Evaluation of Sexual Function in Women with Hypogonadotropic Hypogonadism Using the Female Sexual Function Index (FSFI) and the Beck Depression Inventory (BDI)

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Background: Hypogonadotropic hypogonadism (HH), or secondary hypogonadism, results from reduced secretion of gonadotropins, including follicle-stimulating hormone (FSH) and luteinizing hormone (LH), by the pituitary gland, resulting in lack of production of sex steroids. The aim of this study was to evaluate self-reported sexual function in sexually active women with and without HH using two evaluation methods, the Female Sexual Function Index (FSFI) and the Beck Depression Inventory (BDI).

Material/Methods: The study recruited 88 women who attended an outpatient in vitro fertilization (IVF) clinic in Turkey for primary infertility, between August 2013 and August 2016. All patients were sexually active with an age that ranged from 20–41 years. Following an initial examination, including measurement of FSH and LH levels, all study participants were asked to complete the FSFI and BDI self-reporting questionnaires. Patients were divided into Group 1 (with HH) (N=42) and Group 2 (the control group) (N=46).

Results: Analysis of the patient responses to questions regarding their sexual function in the FSFI and BDI showed that of the 42 patients in Group 1 (the HH group), 27 patients (64.28%) reported sexual dysfunction; of the 46 patients in Group 2 (the control group) 14 patients (30.34%) reported sexual dysfunction. Analysis of the FSFI lubrication scores and orgasm scores showed a statistically significant difference between the two groups (both, p<0.01).

Conclusions: Women with HH require both physical and psychological support to improve their sexual function, self-esteem, mental health, and quality of life.

MeSH Keywords: Anovulation • Hypogonadism • Sexual Dysfunction, Physiological • Women

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Background

Sexual dysfunction is poorly studied in women, particularly in countries such as Turkey. However, sexual dysfunction can adversely affect the quality of life of sexually active women. A previously published study has shown that up to 50% of women in Turkey might have sexual dysfunction [1]. Sexual function in women can be influenced by psychological, biological, and social factors, but some specific risk factors have been identified that include age, adrenal disorders, metabolic syndromes, diabetes, thyroid disease, drug effects, mental health and behavioral disorders, and the use of copper intrauterine devices (IUDs) [2–6].

Hypogonadotropic hypogonadism (HH), or secondary hypogonadism, results from reduced secretion of gonadotropins by gonadotropin-releasing hormone (GnRH), and reduced levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), resulting in lack of production of sex steroids. HH has also been termed by the World Health Organization (WHO) as central hypogonadism, hypothalamic amenorrhea, or Group 1 anovulation [7,8], and between 5–10% of women with anovulation are included in this group.

Primary HH is a rare disease, and apart from the reduced release of GnRH, other hypothalamic and anterior hypophyseal functions are normal. In 2003, de Roux et al. showed that showed that loss of function of G protein-coupled receptor 54 (GPR54) was a cause of HH [9]. In women with HH, serum LH levels are not increased during ovulation, estrogen levels do not rise, and ovulation does not occur, which is why women with HH who are treated for infertility are treated with increased pulse doses of GnRH [10].

Whatever the underlying cause, HH results in mucosal atrophy and dryness of the vagina, vulva, and bladder neck. Vaginal atrophy and reduced vaginal lubrication in women with HH can affect sexual function and can result in discomfort or pain during sexual intercourse. HH may also result in loss of pubic hair, and in loss of fat and subcutaneous tissue of the mons pubis, atrophy of the labia majora, and loss of elasticity of the vaginal wall, with a reduction in vaginal mucosal glandular cells resulting in vaginal dryness, which are also effects associated with estrogen deficiency [11].

Estrogen plays a significant role in spontaneous ovulation and vaginal lubrication, preventing atrophic vaginitis, which might lead to insertional dyspareunia. Women with estradiol levels <50 pg/ml have increased vaginal dryness, dyspareunia, pain, and burning, and report a lower frequency of coital activity when compared to women with normal estradiol levels. Treatment of women with HH with estrogen alone is unlikely to improve these effects and improve sexual function in women, but combined treatment with estrogen and androgen might be the best way to improve sexual dysfunction associated with HH [12]. However, if the main reason for HH-related sexual dysfunction is due to vaginal atrophy, reduced vaginal lubrication, or urogenital atrophy, hormonal replacement therapy might be beneficial, including vaginal estrogen therapy for vaginal atrophy.

