Cardiology in the Young

cambridge.org/cty

Original Article

Cite this article: Hedlund ER, Villard L, Lundell B, and Sjöberg G (2019) Physical exercise may improve sleep quality in children and adolescents with Fontan circulation. *Cardiology in the Young* **29**: 922–929. doi: 10.1017/S1047951119001136

Received: 6 December 2018
Revised: 25 March 2019
Accepted: 25 April 2019
First published online: 20 June 2019

Key words:
Endurance training; Fontan palliation; physical activity; sleep; sleep efficiency

Author for correspondence:
Eva R. Hedlund, MD, PhD, Department of Women's and Children's Health, Karolinska Institutet, Karolinska University Hospital, Astrid Lindgren Children's Hospital Solna, Barnhjärtcentrum, Eugeniavägen 23, C8:34, S-171 76 Stockholm, Sweden.
Tel: +46-707421285; Fax: +46-8-51777778;
E-mail: eva.rylander-hedlund@sll.se

CAMBRIDGE
UNIVERSITY PRESS

Physical exercise may improve sleep quality in children and adolescents with Fontan circulation

Eva R. Hedlund[1], Li Villard[2,3], Bo Lundell[1] and Gunnar Sjöberg[1,4]

[1]Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; [2]Department of Physiotherapy, Karolinska University Hospital, Stockholm, Sweden; [3]Department of Neurobiology, Care Sciences and Society, Division of Physiotherapy, Karolinska Institutet, Stockholm, Sweden and [4]Department of Paediatric Cardiology, Karolinska University Hospital, Stockholm, Sweden

Abstract

Objective: To study physical activity and sleep in Fontan patients and healthy controls before and after an endurance training program, and after 1 year. *Method:* Fontan patients ($n = 30$) and healthy controls ($n = 25$) wore accelerometers for seven consecutive days and nights during a school week before and after a 12-week endurance training program and after 1 year. *Results:* Patients had similar sleep duration and sleep efficiency as healthy controls. Latency to sleep onset in minutes was longer for patients than controls (22.4 (4.3–55.3) minutes versus 14.8 (8.6–29.4) minutes, $p < 0.01$). More time in moderate-to-vigorous activity daytime was correlated with increased sleep time ($p < 0.05$; $r^2 = 0.20$), improved sleep efficiency ($p < 0.01$; $r^2 = 0.24$) and less time as wake after sleep onset ($p < 0.05$; $r^2 = 0.21$) for patients but not controls. Sleep variables did not change after the exercise intervention for patients or controls. After 1 year, patients had decreased total sleep time, decreased sleep efficiency, increased accelerometer counts during sleep and more time as wake after sleep onset during sleep time, but not controls. *Conclusions:* Fontan patients have prolonged latency to sleep onset compared with controls. More time in physical activities was correlated with better sleep quality for the patients. Also, subjects with low sleep efficiency and long latency to sleep onset may benefit most from physical exercise. These patients should be encouraged to engage in individually designed physical exercise as this could improve sleep quality.

Introduction

Children born with univentricular hearts undergo stepwise palliative surgery to a Fontan circulation[1–5] and this has been shown to improve long-term outcomes for these children. There is an increasing concern about heart function, reduced physical activity,[6–8] reduced physical capacity,[8–10] and psychosocial health[6,11–15] in the growing number of children with Fontan palliation who reach adult life. A problem raised by patients and their parents is that these children and adolescents often report disturbed sleep and daily fatigue. Reports of long recovery time with fatigue after physical activity and sports are also common. Sleep analyses can be made from wrist-worn accelerometer recordings. Studies have shown high agreement between accelerometer-recorded sleep–wake scoring and traditional polysomnography in sleep laboratories, regarded as the golden standard for analyses of sleep in children and adults.[16–18]

To our knowledge, there is no previously published study that has focused on sleep and impact of physical activity on sleep in patients with Fontan circulation and a healthy matched control group. Our hypothesis being that Fontan patients may have abnormal sleep patterns, perhaps related to daily activity and physical exercise.

Material

Children with Fontan palliation born between 1990 and 2005 in the Stockholm region, $N = 53$, were considered for participation. Exclusion of 23 patients was made after hospital charts had been reviewed or the patients had declined participation, as described previously.[19] Each patient and their parents were asked to suggest a healthy peer of the same age and gender to serve as a healthy control.

After parental consent and child assent, the study group comprised 30 patients with Fontan circulation and 25 healthy control subjects. Seventeen patients brought a peer each to serve as a healthy control subject. The remaining 13 patients did not want to, or could not, bring a control subject. For the patients who could not bring a peer, eight age- and gender-matched controls were recruited among families and friends of the hospital staff. Cardiac diagnoses in the patient group were 20 children with hypoplastic right ventricle, 9 children with hypoplastic left ventricle, and 1 child with unbalanced atrio-ventricular septal defect. Fontan circulation was completed at median age 2.4 (1.1–6.4) years, all with a synthetic extracardiac conduit and without any fenestrations. Pacemakers with epicardial leads were present in three patients due to sinus node dysfunction. All patients were on anti-coagulation treatment with aspirin (n = 28) or warfarin (n = 2). Enalapril or captopril was prescribed for 19 patients. All patients were in stable medical conditions, and only requiring an annual follow-up appointment. The patient group and the control group were comparable regarding age, weight, and height at the three visits. Growth during the study period of 1 year was similar for patients and controls when analysing length and weight.

