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WPŁYW INTERAKTYWNYCH GIER WIDEO NA AKTYWNOŚĆ I WYDOLNOŚĆ FIZYCZNĄ DZIECI LECZONYCH Z POWODU BIAŁACZKI

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SPIS TREŚCI

WYKAZ SKRÓTÓW UŻYWANYCH W TEKŚCIE

ALAL – białaczka z niezidentyfikowanej linii

ALL – ostra białaczka limfoblastyczna

AML – ostra białaczka szpikowa

CPET – test wydolności krążeniowo-oddechowej o stopniowo narastającym obciążeniu

CRF – wydolność krążeniowo-oddechowa

HBSC – zachowania zdrowotne dzieci w wieku szkolnym

HR – częstotliwość uderzeń serca

HR_{peak} – szczytowa częstotliwość uderzeń serca

IVG – interaktywne gry wideo

ml·kg-1·min-1 – mililitr na kilogram masy ciała na minutę

MVPA – umiarkowana i/lub intensywna aktywność fizyczna

PA – poziom aktywności fizycznej

SST – ilości czasu spędzonego w pozycji siedzącej przed ekranem telewizora/komputera

VO_{2peak} – szczytowy pobór tlenu

VR – wirtualna rzeczywistość

I Wskazanie osiągnięcia wynikającego z art. 187, pkt 3 Ustawy z dnia 20 lipca 2018 r. – Prawo o szkolnictwie wyższym i nauce (Dz.U. 2018 poz. 1668).

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I 1. Tytuł osiągnięcia naukowego/artystycznego:

Wpływ interaktywnych gier wideo na aktywność i wydolność fizyczną dzieci leczonych z powodu białaczki

I 2. Autor/autorzy, tytuł/tytuły publikacji, rok wydania, nazwa wydawnictwa:

1. Kowaluk A, Woźniewski M, Malicka I. *Physical Activity and Quality of Life of Healthy Children and Patients with Hematological Cancers*. Int J Environ Res Public Health. 2019, 16(15), 2776. doi: 10.3390/ijerph16152776.

- Punktacja MNiSW – 140 pkt, wartość wskaźnika IF – 2.849

2. Kowaluk A, Woźniewski M. *Peak Oxygen Uptake and Exercise Capacity of Children Undergoing Leukemia Treatment*. Int J Environ Res Public Health. 2020, 17(23), 8732. doi: 10.3390/ijerph17238732.

- Punktacja MNiSW – 140 pkt, wartość wskaźnika IF – 3.390

3. Kowaluk A, Woźniewski M. *Interactive Video Games as a Method to Increase Physical Activity Levels in Children Treated for Leukemia*. Healthcare 2022, 10(4), 692. https://doi.org/10.3390/healthcare10040692.

- Punktacja MNiSW – 40 pkt, wartość wskaźnika IF – 2.645

Inne publikacje autora rozprawy doktorskiej:

1. Kowaluk A, Woźniewski M. *Physical activity and quality of life in children treated for leukaemia*. Physiother Quart. 2018, 26(2), 9–18. doi: 10.5114/pq.2018.75994

2. Kowaluk A, Woźniewski M. *Interactive video games to promote physical activity among healthy children and youths*. Pediatr Pol 2019, 94 (3): 198–204. doi: https://doi.org/10.5114/polp.2019.86443

II WSTĘP

II 1. Częstość występowania choroby nowotworowej wieku dziecięcego

W dzisiejszych czasach obserwuje się stały wzrost zachorowalności na nowotwory złośliwe. Coraz więcej danych wskazuje na wzrost liczby zachorowań również w grupie dzieci i młodzieży (Smith i wsp., 2010; Hubbard i wsp., 2019). Wynika to między innymi ze zwiększonej ekspozycji na czynniki karcinogenne, działające niekorzystnie już w życiu płodowym, a także z braku przestrzegania podstawowych zaleceń dotyczących zdrowego stylu życia (Carpenter i wsp., 2013; Karalexi i wsp., 2022; Wu i wsp., 2018). Podejmowane są liczne inicjatywy, które mają na celu zwiększenie czujności onkologicznej społeczeństwa oraz wdrożenie działań prewencyjnych, których ważnym elementem jest regularna aktywność fizyczna (Lugo i wsp., 2019; Rock i wsp., 2022).

Statystyki dotyczące nowotworów wieku dziecięcego wskazują, że schorzenia te stanowią zaledwie 1% wszystkich zachorowań u dzieci. Oznacza to, że choroby nowotworowe wieku dziecięcego występują znacznie rzadziej niż w grupie osób dorosłych. Dane dotyczące krajów europejskich wykazują, że każdego roku w Europie u około 15 tys. dzieci w wieku 0–14 lat diagnozuje się nowotwór złośliwy. W grupie młodzieży i młodych dorosłych (15–24 lat) odnotowuje się dodatkowo 20 tys. nowych zachorowań. W Polsce łączna liczba dzieci w grupie wiekowej od 0 do ukończonych 17 lat to około 7 mln, a każdego roku diagnozuje się od 1100–1200 nowych zachorowań na nowotwór (Schüz i wsp., 2022; Kowalczyk i wsp., 2021).

Rozwój metod diagnostyczno-terapeutycznych przyczynia się do stałego wzrostu odsetka wyleczonych dzieci. Zdecydowana większość dzieci zostaje trwale wyleczonych i uzyskuje całkowitą remisję choroby. Dlatego coraz większego znaczenia nabiera sprawność i aktywność fizyczna osób z chorobą nowotworową w wywiadzie, zarówno w życiu codziennym jak i zawodowym. Ważne są działania prewencyjne oraz promowanie aktywności fizycznej już w okresie trwania choroby nowotworowej.

II 2. Nowotwory układu krwiotwórczego

Najczęstszym nowotworem wieku dziecięcego są białaczki. Jest to grupa nowotworów układu krwiotwórczego, która stanowi 28% wszystkich zachorowań na nowotwory w grupie dzieci. Ogólny wskaźnik zachorowalności na białaczkę wieku dziecięcego wynosi 40–50 nowych zachorowań rocznie na 1 mln dzieci. Dane, które dotyczą Polski szacują wskaźnik zachorowalności na poziomie 43.1 na 1 mln dzieci (Kowalczyk i wsp., 2021; Wojciechowska i wsp., 2018).

Większość dzieci z rozpoznaniem białaczki posiada postać określaną jako ostrą białaczkę limfoblastyczną (ALL – acute limfoblastic leukemia). Zachorowania na ten rodzaj nowotworu stanowią 75–85% wszystkich zachorowań na białaczkę w grupie dzieci. Drugim rodzajem białaczek są ostre białaczki szpikowe (AML – acute myeloid leukemia). Ta grupa nowotworów stanowi 10–20% wszystkich zachorowań na białaczki. Niedużą grupę stanowią białaczki, których komórki pochodzą z niezidentyfikowanych linii (ALAL – acute leukemia of ambiguous lineage); <0.5% (Kowalczyk i wsp., 2021).

Różne grupy nowotworów wieku dziecięcego charakteryzują się różną częstością występowania w poszczególnych grupach wiekowych, a także odrębną etiologią. Szczyt zachorowalności na ostrą białaczkę limfoblastyczną przypada na wczesne lata życia dziecka tzn. między 2–4 rokiem życia (Kowalczyk i wsp., 2021). ALL jest schorzeniem charakteryzującym się obecnością komórek białaczkowych wywodzących się z linii limfocytów T lub B. Nieprawidłowości w różnicowaniu się komórek linii limfoidalnej mogą wystąpić na każdym jej etapie. Zmienione patologicznie komórki namnażają się bardzo szybko, w sposób klonalny, co doprowadza do wyparcia prawidłowych komórek szpiku przez komórki białaczkowe. Powoduje to przenikanie i gromadzenia się limfoblastów w węzłach chłonnych, śledzionie wątrobie lub innych narządach (Derwich i wsp., 2012).

Ostre białaczki szpikowe natomiast występują stosunkowo rzadziej. W Polsce w ciągu jednego roku diagnozuje się około 50 nowych zachorowań na AML w grupie dzieci. Współczynnik zachorowalności na ostrą białaczkę szpikową zależy od wieku dziecka i wynosi w grupie niemowląt 1.5/100 tys. dzieci rocznie. Następnie współczynnik ten obniża się i osiąga wartość 0.9/100 tys. dzieci w wieku 1–4 lat oraz 0.4/100 tys. dzieci w wieku 5–9 lat (Kowalczyk i wsp., 2021). Nieprawidłowości związane z rozwojem ostrej białaczki szpikowej mogą dotyczyć wszystkich linii różnicowania się komórek w szpiku. Klonalnie namnażające się komórki białaczkowe doprowadzają do zahamowania prawidłowej czynności szpiku oraz wyparcia komórek niezmienionych chorobowo (Szydłowski i wsp., 2013).

III CEL PRACY

III 1. Cel główny

Celem rozprawy doktorskiej stanowiącej spójny tematycznie zbiór trzech oryginalnych artykułów jest ocena wpływu interaktywnych gier wideo na aktywność i wydolność fizyczną dzieci będących w trakcie leczenia z powodu nowotworów złośliwych.

III 2. Cele szczegółowe

- Publikacja pt.: *Physical Activity and Quality of Life of Healthy Children and Patients with Hematological Cancers.*

Celem przeprowadzonych badań była ocena poziomu aktywności fizycznej i jakości życia dzieci będących w trakcie i po zakończonym leczeniu z powodu choroby nowotworowej.

- Publikacja pt.: *Peak Oxygen Uptake and Exercise Capacity of Children Undergoing Leukemia Treatment*.

Celem przeprowadzonych badań była ocena poziomu wydolności krążeniowo-oddechowej dzieci będących w trakcie leczenia z powodu białaczki oraz porównanie uzyskanych wyników z wynikami dzieci zdrowych.

- Publikacja pt.: *Interactive Video Games as a Method to Increase Physical Activity Levels in Children Treated for Leukemia*.

Celem pracy była ocena skuteczności oraz bezpieczeństwa i możliwości realizacji opracowanego modelu rehabilitacji z zastosowaniem interaktywnych gier wideo (Interactive Video Games - IVG) u dzieci będących w trakcie pierwszego etapu leczenia z powodu białaczki.

IV OMÓWIENIE CYKLU PUBLIKACJI

IV 1. Poziom aktywności fizycznej dzieci leczonych z powodu białaczki

Terapia przeciwnowotworowa jest bardzo agresywna i skierowana na jak najszybsze zniszczenie dużej liczby komórek nowotworowych. Intensywne leczenie w połączeniu z często występującymi powikłaniami oraz działaniem immunosupresyjnym niektórych leków powodują konieczność izolacji dziecka. Przebywanie jedynie w środowisku osób dorosłych i przewaga siedzącego trybu życia niekorzystnie wpływają na poziom ogólnej aktywności leczonych dzieci.

Badania Braam i wsp. potwierdzają, że dzieci z chorobą nowotworową przejawiają niewystarczający poziom aktywności fizycznej (PA) i nie podejmują samodzielnie żadnej formy wysiłku, który mógłby wpłynąć na poprawę ich wydolności. Wykazano, że 80% całego czasu w ciągu dnia dzieci te spędzają w pozycji siedzącej, a ich wysiłek fizyczny jest związany jedynie z wykonywaniem czynności codziennych (Braam i wsp., 2016). Dzieci będące w trakcie leczenia choroby nowotworowej nie podejmują aktywności fizycznej trwającej łącznie co najmniej 60 minut dziennie i tym samym nie spełniają zaleceń dotyczących wskaźnika MVPA (umiarkowana i/lub intensywna aktywność fizyczna; Moderate to Vigorous Physical Activity) (Tan i wsp., 2013). Wartość wskaźnika MVPA zalecana przez Światową Organizację Zdrowia to wysiłek aerobowy trwający co najmniej 60 minut dziennie przez 7 dni w tygodniu o intensywności umiarkowanej lub dużej (Bull i wsp., 2020).

Także badania Anzar i wsp. potwierdzają obniżony wskaźnika MVPA w grupie dzieci z białaczką będących w trakcie leczenia podtrzymującego. W grupie badanej żadne z dzieci nie spełniało przyjętego kryterium minimalnego poziomu aktywności fizycznej (co najmniej 60 minut dziennie, co najmniej 5 dni w tygodniu) (Anzar i wsp., 2006).

