Treatment of Osteonecrosis of the Knee

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Spontaneous Osteonecrosis of the Knee

Spontaneous osteonecrosis of the knee is a unilateral and unifocal disorder commonly affecting the medial femoral condylar epiphysis. The medial tibial plateau, patella or the lateral femoral condyle can also be affected with a lower incidence [1]. Reddy and Frederick reported that the medial femoral condylar predominance can be explained by poor arterial supply of the medial femoral condyle compared with the lateral femoral condyle [2].

Etiology and Pathogenesis

Recent studies suggest that the underlying pathology of spontaneous osteonecrosis of the knee is based on repetitive unstable insufficiency fractures of subchondral bone, not necrosis resulting from poor microcirculation to the subchondral bone. Robertson et al. reported that, 80% of the patients had meniscal posterior horn injury in a series of 30 patients with spontaneous osteonecrosis of the medial femoral condyle [3]. A recent study of 22 knees with spontaneous osteonecrosis in 21 patients reported that, 14 (64%) specimens showed osteopaenia and 15 (68%) evidence of osteoarthritis with no evidence of dead bone or osteonecrosis [4]. Yamamoto et al. reported that the primary event leading to spontaneous osteonecrosis of the knee is a subchondral insufficiency fracture and that the localized osteonecrosis seen in association with this disease is the result of a fracture [5]. Another study supporting this finding showed that, insufficiency fractures are seen on MRI at sub-acute presentation of patients with spontaneous osteonecrosis [6]. These findings imply that, spontaneous osteonecrosis of the knee is a misnomer and actually the underlying pathology is an unstable fracture. The bone death is related to the physiological bone resorption and remodelling of the unstable displaced fracture fragment.

Secondary Osteonecrosis

Secondary osteonecrosis of the knee is a multifocal, generally bilateral, knee-threatening disorder of typically young adults (<45). The epiphysis, metaphysis, and diaphysis can be affected simultaneously (Fig. 1). Silent onset with mild or non-specific symptoms is followed by bilateral joint collapse after multi-focal subchondral fractures leading to the need for arthroplasty. The knee is the second most affected joint after the hip [7, 8].

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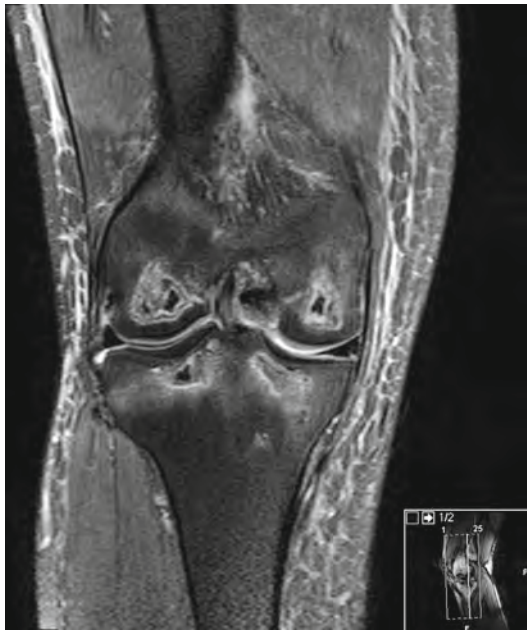

Fig. 1 19 year-old male. Extensive steroid-induced osteonecrosis of the knee. Coronal T2-weighted MRI image demonstrating an area of low signal intensity surrounded by high signal intensity caused by edema of both medial and lateral femoral condyles and tibia

Risk Factors, etiology, and Pathogenesis

Although the pathogenesis of secondary knee osteonecrosis is not well known, there are two conditions leading to focal ischemia and necrosis: elevated intra-osseous pressure and circulatory disruption. Uchio et al. reported that, the intra-osseous pressure of the medial condyle of the knees with osteonecrosis (62.8 ± 27.3 mmHg) is significantly higher than that in the lateral condyle of the knees with osteonecrosis (25.4 ± 18.9 mmHg) and those of both condyles of the knees with osteoarthritis (medial, 31.6 ± 17.4 mmHg; lateral, 29.5 ± 11.0 mmHg) [9]. Elevated intra-osseous pressure and circulatory disruption cause necrotic wedge- shaped osseous regions reaching subchondral bone. Lack of circulation limits repair and causes healing with granulation tissue. Weak subchondral bone without adequate mechanical support causes subchondral fractures and cartilage degeneration further leading to collapse of the related condyle. Multi-focality, size and location of osteonecrosis influence the progression of the disease. Spontaneous resolution may be seen in cases with small, unifocal lesions but generally (>90%) the lesion progresses [10].

