Anaerobic power and muscle strength in young hemophilia patients

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ABSTRACT

FALK, B., S. PORTAL, R. TIKTINSKY, Y. WEINSTEIN, N. CONSTANTINI, and U. MARTINOWITZ. Anaerobic power and muscle strength in young hemophilia patients. *Med. Sci. Sports Exerc.,* Vol. 32, No. 1, pp. 52–57, 2000. **Purpose:** The purpose of this study was to evaluate muscle strength and anaerobic power in young boys with hemophilia compared with healthy boys. **Methods:** Thirteen boys with severe hemophilia (H) (mean (± SD) age = 12.0 ± 3.17 yr) and 16 control (C) boys (age = 11.9 ± 2.8 yr) performed elbow and knee flexion and extension on the Biodex System II dynamometer at two angular velocities. They also performed a Wingate Anaerobic Test (WAnT) for the legs and for the arms. All H subjects received prophylactic factor VIII treatment in the 24 h pretesting, and no test was performed in the presence of hemorrhage. **Results:** C were consistently stronger than H in all dynamic strength measures (e.g., elbow flexors: 0.47 ± 0.15 vs 0.36 ± 0.08 $N \cdot m \cdot kg^{-1}$ for C and H, respectively, $P < 0.05$). Anaerobic mean power was also higher in C compared with H in both upper and lower extremities (arms: 3.08 ± 0.99 vs 2.22 ± 0.46 $W \cdot kg^{-1}$ for C and H, respectively; legs: 6.94 ± 1.62 vs 5.54 ± 1.03 $W \cdot kg^{-1}$ for C and H, respectively, $P < 0.05$). Upper and lower extremity strength, as well as anaerobic power, increased with age in C but not in H. By using the Godin Leisure-Time Exercise Questionnaire, H were found to be much less active, especially in intense activities, compared with C. **Conclusion:** Children and adolescents with hemophilia are characterized by lower muscle strength and anaerobic power compared with age-matched controls. This may be related to their lower leisure-time activity. **Key Words:** ADOLESCENTS, BOYS, CHILDREN, EXERCISE, ISOKINETICS, PHYSICAL ACTIVITY, PHYSICAL FITNESS, WAnT

Hemophilia is an X-linked genetically transmitted disorder that is caused by a deficiency in a circulating blood clotting factor. Hemophilia A is the most common type and is caused by a functional deficiency of factor VIII (15).

The severity of hemophilia can vary from mild to severe, according to the functional plasma levels of the clotting factor and the severity of bleeding. Mild hemophilia is characterized by functional plasma levels above 5% of normal factor VIII levels. Such patients are characterized by rare bleeding, mainly after surgery or trauma. In the moderate form, plasma levels are between 2 and 5% of normal levels, and bleedings characteristically occur several times a year, usually after some trauma. In the severe form of the disorder, plasma levels are below 2% of normal, and patients suffer from spontaneous bleeding even in the absence of trauma (14).

Most bleedings involve the joints, usually those of the lower limbs, and the most common complication is synovitis of the joints, leading to more frequent bleeds. The frequent bleeds again cause recurrent synovitis, and the cycle continues. This can lead to joint degeneration, articular distortion, and, eventually, may require joint replacement.

There are very few quantitative reports in the literature documenting the physical ability of hemophilia patients. Koch et al. (16) reported a low aerobic working capacity in 11 young (15 yr), mild to severe hemophilia patients, compared with age-appropriate norms. This finding was based on the maximal power output attained in a cycle ergometer test to exhaustion. However, no direct measure of oxygen consumption was made. Pietri et al. (20) reported that among 10 young hemophilia patients (8–23 yr) with a history of unilateral hemarthrosis, there was reduced knee extensor strength in the affected limb compared with the unaffected limb. However, no comparison was made with normative or control data. Based on these findings, the authors recommended strength training for the rehabilitation of hemophiliacs.

Greene and Strickler (12) reported that among 32 patients with severe hemophilia, an isokinetic strengthening program was effective in strengthening knee flexors and extensors, although it did not increase the number of knee hemarthroses. Again, no comparison was made to a control group or to normative data.