Methods

Actigraph GT3X accelerometers (Actigraph, Pensacola, Florida, United States of America) were used to record physical activity and sleep–wake scoring for seven consecutive days and nights during a regular school week.[18,20–22] The accelerometer was attached to the non-dominant wrist in order to improve compliance and also to record isolated arm movements.[23] Accelerometer data were sampled with a 12-bit analogue-to-digital converter at 30 Hz and raw data from three axes were stored in a non-volatile flash memory. After the recording period, data were downloaded as 60-second epochs to the ActiLife 6 analysing software (Actigraph). Each individual reported "In Bed Time" and "Out of Bed Time" in a diary while wearing the accelerometer during the seven consecutive days. Using algorithms developed to distinguish between sleep and wakefulness, analyses of accelerometer recordings can be used to measure sleep variables. The clinical use of accelerometers for sleep analysis is that it permits long-term registrations in the individual's own sleep environment and routines.[21]

Sleep analyses were made using ActiLife 6 analysing software (Actigraph). For sleep analyses, the algorithm developed by Sadeh et al[17] was used. This algorithm has been validated and showed that sleep–wake scoring from wrist-worn accelerometers in healthy children and adults reach high agreement with traditional polysomnography for sleep periods.[21] The Sadeh algorithm uses the Y-axis epoch data and scores individual epochs as either sleep or non-sleep. "In Bed Time" and "Out of Bed Time" variables were extracted from self-reported sleep diaries as a complement to the accelerometer-derived analyses with the algorithm by Sadeh et al for each individual. The instructions were to report "In Bed Time" when they put away books or electronic devices, turn off the lights with the intention to sleep.

Total minutes in bed and total sleep time in minutes were analysed. Sleep efficiency (%) was calculated as total sleep time divided by total minutes in bed, that is, the percentage of epoch categorised as asleep within total number of epochs in bed. Total counts summarised from the Y-axis during the night were also extracted. Latency was analysed as number of minutes from "In Bed Time" to sleep onset. Number of awakenings and average length of awakenings were analysed. If at least 10 consecutive minutes are categorised as awake, then the sleep period ended. If an awakening was shorter, it did not interrupt the sleep period. Thus, even though an epoch was categorised as awake, it did not have to be an actual awakening to full consciousness of the subject. Wake after sleep onset was analysed and defined as the total number of minutes the subject was defined as awake during the sleep period. Sleep variables analysed are summarised in Table 1.

Table 1. Sleep variables.

In Bed Time (hh:mm)	Time when subject goes to bed
Out Bed Time (hh:mm)	Time when subject goes out of bed
Total minutes in bed (minutes)	Total minutes between "In Bed Time" and "Out of Bed Time"
Total sleep time (minutes)	Total number of minutes scored as "asleep"
Sleep efficiency (%)	Number of sleep minutes divided by total numbers of minutes the subject was in bed
Total counts night	Total accelerometer counts summed together for the entire sleep period from axis Y
Latency (minutes)	Numbers of minutes from "In Bed Time" to sleep onset
Awakenings (N)	Number of different awakening episodes
Average awakening (minutes)	Average length of all awakening episodes
Wake after sleep onset (minutes)	Total number of minutes scored as "awake" after sleep onset

The total vector magnitude in counts for the whole registration for 1 week was calculated from the three axes, namely $\sqrt{(\text{axis}X^2+\text{axis}Y^2+\text{axis}Z^2)}$. The activity intensity was analysed and categorised in accordance with Evenson's Actigraph cut-off points, which have been shown to provide the most accurate classification for all levels of physical activity intensity in children and adolescents.[24,25] Activities of moderate-to-vigorous intensity were analysed from the accelerometer recordings, as described previously.[6]

Endurance training program and 1-year follow-up

Patients and control subjects, together with at least one parent, were interviewed about the subject's organised physical exercise during an average school week. An individualised endurance training program was designed for each subject based on this history, the results of the ergometer and oxygen uptake tests, time of year, and available sports and instructors near school or home. The endurance training program was to include 2 × 45 minutes of extra instructor-led endurance training every week for 12 consecutive weeks, with maintained baseline activities such as physical education in school and other sports. The endurance training programs included sports like running, jogging, skiing, cycling, riding, swimming, dancing, football, etc. Accelerometer recordings were repeated after the 12-week endurance training program and once again after 1 year, without further encouragement by the study leaders, as described previously.[19] The purpose of the training program was to increase endurance training at a sub-maximal level with the aim to increase load gradually during the training program. The patients were instructed not to perform exercise training at maximal effort. Type of activity and duration in minutes were reported in a logbook and analysed by the study leaders together with the study subjects and a parent. Also, intensity of the activities was reported on the Borg scale which is a method to quantify self-perceived exercise effort on a scale from 6 to 20. The Borg scale has been validated in children with heart defects.[26] Duration and intensity of the training were recorded as weekly average during the training period.

