Robot-assisted kidney transplantation: an update

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ABSTRACT

Renal transplantation has become the gold-standard treatment for the majority of patients with established renal failure. Recent decades have seen significant progress in immunosuppressive therapies and advances in post-transplant management of recipients, resulting in improved graft and patient outcomes. However, the open technique of allograft implantation has stood the test of time, remaining largely unchanged. In a world where major advances in surgery have been facilitated by innovations in the fields of biotechnology and medical instrumentation, minimally invasive options have been introduced for the recipient undergoing kidney transplantation. In this review we present the evolution of minimally invasive kidney transplantation, with a specific focus on robot-assisted kidney transplant and the benefits it offers to specific patient groups. We also discuss the ethical concerns that must be addressed by transplant teams considering developing or referring to robotic programs.

Keywords: chronic renal failure, minimally invasive surgery, obesity, renal transplant, robot-assisted kidney transplant

INTRODUCTION

In the last two decades, major advances in surgery have been facilitated by advances in the field of bioengineering, biotechnology and medical instrumentation. These have led to major patient benefits such as reduced perioperative morbidity and shorter hospital stay in all surgical specialties, in part due to the introduction of minimally invasive and robotic surgery [1]. Over the last half century, renal allotransplantation has developed as a superior renal replacement therapy compared with established dialysis methods [2, 3], becoming the gold-standard treatment for the majority of patients with established renal failure. In recent decades there has been significant progress in immunosuppressive therapies [4, 5] and advances in post-transplant management of recipients, resulting in improved graft and patient outcomes [6]. However, the surgical technique of allograft implantation has remained largely unchanged since the first successful living donor open kidney transplant in identical twins in 1954 [7]; the open surgical approach has stood the test of
time. As with any major open surgical operation, open kidney transplant (OKT) is associated with morbidity such as post-operative pain, surgical site infection (SSI), delayed mobilization, significant time to return to daily activities and long-term complications such as incisional hernia. Transplant recipients with a high body mass index (BMI) face higher incidences of these inevitable risks of undergoing renal transplantation. These patients have higher rates of wound infections, hernia, associated poor graft outcomes [8, 9] and, on occasion, they may not be considered for renal transplantation. To address these issues, transplant teams have explored newer surgical techniques with the aim of further improving patient outcomes following surgery. The advent of robotics and its integration into surgical practice have revolutionized several areas of complex surgical enterprise. Some transplant teams have also incorporated robotic technology into various areas of transplantation, including donor nephrectomy. In this review we provide a contemporary overview and update on robot-assisted kidney transplantation (RAKT).

THE TRADITIONAL SURGICAL APPROACH TO RENAL TRANSPLANTATION

For >60 years, kidney transplantation has been traditionally performed through an open oblique or ‘J-shaped’ incision in the lower lateral abdomen. The exact incision length and position is dependent upon surgeon preference, patient body habitus, BMI and prior transplant history among others. The most common incision used is the oblique or curvilinear incision known as the ‘pelvic Gibson incision’ [10, 11]. Running parallel to the inguinal ligament, the incision extends medially to the midline, 2 cm above the pubis and laterally to the anterior superior iliac spine. The abdominal muscles beneath the incision are divided in the direction of the incision and retracted. The ‘J-shaped’ or ‘hockey stick’ incision has become increasingly popular for kidney transplantation, with its pararectal position continued medially to the midline above the pubic symphysis, allowing division and retraction of the ipsilateral rectus muscle. The kidney graft is placed extra peritoneally, with end-to-side anastomosis of the renal vein and artery to the external iliac vein and artery, respectively (Figures 1 and 2). Following successful reperfusion of the graft, the ureter is anastomosed to the bladder, creating a ureteroneocystostomy (Figure 3). This technique has remained unchanged for many years and provides a reliable method of access and implantation, with good results that are widely reproducible [12, 13]. In selected individuals a transperitoneal approach through a midline or paramedian incision is used if the standard iliac approach could prove problematic [14]. Situations in which this is helpful are in third and subsequent transplants and in paediatric recipients.