Few studies have been undertaken on the causes of sexual dysfunction in women, which has previously been assumed to be due to both organic and psychological factors. However, recent studies have shown that sexual dysfunction in women can be caused by organic factors, which should be diagnosed and treated to reduce stress among couples. Female sexual dysfunction leads to consistent, recurrent problems associated with sexual response in the following six main areas: desire, arousal, lubrication, orgasm, satisfaction, and pain [13,14]. The report of the 2015 International Consensus Development Conference on Female Sexual Dysfunction [13], divided female sexual dysfunction into four distinct disorders: designated desire disorders (DD), arousal disorders (AD), orgasmic disorders (OD) and pain disorders (PD). Information regarding the prevalence of female sexual dysfunction is still limited in the internationally published literature. However, it is estimated that the prevalence of female sexual dysfunction is between 43–90% [15,16]. Previously published studies have shown that hormonal imbalance resulting from endocrinopathies, polycystic ovary syndrome (PCOS), obesity, metabolic syndromes, diabetes mellitus (DM), and some hormonal contraception methods are also associated with female sexual dysfunction [17–19].

Although sexuality is important to the quality of life, in many countries discussion about sexual dysfunction problems are regarded as taboo. Also, there is still the belief that sexual dysfunction is a result of psychopathological disorders. For these reasons, the aim of this study was to evaluate self-reported sexual function in sexually active women with and without HH using two evaluation methods, the Female Sexual Function Index (FSFI) and the Beck Depression Inventory (BDI).

Material and Methods

Ethical statement

This study was supported by an Ethics Committee Report from the Department of Medicine, University of Harran, Turkey. All participants who agreed to participate in the study signed informed consent. This study was conducted following approval and a report from the local Ethics Committee.
Patient recruitment

The study recruited 88 women who attended an outpatient in vitro fertilization (IVF) clinic for primary infertility, between August 2013 and August 2016, in Turkey. All women were sexually active with an age that ranged from 20–41 years. All study participants who attended the outpatient clinical underwent a thorough medical examination that included imaging studies, blood and serum analysis, and laboratory investigations.

Patient groups studied

Two groups of women were studied. Group 1 consisted of patients with hypogonadotropic hypogonadism (HH). Group 2 was the control group, without HH. These two groups had their demographic and clinical data recorded, including age, body mass index (BMI), and serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), prolactin, and thyroid stimulating hormone (TSH).

The diagnostic criteria for HH included a low serum FSH and LH (<1 IU/L), no uterine bleeding on progesterone withdrawal, normal serum prolactin, a normal TSH, and a normal uterus with an endometrial thickness <5mm.

Women were included in the study who were between 20–41 years-of-age, who were sexually active during the previous four weeks, and who used no contraceptive methods.

Exclusion criteria for this study included women who were sexually inactive, younger than 20 years or older than 41 years, women with known systemic disease such as hypertension, diabetes mellitus, or rheumatic diseases, women who had undergone pelvic surgery, including hysterectomy, women with premature menopause, or urinary or fecal incontinence, women who were diagnosed with grade 2 genital prolapse according to the pelvic organ prolapse quantification system (POP-Q), women with a Bartholin’s cyst, endometriosis, vaginismus, chronic pelvic pain, or other pelvic inflammatory diseases, and women who were taking oral contraceptive, antidepressants, and beta blockers.

Self-reported evaluation of sexual function using the Female Sexual Function Index (FSFI)

Following the initial examination, the women who were considered to be suitable for inclusion in the study were asked to complete the Female Sexual Function Index (FSFI) questionnaire and the Beck Depression Inventory (BDI). The participants were informed about the study protocol, their privacy was guaranteed, and participation was voluntary. The study participants were allowed to complete the questionnaire in a single room so that an adequate level of privacy could be assured.