Badania Winter i wsp. donoszą o znacznie obniżonym poziomie aktywności fizycznej w grupie dzieci będących w trakcie leczenia z powodu choroby nowotworowej mierzonym obiektywnie za pomocą monitora aktywności fizycznej StepWatch. Leczone dzieci wykonywały około 2 800 kroków dziennie natomiast ich zdrowi rówieśnicy około 8 100 kroków. Leczone dzieci były bardziej aktywne podczas pobytu w domu w porównaniu do okresów hospitalizacji (około 3 200 vs 1 850 kroków dziennie). Dzieci leczone z powodu białaczki były bardziej aktywne, zarówno podczas pobytu w domu jak i szpitalu, w porównaniu do dzieci z nowotworami zlokalizowanymi w obrębie układu kostno-stawowego (Winter i wsp., 2009).

Wyniki badań Götte i wsp. dowodzą, że poziom aktywności fizycznej dzieci leczonych z powodu choroby nowotworowej ulega istotnemu obniżeniu w okresie leczenia w porównaniu do czasu przed zachorowaniem. Zaobserwowali oni, że w okresach przedłużających się hospitalizacji aż 50% badanych dzieci pozostawało w łóżku w sposób ciągły przez ponad 23 godziny (Götte i wsp., 2014).

W badaniach Rehorst-Kleinlugtenbelt i wsp. zmierzono dzienny poziom aktywności fizycznej za pomocą akcelerometru. Wyniki wykazały, że dzieci z chorobą nowotworową większość czasu w ciągu dnia spędzały w pozycji siedzącej (mediana czasu 1325 min/24 godz.). Dzieci przeznaczały około 111 min/24 godz. na wysiłki lekkie oraz zaledwie 4 min/24 godz. na wysiłki umiarkowane do intensywnych (MVPA). W warunkach szpitalnych dzieci osiągały znacznie niższe poziomy aktywności fizycznej w porównaniu do warunków domowych (Rehorst-Kleinlugtenbelt i wsp., 2019).

Wyniki badań Gaser i wsp. przeprowadzonych w grupie dzieci w wieku 4–18 lat będących w początkowym etapie leczenia (średnio 19.2 ± 12.6 dni od rozpoznania choroby) dowodzą, że dzieci i młodzież w trakcie leczenia onkologicznego przejawiają ograniczone możliwości wykonywania czynności dnia codziennego w warunkach hospitalizacji oraz podczas leczenia ambulatoryjnego już niedługo po postawionej diagnozie choroby nowotworowej. Skutki uboczne związane z chorobą i leczeniem w pierwszych tygodniach intensywnego leczenia nie tylko wpływają na realizację podstawowych czynności dnia codziennego, ale mogą również prowadzić do zmniejszonej sprawności motorycznej i ograniczonego poziomu aktywności fizycznej. Autorzy ci wykazali znacznie obniżony poziom aktywności fizycznej leczonych dzieci. Średnia ilość kroków wykonywanych przez dzieci to 3 126 ± 1 834, natomiast średni czas wysiłków na poziomie MVPA to 17.0 ± 19.0 minut w ciągu jednego dnia (Gaser i wsp., 2022).

Wyniki badań własnych, które zostały przedstawione w pierwszej publikacji naukowej o tytule: *„Physical Activity and Quality of Life of Healthy Children and Patients with Hematological Cancers”*, stanowiącej element cyklu rozprawy doktorskiej (Załącznik nr 1), potwierdzają, że choroba nowotworowa oraz proces jej leczenia istotnie wpływały na zmniejszenie poziomu aktywności fizycznej badanych dzieci (n=88). Celem przeprowadzonych badań była ocena poziomu aktywności fizycznej i jakości życia dzieci będących w trakcie i po zakończonym leczeniu z powodu choroby nowotworowej. Wykorzystano międzynarodowy kwestionariusz dotyczący zachowań zdrowotnych i samopoczucia dzieci w wieku szkolnym (kwestionariusz HBSC - Health Behaviour in School-aged Children). Pytania dotyczyły zachowań związanych z aktywnością fizyczną w ostatnich siedmiu dniach. Dokonano oceny poziomu aktywności fizycznej w trzech grupach dzieci: dzieci w trakcie leczenia choroby nowotworowej *vs.* dzieci, które zakończyły leczenie *vs.* dzieci zdrowe. Wyniki wykazały, że dzieci będące w trakcie leczenia choroby nowotworowej nie wykonywały w tygodniu żadnych wysiłków fizycznych trwających łącznie co najmniej 60 minut dziennie i tym samym nie spełniały zaleceń dotyczących odpowiedniego poziomu codziennej aktywności fizycznej (wskaźnik MVPA). Dzieci po zakończonym leczeniu choroby nowotworowej deklarowały, że co najmniej jeden raz w tygodniu podejmowały wysiłki fizyczne trwające co najmniej 60 minut dziennie. Dzieci zdrowe w 40% podejmowały taką aktywność fizyczną co najmniej 5 dni w tygodniu.

W badaniach własnych ocenie poddano również częstotliwość podejmowania wysiłków fizycznych o dużej intensywności. Dzieci będące w trakcie leczenia choroby nowotworowej w większości (80% dzieci) wcale nie podejmowały wysiłków fizycznych o dużej intensywności, które prowadziłyby do ogólnego zmęczenia. Dzieci po zakończonym leczeniu choroby nowotworowej w 86% przeznaczały co najmniej 30 minut w tygodniu na wysiłki fizyczne o znacznym poziomie. Dzieci zdrowe podejmowały przez co najmniej 2 godziny w tygodniu wysiłek fizyczny o dużej intensywności. Dzieci zdrowe w 36% podejmowały aktywność fizyczną o dużym natężeniu nawet 4–6 razy w tygodniu.

Dzieci leczone z powodu choroby nowotworowej doświadczały nie tylko pogorszenia zdrowia fizycznego, ale również zdrowia psychicznego. Fakt zakończenia leczenia choroby nowotworowej wpływał na wzrost poziomu aktywności fizycznej dzieci, jednak nadal wartości badanych parametrów były niższe w porównaniu do grupy dzieci zdrowych.

IV 2. Poziom wydolności krążeniowo-oddechowej dzieci z chorobą nowotworową

Brak aktywności fizycznej i przewaga czasu spędzonego w pozycji siedzącej dzieci chorych na nowotwory dodatkowo, w postaci „błędnego koła” potęgują stale obniżający się poziom wydolności krążeniowo-oddechowej (cardio respiratory fitness- CRF).

Intensywna terapia przeciwnowotworowa ma niekorzystny wpływ na wydolność fizyczną dzieci i doprowadza do istotnego spadku parametrów wydolnościowych. Potwierdzają to m.in. badania Braam i wsp., w których wartość szczytowa poboru tlenu (VO_{2peak}) dzieci leczonych z powodu choroby nowotworowej wynosiła średnio 31.7 *ml·kg-1·min-1*, podczas gdy średnia wartość przewidywana dla tej grupy wiekowej powinna wynieść 45.1 *ml·kg-1·min-1.* Braam i wsp., wykazali, że ponad 50% dzieci osiągnęło VO_{2peak} poniżej wartości należnej. CRF jest istotnie związane z poziomem aktywności fizycznej oraz nawykami sedenteryjnymi: każda dodatkowa aktywność na minutę powoduje wzrost CRF o 0.05 *ml·kg-1·min-1* VO_{2peak}, a każda dodatkowa minuta siedzenia zmniejsza VO_{2peak} o 0.06 *ml·kg-1·min-1* (Braam i wsp., 2016).

Obniżoną wydolność fizyczną dzieci oraz istotny spadek parametrów wydolnościowych potwierdzają też badania San Juana i wsp. Badane wartości VO_{2peak} w grupie dzieci z ostrą białaczką limfoblastyczną, będących w fazie leczenia podtrzymującego były istotnie niższe w porównaniu do grupy zdrowych rówieśników (25.3 ± 6.5 *ml·kg-1·min-1* vs. 31.9 ± 6.8 *ml·kg-1·min-1*) (San Juan i wsp., 2007). Udowodniono też, że poprawa parametrów wydolnościowych zwiększa wskaźnik przeżywalności leczonych dzieci, natomiast obniżona wartość szczytowego poboru tlenu zaledwie o 3.5 *ml·kg-1·min-1* przyczynia się do obniżenia prawdopodobieństwa przeżycia o 12% (Myers i wsp., 2003).

Również inne badania San Juana i wsp. wykazały obniżony wskaźnik parametrów szczytowego poboru tlenu w grupie dzieci będących po przeszczepie szpiku kostnego (czas od odbytej transplantacji ≤12 miesięcy). Wartość wyjściowa parametru VO_{2peak} w badaniu przeprowadzonym przed rozpoczęciem interwencji treningowej wynosiła w grupie dzieci po odbytym leczeniu z powodu białaczki 25.9 ± 8.9 *ml·kg-1·min-1* (San Juan i wsp., 2008).

Podobne wyniki uzyskali Anzar i wsp., oceniając szczytowy pobór tlenu w teście na bieżni ruchomej. Dzieci leczone z powodu białaczki przejawiały niższy poziom wydolności krążeniowo-oddechowej oceniony na podstawie parametru VO_{2peak} w porównaniu do dzieci zdrowych (25.2 ± 5.9 *ml·kg-1·min-1* vs. 31.2 ± 4.0 *ml·kg-1·min-1*) (Anzar i wsp. 2006).

Wyniki wielu badań potwierdzają obniżone wartości szczytowego poboru tlenu w wysiłkowych próbach ergospirometrycznych, które utrzymują się nawet wiele lat po zakończonym leczeniu choroby nowotworowej wieku dziecięcego. Obniżone parametry wydolnościowe utrzymują się w życiu dorosłym i stanowią ograniczenie do podjęcia wysiłku fizycznego w pełnym zakresie (Yildiz Kabak i wsp., 2019).

Wyniki badań własnych zawarte w drugiej publikacji naukowej: *„Peak Oxygen Uptake and Exercise Capacity of Children Undergoing Leukemia Treatment”,* potwierdziły obniżony poziom wydolności krążeniowo-oddechowej dzieci leczonych z powodu białaczki (Załącznik nr 2). Celem przeprowadzonych badań była ocena poziomu wydolności krążeniowo-oddechowej dzieci będących w trakcie leczenia z powodu białaczki (n=21) oraz porównanie uzyskanych wyników z wynikami dzieci zdrowych. Oceny poziomu wydolności dzieci dokonano w teście ergospirometrycznym według progresywnego protokołu Godfrey’a o stopniowo narastającym obciążeniu, podczas którego przeprowadzono analizę gazów oddechowych. Ponadto oceniono wpływ zastosowanych metod leczenia na poziom wydolności fizycznej dzieci oraz nasilenie zachowań sedenteryjnych.

Zmierzona wartość parametru VO_{2peak} w badanej grupie dzieci wyniosła średnio 22.16 *ml·kg-1·min-1* (SD 2.5). W grupie badanych chłopców parametr ten wyniósł 22.67 *ml·kg-1·min-1* (SD 2.7) natomiast w grupie badanych dziewcząt 21.49 *ml·kg-1·min-1* (SD 2.1). Średnie wartości parametru VO_{2peak} przewidywane dla tej grupy wiekowej to 45.48 *ml·kg-1·min-1* (SD 3.8). Przewidywana wartość parametru VO_{2peak} w grupie zdrowych chłopców to 46.3 *ml·kg-1·min-1* (SD 4.2) natomiast w grupie zdrowych dziewcząt 44.7 *ml·kg-1·min-1* (SD 3.4). Różnica bezwzględna wartości zmierzonej i przewidywanej VO_{2peak} pomiędzy grupami to 23.32 *ml·kg-1·min-1.* W grupie chłopców oraz w grupie dziewcząt różnica ta wyniosła odpowiednio 23.63 *ml·kg-1·min-1* i 23.21 *ml·kg-1·min-1.*

Badania wykazały, że dzieci będące w trakcie leczenia z powodu białaczki charakteryzują się obniżonym poziomem wydolności krążeniowo-oddechowej. Poziom ich wydolności jest zdecydowanie niższy w porównaniu do wartości osiąganych przez dzieci zdrowe będące w tym samym wieku. Niskie wartości parametrów wydolnościowych spowodowane są prawdopodobnie wynikiem zastosowanych metod leczenia, ich skutków ubocznych oraz radykalnej zmiany stylu życia z istotnym ograniczeniem aktywności fizycznej, a wzrostem zachowań sedenteryjnych. Choroba nowotworowa oraz agresywny proces jej leczenia skutkują obniżeniem poziomu parametrów morfotycznych krwi. W konsekwencji doprowadza to do niedotlenienia tkanek i narządów oraz znacznego spadku parametrów wydolnościowych. Brak aktywności fizycznej oraz niespełnione normy dotyczące minimalnego poziomu tygodniowej aktywności fizycznej (wskaźnik MVPA) dodatkowo potęgują ubytek poziomu wydolności leczonych dzieci. Do braku aktywności fizycznej przyczyniają się też czynniki psychospołeczne takie jak brak kontaktu z rówieśnikami, poczucie wyizolowania oraz świadomość choroby zagrażającej życiu, a także nadmierna troska ze strony rodziców i opiekunów leczonych dzieci.

