BMI-z scores of boys with Duchenne muscular dystrophy already begin to increase before losing ambulation: a longitudinal exploration of BMI, corticosteroids and caloric intake

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BMI-z scores of boys with Duchenne muscular dystrophy already begin to increase before losing ambulation: a longitudinal exploration of BMI, corticosteroids and caloric intake

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Abstract

We aimed to investigate BMI-z course in patients with Duchenne muscular dystrophy (DMD) during transition to loss of ambulation, and to explore the contribution of caloric intake and corticosteroid use. A retrospective multicenter longitudinal study was conducted. First, analyses of characteristics at first visit were carried out. Second, discontinuous change models were fitted to explore associations between BMI-z, loss of ambulation, caloric intake and corticosteroid use. 790 visits of 159 patients were collected. Cross sectional first visit analyses showed the presence of overweight and obesity was 44% in the ambulant group and 51% in the non-ambulant group. In the non-ambulatory group, exceeding the recommended caloric intake was associated with higher BMI-z scores (r 0.36, $p = 0.04$). Patients who were using corticosteroids had significantly higher BMI-z scores compared with patients not using corticosteroids (1.06 and 0.51 respectively, $p = 0.02$). Longitudinal analyses on patients ambulant at first visit showed an increase in BMI-z score during transition to the non-ambulatory phase. Caloric intake and corticosteroid use were not associated with BMI-z. Transition to the non-ambulatory phase may be crucial in the development of excessive weight gain. Early measures – starting before this time frame – may contribute to reduce development of obesity.

Keywords: Duchenne muscular dystrophy; BMI; Caloric intake; Corticosteroids; Loss of ambulation; Obesity.

1. Introduction

Duchenne muscular dystrophy (DMD), with an estimated incidence of 1 in 5000 newborn males, is the most common inherited muscular dystrophy. DMD progressively leads to muscle weakness, cardiomyopathy, and decline in pulmonary function [1]. Moreover, patients in later disease stages have a decreased lean body mass and increased fat mass, which decreases energy requirements and puts them more at risk to become overweight [2]. Obesity is a common

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problem for patients with DMD, previous studies reported a prevalence of 54–73% in corticosteroid naive patients [3,4]. An Australian cohort study, in which the majority of patients used corticosteroids, reported that around 50% of patients were obese at 10 years of age [5].

Development of obesity is undesirable, especially in patients with DMD. Obesity hinders movement, accentuates skeletal deformity, potentially reduces the effectiveness of orthopedic surgery, accelerates the reduction of respiratory function in latter disease stages, and can enlarge nursing difficulties [6,7]. Overweight and obesity are associated with insulin resistance and hypertension, which increases the risk for secondary health problems such as diabetes type 2 and cardiovascular disease [8–10].

In clinical practice, weight gain in DMD is often seen during the transition to the non-ambulatory stage, suggesting decrease in physical activity may play an important role, with accompanying changes in body composition. Multiple studies confirm that patients in their non-ambulatory stage have a higher BMI-z score in general [5,11]. Other factors which can cause weight gain are corticosteroid use and caloric intake [12–15]. Corticosteroid use is recommended as treatment in the international guidelines for DMD care as it delays disease progression [16]. It is a risk factor for increased appetite and developing obesity, depending on dose and scheme [17,18]. However, ambulant patients who received corticosteroids intermittently, as is common practice in the Netherlands, showed no significant difference in weight compared to patients who did not use corticosteroids [18]. Further, some studies were not able to detect significant association in the BMI-z score course and the duration of corticosteroid use [5]. The influence of caloric intake on the development of obesity also remains unclear. Caloric intake was studied by Bernabe et al. [11] in a corticosteroid naive DMD population, for which they compared caloric intake with the recommended caloric intake. They found high caloric intake at preschool age compared to the recommended caloric intake and found no associations between caloric intake and prediction of body fat mass and lean mass.

While previous literature gives us insight into BMI-z score course and the possible influence of ambulatory status, caloric intake and corticosteroid use, specific information on the influence of the transition period to non-ambulatory status and the coherence between ambulatory status, caloric intake and corticosteroid use, relative to the BMI-z course, is still lacking. The present study aims to gain insight on weight changes during the disease course of DMD and whether this is associated by ambulatory status, caloric intake, corticosteroid use and ambulatory status.

2. Materials and methods

2.1. Study design and participants

A multicenter retrospective cross sectional and longitudinal study was carried out. Data were collected from patients who visited the outpatient clinics of two large neuromuscular clinics in the Netherlands, annually, between January 2012 and March 2020. Patients were included if DMD was genetically or histologically confirmed and at least one height and weight measurement was available. Exclusion criteria were: being female, having tube feeding, being ambulant after 16 years of age, or conditions that could affect growth and motor development, such as treatment with growth hormone. Data were anonymized and handled according to the guidelines of good clinical practice. The study was approved by the local medical ethical committee, patient consent was not required (no. 2019–5760).

