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Influence of Low Intensity Pulsed Ultrasound on Enhancing Biostimulation of Median Nerve in Patients with Chronic Carpal Tunnel Syndrome

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ABSTRACT

Background: When the median nerve is compressed while passing through the carpal tunnel in the wrist, a condition known as carpal tunnel syndrome (CTS) develops.

Purpose: To examine the impact of low intensity pulsed ultrasound on improving biostimulation of median nerve in patients suffering from chronic CTS.

Study Design: A pretest posttest control group design.

Materials and methods: Fifty-two male and female patients ranging in age from 30 to 50 years old were included in the study with chronic CTS. There were 26 patients in each of the two groups. Those in the 1st group were given through traditional physiotherapy and a low-intensity pulsed ultrasound. The 2nd group of patients served as controls and were given more traditional physiotherapy program, such as the use of splints and rehabilitative exercises. The four weeks of training consisted of three sessions per week. There were pre- and post-treatment assessments of pain levels, distal sensory and motor latencies, pinch grip strengths, and hand functions.

Results: In terms of pain intensity, distal sensory and motor latency, pinch grip strength, as well as functional performance, there were significant differences in both groups both before and after treatment.

Conclusion: Low intensity pulsed ultrasound was showed to be effective in enhancing perceived wrist pain, sensory and motor distal latency, pinch grip strength and functional performance in patients suffering from chronic CTS.

Keywords: *Chronic carpal tunnel syndrome, Low intensity pulsed ultrasound, Median nerve*

1. INTRODUCTION

The median nerve is squeezed as it travels through the carpal tunnel due to an enlarged and inflamed transverse carpal ligament, a condition known as carpal tunnel syndrome (CTS), the most prevalent entrapment mononeuropathy affecting the upper extremities. (1)

Pain, poor motor control of the hand, numbness of the lateral three and half fingers are clinical symptoms of CTS. (2) Pathophysiology of CTS is a multidimensional process; impaired venous return caused by compression generates a set of inflammatory reactions that may induce fibrosis, demyelination, and axonal loss leaving the median nerve hyperemic and edematous. Also, several studies reported that increased prostaglandin E2 expression, vascular endothelial growth factor and interleukin-6, may also be involved in CTS. (3, 4, 5)

To develop an accurate diagnosis, physical examination must be linked with electrodiagnostic modalities, as CTS continues to burden health care practitioners due to its high incidence which creates economic concerns. (6)

Patients suffering from mild to moderate CTS are advised to be involved in a conservative treatment program that may include splinting, exercise and therapeutic ultrasound as surgical treatment can't be considered risk free in spite of its effectiveness (7)

Ultrasound, like all sounds, is made up of waves that carry energy by compressing and releasing material at regular intervals. However, unlike human hearing, the frequency of ultrasound is greater than 20,000 Hz, which is far greater than what is considered normal. A frequency range of 16–20,000 Hz is audible to humans. To optimize the absorption of energy within a depth of 2 to 5 cm of soft tissue, therapeutic ultrasound uses a frequency ranging from 0.7 to 3.3 megahertz (MHz), or 700,000 to 3,300,000 cycles per second. (8)

For almost fifty years, physical therapists have relied on ultrasound (US) for its purported therapeutic benefits on pain and soft tissues. Theoretically, pain alleviation could be transmitted to soft tissues via reparative effects brought about by temperature-induced in vivo cavitation, intracellular alterations, and subsequent increases in blood flow. While ultrasound has shown promise in alleviating musculoskeletal injury pain, the scientific evidence supporting its use in this context is still lacking. (9)

While ultrasound is a powerful tool for therapeutic purposes, it is important to be aware of the potential for unintended adverse bioeffects that could cause serious harm to patients, even death. So, standardization, ultrasound dosimetry, benefits assurance and side-effects risk minimization must be carefully considered to ensure an optimal outcome for the patient. (10)

Numerous studies have shown that low intensity pulsed ultrasound (LIPUS) can enhance cytosolic calcium levels while simultaneously promoting dentinogenesis, cell regeneration, protein production, collagen production, membrane permeability, as well as integrin expression. (11)

Regarding the promotion of tissue/fracture healing along with dental repair, LIPUS has important implications. Furthermore, animal studies suggest it may have restorative effects on brain regeneration. (12)