Despite the standardization and safety of this approach, it is well recognized that open abdominal incisions carry significant morbidity. They are associated with longer wound healing times, higher levels of post-operative pain and the need for higher doses of analgesia, prolonged recovery and hospital stay, incisional hernia as well as inferior cosmetic outcomes compared with minimally invasive surgical approaches [15–18]. Morbidity of open surgery is higher in patients with a high BMI, diabetes mellitus, smokers, renal failure and, importantly for transplant patients, immunosuppressive medication, most specifically steroids.

Minimally invasive surgery, favoured for its lower morbidity, has made significant technological advances and now plays a role in almost all forms of abdominal surgery [19]. It affords patients improved perioperative outcomes, including shorter hospital stay, reduced post-operative pain, lesser rates of wound infection and superior cosmetic results [20]. Minimally invasive surgery already plays a role in renal transplantation, with variations of laparoscopic donor nephrectomy becoming established as the gold-standard worldwide [8, 9]. The 6–10 cm incision required for minimally invasive donor nephrectomy allows safe donation with significant benefits for living donors [10, 11, 15, 19, 20]. For the implantation of grafts, various minimally invasive approaches have been explored to minimize the complications associated with the OKT approach.

MODIFICATIONS OF THE TRADITIONAL SURGICAL APPROACH: MINIMAL SKIN INCISION AND LAPAROSCOPIC KIDNEY TRANSPLANT

To minimize wound-related morbidity, smaller open incisions of 7–10 cm have been trialled with limited success [21, 22]. Utilization of minimally invasive incisions requires careful patient selection, favouring those with lower BMI, thereby precluding its use in patients who may attain the greatest benefit. OKT through smaller incisions also increases the difficulty of already challenging vascular anastomoses, the most crucial technical component of a kidney transplant. The difficulty in balancing a minimally invasive cosmetic incision with a safe, effective vascular anastomosis, in conjunction with a restrictive patient cohort, has led to limited practice.
Following success with laparoscopic donor nephrectomy, attention inevitably moved towards attempting laparoscopic graft implantation. Rosales et al. [23] reported the first case of laparoscopic kidney transplantation (LKT) in 2010, also employing a smaller 7-cm incision to allow the graft to be placed in the abdomen. Modi et al. [24] demonstrated no difference in estimated glomerular filtration rate (eGFR) at 1 and 12 months between kidneys from single donors transplanted open and laparoscopically, respectively. However, operative and anastomotic times in the laparoscopic group were significantly longer. Modi et al. [25] also reported outcomes of 72 laparoscopic living donor transplants with successful outcomes. The LKT group required significantly lower quantities of morphine equivalent analgesia in the first 24 h post-operatively due to the minimally invasive incision. While eGFR was significantly less in the LKT group at days 7 and 30 post-operatively, no difference was observed between LKT and OKT at 3, 6, 12 and 18 months. Patient survival was also similar between the two groups, at 94.1% and 94.7%, respectively, at 22.3 months of follow-up. While the outcomes are comparable between OKT and LKT, the authors acknowledge the steep learning curve (LC) and need for further prospective randomized studies with large patient numbers to evaluate the actual benefits of LKT over OKT.

Despite the successes of Modi et al. [25], LKT has not been widely adopted, likely due to the challenges of performing vascular anastomosis with laparoscopic instruments and two-dimensional vision, causing loss of hand–eye coordination and the long instruments amplifying natural tremor and carrying a fulcrum effect, as well as poor ergonomics promoting surgeon fatigue [26]. These technical difficulties are unlikely to change and therefore LKT is likely to remain in a few highly specialized centres with extensive expertise. This poses a challenge to larger prospective randomized multicentre studies required to robustly assess the potential benefits of LKT versus OKT.

RAKT

Minimally invasive surgery has been enhanced by the introduction of robots (Figure 4), which has a well-established role across several surgical specialties. A robot offers more dexterity, increased geometric accuracy, enhances the abilities to measure surgeon performance and reduces tremors and fatigue.

