ORIGINAL ARTICLE

Cardiovascular Disease Risk Factors and the Relationships With Physical Activity, Aerobic Fitness, and Body Fat in Adolescents and Young Adults With Myelomeningocele

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ABSTRACT. Buffart LM, van den Berg-Emons RJ, Burdorf A, Janssen WG, Stam HJ, Roebroeck ME. Cardiovascular disease risk factors and the relationships with physical activity, aerobic fitness, and body fat in adolescents and young adults with myelomeningocele. Arch Phys Med Rehabil 2008;xx:xxx.

Objectives: To describe cardiovascular disease (CVD) risk factors in adolescents and young adults with myelomeningocele (MMC) and to explore relationships with physical activity, aerobic fitness, and body fat.

Design: Cross-sectional study.

Setting: Outpatient clinic.

Participants: Adolescents and young adults (N=31) with MMC (58% men) age 16 through 30 years; 13 were ambulatory and 18 were nonambulatory.

Interventions: Not applicable.

Main Outcome Measures: We studied biologic and lifestyle-related CVD risk factors, including lipid and lipoprotein profiles, blood pressure, aerobic fitness (Vo_2peak), body fat, daily physical activity, and smoking behavior. We considered subjects at increased CVD risk when 2 or more of the following risk factors clustered: systolic blood pressure, total serum cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and cigarette smoking. Relationships were studied using regression analyses.

Results: Levels of TC, low-density lipoprotein cholesterol, and triglycerides were elevated in 29%, 38%, and 3% of the participants, respectively. HDL-C was reduced in 19%. Hypertension was found in 20%, and 19% were current cigarette smokers. Based on the clustering of risk factors, 42% of the participants were at increased CVD risk: 15% of ambulatory participants and 61% of nonambulatory participants (P=.03). Adjusted for sex and ambulatory status, participants with higher aerobic fitness tended to be more likely to have no CVD risk (odds ratio=13.0; P=.07). CVD risk was not associated to physical activity and body fat.

Conclusions: A large proportion of the study sample was at CVD risk, indicated by clustering of risk factors. Improving aerobic fitness in young adults with MMC may contribute in reducing CVD risk; this needs to be confirmed in future studies.

Key Words: Cardiovascular diseases; Physical fitness; Rehabilitation; Risk factors; Spina bifida cystica.

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LIFESTYLE-RELATED DISEASES such as CVDs are of major concern in industrialized countries.[1,2] Although the clinical manifestations of CVD typically appear in adulthood, the process of atherosclerosis, causing CVD, lies early in childhood[3,4] and seems to increase rapidly during adolescence and young adulthood.[5] During the transition from adolescence to adulthood, people develop their own lifestyles. It may therefore be important to encourage healthy lifestyle behavior at these ages with the aim of delaying the development of atherosclerosis and reducing the incidence of CVD later in life.

The Framingham Heart Study has substantially contributed to the understanding of the causes of CVD and has identified numerous risk factors, such as cigarette smoking, hypertension, high TC, and low levels of HDL-C.[1,6-8] It has been suggested to focus on multiple risk factors rather than on 1 specific risk factor because the severity of atherosclerosis increases as the number of CVD risk factors increases.[4] This clustering of risk factors has proved to be a better measure of cardiovascular health in youth than single risk factors.[9]

Other important risk factors for CVD are physical inactivity, obesity, and low aerobic fitness,[6,7,10-12] which can play a major role in the prevention of CVD.[6] Persons with chronic physical conditions may be at increased risk of developing CVD. Unfavorable CVD risk profiles in persons with an SCI have been

List of Abbreviations

CVD	cardiovascular disease
DBP	diastolic blood pressure
HDL-C	high-density lipoprotein cholesterol
JNC 7	Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
LDL-C	low-density lipoprotein cholesterol
MMC	myelomeningocele
NCEP ATP III	National Cholesterol Education, Adult Treatment Panel III
OR	odds ratio
Vo_2peak	peak oxygen uptake
RC	regression coefficient
SBP	systolic blood pressure
SCI	spinal cord injury
TC	total serum cholesterol
TG	triglycerides

