



Does the Surgical Technique Affect the Results of Partial Nephrectomy Performed for Renal Cell Carcinoma? Single-center 'MIC' Score and 'Trifecta' Results

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Abstract

Introduction: To report the MIC scores and trifecta rates in patients who underwent partial nephrectomy with open (OPN), laparoscopic (LPN) and robot-assisted techniques (RPN) due to kidney tumor.

Methods: Demographic characteristics, tumor characteristics, peri- and post-operative data and complications of the patients who underwent OPN (n=58), LPN (n=32) and RPN (n=126) between 2007 and August 2018 due to kidney tumor and histopathological features were evaluated retrospectively in this study. To report oncological and functional outcomes of nephron-sparing surgery for renal tumors, MIC (surgical margin negativity, ischemia duration less than 20 minutes and lack of complication) and Trifecta (surgical margin negativity, perioperative complications and glomerular filtration rate (GFR) >90% protection rate) were used.

Results: RPN was superior to OPN technique in hospitalization and estimated bleeding. Transfusion rate and all complications were similar in all three techniques. Although OPN had shorter operation time and ischemia time, there was a higher amount of blood loss and hospital stay. No significant difference was found between all three techniques for surgical margin positivity and >90% preservation of GFR. The mean duration of warm ischemia was 23.6 minutes with the longest LPN, followed by a mean of 18.4 minutes with an RPN and a mean of 16.6 minutes with OPN (p=0.003). It was significantly longer. Our MIC score was 79% in OPN, 71% in LPN and 81.7% in RPN (p=0.04). Our Trifecta rates were 87% in OPN, 87.5% in LPN and 93.6% in RPN (p=0.128).

Discussion and Conclusion: Both the 'MIC score system' and the 'Trifecta' system are easy to use and reproducible systems for reporting partial nephrectomy results for renal tumors. Robot-assisted partial nephrectomy is the most powerful alternative technique for open partial nephrectomy with low complication rates, shorter operation time, similar ischemia durations and oncologic outcomes.

Keywords: Laparoscopic; MIC score; open; partial nephrectomy; robotic; trifecta.

Kidney cancers are the third most common urological malignancy, and it is estimated to account for approximately 3% of all cancer-related deaths [1]. According to the International Agency for Research on Cancer (IARC), RCC is the 9th most common malignancy in men and in 2018, over 400.000 new cases were identified. In the U.S., 3.8% of all

cancer cases are kidney tumors, and in 2014, 63.920 new cases and 13.860 kidney cancer-related deaths were estimated [2]. Historically, standard surgical treatment for all kidney masses was radical nephrectomy (RN) [3]. Nephron-sparing surgery has become widespread in small kidney masses due to increased end-stage renal failure and car-

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diac events [4]. Partial nephrectomy (PN) is accepted as the first choice method in the surgical management of local stage T1 (<7cm) renal cell carcinomas (RCCs).

Laparoscopic partial nephrectomy (LPN) has gained popularity as a result of the development of technology and the improvement in imaging and surgical equipment. LPN technique was widely accepted, with decreased blood loss, shortened hospital stay and incisions, and reduced operative morbidity [6]. Because LPN has a long learning curve due to the difficulty of suturing within the body, the minimal invasive technique of robot-assisted partial nephrectomy (RPN), which is an alternative to open and laparoscopic partial nephrectomy has become widespread.

In this study, we aimed to report the surgical, functional and oncological results of PN cases that we are performing with three different techniques in our clinic with the indication of kidney tumor together with their MIC scores and trifecta rates.

Materials and Methods

Following the approval of the institutional ethics committee, data related to 58 OPNs applied by five different surgeons between 2007 and August 2018, 32 LPNs performed by one surgeon between 2010 and 2014, and 126 RPNs realized by three different surgeons between 2008 and August 2018 were retrospectively analyzed by four different surgeons. Abdominal computed tomography (CT) or magnetic resonance (MR) images were examined and the data were recorded.