The da Vinci surgical system (Intuitive Surgical, Sunnyvale, CA, USA) is the most widely used robotic system in many surgical specialities and has demonstrated significant clinical benefits to patients over the last two decades [27, 28]. The three-dimensional views restore hand–eye coordination, with wristed instruments and tracking of movements thousands of times per second providing tremor filtration and scaled motion. These features provide significant operative advantages over laparoscopic surgery, particularly when the operative field is
narrow and deep and fine dissection and microsuturing are required [28], as with the intrapelvic anastomoses of kidney transplantation. Seeking the benefits provided by the robot, several groups have pioneered robot-assisted donor nephrectomy and renal transplantation [29–32], with a significant reduction in surgical complications and graft outcomes compared with OKT. The first robot-assisted kidney transplant was performed in France in 2001 [33], when a cadaveric kidney was transplanted into a 26-year-old male using the da Vinci robot by a remote surgeon in another hospital, with an assistant in the operating theatre. While this ground-breaking achievement demonstrated the feasibility of RAKT, the authors commented that the operative time was greater than standard OKT and the cost of the procedure was extremely high.

Seven years later, Giulianotti et al. [29], from Chicago, performed the first full RAKT in a 29-year-old female with a BMI of 41 kg/m² via a 7-cm midline incision. The outcome was excellent, with immediate graft function, no perioperative complications and the patient safely discharged at day 5 with normal renal function. In 2011, Boggi et al. [30] reported the second European case of RAKT, a successful living-donor transplant from a 56-year-old mother to her 37-year-old daughter. The success of these pioneering single-case reports was built upon by a number of safety and feasibility studies [34,35], which provided improved methods of robotic positioning, access and use of regional hypothermia and graft cooling for implant. Vascular anastomoses take longer when performed robotically, leading to longer warm ischaemic times (WITs), which are known to partially compromise renal function when >30 min [36]. A phase 2a innovation study [35] introduced the technique of RAKT with regional hypothermia provided by a reproducible technique that allows cooling of the graft through a wrapped gauze filled with ice slush, delivered intraperitoneally during implant, creating safe regional hypothermia (see supplementary video). The benefits of RAKT have been reproduced since [31,32,37–40] and the results confirmed by the large prospective multicentre studies of the European Association of Urology: Robotic Urology Section (ERUS)–RAKT working group [41–44]. These reported experiences suggest RAKT achieves comparable patient and graft survival outcomes as compared with OKT, with the added benefits of minimally invasive surgery [45,46]. The ERUS–RAKT group [42] is currently the largest interna-
tional collaborative on RAKT, with 10 centres across Europe maintaining a prospective dataset of >300 patients undergoing RAKT [35]. Their recent update demonstrates good surgical and functional results, comparable with those of OKT [47].

RAKT in the obese patient

Positive outcomes inspired groups to use RAKT in an increasing number of settings, including deceased donation [48], polycystic kidney disease [40] and multiple vessel grafts in living donation [44]. However, most important is the use of RAKT in obese patients. The only current universal indication for RAKT, performed in the context of appropriately monitored prospective studies, is for those obese patients who would not otherwise be able to have a kidney transplant due to an unacceptable risk of morbidity. Obesity in renal transplantation is a growing problem, with the BMI of patients on the waiting list increasing annually [49]. In developed countries, the BMI of the population overall has continued to increase [50] and renal transplant candidates are no exception. An earlier study from the USA reported that between 1987 and 2001, the proportion of obese transplant recipients rose by 116% [51]. Traditionally, increased BMI was seen as a relative contraindication to renal transplantation, but recent data show considerable benefit in obese recipients [52]. Despite this, analysis of the United Network for Organ Sharing (UNOS) database revealed that 21% of transplant centres do not list morbidly obese patients [53], which may be an underestimation. Those listed wait an average of 50 months of a patient compared with the 40 months of non-obese patients [53]. The issue is further compounded by the ‘BMI paradox’, i.e. the fact that in the dialysis population, a high BMI is, up to a point, a marker of improved prognosis [54]. The obese population is at higher risk of post-operative SSI [55], with obese transplant recipients experiencing higher incidences of SSI, prolonged operative times and longer hospital stays [56–58]. Taken together, these facts have prompted a rethink and search for new strategies to address the issue. Bariatric surgery has been advocated in very obese transplant candidates [59], but access to this type of surgery is not universal. New approaches to successfully transplant the obese recipient are therefore eagerly awaited.