Table 2. Results sleep analyses.

	Patients N = 27	Controls N = 22	p
Registered time, nights	18 (17–18)	18 (13–18)	0.16
In Bed Time (hh:mm)	22:39 (20:48–01:19)	22:37 (20:21–02:39)	0.651
Out Bed Time (hh:mm)	07:51 (06:41–10:10)	07:49 (06:37–11:10)	0.740
Total minutes in bed (minutes)	543.9 (424.1–636.4)	559.8 (455.1–643.1)	0.710
Total sleep time (minutes)	437.1 (305.4–511.7)	432.7 (341.8–504.2)	0.880
Sleep efficiency (%)	79.4 (63.0–87.8)	78.4 (68.6–87.3)	0.740
Total counts night	60050 (32089–131082)	55337 (25865–122276)	0.817
Latency (minutes)	22.4 (4.3–55.3)	14.8 (8.6–29.4)	0.008
Awakenings (N)	25.4 (15.2–34.2)	28.1 (13.4–35.8)	0.191
Average awakening (minutes)	3.7 (2.3–7.1)	3.7 (2.7–9.6)	0.952
WASO (minutes)	91.4 (49.4–163.3)	95.1 (50.9–167.7)	0.527

WASO=Wake after sleep onset
Values are presented as median (min–max)
Values are mean values from three separate recordings

Statistical analyses

The statistical analyses between the groups were performed using t-tests, Mann–Whitney U-tests, and chi-square tests as appropriate. Repeated measures ANOVA were carried out to perform analyses over time. A multiple stepwise regression analysis was performed with “Sleep efficiency” as dependent variable, and having a heart defect, gender, age, total vector magnitude and time in moderate-to-vigorous physical activity as independent variables. Statistical significance was set at $p < 0.05$. The statistical program used was Statistica 12 (StatSoft, Inc., Tulsa, Oklahoma, United States of America).

Results

Sleep scoring

Number of nights analysed were similar for patients and controls at baseline (6 (5–6) nights versus 6 (4–6) nights, $p = 0.53$), after training (6 (5–6) nights versus 6 (2–6) nights, $p = 0.58$), and at follow-up after 1 year (6 (5–6) nights versus 6 (3–6) nights, $p = 0.36$). Nights unqualified for analyses were nights with no accelerometer worn by subject and not representative nights due to acute infectious illness and fever. Sleep variables were first analysed as mean values from the three recording periods, see Table 2. Thus, analyses were based on similar total numbers of nights for patients and controls (18 (17–18) nights versus 18 (13–18) nights, $p = 0.16$). One patient did not fulfil the endurance training program and did not come to the follow-up after 1 year. Another patient and two control subjects did not come to the follow-up after 1 year. The reasons for not fulfilling training program or follow-up visits were lack of time and interest. At the follow-up after 1 year, two sleep analyses from one patient and one control were not acceptable for analyses due to lack of corresponding sleep diaries. Number of patients ($N = 27$) and controls ($N = 22$) included in analyses were subjects with three accepted recordings with corresponding sleep diaries.

Total minutes in bed before training were similar for patients and controls (543.9 (424.1–636.4) minutes versus 559.8 (455.1–643.1) minutes, $p = 0.71$). For children below 14 years of age, patients and controls had similar amount of sleep (572.2 (520.6–643.1) minutes versus 569.4 (510.2–636.4) minutes, $p = 0.81$). Also, for children aged 14–17 years, patients and controls had similar results (513.7 (424.1–555.0) minutes versus 514.5 (455.1–577.2) minutes, $p = 0.54$). These results meet novel recommendations for sleep time in children and youth.[27] Latency to sleep onset in minutes were significantly longer for patients than controls (22.4 (4.3–55.3) minutes versus 14.8 (8.6–29.4) minutes, $p < 0.01$). Other sleep variables were similar in both groups. No gender differences were found in sleep variables.

Total sleep time decreased with age in both patients ($p < 0.001$) and controls ($p < 0.001$). Sleep efficiency showed a tendency to decrease in patients ($p = 0.05$) with age, but not for controls ($p = 0.81$) (Fig 1). The slope of the regression line between age and sleep efficiency did not differ between patients and controls ($p = 0.07$) (Fig 1).

Physical activity

Self-reported exercise in minutes per week was lower for patients than for controls before the training program (120 (0–250) minutes per week versus 220 (15–660) minutes per week, $p < 0.001$). Average intensity on the Borg scale for all activities was significantly lower for patients than for controls (13.0 (10.0–18.0) versus 15.0 (10.0–19.0), $p < 0.05$), as described previously.[6]

The total vector magnitude during the whole recording period of seven days and nights was similar in patients and controls (19.0×10^6 (11.0×10^6–27.5×10^6) counts versus 18.9×10^6 (10.6×10^6–28.0×10^6) counts, $p = 0.74$). Time in moderate-to-vigorous physical activity during the 7-day recording was similar in patients and controls (947 (306–1847) minutes versus 1049 (322–1593) minutes, $p = 0.70$) (Table 3). Average time in moderate-to-vigorous activity per day was 148 ± 60 minutes for the patients and 141 ± 54 minutes for the controls ($p = 0.67$). Only three patients and two controls did not exceed an average moderate-to-vigorous activity of 60 minutes per day, as described previously.[6] Male patients had less self-reported exercise at lower intensity than male controls,

