The impact of a specific aqua-training for adult haemophilic patients – results of the WATERCISE study (WAT-QoL)

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Summary. Sport is increasingly recommended for haemophilic patients due to physical and psychological benefits. ‘WATERCISE’ is a specific aqua-training programme for haemophiliacs in which endurance, strength, coordination and mobility are trained. In the WAT-QoL study benefits and risks of regular WATERCISE training sessions were investigated in terms of health-related quality of life (HRQoL), physical functioning (PF), orthopaedic joint status (OJS), bleeding frequency and factor consumption. Patients in the WATERCISE group attended an aqua-training programme once a week for 1 h over 12 months, patients in the control group did not. Patients were matched for clinical and demographic data. Information on clinical data, orthopaedic status, PF (HEP-Test-Q) and HRQoL were collected in both groups at baseline and at follow-up (6 and 12 months). Twenty-eight adult severely affected haemophilic patients (WATERCISE group: 10 haemophilia A (HA), 3 haemophilia B (HB) patients; control group: 12 HA and 3 HB patients) were enrolled (aged 40.68 ± 12.7 years). Baseline data (body mass indices, OJS, sportive activities, HRQoL and PF) were well distributed between groups. After 12 months the WATERCISE group reported a significantly better PF \( M_w = 65.22, SD = 11.3; M_c = 52.5, SD = 15.0 \), especially for endurance \( P < 0.004 \). Although always differently reported by the patients within the WATERCISE group, HRQoL did not prove to be significantly different between groups. WATERCISE seems to have a positive effect on the PF of patients suffering from haemophilia. These study findings need to be further investigated in a larger study group.

Keywords: aqua-gymnastic, haemophilia, Haem-A-QoL, HEP-Test-Q, physical performance, quality of life

Introduction

Haemophilia is an X-linked recessive haemorrhagic disorder mainly affecting males. Two forms of haemophilia can be distinguished according to the factor concerned: haemophilia A (HA; factor VIII) and haemophilia B (HB; factor IX) [1]. With regard to the factor activity different types of severity are classified: ‘severe’ with a factor activity <1%, ‘moderate’ with a factor activity between 1 and 5% and ‘mild’ with a factor activity >5–40% [2]. Haemophilic patients suffer from recurrent joint bleeds leading to progressive joint destruction, arthropathy and disability accompanied by chronic pain [3]. The avoidance of recurrent haemarthroses is the main goal of haemophilia therapy [4,5]. Haemophilia treatment is based on replacement of the deficient coagulation factor regularly (prophylaxis) or when bleeding occurs (on-demand) [6]. Depending on when prophylaxis is initiated, it is possible to distinguish between primary and secondary prophylaxis [7]. Primary prophylaxis is started prior to any clinically evident joint bleeding or prior to the second year of age as a long-term continuous treatment of at least 46 weeks/year [8]. Prophylaxis started after this time is called secondary prophylaxis, where irreversible articular changes may have already occurred [8,9]. Physiotherapy by means of mobilization techniques, muscle strengthening exercises, joint stability training, postural and gait training, and functional training tries
to diminish disabilities, prevent handicaps and reduce pain caused by articular impairments [10].

Until the early 1970s it was recommended for haemophilic patients to avoid any type of sports activity, because of the danger of uncontrollable intra-articular and intra-muscular bleeding [11]. Today persons with haemophilia are advised to actively participate in sports thanks to prophylactic treatment and an increased knowledge in sports therapy [12]. Even though physical and psychological benefits of sport for haemophilic patients are discussed [13–15], sport is not yet recognized as an integral component in haemophilia management [16]. It could be demonstrated that haemophilic patients doing regularly sport are bleeding less. If on prophylaxis, the motor performance and health condition of children with haemophilia was comparable to their healthy peers [16–18]. Although several studies were conducted assessing physical performance in haemophilic patients [19–26], only one study assessed physical performance subjectively [27], in which the subjective measure ‘HEP-Test-Q’ was developed [28]. However, the self-evaluation of patients’ health condition, especially the health-related quality of life (HRQoL), has gained an important role in the past years [29–31].

