Osteoporosis in Women with Eating Disorders: Comparison of Physical Parameters, Exercise, and Menstrual Status with SPA and DPA Evaluation

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Osteoporosis has been reported in anorexia nervosa (AN), but not in other eating disorders. Thirty-three patients, 8 AN, 17 bulimia nervosa (BN), and 8 eating disorder not otherwise specified (EDNOS), were evaluated by bone densitometry (radius, spine, femur) to determine the prevalence and distribution of osteoporosis and the role of physical parameters, exercise and estrogen. All three diagnostic subgroups had evidence of decreased bone density, worst in the EDNOS subgroup and least in the BN subgroup. The most affected site was the femur, least the spine; the radius was intermediate. Age, body surface area, age of onset, and length of illness weakly correlated with the femur and spine density in the BN and EDNOS subgroups. Exercise was related to bone density in the AN subgroup in the femur, moderate exercise having a protective effect and strenuous exercise being detrimental. No significant correlation of bone density measurements with estradiol levels and/or history of amenorrhea was identified. Eating disorder patients are at risk for osteoporosis, which has multiple contributing factors including physical parameters and exercise. Estrogen deficiency by itself may not be a major causative factor.

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Anorexia nervosa (AN) and bulimia nervosa (BN) are eating disorders which afflict ~5%–10% of our adolescent and young adult female population (*1,2*). Anorexia nervosa has recently been recognized as a risk factor for osteoporosis (*3–9*). This association with BN or "Eating Disorder Not Otherwise Specified" (EDNOS), a third subgroup of patients with anorexic or bulimic behavior not meeting the strict criteria for AN or BN, has not been reported.

The distribution of the osteoporosis in eating disorders needs to be determined. Decreased bone density has been measured in multiple sites in AN patients including the radius, spine, and femur. Only one study compared these sites and found that the area most involved was the femur (*7*). Since femoral fractures carry the highest morbidity and mortality of osteoporotic fractures, the distribution pattern of osteoporosis in eating disorders has important future implications for these patients (*10*).

The contributing factors to osteoporosis in AN also are not clearly understood. Physical parameters such as body mass and level of exercise appear to be related (*3,7*). The role of estrogen deficiency, which predisposes the postmenopausal female to osteoporosis, is controversial (*3,4,7*).

In order to determine the prevalence and distribution of osteoporosis in these eating disorder subgroups and the possible contributing factors, we studied hospitalized eating disorder patients from May 1987 to May 1988 by bone densitometry. Clinical parameters including age, body surface area (BSA), age of onset of illness (AO), length of illness (LOI), exercise, and menstrual status were correlated with the bone density measurements.

METHODS

Patient Population

Seventy-two eating disorder patients consecutively hospitalized between May 1987 and May 1988 were evaluated clinically and by bone densitometry. Each subject underwent a thorough psychiatric and medical evaluation upon admission. Those with a history of disease that may affect bone density, i.e., bone, renal, adrenal, or thyroid abnormalities, as well as those on medication that affect bone density, i.e., corticosteroids or anticonvulsants, were excluded from the study. Also excluded were patients less than 20 yr of age because of the lack of normative data in this age group.

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TABLE 1
DSM-III-R Criteria for Eating Disorder Subgroups

Anorexia Nervosa (AN)
A. Refusal to maintain body weight over a minimal normal weight for age and height (e.g., weight loss or failure to make expected weight gain leading to body weight 15% below that expected).
B. Intense fear of gaining weight or becoming fat even though underweight.
C. Disturbance in the way in which one's body weight, size, or shape is experienced.
D. Absence of at least three consecutive menstrual cycles when otherwise expected to occur.

Bulimia Nervosa (BN)
A. Recurrent episodes of binge eating.
B. A feeling of lack of control over eating behavior during the binges.
C. Regular self-induced vomiting, use of laxatives or diuretics, strict dieting or fasting, or vigorous exercise in order to prevent weight gain.
D. A minimum of two binge-eating episodes a week for at least three months.
E. Persistent overconcern with body shape and weight.

Eating Disorder not Otherwise Specified (EDNOS)
Disorders of eating that do not meet the criteria for a specific eating disorder (e.g., all of the features of Anorexia Nervosa except amenorrhea, or all of the features of Bulimia Nervosa except the frequency of binge eating episodes).