2.2. Outcome measures

The following data were collected for each visit to the clinic: date of visit, age at time of the visit, ambulatory status, height (cm), weight (kg), corticosteroid use, functional measures (Brooke and Vignos scale), caloric intake (kcal/day), and recommended caloric intake (kcal/day). Where relevant, age at loss of ambulation was collected. For the model, the date of visit was used to classify whether a patient was ambulant or non-ambulant.

Anthropometric measures were conducted by trained personnel from the neuromuscular team. Weight of ambulatory patients was measured using a digital scale. Non-ambulant patients were weighed on a digital chair scale or in a hoist with spring balancer. Height was measured with a wall-mounted stadiometer. In non-ambulant patients, the ulna length method or arm span was used. We computed height z-scores to be able to investigate the influence of height on the BMI-scores in the study population, as short height is common in DMD patients [13]. BMI- z scores were computed based on the WHO standards [19]. From the age of 19 and older, we used the z-value calculation which is appropriate for the age of 19 years. Because BMI tend to underestimate the presence of obesity in patients with DMD, we chose the norm value of the WHO instead of the CDC, as the CDC charts reflect a heavier sample than the WHO sample [20]. Overweight was defined as BMI-z score between $+1$ SD and $+2$ SD; obesity as BMI-z score $\geq +2$ SD; underweight as BMI-z score ≤ -1 SD [21]. The age at loss of ambulation was determined on month and year. Corticosteroid use was reported as “yes or no” and “type of corticosteroid” for every patient visit, based on whether corticosteroids were prescribed at the previous visit. Intermitted or daily admission was reported, dose and duration of corticosteroid use was not included in the analyses. The Brooke scale reported the functional possibilities of the upper extremities on a 6-point scale [22]. The Vignos scale was used to categorize the functional possibilities of the lower extremities [23]. Caloric intake was reported by patients (and/or their parents) using a form that guided a 48-hour recall of food and drink intake as part of the standard annual assessment within the neuromuscular centers. The Radboudumc started this routinely assessment in 2015, LUMC started with this in 2019. Before this period, the dietician was involved upon request. The average caloric intake per day was calculated by a registered dietician in kcal. The recommended caloric intake was prospective, calculated by the dietician using the Schofield equation considering the age categories [24,25], a physical activity factor, and the individual growth curves (kcal/day) [26,27]. In case an energy restricted diet was recommended, 200–500 kcal were deducted from the reported intake. Intake data were divided by 100, in order to support the interpretation of the results. 'Caloric difference' was defined as the reported caloric intake minus recommended caloric intake.

2.3. Statistical analysis

Statistical analyses were conducted using SPSS version 25.0 (IBM SPSS, Inc., Armonk, New York) and Stata/SE 16.0 for Windows (StataCorp LLC, Texas). Descriptive statistics were used to summarize patient characteristics at first visit (baseline) using mean and standard deviation for continuous variables and frequency (percentage) for categorical variables. T-tests were used to analyze the differences between the ambulant and non-ambulant groups, correlations were calculated using Pearson's correlations. To represent the hypothesis that the trajectory of BMI z-scores over time is not linear, discontinuous change models were specified [28]. These models explored the possibilities of an immediate shift in elevation at the change from ambulant to non-ambulant; an immediate shift in slope after becoming non-ambulant; or shifts in both the elevation and slope. The primary model of interest focused on the relationship between BMI z-score and loss of ambulation (on the study population which lost ambulation during the follow-up period), with the time-dependent covariates of corticosteroid use and caloric intake as potential confounders. Site was also included as a fixed variable in the model. Additional random effects models were fitted to explore the associations between BMI z-score and caloric intake and corticosteroid use. For these models only the longitudinal variable of age was included, with a random slope and intercept specified for age. Missing data were not imputed.

3. Results

3.1. Cross sectional analysis: first visit data, see Table 1

Data of 790 visits of 159 patients was collected (age 2.7–48.3 years), which is on average 5 annual visits per patient. In total, 95 patients were ambulant at the moment of the first visit, as is shown in Table 1. Overall, 54% of all patients used corticosteroids at the first visit, of which majority were using these intermittently. The presence of overweight and obesity was 44% in the ambulant group and 51% in the non-ambulant group ($p = 0.403$). Underweight was present in 6% of the ambulant patients and in 9% of the non-ambulant patients ($P < 0.001$).

The mean 'caloric difference' of the total group ($n = 159$) was 156 kcal/ day (SD 255), which means that the reported caloric intake exceeded the recommended caloric intake by 156 kcal/ day on average (range −500 kcal/ day to 701 kcal/ day). In the non-ambulatory group, the 'caloric difference' was associated with higher BMI-z scores (r 0.36, $p = 0.04$), meaning the degree of exceeding the recommended caloric intake was associated with higher BMI-z scores. The height-z scores were around zero and did not tend to change over time (Correlation with age: r −0.02). Furthermore, patients who were using corticosteroids had a significantly higher BMI-z score compared with patients not using corticosteroids (1.06 and 0.51 respectively, $p = 0.02$). No significant differences were seen on caloric intake between patients using corticosteroids or patients not using corticosteroids.

