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THE DILEMMA OF AVASCULAR NECROSIS

Mohammed Hassan Kubba* Thamer A. Hamdan@

*M.B.Ch.B, D.O.S. Department of Orthopaedic Surgery, Basrah General Hospital, @ FRCS, Professor Orthopaedic Surgery, Medical College, Basrah; IRAQ.

Introduction

Osteonecrosis refers to the in situ death of bone, with the femoral head being the site most commonly affected. (AVN) of the femoral head is a common entity with approximately 20,000 new cases reported each year.

AVN is the underlying diagnosis in as many as 10% of 500,000 total hip arthroplasties performed in the United States. A significant percentage of these hip arthroplasties are done in individuals in their late 30s and early 40s.

To orthopaedic surgeons, however, early osteonecrosis of the femoral head often is silent or presents with non-specific clinical finding, similarly early radiographic finding of the disease also may be inconspicuous and as such, they may impose a challenge for clinicians and radiologists.

The dilemma of this disease is that many surgeons and workers in its field find difficulties and confusion in selecting the appropriate approach to understand or to select the most

acceptable methods or way regarding the aetiology, pathogenesis, classification and the most effective options of treatment.

Here is this review articles we try to clarify or to nearly approximate the most widely acceptable methods of different treatment modalities.

In addition to reviewing the pathology and some other related problems.

The term avascular (AVN), osteonecrosis implies that a segment of bone has lost its blood supply so that the cellular elements die with it.

The phrase "aseptic necrosis" indicates that infection generally plays no part in the process.

Avascular necrosis has long appears as a distinctive feature in a number of non-traumatic disorders.

Sites which are peculiarly vulnerable to ischemic necrosis are the femoral head, the femoral condyles, the head of humerus, the capitulum, proximal part of the scaphoid, talus, patella and the vertebra.

The anatomic course and the nature of the blood vessels, with the characteristic histological structures of the blood vessels in this area probably give a good

Correspondence to:

Dr. Mohammed H. Kubba
Department of Orthopaedic Surgery, Basrah
General Hospital, Basrah; IRAQ.

explanation to the development of (AVN)³.

The subarticular regions of the bone lie at the most distant part of the bone's vascular territory.

The subcondral trabeculae are supplied by endosteal system with limited collateral connection and lastly the vascular sinusoid which nourish the marrow and bone cells, unlike arterial capillaries, have no adventitial layer and their patency is determined by the volume and pressure of the surrounding marrow tissue, which itself is encased in unyielding bone.

The system functions essentially as a closed compartment within which one element can expand only at the expense of the others.

Pathophysiology

Ischemia results in death of haemopoietic tissue within 6-12 hours; 1- the osteoclast, osteoblasts and osteocytes die within 12-48 hours, and if bone marrow fat in 2-5 days. At the bone ends, cartilage receives nutrition from synovial fluid, cartilage and subchondral bone are not therefore necessarily affected⁴.

Revascularization is seen at the live-dead marrow interface. The necrotic zone is invaded by capillaries, fibroblast and macrophages. Fibrous tissue replaces dead marrow and in turn may calcify, new osteotrabeculae lay down fresh woven bone to replace the devitalized trabeculae. This advancing front of neovascularization and ossification has been termed "creeping substitution"⁴⁵.

Reparative new bone formation proceeds slowly and probably does not advance for more than 8-10 mm into the necrotic zone.

With time structural failure begins to occur in the most heavily stressed part of the necrotic segment. Moreover, until very late the articular cartilage retains its thickness and viability.

In the final stages, fragmentation of the necrotic bone leads to progressive deformity and distraction of the joint surface.

The segmental ischemic necrosis rarely increases, indeed, occasionally they even disappear⁵⁰.

Pathogenesis

The pathogenesis of (AVN) still is unknown despite numerous studies.

Various hypothesis have suggested concerning the pathophysiologic mechanisms underlying the disease including fat embolism, intra-vascular coagulation and intraosseous stress.

These theories are for the most part not mutually exclusive. But rather may be thought of as being mutually supportive in most cases⁵¹.

The process of (AVN) can be indicated in at least four different ways:

Severance of the local blood supply.

Intravascular thrombosis.

Venous stasis and retrograde arteriolar stoppage.

Compression of capillaries and sinusoid by marrow swelling.