The remaining patients were categorized into the three diagnostic subgroups, AN, BN and EDNOS, based on the DSM IIIR criteria (Table 1) (*11*). Age, sex, BSA, LOI, AO, history of amenorrhea, fracture history, and exercise history were obtained for each patient.

Fracture history was considered positive if a fracture occurred during the course of the illness.

Exercise was graded as <1 hr/wk (0), 1–6 hr/wk (1+), and >6 hr/wk (2+).

Menstrual status was evaluated by both the history of amenorrhea or the estradiol level (when available). A history of three or more consecutive months without menstruation and/or a serum estradiol level of <20 pg/ml were considered positive for amenorrhea.

Bone densitometry was performed on each subject within the first week of hospitalization. Single-photon absorptiometry (SPA) of the radius at the distal 33% shaft position and dual-photon absorptiometry (DPA) of the femur (neck, trochanter and Ward's triangle) and of the lumbar spine were performed. Only femur and radius measurements were obtained on the first three patients in the study, with the remainder having femur, radius, and spine examined. The instrumentation utilized was the LUNAR SP2 and DP3 (Lunar Radiation Corporation, Madison, Wisconsin).

Measurements of the radius, femur, and spine were obtained on a small control group of normal subjects at our institution, which showed no significant difference from the control data from recent publications and from the Lunar Corporation data base on similar instruments (*12–14*). Using this control data, a standard deviation (s.d.) from normal age/sex matched control values was calculated.

Statistical analysis was performed by analyzing the group as a whole and dividing the group into the three diagnostic subgroups. Using Pearson's linear correlation, the bone density measurements (raw and standardized scores) and the age, BMI, LOI, AO, and estradiol levels (when available) were compared. The comparison of exercise levels between subgroups and the group as a whole with bone density measurements was computed using the one-way ANOVA test. The two-sample t-test was used to determine differences between patient bone density measurements (using s.d.s) and normal controls and between positive amenorrhea and bone density. A p-value less than or equal to 0.05 was considered significant.

Bone biopsies of the iliac crest were performed on five subjects with evidence of severely decreased bone density by bone densitometry.

RESULTS

Patient Selection

Of the 72 eating disorder patients evaluated, 37 were excluded because they were <20 yr of age and 2 because of medical disease. The remaining population of 33 patients consisted of 8 with AN, 17 with BN, and 8 with EDNOS.

Subject Characteristics

All 33 eating disorder patients were female (Table 2). The age ranged from 20 to 53 yr (mean 29); LOI ranged from 0.5 to 26 yr (mean 8); AO ranged from 13 to 50 yr (mean 21); and BSA ranged from 1.34 to 2.16 m^2 (mean 1.6 m^2). Age, BSA, LOI, and AO were not significantly different between the three subgroups.

Menstrual Status

Seventy-five percent of the AN patients were considered positive for amenorrhea by history or low estradiol level. The two patients with AN who were not counted as positive were taking oral contraceptives and had estradiol levels >20 pg/ml. Only 25% of the EDNOS patients and 18% of the bulimics were considered positive.

Exercise History

As a group, the EDNOS patients exercised the least (7 of 8 graded "0"). Comparing the three subgroups, the only statistically significant difference was between the BN and EDNOS subgroups. However, the p value for the AN versus EDNOS subgroups was 0.08.

Fracture History

A fracture history was positive in one AN patient (clavicle fracture) and two BN patients (wrist and ankles fractures).

Statistical Analysis

Comparison of Bone Densitometry Measurements of Patients to Controls. In the group as a whole, statistically significant differences were found between the normal controls and the eating disorder patients with p value below 0.005 in all five sites (Table 3).

Figure 1 compares the mean expected density of normal controls with the eating disorder subgroups.