There is no generally accepted method for treating CTS at this time. While nonsurgical treatments like mobilization and corticosteroid injection can alleviate symptoms in the short term, they cannot restore the microstructure of the nerves, which is essential for the restoration of nerve function (13, 14). Likewise, surgical procedures may relieve nerve pressure through carpal tunnel release. However, no adequate long-term outcomes were found due to issues of scar-tissue growth around the nerve that may induce nerve atrophy. (15, 16)

2. MATERIALS AND METHODS

Study Design

The study was carried out at the outpatient physical therapy clinic of El hilal hospital in the period from November 2022 to April 2024 and complied with the recommendations of the Declaration of Helsinki on the conduct of human research. The study was approved from the Faculty of Physical Therapy, Cairo University's institutional review board (No: P.T.REC/012/004129) prior to the study began. All subjects were asked to provide informed consent concerning the use of their personal information in publications. The study design was a prospective, randomized, single-blind, pre-post-test controlled trial.

Participants

A simple random sample of eighty participants were recruited from Elhilal hospital, Egypt. They were enlisted and assessed for their eligibility; twelve patients were excluded as shown in fig (1). An overall of 68 hands of 68 individuals with clinical and electrophysiological signs of mild to moderate CTS were enrolled in this study. Patients with mild to moderate CTS, as determined by a physician in accordance with the most recent recommendations (19) from the American Association of Electrodiagnostic, were eligible to participate. (3) patients' ages should fall within the 30–50 years old; (4) patients should have a body mass index (BMI) ranging from 18.5 to 29.9 kg/m2; (5) patients should have a history of nocturnal pain, night waking, paresthesia, or numbness within the sensory distribution of the median nerve; and (6) positive clinical special tests for CTS (Tinel test and Phalen test).

The exclusion criteria were: (1) patients with cervical disc; (2) patients with cervical spondylosis; (3) thoracic outlet syndrome; (4) diabetes; (5) hypertension; (6) cardiovascular disorders; (7) pregnant women and (8) patients who had carpal tunnel release surgery.