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associated with inactive lifestyles and low aerobic fitness.[13-15] Furthermore, CVD is among the most important causes of death in persons with SCI,[16-18] occurring with a greater frequency than in the general population.[19] Also, persons with MMC have inactive lifestyles, low aerobic fitness, and excessive body fat.[20-24] Because they may be restricted in physical activity from birth, the risk of developing CVD may even be higher than in persons with an SCI. Furthermore, deteriorating vascular properties in the lower extremities (small diameter, low flow, high shear stress), which are related to CVD, tend to be more pronounced in persons with MMC than persons with SCI.[25] Because many persons with MMC nowadays survive into adulthood,[26] CVD may be of increasing concern.

In contrast with the SCI population, no data are available on the number of deaths caused by CVD in persons with MMC, and information on CVD risk factors other than physical inactivity, poor aerobic fitness, and obesity is limited. Rendeli et al[27] found that girls with MMC (age 1–16y) had higher levels of TC and very low-density lipoprotein than their peers, and TC was higher in nonambulatory than in ambulatory girls. In contrast, Nelson et al[28] did not find differences in lipid and lipoprotein profiles between adolescents with MMC and able-bodied peers. Because of the scarcity of studies, the present study aimed to describe CVD risk factors in adolescents and young adults with MMC, including ambulators and nonambulators. To study whether improving lifestyles might benefit cardiovascular health, we explored whether physical activity, aerobic fitness, and body fat were related to other CVD risk factors.

METHODS

Participants

Recruitment. Adolescents and young adults with MMC (age 16–30y) from 4 university hospitals in the western part of The Netherlands (Rotterdam, Leiden, Utrecht, and Amsterdam) and 5 rehabilitation centers in the adjacent region were invited to participate in a cross-sectional study on physical activity and aerobic fitness. Exclusion criteria were complete dependence on an electric wheelchair, inability to understand the instructions necessary for the study, presence of disorders other than MMC that affected daily physical activity (eg, rheumatoid arthritis), and presence of disorders that contraindicated a maximal exercise test (eg, exercise-induced ischemia or arrhythmias, uncontrolled hypertension, and exercise limitation caused by chronic obstructive pulmonary disease). The inclusion criterion was willingness to undergo blood tests. In total, 31 adolescents and young adults participated in the present study, a subset of a larger cross-sectional study (n=51) on physical activity and fitness in adolescents and young adults with MMC.[24,29] All participants gave written informed consent. The Medical Ethics Committee of Erasmus Medical Center and of all participating institutes approved the study.

Characteristics. The mean age of the participants was 21.4±4.4y, and 18 (58%) were men. We obtained level of lesion and the presence of hydrocephalus from medical records. We defined ambulatory status according to the classification of Hoffer et al,[30] and categorized participants as ambulators (community ambulators, n=8; or household ambulators, n=5) or nonambulators (n=18, also including nonfunctional ambulators).[30]

Personal and condition-related characteristics (ie, age, sex, level of lesion, and presence of hydrocephalus), ambulatory status, blood pressure, sum of 4 skin folds, aerobic fitness, daily physical activity, and smoking behavior did not differ between those who were willing to yield a blood sample (n=31) and those who were not (n=20), as tested with an independent *t* test or Chi-square test (table 1). Furthermore, we found no differences in personal and disease-related characteristics of responders (n=51) and nonresponders of the larger cross-sectional study (n=108).[24]

Table 1: Descriptive Results of Personal and Condition-Related Characteristics, and Biologic and Lifestyle-Related Risk Factors of Cardiovascular Disease of Responders and Nonresponders of This Study