TABLE 2
Summary of Patient Characteristics

	AN	BN	EDNOS	All
Age range	20–53 yr	20–44 yr	21–44 yr	21–44 yr
(mean)	(29.22)	(29.18)	(29.25)	(29.21)
Length of illness range	2–15 yr	2–26 yr	0.5–22 yr	0.5–26 yr
(mean)	(6.89)	(9.18)	(6.85)	(8.02)
Age at onset range	16–50 yr	13–41 yr	15–37 yr	13–50 yr
(mean)	(22.78)	(20)	(22.25)	(21.26)
Body surface	1.38	1.38	1.34	1.34
Area range	−1.62	−2.16	−1.82	−2.16
(mean)	(1.5)	(1.72)	(1.48)	(1.6)
Exercise				
Grade 0	3 (38%)	7 (41%)	7 (88%)	17 (52%)
1	2 (25%)	6 (35%)	1 (13%)	9 (27%)
2	3 (38%)	4 (24%)	0 (0%)	7 (21%)
Positive amenorrhea	6 (75%)	2 (12%)	2 (25%)	10 (30%)
(By estradiol or history)				
Estradiol	5–51	10–204	10–300	5–300
level	(18.3)	(78.69)	(77.5)	(58.16)

Grade 0 = <1 hr/wk; Grade 1 = 1–6 hr/wk; and Grade 2 = >6 hr/wk.

The EDNOS subgroup bone density was the least in all sites, the AN subgroup intermediate, and the BN subgroup the highest.

In the AN subgroup, the trochanter and the neck were significantly different from the controls and almost significantly different in Ward's triangle and the lumbar spine with p = 0.09 and 0.07, respectively. In the BN subgroup, the radius and trochanter were significantly different. In the EDNOS group, all five sites were statistically significantly different (Table 4).

Comparison of the Bone Densitometry Measurements of the Three Subgroups. Significant differences were present in the radius and femur between three subgroups (Table 5). These included in the radius (raw, s.d.) between BN versus EDNOS and AN versus EDNOS; the trochanter (raw, s.d.) between BN versus EDNOS and trochanter (s.d.) between BN versus AN; in the neck (raw, s.d.) BN versus EDNOS; Ward's triangle (raw, s.d.) between BN versus EDNOS. The EDNOS patients always had the lowest bone density, the BN patients the highest, and the AN subgroup was intermediate except for the trochanter (s.d.), where the AN patients had the lowest.

TABLE 3
Comparison of Entire Eating Disorder Group with Normals

	s.d. ± mean	p-value
R	−0.74	0.0001
T	−1.4	0.0001
N	−0.95	0.0001
W	−0.79	0.0012
L	−0.48	0.004

R = radius; N = femoral neck; T = trochanter; W = Ward's triangle; and L = lumbar spine (L2–L4).

Comparison of Physical Parameters to Bone Density Measurements (Table 6). In the eating disorder group as a whole, significant correlations were demonstrated between age versus Ward's triangle (raw data) and trochanter (s.d.); BSA versus trochanter (raw and s.d.), femoral neck (raw and s.d.), lumbar spine (raw) and Ward's triangle (s.d.); LOI versus trochanter (s.d.); and AO versus the femoral neck (raw) and Ward's triangle (raw).

No significant correlation of these physical parameters with the AN subgroup were identified. In patients with BN, a significant correlation between age and trochanter (s.d.), BMI and trochanter (raw and s.d.), LOI and lumbar spine (raw and s.d.), and AO and Ward's triangle (raw) was determined. In patients with EDNOS, correlations were found between age and femoral neck (raw) and Ward's triangle (raw) (Table 7).

Comparison of Exercise to Bone Density Measurements (Table 8). No correlation of bone density with exercise was determined in analyzing the group as a whole. In the AN subgroup, significant differences were found between the 1+ versus 2+ exercise levels in the trochanter (raw), femoral neck (raw and s.d.), Ward's triangle (raw and s.d.), and lumbar spine (s.d.) value. Significant differences also were identified between the 0 versus 1+ exercise levels in the trochanter (raw) and femoral neck (raw); and the 0 and 2+ levels in the density of the femoral neck (s.d.) and Ward's triangle (s.d.). The 1+ level of exercise (moderate) always showed the highest bone density.

In the BN and EDNOS subgroups, no significant correlation with exercise history was identified.

