International Journal of Cardiology 289 (2019) 6–11

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

An RCT of brief cognitive therapy versus treatment as usual in patients with non-cardiac chest pain

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ARTICLE INFO

Article history:
Received 2 August 2018
Received in revised form 5 December 2018
Accepted 21 January 2019
Available online 5 February 2019

Keywords:
Non-cardiac chest pain
Randomised controlled trial
Cognitive behavioural therapy
Emergency department

ABSTRACT

Background: Non-cardiac chest pain (NCCP) is a common reason for presenting to an emergency department (ED). Many patients re-present with similar symptoms despite reassurance.
Objective: To investigate the clinical value of a brief cognitive behavioural treatment (CBT) in reducing re-presentations of patients who present with NCCP.
Method: A randomised controlled trial (RCT) comparing three or four sessions of NCCP directed CBT with treatment as usual (TAU). The primary outcome measure was reducing health service use measured as re-presentations to the ED and hospitalisations for NCCP over 12 months of follow-up. Secondary outcomes were chest pain, health anxiety, depression, anxiety, quality of life and social functioning.
Results: 214 patients received CBT and 210 TAU. There was no difference in ED visits or hospitalisation at three months or 12 months follow-up. Those with prior ED presentations for NCCP were significantly less likely to present with NCCP at three months follow-up but not at 12 months. Health anxiety was less at three months in those who received CBT but this effect was not present at 12 months. No other differences in secondary outcome measures were present.
Conclusions: A brief CBT intervention for NCCP failed to reduce representations or improve psychological health over 12 months. We do not recommend such an intervention to unselected patients with NCCP. Patients presenting with prior episodes of NCCP obtain benefit for a three month period. Working with those patients to sustain their improvement might be worthwhile.

1. Introduction

Chest pain is common and frequently non-cardiac in origin [1]. The lifetime prevalence of non-cardiac chest pain (NCCP) is around 20–33% compared with 6–7% for angina [2]. Chest pain is one of the commonest reasons for attending an emergency department (ED) [3] and 50–60% of chest pain patients have NCCP [4,5], The focus of assessment is the exclusion of coronary artery disease, but typically, once this is excluded NCCP patients are offered no treatment beyond feedback and reassurance that they do not have cardiac disease [6].

While reassurance may be important it is often ineffective for patients with NCCP. Patients are sceptical because of the lethal connotations of chest pain and the fear that something might have been overlooked [7,8]. The lack of specific management of NCCP often leads to chronic symptoms, high levels of psychological distress [6,9–11], increased risk of unemployment and heavy continued use of health care services [9,12–14].

Despite the high levels of suffering and intensive health service use by patients with NCCP there are relatively few studies of positive management strategies. A recent Cochrane Review identified 17 randomised control trials (RCT) of positive management in patients with NCCP which met their criteria for review. The authors concluded that there was modest evidence for benefit in reducing pain and improving quality of life in patients with NCCP in the short term [15]. However, the evidence base was weak; all studies were small, multiple outcome measures were used, participation rates were low and a wide variety of cognitive behavioural therapy (CBT) based approaches were used. It appears that standard CBT models may not be as effective in the treatment of NCCP as in the treatment of anxiety and depression.

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https://doi.org/10.1016/j.ijcard.2019.01.067
0167-5273/

We have developed a treatment model based on the biopsychosocial approach outlined by Esler and Bock [16]. We have called the intervention NCCP directed CBT. In this intervention the focus is not on attribution, as in most CBT models, but on education about and management of chest pain symptoms, cardiac risk factor reduction and stress management. Chest pain is an ideal candidate for this intervention approach since it is a multi-causal interactive condition [17]. Even if symptoms are determined to be non-cardiac other factors may cause or exacerbate symptoms, e.g. gastric reflux or psychological stress. NCCP directed CBT can address most relevant contributions to the patient's condition so is appropriate for a broad spectrum of patients from those who have panic disorder to those who are eventually diagnosed with cardiovascular disease. The intervention focusses on symptoms of chest pain not on the attributed pathology. The intervention is relatively brief since longer interviews are associated with high drop-out rates [15].