Only few data are available on the impact of sport on the HRQoL of haemophilic patients’ [15]. In a Dutch study in haemophilic children it was demonstrated that patients with severe haemophilia with good physical fitness, joint health and no limitations of activities were comparable to healthy peers suggesting a positive impact on HRQoL [32]. By contrast, no correlation between quality of life (assessed via the haemophilia-specific Haemo-QoL) and aerobic fitness in Australian haemophilic children was found [33]. In the German ‘Hemophilia and Exercise Projects’ (HEP) it was shown that 52% of the variance of quality of life of adult haemophilic patients in terms of the physical component score (PCS) of the SF-36 could be explained by subjective physical performance (HEP-Test-Q) and 34% of the variance of the mental component score (MCS) [34].

Even though water activities have been recommended for haemophilics [35–37], up to now only two studies reported the effects of swimming interventions on haemophilic patients [38,39], which might be explained by the logistic difficulties in conducting such an interventional study. Therefore, we designed an interventional controlled study, named WAT-QoL Study (WATERCISE – Quality of Life Study), with the goal of evaluating the impact of a regular aqua-training on HRQoL, subjective physical performance, bleeding frequency, factor consumption and orthopaedic status in adult haemophilic patients compared with a control group of patients not attending the aqua-training over a time period of 12 months. ‘WATERCISE’ is composed out of ‘Water’ and ‘Exercise’ and stands for training exercise in water, which was especially developed for the needs of haemophilic patients. WATERCISE includes exercises out of the field of aqua fitness, aqua aerobics, aqua jogging, but includes as well relaxing aspects. Within WATERCISE, endurance, strength and speed are trained, together with mobility and coordination. It was developed by Medbaik, Germany, and sponsored by CSL Behring, Germany.

**Patients and methods**

**Study design**

We designed an open, non-randomized, interventional, prospective, bi-centre cohort study to evaluate the impact of a regular aqua-training (WATERCISE) on the HRQoL and subjective physical performance of adult haemophilic patients with severe and moderate haemophilia or von Willebrand syndrome (VWS) compared with a control group of haemophilic patients not attending the aqua-training. All outcomes were collected at baseline (before starting the aqua-training), and after 6 and 12 months of follow-up in both groups.

**Study objectives**

The hypotheses of the study were that regular aqua-training (i) has a positive impact on participants HRQoL and (ii) improves their subjective physical performance.

Secondary endpoints of the study were the orthopaedic status, number of bleeds, factor use and number of days off over the study period.

**Inclusion and exclusion criteria**

Male patients with inherited severe (FVIII:C < 1%) or moderate (FVIII:C < 5%) HA or HB and male patients with inherited VWS severely or moderately affected with an age range from 20 to 55 years (or older, if the physical condition allows it) were candidates for inclusion in the study. Their physical condition should allow the participation in the aqua-training, requiring that patients could swim. Non-swimmers had the permission to use swimming aids.

Mild forms of haemophilia or VWS and female patients were excluded as well as patients who did not had the physical condition to participate in the aqua-training. Furthermore, patients who were not giving their consent and who had a likelihood of poor compliance for the regular participation at the aqua-training were excluded.

**Recruitment**

During a patient meeting and via information leaflets sent to patients, eligible haemophilic patients were recruited from two haemophilia centres in Hamburg, Germany, in 2007. Patients who were interested in
participating once a week in an aqua-training (1 h) over a period of 12 months, which was specifically developed for haemophilic patients (WATERCISE), formed the active group; patients who could not commit their regular participation due to work or time issues or lacking interest were assigned to the control group, if comparable to clinical and socio-demographic data (type of haemophilia, age, marital status, living situation, school education and employment status). The study protocol and patient information sheet were approved by the Ethics Committee of the University of Hamburg. Patients gave their written informed consent. In parallel, all WATERCISE patients were provided a special patient insurance in case of covering the financial consequences of injuries during study participation.

WATERCISE

The WATERCISE programme, lead by a physiotherapist, was planned in advance for the entire duration of the study. Exercises contained mobilization and strengthening exercises in the full range of motion. Due to physical conditions of the participants, the progressive training plan had to be modified over the year and within the sessions. Additional tools, such as Aqua-dumbbells, pool-noodles and boards were used to increase resistance. Several sets of each exercise were performed, around 20 repetitions or less in case of muscular fatigue.