Based on these limited data, many physicians and investigators recommend participation in physical activity for young hemophilia patients (3,6). The recommended activities include aerobic-type activities such as swimming

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TABLE 1. Subjects' characteristics; data are means (and SD).

	Hemophilia	Control
No. of subjects	13	16
Age (yr)	12.04 (3.07)	11.86 (2.83)
Body mass (kg)	44.67 (14.71)	45.60 (18.82)
Height (cm)	146.8 (15.1)	150.0 (13.9)
Sum of skinfolds (mm)	59.7* (30.6)	37.9 (19.8)
Body fat (%)	28.1* (12.4)	18.4 (8.0)

* Significant difference between groups ($P < 0.05$).

(1,5,7,17,22,27), as well as controlled resistance training to develop the musculature (12,16,19,20). In fact, resistance training is believed to increase joint stability, decrease the stress on the joint, reduce injuries, as well as reduce the risk of spontaneous bleeding episodes (6,20).

Despite the consensus regarding the benefits of maintenance of well-developed musculature in hemophilia patients, it is surprising that there are no quantitative reports of muscle strength and endurance in such patients compared with healthy individuals. Thus, the purpose of this study was to evaluate muscle strength and anaerobic power in children and adolescents with severe hemophilia and compare them with age-matched healthy boys. It was hypothesized that muscle strength, as well as anaerobic power would be lower in the hemophilia patients.

METHODS

Subjects. A total of 29 children and adolescents, aged 8–18 yr, volunteered to participate in the study. The hemophilia patients were under the care and supervision of the National Hemophilia Center at the Sheba Medical Center in Israel. Twenty-eight patients were contacted by phone, of whom 13 volunteered to participate. All patients were diagnosed with severe hemophilia A and had a bleeding frequency of about once per week. None of the patients was actively bleeding at the time of testing, and all received prophylactic factor VIII treatment in the 24 h preceding the time of testing. No test was performed in the presence of hemorrhage. In situations where the joint was recently post-bleeding, the affected joint was not evaluated. The control subjects were recruited from local schools and were of a similar chronological age. All subjects and their parents were given an explanation of the purpose, procedures, and potential risks and benefits of the study and all gave their informed consent, in accordance with the requirements of our institution's ethical committee. The subjects' age and physical characteristics are described in Table 1.

Tests and measurements. Anthropometric measurements included body mass (accuracy of $\pm$ 20 g), height, and skin-fold thickness at four sites (biceps brachii, triceps brachii, subscapula, and suprailium). Skin-fold thickness was measured in triplicate using Skyndex (Fayetteville, AR) calipers and the mean value at each site was used. Percent body fat was estimated according to Slaughter et al. (23).

The extensors and flexors of both knees and elbows were tested on an isokinetic dynamometer (Biodex, Systems II, Shirley, NY). Previous studies have demonstrated the reliability and validity of isokinetic devices for measuring muscle strength in adults (see 9, for review) as well as in children (18).

The dynamometer was fitted for either leg or arm testing and was individually adjusted for each subject such that the tested joint axis of rotation was aligned with the dynamometer's pivoting axis. To stabilize the hip and the trunk, the subjects sat on a chair with support for the back, and they were restrained with straps at the level of the chest and thigh. Additional back support was provided for the smaller subjects to accommodate their size.

On the testing day, subjects were familiarized with the dynamometer, after which they performed a standardized warm-up for each muscle group. The warm-up included 6 contractions at a progressive effort. Following a 1.5-min rest, subjects were encouraged to exert maximal muscular force (for both flexion and extension) during actual testing. Verbal encouragement and visual feedback of the torque were provided during the test. All tests were conducted at the same time in the afternoon in an air-conditioned room.