Tumor size was recorded as the longest diameter observed in CT or MR. R.E.N.A.L nephelometry scores {Kutikov, 2009 # 53} of all tumors were determined and recorded. Demographic data, mean operation times, the estimated amount of bleeding, warm ischemia times, hospital stay, renal functions before and after the operation, complications and oncological results were recorded. The preoperative serum creatinine level and e-GFR were calculated using the MDRD (Modification of Diet in Kidney Disease) formula {Levey, 2006 # 54}. Patients with a solitary kidney, a follow-up period of fewer than six months and incomplete data were excluded from this study. All complications seen within 30 days were recorded according to the modified Clavien-Dindo classification {Clavien, 2009 # 55}. According to the Modified Clavien-Dindo classification, Grade 1-2 complications were minor complications, and complications of grade 3 and above were major complications.

In the selection of nephron-sparing surgery group of patients, the operation technique was determined by consid-

ering the comorbidities of the patients, their performance status, previous abdominal or kidney surgeries, and localization of tumors, complexity scores and patients' wishes. Mostly, open technique was performed in patients with high cardio-respiratory risk factors who could not tolerate pneumoperitoneum, the patients with a history of abdominal or kidney operation. There was no difference between laparoscopic and robotic surgery techniques for patient selection. While the open technique was applied by five different surgeons, the laparoscopic technique was applied between 2010-2014 by the only surgeon who had open and robotic surgery experience. RPN was performed by three different surgeons with open and laparoscopic surgery experience. The majority of RPN cases have been carried out in the past three years.

The MIC score system for kidney tumors was defined by Buffi et al. [8] in the year 2012 as surgical margin negativity (Margin), warm ischemia times (Ischemia) less than 20 minutes, and lack of any major complications (Complication). The concept of 'Trifecta' comprised components of surgical margin negativity after partial nephrectomy, absence of perioperative complications and preservation of estimated glomerular filtration rate (e-GFR) above 90% [9].

All statistical analyzes were performed using SPSS statistics 20 (IBM, Armonk, NY, USA) software. Descriptive statistics were analyzed using Student's t-test and chi-square test. Nonparametric Mann-Whitney U or Wilcoxon Rank Sum Test was used for variables with non-normal distribution when appropriate. One-way ANOVA analysis was used for triple comparisons. The confidence interval was taken as 95% and $p < 0.05$ was considered to be statistically significant.

Surgical Technique Open Partial Nephrectomy (OPN)

According to the localization of the renal masses, operations were performed with a transperitoneal approach through Chevron incision and with the retroperitoneal approach through the flank incision. Tumor boundaries were determined using intraoperative ultrasound following mobilization of the kidney and dissection of the renal pedicle, arteries and veins. The renal artery was clamped with two bulldog clamps. The tumor was excised with cold scissors, leaving adequate surgical margins. The tumor bed was continuously sutured using 3-0 absorbable sutures that did not slip backward and the parenchyma was approximated. Parenchymal defect was closed using hemostatic agents (Flo seal, Baxter, Inc., Irvine, CA, USA). Renal parenchyma was approximated with 0-0 polyglactin sutures with CT-1 needle and renography was performed by approximating renal parenchyma using hemoclips.

B. Laparoscopic Partial Nephrectomy (LPN)

Following endotracheal intubation under general anesthesia, the patients were laid in a modified 60-degree lateral decubitus position. After pneumoperitoneum was achieved, three ports were placed for the transperitoneal approach. The fourth port was placed for the retraction of the liver in cases with upper pole tumors on the right side. Renal hilum was dissected cranially by medializing the colon and isolating the gonadal vein. Contours and depth of the tumor were determined using intraoperative laparoscopic USG. After the preparation of renal hilum, the Gerota fascia was opened using monopolar scissors and borders of the tumor were marked. Two 15 cm 3.0 polyglacton 26mm 1/2 barbed sutures were placed in the abdomen for the repair of the parenchyma (V-loc, Covidien, Ireland).

Two laparoscopic bulldog clamps were placed in the renal artery and tumor resection was performed with cold scissors. The tumor bed was sutured with a 3.0 absorbable suture that did not slip back continuously. Parenchymal defect was closed using hemostatic agents (FloSeal, Baxter, Inc., Irvine, CA, USA). Parenchyma was sutured using 0-0 polyglactin sutures with CT-1 needle and brought closer with hemoclips using the sliding-clip renorrhaphy technique. After the repair, the bulldog clamps were removed, bleeding was checked, and the operation was terminated by removing the tumor and placing the drain.