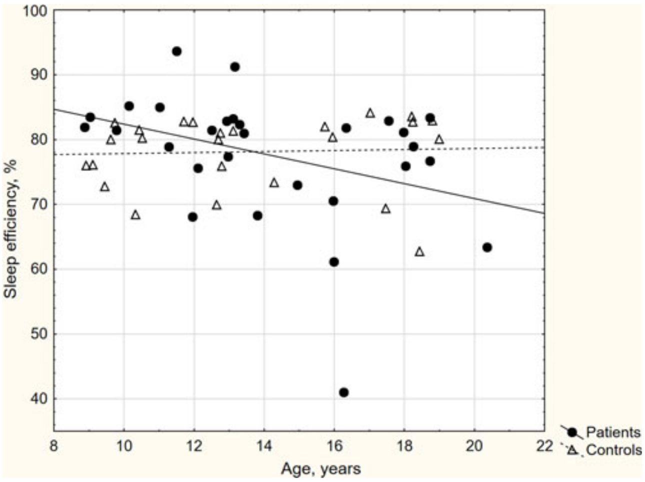

Figure 1. Sleep efficiency in percent versus age in years in Fontan patients ($y = 93.8 – 1.15 \times x$; $r = -0.36$; $p = 0.05$; $r^2 = 0.13$) and controls ($y = 77.0 + 0.08 \times x$; $r = 0.05$; $p = 0.81$; $r^2 = 0.003$).

but they had similar total vector magnitude and time in moderate-to-vigorous activity. Female patients and controls did not differ significantly in these variables.

Sleep versus physical activity

Time in moderate-to-vigorous physical activity during day-time was positively correlated with increased total sleep time ($r = 0.45$; $p < 0.05$; $r^2 = 0.20$), improved sleep efficiency ($r = 0.49$; $p < 0.01$; $r^2 = 0.24$) and less time as wake after sleep onset ($r = -0.46$; $p < 0.05$; $r^2 = 0.21$) for patients, but not for the controls. The slope of the regression line between time in moderate-to-vigorous physical activity and sleep efficiency was different between patients and controls ($p < 0.05$) (Fig 2).

After endurance training program and 1-year follow-up

One patient did not fulfil the training period of 12 weeks. One patient and two control subjects did not come back for the 1-year follow-up visit or accelerometer recording. One patient and one control did not have accepted accelerometer recordings with corresponding sleep diaries at follow-up after 1 year and were excluded from analyses. Characteristics of subjects, physical activity, and sleep variables analysed before and after endurance training and at follow-up after 1 year are presented in Table 3.

Sleep scoring

Total minutes in bed did not change during the whole study for patients and controls. Neither patients nor controls changed their total sleep time after the training program. At follow-up after 1 year, patients decreased their total sleep time ($p < 0.01$), while controls had similar total sleep time ($p = 0.41$). Neither patients nor controls changed their sleep efficiency after the training program. At follow-up after 1 year, patients had a decreased sleep efficiency ($p < 0.05$), while controls had similar sleep efficiency as after training ($p = 0.97$). Moreover, neither patients nor controls changed total accelerometer counts during sleep time after the training program. At follow-up after 1 year, patients increased total accelerometer counts during sleep time ($p < 0.01$), while controls had similar total accelerometer counts during sleep time as after training ($p = 0.77$). Latency to sleep onset did not change after training or at follow-up after 1 year for patients or controls. Neither patients nor controls changed amount of time as wake after sleep onset after the training program. At follow-up after 1 year, patients increased wake after sleep onset ($p < 0.05$), while controls had similar amount of time wake after sleep onset as after training ($p = 0.69$).

In order to study effects within each group, patients and controls were divided into two subgroups, above and below their respective median values for sleep efficiency and latency to sleep onset at baseline. Patients with low sleep efficiency at baseline did increase their sleep efficiency significantly more than subjects with high sleep efficiency at baseline after the training program (+3.2 (−8.6–18.0)% versus −2.6 (−9.1–6.2)%, $p < 0.05$). Controls with low sleep efficiency at baseline did also increase their sleep efficiency more than subjects with high sleep efficiency at baseline after the training program. Moreover, patients with long latency to sleep onset decreased their latency significantly more than subjects with short latency at baseline after the training program (−5.6 (−72–45) minutes versus 11.2 (−3.5–41) minutes, $p < 0.05$). Controls with long latency to sleep onset did also decrease their latency more than subjects with short latency at baseline, after the training program. Changes in sleep efficiency and latency to sleep onset at follow-up after 1 year were similar between subjects with low and high sleep efficiency as well as long and short latency to sleep onset.

