Self-estimated physical functioning poorly predicts actual exercise capacity in adolescents and adults with congenital heart disease

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Aims
The aim of this study is to compare self-reported health-related quality-of-life (HRQoL) with the objective of exercise performance in patients with congenital heart disease (CHD) according to diagnosis.

Methods and results
564 patients (255 females, 14–73 years) with various CHD (62 shunt, 66 left heart obstruction, 33 PS/PR, 47 Ebstein, 96 Fallot, 98 TGA after atrial switch, 38 other TGA, 32 palliated/native cyanotic, 61 others) and a group of 53 healthy controls (18 females, 14–57 years) completed a QoL questionnaire (SF-36) and performed a symptom-limited cardiopulmonary exercise test. Despite several limitations at exercise ($P = 1.30 \times 10^{-23}$), patients only reported reductions in HRQoL concerning physical functioning ($P = 4.41 \times 10^{-15}$) and general health ($P = 6.17 \times 10^{-15}$) and not psychosocial aspects. This could be confirmed in all diagnostic subgroups. Correlation to peak oxygen uptake was found in physical functioning ($r = 0.435, P = 1.72 \times 10^{-27}$) and general health ($r = 0.275, P = 3.79 \times 10^{-11}$). However, there was severe overestimation of physical functioning in most patients when compared with actual exercise test results.

Conclusion
Patients with CHD rate their HRQoL impaired only in physical functioning and general health and not in any psychosocial aspect. Self-estimated physical functioning poorly predicts actual exercise capacity.

Keywords
Congenital heart disease • Quality of life • Cardiopulmonary exercise testing

Introduction
Adults and adolescents with congenital heart disease (CHD) have never experienced unimpaired physical exertion as their healthy counterparts have. They have made lifelong psychosocial adaptations on the basis of their congenital defects both with respect to physical as well as mental aspects and consider their situation as normal. Most studies directly comparing subjective data from quality-of-life (QoL) assessments with objectives of physical parameters are limited to a small number of selected patients 1 with mixed groups of CHDs or lack standardized assessment of specific objective physical data. 2–4 Our previously published pilot study 5 showed no correlation of the results of cardiopulmonary exercise testing (CPET) with psychosocial aspects and only a weak correlation with self-estimated physical function. This was surprising especially for the more severe cardiac defects such as patients with Fontan circulation or cyanotic congenital disease. However, our previous study did not have enough power to analyse according to diagnostic subgroups.

In this study we investigated the correlation between physical fitness expressed by aerobic exercise capacity and the self-reported health-related quality-of-life (HRQoL) according to the underlying defect, in order to prove the hypothesis whether self-estimated physical function predicts actual exercise capacity in patients with CHD.

Methods

Patients
From June 2001 to August 2006, 880 patients were referred for a CPET to our laboratory owing to various clinical indications. During
this period of time 151 of these patients were tested more than once and only the first test was included in this study. Ninety-six patients under the age of 14 were excluded, as the SF-36 questionnaire is not validated for that age-group. Another 31 patients were excluded as they were unable to complete the QoL questionnaire on their own, either because of language barriers or because of cognitive disabilities. Twenty patients with motion sensible rate response pacers were tested on a treadmill and also excluded, as treadmill exercise results in a 10% higher peak oxygen uptake in comparison with bicycle exercise. Another 16 patients were excluded by the attending physician owing to insufficient effort. In total, 564 patients (255 females, 45%) with a median age of 24 years (range 14–73 years) were enrolled in the study. Of these patients, 413 (73%) had surgery of their CHD, some of them more than once. They were grouped into 10 diagnostic groups according to the leading diagnosis (Table 1). We sampled consecutive patients trying to reach a sample size of 30 patients in each diagnostic group in order not to miss correlations with a r > 0.5. Some of the patients were already included in the previously published pilot study. A group of 53 volunteers (18 females, 34%) with a median age of 25 (range 14–57 years) were also tested and analysed separately to show whether some diagnostic groups have normal exercise capacity or a normal QoL. The group consisted of consecutive volunteers without a history of cardiac disease. The anthropometric data are presented in Table 1.

