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Nutritional status at the moment of diagnosis in childhood cancer patients

Stan odżywienia pacjentów w chwili rozpoznania choroby nowotworowej wieku dziecięcego i młodzieńczego

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Abstract

Introduction. Children with a neoplastic disease are highly susceptible to malnutrition. The main objective of the study was to assess the frequency of undernourishment and obesity at the time of the diagnosis of the neoplastic disease at children. **Materials and methods.** The study included 734 patients (58% males) at the age 1–20,25, with the diagnosis of neoplasm in the years 1986–2014. The patients were divided into groups depending on the type of the diagnosis: 1) ALL, 2) ANLL, 3) HL, 4) NHL, 5) NBL, 6) Wilms tumor, 7) mesenchymal malignant tumor. The BMI SDS and the height SDS were evaluated. The difference in the incidence of disorders in each group was examined. **Results.** In the study group at the time of the diagnosis 21.5% of patients were undernourished while 13.8% presented were overweight. Patients in the ALL group were overweight more often than the rest of the study group (RR 1.82, CI 95%1.26–2.63, p=0.002) – 18.6% of them were overweight. However, children with mesenchymal malignant tumor were less susceptible to overweight than the rest of the patients (RR 0.36, CI 95%0.15-0.87, p=0.021) – only 5.4% of them were overweight. Girls with ALL were malnourished more often than other patients (RR 1.72, CI 95%1.08–2.75, p=0.03). There were no significant differences in the malnutrition/obesity frequency in other neoplasms groups. **Summary.** ALL patients are less susceptible to underweight than the patients with the solid tumor. Moreover, the high incidence of overweight in children with ALL is noteworthy.

Key words

malnutrition, neoplastic disease, children, overweigh, obesity

Streszczenie

Wstęp. Dzieci z chorobą nowotworową są znacznie bardziej narażone na niedożywienie. **Celem pracy** jest ocena częstości występowania niedożywienia oraz nadwagi w momencie rozpoznania choroby nowotworowej u dzieci. **Materiał i metody.** Badaniami objęto 734 pacjentów (58% chłopców) w wieku 1–20,25 lat z rozpoznaną chorobą nowotworową w latach 1986–2014. Pacjenci zostali podzieleni na grupy w zależności od rozpoznania:1) ALL, 2) ANLL, 3) HL, 4) NHL, 5) NBL, 6) guz Wilmsa, 7) złośliwy guz mezenchmalny. BMI oraz wysokość ciała przedstawiono w SDS. Oceniano różnice w występowaniu zaburzeń w każdej z tych grup. **Wyniki badań.** W badanej grupie w momencie rozpoznania choroby 21,5% wykazywało niedożywienie, a 13,5% pacjentów miało nadwagę. Pacjenci z ALL byli istotnie częściej otyli w porównaniu do pozostałych grup (RR 1,82, CI 95% 1,26–2,63, p=0,002) – 18,6% z nich miało nadwagę. Dzieci ze złośliwymi guzami mezenchymalnymi są mniej podatne na występowanie nadwagi/otyłosci

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w porównaniu do innych pacjentów (RR 0,36, CI 95% 0,15–0,87, p=0,021) – tylko 5,4% z nich miało nadwagę. Dziewczynki z ALL częściej wykazywały niedowagę w porównaniu do innych badanych grup (RR 1,72, CI 95% 1,08–2,75, p=0,03).W pozostałych grupach badanych nie obserwowano istotnych różnic w występowaniu niedożywienia/otyłości. **Wnioski.** Pacjenci z ALL wykazują większą predyspozycję do niedowagi w porównaniu do pacjentów z guzami litymi. Należy odnotować częstsze występowanie nadwagi u dzieci z ALL w porównaniu do innych grup pacjentów.