Physical activity

Both patients and controls reported increased time in exercise per week after the training program to 175 (0–435) minutes per week for patients and 280 (20–720) minutes per week for controls. At follow-up after 1 year, patients reported a decreased amount of exercise, comparable to the amount before the training program (120 (0–340) minutes per week), while controls reported a maintained amount of exercise as after the training program (240 (0–750) minutes per week). After training, patients reported a significant increase in average intensity on the Borg scale for all activities (14.0 (10.0–17.5)), while the controls reported a similar average intensity (15.0 (11.5–17.0)). At follow-up after 1 year, patients (14.3 (0–17.0)) and controls (15.0 (0–19.0)) reported an average intensity on the Borg scale for all activities similar to after the training program, as described previously.[19] Total vector magnitude and time in moderate-to-vigorous activity did not change for patients or controls after training or at follow-up after 1 year.

Multiple regression model

In the multiple stepwise regression model, significant independent positive predictors of sleep efficiency were female gender ($p < 0.05$) and time in moderate-to-vigorous physical activity ($p < 0.01$). In the patient group, time in moderate-to-vigorous activity was correlated with sleep efficiency, also shown in Fig 2.

Discussion

This is the first study that analyses sleep in patients with Fontan circulation compared with healthy control subjects before and after an endurance training program and at a follow-up after 1 year. Our results show that patients with Fontan circulation have sleep duration and sleep efficiency similar to healthy children. The patients, however, had a prolonged latency to sleep onset compared to healthy control subjects. Moreover, the patients had the same amount of objectively accelerometer-measured physical activity

Table 3. Results at baseline, after endurance training and at 1-year follow-up.

	Baseline			After endurance training			One-year follow-up		
	Patients	Controls	p	Patients	Controls	p	Patients	Controls	p
Characteristics									
Number (N)	30	25		29	25		27	22	
Male/female (N)	16/14	13/12	0.92	16/13	13/12	0.83	15/12	11/11	0.70
Age (years)	13.4 (8.9–20.4)	12.8 (8.9–19.0)	0.42	13.6 (9.3–20.6)	13.1 (9.3–19.4)	0.47	14.4 (9.8–21.4)	13.9 (9.9–20.5)	0.53
Weight (kilogram)	42.4 (24.0–62.0)	48.0 (28.0–89.0)	0.34	41.5 (26.4–66.0)	49.2 (29.0–86.0)	0.28	45.0 (27.0–76.0)	50.0 (31.0–80.0)	0.35
Height (metre)	1.53 (1.28–1.80)	1.61 (1.32–1.90)	0.31	1.54 (1.30–1.80)	1.63 (1.34–1.90)	0.32	1.57 (1.34–1.80)	1.65 (1.36–1.90)	0.34
Physical activity									
Total vector magnitude (counts)	19.0 × 106 (11.0 × 106–27.5 × 106)	18.9 × 106 (10.6 × 106–28.0 × 106)	0.74	18.7 × 106 (10.0 × 106–40.2 × 106)	18.1 × 106 (5.4 × 106–29.2 × 106)	0.47	20.5 × 106 (10.9 × 106–31.6 × 106)	17.4 × 106 (7.7 × 106–27.8 × 106)	0.64
Time in MVPA (minutes)	946.5 (306.0–1847.0)	1049.0 (322.0–1593.0)	0.70	976.0 (264.0–2015.0)	867.0 (188.0–1821.0)	0.61	1114.0 (323.0–2119.0)	974.0 (178.0–1633.0)	0.63
Sleep variables									
In Bed Time (hh:mm)	22:45 (20:42–01:09)	22:22 (20:18–02:43)	0.51	22:46 (21:11–02:00)	22:18 (20:24–02:37)	0.70	23:07 (20:30–02:40)	22:48 (20:05–03:24)	0.74
Out Bed Time (hh:mm)	07:58 (06:04–09:10)	07:35 (06:21–10:53)	0.63	07:55 (06:30–11:02)	07:51 (06:34–12:27)	0.46	07:57 (06:27–12:01)	07:35 (06:40–11:18)	0.69
Total minutes in bed (minutes)	549.0 (439.5–674.3)	560.5 (358.0–642.4)	0.45	550.0 (401.5–675.3)	568.3 (400.8–634.2)	0.71	545.0 (368.3–692.7)	553.1 (471.7–659.2)	0.90
TST (minutes)	440.3 (260.7–517.0)	446.0 (281.8–503.5)	0.70	449.0 (310.5–515.8)	436.2 (270.0–513.8)	0.86	425.2 (296.0–518.5)	419.8 (344.6–508.3)	0.54
SE (%)	81.2 (41.0–93.7)	80.2 (62.8–84.1)	0.69	79.9 (59.0–88.5)	80.2 (59.5–89.6)	0.69	76.8 (62.4–89.9)	79.6 (66.6–91.3)	0.32
Total counts night	50216.7 (25309.5–389149.8)	52048.8 (27001.5–191121.8)	0.94	64743.5 (23138.0–144735.8)	61463.5 (21856.5–192210.3)	0.72	71162.7 (26936.5–177678.5)	53606.5 (23616.7–146978.3)	0.20
Latency (minutes)	16.8 (0.7–163.7)	14.5 (1.5–63.6)	0.27	23.8 (0.0–91.7)	14.3 (1.6–51.0)	<0.05	23.7 (2.3–50.5)	15.3 (4.7–33.8)	<0.05
Awakenings (N)	26.8 (9.5–35.7)	29.2 (13.3–34.8)	0.07	25.7 (14.3–37.2)	27.5 (8.5–35.3)	0.18	25.0 (14.0–37.0)	27.3 (13.2–40.3)	1.00
Average awakening (minutes)	3.7 (2.3–16.0)	3.7 (2.5–8.4)	0.84	3.7 (2.1–44.9)	3.6 (2.4–17.4)	0.82	3.9 (2.4– 10.8)	3.6 (2.4–7.2)	0.62
WASO (minutes)	85.0 (24.2–249.5)	92.7 (55.0–185.5)	0.25	92.3 (35.7–166.2)	105.0 (42.8–190.2)	0.15	97.7 (41.0–196.3)	93.2 (32.2–185.2)	0.85