Isokinetic strength was measured at angular velocities of 1.57 rad·s^{-1} (90°·s^{-1}) and 2.09 rad·s^{-1} (120°·s^{-1}) for the elbow flexors and extensors, and at 1.04 rad·s^{-1} (60°·s^{-1}) and 2.09 rad·s^{-1} (120°·s^{-1}) for the knee flexors and extensors. The range of motion for the knee was 1.57 rad (90°), starting with the knee flexed at 1.57 rad (90°) and ending in full extension. The range of motion for the elbow was 1.74 rad (100°), starting with the elbow fully extended and ending in flexion. The subjects performed five maximal voluntary contractions at each velocity and the highest torque was recorded. The order of testing (upper, lower, right, and left limbs) was randomized.

The Wingate Anaerobic Test (WAnT) was administered on a computerized Fleisch Metabo (Basel, Switzerland) ergometer specially fitted for the subjects' stature, and for either leg or arm ergometry. Resistance was based on body mass with a load of 0.045 kg·kg^{-1} (4.41 J·rev^{-1}·kg^{-1}) and 0.030 kg·kg^{-1} (2.94 J·rev^{-1}·kg^{-1}) for the leg and arm tests, respectively, as recommended by Dotan and Bar-Or (8). In view of the differences in the calculated percent body fat, and therefore in lean body mass, between the two groups, it may have been more appropriate to base the resistance on the calculated lean body mass rather than on total body mass. Basing the resistance on total body mass may have affected the mean power (see below). A 6-min warm-up preceded the test, during which time subjects were familiarized with the test procedures and performed 3 maximal unresisted accelerations. The duration of each acceleration was 3–4 s. The peak rate of unloaded revolutions per minute (RPM) was recorded. The WAnT was performed 3–4 min after the warm-up. Resistance was applied when subjects reached 75% of their predetermined peak RPM. Three performance indices were calculated from the WAnT: peak power (PP) was the highest mechanical power output at any 1-s period, mean power (MP) was the average power

TABLE 2. Performance in the leg and arm WAnT in hemophilia patients and control subjects.

	Hemophilia	Control	*P*
Leg WAnT			
Peak power ($W \cdot kg^{-1}$)			
Per total body mass	7.99 (0.99)	9.37 (1.62)	0.01
Per fat-free mass	11.66 (2.95)	11.71 (3.27)	NS
Mean power ($W \cdot kg^{-1}$)			
Per total body mass	5.54 (1.03)	6.94 (1.62)	0.01
Per fat-free mass	7.99 (1.95)	8.69 (2.94)	NS
Fatigue index (%)	53.6 (17.9)	50.9 (10.9)	NS
Arm WAnT			
Peak power ($W \cdot kg^{-1}$)			
Per total body mass	3.91 (0.67)	4.80 (1.20)	NS (0.08)
Per fat-free mass	5.28 (1.44)	6.10 (2.35)	NS
Mean power ($W \cdot kg^{-1}$)			
Per total body mass	2.22 (0.46)	3.08 (0.99)	0.03
Per fat-free mass	2.96 (0.70)	3.91 (1.75)	NS
Fatigue index (%)	63.0 (15.0)	63.7 (12.8)	NS

attained throughout the entire 30-s test, and fatigue index (FI) was the drop in power from PP to the minimal power, expressed as a percentage of PP. Performance in the WAnT (MP, PP) has been shown to be highly reliable among healthy children (r = 0.96), and feasible for young children with or without a neuromuscular disability (2,24).

Leisure-time physical activity was assessed using the questionnaire developed by Godin and Shephard (11), translated and modified to Hebrew. Its reliability and validity among 5th to 11th grade students have been previously established (21). Its test-retest reliability among 8th and 11th grade Israeli students was examined using an intraclass correlation and found to be 0.92 and 0.83, respectively. Although the questionnaire was validated on a large sample of children (N = 319), it is one of the few quantitative questionnaires which is simple yet valid and reliable in children (21).

Statistical analysis. Differences in the means between the two groups were analyzed using an unpaired *t*-test. Pearson product-moment correlation was used to determine relationships between two variables. Values are reported as means and SD.

RESULTS

There were no differences in age, body mass, or stature between the two groups. However, the sum of four skinfolds and the estimated percent fat were significantly higher in the hemophilia patients (H) compared with the control (C) group. Therefore, all performance variables were corrected for total body mass and for the calculated fat-free mass. The pattern of results was similar whether performance was expressed per unit of body mass or per fat-free mass.