3.2. Longitudinal analyses: age, ambulatory status, BMI-z, corticosteroid use and caloric intake

Fig. 1 shows great variety in BMI-z scores of all first visits included in this study. Additionally it shows that BMI-z scores are generally above 0 and an increasing trend is seen from around the age of 7. Fig. 2 compares longitudinal data between ambulant and non-ambulant participants in different age categories, which also shows an increasing trend of the BMI-z between 7 and 12 and higher BMI-z scores in the non-ambulant patients. Further explorative longitudinal analyses on BMI-z scores were performed on the period around losing their ambulation, as seen in Fig. 3. Again, great variety in BMI-z scores was seen between and within patients over time, however the mean regression line shows that BMI-z scores starts around SD +1, and show an increasing trend starting around one year before losing ambulation until 2 years thereafter.

Mixed model analyses on the transition period, caloric intake and corticosteroid use was performed on the ambulant patients at first visit (542 visits of 95 patients). Table 2 presents the estimated regression coefficients and associated 95% confidence interval and p-values from the analyses. Column 1 shows a significant coefficient of 0.47 for the 'Transition period' variable ($p = 0.004$), meaning that on average, there was an increase of BMI-z score of 0.44 units in the year around loss of ambulation. The other columns of Table 2 show the regression coefficients of the separate variables with adjustment for age at visit only. There was no evidence of an association between BMI z-score and the other variables 'corticosteroid use' and 'caloric intake'.

Finally, a longitudinal exploration was conducted on the caloric intake reports, compared to the national guidelines and the individualized recommended caloric intake. Fig. 4 shows that in the study cohort, the reported caloric intake tended to be lower than recommended in the national guidelines. Under 16 the reported caloric intake seemed to exceed the recommended caloric intake, in the non-ambulatory group this was comparable. Besides, both the reported and recommended caloric intake were decreasing around the age of 10. Moreover, in general the recommended and reported caloric intake of non-ambulant patients tended to be lower than the caloric intake of the ambulant patients.

Table 1
Cohort characteristics at baseline.

	Total group ($n=159$)	Ambulant ($n=95$)	Non-ambulant ($n=64$)
Age Visit, mean (SD)	11.7 (8.1)	6.8 (2.7)	14.3 (3.0)
Age LoA, mean (SD)	10.8 (2.0)	NA*	9.8 (1.8)
Steroid use (y)	85 (54)	49 (52)	36 (56)
Prednison use			
Intermittent, n (%)	71 (45)	41 (43)	30 (47)
Daily, n (%)	2 (1)	2 (2)	0
Deflazacort use			
Intermittent, n (%)	4 (3)	3 (3)	1 (2)
Daily, n (%)	5 (3)	3 (3)	2 (4)

* NA = not applicable.

Table 2
Summary of the results of the longitudinal regression analysis on group 1 ($n=95$, visits = 542).

Variable	All variables included Coefficient (95% CI)	p-value	Transition to LoA Coefficient (95% CI)	p-value	Caloric intake Coefficient (95% CI)	p-value	Corticosteroid use Coefficient (95% CI)	p-value
Age	0.06 (−0.01, 0.14)	0.11	0.06 (−0.01, 0.12)	0.09	0.05 (−0.02, 0.12)	0.135	0.04 (−0.03, 0.11)	0.27
Transition period	0.47 (0.16, 0.77)	0.004*	0.39 (0.15, 0.63)	0.002*				
Period after LoA	−0.03 (−0.16, 0.10)	0.64	−0.10 (−0.21, 0.01)	0.08				
Caloric								
Intake_100	−0.01 (−0.40, 0.20)	0.52			−0.00 (−0.03, 0.04)	0.77		
Corticosteroid use	−0.10 (−0.59, 0.55)	0.94					0.15 (−0.17, 0.85)	0.19

* $p<0.01$Age: BMI-z scores before losing ambulation.Transition period: BMI-z scores during the period patients lose their ambulation.Period after LoA: BMI-z scores after loss of ambulation.Intake_100: caloric intake variable (Kcal/ 100).Cortiocosteroid use: difference in BMI-z in between use of steroids and no steroid use.