Ischemia in the majority of cases is due to combination of several of these factors³.

In traumatic (AVN) the vascular anatomy is particularly important. In fractures, or lesser injuries, also sometime result in subchondral necrosis.

Impact injuries and osteoarticular fractures at any of the convex articular surfaces behave in the same way and often develop localized ischemic changes.

Various mechanisms leading to capillary thrombosis have been demonstrated in patients with non-traumatic (AVN). Over 80% of cases are associated with high-dosage corticosteroid medication or alcohol abuse (or both, acting cumulatively). These conditions give rise to hyperlipidaemia

and fatty degeneration of the liver. At the level of the bone, high dosage corticosteroid administration and alcohol over-use cause fat cell swelling in the marrow, there is a demonstrable rise in intraosseous pressure and contrast venography shows slowing of venous blood flow in the bone.

Jones (1994) has favoured the idea that fat embolism plays a part, given rise to capillary endothelial damage, platelet aggregation and thrombosis²⁸.

Glueck and colleagues observed that patients with very early non-traumatic (AVN) should undergo laboratory test for coagulopathies²⁴.

Sickle-cell disease is a genetic disorder in which the red cell contain abnormal haemoglobin (Hbs). In deoxygenated blood there is increased aggregation of the haemoglobin molecules and distraction of the red cells, which become somewhat sickle - shaped. Chronic haemolytic anaemia and the tendency to clamping of the sickle-shaped cells, which results in, diminished capillary flow and recurrent episodes of intracapillary thrombosis³.

Secondary changes such as trabecular coarsening, infarction of the marrow, periostitis and osteonecrosis are common.

In Gaucher's disease a specific enzyme results in the abnormal storage of glucocerberoside in macrophages of the RE system. The effects are seen chiefly in the liver, spleen and bone marrow, where the large polyhedral (Gaucher cells) accumulate. Bone complications are common and osteonecrosis is among the worst of them.

Bone ischemia is usually attributed to the increase in medullary cell volume and sinusoidal compression. In radiation necrosis unlike the common form of ischemic necrosis it is more diffuse and the effect is more variable. Marrow and bone cells die, but for months or even years there may be no structural change

in the bone, a striking feature is the absence of repair and remodelling.

In dysbaric osteonecrosis a generalized embolic phenomena and intracapillary coagulation occurs. Prolonged compression may also cause swelling of marrow fat cells and decrease intramedullary blood flow, possibly due to oxygen toxicity⁴⁶.

The main conditions associated with non traumatic osteonecrosis includes³.

- I- Infection: osteomyelitis, septic arthritis.
- II- Haemoglobinopathy: sickle cell disease.
- III- Storage disorders: Gaucher's disease.
- IV- Caisson disease: dysbaric osteonecrosis
- V- Coagulation disorders: familial thromophilia, hypofibrinolysis, hypolipoproteinemia, thrombocytopenic purpura.
- VI- Other: perthes disease, corti-sones administration, alcohol abuse, SLE, pregnancy, ionizing radiation.

Classification of (AVN)

A number of systems for the classification of (AVN) of the femoral head had been proposed

The most widely used system is that of Ficat and Arlet¹⁹, which classify hip into:

- Stage I – Symptomatic with normal radiographic finding.
- Stage IIA-diffuse osteoporosis, sclerosis, or cystic.
- Stage IIB- transitional stage (flattening of the femoral head and crescent sign).
- Stage III – collapse

Stage IV- incongruous joint with flattening of the head and decrease joint space.

This system was modified by Hungerford and Lennox to include stage O (an asymptomatic hip with evidence of osteonecrosis on MRI)²⁶.

Steinberg et al.⁵³ later expanded this system to include six stages, with the important addition of quantification of the involvement of the femoral head.

Marcus et al.³⁴ in 1973, also described a six staging system, which included both radiographic changes and clinical signs and symptoms.

In 1987, the Japanese investigation committee⁴¹ for intractable disease, avascular necrosis of the femoral head, developed a classification system that incorporates the size and location of the lesion and has been found, by several authors, to help to predict the outcome.

According to this system, type-A lesions are medial and rarely progress. Type-B lesions are central and there is intermediate progression, and type-C lesions demonstrate lateral involvement of the head and have the worse prognosis.