	Responders (n=31)	Nonresponders (n=20)	
Personal and condition-related characteristics	n (%)	n (%)	*P*
Sex (female)	13 (42)	10 (50)	.77
Ambulatory status (nonambulator)	18 (58)	10 (50)	.78
Lesion level			.37
Sacral	2 (7)	5 (25)	
Lumbosacral	14 (45)	7 (35)	
Lumbar	10 (32)	5 (25)	
Thoraco-lumbar	4 (13)	3 (15)	
Thoracic	1 (3)	0 (0)	
Hydrocephalus	25 (81)	17 (89)	.50
	Mean ± SD	Mean ± SD	*P*
Age (y)	21.4±4.4	20.6±4.8	.55
Biologic risk factors			
Blood lipid and lipoproteins			
Total cholesterol (mmol/L)	4.59±0.94	NA	
High-density lipoprotein (mmol/L)	1.27±0.25	NA	
Low-density lipoprotein (mmol/L)	2.96±0.93	NA	
TG (mmol/L)	1.09±0.32	NA	
Blood pressure			
SBP (mmHg)	123.9±13.2*	122.0±37.5	.55
DBP (mmHg)	80.9±8.6*	80.5±5.6	.88
Body fat, sum of 4 skin folds (mm)	75.4±40.6*	72.4±37.5*	.70
Aerobic fitness, Vo_2peak (L/min)	1.47±0.51	1.51±0.56	.79
Lifestyle-related risk factors			
Daily physical activity (min/d)	77.4±72.1†	85.7±45.5	.65
Smoking behavior (cigarettes/d)	2.0±4.9	0.6±2.4	.25

Abbreviations: NA, not applicable.
*n−1.
†n−2.

Biologic Risk Factors

Blood lipids and lipoproteins. Nonfasting venous blood samples of approximately 10mL were drawn from the vena antecubitus with a Vacutainer needle[a] and collected into an evacuated serum separator tube II (SST II tube[a]) while subjects were seated. TC and TG were determined using an enzymatic calorimetric test (CHOD-PAP and GPO-PAP[b]). HDL-C and LDL-C were determined directly using a homogeneous enzymatic calorimetric test with polyethylene glycol modified enzymes and dextran sulfate (Roche/Hitachi 747, 902[b]).

Blood pressure. We measured blood pressure with an indirect method while subjects were seated for at least 10 minutes prior to the measurement. A standard pressure cuff was placed around the upper arm. SBP and DBP were measured twice

using a sphygmomanometer (Maxi-Stabil 3[c]), and the lowest values were recorded.

Aerobic fitness. We measured aerobic fitness during a progressive maximal exercise test, based on the McMaster All-Out Progressive Continuous Cycling and Arm test.[31] According to Bhambhani et al,[32] who studied persons with cerebral palsy, the main mode of ambulation elicits the highest oxygen uptake. Therefore, depending on whether the main mode of ambulation was walking or wheelchair driving, participants performed the test on an electronically braked cycle ergometer (Jaeger ER800[d]) or an arm ergometer (Jaeger ER800SH[d]), respectively. Detailed descriptions of the test can be found elsewhere.[29] We defined aerobic capacity as the mean oxygen uptake during the last 30 seconds of exercise (Vo_2peak, in L/min).

Body fat. We measured thickness of 4 skin folds (biceps, triceps, subscapular, suprailiac) twice on the right side of the body with a Harpenden caliper[e] and used the average sum (in mm) as an indicator of body fat.

Lifestyle-Related Risk Factors

Level of daily physical activity. We objectively measured the duration of dynamic activities (composite measure of the separately detected activities: walking [including walking stairs and running] cycling, general noncyclic movement, and wheelchair driving) during 2 consecutive weekdays using an accelerometry-based activity monitor[f] (size, 15×9×3.5cm; weight, 500g). The activity monitor has been shown to be a valid and reliable instrument to quantify mobility-related activities, including wheelchair driving.[33,34] We fitted participants with the activity monitor at their homes and instructed them to perform their usual daily activities, except to swim or take a shower or bath during activity monitoring. To avoid measurement bias, we explained the principles of the activity monitor to the participants after the measurements. All participants agreed with this procedure. Detailed procedures are described elsewhere.[24] We defined the level of daily physical activity as the average duration of dynamic activities of the first and second measurement day (expressed in min/d).