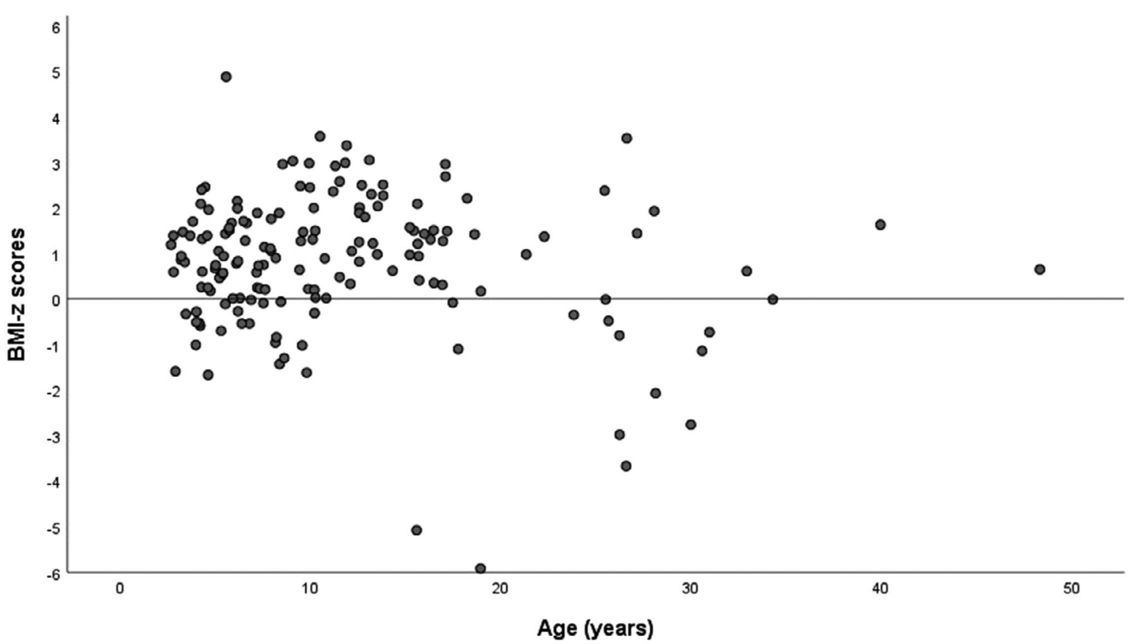

Fig. 1. BMI-z scores and age including all first visits included in the study; 790 observations in 159 patients.

4. Discussion

4.1. BMI-z course in patients with DMD

This retrospective longitudinal analyses aimed to describe changes in BMI-z score over time in boys with DMD, with a focus on the phase around the transition to the loss of ambulation. We also aimed to explore associations between corticosteroid use and caloric intake on the BMI-z course in DMD. The most important results on the first visits were that overweight and obesity are highly prevalent in our population. In the non-ambulatory group, exceeding the recommended caloric intake was correlated with higher BMI-z scores, and BMI-z scores were significantly higher in the group

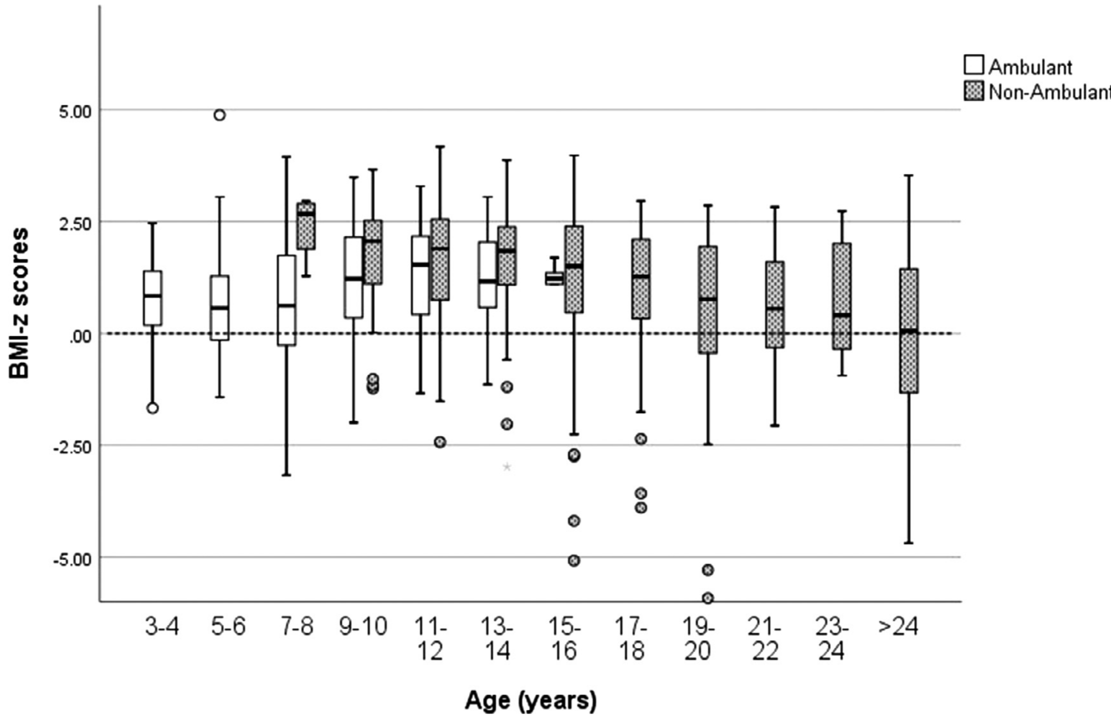

Fig. 2. Longitudinal BMI-z scores of all visits, age interval 2 years in ambulant and non- ambulant patients. For the number of observations per age group, see Table 1 in the supplementary material.

using corticosteroids. However, no significant difference on reported caloric intake was found between patients using corticosteroids or patients not using corticosteroids.

