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ORIGINAL ARTICLE

How fit are children and adolescents with haemophilia in Germany? Results of a prospective study assessing the sport-specific motor performance by means of modern test procedures of sports science

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Summary. There are a lot of publications on the physical fitness of patients with haemophilia (PWH), however, most studies only reflect individual sport-specific motor capacities or focus on a single fitness ability. They involve small patient populations. In this respect principal objective of this study was to compare the physical fitness in all respects and the body composition of young PWH to healthy peers based on the most valid data we could get. Twenty-one German haemophilia treatment centres were visited from 2002 to 2009. PWH between 8 and 25 years were included. They performed a five-stage fitness test covering the sport-specific motor capacities for coordination, measured by one leg stand, strength, aerobic fitness and mobility as well as body composition. The patients' results were compared with age- and gender-specific reference values of healthy subjects. Two hundred and eighty-five PWH (mean age 13.2 ± 4.5 years, 164 PWH with severe disease) were included prospectively in the study. PWH are significantly below the reference values of healthy subjects in the one-leg stand test, the mobility of the lower extremity, the strength ratio of chest and back muscles and the endurance test. In body composition, the back strength and the mobility of the upper extremity PWH are significantly above the reference values. There are no significant differences in abdominal strength. In conclusion we found specific differences in different fitness abilities between PWH and healthy subjects. Knowing this, we are able to work out exercise programmes to compensate the diminished fitness abilities for our PWH.

Keywords: exercise, haemophilia, motor capacities, physical fitness

Introduction

There is a lot of data on the physical fitness of patients with haemophilia (PWH) [1,3–13]. The existing data are sometimes contradictory as the focus is only on selected sport-specific motor capacities, and is usually based on a very small patient population. All values are measured with different tools and not comparable. They do not look at the overall fitness but at only parts of the whole complex. The role of one part of fitness in correlation to all the others is not clear.

The objective of this study was to collect substantial and valid data to be able to describe the fitness of German PWH based on the sport-specific motor capacities like coordination, strength, aerobic fitness and mobility as well as body composition, and compare them with age- and gender-specific reference values. The goal was to find out if the fitness of PWH today is comparable to healthy peers and to discover their individual strengths and weaknesses.

Materials and methods

Method of assessment

The study was conducted between September 2002 and May 2009. During that period, a total of 21

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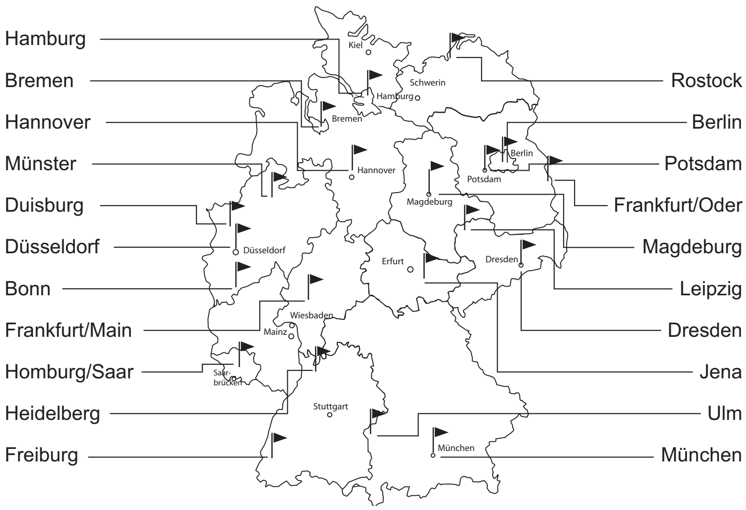

Fig. 1. Haemophilia Treatment Centres (21) in Germany, visited between 2002 and 2009.

haemophilia treatment centres in Germany were visited within the 'Fit for Life' campaign conducted by IPN© (IPN, Institute for Prevention and Aftercare, Cologne, Germany; cf. Fig. 1). All patients diagnosed with haemophilia A or B (all severities) and were able to perform the test procedures we have chosen for the study. Details of the disease, such as the type of haemophilia, residual factor activity and form of treatment (on demand/prophylaxis) were recorded.