Smoking behavior. For each participant, we recorded the number of cigarettes smoked a day and designated the participant as a smoker (1; ≥1 cig/d) or nonsmoker (0).

Statistical Analyses

We expressed results as mean and SD or frequencies. We categorized values of TC, HDL-C, LDL-C, and TG from

Table 2: Descriptive Results and Frequencies of CVD Risk Factors in Adolescents and Young Adults With Myelomeningocele

CVD Risk Factor	Cut-Offs	Total Group (n=31)	Ambulators (n=13)	Nonambulators (n=18)	*P*	Male (n=18)	Female (n=13)	*P*
Physical activity (min/d)		77.4±72.1	121.0±93.2	46.6±26.5	.02	99.1±83.9	46.6±35.5	.05
Aerobic fitness (Vo_2peak, L/min)		1.47±0.51	1.62±0.59	1.36±0.45	.18	1.76±0.47	1.07±0.27	.001
Body fat (sum 4 skin folds, mm)		75.4±40.6	59.1±33.4	88.6±42.0	.05	50.7±24.2	110.4±32.6	<.001
Total cholesterol*	mmol/L							
Desirable	<5.2	71	85	61	.32	78	61	.30
Borderline high	5.2–6.2	26	15	33		17	39	
High	≥6.2	3	0	6		6	0	
Low-density lipoprotein*	mmol/L				.58			.31
Optimal	<2.59	39	39	39		44	31	
Near/above optimal	2.59–3.34	23	31	19		22	23	
Borderline high	3.37–4.12	29	31	28		17	46	
High	4.14–4.86	6	0	11		11	0	
Very high	≥4.92	3	0	5		6	0	
High-density lipoprotein*	mmol/L							
High (no risk)	≥1.56	16	8	22	.43	11	23	.19
In between		65	77	56		78	46	
Low (major risk)	<1.04	19	15	22		11	31	
TG*	mmol/L							
Normative	<1.69	97	92	100	.42	100	92	.42
Borderline high	1.69–2.25	3	8	0		0	8	
High	2.26–5.63	0	0	0		0	0	
Very high	≥5.64	0	0	0		0	0	
Blood pressure[†]	SBP/DBP (mmHg)							
Normative	<120/80	17	33	6	.10	6	31	.20
Prehypertension	120–139/80–89	63	42	78		64	61	
Stage I hypertension	140–159/90–99	17	25	11		24	8	
Stage II hypertension	≥160/100	3	0	6		6	0	
Current cigarette smoker	Yes	19	15	22	.99	17	23	.68
Number of CVD risk factors[‡]					.03			.41
0		3	8	0		0	8	
1		55	77	39		61	46	
2	Increased risk	42	15	61		39	46	

NOTE. Values are percentages and mean ± SD.
*According to the third report of the National Cholesterol Education Program.[8]
[†]According to JNC 7.[35]
[‡]Number of CVD risk factors based on Framingham Risk Assessment (including total cholesterol, high density lipoprotein, systolic blood pressure, smoking).

normative to high according to the third report of the NCEP ATP III[7,8] (cut-offs are presented in table 2). SBP and DBP were categorized according to the JNC 7[35] (see table 2). We tested differences in the proportion of men and women with subnormal levels and differences between ambulators and nonambulators using a Chi-square test. To test differences in physical activity, aerobic fitness, and body fat among subgroups, we used a *t* test for independent samples.

We selected the risk factors included in the Framingham Risk Assessment[8] (ie, TC, SBP, HDL-C, and smoking) to assess the degree of clustering. It was thus possible for a participant to have between 0 and 4 risk factors. We defined clustering of risk to be present in persons with 2 or more risk factors[36] and considered them being at increased CVD risk. Differences in the prevalence of an increased CVD risk between men and women and between ambulators and nonambulators were assessed using a Chi-square test.