Outcomes

The primary endpoints were HRQoL and subjective physical performance. HRQoL was assessed via the generic SF-36 [40] and the haemophilia-specific Haem-A-QoL [41,42] questionnaires. Subjective physical performance was assessed via the HEP-Test-Q [28].

The SF-36 consists of 36 items pertaining to eight dimensions (physical functioning [PF], role PF, bodily pain, general health, vitality, social functioning, role emotional functioning and mental health), which can be summarized to two sum scores (PCS and MCS) [43]. The SF-36 provides values for the subscales and the sum scores ranging from 0 to 100, with a high value indicating a better physical performance.

The Haem-A-QoL consists of 46 items pertaining to 10 dimensions (physical health, feelings, view, sport and leisure, work and school, dealing, treatment, future, family planning, partnership and sexuality), which can be summarized to a sum score. Item responses are scored on a 5-point Likert scale between 1 and 5 (ranging from ‘never’ to ‘always’). The HEP-Test-Q provides values for the subscales and the total scale ranging from 0 to 100, with a high value indicating a better physical performance.

In addition, information on socio-demographic data (such as age, weight, marital status, living situation and school education) and clinical data (such as type and severity of haemophilia, complications, treatment modalities, number of bleedings, days off due to haemophilia and orthopaedic status, which was assessed by the physical examination component of the WFH Orthopaedic Joint Score (OJS) [44] ranging from 0 to 72 (with 0 being a normal joint and 72 being most affected) and information about sport activities (such as doing actually sport, type, frequency and duration of sport) were collected.

Statistics

All statistical analyses were conducted using the SPSS programme version 17.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to depict the study population and are shown as frequency distribution in percentage or as mean (m) ± standard deviation (SD) and range (min–max). Data were tested for normal distribution. \( \chi^2 \)-test was used to compare socio-demographic data between patients and controls. For the comparison of clinical and physical data, unpaired Student’s t-test or Mann–Whitney-U-Test was utilized. Correlations were determined by means of the Pearson or Spearman coefficients. Analysis of variance was used to evaluate differences between the two study groups. Two-sided significance tests were used throughout. \( P \leq 0.05 \) was defined as significant.

Results

Enrolment and follow-up

The aqua-training period was May 2008 to May 2009. Fourteen haemophilic patients were identified for the active WATERCISE group (‘swimmer’) and 15 constituted the passive control group (‘controls’), no patient with VWS was recruited. One patient from the swimmer group was excluded from the analysis because of unmet inclusion criteria (‘mild haemophilia’), but was allowed to attend the aqua-training. In average participants attended 63.9% of the aqua-training units; reasons for not attending were sickness (18.5%), vacation or work-related issues (6.3%) and other reasons (11.3%). Twenty-eight haemophilic patients were eligible and enrolled at baseline, from which 25% were enrolled at baseline, from which 25% had previous experience with any kind of aqua-training or WATERCISE (17.9%).

From baseline to follow-up after 6 months (follow-up 1), three swimmers were excluded from the follow-up
analysis due to lack of regular participation in the weekly training units (>25%). One control patient did not participate at the follow-up evaluation due to lack of interest. From follow-up 1 to follow-up after 12 months (follow-up 2), one swimmer was lost since he moved away from Hamburg, two control patients did not participate at the follow-up 2 evaluation due to lack of interest.

**Baseline data**

Mean age of the whole study population was 40.68 years (SD = 12.7), half of the participants were unmarried (53.6%) and 60.7% were living with their partner. Half of the patients had a lower secondary school level certificate and 57.1% were working part- or full-time. As expected there were no significant differences between swimmers and control patients (see Table 1).

Half of the study population practised actually sport, 50% of this population practised sport alone or with friends (42.9%). This was equally distributed between both groups. Walking (57.1%) and swimming (42.8%) represented the most frequent type of sport, none of the patients played soccer or tennis.

All patients were severely affected and 78.6% suffered from HA. Nearly one-third of the patients (32.1%) were on prophylaxis and in 53.6% of the patients target joints were present. Distribution of clinical parameters such as body mass index (BMI) or OJS was similar between both groups. Walking (57.1%) and swimming (42.8%) were nearly twice the mean values for control patients (1.46 vs. 0.8).