1.1. Research objectives

The objective of this trial was to examine the clinical value of NCCP directed CBT in patients with NCCP who present to an ED. Specifically we hypothesised that, (1) three or four sessions of NCCP directed CBT would be more effective than treatment as usual (TAU) in reducing health service use measured as emergency room visits and hospitalisation in the 12 months after randomisation to the trial (primary outcome) and, (2) result in a reduction in chest pain, health anxiety, general anxiety and depression scores as well as improved quality of life (QOC) and social functioning at three months and 12 months (secondary outcomes).

Treatment as usual in this setting consisted of a brief explanation of likely mechanisms and reassurance about the benign nature of the condition with respect to further heart attacks. Recruiting patients into the study meant they all received a written outline of the diagnosis of NCCP as well as the baseline and follow-up questionnaires".

2. Methods

2.1. Trial design

The study is a single centre pragmatic randomised control trial (RCT) (Trial Registration ACTRN12612000133831) with two parallel aims and equal randomisation of eligible patients to three or four sessions of NCCP directed CBT or TAU.

2.2. Participants & study setting

All participants attending the Christchurch, New Zealand ED with chest pain and in whom acute coronary syndrome or other causes of chest pain requiring inpatient investigation or treatment had been excluded, were eligible for recruitment. Patients were identified at the time of ED presentation and usually recruited after tests (including serum troponin and exercise ECGs) excluding a cardiac cause of chest pain were completed. Participants for inclusion were aged between 18 and 75, able to give informed consent, resident in the Christchurch area and able to read and speak English. The only exclusion criterion was being currently under specialist psychiatric services. The assessments and therapy were all performed in the Department of Cardiology, Christchurch Hospital.

2.3. Assessments

The following assessments were carried out at baseline.

i) The Mini International Neuropsychiatric Interview (MINI) [18] modules for depression, panic disorder, GAD and somatisation disorder.
ii) Demographic data, previous NCCP, other emergency department presentation.

The remaining assessments were carried out at baseline at three months and at 12 months. A trained interviewer who was blind to treatment status interviewed all patients via telephone.

i) The Health Anxiety Questionnaire (HAQ) [19] consists of 21 questions measuring health anxiety. The scale is reliable and discriminates between patients suffering from health anxiety vs generalised anxiety. It is also sensitive to change.
ii) The Hospital Anxiety and Depression Scale (HADS) [20] is a 14 item questionnaire which measures anxiety and depression in the past week. It was specifically designed to be used in patients with medical conditions and has been used in over 500 studies.
iii) SF-12 [21] is a survey of general quality of life. It consists of eight scaled scores which are the weighted sum of questions in their section. It captures practical and valid information about functional health and wellbeing.
iv) The SFQ [22] consists of an eight item self-report developed from the Social Functioning Schedule (SFS). Scores are reliable, valid and stable across normal populations.

2.4. Intervention

The intervention is a flexible three or four session CBT based treatment. Sessions were manualised and structured. A handout explaining the rationale and treatment was given to patients. Session 1 consists of education about the biopsychosocial model of illness, the multiple causes of chest pain and learning to keep an activity record and a mood and anxiety diary. Session 2 focuses on teaching CBT strategies for stress self-management which are diaphragmatic breathing exercise, progressive muscle relation with visualisation and activity scheduling, identification of negative automatic thinking, cognitive misattribution errors and cognitive reframing. Homework practicing these strategies is prescribed. Session 3 reinforces CBT strategies and discusses cardiac risk factors. Handouts summarising cardiac risk factors and cognitive behavioural exercises are given. Homework is prescribed. Session 4 reinforces CBT strategies and alternative strategies for dealing with chest pain as well as an individual relapse prevention model.

Therapists were one clinical psychologist and two cardiac nurses who were trained and worked under the supervision of a clinical psychologist (JZ). Treatment fidelity was promoted in a number of ways; the sessions were comprehensively manualised; staff were trained and supervised; audiotapes of sessions were scrutinised by the supervisor; regular supervision was set up for all therapists.

2.5. Outcome

The primary outcome was hospital attendance with NCCP at three months and 12 months following the intervention. The secondary outcomes for the study were self-reported chest pain, change in health anxiety (measured using the Health Anxiety Inventory (HAI)), change in general anxiety and depression (measured using the Hospital Anxiety and Depression Scale (HADS)), quality of life (using the SF-36) and social functioning (using the Social Functioning Questionnaire (SFQ) at three months and 12 months.