We conducted separate regression analyses to model the outcome measures, each single risk factor from the Framingham Risk Assessment, and the presence (0) or absence (1) of CVD risk. For each outcome measure, we included the following independent variables (continuous data) 1 at a time: (1) physical activity, (2) aerobic fitness, and (3) body fat. Sex (0=male; 1=female) and ambulatory status (0=nonambulator; 1=ambulator) were confounders, adjusted for in all regression analyses. In the regression analyses between aerobic fitness and the CVD risk factors, we used ambulatory status as proxy for type of ergometer because of the high collinearity between the 2 variables.[29] Probability to enter a factor was set at P less than or equal to .05, and the probability to remove was set at P greater than or equal to .10. We calculated RCs and ORs of the models and their 95% confidence intervals. For all tests, we considered P values less than or equal to .05 significant and reported .05 less than P less than or equal to .10 as a trend.

RESULTS

Single CVD Risk Factors

Table 2 presents descriptive results and frequencies of CVD risk factors. Nonambulators had lower levels of daily physical activity (P=.02) and a higher sum of 4 skin folds (P=.05) than ambulators. Women had lower levels of daily physical activity (P=.05), lower aerobic fitness (P<.001), and a higher sum of 4 skin folds (P<.001) than men.

Based on the cut-off points of the NCEP ATP III, levels of TC, LDL-C, and TG were elevated in 29%, 38%, and 3% of the participants, respectively. HDL-C was reduced in 19%. Based on the cut-off points of the JNC 7, 20% of the participants were hypertensive. Of all participants, 19% were current cigarette smokers. We found no significant differences in the proportion of participants with an unfavorable lipid and lipoprotein profile and smoking behavior among subgroups regarding sex and ambulatory status. The proportion of persons with a normative blood pressure tended to be higher in ambulators than in nonambulators (P=.10).

Clustering of CVD Risk Factors

Increased CVD risk, as indicated by clustering of risk factors, was present in 42% of the participants (see table 2). A larger proportion of nonambulatory persons with MMC had increased CVD risk than ambulatory persons (P=.03).

Relations Between CVD Risk Factors and Physical Activity, Fitness, and Body Fat

Physical activity, aerobic fitness, and sum of 4 skin folds were not associated with TC, HDL-C, or smoking after adjusting for sex and ambulatory status (table 3). Results showed that participants with higher values of Vo_2peak had higher values of SBP (RC=12.4; P=.02), and participants with higher sum of 4 skin folds tended to have higher SBP (RC=1.52; P=.07). Furthermore, we found that participants with higher Vo_2peak tended to be more likely to have no CVD risk as indicated by clustering of risk factors (OR=13; P=.07). Levels of physical activity and sum of 4 skin folds were not associated with CVD risk.

DISCUSSION

CVD Risk Factors

The present study provides an overview of biologic and lifestyle-related CVD risk factors in adolescents and young adults with MMC. We did not find differences in blood lipids and lipoproteins values between subgroups regarding sex and ambulatory status.

Table 3: Relationships Between Cardiovascular Disease Risk Factors, Physical Activity, Aerobic Fitness (Vo_2peak), and Body Fat (Sum of 4 Skin Folds)

	Single Risk Factors				Clustering of Risk Factors*				
Variables	TC	HDL-C	SBP	Smoking†	No Risk	Risk			
Independent variable	RC (95% CI)	RC (95% CI)	RC (95% CI)	OR (95% CI)	Mean ± SD	Mean ± SD	OR (95% CI)	R^2	P
Physical activity (min/d)	0.17 (–0.22–0.55)	0.01 (–0.09–0.12)	–2.02 (–6.91–2.87)	1.13 (0.37–3.47)	91±84	60±52	0.94 (0.37–2.38)	0.29	.90
Vo_2peak (L/min)	–0.14 (–1.06–0.79)	0.01 (–0.24–0.26)	12.4§ (1.8–23.0)	0.11 (0.01–1.79)	1.60±0.58	1.30±0.39	13.0 (0.8–204.8)	0.41	.07§
Sum of 4 skin folds (mm)	–0.05 (–0.19–0.09)	–0.02 (–0.06–0.01)	1.52§ (–0.12–3.16)	1.12 (0.75–1.67)	75±44	76±37	1.13 (0.81–1.58)	0.26	.46