HRQoL was similar in both groups for the PCS of the SF-36 and the MCS of the SF-36 (see Table 4). In the Haem-A-QoL both groups reported similar values (Mswimmer = 31.98; SD = 15.5; Mcontrols = 34.01, SD = 18.1). Main impairments were observed in the dimension ‘sport’. A significant difference was found in the dimension ‘relationship’, where controls (Mcontrols = 28.57; SD = 33.9) showed higher impairments than swimmers (Mswimmer = 7.05; SD = 1.2) (P < 0.040).

Subjective physical performance was similar in both groups in the HEP-Test-Q (Mswimmer = 56.69, SD = 19.1; Mcontrols = 54.0, SD = 18.2) (see Table 4). Furthermore,
Follow-up 1 data (after 6 months)

Participants were asked at follow-up 1, if something had changed compared with baseline; 4 of 10 active patients reported about positive changes. Two patients attributed the change to WATERCISE, none of the control patients reported a positive change.

At follow-up 1 no differences were found between the two groups for clinical and HRQoL data. From baseline to follow-up 1, no differences were seen in both groups for clinical data, but for the orthopaedic status (OJS). A significant improvement from baseline (M = 13.8, SD = 7.9) to follow-up 1 (M = 10.8, SD = 7.3) could be demonstrated in the swimmer group (P < 0.035), no difference was found in the control group (see Table 5). Factor consumption increased slightly from baseline to follow-up 1 in the control group whereas it remained nearly constant in the swimmer group. However, due to the low number of study participants, this difference was not significant. No significant difference was furthermore identified for the number of joint bleeds from baseline to follow-up 1 in both groups. In the swimmer group, patients reported an average of 5.1 days off (Median = 0; range 0–50) in the previous 6 months due to haemophilia, which was due to one patient who underwent a total hip endoprothesis procedure compared with control patients who reported a mean of 0.36 days off (Median = 0; range 0–3 days).

No significant differences between swimmers and controls were found for quality of life in terms of PCS (T = 1.38, df = 22, P = 0.191) and MCS (T = 0.98, df = 22, P = 0.364) of the SF-36 and the Haem-A-QoL (Mswimmer = 31.0, SD = 16.6; Mcontrols = 31.78, SD = 19.1; P = 0.919) at follow-up 1; no difference was found as well for physical performance in terms of the HEP-Test-Q (Mswimmer = 60.3, SD = 16.6; Mcontrols = 54.86, SD = 21.4; P < 0.509). In addition, from baseline to follow-up no differences were found for HRQoL and physical performance in both groups (see Table 5). Controls revealed an improved HRQoL in the dimension ‘work’ of the Haem-A-QoL (P < 0.015) from baseline (M = 15.97, SD = 13.9) to follow-up 1 (M = 5.21, SD = 8.77).

Follow-up 2 data (after 12 months)

Five of nine active participants reported at follow-up 2 that in the last 6 months they experienced a positive change due to the participation in the study, two participants associated this to an improvement of their health (increased mobility and better general health status).

At follow-up 2 no differences were observed for the two groups with regard to clinical data. Swimmers had in average 7.14 joint bleeds in the previous 6 months (Median = 4; range 2–25), compared with control patients, who presented with a mean of 9.56 bleeds in the previous 6 months (Median = 8.0; range 1–33). This difference was not significant (P < 0.613). One patient was excluded from the control group due to 400 reported bleeds in the previous 6 months, which were mainly located in the right ankle. After arthrodesis the bleeds decreased dramatically.

With regard to days off due to haemophilia in the previous 6 months the patients in the swimmer group reported in average 0.89 days off (Median = 0; range 0–15), whereas the patients in the control group reported a mean of 2.08 days off (Median = 0; range 0–15). Again, this difference was not significant as well (P < 0.486).

No difference was observed for HRQoL data between the two groups at follow-up 2. However, regarding the physical performance, a significant difference was identified in the dimension ‘endurance’ (P < 0.004) in favour for the patients in the swimmer group (M = 61.81, SD = 13.0) compared with the value for patients in the control group (M = 42.45, SD = 13.7) as well as for the total HEP-Test-Q score (P < 0.047) (Mswimmer = 65.22, SD = 11.3; Mcontrols = 52.50, SD = 15.0) (see Fig. 1).