Comparison of Menstrual Status to Bone Density

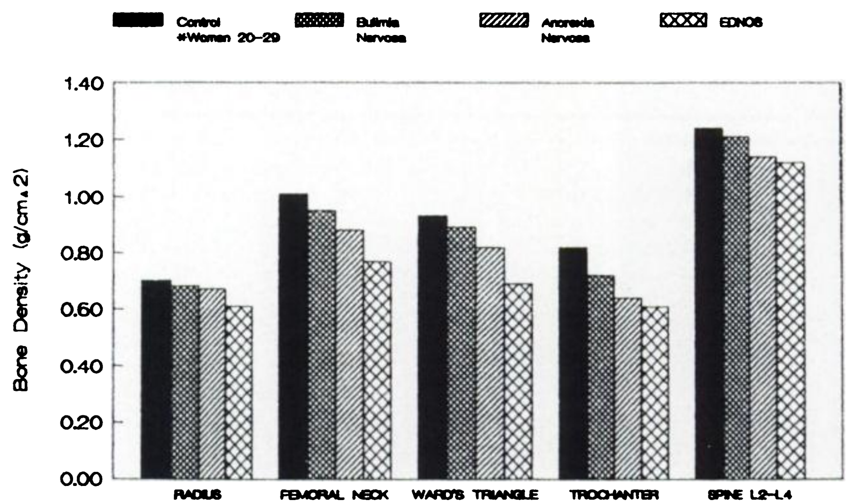

FIGURE 1
Comparison of mean expected density of normal controls with the eating disorder groups.

Measurements. Utilizing both the estradiol levels and the menstrual history, no evidence of a significant correlation of decreased bone density to estrogen deficiency in any of the three diagnostic subgroups or the group as a whole was identified.

Bone Biopsies Results. Bone biopsies were performed on five subjects: two with AN, one with BN, and two with EDNOS. All revealed high-turnover osteopenia.

DISCUSSION

Our results demonstrate that women with eating disorders, including not only AN but also BN and a third subgroup, EDNOS, have evidence of decreased bone mineral density. Based on the results of the bone biopsy in 5 of the 33 patients, this decreased bone density represents osteoporosis. The clinical consequence of this decreased bone density was manifest in three of the patients who suffered fractures during their illness.

TABLE 4
Comparison of Diagnostic Eating Disorder Subgroups with Normal

		s.d. ± mean	p-value
AN	R	−0.56	0.2317
	T	−2.43	0.0050
	N	−1.17	0.0330
	W	−0.94	0.0914
	L	−0.71	0.0783
BN	R	−0.45	0.0234
	T	−0.8	0.0007
	N	−0.34	0.1477
	W	−0.19	0.4420
	L	−0.18	0.3448
ED	R	−1.51	0.0007
	T	−1.66	0.0013
	N	−2.03	0.001
	W	−1.9	0.0007
	L	−0.94	0.0243

R = radius; N = femoral neck; T = trochanter; W = Ward's triangle; and L = lumbar spine (L2–L4).

In our study, the osteoporosis was consistently worse in the EDNOS subgroup and least in the BN subgroup, with the AN patients intermediate. This observation may not be reliable because of the small numbers in each subgroup (8 = AN, 17 = BN, 8 = EDNOS). This finding could also be more related to the exercise level rather than the diagnostic subgroup. The EDNOS patients exercised significantly less than BN subgroup and significantly less than the AN subgroup ($p = 0.08$).

Our bone density results were consistently lowest in the femur and usually highest in the spine with the radius being intermediate. Although this finding could be an incidental observation related to the small number evaluated (33), this preferential loss in the femur over the spine was also detected by Treasure et al. (*7*). As Treasure noted, this pattern of bone loss does not parallel the amount of trabecular bone at each site and is therefore different from postmenopausal osteoporosis where trabecular bone loss predominates (*15*). Possible explanations include lack of bone apposition or cortical bone loss. Further longitudinal studies will be necessary to determine the etiology of this osteoporotic pattern.

Since the highest morbidity and mortality from osteoporotic fractures has been reported in the femur, the greater loss at this site has major future implications for these women. Usually bone mass peaks at ~30 yr of age, therefore, these women will soon or have already reached their highest density. If their highest bone mass attained is lower than normal, they will be prone to fracture at an earlier age than normal women. Such a case has already been reported in a 35-yr-old AN patient who sustained a nontraumatic hip fracture requiring open reduction and pinning (*9*).