Corticosteroid use and alcohol abuse are the most common risk factors associated with secondary knee osteonecrosis by increasing intra-osseous adipocyte size and proliferation. Increased pressure of non-expansile bone resulting from adipocyte hyperproliferation causes vascular collapse and ischaemia, but the specific mechanism is still unclear [11, 12]. Liu et al. reported a correlation between alcohol-induced osteonecrosis and the single nucleotide polymorphisms of methylene tetrahydrofolate reductase (MTHFR) 677 C/T [13]. In an experimental study, Bekler and colleagues noted a significant increase of osteonecrosis after corticosteroid use in rats with serum disease compared to healthy and control groups [14]. Lieberman et al. evaluated 204 patients who underwent cardiac transplantation and were treated with corticosteroids and noted that only 6 (3%) of 204 patients developed symptomatic osteonecrosis of the hip or knee. There was no correlation between steroid dose and development of symptomatic osteonecrosis showing that development of osteonecrosis associated to corticosteroids is an idiosyncratic response to steroids, perhaps related to an underlying hypercoagulable state or hypofibrinolysis [15]. Less common causes like sickle-cell disease and Caisson disease lead to osteonecrosis with direct occlusion of blood vessels. Gaucher disease, coagulation abnormalities, myeloproliferative disorders, inflammatory bowel disease and systemic lupus erythematosus are indirect factors causing secondary osteonecrosis of the knee by increasing intra-osseous pressure [16–20]. Genetic risk factors associated with secondary osteonecrosis have been reported recently by some authors. Their findings may help in better understanding the pathogenesis of secondary osteonecrosis [21, 22]. Liu et al. reported on three families with autosomal dominant inheritance of osteonecrosis by a mutation of type II collagen [23].

Table 1 Comparison of the three forms of osteonecrosis of the knee

	Spontaneous ON	Secondary ON	Postarthroscopic ON
Age	>50	<45	Any
Sex	F/M:3/1	Predominantly in men (except SLE)	Any
Bilaterality	<5%	>80%	No
Multiple joint involvement	No	>90%	No
Risk factors	Idiopathic, chronic mechanical stress, microtrauma	Direct: trauma, Gaucher disease, radiation, Caisson disease, chemotherapy Indirect: alcohol abuse, coagulation abnormalities, corticosteroid use, inflammatory bowel disease, organ transplantation, SLE, smoking	Arthroscopic meniscectomy, anterior cruciate ligament reconstruction, laser or radiofrequency use, cartilage debridement
Mechanism of pathology	Repeating subchondral unstable insufficiency fractures of weight-bearing condyle	Direct cell injury Occlusion of blood supply Increased intra-osseous pressure	Abnormal loading, inflammation, increased intra-osseous pressure, thermal or photoacoustic injury
Pathologic findings	Fibrotic bone with fracture healing, osteopenia and osteoarthritis	Necrotic bone	Fibrotic bone with fracture healing, osteonecrosis with direct injury