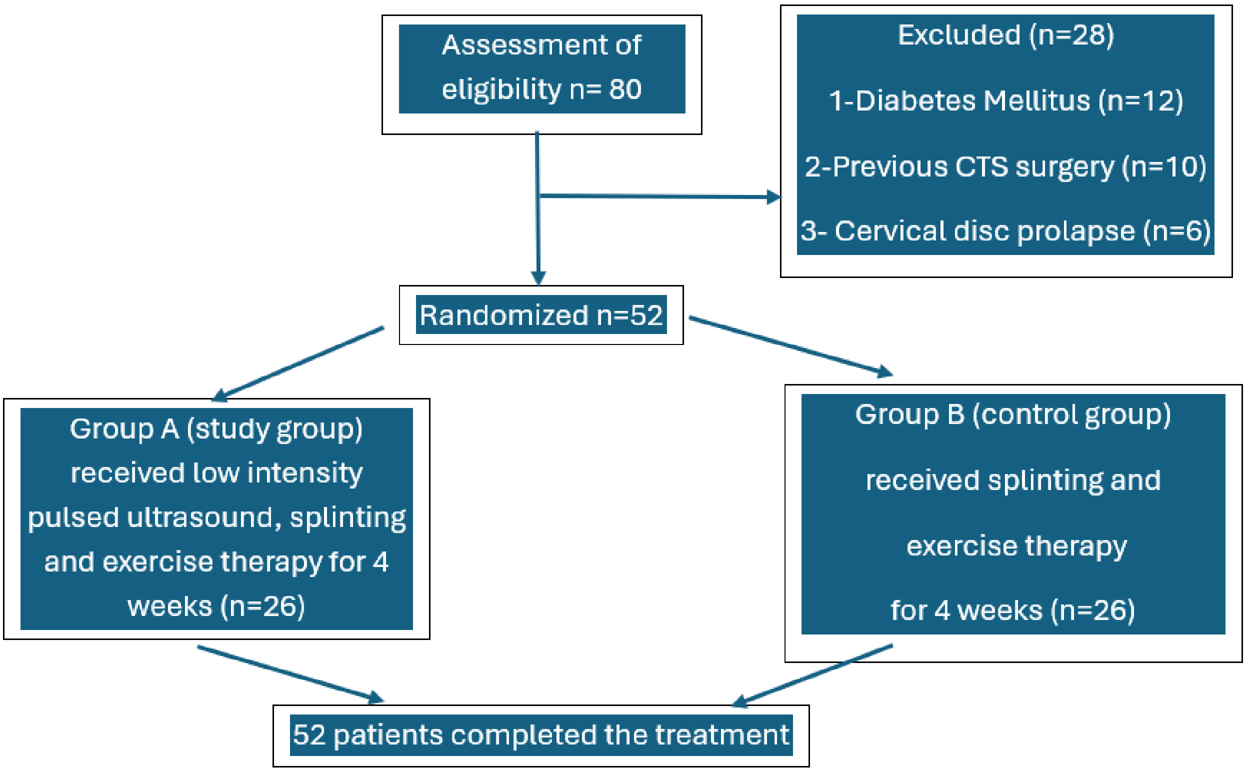

Figure 1: Flowchart diagram for the study.

Randomization

Written informed consents were obtained from the patients after explaining the nature, purpose, and benefits of the study, informing them of their right to withdraw or refuse at any time, and the confidentiality of any obtained data. Utilizing the opaque closed envelope approach, the patients were randomized into two equivalent groups, A and B.

Interventions

Patients in Group A were told to wear a neutral customized volar splint all day and night for four weeks, even while they were doing extremely strenuous activities. At the post-treatment examination, patients were asked to present the forms that they had filled out to verify that they had adhered to the splint application instructions. Splint non-compliance was determined when patients did not check the form more than once weekly.

Also, LIPUS using gymna uniphy ultrasound device was performed over the wrist. The following settings were utilized: a 1 MHz frequency, an intensity of 0.3 W/cm2, as well as pulsed ultrasound waves at a 20% intensity. This treatment was administered three times weekly for four weeks, with each session lasting 20 minutes.

At last, the patients were told for practicing the tendon and nerve gliding exercises that Totten and Hunter (1991) had created (20).

The finger positions were kept distinct throughout the tendon-gliding activities. These will include the following: straight, hook, duck, full fist, as well as straight fist.

To facilitate median nerve mobilization, the following six hand and wrist positions were employed during the glide exercise: The following positions are possible: (A) the wrist was in a neutral position with the fingers and thumb flexed; (B) the wrist is in the same position with the fingers and thumb extended; (C) Wrist and fingers are extended with thumb in neutral position; (D) the wrist, fingers, and thumb are all extended; (E) the wrist, fingers, as well as thumb are all extended with the forearm supinated; (F) the opposite hand gently stretches the thumb as the first hand supinated and extended.

The patient is instructed to hold a neutral position for the neck and shoulders, a forearm supination, and an elbow in 90° flexion for a duration of 5 seconds per position. Ten repetitions of each exercise are to be performed during each session, and patients were advised to perform the exercises three to four times daily for a duration of four weeks.

In Group B, in addition to splinting, nerve and tendon gliding exercises are applied by the same procedure.

3. OUTCOME MEASURES

Visual Analogue Scale

Before and after therapy, patients' levels of hand pain were measured using a 10-point visual analogue scale (VAS; 0 = no pain, 10 = greatest pain).

Electrophysiological studies

Electrophysiological studies (Motor and antidromic sensory distal latencies) were performed based on the American Association of Electrodiagnostic Medicine (AAEM) guidelines (19) with a Neuropack S1 MEB-9004 Nihon Koden (Japan). All experiments were conducted in a controlled environment with a temperature of 25°C. The abductor policies brevis muscle was used for recording compound muscle action potentials (CMAPs) for the median nerve. They were attached to surface electrodes. A handheld stimulator that had a 2-cm interelectrode distance was used for stimulating the median nerve, which was located 8 cm proximal to the anodal electrode. We quantified distal motor latencies as the time it took for the stimulus artifact to appear followed by the commencement of the CMAP. The median nerve's sensory distal latency was measured antidromically using ring electrodes attached to the index finger's proximal as well as distal interphalangeal joints. The stimulus and recording electrode were 14 centimeters apart.