RAKT provides one such hope, with Oberholzer et al. [31] demonstrating successful transplant and favourable outcomes in RAKT compared with OKT in 28 morbidly obese patients. A group from Chicago compared 28 cases (average BMI 42.6) undergoing RAKT to a frequency-matched retrospective cohort of obese patients (average BMI 38.1) undergoing OKT. RAKT patients experienced significantly lower rates of SSI compared with the control group: 28.6% versus 3.6%, respectively. Patient and graft survival were 100% in both groups at 6 months and 6-month creatine was comparable between the two groups: 1.5 mg/dL versus 1.6 mg/dL in RAKT and OKT, respectively. This clearly shows superior outcomes in terms of SSI and the ability to offer transplantation to groups at high risk of complications. The group continues to demonstrate excellent outcomes [31], with recent data on 239 RAKTs with a mean BMI of 41.4 kg/m² highlighting a post-operative SSI rate of just 0.4%. Graft survival at years 1 and 3 was 98% and 93%, respectively, with a mean eGFR at 1 year of 56.5 ± 17.3 mL/min. Importantly, the group also demonstrated a low mortality of 4.6%, with patient survival of 98% and 95% at 1 and 3 years, respectively. While encouraging, the underlying message is that these results are from a dedicated single-centre experience with experienced surgeons who have passed associated LCs.

In addition to RAKT for obese patients, many teams have performed sleeve gastrectomy, and the safety was demonstrated by a randomized trial performed by Spaggiari et al. [60]. Eleven patients were recruited to a robotic sleeve gastrectomy and RAKT group and nine patients to RAKT alone. At the 1-year follow-up there was a significant (P = 0.0041) change in the BMI between the robotic sleeve gastrectomy and RAKT group (8.76 ± 1.82) compared with the RAKT-alone group (1.70 ± 2.30). There was no significant difference between the eGFR, serum creatinine, readmission rates and graft failure rates up to 12 months, although the length of surgery was longer in the robotic sleeve gastrectomy RAKT group (405 versus 269 min; P = 0.00304) with no difference in estimated blood loss.

Patient selection for RAKT

It is imperative that patients offered RAKT are selected on the basis of the following parameters: physiological reserve to undergo surgery using pneumoperitoneum, complexities in the donor kidney and the surgical team’s experience in performing RAKT. Many teams will consider multiple lower abdominal procedures, calcified aorto-iliac vessels and a lack of appropriate team members as absolute contraindications for RAKT. Robotic teams, after the LC, may consider transplanting grafts with multiple vessels and perform RAKT for patients receiving kidneys from deceased donors. However, most units offer RAKT for transplants from live donors only and Vignolini et al. [48] showed a five-phase approach to consider for teams to perform RAKT from deceased donors. They follow the same principles used to perform RAKT from live donors: availability of a team, operating room with a robot, suitable recipient, anatomical variation of the kidney and cold ischaemia time (CIT). Many units may consider offering RAKT from deceased donors in the time ahead, and the experience gained will offer the advantages of minimally invasive kidney transplant to more recipients.

Drawbacks of RAKT

A recent meta-analysis [61] of the six available controlled studies at the time, none of which were randomized, comparing RAKT (263 patients) and OKT (804) concluded that while there was no difference in WITs, RAKT was associated with a significantly longer cold ischaemia (mean difference: 4.78 min), re-warming (mean difference 20.83 min) and total ischaemia times (mean difference 17.82 min). This corresponded to slower improvement in creatinine clearance in the RAKT groups, however, this did not equate to any difference in delayed graft function (DGF), graft failure or all-cause mortality in either group at a relatively short mean follow-up of 31 months. Significantly longer warm ischaemia times have been reported by other groups [41, 42, 46], with long-term follow-up required to assess their impact on long-term patient and graft outcomes, given previous studies in OKT clearly demonstrate adverse long-term patient and graft survival with prolonged WITs [62]. In patients where the graft is placed intraperitoneally, there is a concern that the kidney will slide on the peritoneum, with resultant torsion of the allograft, necessitating fixation in the pelvis, which can make post-transplant biopsy difficult. In one series, seven patients required laparoscopic biopsy, with one converted to open [31]. While dual kidney transplantation, a well-recognized method of expanding criteria for deceased donor transplantation, has been performed robotically [63], the multiple anastomoses result in prolonged operative times and delayed graft function is seen in 33% of patients, making this technique less favourable.
Physiological considerations in RAKT