MVPA=moderate-to-vigorous physical activity; SE=sleep efficiency; TST=total sleep time; WASO=wake after sleep onset
Values are presented as median (min–max)

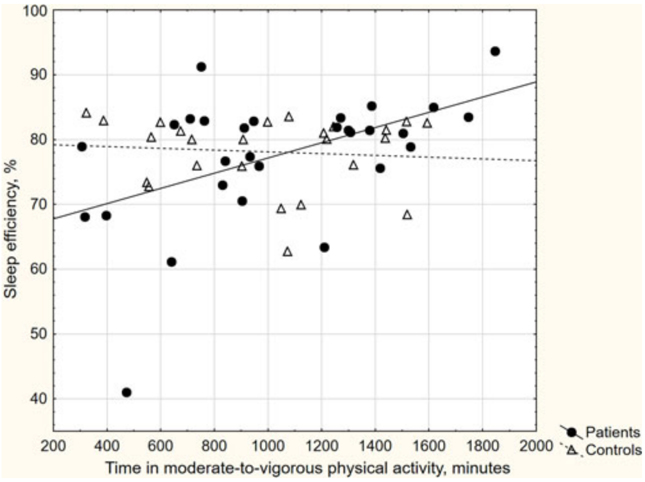

Figure 2. Sleep efficiency in percent versus time in moderate-to-vigorous physical activity in minutes, in Fontan patients ($y = 65.4 + 0.01 \times x$; $r = 0.49$; $p = 0.007$; $r^2 = 0.24$) and controls ($y = 79.5–0.001 \times x$; $r = –0.09$; $p = 0.66$; $r^2 = 0.01$).

but decreased amount of self-reported organised physical exercise compared to healthy children, as described previously.[6] Novel recommendations for health benefits for children and youth are as follows: a daily accumulation of at least 60 minutes of moderate-to-vigorous activity, several hours of light activity, uninterrupted 9–11 hours of sleep per night for those aged 5–13 years and 8–10 hours per night for those aged 14–17 years, and no more than 2 hours of sedentary behaviour.[27] Our study shows that patients and controls had an acceptable average time in moderate-to-vigorous activity per day with only three patients and two controls that did not exceed an average of 60 minutes per day. Patients and controls also met the recommended hours of sleep duration in both younger and older subjects.

Moreover, our results show a tendency to increasing age being associated with decreased sleep efficiency in patients, but not in controls (Fig 1). Also, increased time in moderate-to-vigorous physical activity during daytime was positively correlated with increased sleep efficiency in patients, but not in controls (Fig 2). Lang et al[28] studied healthy adolescents and showed that higher levels of physical activity were related to better subjective and objective sleep and sleep quality. Also, Stone et al[29] showed a positive relationship between physical activity and sleep duration in healthy children. Ortega et al[30] studied sleep duration and activity levels in Estonian and Swedish healthy children and showed that children sleeping longer spent more time in physical activity; however, their findings were fully explained by age and puberty stage. Adolescents sleep shorter time and are less active than younger children, thus a model must adjust for age to avoid misleading results. As our patients and controls were matched for age and gender, we believe this risk is low in our study.

Effects of endurance training on sleep

After endurance training, median total minutes in bed, total sleep time, sleep efficiency, total accelerometer counts during sleep time, latency and time defined as wake after sleep onset did not change for patients or controls. Patients and controls with low sleep efficiency at baseline did, however, increase their sleep efficiency significantly more after the training program than subjects with high sleep efficiency at baseline. Also, patients and controls with long latency to sleep onset decreased their latency significantly more after the training program than subjects with shorter latency at baseline. Changes in sleep efficiency and latency to sleep onset at follow-up after 1 year were similar between subjects with low and high sleep efficiency as well as long and short latency to sleep onset. Thus, it seems as subjects with low sleep efficiency and long latency to sleep onset benefit more after an individualised endurance training program and changes could perhaps be more prominent at follow-up after 1 year if the training had continued in the same way. More studies are needed to clarify these aspects.