Robot-assisted Partial Nephrectomy (RPN)

The operation was started with four ports including three robotic ports and one assist port using a transperitoneal approach for all patients. Following endotracheal general anesthesia, patients were laid in approximately 60 degrees

of modified lateral decubitus position. The fourth port was placed for liver excision in the upper pole tumors on the right side. Da Vinci Si Robot (Intuitive Surgical Inc, Sunnyvale, CA, USA) was used between 2008-2014 and Da Vinci XiRobot (Intuitive Surgical, Sunnyvale, CA, USA) is being used since 2014. In the following stages, the same technique was applied with LPN.

Follow-up

After all patients underwent extensive biochemical examination in the first, third and sixth months after the operation, annual examinations were performed in the first two years and later in six month-intervals. As imaging follow-up, abdominal USG and chest radiograms were evaluated in the first three months and thoracoabdominal computed tomography in the sixth month. Subsequently, follow-ups continued with annual cross-sectional examinations.

Results

A total of 216 patients with complete data were included in our study. Patients who had undergone partial nephrectomies due to indications other than RCC, solitary kidney patients, cases with bilateral kidney tumors or multifocal tumors, patients undergoing cold ischemia, and those with missing data were not included in this study.

In our series, OPN was applied to 58, LPN to 32 and RPN to 126 patients. The demographic characteristics of the patients are summarized in Table 1. The mean ages of the patients were 57 years in OPN, 56 years in LPN and 54 years in RPN groups ($p=0.62$). Average body mass indices were 27.5 kg/m^2 in OPN, 28.2 kg/m^2 in LPN and 28.7 kg/m^2 in RPN groups. The preoperative ASA scores of the patients

Table 1. Demographic data

Demographic data	Group OPN	Group LPN	Group RPN	P
Patients (n)	58	32	126	
Mean±SD, age years	56±13.5	56±15.4	54±12	0.62
Gender, (male/female)	35/21	19/13	87/39	
Mean±SD, body mass indices kg/m^2	27.5±3.3	28.2±3.4	28.7±3.1	0.842
ASA score±SD	1.95±0.5	1.3±0.6	1.85±0.7	0.038
Age-adjusted Charlson comorbidity index, mean±SD	1.55	1.6±0.9	1.91±1.1	0.420
Laterality of the renal tumor (right/left)	35/23	18/14	78/48	0.172
The longest diameters of the tumor mean±SD, cm	4.32±2.3	4.1±1.2	3.88±1.4	0.360
Mean±SD, R.E.N.A.L. nephrometry scores,	6.44±1.8	5.1±4-8	6.1±1.6	0.08
Low complexity (4-6), n (%)	17 (29)	21 (65)	52 (41)	0.238
Moderate complexity (7-9), n (%)	29 (50)	7 (21)	47 (37)	0.198
High complexity (10-12), n (%)	12 (21)	4 (12)	27 (22)	0.525
Mean±SD, preoperative hematocrit, %	40.1±5.2	40.7±4.1	39.8±3.7	0.243

Table 2. Perioperative features

Perioperative features	Group OPN	Group LPN	Group RAPN	p
Mean±SD, operation times, min	145±18	195±26	184±42	0.002
Estimated blood loss, ml±SD	154±85	218±104	110±81	0.012
Warm ischemia time, min±SD	16.6±3.8	23.6±9.4	18.4±8.2	0.003
Hilar clamping, n (%)	58 (100)	32 (100)	126 (100)	
Average duration of drainage days	3.853.5	3.1	0.37	
Mean±SD, hospital stay, days	5.6±2	4.2±2.2	3.8±1.5	0.04
Transfusion rate, n (%)	5/58 (8.6)	2/32 (6.2)	6/126 (4.7)	0.18
Intraoperative complications, n (%)	2/58 (3.4)	3/32 (9.3)	3/126 (2.3)	0.125
Postoperative complications, n (%)	7/586/32	9/126	0.63	
Clavien I-II	4/584/32	6/126	0.80	
Clavien>III	3/58 (5.1)	2/32 (6)	3/126 (2.3)	0.42