Słowa kluczowe

niedowaga, choroby nowotworowe , dzieci, nadwaga, otyłość

Introduction

Nutritional status at the time of the diagnosis is an important factor which influences the response to the treatment as well as the possibility of recovery [1]. Children suffering from the neoplastic disease generally present malnutrition. This happens both because of the disease and its severity in extreme situations causing cachexia. These patients require special care in order to compensate for their nutritional deficiencies. Moreover, the presence of malnutrition correlates with a greater number of the complications and relapse as well as with a decreased level of recoveries [1,2]. In order to better prevent and treat malnutrition it is vitally important to define the frequency of nutritional deficiencies and factors responsible for them [3]. The growing level of the overweight and obesity should be taken into consideration as they negatively influence the response to the treatment and lead to the decreased level of the curability [1,4]. Some other studies confirmed influence of weight disturbances on survival [5–8]. Furthermore, obesity at ALL diagnosis could be linked to poor prognosis (5 year free survival) and increased risk for pancreatic and liver toxicity when compared to non-obese patients [6,7]. This could be a result of inadequate doses of chemotherapy based on body's surface area or different pharmacokinetics of drugs [4]. Veal et al. claimed that surface area-based dosing is not optimal and suggested that drug concentration could be related to patient weight and age [9]. In contrary Hijiya et al. found no relevant associations between BMI and anti-cancer treatment outcomes, chemotherapy pharmacokinetics or toxicity in ALL patients [10]. Furthermore, Conrad et al. found no increased risk for relapse in a large study group conmposed of patients with Wilms' tumor [11]. Viana et al. reported that on the other hand, malnutrition also could be an important prognostic factor for relapse [6]. Murry et al. associated malnutrition with changes in pharmacokinetic features of antineoplastic agents, however the role of this variability has not been well-understood yet [12].

The aim of the study was to assess children's nutritional disorders at the moment of cancer diagnosis.

Materials and methods

The study group comprised 734 patients (58% males) aged 1-20,25 years with childhood neoplasms diagnosed between 1986 and 2014 in the Department of Pediatric Bone Marrow Transplantation, Oncology and Hematology, Wroclaw Medical University, in Wroclaw, Poland. The patients were divided into groups depending on the type of neoplasms: ALL- Acute lymphoblastic leukemia, ANLL- Acute non-lymphoblastic leukemia, Hodgkin lymphoma (HL), Non-Hodgkin lymphoma (NHL), Neuroblastoma (NBL), Wilms' tumor and mesenchymal malignant tumor (MMT). Body weight and height were measured at the time of the diagnosis. Body mass index (BMI) was calculated from the formula: BMI=weight/height^2 (kg/m^2). Body weight, height and BMI values were calculated as SDS values. The patients were then divided into groups of under-, normal- and over-weight children according to BMI SDS ranges. Underweight was defined as BMI SDS ≤-1.6 (≤10th percentile), normal-weight as (-1.6-1.6) (10th percentile-90th percentile) and overweight as ≥1.6 (≥90th percentile). Height deficiency was defined as height SDS ≤-1.6(≤10th percentile). Statistical analyses were performed using Statistica 10 and EpiInfo 6 software. The prevalence of underweight, normal-weight and overweight in different cancer groups was calculated by the chi-square test χ^2_{df} with corresponding degree of freedom df (df=(m-1)*(n-1), where m – number of rows, n – number of columns). For 2x2 tables relative risk and 95% confidence interval for it were also calculated. A p value of less than 0.05 was required to reject the null hypothesis.

Results

There was a male predominance of 58% (426 males) in the overall study group as well as in particular cancer groups, besides Wilms' tumor and MMT group, which were characterized by female predominance (table I). At cancer diagnosis moment, 21.5% (158) of the patients were underweight, 64.7% (475) weighed properly and 13.8% (101) were overweight (table II). Height deficiency was observed in 8% (57) of the patients, 10% (34) of the boys and 9% (23) of the girls. Both underweight and short stature were found in 2% (15) of the patients. There were no significant differences considering height deficiencies between cancer groups.