Post-arthroscopic Osteonecrosis of the Knee

Post-arthroscopic osteonecrosis of the knee is an extremely rare but often a destructive disorder. The pathophysiology of this disorder is still unclear. Different mechanisms are advocated. MacDessi et al. reported on a case series of eight patients with osteonecrosis who had undergone arthroscopic medial meniscectomy. Four patients had essentially intact articular cartilage overlying the lesion, which was characterized by disruption of the trabecular architecture indicative of subchondral bone fracture [24]. Bonutti et al. reported that arthroscopic procedures may play a role in the development of the osteonecrosis [25]. Post-arthroscopic osteonecrosis may be a result of the increased stress after meniscectomy acting across the joint leading to insufficiency fractures or microfractures of the subchondral bone in spite of intact cartilage [26]. Another possible mechanism described by some authors is direct thermal damage and photo-acoustic shock leading to an inflammatory process at the subchondral bone causing edema and necrosis [27–29]. Pape et al. underlined a terminologically important point about this devastating complication of arthroscopic surgery. The term "Post-arthroscopic osteonecrosis" may be medico-legally problematic and wrongly regarding the arthroscopic surgery as the primary cause for osteonecrosis and suggested using the descriptive term "Osteonecrosis in the post-operative knee". This would accommodate the possibility of undiagnosed early stage preoperative spontaneous osteonecrosis [30].

The comparison of the three types of knee ON is summarized in Table 1.

Diagnosis

Clinical Investigations

Patients with osteonecrosis often have nonspecific knee pain similar to patients with meniscal or ligamentous injury. However, the possible devastating results of osteonecrosis makes early diagnosis important. The patient may have a trauma history that can aggravate the symptoms.

Clinical assessment has a significant value for the diagnosis of osteonecrosis. The clinician should be suspicious of demographic factors and risk factors associated with osteonecrosis. Despite spontaneous osteonecrosis, secondary osteonecrosis is more common in men than women with the exception of SLE. Secondary osteonecrosis is typically seen in young adults often aged <45 years. Because of bilateral and multiple joint involvement of secondary osteonecrosis, other joints should be carefully examined too.

Radiographic Investigations

Current opinion underlines the importance of MRI for early diagnosis and plain radiographs for staging. Bilateral AP and lateral radiographs should be initially evaluated for all affected joints. Although no radiographic evidence or minimal sclerosis should be seen in early phases of osteonecrosis, radiographic screening is an inexpensive way to help with differential diagnosis, classification and assessment of progression. MRI is the radiographic "gold standard" for early diagnosis of osteonecrosis, but initial findings of ischaemia are generally non-specific. MRI is very sensitive for the detection of marrow abnormalities. The initial finding of osteonecrosis "bone marrow edema" is seen as an area of low signal intensity on T1-weighted images, associated with intermediate or high signal intensity findings on T2-weighted images but is a non-specific finding with multiple etiologies such as trauma or non-traumatic disorders: red marrow proliferation, stress, osteochondral lesions, osteonecrosis, bone marrow edema syndrome, arthropathy, infection, Paget's disease, and marrow replacement disorders. The clinician should be conscious of disease–specific signs like serpentine signs with a demarcation line for patients with one or more risk factors [31]. Secondary osteonecrosis of the knee is a multi-focal and bilateral disorder with common involvement of the hips. After detailed clinical examination, suspected joints should be assessed with MRI and bilateral plain radiographs. There are several reports pointing out non-symptomatic multi-joint involvement in secondary osteonecrosis diagnosed with MRI. Mont et al. reported symptomatic or non-symptomatic hip joint involvement in 67% of patients with secondary osteonecrosis [8].

Previously, radionucleotide bone scanning was advocated for diagnosis of early stage osteonecrosis, but recent studies comparing the sensitivity and specificity of bone scanning to MRI showed that bone scanning is no longer recommended for diagnosis or screening. Mont et al. reported that bone scanning identified 56% of histologically-confirmed lesions in patients with symptomatic disease while MRI identified 100% of the lesions [32]. Another study noted that, sensitivity, specificity, and accuracy of bone scanning for detection of osteonecrosis of the femoral condyles were 63%, 71%, and 68%, respectively [33].

Sizing the lesions and staging the disease is important for managing osteonecrosis. The most commonly used grading system was described by Ficat et al. Assessment of the following three radiographic criteria defines the stage of the disorder: joint space narrowing, chondral collapse, and trabecular pattern. Stage I defines early stage osteonecrosis diagnosed by MRI or without any evidence of osteonecrosis on plain radiograms. Stage II is defined as mottled sclerosis with normal curvature of the knee. Stage III is the deadline for non-surgical management of the disease. The "Crescent" sign indicates the subchondral fracture and disturbance of the normal curvature leading to collapse of the joint. Stage IV is the end-stage characterized by the joint collapse [34]. Several methods are described for sizing the lesion measuring the width or wedge angle on AP and lateral radiographs [8, 35–37].The size of the lesion is a prognostic factor and is more valuable when evaluated with the location.