2.6. Sample size

The sample size for the present trial was 400 participants. Based on a re-presentation rate of 38% (calculated using Emergency Department historical data) and assuming a 30% reduction in re-presentation rate and an estimated 20% drop-out rate, we calculated that the trial had over 90% power to detect a difference at a significance level of 0.05 or less.

2.7. Randomisation, allocation, implementation and blinding

Participants were randomly assigned to the treatment or control groups using block randomisation, in blocks of six participants. Randomisation was conducted by the statistician (author JMB) using Random Allocation Software [23], with the randomisation procedure being fully blinded to all other investigators and clinical staff.

2.8. Statistical methods

The statistical analyses for the present study employed an intention-to-treat approach. Comparisons between treatment and control groups on demographic and clinical variables were tested for significance using paired *t*-tests.

The primary endpoint for the study (re-presentation at hospital for non-cardiac chest pain within three months and one year of initial visit) was modelled using logistic regression, as a function of treatment (intervention/control), prior history of presenting for non-cardiac chest pain, and treatment × prior presentation interactions.

Secondary outcomes for the study (self-reported chest pain; health anxiety; depression/anxiety; mental quality of life; physical quality of life; social functioning) at three and 12 months follow up were compared across treatment and control groups using paired *t*-tests. In all cases, missing data were treated as missing at random in all analyses, with no imputation.

2.9. Methods of overcoming bias

The independent central computerised system and blinding involved in randomisation ensures no bias in treatment allocations. However, since this is a single blind study there is danger of disclosure. This is minimised by the research assessors and therapists being completely separate, the research assessors being blind to the patient's allocation status and asking the patient not to disclose their treatment.

3. Results

3.1. Participant flow

Fig. 1 shows how patients moved through the study. After randomisation to NCCP, modified CBT or the control arm, all patients were followed up at three months ($n = 197$ controls; $n = 175$ modified CBT) and 12 months ($n = 192$ controls; $n = 165$ modified CBT).

