine with lithotomy, table at 15° Trendelenburg	Supine with lithotomy, table at 30° Trendelenburg	Supine with lithotomy, table at 15° Trendelenburg
Docking of robot	Right side of patient	Right side of patient	Between two legs	Right side of patient	Right side of patient	Not specified
Incision for graft placement	Paraumbilical vertical	Suprapubic horizontal	Paraumbilical vertical	Gibson incision	Paraumbilical vertical	Transvaginal
Graft placement	Transperitoneal with final retroperitonea lization	Transperitoneal with final retroperitonea lization	Transperitoneal with final retroperitonea lization	Extraperitoneal	Transperitoneal with final retroperitonea lization	Transperitone al with final retroperitonea lization
Use of regional hypothermia	No	No	Yes; ice-slush	No	Yes; ice-slush	No
Patient group	Obese	Nonobese	Nonobese	Nonobese	Nonobese	Not specified
Ureteric reimplantation	Robotic	Open surgery	Robotic	Open surgery	Robotic	Robotic

and the average post-transplant hospital stay was 13.6 ± 3.5 days.²³

Furthermore, in 2016, Breda et al reported the first Spanish transperitoneal pure RAKT from a living-related donor and was presumably the second pure RAKT case performed in Europe. The patient was a woman who suffered ESRD due to Alport disease and the donor was her mother. After induction of general anesthesia, four trocar ports were introduced and positioned according to the technique used by Menon et al. The patient was moved to lithotomy position with a 30° Trendelenburg tilt and the dVss robot was docked. During the surgery, GelPOINT® device was used and inserted through a 6-cm vertical periumbilical incision. This was to allow easy introduction of the graft, bulldogs and ice slush. Following vascular dissection, the graft was introduced via the GelPOINT® and positioned intraperitoneally lateral to the iliac vessels. After arterial and venous anastomoses, the graft was retroperitonealized by approximating the peritoneal flaps previously prepared. Ureteral implantation was also done robotically. Surgical time was 120 min and the patient was ambulating and started oral intake during the first post-operative day. Pain was minimal, and no analgesia was required after 48 h. No compli-cation was recorded.24

Doumerc et al from the University Hospital of Toulouse, France performed the first transvaginal RAKT in the world. Their report was published in 2015. The patient was a 50-year-old woman receiving a living donor transplant. Following standard ports placement, transperitoneal dissection of the external vessels was performed. The uterus was mobilized with transparietal stitching to allow full visualization of the posterior vaginal wall that was going to be utilized for graft insertion. Subsequent to vascular anastomosis, the kidney was moved to the retroperitoneum. Ureterocystostomy anastomosis was also performed robotically. The operative time was 200 min and vascular anastomosis time was 55 min. No intra- or postoperative complications were observed.²⁵

DISCUSSION

There are a great number of research and trials being conducted on KT. KT performed with the aid of a robotic surgical system, the dVss, is an emerging modality of minimally-invasive surgery, and surgeons in Europe and the US are developing it in different ways. It overcomes the limitations and pitfalls of standard laparoscopic surgery without

omitting its benefits. The dVss enables surgeons to perform delicate and complex operations through a few small incisions. The surgeon controls the dVss, which translates his or her hand movements into smaller, more precise movements of tiny instruments. Despite all the enthusiasm, the major drawback of RAKT is the expenses incurred by the device and its maintenance. Furthermore, a level of expertise is needed to perform the surgery with the aid of the dVss. Nevertheless, the promising results in term of patient's and graft's survivals so far will compensate the financial issue and will prove beneficial in the future, with the number of the device increases and alternative systems being invented by other companies.

CONCLUSION

The invention of RAKT as a minimally-invasive KT technique has enabled surgeon to perform surgeries when the operative field is deep and narrow and when fine dissection and microsuturing are required.

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