The FSFI is a valid, reliable, and anonymously designed questionnaire with six areas (desire, subjective arousal, lubrication, orgasm, satisfaction, pain), and includes 19 questions that measure female sexual function [14]. The Turkish version of the FSFI was determined to be valid and reliable for the Turkish women [20]. The questions and the FSFI scale is shown in Appendix A.

A scoring algorithm for the FSFI was developed to evaluate every area so that an aggregate score could be generated. Scoring ranges for items 3–14 and 17–19 were between 0–5; scoring ranges for items 1, 2, 15 and 16, were between 1–5. By accumulating the scores of each item that constituted the domain and multiplying the total by the domain factor, separate domain scores were acquired. Factors were 0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, satisfaction, and pain. The aggregate score was acquired by accumulating the six domain scores. The full-scale score range was from 2.0–36.0, with higher scores related to a lower degree of sexual dysfunction (Appendix B). Scores that were <65% in each domain were considered to represent sexual dysfunction in that domain. Therefore, scores <3.9 in all six domains represented sexual dysfunction. Every domain was given a minimum and a maximum score, and the total score is evaluated from all domains. A score <6.5 was considered to represent female sexual dysfunction [21]. A higher score for an individual domain or a higher total score represented better sexual function.

Self-reported evaluation of sexual function using the Beck Depression Inventory (BDI)

The BDI is a multiple-choice self-reporting scale that included 21 questions. The BDI is a mostly used as a tool to assess both the presence and the seriousness of depression [22]. Every question had a four-point scale of answers regarding the intensity of depression symptoms (0–3), with a total score range of 0–63. BDI was also re-designed for the Turkish population and the cut-off value considered to be ≥17 [23]. In this study, the presence of depression was considered to be present when the BDI score was >17.

Statistical analysis

The clinical findings of Group 1 (with HH) and Group 2 (controls) were compared. The comparison was also made of the parametric data of the participants using independent sample t-test. Data were presented as the mean ± standard deviation (SD), and nonparametric data were analyzed using a chi-squared ($\chi^2$) test and Mann-Whitney U test (median, range). Statistical analysis was performed using with SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). The significance level was determined to be $p < 0.05$. 

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There were 88 women with primary infertility who participated in the study, and who were recruited from an outpatient clinic, including 42 patients with hypogonadotropic hypogonadism (HH) (Group 1) and 46 patients without HH (Group 2). Of the 42 women in Group 1, 27 women (64.28%) were diagnosed with sexual dysfunction following analysis of the scores from the Female Sexual Function Index (FSFI) questionnaire and the Beck Depression Inventory (BDI). However, of the 46 women in Group 2 (control group), 14 women (30.43%) were also found to have sexual dysfunction.

Table 1 summarizes the basic demographic and clinical characteristics of the patients in Group 1 and Group 2 of this study. The average age of the women in Group 1 and Group 2 was 28.93±4.05 years and 28.93±4.78 years, respectively, which were not significantly different (p>0.05). Similarly, the average body mass index (BMI) values between the two groups, showed no significant difference (p>0.05). Analysis of serum hormonal levels showed no significant difference between Group 1 and Group 2 for the mean prolactin level and the mean thyroid stimulating hormone (TSH) levels (p>0.05). However, the mean levels of follicle-stimulating hormone (FSH) levels of the women in Group 1 were 0.35±0.28 mIU/mL and in Group 2 were 5.45±1.93 mIU/mL, representing a statistically significant difference between HH patients and the control group (p<0.05). Likewise, there was a significant difference between the two groups in the mean levels of luteinizing hormone (LH) levels (p<0.01 and the mean levels of estradiol between women with HH and the control group (p<0.01).

Table 2, Figure 1 shows that there was no significant difference between women in the HH group and the control group in terms of average satisfaction scores (p>0.05). Comparison of the mean BDI scores between Group 1 and Group 2 did not show a significant difference (p>0.05). However, in terms of mean desire scores and mean arousal scores, a statistically significant difference was found between the two groups (p<0.05). Also, the mean lubrication scores and orgasm scores showed a statistically significant difference between the two groups (p<0.01) and (p<0.01), respectively. In terms of pain and overall FSFI scores, there was no statistically significant difference between women with HH patients and the control group (p>0.05) and (p>0.05), respectively.