There were significant differences between the abovementioned groups (table II). Children diagnosed with ALL significantly varied from the rest of the study group considering underweight/normal weight/overweight status of the patients (p=0,0029). In ALL patients 18.6% (58) were overweight (table II). ALL children had an increased risk of being overweight at the cancer diagnosis moment compared to the other patients (RR= 1.82, CI 95%= 1.26-2.63, p, value=0.002) (table III). Children with mesenchymal malignant tumors also varied from the rest

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Table I. Basic characteristics of the cancer groups
Tabela I. *Charakterystyka badanej grupy*

Cancer groups	No	Mean age at cancer diagnosis (yrs)	Boys (%)	Girls(%)
Overall	734	7.78±5.3	426(58)	308(42)
ALL	312	7±4.61	181(58)	131(42)
ANLL	48	7.88±5.6	28(58)	20(42)
NHL	77	10.63±4.4	58(75)	19(25)
HL	75	12.71±4	50(67)	25(33)
NBL	68	3.39±3.9	39(57)	29(43)
Wilms' tumor	62	3.02±2	25(40)	37(60)
MMT	92	10.39±5.1	44(48)	48(52)

Table II. Distribution of the patients in under-/normal-/over-weight children groups. Comparison of the cancer group the rest of study group
Tabela II. *Rozkład pacjentów z niedoborem masy ciała/prawidłową masą ciała/nadmierną masą ciała. Porównanie grup*

Cancer groups	No	Under-Weight (%)	Normal-weight(%)	Overweight /Obesity (%)	p, value[1]
Overall	734	158(21.5)	475(64.7)	101(13.0)	–
ALL	312	58(18.6)	196(62.8)	58(18.6)	**0.0029**
ANLL	48	13(27.1)	28(58.3)	7(14.6)	0.58
NHL	77	16(20.8)	50(64.9)	11(14.3)	0.98
HL	75	14(18.7)	54(72)	7(9.3)	0.333
NBL	68	18(26.5)	42(61.8)	8(11.8)	0.557
Wilms' tumor	62	16(25.8)	41(66.1)	5(8.1)	0.334
MMT	92	23(25)	64(69.6)	5(5.4)	**0.043**

Each of the cancer groups was divided in to subgroups (under-/normal/-over-weight). Then, the difference in prevalence of under-/normal/-over-weight between the cancer group and the rest of the study group was calculated by the chi-square test χ^2_{df}

Table III. *Relative Risk* of underweight and overweight/obesity in particular cancer groups compared to the rest of the study group
Tabela III. *Relatywne ryzyko niedoboru masy ciała oraz nadmiaru masy ciała w poszczególnych grupach w porównaniu do pozostałej grupy*

Cancer	Underweight			Overweight/obesity		
	RR	CI 95%	P value	RR	CI 95%	P value
ALL	0.78	0.59–1.05	0.12	**1.82**	**1.26–2.63**	**0.002**
ANLL	1.28	0.79–2.08	0.43	1.06	0.52–2.16	0.96
NHL	0.86	0.53–1.42	0.66	1.07	0.6–1.91	0.96
HL	0.87	0.53–1.42	0.67	0.65	0.32–1.36	0.32
NBL	1.26	0.83–1.92	0.38	0.84	0.43–1.66	0.75
Wilms' tumor	1.22	0.78–1.91	0.49	0.56	0.24–1.33	0.24
MMT	1.19	0.81–1.75	0.46	**0.36**	**0.15–0.87**	**0.021**

of the study group considering underweight/normal weight/overweight status of the patients (p=0.043) (table II). Children with MMT had a decreased risk of being overweight compared to the rest of the patients (RR= 0.36, CI 95%=0.15-0.87, p=0.021) and only 5.4%(5) of them were overweight, indeed (table II, III). In other cancer groups there was no increased risk of weight disturbances (under-/overweight) (table III).