The most important explorative longitudinal results showed that the BMI-z scores tended to increase between 7 and 12 years, i.e. the period around loss of ambulation was significantly associated with an increase in BMI-z scores. Mixed model analyses confirmed an increase of BMI-z scores in the transition period to losing ambulation. Finally, caloric intake was generally below the recommended intake according to the national guidelines, but exceeded the individual recommendations, especially in the ambulatory group under 16 years of age. Recommended and reported caloric intake both tended to decrease after the age of 10. After the age of 17 a decreasing trend is seen in BMI-z scores, which emphases that weight stays an important assessment in DMD throughout the full disease course.

4.2. Strengths and weaknesses

These results should be interpreted in the context of the strengths and weaknesses of the study design. A main strength is the large sample size with a mean follow-up of five years, resulting from the integration of two longitudinal cohorts from two muscular centers. There are also limitations to this study. First, it is controversial to use BMI for estimating the presence of obesity in patients with DMD as it fails to differentiate changes in muscle mass, fat mass, or edema, all occurring in DMD [6,12,29,30]. We therefore also take into account an underestimation of the number of patients with obesity in our results. However, it is necessary to account for reduced stature in patients with DMD, and until now, no other disease specific measures exists which take height into account [5,13,31]. Moreover, when using BMI, z-scores can be calculated based on norm scores of the general population. Nevertheless, further research on user-friendly and accurate measures on body composition in DMD is warranted. Secondly, in practice two different height measurements were used for ambulant and non-ambulant patients, which could lead to a misinterpretation of height. In our clinic, the previous growth curve of the patients were taken into account, to correct for this. However, we recommend to additionally apply ulna length measurements in ambulant patients in the future. Thirdly, because of the retrospective nature of this current study, the observed association may not be interpreted as a causal relationship. Also, inaccuracies in measurement and reporting of anthropometric measures may have influenced the findings. Finally, the 48-hour recall procedure to estimate the caloric intake can induce mis-reporting. Especially underreporting is known to be common [32]. Regarding the latter, however, involvement of parents may help to improve the accuracy and at this moment, this is simply the gold standard for measuring caloric intake. Because reporting caloric intake was introduced to the standards of care after 2015, missing data on intake were present, especially in the early observations, which could also be of influence on the findings. The current study emphasizes the importance of monitoring caloric intake during every visit, which means a dietician should be a part of any neuromuscular team.

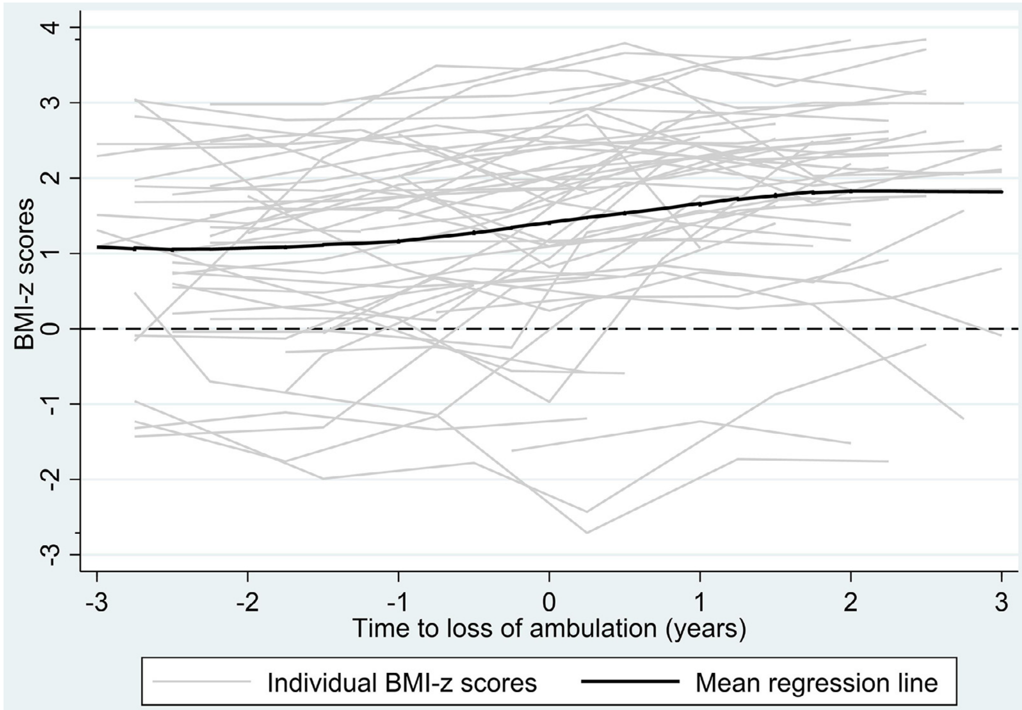

Fig. 3. Longitudinal data of the group losing ambulation during the follow up period in 3 years before and after losing ambulation. ($n = 53$, 258 visits).