**Discussion**

The aim of this study was to evaluate self-reported sexual function in sexually active women with and without hypogonadotropic hypogonadism (HH) using two evaluation methods, the Female Sexual Function Index (FSFI) and the Beck Depression Inventory (BDI). The findings showed a significant difference in sexual function parameters for women with HH when compared with the control group.

Because sexual dysfunction can have a profound effect on the quality of life, and because the effects of hormonal and
other clinical abnormalities on women’s sexual function have been poorly studied, the findings of this study might contribute to awareness of the importance of sexual health on mental health and quality of life [24,25]. Out of 42 patients with HH in Group 1, 27 women (64.28%) were diagnosed with sexual dysfunction. Out of 46 participants in Group 2 (control group), 14 women (30.43%) were found to have sexual dysfunction.

The use of the FSFI self-reported questionnaire forms is considered to be the gold standard for determining sexual dysfunction. Therefore, this approach was chosen for this study to determine female sexual dysfunction. Each domain of the FSFI is given a minimum and a maximum score, and a total score is calculated from all the domains, and patients with a score <26.5 are regarded to have female sexual dysfunction [21]. However, to determine the exact prevalence of female sexual dysfunction in patients with HH, larger scale studies are required.

In this study, the sexual functional characteristics of desire, arousal, lubrication, orgasm, pain, and the overall FSFI scores of HH patients were significantly lower when compared with those of the control group (p<0.05). However, it was also shown in the present study that desire, arousal, pain and lubrication scores were significantly greater when compared with orgasm scores. However, regarding the satisfaction score, there was no significant difference (p>0.05).

When the average BDI scores of both groups are compared, no statistically meaningful difference was observed (p>0.05). A previously reported study claimed that sexual dysfunction was more common in men and women with poor emotional health and that women from different ethnic or racial backgrounds might have different types of sexual dysfunction problems [26]. It has also been reported that the prevalence of sexual dysfunction was 43% for women, and 31% for men [26].

In women with isolated HH, there is a gonadotropin deficiency throughout their lives, with low estrogen levels, a reduced

Table 2. Female Sexual Function Index (FSFI) and Beck Depression Inventory (BDI) scores in the control group and the patients with hypogonadotropic hypogonadism (HH).

| Female Sexual Function Index (FSFI) domain score | Control (N=46) | Hypogonadotropic hypogonadism (HH) (N=42) | p-Value |
|------------------------------------------------|---------------|-------------------------------------------|---------|
| Desire                                          | (1.20–6.0)    | (1.8–5.40)                                | 0.044** |
|                                                 | (4.25±1.37)   | (3.65±1.40)                               |         |
| Arousal                                         | (2.1–6.0)     | (2.6)                                     | 0.012** |
|                                                 | (4.82±1.04)   | (4.16±1.32)                               |         |
| Lubrication                                     | (3.0–6.0)     | (2.7–6.0)                                 | 0.004*  |
|                                                 | (5.20±0.67)   | (4.63±1.07)                               |         |
| Orgasm                                          | (3.0–6.0)     | (2.0–4.8)                                 | 0.000*  |
|                                                 | (4.71±0.87)   | (3.93±0.78)                               |         |
| Satisfaction                                    | (3.2–6.0)     | (3.0–6.0)                                 | 0.078   |
|                                                 | (4.75±0.88)   | (4.41±0.89)                               |         |
| Pain                                            | (3.0–6.0)     | (2.0–5.0)                                 | 0.010** |
|                                                 | (4.37±0.62)   | (3.98±0.75)                               |         |
| Total FSFI score                                | (17.40–34.20) | (15.70–32.40)                             | 0.002*  |
|                                                 | (28.1±4.33)   | (24.7±5.40)                               |         |
| Beck Depression Inventory                       | (6.0–17.0)    | (7.0–21.0)                                | 0.083   |
|                                                 | (12.28±3.58)  | (13.74±4.21)                              |         |

* p<0.05; ** p<0.01.

Figure 1. Comparison of FSFI domain outcomes for control group.