Performance in both the leg and arm versions of the WAnT was lower in H compared with C. Statistical significance was reached when values were expressed relative to total body mass but not relative to fat-free mass (Table 2).

Values of dynamic strength for the right elbow and right knee extensors and flexors are presented in Figure 1. Values and differences between groups were similar for the left limbs. Although the pattern of results was similar when values were expressed relative to body mass or relative to fat-free mass, significance was not reached in the latter case.

Activity scores were significantly lower in H compared with C (31.8 ± 22.7 vs 83.4 ± 64.6, respectively), which is mainly a reflection of the lower involvement in intense activity among H compared with C (1.38 ± 2.06 vs 6.31 ± 5.38 times per week, respectively).

As expected, among C, performance variables in the WAnT correlated well with age, whether expressed per body mass (r = 0.75–0.91) or per fat-free mass (r = 0.80–0.88). However, this was not the case in H, where the only significant correlation with age was in leg PP per body mass (r = 0.53, P = 0.04). All other WAnT performance indices in H did not correlate with age. A careful analysis of the individual data, however, revealed that the difference in performance variables between the older hemophilia subjects (>16 yr, N = 2) and their age-matched control subjects was much bigger than the respective difference among the younger subjects (see Fig. 2). Correlation coefficients among subjects below 16 yr of age were similar in the two groups (although performance values were lower among H).

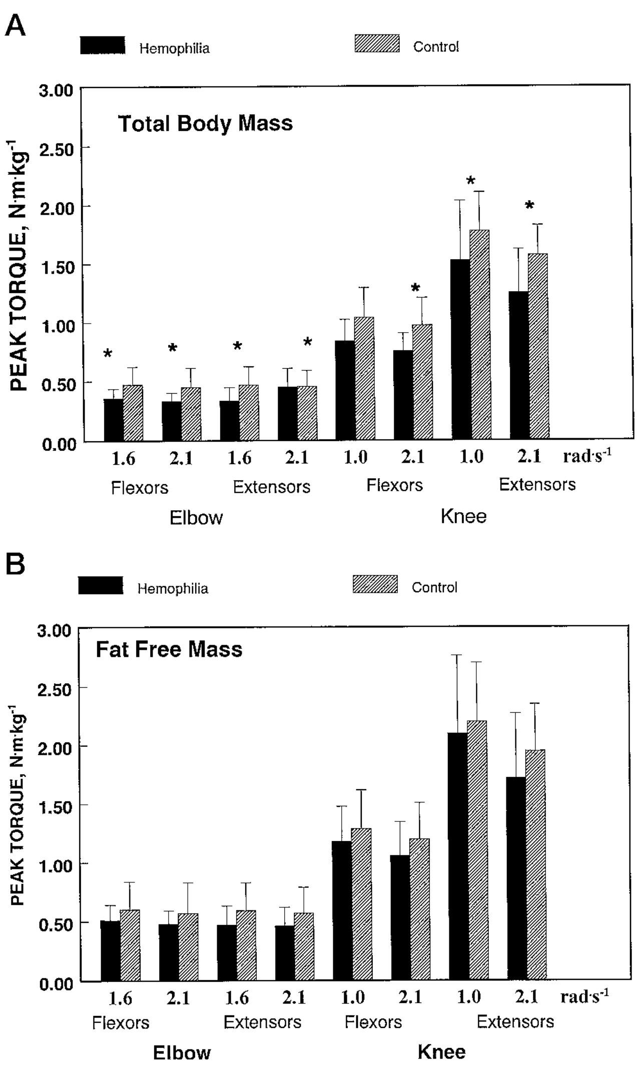

Figure 1—Peak torque per kg body mass (A) and per kg fat-free mass (B) in hemophilia patients and control subjects for the right elbow and right knee flexors and extensors. Values are mean and SD.