Quality-of-life

HRQoL was measured by the medical outcomes study 36 item short form (SF-36) that has an acceptable internal consistency and has proven useful in various specialties of medicine without any bias for symptoms of a specific disease. We used the German version of the self-report form with a window of four weeks. The SF-36 is multidimensional and composed of 36 items scored in eight scales: physical functioning (10 items), role limitations owing to physical functioning (role physical, four items), bodily pain (two items), general health (five items), vitality (four items), social functioning (two items), role limitations because of emotional problems (role emotional, three items), and mental health (five items). A single item health transition assesses health changes within the last year, yet is not scored as a separate dimension. The responses to each question within a scale are combined to generate a score from 0 to 100, with higher scores reflecting better QoL.

Cardiopulmonary exercise test

After completing the SF-36 QoL survey, all patients and healthy volunteers underwent a symptom-limited CPET on an upright bicycle ergometer. Initially several step protocols were used. Ultimately and in most patients, a three-minute warm-up without load was followed by a ramp-wise increase of work load of 10 or 20 W/min according to the estimation of the attending physician/technician in order to reach a cycling time of about 8–12 min after the warm-up. The end of the CPET was marked by symptom limitation and was followed by a 5-min recovery period without cycling.

Oxygen uptake was measured breath by breath using a metabolic chart (Vmax 229, SensorMedics, Viasyis Healthcare, Yorba Linda, CA, USA). Peak oxygen uptake was defined as the highest mean uptake of any 30 s time interval during exercise. Reference values (mL/kg/min) were calculated according to Cooper and Storer:

\[
\text{female: } \text{VO}_2 \text{ peak} = 5.8 + (62.6 \times \text{height(m)} - 45.5) \times (37.03 - 0.371 \times \text{age(years)})/\text{weight(kg)}
\]

\[
\text{male: } \text{VO}_2 \text{peak} = 5.8 + (71.6 \times \text{height(m)} - 51.8) \times (44.22 - 0.394 \times \text{age(years)})/\text{weight(kg)}
\]

Table 1 Anthropicometric data according to diagnostic groups

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Sex (males/females)</th>
<th>Age (median/range)</th>
<th>BMI (median/range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanotic (with/without palliative surgery)*</td>
<td>32</td>
<td>14/18</td>
<td>26.9/16.8–65.2</td>
<td>20.9/15.0–32.0</td>
</tr>
<tr>
<td>Fontan circulation</td>
<td>31</td>
<td>16/15</td>
<td>22.1/14.9–42.8</td>
<td>21.3/17.1–30.5</td>
</tr>
<tr>
<td>TGA after atrial switch</td>
<td>98</td>
<td>63/35</td>
<td>24.0/14.0–40.4</td>
<td>22.8/16.0–36.0</td>
</tr>
<tr>
<td>TGA (no atrial switch)†</td>
<td>38</td>
<td>21/17</td>
<td>27.5/14.3–59.8</td>
<td>23.2/15.6–32.0</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>96</td>
<td>57/39</td>
<td>25.3/14.3–58.1</td>
<td>22.0/14.8–31.7</td>
</tr>
<tr>
<td>Ebstein anomaly</td>
<td>47</td>
<td>16/31</td>
<td>33.1/14.6–73.2</td>
<td>21.5/15.2–34.4</td>
</tr>
<tr>
<td>PS/PR</td>
<td>33</td>
<td>18/15</td>
<td>23.3/14.1–67.3</td>
<td>22.6/15.7–30.5</td>
</tr>
<tr>
<td>Left-heart obstruction AS/CoA</td>
<td>66</td>
<td>53/13</td>
<td>22.0/14.1–56.3</td>
<td>23.4/15.4–38.3</td>
</tr>
<tr>
<td>Isolated shunt</td>
<td>62</td>
<td>24/38</td>
<td>24.2/14.5–56.7</td>
<td>22.1/15.7–31.3</td>
</tr>
<tr>
<td>Others†</td>
<td>61</td>
<td>27/34</td>
<td>21.6/14.4–68.1</td>
<td>21.4/15.4–32.8</td>
</tr>
<tr>
<td>Total</td>
<td>564</td>
<td>309/255</td>
<td>24.3/14.0–73.2</td>
<td>22.2/14.8–38.3</td>
</tr>
<tr>
<td>Control Group</td>
<td>53</td>
<td>35/18</td>
<td>25.2/14.4–57.0</td>
<td>22.3/17.2–27.9</td>
</tr>
</tbody>
</table>

AS, aortic stenosis; CoA, coarctation of the aorta; PR, pulmonary regurgitation; PS, pulmonary stenosis; TGA, transposition of the great arteries; BMI, body mass index.