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endometrial thickness, and without progesterone withdrawal bleeding every month [27]. In a previous study, it has been reported that pulsatile gonadotropin-releasing hormone (GnRH) treatment is a suitable and efficient method to maintain normal ovarian function in HH [28]. These previous findings support the results of the present study, which showed a statistically significant difference between the mean estradiol levels when Group 1 (with HH) and Group 2 (normal) were compared (p<0.01).

Sexual function is influenced by psychological, physiological, anatomical, and social factors, and may cause impairment in the quality of life. Since HH is rare, there have been few previously published studies that have examined the effects of HH on fertility and sexual dysfunction problems of women with HH.

Sexual dysfunction influences the self-esteem of women, causes emotional distress, and reduces the quality of life. Data associated with female sexual dysfunction are limited in Turkey, as the discussion of sexual behavior by women can be a taboo subject, as a result of religious and cultural factors. There have been few studies on the topic of HH and female sexual dysfunction published in the literature. However, a study previously conducted in Turkey, and using the FSFI score, showed that 48.3% of women reported having female sexual dysfunction (with an FSFI score <25), and the prevalence of female sexual dysfunction was reported to be 41% for women between 18–30 years, 53.1% for women between 31–45 years, and 67.9% for women between 46–55 years [29]. It has also been claimed that the FSFI score decreases with age, with other significant risk factors for female sexual dysfunction reported to be smoking, poor diet, menopausal status, and marital status [29]. However, in the present study, there was no statistically meaningful relationship between age and sexual functions in women with HH.

The findings of the present study showed that HH was a significant factor associated with sexual dysfunction problems for infertile women. However, apart from HH, there are many other risk factors as confounders, which were not analyzed, including sexual problems of the partner, work or life stress factors, and other personal or psychological problems. However, based on the findings of this study, female sexual dysfunction is more frequently seen in women with HH when compared with the women without HH (the control group).

The present study had several limitations. First, this was a small pilot study from a single center, which was a private hospital, but with a good clinical network and a reliable patient database. Therefore, multi-center studies that include a larger study population are recommended.

Conclusions

There have been few previous studies conducted on female sexual dysfunction in Turkey. In this study on sexual function in women with hypogonadotropic hypogonadism (HH) two self-reported evaluation methods were used, the Female Sexual Function Index (FSFI) and the Beck Depression Inventory (BDI), which allowed women to give answers to very personal questions confidentially and in private. The findings from this study showed that there was a relationship between HH and sexual dysfunction, which was most likely due to the effects of reduced levels of ovarian hormones. Because sexual dysfunction can impair the quality of life and mental health, the findings of this study highlight that women with HH should be both physically and psychologically supported to improve their state of mind, self-esteem, and quality of life.
## Appendix A. Female Sexual Function Index (FSFI) questions and scoring system.