The patients performed a 5-stage fitness test, always in the same sequence [15]. At the beginning, the anthropometric data (weight and height) and resting pulse were recorded (after a resting period over 5 min by using a infrared earlobe sensor (PL 6000 by Catye, Osaca, Japan).

Thereafter, one leg stand and mobility tests, body fat analysis, strength test and endurance tests were performed.

All tests were compared to reference values of healthy peers. For comparability, the average of the healthy peers is presented by 100%. The results of PWH are expressed in percentage as well.

Statistics

Statistical analysis of the data was performed using the software Microsoft Excel 2003 and (SPSS Statistics 22 IBM, New York, USA) for Windows.

The distribution of the measured values was analysed with the Kolmogorow–Smirnov-test. The test showed normal distribution so we used a one sample *t*-test (hypothesis H_0: Measured values of PWH are equal to the average of the healthy peers) to find out if the results of PWH differ significantly from the average of the healthy peers.

The degree of correlation between two random variables was established by determination of spearman's correlation coefficient *r*.

Test procedures

Coordination test. Coordination was measured using the one-leg stand test [1,16,17] on the Posturomed (Posturomed® by Haider Bioswing, Pullenreuth). It was equipped with a Digimax measuring system (Digimax GmbH, Hamm). This testing procedure is reliable and valid [18,19].

The duration of the test is 20 s. The subject is asked to stand as still as possible testing one leg after the other. The measuring plate is freely suspended on springs. Any balancing motions will cause the measuring plate to swing. The resulting movements of the plate are identified and recorded by a computer as deviations from the neutral position. At the end of 20 s, the summarized oscillation length in millimetres is compared with age- and gender- specific reference values and transformed into a score. For further data processing, the worst of both legs was used as it represents the limiting factor for coordination.

If a subject has to stop the test early in order to avoid tumbling, the most negative result will automatically be assumed. Reference values for the test did not exist when the study started [18,19] so our reference values are based on studies by IPN, including more than 1000 subjects of all age groups and were published in 2009 [20].

Mobility test. Mobility testing involved determination of the passive mobility of the ischiocrural muscles for the lower extremity, and the passive mobility of the chest muscles (m. pectoralis major, pars sternalis). The range of motion was measured by an electronic inclinometer (UMAREX Laserliner, Arnsberg, Germany), with an accuracy of one degree and then compared with reference values.

The measurement for the lower extremity was performed with the patient lying in the supine position on a treatment table with straight knees [21]. The tester elevates the straight leg by increasing hip flexion. The upper ankle joint is kept in the neutral position and the lumbar spine and opposite leg are kept in permanent contact with the table. The test was performed on both sides. The inclinometer was placed on the lateral malleolus.

The measurement for the upper extremity was performed with the patient lying on a treatment table in the supine position on the edge of the table with flexed knees and straight arms next to the trunk [21]. The tester elevates the arm in 135° abduction position with outwards rotated shoulder joint and takes care that the lumbar spine keeps permanent contact with the table. The test was performed on both sides. The inclinometer was placed on the proximal ulna. The stopping of the stretch has been defined based on the following criteria:

Definite tactile resistance of the target muscle-tendon area without pain or evasive movements.
There was no case of induced neural pain defined by a positive Lasegue sign in the lower extremity test all PWH could perform the test.

Trunk strength test. Trunk strength testing was performed using the Back Check® (Dr. Wolf GmbH, Arnsberg, Germany). This involved measuring the isometric maximum trunk extensor and flexor strength while standing [22]. For that purpose, the subject is fixed in a position with the knees slightly bent (with knee joint angle of 15°) and the hip immobilized through pads. The subject is then asked to perform maximum contractions first of the abdominals and then of the back extensors against force plates. Contraction involves one continuous regular exhalation and is recorded using a load cell. The testing meets the highest standards in terms of reliability and validity [23].

The maximum strength of trunk flexors and extensors was assessed as well as the balance between these two muscle groups described by a ratio [back strength (extension)/abdominal strength (flexion)]. Then, comparison was made against the reference values, resulting in individual assessments of flexion, extension and the ratio between flexion and extension [24,25].