RAKT relies on insufflation of carbon dioxide to create pneumoperitoneum required for access, which provides unique physiological challenges. Renal function and renal blood flow are decreased during pneumoperitoneum [65, 66], with the magnitude of the decrease dependent on several factors, including the level of hydration and patient positioning, as well as the level and duration of pneumoperitoneum. Chiu et al. [67] demonstrated that at standard pneumoperitoneal pressures (12–15 mmHg), renal blood flow decreased to 25% of baseline. The graft kidney may therefore suffer a pneumoperitoneal injury during recipient surgery, compounded by potential previous injury if retrieval was performed laparoscopically from a living donor. From a physiological standpoint, the pneumoperitoneal injury in recipient surgery is only experienced after reperfusion of the graft. While some groups report no effect of pneumoperitoneum on early graft function [41], some RAKT groups routinely reduce the intra-abdominal pressures to 10 mmHg [47, 68] and even use a retroperitoneal approach [38] in an effort to reduce the deleterious effects of higher pressures on graft function. The Trendelenburg position (head down and elevation of the feet) used in RAKT can predispose the patient to head and neck oedema, including cerebral, tracheal and optic oedema [69–71]. In addition, the current da Vinci XI system allows patients to be positioned after docking the robot, thereby reducing the degree of Trendelenburg position required. In order to avoid these negative effects, intra-operative fluid infusion must be carefully titrated while maintaining adequate graft perfusion [72], highlighting a specific training requirement of anaesthetic teams in the peri-operative management of these patients.

Table 1. Advantages and disadvantages of RAKT

| Advantages | Disadvantages |
|------------|--------------|
| Intra-operative ease | Long operative times |
| – Magnification | \ |
| – Three-dimensional high definition | \ |
| – Higher degrees of freedom with robotic arms | \ |
| – Tremor filtration | \ |
| Improved post-operative recovery | Longer cold ischaemia, rewarming and total ischaemia times |
| – Reduced post-operative pain and analgesic requirement | \ |
| – Reduced length of hospital stay | \ |
| Reduced wound complications (e.g., surgical site infection, incisional hernia) | Difficult post-operative biopsy of transplant kidney |
| Improved cosmetic outcome | High cost |

Almost all of the studies previously discussed acknowledge that total cost is significantly higher in the robotic groups. With the increased use of robot-assisted surgery, new types of robots are being introduced to clinical practice (Figure 4), such as Versius by CMR Surgical (Cambridge, UK) and the Hugo Robotic System by Medtronic (Minneapolis, MN, USA), with the main advantages of these new systems being their reduced cost, and they are expected to increase access to robotic programmes across the globe. At present there are a lack of cost–benefit studies on the use of RAKT versus OKT and the proposed Markov model analysis from a group in Pittsburgh [64] is eagerly awaited. The above drawbacks of RAKT are not insignificant and the potential advantages (Table 1) for only a highly select group of patients must be considered and weighed carefully on a patient-by-patient basis.

LC

Every newly acquired technical skill comes with an associated LC, which in this case refers to the period of time during which surgeons find a procedure more difficult, take longer to perform it and observe a higher rate of complications with lower efficacy because of inexperience [73, 74]. Defining and objectively measuring a LC with set variables is not always possible because of unique procedure-specific steps. Therefore studies aiming to evaluate this LC set out to define the number of sequential procedures required to overcome the LC [74, 75]. The reported LC of RAKT is relatively short, with studies suggesting 20–35 cases are required to achieve operative and graft rewarming times competitive with those of OKT [47, 76, 77]. While the LC is currently assessed by time, it is suggested that neither total operative nor rewarming times correlate with post-operative serum creatinine levels at 7 and 30 days post-operatively or at the 1-year follow-up [77]. Therefore, other varied and more robust methods of assessment are required to ensure safe determination of graft-independent competency in RAKT.