*Presently cyanotic patients independent of the underlying diagnosis with or without palliative surgery.
†Congenitally corrected TGA (n = 20), TGA after Rastelli procedure (n = 7), TGA after arterial switch operation (n = 10), and TGA after Kawashima procedure (n = 1).
‡Persistent foramen ovale (n = 13), anomalous left coronary artery from the pulmonary artery (ALCAPA, n = 10), mitral valve prolapse (n = 8), arrythmias (n = 13).
§Cardiomyopathy (n = 7), aortic regurgitation (n = 2), M. Osler (n = 1), bronchopulmonary dysplasia (n = 1), left ventricular aneurysm (n = 1), exercise hypertonus (n = 1), Yacoub-OP (n = 1).
Statistical analysis

The collected data were analysed with a standard statistical package (SPSS 15.0, SPSS Inc., Chicago, IL, USA). As the patient groups differed in age and sex, all statistical tests were performed as % of sex and age-dependent reference values. Kolmogorov–Smirnov test showed that most of the variables were skewed and therefore results are expressed as median (range) and non-parametric tests were performed. Primarily significant differences in the constellation of the diagnostic groups were identified using a two-sided Kruskal–Wallis test. At significant Kruskal–Wallis test, the whole cascade down to the pair-wise tests were calculated. The pair-wise tests were only considered significant, if all the tests in the entire cascade were significant. The nine HRQoL scales of the SF-36 scores were then correlated with peak oxygen uptake measured in the CPET. Standard deviation of the correlation factor was estimated by the Jack-knife method. Owing to multiple testing, only P < 0.05/10 (P < 0.005) were accepted as significant according to the Bonferroni correction.

To test whether there are any differences in the correlation factors between the diagnostic groups, we performed Fisher’s Z-transformation on all correlation factors (r)

\[ Z(r) = 0.5 \times \ln[(1 + r)/(1 - r)] \]

and calculated

\[ \chi^2 = \Sigma(n - 3)(u_i - U)^2 \text{ with } U = \Sigma(n - 3)u_i/\Sigma(n - 3), \]

which is \( \chi^2 \) distributed with (k − 1) degrees of freedom.10

Results

Quality-of-life

In five patients with CHD and one healthy volunteer, in total 20 sub-scales of the SF-36 questionnaire could not be calculated because of missing items. These missing dimensions were removed from the statistical analysis. Table 2 shows the results of the individual diagnostic groups depicted as percent of gender and age-related reference values. Patients in all diagnostic groups with CHD report good HRQoL showing significant differences within the individual groups only in the scales of physical functioning and general health.

Patients within all diagnostic groups except for left heart obstructions (aortic stenosis, AS; aortic coarctation, CoA) reported significantly lower physical functioning scores in comparison with the control group. Furthermore, the cyanotic group showed a lower score compared with the shunt group, the left-heart obstructions (AS/CoA), pulmonary stenosis (PS)/pulmonary regurgitation (PR), tetralogy of Fallot, transposition of the great arteries (TGA) not corrected by atrial switch operations, and the group of other congenital heart defects. All other pairs failed to be significant in the Kruskal–Wallis cascade. A significant reduction of the QoL item general health was reported only in the cyanotic group and the patients with Fontan circulation.

Cardiopulmonary exercise test

The 564 patients as well as the 53 healthy controls performed the CPET without complications and no exercise test had to be interrupted by the attending physician. Although some patients had excellent results far above their expected values, the total study group showed significantly lower peak oxygen uptake. Figure 1 depicts the peak oxygen uptake in mL/kg/min of all the diagnostic groups. There were significant differences in exercise capacity (peak oxygen uptake) between the individual groups and the control group (Table 2). This finding holds true for every single diagnostic group, even the most simple ones.