Management

Non-surgical Management

Initial treatment of early stage osteonecrosis is protected weight-bearing, analgesics and non-

steroidal anti-inflammatory drugs, if tolerated. Uchio et al. reported good results with the use of weight-reducing wedge insoles to transfer the body weight away from the affected condyle and noted that, the best results were achieved in early stage small lesions. Success of the initial non-surgical treatment depends on the size, stage and multi-focality of the lesion [38]. Lotke et al. reported that 32 of 36 knees with stage I spontaneous osteonecrosis of the knee remained asymptomatic over a range of 9 to 15 months after initial treatment with protected weight-bearing and analgesia [39]. Another study reported similar good results of non-surgical management of early stage spontaneous osteonecrosis and noted that, the lesions resolved in all patients at a mean time of 8 months [40].

Whereas good results are reported for the non-surgical treatment of early stage spontaneous osteonecrosis, secondary osteonecrosis often progresses to advanced stage joint disease, at a rate of 80% [8].

The success of non-surgical treatment for post-arthroscopic osteonecrosis of the knee is unclear due the low incidence of this disease. Individual case reports demonstrated resolution of symptoms with non-surgical management but there are no published results supporting the effectiveness of conservative care in post-arthroscopic osteonecrosis [29, 41]. The use of pharmacologic agents like, vasodilatators, anti-coagulants and bisphosphonates agents to manage osteonecrosis have been reported, but large randomized trials are needed to confirm the efficacy and reliability [42, 43].

Joint-Preserving Procedures

Joint-preserving procedures may be used in patients who remain symptomatic after protected weight-bearing. Core decompression can be beneficial by reducing intra-osseous pressure and stimulating neo-vascularization. Related studies reported clinical improvements with early stage pre-collapse osteonecrosis for either secondary and spontaneous forms. Authors prefer restricted weight-bearing with crutches for 1 month after the surgery [44–46]. Deie et al. reported, significant improvement with core decompression using artificial bone grafting in 12 knees with spontaneous osteonecrosis. None of them underwent total knee arthroplasty at a mean follow-up time of 25 months after surgery [47].

Arthroscopic procedures like debridement or microfracture are also suggested by some authors for the treatment of spontaneous osteonecrosis. Miller et al. reported clinical improvement in four of five patients after arthroscopic debridement and 1 month protected weight-bearing [48]. Akgun et al. performed arthroscopic microfracture for the patients with spontaneous osteonecrosis and reported 96% clinical improvement at a mean follow-up of 27 months [49].

In our institution, we have performed vascularized free fibula transfer for extensive secondary osteonecrosis in 32 knees (28 patients). At a mean follow-up of 35 months, the average Knee Surgery Scores had improved from 67 (preoperative) to 89 [50]. Regression of the bone marrow edema and necrotic areas can be seen on MRI (Fig. 2a, b). Patients with later stages of osteonecrosis with subchondral collapse may benefit from osteochondral autologous transplantation according to lesion size and localization. A recent study by Duany and colleagues reported good results after osteochondral autologous transplantation at a mean follow-up time of 42 months. The authors suggested 4 weeks of rehabilitation and restricted weight-bearing after such surgery [46]. High tibial osteotomy can be used for transferring weight-bearing loads to the unaffected lateral condyle and re-alignment of varus deformity. Koshino et al. reported significant improvement with high tibial osteotomy, and also noted better roentgenographic improvement in those knees in which tibial osteotomy was performed concomitantly with bone-grafting or drilling [51]. Autologous and/or fresh-frozen bone grafting is beneficial in persons with early stage osteonecrosis. Bone grafting introduced from an extra-articular cortical window provides a structural support to the subchondral bone. Two studies report good results and delayed need for joint arthroplasty at a mean follow-up of 2 and 8 years. The use of