The contributing factors to this osteoporosis are multiple. We found that physical parameters including age, BSA, AO, and LOI were related to the bone density of

TABLE 5
Comparison of Bone Density by Type of Diagnosis: Significant Differences

Area measured	AN mean	BN mean	EDNOS mean	p-value	Significant difference
R RAW	0.66600	0.67735	0.60850	0.009	BN vs. ED; AN vs. ED
T RAW	0.62375	0.72235	0.60875	0.008	BN vs. AN; BN vs. ED
N RAW	0.86125	0.95176	0.77375	0.001	BN vs. ED
W RAW	0.79500	0.89176	0.69000	0.004	BN vs. ED
R STD	−0.55800	−0.45647	−1.5412	0.021	BN vs. ED; AN vs. ED
T STD	−2.4375	−0.80294	−1.6637	0.004	BN vs. AN
N STD	−1.1750	0.34529	−2.0375	0.001	BN vs. ED
W STD	−0.94250	−0.19823	−2.9000	0.004	BN vs. ED

RAW = raw bone mineral density data; s.d. = standard deviation from normal age/sex matched controls; R = radius; N = femoral neck; T = trochanter; W = Ward's triangle; and L = lumbar spine (L2–L4).

the spine and femur in the group as a whole and in the BN and EDNOS subgroups. This agrees with the positive correlation previously noted between body mass and bone density by Treasure et al. in the femur and spine in 31 AN patients (*7*). The lack of correlation of physical parameters in our AN subgroup may be related to the small number of patients.

Exercise has been considered an important factor in bone density. Rigotti found that anorexics with a high physical activity level had greater radial bone density and concluded that a high level of physical activity may protect the skeletons of anorexics. They evaluated two levels of exercise, highly active (vigorous exercise at least three times a week) and less active (*3*).

We found that exercise only showed a significant correlation in the AN subgroup. In contrast to Rigotti, we divided the exercise habits into three levels (<1 hr/wk, 1–6 hr/wk, and >6 hr/wk) and discovered that exercising moderately (1–6 hr/wk) was protective of bone mass whereas minimal or strenuous exercise was detrimental. We also observed that the EDNOS subgroup, which exercised the least, had the lowest bone density values. This finding could be meaningful in the prevention and treatment of osteoporosis in eating disorder patients. An exercise regime with a moderate level of activity might be recommended whereas high or low levels of activity would be discouraged.

TABLE 6
Correlations Between Age, BMI, LOI, AO and Bone Densitometry of the Entire Group

	AGE	BMI	LOI	AO
RRAW	—	—	—	—
TRAW	—	0.009	—	—
NRAW	—	0.04	—	0.03
WRAW	0.03	—	—	0.007
LRAW	—	0.05	—	—
RSTD	—	—	—	—
TSTD	0.005	0.02	0.05	—
NSTD	—	0.01	—	—
WSTD	—	0.01	—	—
LSTD	—	—	—	—

RAW = raw bone mineral density data; s.d. = standard deviation from normal age/sex matched controls; R = radius; N = femoral neck; T = trochanter; W = Ward's triangle; and L = lumbar spine (L2–L4).

Because estrogen deficiency predisposes to osteoporosis, the decreased bone density in AN has been presumed to be related to the hypoestrogenic effect from amenorrhea (*4,5*). Two studies addressing this aspect in eating disorders have previously been reported which reached different conclusions. Rigotti observed no significant correlation of the estradiol levels of 18 AN patients to bone density of the radius (*3*). Treasure found a negative correlation of duration of amenorrhea (based on history) with bone density of the femur and spine in 31 AN patients (*7*).

We found an accurate history of length of amenorrhea difficult to reliably obtain and that patients were frequently taking estrogen supplementation (birth control pills). Because of the questionable validity of history alone, we analyzed the menstrual status of the patients by two methods:

1. "Positive" amenorrhea (history of three consecutive months of amenorrhea and estradiol below 20 pg/ml when available) versus bone density by the two-sample t-test.
2. Estradiol level versus bone density values by Pearson's correlation coefficient.

Neither method demonstrated that estrogen deficiency was related to decreased bone density, although this observation could be related to the limited number considered estrogen-deficient (only 10 of the 33 subjects).