IV 3. Interaktywne gry wideo jako atrakcyjna metoda zwiększająca poziom aktywności fizycznej dzieci z chorobą nowotworową

Aktywność fizyczna jest bardzo ważnym i wciąż jeszcze zbyt mało docenianym elementem prewencji pierwotnej i wtórnej chorób nowotworowych. Ćwiczenia fizyczne mają korzystny wpływ zarówno na chorych w trakcie leczenia, jak i po przebytej chorobie nowotworowej (Dimeo i wsp., 2008). Istnieje stereotypowe przekonanie o szkodliwym wpływie wysiłku fizycznego na proces leczenia choroby nowotworowej. Obecnie zmienia się to podejście i coraz częściej dostrzega się korzystny wpływ wysiłku fizycznego na organizm leczonych dzieci. Aktywność fizyczna ma wyraźny udział w rozwoju somatycznym i motorycznym, ma duże znaczenie dla zdrowia i dobrostanu dzieci i młodzieży oraz daje wyraźne korzyści fizyczne, psychiczne i społeczne (Morales i wsp., 2008). Aktywność fizyczna dziecka będącego w trakcie leczenia choroby nowotworowej zapobiega wielu deficytom czynnościowym oraz skraca czas rekonwalescencji (Daniel i wsp., 2015).

Istotne znaczenie w zwiększeniu poziomu aktywności fizycznej dzieci chorych na nowotwory mogą mieć interaktywne gry wideo stanowiące atrakcyjną formę ćwiczeń w tej grupie wiekowej pacjentów. Do tej pory IVG używane w celu zwiększenia poziomu aktywności fizycznej znalazły szerokie zastosowanie w grupie dzieci zdrowych i młodych dorosłych, dzieci z nadwagą i otyłością oraz w grupie osób dorosłych (Liang i wsp., 2014; Biddiss i wsp., 2010; Guy i wsp., 2011; Lu i wsp., 2013; Oliveira i wsp., 2020; Vázquez i wsp., 2018). IVG znalazły też zastosowanie w grupie dzieci z zaburzeniami rozwojowymi i nieprawidłowościami wzorców motorycznych. Interaktywne gry korzystnie wpłynęły na poprawę badanych parametrów: motorykę małą i dużą, równowagę, koordynację, naturalne formy ruchu i lokomocji (bieganie, chodzenie, skakanie) (Page i wsp., 2017). IVG używane były również jako element programu rehabilitacji dzieci z porażeniem mózgowym oraz po amputacjach (Howcroft i wsp., 2012; Andrysek i wsp., 2012). Interaktywne gry wykorzystywano również w usprawnianiu dzieci z mukowiscydozą (Carbonera i wsp., 2016).

Nowe technologie, takie jak wirtualna rzeczywistość (virtual reality- VR), są również często wykorzystywaną techniką, zarówno w grupie dzieci zdrowych jak i chorych. Liczne badania wykazały, że VR może skutecznie zmniejszyć lęk, niepokój, ból związany z oparzeniem, ból okołooperacyjny, ból związany z jednorazowym lub częstym nakłuciem żył. W grupie dzieci z chorobą nowotworową wirtualna rzeczywistość znalazła również zastosowanie i uzyskuje pozytywne efekty (Sajeev i wsp., 2021). VR to metoda często stosowana w grupie dzieci z chorobą nowotworową jako element terapii długotrwałego bólu, lęku oraz objawów depresyjnych (Ahmad i wsp., 2020; Lopez-Rodriguez i wsp., 2020).

Natomiast interaktywne gry wideo nie znalazły jak dotąd powszechnego zastosowania w grupie dzieci leczonych z powodu nowotworów złośliwych (Kauhanen i wsp., 2014).

IVG to gry elektroniczne, które umożliwiają fizyczną interakcję ciała osoby grającej z obrazem wyświetlanym na ekranie w różnych działaniach, takich jak sport, ćwiczenia fizyczne, taniec, zabawy zręcznościowe. IVG nowej generacji skutecznie zwiększają wydatek energetyczny oraz poziom aktywności fizycznej dzieci zdrowych (LeBlanc i wsp., 2013; Allsop i wsp., 2016). Ponadto zmieniają nieprawidłowe nawyki ograniczając zachowania sedenteryjne.

Coraz większa liczba dzieci i młodzieży nie spełnia podstawowych zaleceń dotyczących odpowiedniego poziomu aktywności fizycznej. Badania Maloney i wsp. potwierdzają korzystny wpływ IVG na poziom aktywności fizycznej w grupie zdrowych dzieci. Zaobserwowano zmniejszenie częstotliwości podejmowania wysiłków lekkich na rzecz wysiłków fizycznych o znacznym poziomie. Wykazano również istotne skrócenie ilości czasu spędzonego w pozycji siedzącej przed ekranem telewizora (sedentary screen time-SST) w grupie badanych dzieci (Maloney i wsp., 2008). Badania dowodzą, że stosunkowo krótka, 20 minutowa sesja interaktywnych gier wideo skutecznie zwiększa wydatek energetyczny zdrowych dzieci. Wydatek energetyczny podczas IVG był znacząco wyższy w porównaniu do wydatku podczas nieaktywnych gier wideo w pozycji siedzącej. Stosunkowo krótkie okresy aktywności podczas interaktywnych gier wideo mają podobną intensywność do takich aktywności jak chodzenie, skoki czy bieganie (Maddison i wsp., 2007). IVG sprawiają, że dzieci stają się bardziej aktywne, a poziom tej aktywności odpowiada co najmniej marszowi o niskiej intensywności (Lanningham-Foster i wsp., 2009; Mitre i wsp., 2011), natomiast badania Mellecker i wsp. donoszą nawet o 4 - krotnym wzroście wydatku na energię podczas gry (Mellecker i wsp., 2008).

Chociaż interaktywne gry nie zawsze są skutecznym rozwiązaniem zwiększającym poziom aktywności fizycznej dzieci zdrowych (Graves i wsp., 2010) to w grupie dzieci chorych wykazują wyższą skuteczność (Kauhanen i wsp., 2014; Fazelniya i wsp., 2017). Potrzeba izolacji oraz wysokie ryzyko infekcji powodują, że hospitalizowane dzieci mają ograniczone możliwości korzystania z ogólnie dostępnych form aktywności fizycznej (Winter i wsp., 2010). Interaktywne gry mogą być sposobem na przerwanie siedzącego trybu życia, są bezpieczne i mogą być stosowane w salach chorych bez kontaktu z innymi osobami. Dzieci podczas hospitalizacji chętnie biorą w nich udział ponieważ są one ciekawą rozrywką i pozwalają na chwilowe odwrócenie uwagi od bolesnych i nieprzyjemnych procedur medycznych (Ghazisaeidi i wsp., 2017).

Dotychczasowe badania dowodzą, że dzieci podczas interaktywnej gry osiągają aktywność fizyczną na poziomie lekkim lub umiarkowanym (Biddiss i wsp., 2010; Barnett i wsp., 2011), czyli takim jaki zaleca się dzieciom podczas leczenia choroby nowotworowej (White i wsp., 2005). Dodatkowo badania dowodzą, że interwencje kontrolowane i monitorowane w czasie rzeczywistym dają znacznie korzystniejsze wyniki w porównaniu do gry spontanicznej, pozwalającej dziecku na dowolność (Baranowski i wsp., 2012). Dlatego słusznym wydaje się zastosowanie indywidualnie dobranego treningu z wykorzystaniem interaktywnych gier wideo w grupie dzieci będących w trakcie hospitalizacji i leczenia z powodu choroby nowotworowej.

Wyniki badań własnych zawarte w trzeciej publikacji naukowej: *„Interactive Video Games as a Method to Increase Physical Activity Levels in Children Treated for Leukemia”,* potwierdziły, że interaktywne gry wideo mogą stanowić skuteczną metodę zwiększającą poziom aktywności fizycznej leczonych dzieci (Załącznik nr 3). Celem pracy była ocena skuteczności oraz bezpieczeństwa i możliwości realizacji opracowanego modelu rehabilitacji z zastosowaniem IVG u dzieci będących w trakcie pierwszego etapu leczenia z powodu białaczki. Ponadto oceniono poziom wydolności krążeniowo-oddechowej (badanie ergospirometryczne na cykloergometrze – protokół progresywny Godfrey'a), aktywność fizyczną i siedzący tryb życia (kwestionariusz HBSC) dzieci podczas hospitalizacji oraz w badaniach kontrolnych (14 miesięcy od zakończenia interwencji IVG). Podczas gry poziom wysiłku (intensywność) kontrolowano za pomocą monitora aktywności fizycznej (Polar M 430). Było to dodatkowe narzędzie, które umożliwiało monitorowanie HR w czasie rzeczywistym i ocenę intensywności wysiłku dzieci podczas interwencji treningowej IVG.

Podział dzieci (n=21) na grupę badaną i kontrolną pozwolił ocenić wpływ programu IVG na poziom wydolności fizycznej i zmianę nawyków związanych z regularną aktywnością fizyczną. Dodatkowo pozwolił ocenić czy nabyte nawyki zdrowotne były trwałe i czy znacząco poprawiły parametry wydolnościowe. Dzieci z grupy kontrolnej nie były objęte żadnym programem rehabilitacyjnym.

Ocena uzyskanych wartości częstości akcji serca (HR) w poszczególnych fazach treningu wykazała, że w badanej grupie dzieci osiągały zakładane wartości HR treningowego, co było szczególnie widoczne w końcowych etapach kolejnych faz treningu IVG. Wymagane wartości częstości akcji serca dla każdej fazy treningowej (70% HR_{peak}, 75% HR_{peak} i 80% HR_{peak}) zostały osiągnięte, a w niektórych przypadkach nawet przekroczone i dzieci osiągnęły wyższe wartości HR niż przewidywano. W końcowej fazie programu rehabilitacji z wykorzystaniem IVG wszystkie badane osoby osiągnęły założone wartości HR, co oznaczało, że trening IVG był bezpieczny i możliwy do przeprowadzenia w grupie dzieci z białaczką.

We wczesnym etapie leczenia choroby nowotworowej dzieci z grupy interwencyjnej podejmowały aktywność fizyczną podczas treningów IVG i tym samym spełniały zalecenia dotyczące odpowiedniego poziomu MVPA. Wyniki badań kontrolnych przeprowadzonych 14 miesięcy od zakończenia programu IVG wykazały, że dzieci te kontynuowały regularną aktywność fizyczną, a ich poziom PA był nawet porównywalny do tego podczas interwencji treningowej IVG (brak statystycznie istotnej różnicy w PA pomiędzy badaniem bezpośrednio po interwencji a badaniem kontrolnym). Po 14 miesiącach od interwencji IVG dzieci nie odbywały już tak intensywnego leczenia jak w pierwszym etapie, a ich parametry wydolnościowe były lepsze, co wykazały wyniki ponownego testu CPET (czas trwania testu był wydłużony, a szczytowa wartość częstości akcji serca była wyższa). W badaniu kontrolnym 14 miesięcy po interwencji IVG zaobserwowano istotny statystycznie wzrost poziomu wydolności krążeniowo-oddechowej w grupie interwencyjnej w porównaniu do wartości osiąganych przez dzieci przed interwencją treningową. Natomiast w grupie kontrolnej nie zaobserwowano istotnej statystycznie różnicy w poziomie wydolności krążeniowo-oddechowej pomiędzy badaniem wyjściowym a badaniem kontrolnym (14 miesięcy później).