Body fat analysis. Body fat percentage was determined using a Futrex® infrared analyser (Vicmedic Systems GmbH, Filderstadt, Germany), for this purpose, a measuring head is attached to the biceps brachii muscle, midway between the bend of the elbow and the armpit, which emits infrared rays into the underlying tissue. The different properties of fat and muscle tissue with regard to absorption and reflection of infrared rays permit quantitative assessment of the tissue composition, expressed as the percentage of body fat in the total body mass [26]. This percentage is compared with age- and gender-specific reference values [27].

Endurance test. In order to determine aerobic fitness, a two-stage endurance test of 2 min each was performed on a bicycle ergometer based on the principles of the IPN endurance test (IPN-Ausdauertest®) [2,28]. The test is based on submaximal loading as is recommended for PWH [3].

At the beginning of the test, a target heart rate and a target performance based on the subject's age, resting heart rate and training condition are given to the patient, according to an established algorithm [2].

On the basis of the target performance, the subject completes the first stage of the test with a workload of 50% of the target performance, and then with the full target performance during the second stage.

Upon completion of the test, calculations are made to determine the performance capacity the subject achieved with the target heart rate. This performance capacity is then compared with reference values [2].

Results

Patients

In the study, a total of 285 PWH aged between 8 and 25 years were included prospectively. All included PWH are male. The mean age at the time of testing was 13.2 ± 4.5 years; the patients were on average 159.5 ± 18.9 cm in height and 53.2 ± 20.4 kg in weight. Two hundred and forty-nine patients were having haemophilia A and 36 haemophilia B. One hundred and sixty-four patients were suffering from severe haemophilia with a residual activity of less than

Table 1. Epidemiology of the patients.

Epidemiology	
Tested haemophiliacs altogether ($n = x$)	285
Sex	
Male	285
Anthropometry	
Age (years)	13.2 ± 4.5
Height (cm)	159.5 ± 18.9
Weight (kg)	53.2 ± 20.4
Diagnosis	
Haemophilia A	249
Haemophilia B	36
Residual activity	
<1%	164
1–3%	33
3–5%	23
>5%	65
Treatment	
Prophylactic	198
On demand	87
Inhibitors	
Yes	26
No	259

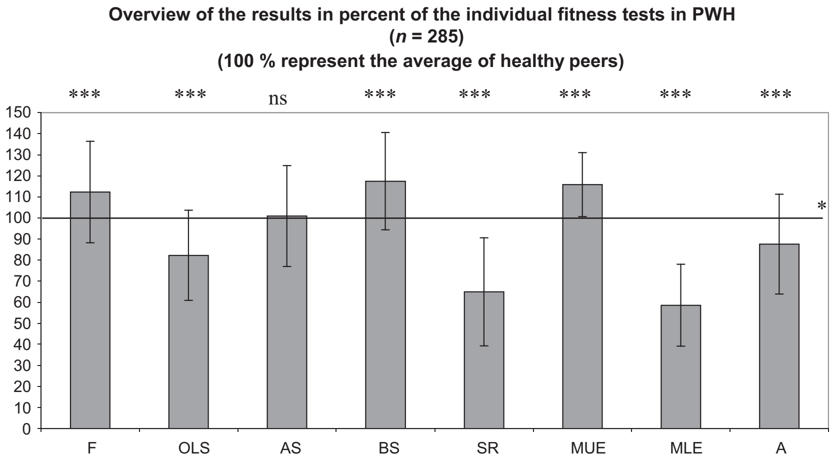

Fig. 2. Overview of the results of the individual fitness tests. ***represents a significance level p < 0,001.*The horizontal line represents the statistical average of healthy peers. F, body fat analysis; OLS, one-leg stand test; AS, trunk muscle strength flexion (abdominal muscle strength); BS, trunk muscle strength extension (back muscle strength); SR, strength ratio (back strength/abdominal strength); MUE, mobility of upper extremity; MLE, mobility of lower extremity; A, aerobic fitness.