Table 3. Complications

Complications	Time	Treatment	Clavien Grade	OPN	LPN	RPN
Perirenal hematoma	Early post-operative	Medical treatment	2	2	1	4
Hematuria/hematoma	Early post-operative	Medical treatment	2	1	1	2
Hematuria/hematoma	Early post-operative	Blood transfusion	2	2	2	2
Hematuria/hematoma	Early post-operative	Angioembolization	3	3	2	3
Pleura injury	Intraoperative	Intraoperative repair	-	2	1	2
Renal vein injury	Intraoperative	Intraoperative repair	-	1	1	2
Vena cava inferior injury	Intraoperative	Intraoperative repair	-	-	-	1

were 1.95 (0.5) in the OPN group 1.3 (0.6) in the LPN group and 1.85 (0.7) in the RAPN group. ASA scores of the RAPN and OPN groups were significantly higher than those of the LPN group ($p=0.038$).

Mean values for the longest diameters of the tumors were 4.32 ± 2.3 cm in the OPN, 4.1 ± 1.2 cm in the LPN and 3.88 ± 1.4 cm in the RPN groups. Mean R.E.N.A.L. nephrometry scores were 6.44 ± 1.8 in the APN, $5.1\pm 4-8$ in the LPN and 6.1 ± 1.6 in the RPN groups. Mean operation times were 145 ± 18 min in OPN, 195 ± 26 min in LPN, 184 ± 42 min in RPN groups. Statistically significant differences were detected in operation times with the shortest and longest operation times being detected in OPN and ILPN groups, respectively ($p<0.002$). Mean values for the estimated amount of blood loss were 154 ± 85 ml in OPN, 218 ± 104 ml in LPN and 110 ± 81 ml in RAPN ($p=0.012$). Mean values for warm ischemia times were statistically significant and they were 16.6 ± 3.8 min in the OPN, 23.6 ± 9.4 min in the LPN and 18.4 ± 8.2 min in the RPN groups.

Warm ischemia times were less than 20 min in 94%, 81.24%, and 90% of the patients in the APN, LPN and RPN groups, respectively. The average hospital stay was 5.6 ± 2 days in the OPN, 4.2 ± 2.2 days in the LPN, and 3.8 ± 1.5 days in the RPN

groups. There was a significant statistical difference among all three groups in terms of hospital stay ($p=0.04$). There was no significant difference in transfusion rates among OPN (8.6%), LPN (6.2%), and RPN (4.7%) groups ($p=0.18$) (Table 2).

In our study, postoperative grade 1-2 complication rates according to the modified Clavien-Dindo classification were determined as 6.86% (4/58) in OPN, 12.5% (4/32) in LPN and 4.7% (6/126) in RPN groups. According to the modified Clavien-Dindo classification, grade 3 and above complications were 5.1% (3/58) in the APN, 6% (2/32) in the LPN and 2.3% (3/126) in the RPN groups without any statistically significant difference among groups ($p=0.125$) (Table 3).

The change in estimated glomerular filtration rates (e-GFR) was found by comparing the preoperative values with those obtained at postoperative third months. The average preoperative e-GFR was 87 ml/min in the OPN group, with an 8% decrease; it dropped to 80 ml/min in the postoperative 3rd month. The average preoperative e-GFR was 89 ml/min in the LPN group, with a 12.3% decrease; it dropped to 78 ml/min at the post-operative 3rd month. The average preoperative e-GFR was 94 ml/min in the RPN group, with an 8.5% decrease; it dropped to 86 ml/min at the postoperative 3rd month. Estimated glomerular filtration rates were

Table 4. Preoperative and postoperative renal functions

Preoperative and postoperative functions	Group OPN	Group LPN	Group RPN	p
Mean serum creatinine (mg/dl)				
Preoperative	0.93	0.96 (0.71-2.28)	0.89	0.90
Postoperative first day	1.22	1.05	1.16	0.48
Postoperative third month	1.02	1.02	0.98	
p	0.002	<0.001	0.003	
Mean e-GFR (ml/min/1.73 m ²)				
Preoperative	87	89	94	0.44
Postoperative third month	80	78	86	0.36
Decrease in e-GFR	8ml/min	12.3 ml/min	8.5 ml/min	0.40
>90% preservation of e-GFR	53/58 (92%)	28/32(87.5%)	114/126 (90.4%)	0.24