4.3. Increase BMI-z score leading up to loss of ambulation

Notwithstanding the limitations of our study, the average increase of BMI-z course which starts already before the actual loss of ambulation is evident. We hypothesize multiple factors may be of influence. In the first place a decrease in physical activity. Before losing ambulation, patients increasingly depend on their wheelchair. Heutinck et. al [33]., studied the amount and perception of physical activity in boys with DMD and found that physical activity was lower and less demanding compared to healthy pears, and further decreases in the non-ambulatory stages. Barriers to perform physical activity for patients with DMD were lack of sport facilities and insufficient health. Although physical abilities decrease inevitably, it is important that patients stay active, for example with adjusted sports, use of electric wheels on manual wheelchair or supported gaming facilities. Second, there is progressive replacement of muscle tissue with fat and fibrosis, a recent study found a direct relation between fat fraction of the vastus lateralis and the loss of ambulation [34]. This means that before and during the transition period, body composition is changing, which may be of influence on resting energy expenditure (REE) and consequently on weight.

4.4. The role of caloric intake

Saure et al. [6] investigated energy expenditure and body composition in patients with DMD and found that patients with DMD presented a medium REE of 1061 kcal/ day, which was lower than their obese peers. They did not found differences in energy expenditure between ambulant patients and non-ambulant patients. Hankard et al. [2] reported a 13% decrease in REE as well and a muscle mass decline of 71% at ten years of age. With this knowledge, dieticians tend to advice non-ambulant patients with DMD a daily caloric intake of 1000–1500 kcal/ day. If we apply this rule of thumb to Fig. 4a it is seen that most of the patients, especially non-ambulatory patients, reported their caloric intake in this bandwidth. In the current study as well as the previous study of Bernabe [11], no association was found between a high caloric intake and obesity for the total group. This can be explained by the fact that non-ambulant (older) patients have higher BMI-z scores and have a lower caloric intake, for example because of feeding difficulties. We did found in the first visit analysis that within non- ambulant patients exceeding the recommended caloric intake was associated with higher BMI scores. Moreover, we see that BMI-z scores are increasing from the age of 7 and the recommended and reported caloric intake decreases around the age of 10. We hypothesize that if the daily caloric intake is restricted earlier, possibly from the moment the diagnosis is known, or when patients reach their plateau phase, especially when starting corticosteroids, the onset of overweight and obesity can be prevented.

4.5. The role of corticosteroid use

In the longitudinal current study, corticosteroid use was not associated with BMI-z scores. This in contrast to the