NOTE. For each risk factor, the independent variables were included in the model 1 at a time, adjusted for sex (0=male; 1=female) and ambulatory status (0=nonambulator; 1=ambulator). In the logistic regression analyses, physical activity is expressed in hours a day. In the logistic regression analyses, the sum of 4 skin folds is expressed in centimeters.
Abbreviation: CI, confidence interval.
*0=Increased risk; 1=no risk.
†0=Smoker; 1=nonsmoker.
‡$P \leq .05$.
§$.05 < P \leq .10$.

Average values of lipid and lipoproteins were comparable to those reported in the general male and female Dutch population of similar ages.[37] This is in line with results from Nelson et al,[28] who did not find differences in lipid and lipoprotein profiles between persons with MMC and able-bodied peers. However, although average values seem normative, according to the NCEP ATP III guidelines, we found unfavorable TC, LDL-C, and HDL-C in 29%, 38%, and 19% of the participants, respectively. TC values 5.2mmol/L or higher were reported in approximately 4% and 15% of the general Dutch male and female population age 16 to 19 years, respectively.[37] We found that 24% of the men were hypertensive, which is somewhat higher than the 13% reported in the general Dutch male population age 20 to 29 years.[37] The proportion of hypertensive women with MMC (7%) was comparable to the general Dutch female population age 20 to 29 years (8%).[37] In addition, in our study a large proportion of adolescents and young adults with MMC was prehypertensive and therefore at increased risk for progression to hypertension.[35] According to the JNC 7, people with prehypertension require health-promoting lifestyle modifications. In the general population, 10kg weight loss can reduce SBP by 5 to 20mmHg,[35,38,39] and regular aerobic physical activity can reduce SBP by 4 to 9mmHg.[35,40,41] Considering the high body fat and the poor levels of physical activity and aerobic fitness found in persons with MMC,[20,22-24,29] sufficient reductions in blood pressure might be achieved from counseling aimed at reducing body fat and increasing physical activity and aerobic fitness. However, the present results do not support the hypothesis that in persons with MMC, health-promoting lifestyle modifications will reduce SBP. Unexpectedly, after adjusting for sex and ambulatory status, we found that higher SBP was associated with higher fitness. Possibly, factors other than sex and ambulatory status may also play a role in the relationship between SBP and fitness in persons with MMC, but the small sample size limited further adjustments for confounders. Therefore, the data remain inconclusive about the relation between blood pressure and fitness, and future studies on fitness training with close monitoring of blood pressure are warranted in persons with MMC.

CVD Risk

It is assumed that clustering of risk factors is a better measure of CVD risk than single risk factors.[4,9] Results showed that clustering was present in a large proportion (42%) of participating adolescents and young adults with MMC, particularly in nonambulators. Berenson et al[4] reported that 2 or more risk factors were present in 23% and Andersen et al[36] reported clustering of risk to be present in approximately 15% of able-bodied adolescents and young adults. Although the proportion with multiple risk factors seems higher in persons with MMC, it is difficult to draw conclusions because of the summing of different risk factors among studies.

The only factor that tended to be associated with the clustering of risk factors was aerobic fitness. This implies that increasing aerobic fitness may lower the CVD risk in adolescents and young adults with MMC. It is known that aerobic exercise training may lead to a 10% to 20% increase in Vo_2peak.[42] Results showed that people are 13 times more likely to have no CVD risk with every liter increase in Vo_2peak. Correspondingly, with every 220mL increase in Vo_2peak (which is an increase of approximately 15%), people with MMC are 1.8 times more likely to have no CVD risk; future longitudinal studies are needed to confirm this relationship. In the general population, improvements in aerobic fitness over time have been shown to improve the prognosis of developing CVD.[11,43]