Table 5. Oncological results

Oncological Results	OPN	LPN	RAPN	p
Malignant histology (RHK), n (%)	54/58 (93)	29/32 (90.6)	113/126(89.6)	0.186
Subtypes, n (%)				0.360
Clear cell type	39 (72)	20 (68)	87 (76)	
Papillary type	9 (16)	6 (21)	17 (15)	
Chromophobe type	6 (11)	3 (11)	9 (7.9)	
Pathologic grade of malignant tumors (%)				0.248
Pt1a	34 (62.9)	20 (68.9)	83 (73.4)	
Pt1b	13 (24)	7 (24)	24 (21.2)	
Pt3a	8 (14.8)	2 (6.8)	6 (5.3)	
Fuhrman grade, n (%)				0.796
1	7 (13)	6 (20)	28 (24)	
2	41 (75)	16 (55)	58 (51)	
3	4 (7.4)	5 (18)	19 (17)	
4	2 (3)	2 (7)	7 (6)	
Benign histology, n (%)	4 (6.8)	3 (9.3)	13 (10.3)	0.644
Subtypes, n (%)				
Angiomyolipoma	2 (3.4)	1 (3.1)	4 (3.1)	
Oncocytoma	2 (3.4)	2 (6.2)	6 (4.7)	
Benign cyst	-	-	3 (2.3)	
Surgical margin positivity, n (%)	2 (3.7)	2 (6.8)	6 (5.3)	0.18
Local recurrence, n	1 (1.7)	1 (3.1)	4 (3.1)	
Average follow-up period, month (SD)	33 (20)	36 (12)	42 (8)	
Margin, ischemia, complication (MIC) Scores	46/58 (79.3)	23 (71)	103 (81.7)	0.04
Trifecta rates	51/58 (87)	4/32 (87.5)	118/126 (93.6)	0.128

maintained above 90% in 92% (53/58), 87.5% (28/32), and 90.4% (114/126) of the patients in the OPN, LPN, and RPN groups, respectively without any significant difference in the preservation rates of e-GFR among techniques (Table 4).

The oncological results of the patients are summarized in Table 5. The malignant histology was found in 93% (54/58), 90.6% (29/32), and 89.6% (113/126) of the patients in the APN, LPN, and RPN groups, respectively. Surgical margin

positivities were found in 3.7% (2/58), 6.8% (2/32), and 5.3% (6/126) of the patients in the OPN, LPN, and RPN groups, respectively without any statistically significant difference among groups as for surgical margin positivity (p=0.18).

The MIC scores which include surgical margin negativity, ischemia times less than 20 minutes, and absence of Clavien-Dindo grade ≥ 3 complications, were found in 79.3%, 71%, and 81.7% of the patients in our OPN, LPN, and RPN series,

respectively. The difference was statistically significant ($p=0.04$) with a statistically significant difference among groups.

Our 'Trifecta' rates which take surgical margin negativity, lack of modified Clavien-Dindo grade ≥ 3 complications and preservation of e-GFR over 90% into account were estimated as 87%, 87.5% and 93.6% of our patients in our OPN, LPN and RPN series, respectively without any statistically significant difference among techniques concerning Trifecta rates ($p=0.124$).

Discussion

In international guidelines, partial nephrectomy for kidney tumors in the clinical T1 (<7 cm) stage has been reported to provide cancer-specific survival rates comparable to radical nephrectomy [5]. OPN has been used as the gold standard treatment method for many years. Minimally invasive surgical techniques as LPN and RPN have found widespread use in urological surgery in recent years and have become an important alternative to open technique. Main objectives in nephron-sparing surgery are oncological control, preservation of renal functions with lower morbidity and complication rates.

Since the LPN technique requires an advanced laparoscopic experience and ability, its learning and education have been limited apart from experienced laparoscopic surgery centers. In contrast, the RPN technique has improved the functional outcomes by providing shorter console and ischemia times by overcoming the difficulties in learning, such as the two-dimensional view of the conventional laparoscopy, and limitations in wrist movements.

In our series, surgical margin positivity rates were 3.7% (2/58) in OPN, 6.8% (2/32) in LPN, and 5.3% (6/126) RPN groups. In a study by Masson-Lecomte et al. surgical margin positivity rates were reported as 6.9% in open nephrectomy, and 2.4% in robot-assisted partial nephrectomy [10] Ricciardulli et al. [11] reported surgical margin positivity rates in laparoscopic and robot-assisted partial nephrectomies as 5%, and 8.3%, respectively. Our surgical margin positivity rates were similar to the studies reported in the literature.