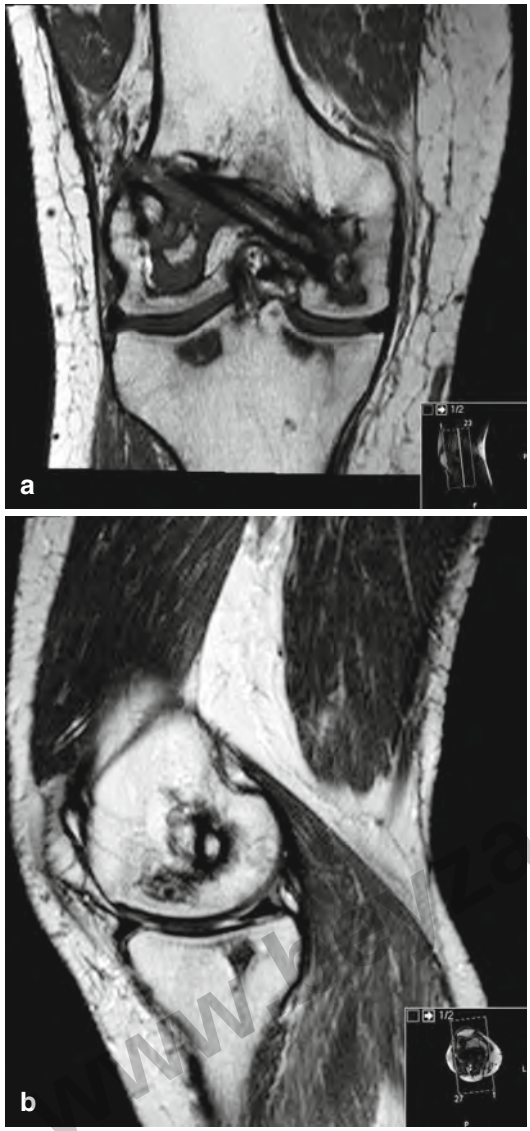

Fig. 2 (**a**, **b**) Coronal T-1 weighted and sagittal T-2 weighted images of the patient in Fig. 1, 4 years after vascularized free fibula grafting surgery. Regression of the bone marrow oedema and native bone around viable fibular graft can be seen. Joint curvature is still preserved 4 years after the surgery

osteochondral grafts for secondary osteonecrosis is not recommended because of impaired healing potential and multi-focality of the lesions. Nevertheless, Rijnen et al. reported good result for the treatment of corticosteroid-induced osteonecrosis even with collapse [52, 53].

Arthroplasty

Patients with progressive osteonecrossis are candidates for Total Knee Arthroplasty (TKA), Unicondylar Knee Arthroplasty (UKA) or limited resurfacing arthroplasty. With the development of modern cemented TKA designs outcomes have reached better levels, similar to osteoarthrosis. UKA is generally not recommended for secondary osteonecrosis because of multi-focality and bone involvement but a recent study reported good result of UKA for secondary osteonecrosis [54]. Myers et al. reported good to excellent outcomes of TKA for secondary osteonecrosis and both TKA and UKA for spontaneous osteonecrosis. The same authors noted a significant improvement of the result after 1985; revision rates decreased from 24% to 3% [55]. Several authors reported similar outcomes [25, 56].

Limited re-surfacing arthroplasty is a novel technique for the treatment of focal chondral lesions that preserves subchondral bone. In our institution, we have performed limited re-surfacing arthroplasty for two knees with stage 2 spontaneous osteonecrosis of medial femoral condyle combined with core decompression. The mean KSS improved from 64 before surgery to 98 at a mean follow-up of 23 months. There was no radiographic collapse in both patients (Fig. 3a–c).

Conclusion

ON is a joint-destroying, progressive disease that can be difficult to manage. Early spontaneous and post-arthroscopic ON can be treated conservatively. Better joint-preserving techniques with comparative studies are needed. Treatment for end-stage disease is replacement arthroplasty.