Finally, the association research circulation osseous (ARCO)⁷ recently proposed a new international classification system. That system represents an attempt to incorporate features of the classification system of Ficat and Arlet, to quantify the involvement as described by Steinberg et al, and to determine the anatomical location of involvement as proposed by the Japanese investigation committee.

The proposed pittsburgh classification⁴³, is based on three major parameters:

- 1- Magnetic resonance imaging (MRI)
- 2- Structure of the femoral head and,
- 3- Contour of the femoral head as seen on plain radiographs.

Stage	MRI	Plain radiographs of the femoral head	
		Structure	Contour
1	Abnormal	Normal	Normal
2	Abnormal	Abnormal	Normal
3	Abnormal	Abnormal	Abnormal

The three-stage classification is proposed as an easy and reproducible system that will allow a more uniform assessment of outcome.

Investigation

In many cases of (AVN) the history is important to suggest the underlying causes. A known episode of trauma, an occupation and a family background of Gaucher's disease or sickle cell disease.

There may be a record of high dosage corticosteroid administration. Alcohol, corticosteroids, immunosuppressions and cytotoxic drugs either singly or in combination are the commonest causes of non-traumatic (AVN)³.

It has been suggested that patients with very early traumatic osteonecrosis should undergo laboratory test for coagulopathies.

In cases of suspected SLE, antiphospholipid antibodies may be measured.

In early (AVN) both the intramedullary pressure and the response to saline injection may increase three or four fold. Venous stasis can also be demonstrated by venography after injection of radio-opaque medium in to the bone⁶³.

Uchio et al. study the angiokinematic factor of (AVN) the early results of the study suggest that disturbed venous drainage and increase intraosseous pressure might be important factor in the pathogenesis of (AVN).

Because typical radiographic finding of AVN most commonly appears relatively late in the disease process, that is, after the onset of clinical manifestation, radiographs may lack sensitivity in detecting early disease⁴⁹.

Small lesions may not be detected on conventional radiographs because they may be obscured by the abnormally mineralized underlying bone⁴⁹.

With the advent of more sophisticated imaging modalities, including radio-nuclide bone scintigraphy, computed tomography (CT), and magnetic resonance imaging (MRI), substantial gains in the diagnosis of osteoneurosis on early, pre collapse stages have been achieved^{4,36}.

In the clinical setting, imaging is considered a valuable tool for providing an early and definitive identification of the osteoneurotic lesion, evaluating its type and extent, determining prognosis, and monitoring the effect of treatment. Differential diagnosis particularly challenging cases with an atypical initial presentation.

Moreover, characterization of the infarcted segment, in terms of identification of its precise location in relation to the weight bearing surface of the femoral head⁴⁰, accurate quantification of its extent, and evaluation of collapse are extremely important parameters influencing the choice of conservative or operative treatment.

Although the diagnostic role of bone scintigraphy with technetium labeled-diphosphonates in AVN has not been well defined, it is generally accepted that the detection of cold lesion is highly sensitive for early disease indicating devascularization of the femoral head^{9,49}.

However, because of its capability to detect bone marrow abnormalities, MRI has been described to detect osteoneurosis of the femoral head with a sensitivity approaching 100%^{30,35}.

In this regard, MRI has been found to be effective in evaluating osteoneurosis where conventional radiography and bone scintigraph are negative or equivocal.

Treatment

It is generally agreed that without specific treatment the large majority of clinically diagnosed cases of AVN will progress to collapse of the femoral head and require some form of arthroplasty.

Orthopaedic surgeons have been challenged to find surgically effective solutions for the treatment of this disabling disease, but to date no solution has been totally satisfying.

Mechanical procedures, such as cup arthroplasty or osteotomies are limited in their indications by the extent of the sequestrum, whereas biologic procedures attempt either to reinforce the sequestrum or to revascularize the necrotic bone.

Osteoneurosis in adults lead to progressive osteoarthritis once subcondral and loss of joint congruity occurs.

However, the natural history in younger patient is defined less clearly because of their increased remodeling capacity.

Statins are lipid-clearing agents that dramatically reduce lipid levels in blood and tissues.

Statins are widely used to prevent cardiovascular disease and have been shown to reduce the adverse effects of steroids on lipid metabolism.