Correlation of QoL scores with CPET results

Correlation to peak oxygen uptake was found with the scales of physical functioning (r = 0.435, P = 1.72 x 10−22) and general health (r = 0.275, P = 3.79 x 10−11) (Table 2). In addition, a weak correlation was found to role physical (r = 0.140, P = 0.001) and vitality (r = 0.140, P = 0.001). No correlation was observed within any of the other scales of HRQoL. After considering the effects of the diagnosis by partial correlation, similar results were obtained but in addition included a week correlation to role emotional (r’ = 0.147, P = 0.001).

The correlation within the diagnostic groups and the item physical functioning are depicted in Figure 2. It shows that there is no pattern of better or worse correlation in the more severe defects. Also statistical testing could not find any differences in the correlation factors of the different diagnostic groups (χ^2 = 11.872, df = 9, P = 0.221).

The scatter plot (Figure 3) depicts the best correlation between peak oxygen uptake, the objective exercise capacity criterion, and physical functioning, the self-reported exercise capacity, of all 564 patients. One would initially expect a scatter cloud around a line of patients reporting low scores in self-estimated physical functioning with a low peak oxygen uptake and patients with high self-reported physical functioning and high peak oxygen uptake. However, the scatter plot has the distinct shape of a triangle. Patients reporting a low score in self-reported physical functioning had low peak oxygen uptake, whereas peak oxygen uptake varied broadly among patients reporting good physical functioning on the SF-36. This was seen in both male and female patients, in patients with native congenital defects and patients after corrective surgery, as well as in patients of any diagnostic group.

Discussion

Quality-of-life

This study showed that patients with CHD report excellent QoL in most aspects. This could be seen in all diagnostic groups despite considerable limitations in exercise capacity. Reductions were only reported concerning physical characteristics, whereas all psychosocial aspects are congruent with a healthy population. This has previously been reported for mixed groups of congenital defects.2,5,11 The present study was adequately powered to analyse several subgroups and confirmed that this good QoL in the psychosocial aspects holds true for all examined diagnostic groups, including the most severe defects.

This is of major importance as one has to distinguish between QoL and health status as patients perceive these aspects as two distinct constructs.12 The SF-36 questionnaire incorporates psychosocial aspects of QoL, including mental health, which has shown substantial concordance with patients’ perception of their
Table 2 Results of the SF-36 quality-of-life instrument and the cardiopulmonary exercise test (CPET)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>SF-36 health-related quality-of-life evaluation</th>
<th>CPET</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Physical functioning*</td>
<td>Role physical</td>
</tr>
<tr>
<td>Cyanotic (with/without palliative surgery)</td>
<td>32</td>
<td>67 (16–100)</td>
<td>103 (0–115)</td>
</tr>
<tr>
<td>Fontan circulation</td>
<td>31</td>
<td>85 (0–101)</td>
<td>104 (0–114)</td>
</tr>
<tr>
<td>TGA after atrial switch</td>
<td>98</td>
<td>92 (21–106)</td>
<td>104 (0–114)</td>
</tr>
<tr>
<td>TGA (no atrial switch)</td>
<td>38</td>
<td>87 (42–113)</td>
<td>102 (0–120)</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>96</td>
<td>94 (16–110)</td>
<td>104 (0–115)</td>
</tr>
<tr>
<td>Ebstein anomaly</td>
<td>47</td>
<td>89 (23–158)</td>
<td>104 (0–138)</td>
</tr>
<tr>
<td>PS/PR</td>
<td>33</td>
<td>96 (40–123)</td>
<td>102 (0–138)</td>
</tr>
<tr>
<td>Left-heart obstruction (AS/CoA)</td>
<td>66</td>
<td>99 (22–110)</td>
<td>102 (0–120)</td>
</tr>
<tr>
<td>Isolated shunt</td>
<td>62</td>
<td>95 (11–106)</td>
<td>102 (0–115)</td>
</tr>
<tr>
<td>Others</td>
<td>61</td>
<td>94 (21–110)</td>
<td>102 (0–115)</td>
</tr>
<tr>
<td>Total</td>
<td>564</td>
<td>94 (0–158)</td>
<td>104 (0–138)</td>
</tr>
</tbody>
</table>