Dzieci z grupy kontrolnej w badaniu porównawczym (na początku badania i po 1 miesiącu w badaniu ponownym) nie zwiększyły poziomu aktywności fizycznej w okresie hospitalizacji. Po zakończonym okresie hospitalizacji zwiększyły one codzienną aktywność fizyczną, na co wskazują wyniki badania po 14 miesiącach.

Zaobserwowano istotny statystycznie wzrost poziomu PA w grupie interwencyjnej i kontrolnej 14 miesięcy po interwencji IVG w stosunku do okresu przed interwencją. W badaniu przeprowadzonym 14 miesięcy po zakończeniu interwencji IVG nie stwierdzono istotnych różnic poziomu aktywności fizycznej i wydolności krążeniowo-oddechowej między grupą badaną i kontrolną.

Trening IVG z intensywnością określoną na podstawie wyjściowego testu wydolności krążeniowo-oddechowej jest bezpieczny i może stać się częścią programu rehabilitacji dzieci leczonych z powodu białaczki. Badani z grupy interwencyjnej ukończyli wszystkie etapy progresywnego programu treningowego. Dowiodło to, że możliwe jest podejmowanie takiego wysiłku fizycznego przez dzieci podczas leczenia choroby nowotworowej, a nawet w okresie hospitalizacji. Co więcej, subiektywna ocena zadanego dzieciom wysiłku fizycznego podczas sesji ćwiczeń wykazała, że trening IVG wymagał lekkiego lub umiarkowanego wysiłku, pomimo osiąganych przez dzieci wysokich wartości wydatku energetycznego. Dzieci po zakończeniu intensywnego etapu leczenia białaczki są poddane leczeniu podtrzymującemu. W tym okresie dzieci są zdolne do podjęcia wysiłku fizycznego na poziomie umiarkowanym lub znacznym. Może to wskazywać na konieczność prowadzenia programów rehabilitacyjnych dla dzieci przez cały okres leczenia onkologicznego.

IV 4. Indywidualny dobór parametrów treningowych na podstawie wyników wyjściowej próby wysiłkowej

Nieprawidłowe nawyki nabyte w czasie leczenia często utrwalają się i pozostają obniżone nawet po zakończeniu leczenia. Obniżona wartość szczytowego poboru tlenu jest ważnym predyktorem przedwczesnej umieralności. Dlatego tak ważne jest, aby na każdym etapie leczenia choroby nowotworowej dzieci podejmowały aktywność fizyczną i utrzymywały wysokie wartości VO_{2peak} (Stolley i wsp., 2010; Blair i wsp., 1989; Myers i wsp., 2002).

Spośród metod oceny tolerancji wysiłkowej obrazującej poziom wydolności układu krążeniowo-oddechowego najbardziej wiarygodnym i najczęściej stosowanym jest pomiar szczytowego poboru tlenu za pomocą analizy gazów oddechowych wykonywany podczas testu o stopniowo narastającym obciążeniu (Cardio-Pulmonary Exercise Test - CPET) (American Thoracic Society, 2003).

Test CPET został wykorzystany w badaniach własnych jako metoda diagnostyczna, a wyniki zostały przedstawione w publikacji z 2020 roku: *Peak Oxygen Uptake and Exercise Capacity of Children Undergoing Leukemia Treatment"* (Załącznik nr 2). Metoda analizy gazów oddechowych została wykorzystana w badaniach własnych również jako metoda pozwalająca na indywidualny dobór parametrów programu rehabilitacji z wykorzystaniem IVG. Wyniki przedstawione zostały w publikacji z 2022 roku: *„Interactive Video Games as a Method to Increase Physical Activity Levels in Children Treated for Leukemia"* (Załącznik nr 3). Pomiary dokonywane w teście CPET są uważane przez Światową Organizację Zdrowia za złoty standard oceny zdolności do ćwiczeń aerobowych (Shephard i wsp., 1968). Wartość szczytowa poboru tlenu jest uważana za najbardziej obiektywny i miarodajny parametr oceniający poziom wydolności wysiłkowej. Wyniki testu CPET dostarczają informacji przydatnych klinicznie i są pomocne w obrazowaniu reakcji fizjologicznych organizmu na zadany wysiłek fizyczny (Braam i wsp., 2016; American Thoracic Society, 2003). Pomiar ten wykonywany u dzieci leczonych z powodu białaczki również jest przydatnym badaniem dodatkowym oceniającym stopień nasilenia zaburzeń układu krążeniowo-oddechowego (Thorsteinsson i wsp., 2017).

W trakcie leczenia przeciwnowotworowego dzieci poddawane są rehabilitacji, która jest głównie skierowana na łagodzenie objawów leczenia. Dzieci nie są objęte całościowym programem, a stosowana rehabilitacja często jest jedynie metodą doraźną. Ważne jest, aby u dzieci od samego początku leczenia stosować programy ćwiczeń aerobowych, które będę zapobiegały nadmiernemu spadkowi wydolności wysiłkowej (Huang i wsp., 2011).

Jest wiele badań, które potwierdzają korzystny wpływ programów ćwiczeń aerobowych na organizm leczonych dzieci. Mogą one zapobiegać powstawaniu odległych deficytów sprawności fizycznej, jeśli zostaną włączone już w trakcie leczenia choroby nowotworowej (Liu i wsp., 2009).

Pomiar wyjściowego poziomu parametru VO_{2peak} wykonany na początku leczenia pozwala ocenić sprawność układu sercowo-oddechowego oraz indywidualnie dobrać program ćwiczeń aerobowych. Okresowa kontrola i monitorowanie parametrów krążeniowo-oddechowych w teście CPET umożliwiają modyfikację indywidualnego programu rehabilitacji i dostosowanie go do aktualnego stanu dziecka (San Juan i wsp., 2008). Ważne jest, aby porównywać wyniki poziomu wydolności dzieci objętych procesem leczenia z poziomem wydolności dzieci zdrowych. Wykaże to w jakim stopniu choroba nowotworowa wpłynęła na obniżenie wydolności organizmu leczonych dzieci. Test CPET jest cennym badaniem, ale stosunkowo rzadko wykonywanym w klinikach onkologicznych ze względu na koszty, konieczność zastosowania specjalnego sprzętu do analizy gazów oddechowych oraz wyszkolonego personelu (Dencker i wsp., 2008).

V PODSUMOWANIE

Brak aktywności fizycznej i przewaga czasu spędzonego w pozycji siedzącej dzieci chorych na nowotwory znacząco obniżają wydolność krążeniowo-oddechową. Świadczą o tym niskie wartości szczytowego poboru tlenu uzyskane w teście wydolności krążeniowo-oddechowej porównywane do wartości przewidywanych norm. CRF jest istotnie związane z poziomem aktywności fizycznej oraz nawykami sedenteryjnymi. Częste hospitalizacje, ograniczony kontakt z rówieśnikami i przebywanie jedynie w środowisku osób dorosłych wpływają negatywnie na proces socjalizacji dziecka, który w ten sposób zostaje zaburzony. Doświadczenie izolacji społecznej oraz brak przynależności do wspólnoty wzmagają niejednokrotnie poczucie odrębności i wyobcowania dziecka.

Ocena poziomu aktywności fizycznej ma istotne znaczenie dla opracowania indywidualnych programów rehabilitacji dzieci leczonych z powodu nowotworów, a wyniki testów wydolnościowych stanowią podstawę efektywności zaplanowanego programu rehabilitacji. Okresowa kontrola badanych parametrów oraz stałe monitorowanie częstości skurczów serca w czasie trwania ćwiczeń (np. za pomocą prostych urządzeń takich jak sport tester) zapewni bezpieczny przebieg całego procesu rehabilitacji. Przeciwdziałanie siedzącemu trybowi życia i utrzymanie jak najbardziej normalnego poziomu aktywności fizycznej zbliżonego do zdrowych rówieśników korzystnie wpływa na prawidłowy rozwój dziecka chorego na nowotwór oraz jego samodzielność i niezależność, przyczyniając się do zwiększenia skuteczności leczenia choroby nowotworowej oraz zmniejszenia ryzyka jego skutków ubocznych. Zwiększony poziom PA wpływa na zwiększenie poziomu szczytowego poboru tlenu, którego niska wartość jest predyktorem przedwczesnej umieralności. Osoby, które chorowały na nowotwór w dzieciństwie charakteryzują się zwiększonym ryzykiem wystąpienia chorób sercowo-naczyniowych, otyłości, osteoporozy oraz przedwczesnej śmierci. Obecnie rekomenduje się aktywność fizyczną na każdym etapie leczenia choroby nowotworowej, chociaż pozostaje ona nadal mało docenianym komponentem profilaktyki i terapii choroby nowotworowej. Trening z zastosowaniem IVG może stać się integralną częścią procesu rehabilitacji wewnątrzszpitalnej.

Aktywność fizyczna z wykorzystaniem IVG, dostarczona dziecku w formie zabawy może przyczynić się do zwiększenia poziomu wydatku energetycznego oraz poprawy parametrów wydolnościowych. Ponadto taka forma aktywności fizycznej może dać wytchnienie w chorobie i odwrócić uwagę dziecka od nieprzyjemnych procedur medycznych. Dzieci z chorobą nowotworową, które podejmują wysiłek fizyczny podczas procesu leczenia będą mogły w przyszłości aktywniej uczestniczyć w życiu społecznym i zawodowym.

VI WNIOSKI

Wyniki przeprowadzonych badań poziomu aktywności i wydolności fizycznej dzieci leczonych z powodu białaczki oraz wpływu interaktywnych gier wideo na badane parametry pozwoliły na sformułowanie następujących wniosków:

1. Poziom aktywności fizycznej dzieci będących w trakcie i po zakończonym leczeniu z powodu choroby nowotworowej był znacznie niższy w porównaniu do poziomu PA dzieci zdrowych.

2. W czasie odbywania intensywnego leczenia i hospitalizacji dzieci leczone z powodu choroby nowotworowej nie spełniały zaleceń dotyczących odpowiedniego poziomu wskaźnika MVPA.

3. Poziom wydolności krążeniowo-oddechowej dzieci będących w trakcie leczenia z powodu białaczki był istotnie niższy w porównaniu do wartości przewidywanych dla grupy dzieci zdrowych.

4. Trening IVG z intensywnością określoną na podstawie wyjściowego testu wydolności krążeniowo-oddechowej był bezpieczny i wykonalny oraz możliwy do realizacji w warunkach szpitalnych podczas intensywnego procesu leczenia z powodu białaczki.

5. Trening IVG zastosowany podczas hospitalizacji wpłynął na zwiększenie poziomu aktywności fizycznej dzieci oraz poprawę wskaźnika MVPA.

6. Wyniki badań kontrolnych przeprowadzonych 14 miesięcy od zakończenia programu IVG wykazały, że dzieci kontynuowały aktywność fizyczną, a poziom jej był porównywalny do osiąganego podczas interwencji treningowej IVG.

7. W badaniu kontrolnym 14 miesięcy po interwencji IVG zaobserwowano istotny statystycznie wzrost poziomu wydolności krążeniowo-oddechowej w grupie

interwencyjnej w porównaniu do wartości osiąganych przez dzieci przed interwencją treningową.

8. W grupie kontrolnej nie zaobserwowano istotnej statystycznie różnicy w poziomie wydolności krążeniowo-oddechowej pomiędzy badaniem wyjściowym a badaniem kontrolnym (14 miesięcy później).

9. Poziom aktywności fizycznej w badaniu przeprowadzonym 14 miesięcy po interwencji IVG nie różnił się istotnie statystycznie między grupą badaną i kontrolną.

10. W badaniu przeprowadzonym 14 miesięcy po interwencji IVG poziom wydolności krążeniowo-oddechowej dzieci z grupy badanej i kontrolnej nie różnił się istotnie statystycznie.

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VIII STRESZCZENIA PRACY

VIII 1. Streszczenie w języku polskim

WPŁYW INTERAKTYWNYCH GIER WIDEO NA AKTYWNOŚĆ I WYDOLNOŚĆ FIZYCZNĄ DZIECI LECZONYCH Z POWODU BIAŁACZKI

Słowa kluczowe: białaczka, dzieci z chorobą nowotworową, aktywność fizyczna, wydolność krążeniowo-oddechowa, interaktywne gry wideo.