Underweight was found in 27% (82) of the girls and in 18% (76) of the boys in the overall study group (table IV). The girls and the boys varied from oneanother considering the prevalence of underweight/normal weight/overweight status at the moment of diagnosis in overall (p=0.013) and in MMT group (p=0.046). In the groups with ALL and NHL the difference between the girls and the boys was almost statistically significant (p=0.061) (table IV). In the whole study group the girls were at a higher risk of underweight then the boys (RR=1.49, CI 95%=1.49-1.97, p value<0.01). A similar result was found in the girls diagnosed with ALL (RR=1.72, CI 95%=1.08-2.75, p, value=0.03) (table

Table IV. Comparison of the cancer groups considering sexes
Tabela IV. *Porównanie badanej grupy przy podziale płci*

Cancer groups	N	Under-weight (%) weight (%)	Normal-weight (%)	Overweight/ Obesity (%)	p, value[1]
Overall					
Girls	308	82(26.6)	183(59.4)	43(14)	**0.013**
Boys	426	76(17.8)	292(68.5)	58(13.6)	
ALL					
Girls	130	32(24.6)	74(56.9)	24(18.5)	0.061
Boys	182	26(14.2)	122(67)	34(18.7)	
ANLL					
Girls	20	6(30)	11(55)	3(15)	0.915
Boys	28	7(25)	17(60.7)	4(14.3)	
NHL					
Girls	19	1(5.3)	13(68.4)	5(26.3)	0.061
Boys	58	15(25.9)	37(63.8)	6(10.4)	
HL					
Girls	25	4(16)	20(80)	1(4)	0.614
Boys	50	10(20)	34(68)	6(12)	
NBL					
Girls	29	10(34.5)	16(55.2)	3(10.4)	0.434
Boys	39	8(20.5)	26(66.7)	5(12.8)	
Wilms' tumor					
Girls	37	13(35.1)	21(56.8)	3(8.1)	0.116
Boys	25	3(12)	20(80)	2(8)	
MMT					
Girls	48	16(33.3)	28(58.3)	4(8.3)	**0.046**
Boys	44	7(15.9)	36(81.8)	1(2.3)	

[1]Each of the cancer groups were divided in to subgroups (under-/normal/-over-weight). Then, the difference in prevalence of under-/normal/-over-weight between the girls and the boys was calculated by the chi-square test χ^2_{df}

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V). Differences between the girls and the boys considering underweight were almost statistically significant in the groups diagnosed with Wilms tumor (RR=1.56; CI 95%=1.08-2,24; p=0.08) and MMT (RR=2.1; CI 95%=0.95-4,6; p=0.09). Overweight or obese children were found in 13.96% (43) of the girls and 13.92% (58) of the boys. There were no significant differences in overweight prevalence between the sexes (table V).

Discussion

Many former and recent studies investigated the issue of weight disturbances in children diagnosed with cancers. However, authors of these studies used different values to define malnutrition and overweight which made their results difficult to compare.Nutritional status at the time of cancer diagnosis is dependent on a cancer type, its localization, and clinical stage of the disease [1]. Children with advanced stage of Wilms tumors, neuroblastoma, rhabdomyosarcoma are at a higher risk of undernourishment [13]. Undernourishment occurs less frequently in patients with non-metastatic tumors [14]. Brinksma et al. in their metaanalysis observed high prevalence of malnutrition (up to about 50%) in children diagnosed with neuroblastoma. Unfortunately, the size of the study groups were small and there was no information about the stage of the neuroblastoma [3]. In another study the prevalence of malnutrition at diagnosis in the group of patients with neuroblastoma was about 24% [15]. In our study 26.8% (16) of children with neuroblastoma were underweight at the time of cancer diagnosis, but we also did not included in our analysis the factor like stage of the neuroblastoma. Considering other solid tumors, malnutrition at the diagnosis is presented in 0–30% of the patients [3]. Unfortunately, most of the studies investigating the incidence of malnutrition in solid tumors are based on small groups of patients. Garfólo et al. reported that patients with solid tumors presented malnutrition more frequently compared to haematological malignancies [16]. In contrary, the other authors found no differences in malnutrition frequency between haematological malignancies and solid tumors [17,18]. In our study patients with soft tissue tumors were ata lower risk of being overweight at diagnosis compared to the other cancer groups. Brinksma et al. in their metaanalysis observed lower malnutrition prevalence of about 5–10% in leukemia patients. [3] Interestingly, we found in ALL group a high prevalence of not only underweight (18.6%), but overweight as well (18.6%). Moreover, children with ALL were at a higher risk of overweight than the rest of the study group. The time of cancer development is shorter in haematological malignancies than solid tumors. If the cancer develops more rapidly, the shortage of weight is smaller. That could explain high prevalence of overweight in ALL patients as those patients had not enough time to develop severe malnutrition.