Statins appear to offer protection against having osteoporosis and osteoneurosis when steroids are necessary⁴⁴.

More recently a course of hyperbaric oxygen treatment is effective in the treatment of idiopathic stage - I (AVN). It may be used in conjunction with core decompression, fenestration and drilling or other forms of orthopaedic intervention⁴⁷.

During the early 1960s Arlet and Ficat⁵ performed core biopsies in order to examine the pathological changes taken place in femoral head.

This procedure frequently produce immediate relief of preoperative pain,

and it was felt that this was because of decompression of the increased intraosseous pressure which found to be present in the femoral head used as therapeutic rather than as a diagnostic procedure and was referred as core decompression.

Initially, Ficat²⁰ as well as Hungerford and Lennox²⁶ reported high rates of success with use of this procedure. However, their results have not been duplicated by other investigators and enthusiasm for core decompression has recently waned.

In 1980, after experiencing poor results treating patients with (AVN) conservatively Steinberg⁵⁴ and colleagues began to perform a modified type of core decompression with supplemental cancellous bone graft.

It was shown that is properly performed to procedure had an extremely low incidence of complication and was effective in treating patients with earlier stages of (AVN) as compared with patients who were treated non-operatively or patients who received symptomatic treatment.

Osteotomy techniques

In an effort to improve the prognosis of patients with (AVN), several surgical procedure have been proposed with the aim of slowing down the progress of degenerative changes. Various osteotomy techniques have been proposed to remove the necrotic area, which is usually located in the antero-superior part of the femoral head, out of the weight bearing zone.

However, the most effective type of osteotomy is still controversial because osteotomies have been proposed on approximately every plane, each with its own rationale.

The surgical procedure of osteotomy is more technically demanding than hip replacement, requires a lengthy period of disability for the patient, and does not

appear to give totally predictable results²⁰.

In 1972, Sugioka⁵⁸ devised a trochantric rotational osteotomy of the femoral head for idiopathic (AVN) to prevent progressive collapse of the articular surface and to improve the congruity of the hip joint when articular collapse followed femoral head subluxation.

Merele D Aubigne et al.³⁹ first introduce varus osteotomy to load the most lateral part of the femoral head which is usually not involved by the necrosis.

Avalgus Extension osteotomy was proposed by Pawels⁴² to move the necrotic area laterally and posteriorly and to enlarge the weight bearing surface by loading the capital drop osteophyte.

Sugioka stated that the best results were obtained when the osteotomy was performed during the early stage of necrosis or in extensive lesions in the absence of advanced collapse⁵⁹.

More specifically, of patient characteristics, young patient have been reported to be the best candidates for intertrochanteric osteotomy with upper age limits generally around 45 year^{20,33}.

Patients with Ficat stage III lesion or late stage II can be treated successfully with intertrochanteric osteotomy.

The operation has to be avoided if there is poor patient compliance and if the patient is not highly motivated to accept a lengthy disability period.

However, intertrochanteric osteotomy should be avoided in patients with underlying metabolic disease or in patients with systemic conditions treated with chemotherapy or corticosteroids.

Free vascularized fibular graft

An appealing to maintain available femoral head without violating the joint capsule in free vascularized fibular grafting (FVFG).

In most of the types of free vascularized fibular graft procedures two teams of surgeons worked simultaneously. One team isolated the middle 1/3 of the contralateral fibula and the other team working of the hip region.

Harvesting the fibula according to the method of Gilbert technique.

The placement of the fibula to the head of the femur is done either by direct approach, intra capsular, or by extra capsular placement of the fibular graft.

The technique of intra capsular involve the total excision of the necrosed bone then replaced by autogenous cancellous bone associated with a bone vascularized graft taken from the contralateral fibula. The articular cartilage that normally remains preserved for a long time during the natural history of the disease is protected and used to cover the grafted area.

The extra capsular placement of vascularized fibular graft in the subchondral region of the femoral head is widely accepted method for treating patient with (AVN).

The rationale for its use includes; the femoral head is decompressed, necrotic bone is removed, fresh autogenous cancellous and vascularized cortical bone grafts are added, and new bone formation that fuses with the affected subcondral bone is induced, this prevent will collapse of the articular cartilage^{4,18,53,61}.

Urbaniak and colleagues have remained leader in the field of osteonecrosis during the course of its study.