WSTĘP: W dzisiejszych czasach obserwuje się stały wzrost zachorowalności na nowotwory złośliwe. Coraz więcej danych wskazuje na wzrost liczby zachorowań również w grupie dzieci i młodzieży.

Rozwój metod diagnostyczno-terapeutycznych przyczynia się do stałego wzrostu odsetka wyleczonych dzieci. Dlatego coraz większego znaczenia nabiera sprawność i aktywność fizyczna osób z chorobą nowotworową w wywiadzie, zarówno w życiu codziennym jak i zawodowym. Ważne są działania prewencyjne oraz promowanie aktywności fizycznej już w okresie trwania choroby nowotworowej. Dzieci z chorobą nowotworową przejawiają niewystarczający poziom aktywności fizycznej (PA) i nie podejmują samodzielnie żadnej formy wysiłku, który mógłby wpłynąć na poprawę ich parametrów wydolnościowych.

CEL PRACY: Celem rozprawy doktorskiej stanowiącej spójny tematycznie zbiór trzech oryginalnych artykułów jest ocena wpływu interaktywnych gier wideo na aktywność i wydolność fizyczną dzieci będących w trakcie leczenia z powodu nowotworów złośliwych.

METODY BADAWCZE: W celu oceny poziomu aktywności fizycznej dzieci i nasilenia zachowań sedenteryjnych wykorzystano międzynarodowy kwestionariusz dotyczący zachowań zdrowotnych i samopoczucia dzieci w wieku szkolnym (kwestionariusz HBSC - Health Behaviour in School-aged Children). Pytania dotyczyły zachowań związanych z aktywnością fizyczną w ciągu ostatnich siedmiu dni. Oceny poziomu wydolności krążeniowo-oddechowej dzieci dokonano w teście ergospirometrycznym według progresywnego protokołu Godfrey'a o stopniowo narastającym obciążeniu, podczas którego przeprowadzono analizę gazów oddechowych. Podczas interwencji treningowej poziom wysiłku (intensywność) kontrolowano za pomocą monitora aktywności fizycznej (Polar M 430).

WYNIKI: Wyniki wykazały, że dzieci będące w trakcie leczenia choroby nowotworowej nie wykonywały w tygodniu żadnych wysiłków fizycznych trwających łącznie co najmniej 60 minut dziennie i tym samym nie spełniały zaleceń dotyczących odpowiedniego poziomu codziennej aktywności fizycznej (wskaźnik MVPA). Badania wykazały, że dzieci będące w trakcie leczenia z powodu białaczki charakteryzują się obniżonym poziomem wydolności krążeniowo-oddechowej i jest to szczególnie widoczne w badaniach porównawczych (porównanie do wyników osiąganych w grupie dzieci zdrowych). Ocena uzyskanych wartości częstości akcji serca (HR) w poszczególnych fazach treningu z wykorzystaniem IVG wykazała, że w badanej grupie dzieci osiągały zakładane wartości HR treningowego, co było szczególnie widoczne w końcowych etapach kolejnych faz treningu IVG. Wymagane wartości częstości akcji serca dla każdej fazy treningowej (70% HR_{peak}, 75% HR_{peak} i 80% HR_{peak}) zostały osiągnięte, a w niektórych przypadkach nawet przekroczone i dzieci osiągnęły wyższe wartości HR niż przewidywano. W końcowej fazie programu rehabilitacji z wykorzystaniem IVG wszystkie badane osoby osiągnęły założone wartości HR, co oznaczało, że trening IVG był bezpieczny i możliwy do przeprowadzenia w grupie dzieci z białaczką. W badaniu kontrolnym 14 miesięcy po interwencji IVG zaobserwowano istotny statystycznie wzrost poziomu wydolności krążeniowo-oddechowej w grupie interwencyjnej w porównaniu do wartości osiąganych przez dzieci przed interwencją treningową. Natomiast w grupie kontrolnej nie zaobserwowano istotnej statystycznie różnicy w poziomie wydolności krążeniowo-oddechowej pomiędzy badaniem wyjściowym a badaniem kontrolnym (14 miesięcy później).

WNIOSKI: Wyniki przeprowadzonych badań poziomu aktywności i wydolności fizycznej oraz wpływu interaktywnych gier wideo na oceniane parametry pozwoliły sformułować następujące wnioski:

1. Poziom aktywności fizycznej dzieci będących w trakcie i po zakończonym leczeniu z powodu choroby nowotworowej był znacznie niższy w porównaniu do poziomu PA dzieci zdrowych.

2. W czasie odbywania intensywnego leczenia i hospitalizacji dzieci leczone z powodu choroby nowotworowej nie spełniały zaleceń dotyczących odpowiedniego poziomu wskaźnika MVPA.

3. Poziom wydolności krążeniowo-oddechowej dzieci będących w trakcie leczenia z powodu białaczki był istotnie niższy w porównaniu do wartości przewidywanych dla grupy dzieci zdrowych.

4. Trening IVG z intensywnością określoną na podstawie wyjściowego testu wydolności krążeniowo-oddechowej był bezpieczny i wykonalny oraz możliwy do realizacji w warunkach szpitalnych podczas intensywnego procesu leczenia z powodu białaczki.

5. Trening IVG zastosowany podczas hospitalizacji wpłynął na zwiększenie poziomu aktywności fizycznej dzieci oraz poprawę wskaźnika MVPA.

6. Wyniki badań kontrolnych przeprowadzonych 14 miesięcy od zakończenia programu IVG wykazały, że dzieci kontynuowały aktywność fizyczną, a poziom jej był porównywalny do osiąganego podczas interwencji treningowej IVG.

7. W badaniu kontrolnym 14 miesięcy po interwencji IVG zaobserwowano istotny statystycznie wzrost poziomu wydolności krążeniowo-oddechowej w grupie interwencyjnej w porównaniu do wartości osiąganych przez dzieci przed interwencją treningową.

8. W grupie kontrolnej nie zaobserwowano istotnej statystycznie różnicy w poziomie wydolności krążeniowo-oddechowej pomiędzy badaniem wyjściowym a badaniem kontrolnym (14 miesięcy później).

9. Poziom aktywności fizycznej w badaniu przeprowadzonym 14 miesięcy po interwencji IVG nie różnił się istotnie statystycznie między grupą badaną i kontrolną.

10. W badaniu przeprowadzonym 14 miesięcy po interwencji IVG poziom wydolności krążeniowo-oddechowej dzieci z grupy badanej i kontrolnej nie różnił się istotnie statystycznie.

VIII 2. Streszczenie w języku angielskim

ABSTRACT

THE INFLUENCE OF INTERACTIVE VIDEO GAMES TRAINING ON PHYSICAL ACTIVITY LEVEL AND CARDIORESPIRATORY FITNESS OF CHILDREN TREATED FOR LEUKEMIA

Keywords: leukemia, children with cancer, physical activity, cardiorespiratory fitness, interactive video games.

INTRODUCTION: Nowadays, we can observe a steady increase in the incidence of malignant neoplasms. Many data indicate an increase in the number of cases also in the group of children and adolescents.

The development of diagnostic and therapeutic methods contributes to a steady increase in the percentage of cured children. Therefore, the fitness and physical activity of people with a history of cancer, are becoming more important both in everyday and professional life. The prevention and promotion of regular physical activity during cancer disease are essential. Children with cancer have an insufficient level of physical activity (PA) and do not undertake any form of exercise which could improve their cardiorespiratory parameters.

THE AIM OF THE STUDY: The aim of the doctoral dissertation, which is a thematically coherent collection of three original articles, was to assess the impact of interactive video games on the physical activity level and cardiorespiratory fitness of children undergoing treatment for malignant tumors.

METHODS: The international questionnaire of health behavior in school-aged children (HBSC) was used to assess the level of physical activity and sedentary behavior. The questions concerned the last seven days. The level of cardiorespiratory fitness was assessed in the ergospirometric test according to the progressive Godfrey protocol with gradually increasing load, during which the respiratory gas analysis was carried out. During the training intervention, the exercise intensity was monitored with a physical activity monitor (Polar M 430).

RESULTS: The results showed that children undergoing cancer treatment did not perform any physical activity for a total of at least 60 minutes a day and they did not meet the recommendations for an appropriate level of daily physical activity (MVPA index). The

study showed that children undergoing leukemia treatment had a reduced level of cardiorespiratory fitness. It was especially evident in comparative studies (comparison study with the results obtained in the group of healthy children). The evaluation of the obtained values of heart rate (HR) in particular phases of training with the use of IVG showed that in the examined group children achieved the assumed values of training HR. It was particularly visible in the final stages of the subsequent phases of IVG training. The required HR values in each training phase (70% HR_{peak}, 75% HR_{peak}, and 80% HR_{peak}) were achieved and in some cases even exceeded. Sometimes children even achieved higher HR values than predicted. In the final phase of the rehabilitation program with the use of IVG, all children from the intervention group achieved the assumed HR values. It confirmed that IVG training was safe and possible to be carried out in the group of children with leukemia. In the follow-up study 14 months after the IVG intervention, a statistically significant increase was observed in the level of cardiorespiratory fitness in the intervention group compared to the values achieved by children before the intervention. However, in the control group, there was no statistically significant difference in the level of cardiorespiratory fitness between the baseline and the examination conducted 14 months later.

CONCLUSIONS: The results of conducted studies allowed for the following conclusions:

1. The level of physical activity of children during and after cancer treatment was significantly lower compared to the PA level of healthy children.

2. During intensive treatment and hospitalization, children treated for cancer disease did not meet the recommendations regarding the appropriate level of the MVPA index.

3. The level of cardiorespiratory fitness of children undergoing treatment for leukemia was significantly lower than the values predicted for the group of healthy children.

4. IVG training with the intensity determined during the baseline cardiorespiratory fitness test was safe, feasible, and possible to be carried out in hospital settings during the intensive leukemia treatment.

5. IVG training applied during hospitalization increased the level of physical activity in children and improved their MVPA index.

6. The results of the follow-up study carried out 14 months after the end of the IVG training showed that the children continued their physical activity, and the level of PA was comparable to the level of PA achieved during the IVG training intervention.

7. In the study group there was a statistically significant increase in the level of cardiorespiratory fitness between the baseline and the follow-up study (14 months later).

8. In the control group there was no statistically significant difference in the level of cardiorespiratory fitness between the baseline and the follow-up study (14 months later).

9. The level of physical activity in the study carried out 14 months after IVG intervention was not statistically significant between the study and control groups.

10. In the study carried out 14 months after IVG intervention, the level of cardiorespiratory fitness of children from the study and control groups did not differ statistically significantly.

IX ZAŁĄCZNIKI

1. Artykuł nr 1 wchodzący w skład przedstawionego osiągnięcia naukowego o tytule: *Physical Activity and Quality of Life of Healthy Children and Patients with Hematological Cancers.*

2. Artykuł nr 2 wchodzący w skład przedstawionego osiągnięcia naukowego o tytule: *Peak Oxygen Uptake and Exercise Capacity of Children Undergoing Leukemia Treatment.*

3. Artykuł nr 3 wchodzący w skład przedstawionego osiągnięcia naukowego o tytule: *Interactive Video Games as a Method to Increase Physical Activity Levels in Children Treated for Leukemia*

4. Oświadczenia autora pracy i współautorów (prof. dr. hab. Marka Woźniewskiego oraz dr. hab. Iwony Malickiej prof. AWF).

Załącznik nr 1

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Physical Activity and Quality of Life of Healthy Children and Patients with Hematological Cancers

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Abstract: The aim was to assess the level of physical activity and the quality of life of children undergoing cancer treatment, during and after the completion of the treatment. Eighty-eight children aged 11–15 were enrolled. Three groups of children were assessed, i.e., children undergoing cancer treatment ($n = 30$), children after cancer treatment ($n = 28$), and healthy children ($n = 30$). The level of physical activity in children was assessed using the questions from the Health Behavior in School-Aged Children (HBSC) questionnaire. The assessment of children's quality of life was conducted using the KIDSCREEN-10 Index. The chi-square test was used to assess the statistical significance of the differences in the results between the study groups in the case of both HBSC and KIDSCREEN-10 questionnaires. Children undergoing cancer treatment did not perform any physical activity of at least 60 min (in total) per day, during the week. Therefore, they did not meet the recommendations related to the appropriate level of daily physical activity (Moderate-to-Vigorous Physical Activity; MVPA). Children after cancer treatment and healthy children significantly more frequently undertook physical activity. The quality of life of children with cancer is significantly lower and different from the quality of life of healthy children.