Grip strength

The same researcher also assessed pinch grip strength, which is expressed as a kilogram. The strength of the pinch grip was measured utilizing a baseline hydraulic dynamometer in accordance with the protocols established by the American Society of Hand Therapists (26). When the patient was seated, their arm was held in the neutral position with the shoulder was in adduction and neutral rotation, elbow at 90° flexion, forearm, and wrist neutral. As part of the exercise, patients were told to apply full force to the handle and hold that position for two to five seconds. With a 30-second rest in between each trial, this process was performed three times for each hand. The average score from all three trials was determined.

Hand function

Boston Carpal Tunnel Questionnaire was used to assess the patients' pre and post treatment levels of hand function level. It consists of the Symptom Severity Scale (SSS) containing 11 questions, and it employs a five- point rating scale, as well as Functional Status Scale (FSS), which comprises 8 items evaluating the degree of complaints on a five-point scale. We estimated the mean totals of the two scales and utilized them for our study.

Statistical analysis

The proper sample size for this investigation was determined utilizing the "t tests" option in G-power 3.1.9.4, which yielded a preliminary power analysis with parameters of power= 0.8 and α= 0.05. An examination of two other research' findings (27, 28) indicated that a minimum of 52 individuals, divided equally between the two groups, would be sufficient for this study. A Shapiro-Wilk test was used to determine if the data was normally distributed. Due to the regularly distributed nature of all variables, a parametric test was employed. Statisticians from SPSS, Inc. in Chicago, IL, used SPSS for Windows, version 20, to analyze the data. For this reason, we employed parametric statistical tests, namely a dependent t test, to compare the groups' "pre" and "post" therapy, and a "independent t test" to compare the two groups' "pre" and "post" treatment. A significance level of 0.05 was used.

4. RESULTS

Baseline and demographic data

According to Table 1, there were no significant differences (P>0.05) in terms of age, weight, height, or BMI among the two groups of subjects.

Table 1: Descriptive statistics and independent t tests for the participants in both groups:

Parameters	**Age (Years)**		**Weight (kg)**		**Height (cm)**		**BMI (kg/m^2)**	
Groups	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**
Mean ± SD	43.5 ±4.2	41.2 ±5.4	69.8 ±6.4	68.5 ±7.3	172.1 ±7.3	170 ±6	23.5 ±0.6	23.7 ±1.5
t value	1.7		0.6		1.1		0.5	
p value	0.085		0.521		0.260		0.640	
Sig.	NS		NS		NS		NS	

*SD: standard deviation, P: probability S: significance, NS: nonsignificant, kg: Kilogram, cm: centimeter, BMI: Body mass index.

Comparison of Pain, Median nerve sensory distal latency, motor distal latency, pinch grip strength and hand function in the two groups measured pre and post-treatment:

There was a significant reduction in pain, median nerve sensory distal latency, and motor distal latency when comparing among groups. Additionally, both groups showed a statistically significant improvement in hand function and pinch grip strength after treatment as compared to their pre-treatment levels ($p < 0.05$). According to table 2 In terms of pain, median nerve sensory distal latency, as well as motor distal latency, Group A demonstrated a statistically significant decrease compared to Group B ($p<0.05$). The results showed that group B had significantly better hand function along with pinch grip strength ($p<0.05$) (Table 2)

Table 2: The two groups' mean ± standard deviation and p-values for pain intensity, median nerve sensory distal latency, motor distal latency, pinch grip strength, as well as hand function before and after treatment:

Pain Intensity

Parameters	**Group A**	**Group B**	**MD**	**t value**	**p value**	**Sig.**
Pre treatment	8.3 ± 0.4	8.4 ± 0.4	0.1	2.7	0.109	NS
Post treatment	5 ± 0.9	6 ± 1.3	1.0	11.8	0.001*	**S**
% Change	**40** %	**28**.6 %				
p value	0.001*	0.001*				
Sig.	**S**	**S**				

Sensory Distal Latency

Parameters	**Group A**	**Group B**	**MD**	**t value**	**p value**	**Sig.**
Pre treatment	3.75 ± 0.14	3.75 ± 0.12	0.002	0.01	0.914	NS
Post treatment	3.1 ± 0.12	3.25 ± 0.09	0.010	37	0.0001*	**S**
% Change	17.3%	13.3%				
p value	0.001*	0.001*				
Sig.	**S**	**S**				