Data over 12 months

Time and interaction effects between the groups were analysed for clinical and HRQoL data and for physical performance over time from baseline over follow-up 1 to follow-up 2. No significant time and interaction

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### Table 5. Follow-up 1 clinical data, HRQoL and physical performance of both study groups.

<table>
<thead>
<tr>
<th>Clinical and PRO data</th>
<th>Patients (n = 10)</th>
<th>Controls (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (M (SD))</td>
<td>Follow-up (M (SD))</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OJS</td>
<td>13.80 (7.9)</td>
<td>10.80 (7.3)</td>
</tr>
<tr>
<td>Number of joint bleeds in previous 6 months</td>
<td>8.00 (8.0)</td>
<td>7.13 (8.6)</td>
</tr>
<tr>
<td>Factor consumption U/kg in previous 6 months</td>
<td>1020.12 (851.1)</td>
<td>1029.76 (747.2)</td>
</tr>
<tr>
<td>PCS (SF-36)</td>
<td>42.29 (10.2)</td>
<td>43.45 (8.9)</td>
</tr>
<tr>
<td>MCS (SF-36)</td>
<td>49.58 (8.2)</td>
<td>46.91 (9.6)</td>
</tr>
<tr>
<td>Haem-A-QoL</td>
<td>33.68 (17.4)</td>
<td>31.0 (16.6)</td>
</tr>
<tr>
<td>HEP-Test-Q</td>
<td>60.90 (18.7)</td>
<td>60.30 (16.6)</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>13.75 (11.7)</td>
<td>11.75 (9.3)</td>
</tr>
<tr>
<td></td>
<td>11.89 (12.0)</td>
<td>9.56 (9.2)</td>
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<tr>
<td></td>
<td>653.11 (378.4)</td>
<td>900.67 (840.1)</td>
</tr>
<tr>
<td></td>
<td>36.62 (9.8)</td>
<td>42.94 (8.9)</td>
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<td></td>
<td>47.64 (8.9)</td>
<td>46.54 (8.6)</td>
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<tr>
<td></td>
<td>33.91 (18.8)</td>
<td>31.78 (19.1)</td>
</tr>
<tr>
<td></td>
<td>50.36 (17.5)</td>
<td>54.86 (21.4)</td>
</tr>
</tbody>
</table>
The effect was identified for the number of bleeds per month. For the orthopaedic joint score a significant time effect was observed ($df = 1.5$, $F = 4.874$, $P < 0.024$), but no interaction effect between time and group (see Fig. 2). No significant time or interaction effect was seen with regard to HRQoL. Regarding the physical performance no significant time or interaction effect was documented, even though there was a trend showing that the swimmer group improved over time. For the dimension ‘endurance’ of the HEP-Test-Q a significant interaction effect was shown over time between the groups ($df = 2$, $F = 3.553$, $P < 0.038$) demonstrating that the swimmer group improved their ‘endurance’ over time (see Fig. 3).

Discussion

Participants of both groups in the WAT-QoL Study showed at baseline some impairment in their OJS, which was slightly worse in the swimmer group compared with the baseline value of patients in the control group. However, this was not significantly different between groups.

The mean values for the target joints at baseline between groups were not significantly different, which is probably due to the small sample size.

In addition, only swimmers attended physiotherapy at baseline, by contrast none of the controls. This demonstrates at least the bias that study participants were not randomized to study groups and the patients in the swimmer group were of course more interested in their treatment and more active in this regard.

No differences between ‘swimmers’ (active patients) and ‘controls’ (non-active patients) were identified at baseline for socio-demographic, clinical (e.g. BMI), HRQoL data and subjective physical performance.

At follow-up 1, a significant improvement could be demonstrated for the OJS in the swimmer group compared with the OJS in the non-swimmer group, no improvement was found for HRQoL and physical performance. This difference between groups could not be confirmed at follow-up 2 and interestingly, the OJS in both groups improved significantly over time.

Interestingly, at follow-up 2, a significant improvement in physical performance was observed in the swimmer group with regard to ‘endurance’ and total score. Over the 12 months period a significant improvement was identified in the swimmer group for the dimension ‘endurance’ of the HEP-Test-Q.

With regard to days off due to haemophilia in the previous 6 months the patients in the swimmer group reported in average 0.89 days off (Median = 0; range 0–15), whereas the patients in the control group reported a mean of 2.08 days off (Median = 0; range 0–15) during follow-up 2. This again would become significantly different in greater sample sizes.