| Spearman correlation to peak VO₂ (R)   | 0.435 ± 0.037² | 0.140 ± 0.041² | 0.014 ± 0.043 | 0.275 ± 0.040² | 0.140 ± 0.042² | 0.095 ± 0.042 | 0.112 ± 0.043 | 0.009 ± 0.042 | 0.064 ± 0.045 |
| Spearman correlation to peak VO₂ (P)   | 1.72 × 10⁻²⁷ | 0.001 | 0.734 | 3.79 × 10⁻¹¹ | 0.001 | 0.025 | 0.008 | 0.828 | 0.13 |
| Partial correlation (r*)              | 0.37² | 0.184² | 0.400 | 0.251² | 0.177² | 0.119 | 0.147² | 0.035 | 0.107 |
| Partial correlation (P*)              | 4.79 × 10⁻²⁰ | 1.36 × 10⁻⁵ | 0.353 | 2.4 × 10⁻⁹ | 3.14 × 10⁻⁵ | 5.24 × 10⁻³ | 5.27 × 10⁻⁴ | 0.411 | 0.012 |
| Control group                         | 53 | 104 (42–120) | 104 (0–129) | 112 (46–132) | 104 (39–164) | 99 (27–137) | 107 (40–117) | 106 (0–114) | 109 (56–137) | 94 (0–187) | 112 (57–200) |
| Kruskal–Wallis test (P)               | 4.41 × 10⁻¹⁵ | 0.396 | 0.403 | 6.17 × 10⁻⁵ | 0.063 | 0.609 | 0.232 | 0.086 | 0.599 | 1.30 × 10⁻³³ |

AS, aortic stenosis; CoA, coartation of the aorta; KW, Kruskal–Wallis; PR, pulmonary regurgitation; PS, pulmonary stenosis; TGA, transposition of the great arteries. Results of 564 patients with congenital heart disease and 53 healthy controls depicted as percent (%) of gender- and age-dependent reference values—median (range).

*Significant differences in diagnostic group in a Kruskal–Wallis test (P<0.005).

†Correlation to peak VO₂ (standard deviation estimated by Jack-knife method).

‡Partial correlations of rank considering diagnostic groups.

A. Gratz et al. 2000
Figure 1  Peak oxygen uptake (mL/kg/min) according to diagnostic groups depicting significant reductions in exercise capacity in all diagnostic groups. Box plots express median and quartiles. Whiskers represent minimum and maximum excluding outliers (values between 1.5 and 3 inter-quartile ranges from the end of the box) expressed as circles.

Figure 2  Spearman correlation factor (and 95% confidence intervals) of physical functioning according to diagnosis.
definition of QoL. On the other hand, the SF-36 also includes physical aspects like the physical functioning scale expressing the self-reported health status. This means for our results, where psychosocial aspects and especially mental health were not diminished, that patients with CHDs express no limitations in ‘true’ QoL and only minor impairment in their health status.

The majority of studies concerning QoL in children and adults with CHD focus on psychosocial items and are in concordance with our results. Moons et al. found satisfactory QoL in a selected group of patients with univentricular heart. However, Kaeenmerer and colleagues collected psychosocially relevant data in a group of 146 patients with mixed CHD and found that more than one-half of the patients felt unhealthy and impaired. In contrast to our data, Utens et al. used emotional and behavioural checklists to evaluate the psychological situation in children and adolescents with operated CHD more objectively. They found clear limitations based on the number of heart operations and deep hypothermic circulatory arrest.

Meijboom et al. were the first to use standardized questionnaires in their follow-up studies of patients after operative closure of atrial septal defects, ventricular septal defects, repair of tetralogy of Fallot, as well as of TGA. Contrary to our results they showed that patients with septal defects perform near normal at exercise tests and self-reported a good health, whereas patients with corrected tetralogy of Fallot and TGA performed worse than predicted at exercise with reduced self-reported health status. With respect to the simpler congenital lesions, the difference in exercise performance may be owing to a referral bias of our patients, whereas Meijboom et al. claim a rather complete follow-up cohort.