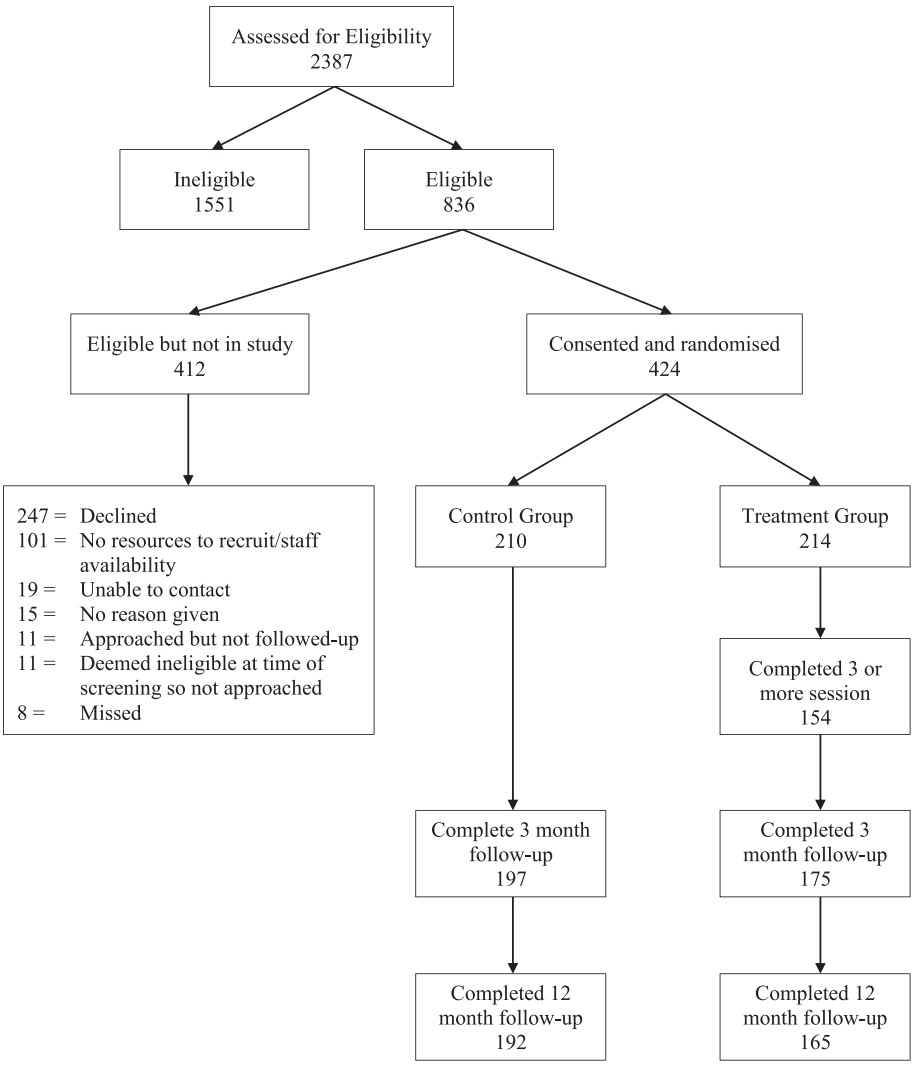

Fig. 1. Participant flow.

3.2. Baseline demographic and clinical characteristics

The baseline demographic characteristics for the sample are shown in Table 1a. The Table shows that those in the control group were marginally older than those in the treatment group, but that there were no differences in the distribution of gender or ethnicity (New Zealand European/other European vs other ethnicities).

Table 1b shows the baseline clinical characteristics of the two groups. There were no statistically significant differences between the treatment and control groups on the measure of prior presentation, or the baseline clinical measures.

3.3. Primary outcome measure – main effects tests

The primary outcome measure in the study was the percentage of participants who reported attending hospital at the three month and twelve month follow-up. The risks of self-reported hospital attendance for the treatment and control groups, at the three month and twelve-month follow ups are shown in Table 2. The Table shows while rates of hospital attendance were slightly lower for the treatment group, there was no evidence of statistically significant differences between the treatment and control groups in terms of risk of hospital attendance, either at three months follow-up or twelve-months follow up (three month RR = 1.14; 12 month RR = 0.84).

3.4. Primary outcome measure - tests of interaction

The logistic regression models used to model the main effects of treatment on risk of hospitalisation at three and 12 months follow up were extended to include a treatment × prior presentation interaction term. The results of these analyses are shown in Table 3, which depicts the percentage of participants who re-presented to hospital with non-cardiac chest pain at either three or 12 months follow up. The Table shows there was evidence of a statistically significant treatment × prior presentation interaction for re-presentation for chest pain at the three month follow up. Simple main effects analyses showed that, for the treatment condition, those participants who had previously presented with chest pain were significantly less likely to have re-presented to hospital with non-cardiac chest pain at the three month

Table 2
Primary outcome – main effect for treatment condition at three months and 12 months post-presentation for non-cardiac chest pain.

Measure	Treatment group %	Control group %	p[a]
Re-presentation (3 months)	16.2	18.4	>0.50
Re-presentation (12 months)	28.5	24.0	>0.30

[a] *P*-value derived from logistic regression.

Table 3
Primary outcome – tests of interaction for treatment condition at three months and 12 months post-presentation for non-cardiac chest pain.

	% re-presentation (3 months)			% re-presentation (12 months)	
	Treatment	Control		Treatment	Control
Prior presentation	11.9	27.0	Prior presentation	26.3	29.2
No prior presentation	17.6	13.3	No prior presentation	27.8	18.4
Test of interaction: Wald $\chi^2(1) = 4.74$, $p < .05$			Test of interaction: Wald $\chi^2(1) = 1.67$, $p > .10$		

follow up, as compared with those in the control condition (three month RR = 2.26; 12 month RR = 1.11).

3.5. Secondary outcome measures

A series of secondary outcomes were also measured in the present trial. These included: self-reported chest pain; health anxiety; anxiety and depression (measured by the HADS); mental and physical quality of life, and social functioning. Table 4 shows mean scores for both the treatment and control groups on each of these measures at the three month follow-up, and 12 month follow-up. The Table shows that there was little evidence of differences between treatment and control groups on any measures at three and 12 months. The only exception to this pattern of findings was for the measure of health anxiety. At three months, the treatment group reported significantly ($p < .01$) lower scores on the measure of health anxiety than those in the control group. By twelve months, the magnitude of this difference had reduced to marginal significance ($p < .10$). The use of a Sidak-corrected p-value cutoff (for multiple comparisons) of $p = .006$ did not materially alter the results of these analyses.