During the procedure the femoral head is decompressed, which may interrupt the cycle of ischemia and intraosseous hypertension that is thought to contribute to the disease.

The necrotic bone is then excised, possibly by removing the obstacle to revascularization, the defect then is filled with osteoinductive cancellous graft and a viable cortical strut to support the subchondral surface. A

period of limited weight bearing protects the healing construct¹⁵.

The loannina technique uses serial CT scan of the proximal femur to identify the configuration of the femur and the size, location, and configuration of the lesion with a computer-aided design and computer aided manufacturing process. Optimal graft placement is determined and a guide wire canal is drilled in patient-specific aiming device.

The aiming device resulted in good placement of the fibular graft in 89% of the patients studied to date.

Beris and Soucacos et al.⁸ present the loannina technique. The goal of this technique was to optimize the length and position of the fibular graft in the necrotic defect, and to diminish the x ray exposure and preparation time.

To date, there is still no agreement on the best surgical method for preserving the hip in adult with (AVN) of the femoral head. In general, either free vascularized fibula transplants or vascularized iliac crest transplants are used.

The insertion of corticospongious iliac crest transplant perfused by the circumflex ilium profunda artery in the femoral head places a high quality autogenous bone transplant in a weak host bed.

And lastly this type of vascularized graft lack the need for vessel anastomosis¹⁶.

Although retention of the femoral head is accepted as the goal of early treatment, methods for treating osteonecrosis of the femoral head remain controversial.

Once-end-stage osteonecrosis has developed with collapse of the femoral head, total hip arthroplasty has become the accepted means for surgical management of pain and restoration of function⁶⁴.

Discussion

In many cases of (AVN) an underlying disorder will be obvious from the history: a known episode of trauma, is a more obvious cause an occupation such as deep-sea diving or working under compressed air, a family background of Gaucher's disease or sickle cell disease.

Drugs use such as corticosteroid, immunosuppressive and cytotoxic either singly or in combination are the commonest cause of non-traumatic osteonecrosis. The threshold depends not only on the total intake but also on the time over the intake, and the presence of associated disorder which in themselves may predispose to osteonecrosis³.

Accumulative dose of 2000mg of prednisolone equivalent administration over several years is less likely to cause (AVN) than the same dose given over a period of months.

It is important to bear in mind that multiple causative agent have an additive effect for the development of (AVN)⁵⁷.

The threshold dose for alcohol is equally vague, base on the known dose relationship of alcohol-induced fatty degeneration of the liver, it may be around 150mg of ethanol per day, for men and considerably less for woman.

Steroid treatment produce a hyperlipidemic state that often leads to osteoporosis, however, at least 1/3 of the cases of (AVN) have been associated with steroid treatment⁴⁴.

There is no clear relationship to etiology was observed except in patient exposed to combination of steroids and alcohol in whom the prognosis seemed to be somewhat worse⁵².

Given the unpredictable natural history of (AVN) that usually progresses to structural failure, it is conceivable that early diagnosis is crucial in selecting the appropriate treatment options that eventually may halt the evolutionary and debilitating course of this disease.

To orthopaedic surgeon, however early (AVN) of the femoral head often is silent or present with non-specific clinical finding⁶⁰.

Thornhill et al.¹³ their result stress the importance of distinguishing between patient who have sclerotic changes only, they demonstrated that patients who do not have cystic changes or collapse of the femoral head are most likely to benefit from core decompression.

We see that the proposed classification by Pittsburgh has excellent agreement and is anticipated to be more helpful in comparing methods of treatment in multicentre studies⁴³.

Given that many theories regarding the pathogenesis of (AVN) of the femoral head have been proposed, it is not surprising that a wide variety of treatment options have been advocated for this disease. These modalities have included non-operative measures, electrical stimulation, hyperbaric oxygen therapy, statin drug therapy, corrective osteotomy, vascularized and non-vascularized bone graft, core decompression with and without bone graft, arthrodesis and endoprosthetic replacement.

Each patient should be evaluated preoperatively on the basis of medical history, associated risk factors, the results of physical examination anteroposterior and lateral radiographs, technetium-99 bone scan and MRI.

It is generally agreed that without specific treatment the majority of clinically diagnosed cases will progress to collapse of the femoral head and the head require some form of arthroplasty if the initial treatment consisted of non-operative measures only^{38,52,53}.