Our patients and their parents reported a long recovery time after physical activity and fatigue the day after physical exercise. A long recovery time must be taken into consideration and even more individually designed physical activities in schools and in the community should be available for children with complex congenital heart malformations. Kredlow et al[31] reviewed studies of effects of physical activity on sleep in adults and showed acute benefits of exercise on many sleep parameters, and also greater subjective and objective sleep benefits of regular exercise over longer time. Our training programs could have been of suboptimal duration and/or intensity for maximal positive effects for our patients and more research is needed to understand effects of exercise on sleep in this patient group.

At follow-up after 1 year, however, patients had decreased their total sleep time, decreased sleep efficiency, increased total accelerometer counts during sleep time and increased time as wake after sleep onset during sleep time. These changes were not seen in the control group. Thus, patients and controls differ at follow-up after 1 year which is concerning. Even though, objectively measured activity did not change for patients or controls after training or at follow-up after 1 year, self-reported activity decreased for patients but not for controls at follow-up after 1 year. This could explain a worsening sleep pattern in the patient group over time; however, one cannot rule out that worsening sleep patterns may have a negative impact on a child’s ability to engage in exercise and sports.

Multiple regression model

In the multiple regression model, positive predictors of sleep efficiency were female gender and time in moderate-to-vigorous physical activity. Age was not a predictor of sleep efficiency in our model, but increased age can be associated with decreased time in physical activity, described earlier,[6,32] and thus, this could be one explanation for the tendency of negative correlation between age and sleep efficiency seen in Fig 1. However, more research is needed to better understand mechanisms for sleep duration, sleep quality, and effect of physical activity in this patient group.

Limitations

This is a new field of research on patients with Fontan circulation. This study enlightens sleep patterns and effect of physical activity on sleep in this patient group but more research is needed to study sleep and sleep disturbance in this patient group. The number of patients was based on the size of our Fontan cohort in Stockholm. One could speculate as to whether the patients who chose to participate represented a group with more favourable outcomes than the patients who chose not to participate. The self-selection of control subjects can be questioned, but we felt it was important to compare physical activity and sleep in peers with whom the patients are likely to compare themselves with.

Latency to sleep onset was longer for patients than controls. The instructions were to report “In Bed Time” when you put away books or electronic devices and turn off the lights with the intention to sleep. However, we do not know if they have followed these instructions properly but the instructions were identical to patients and controls. Number of awakenings was high in both patients and controls. An awakening shorter than 10 minutes did not have to be an actual awakening to full consciousness as described, but it could be a sign of high motor activity in children. Perhaps the algorithm was not optimal for this variable; however, the same analyses were made in both groups. Moreover, endurance training programs with another duration, frequency and/or intensity could have given other results. More research is needed to find optimal regimes regarding exercise and its effect on sleep.

Conclusions

Children and adolescents with Fontan circulation have similar sleep duration and sleep efficiency as healthy controls. However, it seems as they have a prolonged latency to sleep onset. Increased time in physical activities seems to be associated with better sleep quality in patients with Fontan circulation. Also, both patients and controls with low sleep efficiency and long latency to sleep onset may benefit the most from physical exercise. The clinical importance of our results is that if increased physical activity is likely to be beneficial for sleep and sleep quality in this patient group, patients with Fontan circulation should be encouraged to engage in regular sports and activities that are individually designed. More research is however needed on how to individualise recommendations for physical activities from early age for these patients and also to find optimal regimes for exercise training with regard to sleep and other health issues.

Acknowledgements. The statistical analysis was supervised by Elisabeth Berg, statistician at Unit for Medical Statistics, Department of Learning, Informatics, Management and Ethics (LIME), Karolinska Institutet.

Financial Support. This research was financed by the Swedish Order of Freemasons, the Mayflower charity foundation for children, the Samariten foundation for paediatric research, Sällskapet Barnavård, and the Swedish Heart-Lung Foundation.

Conflicts of Interests. None.

Ethical Standards. The study was approved by the Ethical Review Board at Karolinska Institutet (DNR 2010/84-31/4), Stockholm.