As three patients missed more than 25% of the training units and one patient did not fulfil the inclusion criteria only nine active patients remained be analysed over time compared with 12 patients in the control group.
group, which is quite a low number. However, the number of active participants is already limited due to the size of the swimming pool and the practicability of the training units, where a maximal number of participants should not exceed 15–20 people.

In addition, it has to be kept in mind that the study logistics involved in the conduct of such a study is demanding. Beside regulatory and insurance issues, the simple organization of weekly WATERCISE sessions for haemophilic patients asks for a high degree of compliance. This is also the main reason for our low number of patients who could be motivated for study conduct.

On the other hand this is the first interventional study in haemophilic patients attending an aqua-training over a long period of 12 months, where objective and subjective data are assessed together.

Another study in Spain investigated the effect of a specially designed aquatic training on the motor performance of HA patients, which revealed improved aerobic and mechanical capacity without causing adverse effects [39]. However, no subjective effects of the aquatic training were assessed.

In the German Haemophilia & Exercise Project (HEP) the subjective and objective physical performance in adult haemophilic patients was investigated. It was demonstrated that objective outcomes such as one-leg-stand and 12-min-walk test were correlated with the subjective HEP-Test-Q and that haemophilic patients showed a significantly more impaired subjective physical performance than age-matched healthy controls [45].

A correlation between subjective outcome (pain intensity) and objective outcomes (clinical pathology and radiographic joint damage) was found in another German study in 60 adult haemophilic patients; the more pronounced was the objective damage, the higher was the likelihood of severe joint pain and reduced activities [46].

Our study could demonstrate that subjective assessment of physical performance is an important indicator of the condition of haemophilic patients and that it can be improved over time with a specific aqua-training. As sport can not only influence positively the physical health, but as well the socialization and self-esteem of persons with haemophilia, supervised sport activities should be considered among the aims of a global approach to haemophilia management, which is as well in line with the recommendations of Seuser et al., who stated that after adequate physical evaluation and preparation, haemophilic patients can benefit physically and emotionally from participation in sports [47].

In conclusion, a significant improvement of the orthopaedic joint score over time could be demonstrated in both groups, which might be explained as well by the Hawthorne effect [48] (a form of reactivity whereby subjects modify an aspect of their behaviour in response to the fact that they know they are being studied), that also the control patients took care of their joints due to the fact that they were participating in the WAT-QoL study.

Compared with controls active patients reported a higher endurance in their PF which was significant as well over time. We also identified a trend for less bleeds in the swimmers group over time and in the data over 6 months time, a higher factor consumption was observed in patients of the control group compared with patients in the swimmer group (swimmer group: 1,020.12 IU/kg b.w. at baseline; 1,029.76 IU/kg b.w. at 6 months; control group: 653.11 IU/kg b.w. at baseline; 900.67 IU/kg b.w. at 6 months). Again, this finding did not remain constant, but if physiotherapy improved also in the non-swimmers, this could have had an impact on bleeds and factor consumption in control patients.

No further differences were found for other clinical or subjective parameters and it is of great interest that we were unable to confirm a significant difference in HRQoL although the swimmers reported an increase in HRQoL over the whole conduct of the study. The reason for this has to be explored further.

In conclusion, even with this small number of patients it could be demonstrated that sportive activities, such as aqua-training (WATERCISE), have a positive effect on haemophilic patients. These findings need to be replicated in a larger cohort including further objective measures with study participants randomized to treatment and non-treatment where we feel that most of the parameters that were already different between groups in our study may turn into significant differences.

Author contributions

SvM, WZ and BE: designed the research study; JK: developed in cooperation with CSL Behring the WATERCISE training programme; DZ: coordinated the logistics with the patients from both haemophilia treatment centres; AW: performed the aqua gymnastic training with the haemophilic patients; SvM: analysed the data; SvM: wrote the manuscript and WZ; was the study coordinator and contributed to the writing of the manuscript.

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Disclosures

SvM and WZ have received research grants from CSL Behring for conducting the study. DZ served as a study nurse during the study. AW was paid by CSL Behring for performing the WATERCISE training with the active patients. BE and JK received a consultancy fee from CSL Behring.
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