BMI values were concerned not to be the best method of defining nutritional status in patients with neoplasm diseases. It is especially so in patients with advanced abdominal solid tumors, because tumor mass could constitute over 10% of the total body weight [1]. These patients might present normal body weight despite severe malnutrition [14]. Other methods like Triceps skinfold thickness (TSFT), mid-upper arm circumference (MUAC) and arm muscle circumference (AMC) were discussed in terms of their usefulness. TSFT, MUAC, AMC could be more adequate indicators of nutritional status than simple measurements of body weight and height [14,16]. However, skinfold measurements results are strongly dependent on physician's experience in such measurements and, therefore, this could contribute to variability of results of the same measurements performed by a different person. Another po-

Table V. *Relative Risk* of underweight and overweight/obesity comparing girls to boys
Tabela V. *Relatywne ryzyko niedoboru i nadmiaru masy ciała porównanie dziewcząt do chłopców*

Cancer	Underweight			Overweight/obesity		
	RR	CI 95%	P value	RR	CI 95%	P value
Overall	**1.49**	**1.49–1.97**	**0.006**	1.03	0.71–1.48	0.98
ALL	**1.72**	**1.08–2.75**	**0.03**	0.99	0.62–1.58	0.92
ANLL	1.2	0.47–3.03	0.96	1.05	0.26–4.18	0.73
NHL	0.2	0.03–1.44	0.11	2.54	0.87–7.4	0,.18
HL	0.8	0.28–2.32	0.92	0.33	0.04–2.62	0.48
NBL	1.68	0.76–3.73	0.31	0.81	0.21–3.11	0.95
Wilms' tumor	1.56	1.08–2.24	0.08	1.01	0.18–5.64	0.68
MMT	2.1	0.95–4.6	0.09	0.81	0.21–3.11	0.95

tentially useful method presented by Murphy et al. was total body potassium counting (TBK), which measures body cell mass (BCM) [18]. Murphy et al. used BCMI (BCM index-BCM adjusted for height) to compare nutritional status of patients undergoing cancer treatment and healthy control subjects. The patients had lower BCMI than the control subjects, but there were no significant differences concerning BMI values between the treated patients and the healthy control group. Unfortunately, the authors emphasised high costs and time-consuming examination as main and significant drawbacks of BCMI[18]. Nutritional status in children diagnosed with cancer could also be measured using more adequate methods of assessing body's composition. Methods like dual energy X-ray absorptiometry (DEXA) or Score Patient-Generated Subjective Global Assessment (PG-SGA) were suggested to be useful [19–21]. Several biochemical markers, such as serum levels of albumin, transferrin or Insulin like growth factor (IGF-1) were reported to be useful in monitoring nutritional status [12,22].

Conclusion

Children diagnosed with cancers are in a high risk of weight disturbances. Therefore, physicians ought to pay attention to this problem and diagnose these disturbances. Underweight in the patients diagnosed with ALL is not characteristic. Patients with ALL were more often overweight at the time of cancer diagnosis. Girls with ALL compared to the boys are more often underweight. Children with MMT are less susceptible to overweight than the rest of types of cancers.

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