References

1. Bjork VO, Olin CL, Bjarke BB, Thoren CA. Right atrial-right ventricular anastomosis for correction of tricuspid atresia. J Thorac Cardiovasc Surg 1979; 77: 452–458.
2. de Leval MR, Kilner P, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. Experimental studies and early clinical experience. J Thorac Cardiovasc Surg 1988; 96: 682–695.
3. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971; 26: 240–248.
4. Gewillig M, Brown SC. The Fontan circulation after 45 years: update in physiology. Heart 2016; 102: 1081–1086.
5. Kanakis MA, Petropoulos AC, Mitropoulos FA. Fontan operation. Hellenic J Cardiol 2009; 50: 133–141.
6. Hedlund ER, Lundell B, Villard L, Sjoberg G. Reduced physical exercise and health-related quality of life after Fontan palliation. Acta Paediatr 2016; 105: 1322–1328.
7. Longmuir PE, Corey M, Faulkner G, Russell JL, McCrindle BW. Children after Fontan have strength and body composition similar to healthy peers and can successfully participate in daily moderate-to-vigorous physical activity. Pediatr Cardiol 2015; 36: 759–767.
8. McCrindle BW, Williams RV, Mital S, et al. Physical activity levels in children and adolescents are reduced after the Fontan procedure, independent of exercise capacity, and are associated with lower perceived general health. Arch Dis Child 2007; 92: 509–514.
9. Jenkins PC, Chinnock RE, Jenkins KJ, et al. Decreased exercise performance with age in children with hypoplastic left heart syndrome. J Pediatr 2008; 152: 507–512.
10. Muller J, Christov F, Schreiber C, Hess J, Hager A. Exercise capacity, quality of life, and daily activity in the long-term follow-up of patients with univentricular heart and total cavopulmonary connection. Eur Heart J 2009; 30: 2915–2920.
11. Dulfer K, Bossers SS, Utens EM, et al. Does functional health status predict health-related quality of life in children after Fontan operation?. Cardiol Young 2016; 26: 459–468.
12. Knowles RL, Day T, Wade A, et al. Patient-reported quality of life outcomes for children with serious congenital heart defects. Arch Dis Child 2014; 99: 413–419.
13. McCrindle BW, Williams RV, Mitchell PD, et al. Relationship of patient and medical characteristics to health status in children and adolescents after the Fontan procedure. Circulation 2006; 113: 1123–1129.
14. Uzark K, Jones K, Slusher J, Limbers CA, Burwinkle TM, Varni JW. Quality of life in children with heart disease as perceived by children and parents. Pediatrics 2008; 121: e1060–1067.
15. Uzark K, Zak V, Shrader P, et al. Assessment of quality of life in young patients with single ventricle after the Fontan operation. J Pediatr 2016; 170: 166–172 e161.
16. Cole RJ, Kripke DF, Gruen W, Mullaney DJ, Gillin JC. Automatic sleep/wake identification from wrist activity. Sleep 1992; 15: 461–469.
17. Sadeh A, Sharkey KM, Carskadon MA. Activity-based sleep-wake identification: an empirical test of methodological issues. Sleep 1994; 17: 201–207.
18. Weiss AR, Johnson NL, Berger NA, Redline S. Validity of activity-based devices to estimate sleep. J Clin Sleep Med 2010; 6: 336–342.
19. Hedlund ER, Lundell B, Soderstrom L, Sjoberg G. Can endurance training improve physical capacity and quality of life in young Fontan patients? Cardiol Young 2017: 1–9.
20. Corder K, Brage S, Ekelund U. Accelerometers and pedometers: methodology and clinical application. Curr Opin Clin Nutr Metab Care 2007; 10: 597–603.
21. de Souza L, Benedito-Silva AA, Pires ML, Poyares D, Tufik S, Calil HM. Further validation of actigraphy for sleep studies. Sleep 2003; 26: 81–85.
22. Trost SG, Pate RR, Freedson PS, Sallis JF, Taylor WC. Using objective physical activity measures with youth: how many days of monitoring are needed?. Med Sci Sports Exerc 2000; 32: 426–431.
23. Fairclough SJ, Noonan R, Rowlands AV, Van Hees V, Knowles Z, Boddy LM. Wear compliance and activity in children wearing wrist- and hip-mounted accelerometers. Med Sci Sports Exerc 2016; 48: 245–253.
24. Evenson KR, Catellier DJ, Gill K, Ondrak KS, McMurray RG. Calibration of two objective measures of physical activity for children. J Sports Sci 2008; 26: 1557–1565.
25. Trost SG, Loprinzi PD, Moore R, Pfeiffer KA. Comparison of accelerometer cut points for predicting activity intensity in youth. Med Sci Sports Exerc 2011; 43: 1360–1368.
26. Eakin BL, Finta KM, Serwer GA, Beekman RH. Perceived exertion and exercise intensity in children with or without structural heart defects. J Pediatr 1992; 120: 90–93.
27. Tremblay MS, Carson V, Chaput JP, et al. Canadian 24-Hour movement guidelines for children and youth: an integration of physical activity, sedentary behaviour, and sleep. Appl Physiol Nutr Metab 2016; 41: S311–327.
28. Lang C, Brand S, Feldmeth AK, Holsboer-Trachsler E, Puhse U, Gerber M. Increased self-reported and objectively assessed physical activity predict sleep quality among adolescents. Physiol Behav 2013; 120: 46–53.

29. Stone MR, Stevens D, Faulkner GE. Maintaining recommended sleep throughout the week is associated with increased physical activity in children. Prev Med 2013; 56: 112–117.
30. Ortega FB, Ruiz JR, Labayen I, et al. Sleep duration and activity levels in Estonian and Swedish children and adolescents. Eur J Appl Physiol 2011; 111: 2615–2623.
31. Kredlow MA, Capozzoli MC, Hearon BA, Calkins AW, Otto MW. The effects of physical activity on sleep: a meta-analytic review. J Behav Med 2015; 38: 427–449.
32. Raustorp A, Pagels P, Froberg A, Boldemann C. Physical activity decreased by a quarter in the 11- to 12-year-old Swedish boys between 2000 and 2013 but was stable in girls: a smartphone effect?. Acta Paediatr 2015; 104: 808–814.