Motor Distal Latency

Parameters	**Group A**	**Group B**	**MD**	**t value**	**p value**	**Sig.**
Pre treatment	4.6 ± 0.2	4.6 ± 0.2	0.001	0.8	0.784	NS
Post treatment	3.13 ± 0.2	3.58 ± 0.16	3.045	110	0.0001*	**S**
% Change	32%	22%				
p value	0.0001*	0.0001*				
Sig.	**S**	**S**				

Pinch Grip Strength

Parameters	**Group A**	**Group B**	**MD**	**t value**	**p value**	**Sig.**
Pre treatment	11.8 ± 1.4	12.5 ± 1.2	0.7	3.66	0.061	NS
Post treatment	17.7 ± 1.5	16.3 ± 1.4	1.4	11.65	0.001*	**S**
% Change	**50%**	**30%**				
p value	0.001*	0.001*				

Sig.	**S**	**S**

Hand Function

Parameters	Group A	Group B	MD	t value	p value	Sig.
Pre treatment	60 ± 3.8	58.8 ± 3.7	1.2	1.4	0.246	NS
Post treatment	18.4 ± 2.3	21.5 ± 3	3.1	16.7	0.001*	**S**
% Change	69.3%	63.4%				
p value	0.001*	0.001*				
Sig.	**S**	**S**				

*Significant level is set at alpha level <0.05 SD: standard deviation

MD: Mean difference p-value: probability value S: significance

NS: non-significant MDL: Motor distal latency SDL: Sensory distal latency kg: Kilogram VAS: Visual analogue scale msec: Millisecond

5. DISCUSSION

The median nerve runs through the carpal tunnel, which can cause mechanical irritation, compression, or stretching, leading to CTS, a type of mononeuropathy. Annual surgical expenditures are close to $2 billion USD. Unfortunately, there is currently no universally accepted method for treating CTS, despite the fact that patients with this condition are among the most likely to miss work due to their condition (17)

Therapeutic ultrasound has a long history of usage in the conservative management of chronic CTS, with numerous research confirming to its effectiveness18-19-20. Studies showing the effectiveness of US should be backed by placebo-controlled trials due to methodological discrepancies and differences in type, intensity, as well as frequency of therapy. (10-19-20)

In the present study which aimed to examine the impact of LIPUS on Pain intensity, sensory distal latency (SDL), motor distal latency (MDL) of the median nerve, pinch grip strength as well as hand function in patients suffering from chronic CTS there was significant improvement in pain intensity, SDL and MDL of median nerve, pinch grip strength and hand function in experimental group who received LIPUS in addition to conventional physical therapy program

The findings corroborated those of Sinan Bagcaci et al. 2023, who studied the effectiveness of underwater therapeutic pulsed ultrasound for mild to moderate cases of CTS. Seventy-five patients were recruited and received 10 session of underwater pulsed ultrasound for 2 consecutive weeks. improvement in pain, SDL, MDL and hand grip strength were noted after treatment (21)

Also in the current study, patients in group (A) reported improvement in pain intensity, pinch grip strength, median nerve sensory and motor distal latencies and hand function after application of LIPUS, these results came in agreement with Muhammad Ljaz et al 2022 while the study found that both groups of patients with mild to moderate CTS benefited from physical therapy, the neuromobilization group demonstrated a statistically significant improvement in flexion and extension, pain reduction, SSS and FSS reduction, and BCTQ compared to the traditional physiotherapy group. (22)

In addition, those suffering from mild to moderate CTS were the subjects of a 2017 study by Tomasz W et al. that compared the effectiveness of electro physical modalities, such as ultrasound therapy, with manual therapy, which included neurodynamic techniques, and found that both treatments improved nerve conduction, pain levels, functional status, as well as subjective symptoms. Nevertheless, the MT group had superior outcomes in terms of pain elimination, subjective symptoms, in addition to functional status. (23)

In a recently published meta-analysis, Konstantin et al. (2018) demonstrated that low-intensity ultrasound may enhance functional results by experimentally promoting nerve regeneration. Their goal is to show how low-intensity ultrasound promotes nerve regeneration in an experimental setting, as well as the present status of research into this topic and its potential future therapeutic uses. (24)