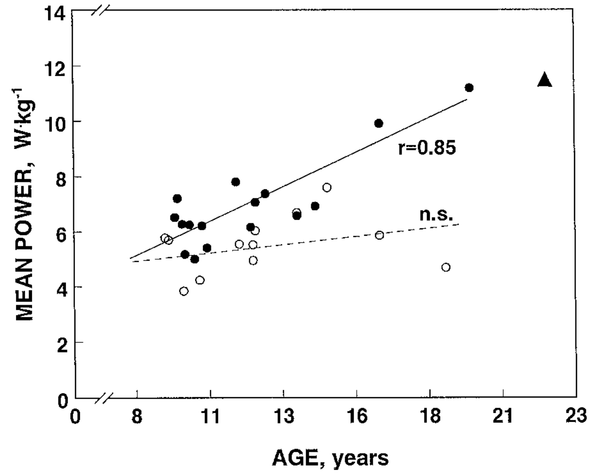

Figure 2—Correlation between age and leg mean power per kg body mass in the WAnT in hemophilia patients ($P > 0.05$, *unfilled circles*) and control subjects (r = 0.85, $P < 0.001$, *filled circles*). The *filled triangle* is a hemophilia patient who has been training intensively for over 10 yr (see text for details).

Similarly, variables of dynamic strength correlated well with age in C (r = 0.48–0.90) but not in H. The only significant correlation between a strength variable and age in H was observed in the right elbow flexion peak torque per body mass (r = 0.49, $P = 0.05$) (Fig. 3). As was the case for the WAnT performance indices, dynamic strength variables correlated with age to a similar degree in the two groups when the analysis was performed among subjects below age 16 (although values were lower among H).

A significant correlation was found between leg MP in the WAnT and the calculated activity score in H (r = 0.62, $P = 0.02$), but not in C. None of the other WAnT performance indices correlated with the activity scores in either group. Variables of dynamic strength generally correlated well with the level of activity in H (r = 0.51–0.82) but not in C (most correlations were not significant and others were negative, r = −0.44–0.64; Fig. 4). Activity scores were not related to age. Therefore, a similar pattern was apparent when correlation analysis was performed between performance variables and activity scores among subjects below the age of 16 yr.

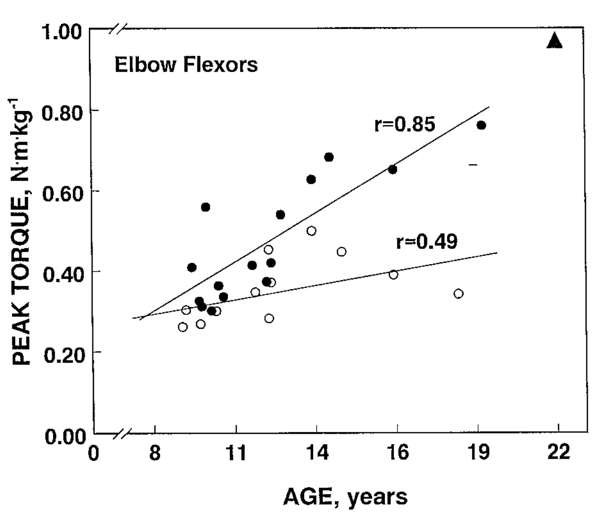

Figure 3—Correlation between age and right elbow flexors peak torque at 1.56 rad·s^{-1} (90°· s^{-1}) in hemophilia patients (r = 0.49, P = 0.05, *unfilled circles*) and control subjects (r = 0.85, $P < 0.001$, *filled circles*). The *filled triangle* is a hemophilia patient who has been training intensively for over 10 yr (see text for details).