4. Discussion

4.1. Summary of findings

In the present study patients who presented at ED with NCCP and were randomised to three or four sessions of NCCP modified CBT, did not report any significant reduction in hospital attendance for NCCP at three months or 12 months. Patients receiving NCCP modified CBT had significantly lower health anxiety scores at three months but not at 12 months. Patients who had at least one prior ED presentation with NCCP were significantly less likely to re-present with NCCP up to three months but not less likely to re-present over 12 months.

These findings suggest that a brief psychotherapeutic intervention is feasible and acceptable to cardiac patients. However, in our sample the intervention has a modest and transient clinical impact. Overall by 12 months there was no significant difference in primary or secondary outcome measures. The intervention significantly reduced health anxiety scores over the short term but this reduced to marginal significance at 12 months. The intervention also helped the subgroup of patients, around one third of the sample, who had a least one prior presentation for NCCP. These patients were significantly less likely to re-present with NCCP in the first three months after discharge. However, this effect was not sustained over the next nine months.

Table 4
Secondary outcomes – main effects for treatment condition at three months and 12 months post-presentation for non-cardiac chest pain.

Measure	Treatment group	Control group	p[a]
	Mean (SD)/%	Mean (SD)/%	
Self-reported chest pain (3 months)	37.0	35.7	>0.70
Self-reported chest pain (12 months)	33.3	38.0	>0.30
Health anxiety (3 months)	4.51 (4.08)	6.00 (6.31)	<0.01
Health anxiety (12 months)	4.58 (4.46)	5.54 (5.39)	<0.10
Depression/anxiety (3 months)	4.88 (4.61)	5.73 (5.50)	>0.10
Depression/anxiety (12 months)	4.20 (4.70)	4.67 (4.46)	>0.30
Mental quality of life (3 months)	43.20 (5.05)	42.78 (5.62)	>0.40
Mental quality of life (12 months)	42.94 (5.51)	42.66 (5.64)	>0.60
Physical quality of life (3 months)	48.83 (4.29)	48.57 (4.89)	>0.50
Physical quality of life (12 months)	48.51 (4.62)	47.91 (4.78)	>0.20
Social functioning (3 months)	2.15 (2.32)	2.22 (2.56)	>0.70
Social functioning (12 months)	2.10 (2.39)	2.33 (2.22)	>0.30

[a] p-Value derived from paired t-tests.

4.2. Comparison with other studies

As noted above the recent Cochrane review reported a total of 17 RCTs assessing psychological intervention for non-specific chest pain. The primary outcome reported in most studies was chest pain. We report that our intervention had no effect on self-reported chest pain. The Cochrane studies were small with the number of subjects randomised ranging from 21 to 115 and only two studies had >70 subjects. Participation rates were modest with 40–60% of eligible subjects agreeing to participate, compared with 63% in our study. Our drop-out rate was 28%. It is of note that in the five largest studies, involving 331 patients, the drop-out rates ranged between 28% and 57%. Our follow-up rate was also superior to the reviewed RCTs with 84% of subjects completing the 12 month follow-up. The present study is therefore by far the largest to evaluate a psychotherapy for non-cardiac chest pain. It also has a 12 month follow-up which most comparable studies did not have. The negative finding we report is therefore important.

4.3. Generalisability

Since the ED is the only one available for the acute presentation of chest pain in the Christchurch region, the sample studied is highly representative of the general population. All ages, ethnicities, socio-economic states and gender in the catchment area attend this single ED. All those attending ED were eligible for the study. Our patients were unselected. Comparable studies all used selected patient groups who had evidence of persistent NCCP. Jonsbu et al. [24] for example, selected patients with persistent pain for six months. Others had patients who were referred by cardiologists [25], or undergoing angiography [26,27], had NCCP occurring at least once per month [28], or had a HADS subscale score of eight or above [29].