The finding that aerobic fitness was related to the CVD risk, whereas physical activity was not, is in line with the general conclusion emerging from 6 longitudinal observational studies in the general population[44-49] in which aerobic fitness was found to be predictive for a healthy CVD risk profile at a later age, whereas physical activity was not.[50] In these longitudinal studies, physical activity was assessed by means of questionnaires, and therefore, measurements of fitness offered greater objectivity than physical activity, which might have contributed to this conclusion. In contrast, the present study objectively assessed both aerobic fitness and physical activity. Because we found no relation with physical activity, this might contribute to the evidence that aerobic fitness seems to be more directly associated with the quality of the cardiovascular system than physical activity.[50] A possible explanation might be that physical activity is, in contrast to aerobic fitness, a behavior; therefore, measurements of physical activity could be momentary, whereas aerobic fitness is an attribute that people have or achieve[51] and thus is more or less the result of an active lifestyle over time. The history and intensity of physical activity were not assessed in the present study, but they may play a role in the relation with CVD risk.

Although obesity is considered a CVD risk factor, we found no relation between body fat and CVD risk. In persons with MMC, besides ambulatory status, perhaps factors such as aerobic fitness are more important for determining CVD risk than body fat. Similarly, Myers et al[12] found that aerobic fitness was the most important predictor of CVD mortality in able-bodied adult men and that it was more powerful than other established risk factors.

Study Limitations

The present study had some limitations. First, the small sample size may hamper the generalization of the results, as indicated by the relatively large confidence intervals. However, because personal and disease-related characteristics did not differ between participants and nonparticipants of the present study or between participants and nonparticipants of the larger cross-sectional study, we consider the results to be sufficiently representative. Furthermore, results will have to be interpreted with some caution because the sample size was rather small with regard to the number of independent variables (n=3) in the regression models.

Second, for practical reasons, we did not obtain a fasting blood sample for the measurements of blood lipids and lipoproteins, which may have influenced the values. However, there is evidence that differences between nonfasting and fasting levels of TC, HDL-C, and LDL-C are clinically irrelevant,[52-54] and the NCEP ATP III guidelines consider nonfasting values for TC and HDL-C to be appropriate.[7] Nonfasting TG levels must be interpreted carefully because they are significantly higher than fasting TG.[52,53] Because we did not include TG in the clustering of CVD risk factors, we assumed that the relationships between CVD risk and levels of physical activity, aerobic fitness, and body fat were not influenced by the nonfasting blood samples.

Third, we used the presence of clustering of risk factors to determine whether a participant was at increased CVD risk, but unlike the Framingham Risk Assessment, the risk factors were not weighted. However, because the Framingham Risk Assessment is validated only for participants age 20 years and older, we were restricted to study unweighted clustering of risk factors. Considering that the purpose of this study was not to predict future CVD events but to study whether levels of physical activity, aerobic fitness, and body fat were associated with CVD risk, we consider our approach valid.

Finally, objective monitoring of physical activity with the activity monitor was restricted to 2 days. The strength of the activity monitor measurements is that they provide detailed objective information on mobility-related physical activities in both ambulatory and nonambulatory persons. However, we did not characterize an individual's actual activity pattern, which needs at least 7 days of activity monitoring.[55] Therefore, we may have underestimated the relation between physical activity and CVD risk. In a previous study, White et al[56] found evidence that a 24-hour measurement with the activity monitor is of adequate duration to assess activity level. Analyses of variance showed that the variance between the 2 measurement days was small enough to be able to distinguish active and inactive people (intraclass correlation coefficient=.89). Therefore, we assumed that a sample of 2 random days during the week was sufficient to assess an individual's physical activity level adequately.

CONCLUSIONS

We found that a large proportion of the sample of adolescents and young adults with MMC, particularly the nonambulators, was at increased CVD risk as indicated by the clustering of risk factors. Participants with higher aerobic fitness tended to be more likely to have no CVD risk. Improving aerobic fitness in persons with MMC deserves attention in health care because it may contribute in reducing cardiovascular risk. This needs to be confirmed in future studies.

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