The warm ischemia times were 16.6 (3.8) min in the OPN and 23.6 (9.4) min in the LPN, and 18.4 (8.2) min in the RPN groups, with a statistically significant intergroup difference ($p=0.003$). Warm ischemia times were less than 20 min in 94%, 81.24%, and 90% of the patients in OPN, LPN and RPN groups, respectively. In a study by BM Benway et al., [12] average warm ischemia times were found as 28.4 min in LPN,

and 19.7 min in RPN. In a study by LA Deane et al., warm ischemia times were found as 35.3 min for LPN and 32.1 min for RPN. While our warm ischemia times in OPN were similar to the studies in the literature but shorter than indicated for RPN and LPN. As a result, we think that our clinic is an experienced clinic in robotic surgery and its effective because these surgeries are being performed by surgeons who have completed their learning curves in RPN and LPN.

In our study, our intraoperative complication rates were 3.4% (2/58) in OPN, 9.3% (3/32) in LPN and 2.3% (3/126) in RPN groups. According to the modified Clavien-Dindo classification, postoperative grade 1-2 complication rates were 6.86% (4/58) in OPN, 12.5% (4/32) in LPN and 4.7% (6/126) in RPN groups. According to the Modified Clavien-Dindo classification, postoperative grade ≥ 3 complication rates were (5.1%) (3/58) in OPN, 6% (2/32) in LPN, and 2.3% (3/126) in RPN groups, without any statistically significant difference among groups ($p=0.125$). In a study where Ricciardulli et al. compared laparoscopic and robot-assisted partial nephrectomies concerning intraoperative complication rates, complication rates were reported as 10.5% in LPN and 6.9% in RPN groups [11]. Minervini et al. [14] compared open and robot-assisted partial nephrectomy results, and reported the rates of all complications as 17.9% in OPN, 15% in RPN groups without any statistically significant intergroup differences. They also reported comparable Clavien grade 2-3 complication rates. Our intraoperative and postoperative complication rates were similar for all three techniques to those cited in the literature.

In our study, MIC scores were 79.3% in OPN, 71% in LPN and 81.7% in RPN series without any statistically significant intergroup differences ($p=0.04$). In their study comparing laparoscopic and robot-assisted partial nephrectomies, Ricciardulli et al. [11] reported their MIC scores as 55% for LPN and 65.5% for RPN techniques. Buffi et al. reported their MIC score as 75.8% for RPN. As the surgical experience increased, the average MIC score of 66.7% in the first third part of the study increased to 87.9% in the last third part [8]. We determined that our MIC scores were higher than the studies reported in the literature.

Our "Trifecta" rates were 87% in OPN, 87.5% in LPN, and 93.6% in RPN series, without any statistical significance among techniques concerning Trifecta rates ($p=0.124$). Minervini et al. [14] reported their trifecta rates in their laparoscopic partial nephrectomy series as 78.6% in OPN and 74.3% in LPN without any statistical significance between techniques in terms of trifecta rates. Similar to the studies in the literature, we found that our trifecta rates were sim-

ilar for all three techniques. We have determined that our Trifecta results are superior to the results reported in similar studies. In our series, the results of the robotic technique can be seen to be more successful than those reported in the literature, and that our clinic is a center with more than 1500 robotic case experiences and it can be applied by three surgeons who have completed the learning curve in open surgery. Laparoscopic operations were performed by the only surgeon with open and robotic surgery experience.

Conclusion

Both the "MIC score system" and the "Trifecta" system can provide an objective standardization in reporting the partial nephrectomy results applied for kidney tumors. Robot-assisted partial nephrectomy is the strongest alternative technique to open partial nephrectomy with low complication rates, while shorter operation time compared to laparoscopic technique, with warm ischemia times, and oncological results similar to open surgery. Learning and teaching the laparoscopic technique are very dependent on surgical ability and clinical possibilities; thus, it is difficult to report objective results.

Ethics Committee Approval: The Ethics Committee of Umraniye Teaching Hospital provided the ethics committee approval for this study (08.09.2018-2018/108).

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