Keywords: physical activity level; quality of life; child health; cancer

1. Introduction

The increasing effectiveness of treatment in pediatric oncology results in the fact that more children are successfully cured or achieve a long-term remission [1]. In light of the above information, future health and the quality of life of these children become more significant. Treatment of childhood cancer is long-lasting and aggressive. Frequent hospitalizations, invasive examinations, lack of contact with peers, and subordination of life to the disease [2,3] lead to a decreased quality of life [4] and a significant reduction in the level of physical activity [5]. The prolonged periods of inactivity contribute to the reduced capacity of the cardiovascular system, reduced bone mineral density and muscle strength, and deterioration of physical fitness [6–8]. Decreased ability to perform daily activities [9] adversely affects the well-being and significantly reduces the quality of life of children undergoing treatment [4]. As a result, the dynamic development of the child's psychological and social spheres during the treatment and at the time of recovery is disturbed [10,11].

Physical activity in children was previously an underrated part of the cancer treatment process. Currently, this approach has changed and physical activity is promoted at every stage of the treatment [12–14]. Studies revealed that physical activity in a child undergoing cancer treatment prevents many functional deficits and shortens the convalescence time [15]. Additionally, it has a beneficial effect on the specific immune response in children, after a bone marrow transplantation [16].

Due to their health conditions, children undergoing cancer are reluctant to undertake physical activity, which is an essential part of the child's balanced development [17]. There are many guidelines on the forms of physical activity for adult cancer patients, which are clearly defined [18]. In the group of children with cancer, no uniform recommendations have been developed yet. Studies showed a positive effect of physical exercise on the physical and psychosocial spheres in children. Adverse effects related to such activities have not been observed. Children undergoing cancer treatment should also undertake physical activity and should not be deprived of it [12–16].

It was revealed that the physical activity of children after cancer is still reduced and it is not only due to treatment-related adverse effects but also due to bad habits acquired during cancer and the overly cautious attitude of parents and educators [19]. An adequate level of physical activity in childhood determines the fitness and health of adults. It is also a preventive factor for the diseases of affluence.

Promotion of physical activity in children during and after cancer treatment is of great importance. The physical activity in such patients is not contraindicated. Quite the contrary, it should be promoted. Adjusting the type and intensity of exercise to individual abilities of each child and to the stage of cancer treatment is also of crucial significance [12,20,21]. Carefully selected exercise programs can help alleviate the adverse effects of cancer treatment, minimize functional deficits, and significantly reduce the convalescence time [15].

The present recommendations on the level of physical activity are mainly related to healthy children. The recommended intensity of physical activity that is necessary for the proper development of a child should be at least at the moderate level, minimum 5 days per week, each lasting at least 1 h [22,23]. Studies confirm a beneficial effect of moderate to vigorous physical activity (MVPA) on health indicators in children and adolescents [22,24]. However, they are usually related to meeting the recommendations on the appropriate level of MVPA in the group of healthy children [25]. The importance of MVPA should not be overestimated. Some reports indicate that physical activity of light intensity has a positive effect on children's health indicators [26]. Activity in any form is important to children.

The aim of the study was to assess the level of physical activity and the quality of life of children during and after cancer treatment. This assessment might help to develop rehabilitation programs and to determine an individual's level of physical activity.

2. Materials and Methods

2.1. Study Group

Eighty-eight children aged 11–15 were enrolled in the study (Table 1). Three groups of children were examined, i.e., children undergoing cancer treatment, children after cancer treatment, and healthy children. The groups were selected in such a manner as to show to what extent cancer and its treatment influenced the daily activity and the quality of life of children. The selection of such groups also allowed to determine to what extent these parameters were different from the results of healthy children. Additionally, it allowed us to assess whether past cancer treatment affected the physical and psychosocial spheres in children. The inclusion and exclusion criteria were defined (Table 2).

Table 1. Characteristics of the study groups.

Parameter	Group I Children Undergoing Treatment	Group II Children after Treatment	Group III Healthy Children
Age [years]	13 ± 1.5	13 ± 1.9	13 ± 0.47
Weight [kg]	47 ± 13	51 ± 11	50 ± 10
Height [cm]	156 ± 13	159 ± 12	163 ± 8.7

Table 2. Inclusion and exclusion criteria in the study groups.

Group I	Group II	Group III
	Inclusion Criteria	
- diagnosed cancer disease - hospital treatment - duration of hospital stay > 7 days - chemotherapy	- past history of cancer - completed cancer treatment > 1 year - past chemotherapy - no contraindications to physical activity confirmed by the medical certificate	- no history of cancer disease - no medical contraindications to participate in physical education classes in school
	Exclusion Criteria	
- lack of informed consent from parents or the child - intellectual disability of the child	- lack of informed consent from parents or the child - intellectual disability of the child - practicing competitive sports	- lack of informed consent from parents or the child - intellectual disability of the child - practicing competitive sports

Group I consisted of the patients of the Department of Pediatric Bone Marrow Transplantation, Oncology and Hematology, University Teaching Hospital, Wrocław, Poland. Group II was comprised of children who were the participants of the Lower Silesian Onco-Olympic Games of Children and Adolescents (sports competition aimed at promoting physical activity among children treated for cancer). Group III consisted of junior high school students with a negative history of cancer.

The groups were comparable in terms of the number of subjects, age, gender, weight, and height (Table 1). Group I consisted of 30 children, i.e., 13 girls and 17 boys who were hospitalized due to acute lymphoblastic leukemia ($n = 24$) and acute myeloid leukemia ($n = 6$). Chemotherapy was the form of treatment in Group I (mean treatment duration 2.2 years). Group II consisted of 28 children after cancer treatment (girls $n = 17$, boys $n = 11$). These subjects had been previously diagnosed with acute lymphoblastic leukemia ($n = 16$), acute myeloid leukemia ($n = 4$), Ewing's sarcoma ($n = 3$), and Hodgkin's lymphoma ($n = 5$). Chemotherapy was the basic form of treatment in Group II. The time from treatment completion in children from Group II was > 1 year. Group III ($n = 30$) included healthy children with no history of cancer or other chronic diseases (girls $n = 14$, boys $n = 16$).

2.2. Research Methods

The level of physical activity of the subjects was assessed using the questions from the Health Behavior in School-Aged Children (HBSC) questionnaire from the section related to health behavior. The questions were connected with physical activity within the last seven days. We assessed the number of days in a week during which children exercised for at least 60 min—MVPA. The task of the subjects was to estimate the total daily amount of time they spent on physical activity. The frequency and duration of significant physical effort were also assessed. The effort was defined as any activity that resulted in an increased heart rate, temporary shortness of breath, and increased sweating. The questionnaire also included three questions related to sedentary behavior and the time spent in a sitting position in front of a TV or a computer screen.

The assessment of the quality of life of the subjects was conducted using the KIDSCREEN-10 (the short health-related quality of life questionnaire). The short version of the questionnaire assesses the health-related quality of life of children and adolescents. The answers are given based on the last seven days. Subjective feelings of the children related to the condition of their physical and mental health were assessed on the basis of the first four questions of the questionnaire. The relationships with parents and peers, the child's autonomy, and feelings related to the school environment were also assessed.

In each study group, an anonymous questionnaire survey was conducted in the traditional paper form.

2.3. Ethics

The study was approved by the Local Bioethics Committee at the University of Physical Education in Wroclaw, Poland (consent no 22/2018).

2.4. Statistical Analysis

Statistical analysis was performed in GraphPad Prism 7 (Institute of Immunology and Experimental Therapy, Wroclaw, Poland). The normality of the data distribution was assessed using the Shapiro-Wilk test. Parameters defining the characteristics of the study groups were presented by providing the descriptive statistics, such as arithmetic mean, median, and lower and upper quartile. The chi-square test was used to assess the statistical significance of the differences in the results between the study groups in the case of HBSC and the KIDSCREEN-10 questionnaires. The level of significance was set at $p < 0.05$.

3. Results

3.1. Physical Activity Level

Children undergoing treatment did not perform any physical activity during a week that lasted at least 60 min in total daily and, therefore, they did not meet the recommendations related to the appropriate level of daily physical activity (MVPA). After completing cancer treatment, the subjects declared that they were physically active at least once a week for a minimum period of 60 min per day, compared to children undergoing treatment. Healthy children (40%) undertook such physical activity at least 5 days per week (Table 3).

Table 3. Physical activity level in children. The percentage of the respondents providing a given answer [%].

Question/Variable	Answer	Group I	Group II	Group III
The number of days per week in which the child performed the physical activity of at least 60 min (MVPA)—HBSC 1	0 days	100.00	17.9	-
	1 day	-	10.7	-
	2 days	-	25.0	-
	3 days	-	21.4	20.0
	4 days	-	-	40.0
	5 days	-	-	20.0
	6 days	-	7.1	6.7
	7 days	-	17.9	13.3
p	* <0.0001	** <0.0001	*** <0.0001	**** <0.0001
Frequency of undertaking vigorous physical activity—HBSC 2	daily	-	14.3	16.7
	4–6 times/week	-	7.1	36.7
	2–3 times/week	-	28.6	33.3
	once a week	-	17.9	10.0
	once a month	-	10.7	-
	< once a week	23.3	7.1	3.3
	never	76.7	14.3	-
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.026
The number of hours per week devoted to vigorous physical activity—HBSC 3	none	80.0	14.3	-
	about 30 min	20.0	21.3	-
	about 1 h	-	17.9	-
	about 2 h	-	17.9	10.0
	about 3 h	-	10.7	23.3
	about 4 h	-	3.6	36.7
	about 5 h	-	3.6	16.7
	about 6 h	-	-	3.3
	about 7 h or more	-	10.7	10.0
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.0003

Chi square test: * all groups, ** Group I versus Group III, *** Group I versus Group II, **** Group II versus Group III.

In the majority of cases, children undergoing cancer treatment did not undertake significant physical activity that led to general fatigue. After completing the cancer treatment, the subjects spent at least 30 min per week doing vigorous physical activity. Eighty percent of children undergoing cancer treatment did not undertake vigorous physical activity. Thirty six percent of children undertook vigorous physical activity even 4–6 times per week, which lasted at least 2 h per week (Table 3).

Almost 90% of children undergoing cancer treatment spent at least two hours per day in front of a TV screen. Children after treatment completion and healthy subjects spent significantly less time during the day in front of a TV screen. A comparable number of the subjects spent more than 2 h per day watching TV (67.8% of children from Group II and 60.0% from Group III; Table 4).

Table 4. Time spent in front of a computer/TV screen per week. The percentage of respondents providing a given answer [%].

Question/Variable	Answer	Group I	Group II	Group III
The number of hours in front of a TV screen per week—HBSC 4.1	none	-	17.9	16.7
	about 30 min/day	-	14.3	6.7
	about 1 h/day	13.3	-	16.7
	about 2 h/day	40.0	25.0	36.5
	about 3 h/day	33.4	21.4	-
	about 4 h/day	13.3	10.7	6.7
	about 5 h/day	-	7.1	6.7
	about 6 h/day	-	-	6.7
	about 7 h or more/day	-	3.6	3.3
p	* 0.0101	** 0.0101	*** 0.0102	**** 0.0652
The number of hours spent playing games per week—HBSC 5.1	none	33.3	32.2	33.4
	about 30 min/day	10.0	10.7	3.3
	about 1 h/day	40.0	7.1	13.3
	about 2 h/day	16.7	10.7	13.3
	about 3 h/day	-	14.3	23.4
	about 4 h/day	-	7.1	10.0
	about 5 h/day	-	3.6	-
	about 6 h/day	-	3.6	-
	about 7 h or more/day	-	10.7	3.3
p	* 0.0324	** 0.0132	*** 0.0169	**** 0.6676
The number of hours spent in front of a computer screen per week—HBSC 6.1	none	-	17.9	6.7
	about 30 min/day	43.3	-	6.7
	about 1 h/day	56.7	32.1	13.3
	about 2 h/day	-	17.9	23.3
	about 3 h/day	-	14.3	10.0
	about 4 h/day	-	3.6	20.0
	about 5 h/day	-	3.6	10.0
	about 6 h/day	-	-	6.7
	about 7 h or more/day	-	10.6	3.3
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.1050

Chi square test: * all groups, ** Group I versus Group III, *** Group I versus Group II, **** Group II versus Group III.