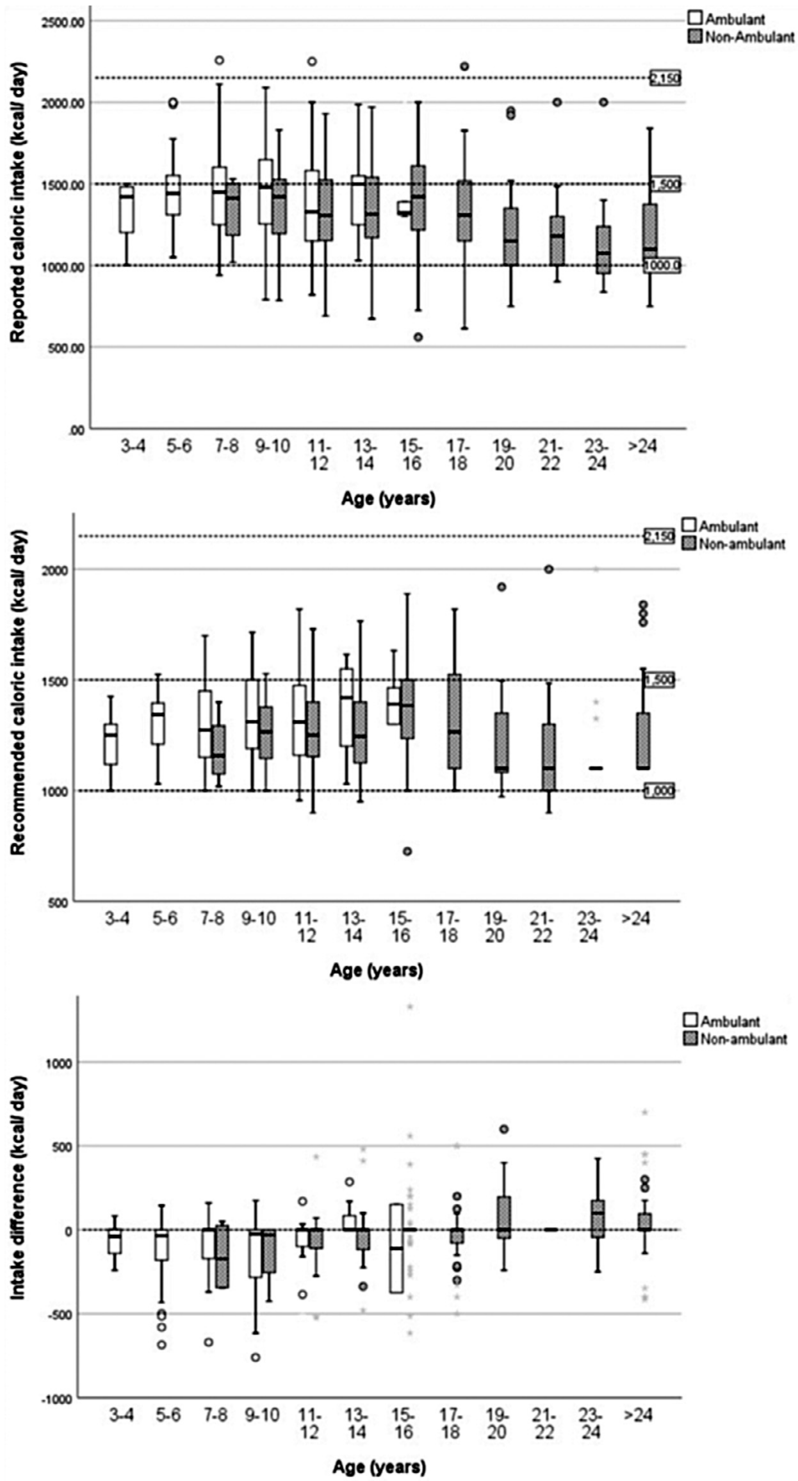

Fig. 4. Longitudinal data of all visits; ambulant compared non- ambulant patients in different age categories on a) reported caloric intake, b) recommended caloric intake, and c) caloric difference (reported caloric intake-recommended reported intake).
Reference lines represent the norm values of daily caloric intake in different age categories: 4–8 years: 1500 kcal, 9–13 years: 2150 kcal, 14–18 years: 2700 kcal (out of range of this figure), 19–20 years: 2600 kcal (out of range of this figure).

first visit analysis, where a significant difference did exist between the corticosteroid use group and patients not using corticosteroids. Possible explanations for not finding an association in the longitudinal analyses are that only the patients who were ambulant at first visit were included in further analysis and within this group the amount of patients not using corticosteroids was very small. Second, majority used intermittent use of corticosteroids, which can reduce the effect on appetite and weight, as described before [18]. As corticosteroid use delays disease progression, it is still strongly recommended however, that parents, carers and patients should be aware from the beginning of the possible effects on both appetite and weight.

5. Conclusions

Obesity is a common problem in patients with DMD. This study showed that even a year before losing ambulation, BMI-z scores increased. Therefore, preventive measures are needed before this time frame. Earlier intervention in caloric intake may help to prevent obesity. Besides, stimulation of (adjusted or supported) physical activities during all disease stages can additionally prevent overweight and obesity in the later disease stages.

Declaration of Competing Interest

None.