1%, 56 patients from moderate haemophilia with a residual activity of 1–5%, and 65 patients have mild haemophilia with a residual activity of more than 5%. The vast majority of patients receive prophylactic treatment (198). Eighty-seven patients are treated on demand. Twenty-six patients had a history of inhibitors (Table 1).

Results of the fitness test

The general overview (Fig. 2) shows the results of PWH in comparison to reference values of healthy peers. All results are related to mean values of the healthy peers represented by 100% and shown as a horizontal line in the figure. A result above 100% indicates a fitness level of PWH above the reference and vice versa.

We found marked deficits of PWH, compared to the age-related reference values of healthy persons, in mobility of the lower extremity, the one leg stand test, the strength ratio and the endurance test. Values above the 100% were found in body fat analysis, back extension strength (back strength) and mobility of the upper extremity. PWH are in the range of health peers in the trunk flexion strength (abdominal strength).

Discussion

We investigated a large cohort of young German PWH to assess the overall fitness based on the sport-specific motor capacities for coordination, strength, aerobic fitness and mobility as well as body composition.

The test procedures were chosen to safely and objectively measure the basic motor skills [29] of PWH in a reasonable time. All tests show proven validity and reliability in literature.

Because of the normal distribution and interval scaling of all measured results, we were able to set the average fitness of healthy subjects to 100% and compare the results of PWH to this standard.

Results of fitness tests

The results of PWH differed in all tests statistically significant from the reference values for healthy peers except the abdominal strength. In this test, there were no differences found. But we found as many deficits as advantages in comparison to the healthy group so that we cannot state in general if the fitness of PWH is comparable to healthy peers. We have to evaluate each test for itself.

An overview of the results shows that the differences are biggest in the mobility of the lower extremity. In contrast, PWH scored considerably higher than the reference group in the mobility test of the upper extremity. No differences in mobility were found in studies conducted by Schoenmakers *et al.* They compared 39 PWHs with the reference values of non-haemophiliacs [30]. The joints examined were the knee, elbow and ankle joints. They measured the range of motion of the single joints and not the overall mobility in the motion chain. The results are not comparable because the mobility of one joint can be normal whereas the mobility of the motion chain can be limited.

With regard to injury protection, however, the shortened ischiocrural muscles, which were assessed within the mobility testing of the lower extremity, seem to be of particular relevance. Because shortened knee flexors seem to increase the risk of sport injury [31].

In the one leg stand test, the group of PWH was below the reference values, which corresponds with the data of Hilberg *et al.* on 12 [1] and 9 patients [4] and the data by Fearn *et al.* [32] on 20 PWH, dealing only with adult PWH.

In the strength test, PWH showed individual changing results as well. Although here were no significant differences in abdominal strength, PWH were even better than their healthy peers in back strength. The data in the literature are contradictory due to the use of different methods of examination.

Falk *et al.* identified strength deficits in the flexor and extensor muscles of PWH during isokinetic measurements in the elbow and knee joints, compared to healthy subjects in 13 [5] and 27 [6] patients, respectively. Gonzalez *et al.* performed isometric measurements on quadriceps muscles in 28 PWH [7] and showed differences from healthy subjects. No deficits compared to the reference values of healthy subjects were found by Douma-van Riet *et al.* in isometric measurements in 158 [8] patients and by Engelbert *et al.* [9] in 47 patients when assessing the flexor and extensor muscles in the elbow, knee and upper ankle joints. Broderick *et al.* [10] found PWH slightly stronger than the healthy peers measured by a basketball chest pass.

We used trunk strength measurement because there is no data on PWH yet. As our PWH get older, we need data to give advice for the prevention of back pain. Additionally the trunk muscles stabilize the motion chain and the force transfer from the upper body to lower extremities and vice versa due to their task as core muscles. Abdominal and back strength are not normally balanced. That is why we looked at the ratio as well (normal ratio 1:1.3 male and 1:1.5 female [24,25]). We could demonstrate an unbalanced muscular ratio in the strength test in our patient group. Patients with chronic back pain also tend to have an unfavourable trunk strength balance [24].

In the endurance test, PWH scored lower than the reference group. Similar to the strength test, the literature on this aspect is contradictory. The data are obtained with differing measurement tools that vary in quality.