The whole group of children undergoing cancer treatment used a computer for 30–60 min per day. Almost 70% of children from Group I reported that they also played games in addition to performing other activities that required the use of a computer. The subjects from Groups II and III spent significantly more time in front of a computer screen. The vast majority of children from Groups II and III spent at least one hour per day in front of a computer screen (82.1% and 86.6%, respectively; Table 4).

On off-days, children from Group I spent more time in front of a TV screen (at least 2 h per day) compared to other days of the week. Almost 68% of the subjects from Group II and 73% of the subjects from Group III spent at least 2 h per day in front of a television screen on off-days. The amount of time devoted to playing games on off-days increased in each group compared to other days of the week. The percentage of the children who played games at least 30 min per day was as follows—86.7% from Group I, 78.5% from Group II, and 83.3% from Group III (Table 5).

Table 5. Time spent in front of a computer/TV screen on off-days. The percentage of respondents providing a given answer [%].

Question/Variable	Answer	Group I	Group II	Group III
The number of hours in front of a TV screen at the weekend—HBSC 4.2	none	-	14.3	16.7
	about 30 min/day	-	10.7	3.3
	about 1 h/day	-	7.1	6.7
	about 2 h/day	20.00	14.3	6.7
	about 3 h/day	50.00	17.9	33.2
	about 4 h/day	30.00	25.0	16.7
	about 5 h/day	-	3.6	6.7
	about 6 h/day	-	-	3.3
	about 7 h or more/day	-	7.1	6.7
p	* 0.0876	** n/a	*** n/a	**** n/a
The number of hours spent playing games at the weekend—HBSC 5.2	none	13.3	21.5	16.7
	about 30 min/day	30.0	7.1	3.3
	about 1 h/day	16.7	-	6.7
	about 2 h/day	26.7	17.9	10.0
	about 3 h/day	13.3	7.1	20.0
	about 4 h/day	-	14.3	10.0
	about 5 h/day	-	10.7	10.0
	about 6 h/day	-	7.1	10.0
	about 7 h or more/day	-	14.3	13.3
p	* 0.0077	** 0.0028	*** 0.0021	**** 0.7355
The number of hours spent in front of a computer screen at the weekend—HBSC 6.2	none	-	10.7	-
	about 30 min/day	-	7.1	3.3
	about 1 h/day	43.3	3.6	3.3
	about 2 h/day	56.7	25.0	23.3
	about 3 h/day	-	17.9	16.7
	about 4 h/day	-	17.9	10.0
	about 5 h/day	-	7.1	16.7
	about 6 h/day	-	-	6.7
	about 7 h or more/day	-	10.7	20.0
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.4277

Chi square test: * all groups, ** Group I versus Group III, *** Group I versus Group II, **** Group II versus Group III.

3.2. *Quality of Life*

All of the subjects who were undergoing treatment for cancer did not feel fit or well. The children who completed cancer treatment assessed their well-being and physical fitness significantly better. Almost 36% of the subjects from Group II reported at least very good well-being and physical fitness, whereas 83.3% of the children from Group III assessed their health as at least very good. All children undergoing cancer treatment reported the lack of energy and fatigue and 86% of the subjects from Group II reported at least a frequent feeling of energy and willingness to undertake the physical activity. Seventy percent of the healthy children reported an increased energy level and willingness to undertake physical activity. All subjects undergoing cancer treatment experienced sadness within the last 7 days. The subjects who completed the treatment and the healthy subjects reported the absence of low mood within the last 7 days (35.7% and 30%, respectively). The distribution of the answers of the subjects from Groups II and III to the question related to the mood and the feeling of sadness within the last seven days was similar. A comparable number of the subjects from each group rarely felt lonely (Table 6).

Table 6. Self-assessment of physical and mental health (KIDSCREEN). The percentage of respondents providing a given answer [%].

Question/Variable	Answer	Group I	Group II	Group III
Feeling fit and well—KID 1	not at all	40.00	3.6	-
	slightly	60.00	7.1	6.7
	moderately	-	53.6	10.0
	very	-	14.3	53.3
	extremely	-	21.4	30.0
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.0022
Feeling of strength and energy—KID 2	never	23.3	-	-
	seldom	76.7	14.3	6.7
	quite often	-	46.4	23.3
	very often	-	14.3	26.7
	always	-	25.0	43.3
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.1364
Feeling of sadness—KID 3	never	-	35.7	30.0
	seldom	-	46.4	56.7
	quite often	40.00	17.9	13.3
	very often	60.00	-	-
	always	-	-	-
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.7302
Feeling of loneliness—KID 4	never	26.7	-	53.4
	seldom	50.0	50.0	40.0
	quite often	23.3	39.3	3.3
	very often	-	10.7	-
	always	-	-	3.3
p	* <0.0001	** 0.0367	*** 0.0078	**** <0.0001

Chi square test: * all groups, ** Group I vs. Group III, *** Group I vs. Group II, **** Group II vs. Group III.

The level of autonomy of the subjects undergoing cancer treatment was significantly lower compared to the subjects from Groups II and III. As many as 43% of the subjects undergoing cancer treatment reported that they had an insufficient amount of time for themselves. The vast majority of the subjects from Groups II (64.3%) and III (66.7%) reported that they had time for themselves at least very often (Table 7).

Table 7. The ability to set standards for yourself (the autonomy of the child). The percentage of respondents providing a given answer [%].

Question/Variable	Answer	Group I	Group II	Group III
Having enough time for yourself—KID 5	never	-	-	3.3
	seldom	43.3	7.1	6.7
	quite often	53.4	28.6	23.3
	very often	3.3	39.3	36.7
	always	-	25.0	30.0
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.8699
Performing the things that you want to do—KID 6	never	3.3	3.6	3.3
	seldom	30.0	7.1	3.3
	quite often	63.4	17.9	26.7
	very often	3.3	50.0	40.0
	always	-	21.4	26.7
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.8446

Chi square test: * all groups, ** Group I versus Group III, *** Group I versus Group II, **** Group II versus Group III.

The subjects from Groups I, II, and III reported very good relations with their parents. The subjects undergoing cancer treatment mostly reported an insufficient contact with their peers (Table 8).

Table 8. Relationships with parents and peers. The percentage of respondents providing a given answer [%].

Question/Variable	Answer	Group I	Group II	Group III
Being treated fairly by parents/Good relations with parents—KID 7	never	-	-	-
	seldom	-	-	-
	quite often	-	7.1	20.00
	very often	10.00	42.9	13.3
	always	90.00	50.00	66.7
p	* 0.0008	** 0.0008	*** 0.0032	**** 0.0302
Good relations with peers, fun—KID 8	never	40.00	3.6	6.7
	seldom	60.00	7.1	3.3
	quite often	-	14.3	13.3
	very often	-	53.6	40.0
	always	-	21.4	36.7
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.6618

Chi square test: * all groups, ** Group I versus Group III, *** Group I versus Group II, **** Group II versus Group III.

As many as 90% of the subjects undergoing cancer treatment reported the lack of satisfactory results at school. Children after the completion of cancer treatment and healthy subjects reported significantly greater satisfaction with their school results. All subjects from Group I reported decreased concentration and attention-related problems. The subjects from Groups II and III reported good concentration (89.3% and 90%, respectively) (Table 9).

Table 9. School-related environment, concentration, and attention. The percentage of the respondents providing a given answer [%].

Question/Variable	Answer	Group I	Group II	Group III
Positive feelings related to the school environment—KID 9	not at all	26.7	-	-
	slightly	63.3	3.6	3.3
	moderately	10.0	42.9	30.0
	very	-	39.2	40.0
	extremely	-	14.3	26.7
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.6284
Ability to pay attention—KID 10	never	23.3	3.6	-
	seldom	76.7	7.1	10.0
	quite often	-	46.5	23.4
	very often	-	21.4	33.3
	always	-	21.4	33.3
p	* <0.0001	** <0.0001	*** <0.0001	**** 0.2938

Chi square test: * all groups, ** Group I versus Group III, *** Group I versus Group II, **** Group II versus Group III.

4. Discussion

Cancer treatment process is long-lasting and debilitating. It adversely affects the level of physical activity and the quality of life of pediatric patients and survivors.

Aggressive protocols for anticancer therapy lead to many adverse effects that are observed during treatment and many years after its completion. Sarcopenia is one of the most common problems resulting from the catabolic action of several chemotherapeutic agents. The occurrence of muscular atrophy results in reduced muscle strength and a significant decline in physical performance [27,28]. Limited exercise capacity enhances protective lifestyle and the cessation of daily physical activity [29].

Treatment duration of childhood cancer significantly reduces the frequency of performing even light physical activity and recreational sports, such as everyday walks and playing with peers in the open air. The level of physical activity of children with cancer also decreases significantly compared to the time before the disease. Reduced level of physical activity is observed in children suffering from cancer, during their stay at home and during hospitalization, which was found to be reduced by 74% to 91%, respectively [30].

During the cancer treatment, none of the subjects met the recommendations related to the appropriate level of physical activity per week. These criteria were met by 25% of the subjects after the completion of treatment, while they were met by 40% of the healthy children. Similar results were presented by Tan et al. Their subjects undergoing cancer treatment did not undertake the physical activity lasting a total of at least 60 min daily (MVPA) [5]. Additionally, Anzar et al. confirmed the decreased MVPA. In their study group, none of the children performed a 60-min physical effort for a minimum of five days per week [19].

The subjects, regardless of the group, preferred a sedentary lifestyle; all subjects also reported that they used a computer every day. In this case, however, both the subjects after cancer treatment and the healthy subjects spent significantly more time on this activity. It probably resulted from more activities related to learning and communication with peers. The amount of time in front of a computer/TV screen increased in each group during the days free of classes.

Lack of physical activity and the majority of time being spent in the sitting position in children with cancer, significantly reduced CRF. It is manifested by a lower peak oxygen uptake (VO2peak) in relation to the normal range (31.7 versus 45.1 mL/kg/min). Braam et al. showed that over 50% of children undergoing cancer treatment had a VO2peak below the normal value. Cardiorespiratory fitness is significantly associated with the level of physical activity and sedentary habits—any additional activity per minute results in an increase in VO2peak by 0.05 mL/kg/min, whereas each additional minute of sitting reduces VO2peak by 0.06 mL/kg/min [21].

A complete lack of physical activity among cancer children is a decisive factor that negatively affects the quality of life of these children and forms the belief about lack of independence [4]. Our study results showed that the children undergoing cancer treatment presented with a lack of well-being and decreased physical fitness. Children after cancer treatment had significantly better well-being and physical fitness.

Significant deterioration of physical and mental health, especially in the group of children who underwent chemotherapy and radiotherapy, was also confirmed by Bhat et al. Children manifested disorders related to emotional and social functioning [31].

In our studies, as many as 90% of the subjects undergoing cancer treatment reported learning difficulties and all of these subjects reported attention- and concentration-related problems. Both, the subjects after cancer treatment and the healthy children reported significantly greater satisfaction with their results at school, which is in line with observations of Bhat et al. Lack of contact with peers and the social environment might be the reason for social isolation and future communication problems [31].

All subjects undergoing cancer treatment were also characterized by excessive fatigue and a frequent lack of energy. Davies et al. reported that cancer treatment-related fatigue additionally enhances a protective lifestyle and the cessation of physical activity. Children manage their dwindling energy and minimized further loss of energy through preserving strategies, which include reduced physical activity and a sedentary lifestyle [32].

Physical activity is a factor that significantly determines the quality of life of children undergoing cancer treatment, which is confirmed by Speyer et al. and San Juan et al. Children who are physically active during hospitalization are characterized by a higher quality of life, and their self-esteem and activity-related satisfaction are improved [13,33].

Sadness is predominant in the subjects undergoing cancer treatment, compared to the other study groups. Moody et al. showed that a lack of contact with peers, health-related, and future-related anxiety and excessive concern of parents and of the medical personnel adversely affect satisfaction and the well-being of hospitalized children [34].