Key to reducing the steepness of the LC is appropriate training. In RAKT, groups have developed laboratory training models with excellent results. Khanna et al. [78] describe a simple model of ex vivo kidney transplantation using the robotic technique, where vascular anastomoses were performed in 10 euthanized pig kidneys. With each sequential anastomosis there was improvement in the time taken to complete the procedure as well as a reduction of anastomotic leaks and ‘wasted moves’. Appropriate training also encompasses an essential extensive experience of both OKT and robotic surgery; only in those surgeons experienced in both is the LC of RAKT as short as the suggested 20–35 cases. Sood et al. [79] highlighted the importance of prior experience in both settings, with a well-constructed prospective study aiming to overcome the retrospective nature of LC assessment using subjective trajectories that limit generalisability. Data were prospectively collected in 41 patients undergoing RAKT with regional hypothermia, classified into three groups determined by surgeon training and OKT experience. Group 1 (n = 7) was a single surgeon with extensive robotic experience (>2000 cases) but limited OKT experience (<100 cases); Group 2 (n = 20) was a single surgeon with extensive robotic and OKT experience (>300 robotic and >2000 OKT cases) and Group 3 (n = 14) was a single surgeon with extensive OKT experience but limited robotic experience (>2000 OKT and <10 robotic cases).

The study showed the LC was minimal or absent in the robotic-trained groups compared with the significant LC seen in the non-robotic-trained group. The LC was not significantly affected by...
Kidney transplantation experience, likely because all surgeons were familiar with the pelvic anatomy. This highlights the importance of developing skills safely using simulated and cadaveric studies in preparation for adoption of a new technical interface, which could help reduce the LC in real-life patients [80]. The robot also provides the opportunity to monitor, track and analyse all movements of the surgeon. With the adjunct of artificial intelligence, this can provide user-specific feedback to help surgeons identify their strengths and weaknesses for better learning. It is imperative that centres considering the development of RAKT programmes ensure surgeons are well trained in robotic surgery as a priority, as well as OKT.

**ETHICAL CONSIDERATIONS**

While creativity and the introduction of novel technologies to improve outcomes and patient experiences is the norm in modern surgical practice, RAKT is perhaps a surgical field that highlights the ethical challenges of surgical innovation [81]. The primary endpoint of surgical transplantation is successful graft function that lasts for a lifetime. The ethical criteria that need to be considered by departments and individual surgeons seeking to introduce RAKT is whether robot-assisted transplantation provides a similar or better technical vascular anastomosis than an open approach and if incision-related morbidity is less than with an open procedure. These ethical considerations are similar to Knight’s assessment of innovations in cardiothoracic surgery, including minimally invasive cardiac surgery [82]. Based on these, any surgeon carrying out an RAKT should ask, ‘Can I, with my skill set, in my demographic practice, provide as good or better transplant graft and patient outcomes, when compared with an open implant, with a similar tariff?’ The variables addressed in such self-reflection should be openly discussed with the patient during the consent process, alongside the overall effectiveness of robotic procedures relative to other approaches.

Regular appraisal of surgical ability and outcomes, combined with institutional support for pioneering intervention, will allow safe and efficient progress. With every new approach that evolves, it is essential to continually assess the goals and outcomes that must be achieved, ensuring the procedure is held to the correct standard and patient safety preserved. Robotic surgery is still maturing and long-term follow-up of RAKT patients is as yet not available; we may find that outcome measures and early perceived benefits must be reassessed in light of long-term results. This is essential for all multidisciplinary teams and should be sought by referring physicians and funding bodies as well as surgical teams. Cost must also be borne in mind, ensuring a fair distribution of funding, particularly when transplant patients comprise a relatively small proportion of the wider populations that healthcare services treat.

Ultimately it is of the utmost importance that patients chose the right procedure for them, with the support of their team and careful explanation of appropriate literature, alongside honest conversations about risk, local expertise and the LC involved—true evidence-based medicine.

**CONCLUSIONS AND FUTURE DIRECTIONS**

The use of RAKT for better clinical outcomes has been established in the subgroup of patients who are obese and who may be declined by transplant programmes or who may develop complications after transplantation. Good outcomes have also been demonstrated in the non-obese patient cohort. However, there remain several important considerations before RAKT can be universally offered to all kidney transplant recipients. With the exponential integration of technological advances into surgical practice, it is likely that the integration of these techniques with RAKT will permit further refinements. While outcomes are still very much dependent on individual surgeon expertise, it is envisaged that in the next decade the integration of further digitization, ergonomic instrumentation and artificial intelligence within robotics will exponentially improve RAKT outcomes.

**SUPPLEMENTARY DATA**

Supplementary data are available at *ckj* online.

**CONFLICT OF INTEREST STATEMENT**

A.W. is a member of the *CKJ* Editorial Board. This article has not been published previously, in whole or in part.

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