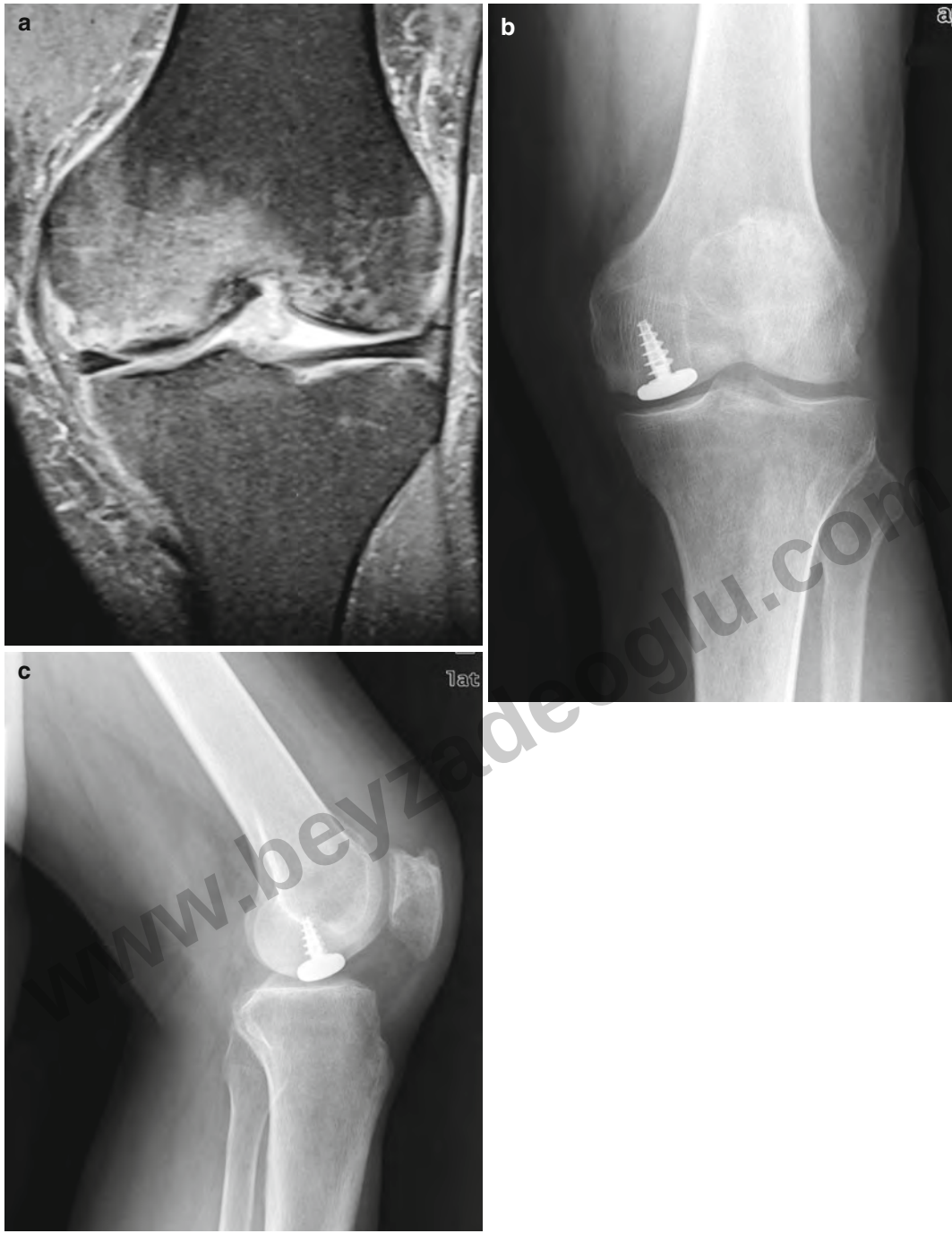

Fig. 3 (**a**) 63 year-old male. Coronal T2-weighted MRI image showing low signal intensity subchondral area isolated at medial femoral condyle demonstrating stage 2 spontaneous osteonecrosis of the knee (**b**, **c**) Post-operative AP and lateral radiographies of the same patient 2 years after limited resurfacing arthroplasty. Joint curvature is smooth on both views without any evidence of collapse

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