4.4. Clinical implications

While the present study did not report a significant effect of a brief psychological intervention, there are possible clinical implications. The first is that a brief intervention appears to be acceptable to cardiac patients with most completing treatment. The second is that cardiac nurses can be trained to competently deliver such a psychological intervention. The third is that offering a psychological intervention to all patients presenting at an ED with NCCP is unlikely to be effective overall in preventing re-presentation or improving psychological health in the longer term. The fourth is that the patients to focus on for any intervention are those that have previously presented with NCCP. In this study, they at least derive some temporary benefit from treatment and the reduction in costs associated with re-presentation to ED and possible admission may offset the cost of the intervention. The fifth is that some type of maintenance or booster therapy after three months may be useful in this group to maintain the benefits.

These suggestions are supported by the result of a similar study in the United Kingdom which showed significant cost-savings and greater benefit over 12 months in a selected group who had presented at least twice with NCCP [30].

One possible explanation for the lack of efficacy in our study is that the treatment was too brief. This would need to be tested in another study. However, any significant increase in treatment length will almost certainly lead to lower participation rates. Despite NCCP being a very common problem, most studies which have used longer treatments report low recruitment rates and poor retention rates [15]. A brief treatment with booster sessions might be more acceptable. In addition NCCP is not a unitary diagnosis and it is possible that more evaluation of the potential mechanisms of the pain and targeting treatment more specifically might be effective. It is also possible that the interventions might have been effective if we used highly trained clinical psychologists rather than nurses.

4.5. Limitations

The modified brief CBT used in the study has not been specifically evaluated before. While it follows the general principles used in CBT in patients with health anxiety it is possible that the intervention was not a useful one and an alternative model might be effective.

Due to the nature of the interventions it is impossible to blind therapists. However, the follow-ups were assessed blindly with the patients explicitly told not to reveal whether they were in the treatment arm or not. The interventions were manualised and monitored for treatment fidelity. Participation rates were high for this type of study but over 30% of patients did not want to take part.

5. Conclusions

A brief psychological intervention for NCCP failed to reduce representations or improve psychological health over the next 12 months. We therefore do not recommend such an intervention to unselected patients with NCCP although they did obtain some temporary reduction in health anxiety. Patients presenting in ED with at least two episodes of NCCP (ie more severe patients) appear to have obtained some temporary benefit and are less likely to re-present with NCCP for the first three months. Focussing on this group of patients using booster sessions or a longer CBT intervention might led to a more sustained improvement.

Acknowledgements

We thank the therapists, Katie Douglas, Judy Ward and, Berny Holtmark van Dijkerhof. We thank Wendy Mayes for interviewing and data management of the study and Andrea Bartram for data management.

Author contributors

RM was the Principal Investigator who obtained the research grant, designed the study, helped supervise the treatment and was the principal author on the paper.

JZ contributed to this manuscript in terms of designing the format and content of the treatment sessions for the CBT arm. Thereafter she taught, then supervised cardiology nurses and a psychology intern in the recruitment of potential study candidates, randomisation, and delivery of treatment sessions. She was responsible for monitoring, collection and storage of all data related to this RCT.

JB undertook randomisation procedures and the statistical analysis.

CM Helped in the design of the study, particularly in relationship to Maori participants who were recruited.

PT helped in the literature search, the choice of measures of outcome and in the interpretation of the data.

HT assisted in the design of the study and in the supervision of therapy in the CBT group.

MT participated in the preliminary data analysis to determine study feasibility, study design and trial process planning, contributed to the interpretation and analysis of study findings, and undertook review of first and final manuscript versions.

RT contributed to study design, data collection, protocol implementation, review of data and manuscript.

Sources of funding

Health Research Council of New Zealand (11/259). Health Anxiety CBT vs TAU for patients with non-cardiac chest pain. $726,683 (3 years). 2011. Mulder RT, Lacey C, Tyrer H, Than M, Zarifeh J, Troughton R, Boden J.

The funder had no input into the design, conduct or reporting of the study.

Disclosure

The authors report no relationships that could be construed as a conflict of interest.

Ethical approval

Approval was granted by the Health and Disability Ethics Committee – Southern Branch (New Zealand). The Ethics reference is URB/12/02/007.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.01.067.

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