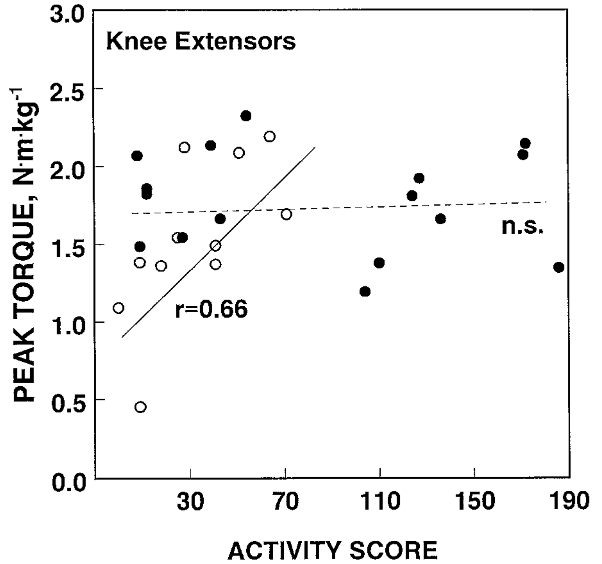

Figure 4—Correlation between right knee extensors peak torque at 1.04 rad·s^{-1} (60°·s^{-1}) and activity scores in hemophilia patients (r = 0.66, $P < 0.05$, *unfilled circles*) and control subjects ($P > 0.05$, *filled circles*).

DISCUSSION

The main findings in this study are the lower anaerobic power and dynamic strength among the hemophilia patients compared with age-matched controls. The lower performance capacity was apparent whether values were absolute or corrected for body mass. A similar tendency was observed when values were corrected for adiposity. The reduced muscular performance capacity among the hemophilia patients may be explained, at least in part, by their lower level of reported leisure-time activity. In fact, among the hemophilia patients, there was a close relationship between the mean power in the WAnT performance and strength on the one hand, and activity scores on the other.

It is important to emphasize that strength and anaerobic capacity were consistently lower in the hemophilia patients, even when values were corrected for fat-free mass, although the differences did not often reach statistical significance. The consistently lower values suggest that the differences may be attributed to a lower muscular performance capacity and are not a consequence of a higher adiposity. It is likely that statistical significance was not reached due to the higher variability when correcting for fat-free mass compared with correcting for total body mass.

The findings of lower anaerobic power and muscle strength among our young hemophilia patients are in line with the lower aerobic working capacity reported by Koch et al. (16) in hemophilia patients of a similar age. The patients in the latter study claimed that "their activity levels do not differ from those of their peers," although the authors did not state whether this claim was made informally or whether it was borne out using a standardized method such as a questionnaire or interview. Nevertheless, the authors suggest that the patients' lower physical working capacity was due to their lack of conditioning, higher proportion of body fat (not reported), and reduced exercise participation. The results of the present study quantitatively support the suggestions made by Koch et al. (16). In the present study, the hemophilia patients indeed had a higher percentage of body fat. Additionally, their lower physical capacity was consistently related to their lower level of activity, as determined by a standardized questionnaire.

An alternative hypothesis explaining the lower muscular performance capacity among the hemophilia patients may be related to direct damage to joints and muscle due to intra-articular and intra-muscular bleedings. These may have caused muscle atrophy that, in turn, would result in reduced strength and anaerobic power among the hemophilia patients. Although all patients were characterized by a bleeding frequency of about once per week, we have no detailed records of their bleeding history. Future studies should investigate the relationship between bleeding history, possible muscle atrophy, and muscular performance capacity.

Very few quantitative studies of muscle function in hemophilia patients have been published, none of which provide a comparison with control subjects. Two studies used isokinetic dynamometers with hemophilia patients, although values were reported for the lower limbs only. Greene and Strickler (12) reported on dynamic strength, as measured on a Cybex II machine, in 7- to 51-yr old patients. No attempt was made to correct for body size. Additionally, the speed of contraction was much slower than in the present study (0.52 vs 1.04 rad·s^{-1} or 30 vs 60°·s^{-1}). More recently, Pietri et al. (20) reported isokinetic strength values for the knee flexors and extensors in ten 8- to 23-yr old hemophilia patients, as measured on the Cybex 340, comparing knees with a history of hemarthrosis (affected) with unaffected knees. Again, no attempt was made to correct for body size. Both studies reported a wide range of peak torque for both knee extensors (49.8–115.2 N·m) and knee flexors (30.4–59.7 N·m). The fact that no correction was made for body size and that different types of dynamometers were used in both studies makes it difficult to compare these results with the ones of the present study. Nevertheless, Greene and Strickler (12) report a correlation between age and strength of knee flexors (no r value reported), which agrees with our finding of increased dynamic strength with increased age.