Falk *et al.* detected deficits during anaerobic tests on a bicycle ergometer in 13 patients [5]. Koch *et al.* found values below the healthy average when assessing the maximum performance on a bicycle ergometer in 11 patients [11]. Engelbert *et al.* [9] and Groen *et al.* [12] found deficits during spiroergometry on a bicycle ergometer each in 47 patients.

No differences to healthy subjects were found by Douma-van Riet *et al.* in a 6-min walk test with 158 patients [8], van der Net *et al.* during spiroergometry on a bicycle ergometer with 13 PWH [13] and Broderick *et al.* [10] measured by a Multistage fitness test.

As to body composition, PWH scored higher than the healthy reference group in our study showing a lower body fat percentage. This contradicts the results of skin-fold measurements by Falk *et al.* in 13 patients [6] where PWH performed badly and the results of Broderick *et al.* [10] wherein PWH showed no differences in BMI compared to healthy controls.

In general, adipositas seems to be a growing problem in PWH, especially with growing age [14,33]. It would be of scientific interest if increased body weight correlates with decreased fitness in PWH as it is proved for healthy German children [34].

In this context, it is worth mentioning, that the highest correlation of individual test and overall result (by addition of all single tests) was observed for body fat analysis, with $\rho = 0.68$ ($P < 0.001$). Correlation in all the other tests was less marked.

In conclusion, the considerable differences in performance by PWH compared to healthy peers, as stated in the literature, were confirmed by the study on hand. Although PWH proved better than their healthy peers in several individual tests (body fat, flexor strength and mobility of the upper extremity).

Patients with haemophilia scored lower than the reference group in the one leg stand test, the mobility of the lower extremity and the endurance test.

In comparisons with existing contradictory data, the biggest differences are the different methods of examination as well as the small number of PWH.

All tested PWH were patients from Germany's major haemophilia treatment centres (Fig. 1). The oldest subject was born in 1978. Thus, 'physician-controlled self-treatment', which was introduced in Germany as early as 1972, was available to all patients [35]. It can therefore be assumed that the patients had been receiving optimal treatment from the start.

In Germany there are 9.5 million male Germans within that age group 8–25 years (source: German Federal Statistical Office). The incidence of haemophilia A is approx. 1/10 000 and of haemophilia B approx. 1/30 000 male newborns. This study covers about one-quarter of all haemophilia patients in Germany within the tested age group and more than one-third in the group between 8 and 18 years of age.

All patients participated voluntarily in the tests upon invitation from their treating physician. This involves the risk of a bias as the haemophilia patients less interested in sports may not have participated in the study in the first place.

The composition of the group of PWH matches the statistical expectations. The distribution of haemophilia A to haemophilia B patients is 87–13%. More than 55% of the patients have a residual activity below 1%. More than 75% of the patients were 25 years old and suffering from severe or moderate haemophilia and on prophylactic treatment.

Conclusions

We find as many deficits as advantages in comparison to the healthy group, so there is no general inferiority of PWH in fitness. This is might be a result of modern substitution therapy and the fact that activity is widely accepted and advised as a prophylaxis against joint deterioration [1,4,8,15,17,36–39].

The specific deficits should be basis for an individualized exercise therapy. It will be of further interest to find correlations between fitness level and disease progression, age and treatment.

Another aspect is the decreasing fitness in healthy children and young adults [34]. Could that be true for our PWH as well or do we face an increased awareness of the beneficial activities and sports with an increasing fitness level in this group?

Future publication should focus on the comparison of the fitness results of PWH with the results of their healthy family members. If we do not find differences the course of illness might not be the major reason for our results but as well the influence of the socio-economic context.

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Disclosures

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

Author contributions

Axel Seuser designed the study, controlled the measurement and wrote the paper. Peter Böhm analysed the data, performed the research and wrote the paper. Sebastian Ochs organized, controlled and performed the measurement and gave expert advice on Questions of sports science. Elmar Trunz-Carlisi analysed the data, performed the research and gave advice on Questions of sports science. Susan Halimeh gave advice on clinical questions and revised the paper. Robert Klamroth designed the study, gave advice on clinical questions and revised the paper.

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