| Question | Response options |
|----------|------------------|
| **Q1.** Over the past 4 weeks, how often did you feel sexual desire or interest? | 5 = Almost always or always  
4 = Most times (more than half the time)  
3 = Sometimes (about half the time)  
2 = A few times (less than half the time)  
1 = Almost never or never |
| **Q2.** Over the past 4 weeks, how would you rate your level (degree) of sexual desire or interest? | 5 = Very high  
4 = High  
3 = Moderate  
2 = Low  
1 = Very low or none at all |
| **Q3.** Over the past 4 weeks, how often did you feel sexually aroused (“turned on”) during sexual activity or intercourse? | 0 = No sexual activity  
5 = Almost always or always  
4 = Most times (more than half the time)  
3 = Sometimes (about half the time)  
2 = A few times (less than half the time)  
1 = Almost never or never |
| **Q4.** Over the past 4 weeks, how would you rate your level of sexual arousal (“turn on”) during sexual activity or intercourse? | 0 = No sexual activity  
5 = Very high  
4 = High  
3 = Moderate  
2 = Low  
1 = Very low or none at all |
| **Q5.** Over the past 4 weeks, how confident were you about becoming sexually aroused during sexual activity or intercourse? | 0 = No sexual activity  
5 = Very high confidence  
4 = High confidence  
3 = Moderate confidence  
2 = Low confidence  
1 = Very low or no confidence |
| **Q6.** Over the past 4 weeks, how often have you been satisfied with your arousal (excitement) during sexual activity or intercourse? | 0 = No sexual activity  
5 = Almost always or always  
4 = Most times (more than half the time)  
3 = Sometimes (about half the time)  
2 = A few times (less than half the time)  
1 = Almost never or never |
| **Q7.** Over the past 4 weeks, how often did you become lubricated (wet) during sexual activity or intercourse? | 0 = No sexual activity  
5 = Almost always or always  
4 = Most times (more than half the time)  
3 = Sometimes (about half the time)  
2 = A few times (less than half the time)  
1 = Almost never or never |
| **Q8.** Over the past 4 weeks, how difficult was it to become lubricated (wet) during sexual activity or intercourse? | 0 = No sexual activity  
1 = Extremely difficult or impossible  
2 = Very difficult  
3 = Difficult  
4 = Slightly difficult  
5 = Not difficult |
| **Q9.** Over the past 4 weeks, how often did you maintain your lubrication (wetness) until completion of sexual activity or intercourse? | 0 = No sexual activity  
5 = Almost always or always  
4 = Most times (more than half the time)  
3 = Sometimes (about half the time)  
2 = A few times (less than half the time)  
1 = Almost never or never |
| **Q10.** Over the past 4 weeks, how difficult was it to maintain your lubrication (wetness) until completion of sexual activity or intercourse? | 0 = No sexual activity  
1 = Extremely difficult or impossible  
2 = Very difficult  
3 = Difficult  
4 = Slightly difficult  
5 = Not difficult |
| **Q11.** Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you reach orgasm (climax)? | 0 = No sexual activity  
5 = Almost always or always  
4 = Most times (more than half the time)  
3 = Sometimes (about half the time)  
2 = A few times (less than half the time)  
1 = Almost never or never |
| **Q12.** Over the past 4 weeks, when you had sexual stimulation or intercourse, how difficult was it for you to reach orgasm (climax)? | 0 = No sexual activity  
1 = Extremely difficult or impossible  
2 = Very difficult  
3 = Difficult  
4 = Slightly difficult  
5 = Not difficult |
Question | Response options
--- | ---
Q13. Over the past 4 weeks, how satisfied were you with your ability to reach orgasm (climax) during sexual activity or intercourse? | 0 = No sexual activity  1 = Very dissatisfied  2 = Moderately dissatisfied  3 = About equally satisfied and dissatisfied  4 = Moderately satisfied  5 = Very satisfied

Q14. Over the past 4 weeks, how satisfied have you been with the amount of emotional closeness during sexual activity between you and your partner? | 0 = No sexual activity  1 = Very dissatisfied  2 = Moderately dissatisfied  3 = About equally satisfied and dissatisfied  4 = Moderately satisfied  5 = Very satisfied

Q15. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner? | 0 = No sexual activity  1 = Very dissatisfied  2 = Moderately dissatisfied  3 = About equally satisfied and dissatisfied  4 = Moderately satisfied  5 = Very satisfied

Q16. Over the past 4 weeks, how satisfied have you been with your overall sexual life? | 0 = No sexual activity  1 = Very dissatisfied  2 = Moderately dissatisfied  3 = About equally satisfied and dissatisfied  4 = Moderately satisfied  5 = Very satisfied

Adapted from Rosen et al. [14].

### Appendix B. Female Sexual Function Index (FSFI) domain scores and total scale Scoring System.

| Domain | Questions | Score range | Factor | Minimum score | Maximum score |
| --- | --- | --- | --- | --- | --- |
| Desire | 1, 2 | 1–5 | 0.6 | 1.2 | 6.0 |
| Arousal | 3, 4, 5, 6 | 0–5 | 0.3 | 0 | 6.0 |
| Lubrication | 7, 8, 9, 10 | 0–5 | 0.3 | 0 | 6.0 |
| Orgasm | 11, 12, 13 | 0–5 | 0.4 | 0 | 6.0 |
| Satisfaction | 14, 15, 16 | 0 or 1–5 | 0.4 | 0 | 6.0 |
| Pain | 17, 18, 19 | 0–5 | 0.4 | 0 | 6.0 |

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