For cases of mild to severe idiopathic CTS, researchers Amir and Ali (2004) evaluated the effectiveness of ultrasound and laser therapy. When comparing ultrasound and laser therapy for CTS, they found that ultrasound was superior. The efficacy of these therapies in combination therapy for CTS patients need more investigation. (25)

Through improving Schwann cell-mediated cavernous nerve regeneration, Zitaiyu L. 2023 found that lLIPUS alleviated erectile dysfunction caused by bilateral cavernous nerve damage and concluded that LIPUS promoted nerve regeneration and ameliorated erectile function by enhancing Schwann cells proliferation, migration, and neurotrophic factor nerve growth factor expression. The stimulation of Schwann cells by low-intensity pulsed ultrasound may be mediated via the TrkB/Akt/CREB axis. A new approach to treating neurogenic erectile dysfunction caused by cavernous nerve damage may be LIPUS therapy. (26)

Cameron (M) 2022 confirmed that Ultrasound has the potential to manage pain in two ways: by influencing how the body perceives and transmits pain, or by addressing the underlying cause of the pain. These effects may be the result of The nonthermal effects of ultrasound which may reduce pain by modulating inflammation or neuronal pain signaling. .(9)

The mechanical processes generated by ultrasound, such as cavitation, microstreaming, as well as acoustic streaming, are responsible for these nonthermal ultrasonic effects. Ultrasound causes gas-filled bubbles to develop, expand, and pulsate, a process known as cavitation. Ultrasound waves have two distinct phases: compression, when they reduce tissue bubbles, and rarefaction, when they enlarge them. Inertial cavitation is one kind of cavitation, whereas transient cavitation is another. In stable cavitation, the size of the bubbles varies periodically without bursting. Unstable cavitation occurs when bubbles expand across several cycles before abruptly collapsing. The production of free radicals and massive, transient localized increases in pressure and temperature are the results of this implosion. One theory for ultrasound's nonthermal therapeutic benefits is stable cavitation, whereas another holds that therapeutically-used ultrasonic levels do not cause unstable cavitation. James Cameron 2022. (9)

The present study's findings were in contradiction with Jeremy D. and Kamalakannan P. 2019 who compared therapeutic ultrasound for mild to moderate CTS in a randomized controlled study. 40 individuals were observed for one year after treatment with wrist splints as well as either real or sham therapeutic ultrasonic. Symptom severity scale score change was the primary outcome measure. Neuron conduction investigations, ultrasound examination of the median nerve, as well as functional status scale score were secondary results. At 6 and 12 months, both groups demonstrated significant improvements in clinical and neurophysiological outcomes as compared to their baseline conditions. No significant differences were observed between groups at any time. In a multivariate analysis, the only independently significant predictors of the primary outcome were pretreatment symptom severity and additional treatments during follow-up and they came to the conclusion that treating CTS with ultrasound does not provide any significant improvement in clinical outcomes (27)

Additionally, Simeon i et al. (2018) used sixty rats in their study. The rats were randomly divided into five groups of 12 and each group got primary epineural nerve reconstruction as well as median nerve transection. After surgery, patients were given ultrasonic treatment once, three times, or daily for up to two minutes at a time with a frequency of 1.5 MHz, a pulsed SATA intensity of 30 mW/cm2, a repetition rate of 1.0 kHz, and a duty cycle of 20%. A control group and an every-day sham group were used as references. After comparing the results to those of control and sham groups, they determined that the FDA-approved ultrasound device that is now available for clinical use didn't improve axonal regeneration after nerve damage. Since the ultrasound-intensity was just 30 mW/cm2, this goes against the grain of the non-conclusive preclinical data. Clinical trials with 200-300 mW/cm^2 are suggested (28)

The conflicting results may be due to different ultrasound parameters used such as frequency, intensity, mode and duration. In previous studies, authors used various parameters that differ than parameters used in the current study which allowed utilization of therapeutic window that has biostimulation effect that promote median nerve regeneration.

6. CONCLUSIONS

This study provides evidence of the effectiveness of LIPUS in improving patient symptoms and hand function in CTS. The use of selected ultrasound parameters in electro therapy techniques may provide avenues to help clinicians in treating neuromuscular disorders.

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