Similar studies have been performed in amenorrheic female athletes, which further address the role of estrogen in osteoporosis. Drinkwater et al. found that amen-

TABLE 7
Correlations Between Age, BMI, AO, LOI and Bone Densitometry Measurements by Diagnostic Subgroup

Variable	Age			BMI			LOI			AO		
	AN	B	ED	AN	B	ED	AN	B	ED	AN	B	ED
RRAW	—	—	—	—	—	—	—	—	—	—	—	—
TRAW	—	—	—	—	0.02	—	—	—	—	—	—	—
NRAW	—	—	0.009	—	—	—	—	—	—	—	—	—
WRAW	—	—	0.008	—	—	—	—	—	—	—	0.05	—
LRAW	—	—	—	—	—	—	—	0.02	—	—	—	—
RS.D.	—	—	—	—	—	—	—	—	—	—	—	—
TS.D.	—	0.03	—	—	0.03	—	—	—	—	—	—	—
NS.D.	—	—	—	—	—	—	—	—	—	—	—	—
WS.D.	—	—	—	—	—	—	—	—	—	—	—	—
LS.D.	—	—	—	—	—	—	—	0.008	—	—	—	—

RAW = raw bone mineral density data; S.D. = standard deviation from normal age/sex matched controls; R = radius; N = femoral neck; T = trochanter; W = Ward's triangle; and L = lumbar spine (L2–L4).

orrhea in female athletes was accompanied by a significant decrease in density of the lumbar spine when compared to similar eumenorrheic controls with no significant change in the density of the radius. However, the amenorrheic group also had a significantly higher level of exercise than their eumenorrheic control group (*16*).

Another more recent report verified the decreased lumbar spine density in amenorrheic female distance runner athletes and the lack of change in the radius. However, the amenorrheic athletes in this study were significantly different from the controls in that the amenorrheic females began serious training very close to or even before menarche while the eumenorrheic females began training intensively at a mean of 5 yr after menarche (*17*).

Our results in combination with these other reports pose some important unresolved issues. First, does strenuous exercise regardless of menstrual status result in decreased bone density? Second, is the relation of the onset of the eating disorder to menarche the critical factor in the degree of decreased bone density rather than the length of amenorrhea?

TABLE 8
Exercise Level and Bone Density in Anorexia Nervosa

Area Measured	Grade 0 mean	Grade 1+ mean	Grade 2+ mean	p-value
T RAW	0.6576	0.6780	0.6663	0.0054
N RAW	0.5900	0.7950	0.5433	0.018
W RAW	0.8433	1.030	0.7666	0.047
N STD	−0.8333	0.2000	−2.433	0.02
W STD	−0.3800	0.4000	−2.400	0.01
L STD	−0.5100	0.2450	−1.500	0.04

RAW = raw bone mineral density data; S.D. = standard deviation from normal age/sex matched controls; R = radius; N = femoral neck; T = trochanter; W = Ward's triangle; and L = lumbar spine (L2–L4).

Another contributing factor may be malnutrition, which was not analyzed in our study. Garn et al. suggested that endosteal resorption of bone occurs in cases of severe malnutrition from lack of protein (*18*). Further evaluation of the dietary intake of nutrients, including proteins and carbohydrates, would be helpful to better determine the effect of diet.

Other important factors may be the effect of the eating disorder on the function of organs such as the kidneys, adrenal, thyroid, parathyroid, and pituitary glands. Several of these parameters have also been evaluated in the patients in this study and will be published in a separate manuscript.

Further studies to determine whether these patients can restore their bone density with return to a normal diet need to be performed. Treasure et al. reported that bone mineral density did improve with weight gain in patients with AN and was normal in patients who had recovered from the disorder (*19*). We have followed a limited number of these subjects (13) by bone densitometry and have found that the return of body weight did not reverse the osteoporosis. Therefore, "cure" of the eating disorder by weight gain alone may not restore the bone loss. More aggressive measures, such as how much vitamin D or fluoride therapy, may be required.

In conclusion, women with eating disorders including BN, EDNOS, and AN are at risk for osteoporosis. Since the femur is the most affected site in this population, the possibility of future morbidity and mortality is of major concern. The contributing factors of this osteoporosis are multiple, including physical parameters and exercise. Moderate exercise appears to be protective, but minimal or strenuous exercise may be harmful. Estrogen deficiency by itself may not be a major causative factor.

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