Pietri et al. (20) reported differences in dynamic strength between affected and unaffected knees only in low angular velocities (1.04 rad·s^{-1} or 60°·s^{-1}). The authors suggested that this may be due to selective atrophy or loss of slow twitch muscle fibers in the affected limb. In the present study, differences between control and hemophilia patients were similar in the slow (1.04 rad·s^{-1} or 60°·s^{-1}) and faster angular velocities (2.09 rad·s^{-1} or 120°·s^{-1}). Although our "fast" velocity was slower than the one used by Pietri et al. (20) (3.13 rad·s^{-1} or 180°·s^{-1}), the findings of the present study do not support the suggestion of selective slow fiber atrophy.

Muscular performance capacity increased with age in the control subjects, which is in agreement with previous reports (e.g., 4,10,13). This was not the case with the hemophilia patients. As seen in Figures 2 and 3, the low correlations between muscular performance capacity and age among these patients may be explained by the low strength and anaerobic power attained by the two older patients. We have no indication that these patients were clinically different than the rest of the hemophilia patients. Furthermore, their activity scores were not distinctly low compared with the group range (9 and 41, group range = 0–71). It is possible that their lower muscular performance capacity is a characteristic outcome of a general deterioration in physical ability which may occur in hemophilia patients. That is, it is possible that the accumulated damage of intra-articular or intra-muscular bleedings experienced by these older patients contributed to greater muscle atrophy and thus, reduced muscular performance capacity. Additionally, the reduced physical activity in hemophilia patients may have a more pronounced effect on muscular performance capacity with an increase in age or with maturation. In view of the small number of older subjects, further research is recommended to examine the effect of age and maturation, as well as the effect of physical activity on muscular performance capacity in hemophilia patients.

It should be noted that pubertal stage was not determined among subjects. Because muscular ability may increase with pubertal maturity, independent of age, relating the results to pubertal stage, rather than chronological age, may theoretically influence the results. However, we have no reason to believe that progression through puberty is different in boys with hemophilia compared with healthy boys. Therefore, any possible bias is similar in both groups.

In addition to the known health benefits of physical activity to the general population, children as well as adults (26), physical activity is argued to have added benefits among hemophilia patients. These include increased joint stability, reduced risk of injury, and a reduction or prevention of intra-articular hemorrhages (see reviews by Beardsley (3) and Buzzard (6)). The findings of this study cannot directly support the claim of reduced hemorrhages. However, the correlations that were observed among the hemophilia patients between physical activity scores, on the one hand, and muscular strength and anaerobic power ($r = 0.51–0.82$), on the other, strengthen the above arguments for the added benefits of physical activity among these patients.

Of special interest is a severe hemophilia patient at our clinic who began sports participation at a young age. At the age of 22, he still trains intensively and competes at top national and international level karate competitions. In fact, he was recently declared the Israeli champion in the <80 kg weight category. He suffers from bleeding episodes only after trauma (and even this very rarely) and no spontaneous bleeding, although his factor VIII level is below 1%. This and similar cases of reduced bleeding in patients who exercise regularly have been recently reported (25). His muscular strength and anaerobic power values were much higher than those of the hemophilia patients in the present study. More importantly, his values were on the control group's extended regression lines of the anaerobic power vs age and the muscular strength versus age, as seen in Figures 2 and 3, respectively.

In summary, this study quantitatively demonstrates that muscular strength and anaerobic power in young hemophilia patients is lower compared with an age-matched healthy control group. Additionally, the muscular strength and anaerobic power among the hemophilia patients was directly related to their level of reported physical activity. The findings thus support the common recognition among those who treat hemophilia patients that physical activity and exercise can be beneficial to this population. Future research is needed to examine the effects of regular exercise, especially strengthening exercise, on joint stability, and the incidence of injury and of intraarticular spontaneous bleeding.

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