Mir et al. also used the SF-36 to measure HRQoL in 169 patients with CHD and concluded that patients must be very closely and interdisciplinarily followed-up because of their reduced HRQoL in most aspects including the psychosocial ones. A substantial difference in observation by Mir et al. was a significantly lower mental health in all of their patients except for CoA. One way to explain these differences is the fact that their patients answered the SF-36 at home in the context of friends and family, whereas we ensured that our patients completed the questionnaire without help and external influence.

Lane and colleagues examined the QoL of 276 patients with CHD also using the SF-36. They studied a mixed population categorized based on their clinical management at the time of survey in groups of surgically cured, surgically corrected, surgically palliated, and family, whereas we ensured that our patients completed the questionnaire without help and external influence.

Lane and colleagues examined the QoL of 276 patients with CHD also using the SF-36. They studied a mixed population categorized based on their clinical management at the time of survey in groups of surgically cured, surgically corrected, surgically palliated, no indication for surgery, and inoperable. Lane et al. reported results similar to Mir et al. and in concordance to our findings concerning a comparatively poor physical functioning and general health perceptions, however, in contrast to our findings concerning psychosocial QoL, including mental health. Again, this may be explained by the fact that their patients answered the SF-36 at home.

**Correlation of objectively measured aerobic physical capacity and self-estimated physical functioning in 564 adolescents and adults with congenital heart disease**

**Cardiopulmonary exercise test**

The results from the CPETs showed a substantial reduction in all diagnostic groups, including the most simple lesions. These findings are in concordance with previous studies that have reported exercise limitations in patients with diverse CHD. Also, smaller studies within one diagnosis confirmed this general finding.

Especially Diller et al. showed very clearly that patients with CHD have a peak oxygen uptake significantly reduced in all diagnostic groups, including minor defects like CoA and corrected septal defects. Secondly, and most important, they showed that impaired peak oxygen uptake predicts hospitalization and death over the following year even after accounting for age, gender, NYHA class, laboratory parameters, and underlying cardiac lesions.

**Correlation of quality-of-life scores with cardiopulmonary exercise test results**

In the previously published pilot study there was no correlation of peak oxygen uptake to any of the psychosocial scales of the SF-36. This study confirms this finding throughout all of our diagnostic groups, including the most severe CHDs. As was seen in the pilot study, the reductions in physical functioning and general health do correlate with peak oxygen uptake during a CPET, but the individual predictability of self-estimated physical function and actual capacity is low.

Our study stands in contrast to the growing evidence in studies concerning acquired heart disease suggesting that physical exercise capacity is associated with well-being and improvements in psychosocial aspects of QoL. Patients in our study showed significant, in part severe limitations in exercise capacity, however, reported no reductions in psychosocial HRQoL.
patients with acquired heart diseases our patients have made life-long adaptations on the basis of their congenital defects both with respect to physical as well as mental aspects and consider their situation as normal. They have not experienced unimpaired physical exertion the way patients with acquired heart failure have.

However, concluded from a more detailed analysis of Figure 3, most patients with CHD in part severely overestimated their physical abilities, whereas almost none underestimated their physical function. This was observed in any diagnostic group, as well as in both male and female patients. This is contrary to the findings by Salzer-Muhar et al.,31 who concluded that especially male adolescents with CHD perceive a reduced capacity and lack self-esteem on account of their reduced physical ability. This overestimation is seen in patients after corrective surgery, palliative surgery, and in patients without surgery. Therefore, the surgical term total correction, which is applied to many operative repairs of complex congenital anomalies,32 is not the only reason for the misconception of being cured and individual physical abilities being restored to near normal. A similar effect was previously observed by Rogers et al.,33 who concluded that especially male adolescents with CHD perceive a reduced capacity and lack self-esteem on account of their reduced physical ability. This overestimation is seen in patients after corrective surgery, palliative surgery, and in patients without surgery. Therefore, the surgical term total correction, which is applied to many operative repairs of complex congenital anomalies,32 is not the only reason for the misconception of being cured and individual physical abilities being restored to near normal. A similar effect was previously observed by Rogers et al.,33 who concluded that especially male adolescents with CHD perceive a reduced capacity and lack self-esteem on account of their reduced physical ability. This overestimation is seen in patients after corrective surgery, palliative surgery, and in patients without surgery. 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