There is general agreement in the literature that core decompression is most effective in the earlier stages of the disease, however, the overall rate of success of this procedure for the treatment of non-traumatic osteonecrosis has varied widely from as low as 17% to

as high as 89%^{17,37,56}. It is effective in hips treated prior to collapse, especially in those with smaller lesion. Among the advantages are the following, it is a procedure with long time of experience (30 years), it is relatively simple and requires no special equipment, it is a short procedure with little blood loss and if done carefully, the complication rate is extremely low and protected weight bearing is required for only 6-12 weeks and finally it can be done bilaterally.

The major disadvantage of core decompression is that it is not as effective as we would like it to be especially in treating hip with larger lesions or in those after collapse has already began. However, even in this group results are significantly better than with conservative management.

The result of core decompression is limited to the stage I and stage IIA of the sclerotic type, where as the result is limited in cases of stage IIA (cystic type).

Mont and Hungerford³⁷ reported that radiolucenced or cystic area on plain radiographs represent regions of resorption of bone and corresponded to the fibrous or granulation tissue seen in histological section.

Similarly, osteosclerotic changes bordering the necrotic area corresponded histological in section⁵⁴ to the region of repair with newly formed bone laid on dead trabeculae.

For this reason Thornhill et al. in their study believe that preservation of the joint should be the goal of treatment of early stage of non traumatic (AVN), furthermore they found that both a rapid onset of symptoms and the use of corticosteroid are independently associated with poor outcome.

Steinberg M.⁵⁵ after performing 406 procedures perform a modified type of core decompression with a supplemental cancellous bone graft taken from the intertrochanteric area. They concluded that, compared to nonoperative or symp-

tomatic management, core decompression with or without a cancellous bone graft was a safe and effective procedure for treatment of early stages of AVN.

Recently there has been increasing interest in free vascularized fibular grafting (FVFG), and some of the reports cited indicate that it may be one of the most effective treatment, especially after femoral head collapse.

FVFG with this procedure is applied to patient younger than 40 years who have stage II of stage III osteonecrosis with good spherically of the femoral head and a healthy shell of cartilage²⁹.

Other studies indicate that equal or nearly equal results can be obtained with simpler procedure such as non-vascularized tibia or fibular^{9,12} allograft or with cancellous grafting^{21,48}.

The major disadvantage of this procedure are associated with the need to harvest the patient own fibula and perform to microvascular anastomosis.

In a recent comparison between core decompression and (FVFG) it was found that the increased morbidity of the FVFG is justified by the associated delay in or prevention of articular collapse in hip with stage II or III disease (FVFG) is an appealing alternative to all of the other mentioned methods of treatment. During the procedure the femoral head is decompressed, which may interrupt the cycle of ischemia and intra osseous hypertension that is thought to contribute to the disease.

The necrotic bone is then is excised, possibly removing the obstacle to revascularization.

The defect then is filled with osteoinductive cancellous graft and available strut to support the subcondral surface. A period of limited weight-bearing protect the healing construct¹⁵.

Vascularized iliac crest transplant is another salvage procedure for the AVN of the head of the femur in which the

necessity for microvascular surgery is omitted¹⁵.

Osteotomies of the femur and acetabulum have been recommended as a way to unload the necrotic segment of the femoral head and redirect weight bearing through a more viable area.

Sugioka et al. reported excellent results with their technique of rotational osteotomy, however, similar success rates have not achieved elsewhere.

Patient with Ficat stage II lesions or late stage II lesions can be treated successfully with intertrochanteric osteotomy.

In terms of pathogenesis, idiopathic avascular necrosis represents the best indication. However, intertrochanteric osteotomy should be avoided in patients with underlying metabolic disease or in

patients with a systemic condition who have been treated with chemotherapy or corticosteroid²⁰.

Different types of electrical stimulation, both alone and supplement to operative procedures, have been used to treat (AVN). Promising results have been reported with the use of pulsing electromagnetic field^{1,2,27}.

There is a great deal of controversy about the recommended treatment of so-called silent or asymptomatic hip with early stage osteonecrosis. Some authors emphasized the importance of long-term follow-up in order to determine the true rates of radiographic and clinical progression^{10,32}.

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