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Supplementary materials

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References

[1] Mendell JR, Lloyd-Puryear M. Report of MDA muscle disease symposium on newborn screening for Duchenne muscular dystrophy. Musc Nerve 2013;48:21–6.
[2] Hankard R, Gottrand F, Turck D, Carpentier A, Romon M, Farriaux JP. Resting energy expenditure and energy substrate utilization in children with Duchenne muscular dystrophy. Pediatr Res 1996;40:29–33.
[3] Willig TN, Carlier L, Legrand M, Riviere H, Navarro J. Nutritional assessment in Duchenne muscular dystrophy. Dev Med Child Neurol 1993;35:1074–82.
[4] Martigne L, Salleron J, Mayer M, Cuisset JM, Carpentier A, Neve V, et al. Natural evolution of weight status in Duchenne muscular dystrophy: a retrospective audit. Br J Nutr 2011;105:1486–91.
[5] Davidson ZE, Ryan MM, Kornberg AJ, Sinclair K, Cairns A, Walker KZ, et al. Observations of body mass index in Duchenne muscular dystrophy: a longitudinal study. Eur J Clin Nutr 2014; 68:892–7.
[6] Saure C, Caminiti C, Weglinski J, de Castro Perez F, Monges S. Energy expenditure, body composition, and prevalence of metabolic disorders in patients with Duchenne muscular dystrophy. Diabetes Metab Syndr 2018;12:81–5.
[7] Zanardi MC, Tagliabue A, Orcesi S, Berardinelli A, Uggetti C, Pichiecchio A. Body composition and energy expenditure in Duchenne muscular dystrophy. Eur J Clin Nutr 2003;57:273–8.
[8] Rodríguez-Cruz M, Sanchez R, Escobar RE, Cruz-Guzmán Odel R, López-Alarcón M, Bernabe García M, et al. Evidence of insulin resistance and other metabolic alterations in boys with duchenne or becker muscular dystrophy. Int J Endocrinol 2015;2015:867273.
[9] Bostock EL, Edwards BT, Jacques MF, Pogson JTS, Reeves ND, Onambele-Pearson GL, et al. Impaired Glucose Tolerance in Adults with Duchenne and Becker Muscular Dystrophy. Nutrients 2018;10.
[10] van de Velde NM, Roest AAW, van Zwet EW, Niks EH. Increased blood pressure and body mass index as potential modifiable factors in the progression of myocardial dysfunction in duchenne muscular dystrophy. J Neuromusc Dis 2019;6:65–73.
[11] Bernabe-Garcia M, Rodriguez-Cruz M, Atilano S, Cruz-Guzman ODR, Almeida-Becerril T, Calder PC, et al. Body composition and body mass index in Duchenne muscular dystrophy: role of dietary intake. Muscle Nerve 2019;59:295–302.
[12] Sarrazin E, von der Hagen M, Schara U, von Au K, Kaindl AM. Growth and psychomotor development of patients with Duchenne muscular dystrophy. Eur J Paediatr Neurol 2014;18:38–44.
[13] Wood CL, Straub V, Guglieri M, Bushby K, Cheetham T. Short stature and pubertal delay in Duchenne muscular dystrophy. Arch Dis Child 2016;101:101–6.
[14] West NA, Yang ML, Weitzenkamp DA, Andrews J, Meaney FJ, Oleszek J, et al. Patterns of growth in ambulatory males with Duchenne muscular dystrophy. J Pediatr 2013;163:1759–63 e1.
[15] Bianchi ML, Biggar D, Bushby K, Rogol AD, Rutter MM, Tseng B. Endocrine aspects of Duchenne muscular dystrophy. Neuromusc Disord 2011;21:298–303.
[16] Birnkrant DJ, Bushby K, Bann CM, Apkon SD, Blackwell A, Brumbaugh D, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol 2018;17:251–67.
[17] Manzur AY, Kuntzer T, Pike M, Swan A. Glucocorticoid corticosteroids for Duchenne muscular dystrophy. Cochrane Database Syst Rev 2008:Cd003725.
[18] ten Dam K, de Groot IJ, Noordam C, van Alfen N, Hendriks JC, Sie LT. Normal height and weight in a series of ambulant Duchenne muscular dystrophy patients using the 10 day on/10 day off prednisone regimen. Neuromusc Disord 2012;22:500–4.
[19] https://apps.cpeg-gcep.net/quickZ_WHO/.
[20] de Onis M, Garza C, Onyango AW, Borghi E. Comparison of the WHO child growth standards and the CDC 2000 growth charts. J Nutr 2007;137:144–8.
[21] Worldwide trends in body-mass indexunderweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128•9 million children, adolescents, and adults. Lancet (London, England) 2017;390:2627–42.
[22] Connolly AM, Malkus EC, Mendell JR, Flanigan KM, Miller JP, Schierbecker JR, et al. Outcome reliability in non-ambulatory boys/men with Duchenne muscular dystrophy. Muscle Nerve 2015;51:522–32.
[23] Berard C, Payan C, Fermanian J, Girardot F. [A motor function measurement scale for neuromuscular diseases - description and validation study]. Rev Neurol (Paris) 2006;162:485–93.
[24] Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. Human nutrition. Clin Nutr 1985;39(1):5–41 Suppl.
[25] Firouzbakhsh S, Mathis RK, Dorchester WL, Oseas RS, Groncy PK, Grant KE, et al. Measured resting energy expenditure in children. J Pediatr Gastroenterol Nutr 1993;16:136–42.
[26] van der Kuip M, de Meer K, Westerterp KR, Gemke RJ. Physical

activity as a determinant of total energy expenditure in critically ill children. Clin Nutr 2007;26:744–51.
[27] Joint FAOWHOUNUECoE, Protein R, Food, Agriculture Organization of the United N, World Health O, United Nations U Energy and protein requirements: report of a joint fao/who/unu expert consultation [held in Rome from 5 to 17 October 1981]. Geneva: World Health Organization; 1985.
[28] Singer JD, Willett JB, Willett JB. Applied longitudinal data analysis: modeling change and event occurrence. Oxford university press; 2003.
[29] Mok E, Letellier G, Cuisset JM, Denjean A, Gottrand F, Hankard R. Assessing change in body composition in children with Duchenne muscular dystrophy: anthropometry and bioelectrical impedance analysis versus dual-energy X-ray absorptiometry. Clin Nutr 2010;29:633–8.
[30] Chew K, Carey K, Ho G, Mallitt KA, Widger J, Farrar M. The relationship of body habitus and respiratory function in Duchenne muscular dystrophy. Respir Med 2016;119:35–40.
[31] Nagel BH, Mortier W, Elmlinger M, Wollmann HA, Schmitt K, Ranke MB. Short stature in Duchenne muscular dystrophy: a study of 34 patients. Acta Paediatr 1999;88:62–5.
[32] Walker JL, Ardouin S, Burrows T. The validity of dietary assessment methods to accurately measure energy intake in children and adolescents who are overweight or obese: a systematic review. Eur J Clin Nutr 2018;72:185–97.
[33] Heutinck L, Kampen NV, Jansen M, Groot IJ. Physical activity in boys with duchenne muscular dystrophy is lower and less demanding compared to healthy boys. J Child Neurol 2017;32:450–7.
[34] Barnard AM, Willcocks RJ, Triplett WT, Forbes SC, Daniels MJ, Chakraborty S, et al. MR biomarkers predict clinical function in Duchenne muscular dystrophy. Neurology 2020;94:e897–909.