The effectiveness of treatment in pediatric oncology is increasing, and hence there is a higher number of survivors. Consequently, issues related to future health and the quality of life of these individuals become more significant. Individuals who were diagnosed in childhood with cancer are characterized by an increased risk of cardiovascular diseases [35], obesity [36], osteoporosis [37], and premature death [38]. Currently, physical activity is recommended at every stage of cancer treatment despite the fact that it remains an underappreciated component of cancer prevention and therapy [12,39]. Children with cancer who undertake physical activity during the treatment process are able to participate more actively in social and professional life, in future.

5. Limitations

Certain study limitations should be considered. Further studies are warranted to confirm the results of the present study. Such studies should be conducted on larger samples with longer follow-up periods. The results of other studies assessing the level of physical activity of children undergoing treatment for cancer are in line with the results of our study [19,30]. The questionnaire methods are easily accessible and are quick diagnostic tools. However, the use of objective methods to assess the level of physical activity, such as an accelerometer, would practically allow the assessment of the activity and sedentary behavior in children. Another limitation is also related to the fact that the subjects presented with different diagnoses, particularly in the group of children after the completion of cancer treatment.

6. Future Research Directions

Further studies should focus on developing and verifying the effectiveness of the training program in children undergoing cancer treatment. Such a program should be directed primarily at increasing the level of daily physical activity and counteracting the sedentary lifestyle in this group of patients. The different forms of physical activity should be personalized, diverse, and attractive and should meet the expectations of pediatric patients. Any form of physical activity is important, including low-intensity activity, such as games or plays.

Educational programs for children, parents, and health professionals should be created. An overly cautious approach of caregivers of cancer children might lead to a situation when the daily life of these patients is subordinated to the disease. As a result, these children lose their natural need for physical activity. Promotion of physical activity should occur at every stage during and after cancer treatment.

7. Conclusions

Cancer and its treatment significantly reduce the level of physical activity in children. The subjects undergoing treatment for cancer had a significantly lower level of physical activity compared to children who have already undergone cancer treatment and healthy children. The quality of life of children with cancer is significantly lower and is definitely different from the quality of life of healthy children. Our subjects with cancer experienced deterioration in both physical and mental health. The completion of cancer treatment resulted in increased physical activity and the quality of life. However, the values of these parameters were lower compared to the group of healthy children.

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Peak Oxygen Uptake and Exercise Capacity of Children Undergoing Leukemia Treatment

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Abstract: The aim of the study was to assess the exercise capacity (VO_{2peak}) of children undergoing leukemia treatment and to compare the results with healthy children. Furthermore, we assessed the influence of treatment methods on the level of exercise capacity and the increase in sedentary behaviors. The study comprised 21 children (12 boys and 9 girls) undergoing treatment for acute lymphoblastic leukemia (ALL) ($n = 13$) and acute myeloid leukemia (AML) ($n = 8$). The subjects were aged 7–13 years (mean age 10.7, SD 2.0 years). Cardiorespiratory fitness was assessed by using the ergospirometry test. Progressive Godfrey protocol was performed. The level of physical activity was assessed by using the questions from the Health Behavior in School-Aged Children (HBSC 2018) questionnaire. The study results showed that children undergoing leukemia treatment were characterized by a reduced level of exercise capacity. The measured value of VO_{2peak} in the group of treated children was, on average, 22.16 $mL \cdot kg^{-1} \cdot min^{-1}$. The mean values of VO_{2peak} predicted for this age group were 45.48 $mL \cdot kg^{-1} \cdot min^{-1}$ (SD, 3.8). The measured value of VO_{2peak} in the study group with the division into age groups was, on average, 21.21 $mL \cdot kg^{-1} \cdot min^{-1}$ in the group of children aged 7–10 years. In the group of children aged 11–13 years, this parameter was 22.64 $mL \cdot kg^{-1} \cdot min^{-1}$. Lack of physical activity and failure to meet the standards for the minimum level of weekly physical activity (MVPA index—moderate-to-vigorous physical activity) probably contribute to the deterioration in exercise capacity level of cancer-treated children.

Keywords: cardiorespiratory fitness; children; leukemia; physical activity; morphotic parameters; blood

1. Introduction

Leukemia is one of the most common childhood cancers, and the effectiveness of its treatment is steadily increasing. However, cancer therapy is aggressive, and it leads to many side effects that occur during treatment [1,2] and many years after its completion [3]. One of the most common complications of cancer treatment is a large decrease in morphotic parameters of blood. Low blood counts, especially the decrease in hemoglobin concentration, are the reason of insufficient oxygen transport to the working muscles and other tissues [4,5]. Anemia and reduced blood perfusion in skeletal muscles are the causes of insufficient oxygen supply during physical effort, which leads to a reduction in cardiorespiratory fitness that manifests by decreased exercise tolerance [6]. As a result, children who undergo cancer treatment reduce their daily physical activity and prefer a sedentary lifestyle [7]. Such habits and a reduced level of exercise capacity can persist in adult childhood-cancer survivors [8].

Intensive anticancer therapy leads to a significant decrease in exercise capacity parameters in children, which was confirmed by San Juan et al. Peak oxygen uptake values (VO_{2peak}) in the group of children with acute lymphoblastic leukemia (ALL) undergoing the maintenance phase of the treatment were significantly lower when compared to the group of healthy peers (25.3 ± 6.5 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 31.9 ± 6.8 $mL \cdot kg^{-1} \cdot min^{-1}$) [9]. These results confirm the essence of the treatment-induced problem with cardiorespiratory fitness impairment and the insufficient implementation of rehabilitation methods to combat the problem of inactivity. It has also been shown that the improvement in exercise capacity parameters increases the survival rate, while reduced exercise capacity already at the level of 3.5 ($mL \cdot kg^{-1} \cdot min^{-1}$) contributes to the decrease in survival rate by 12% [10].

During anticancer therapy, children often participate in rehabilitation activities. However, it is primarily aimed at relieving the symptoms of treatment, such as reducing contractures and muscle atrophy. Children who undergo treatment are not included in a comprehensive program. The rehabilitation is often aimed only at reducing patients' temporary problems. Exercise is rarely used to keep children physically active and ensure at least a moderate level of exercise capacity. It is crucial to implement aerobic exercise programs at the very beginning of treatment, to prevent an excessive decrease in VO_{2peak} [11].

There are many studies that confirm the beneficial effects of aerobic exercise programs in the group of children undergoing cancer treatment. They can also prevent the development of long-term deficits in cardiorespiratory fitness and peak oxygen values if they are implemented early [12]. The measurement of the baseline peak oxygen uptake at the beginning of the treatment allows for the assessment of the cardiorespiratory fitness and the choice of an individual aerobic exercise program. Periodic follow-up and monitoring of the cardiorespiratory parameters allow the modification of the individual rehabilitation program to the current condition of children [13]. It is important to compare the level of exercise capacity of treated children with the results of healthy children. This will show how the extent of cancer disease has reduced the capacity level of children undergoing leukemia treatment.

The Cardio-Pulmonary Exercise Test (CPET) is a valuable tool. However, it is relatively rarely used in oncology clinics due to costs, the need for special equipment for respiratory gas analysis, and trained personnel [14]. CPET is one of the methods used to assess exercise tolerance, which reflects the level of cardiorespiratory fitness. This test is the most reliable and commonly used tool to measure the peak oxygen uptake value using respiratory gas analysis [15]. This measurement is considered by the World Health Organization to be the gold standard for assessing aerobic fitness [16]. Peak oxygen uptake is regarded as the most objective and reliable parameter for assessing exercise capacity. CPET results provide clinically useful information and are helpful in visualizing the body's physiological responses to a given physical effort [15,17]. This test performed in children during leukemia treatment is also a useful additional measurement for assessing the severity of cardiopulmonary disorders [18]. The results of these clinical trials may be useful in creating new, or improving the already existing, models of rehabilitation in children during treatment. Such models should prevent the excessive decline in exercise capacity among children both during and after treatment.

The aim of the study was to assess the peak oxygen uptake in children undergoing leukemia treatment and to compare the results with the group of healthy children. Furthermore, we assessed the influence of treatment methods on the level of exercise capacity in children and sedentary behaviors.

2. Materials and Methods

2.1. Study Group

A total of 30 children were recruited in the research. Four children refused to take part in the cardiorespiratory fitness test. Two children manifested the symptoms of prolonged malaise. Moreover, on the research day, in three children, the level of platelet count was too low to take physical effort.

The study was comprised of 21 children (12 boys, 9 girls) undergoing treatment for ALL (n = 13) and acute myeloid leukemia (AML) (n = 8). The subjects were aged 7–13 years (mean age 10.7, SD 2 years; mean height 144, SD 16 cm; mean weight 41.28, SD 13.82 kg) (Table 1).

Table 1. Patient characteristics by sex.

Variables	All Participants n = 21		Boys n = 12		Girls n = 9	
	Mean	SD	Mean	SD	Mean	SD
Determinant variables						
Age (years)	10.7	2.0	10.7	2.1	10.7	2.0
Height (cm)	144.0	16.0	147.0	18.0	141.0	13.0
Weight (kg)	41.28	13.82	42	14.99	40.32	12.91
Treatment duration (months)	6.0	2.0	6.0	2.0	6.0	1.0
HGB (g/dL) *	8.34	0.18	8.32	0.18	8.36	0.19
PLT (G/L) *	157.3	66.15	135.8	71.59	186	47.69
RBC (T/L) *	3.49	0.3	3.46	0.32	3.55	0.29
WBC (G/L) *	2.1	0.96	2.29	1.19	1.84	0.49
HR (at rest) *	85.67	3.812	85.58	4.48	85.78	2.95
Outcome variables						
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) *	22.16	2.46	22.67	2.67	21.49	2.11
HR_{peak} *	139.5	21.32	142	24.15	136.1	17.65
VO_2 ($mL \cdot min^{-1}$) *	1628	2277	1244	293.2	2140	3511
VCO_2 ($mL \cdot min^{-1}$) *	1130	453.4	1284	461.2	924.9	372.3
VE ($L \cdot min^{-1}$) *	28.94	7.65	30.6	6.43	26.72	8.92
VE/VCO_2*	27.73	4.99	26.02	4.51	30	4.91
RQ = $VCO_{2\ exhaled}/VO_{2\ uptake}$ *	0.93	0.24	1.0	0.17	0.82	0.29
MET *	6.28	0.7	6.4	0.76	6.1	0.6
Test duration (s)	470.67	33.91	471.5	35.75	469.55	31.26

* HGB, hemoglobin level; PLT, blood platelet count; RBC, red blood cell count; WBC, white blood cell count; HR (at rest), resting heart rate; VO_{2peak},peak oxygen uptake; HR_{peak}, peak heart rate; VO_2, volume of O_2 uptake; VCO_2, volume of exhaled CO_2; VE, minute ventilation; VE/VCO_2,ventilatory equivalent of carbon dioxide; RQ, respiratory quotient; MET, metabolic equivalent of task.

The subjects were also divided into two separate groups. The criterion for the division was the age of children (7–10 years and 11–13 years). Separate descriptive statistics were used in the groups (Table 2). Children undergoing treatment for cancer disease were examined. The subjects were the patients of the Department of Pediatric Bone Marrow Transplantation, Oncology and Hematology at the University Hospital in Wroclaw, Poland. All children underwent cycles of chemotherapy which were administered in hospital settings. The mean treatment duration was 6.19 (SD, 1.63 months). No comorbidities were reported in patients such as pulmonary disease, musculoskeletal disease, osteoarthritis, or psychiatric disease.

Based on many specific tests, including cytological assessment, immunophenotyping, and genetic and molecular evaluation, children were qualified for treatment with the AIEOP-BFM ALL 2017 protocol or the AML-BFM 2012 protocol. Children treated for ALL (n = 13) were included in the AIEOP-BFM ALL 2017 protocol, while those (n = 8) treated for AML were included in the AML-BFM 2012 protocol. Depending on the type of ALL, the treatment was different according to the B-ALL (n = 7) or the T-ALL regimen (n = 6). All children after the first stage of treatment, i.e., after induction, were enrolled in three risk groups based on the following criteria: age, leukocyte count, type of leukemia, treatment response rate, remission, and cytogenetic results. Six children were enrolled in the standard risk (SR) group and 3 children in the intermediate risk (IR) group. The largest group included children who were enrolled in the high risk (HR) group (n = 12). In the study group, 13 subjects were given glucocorticoids during treatment, while 8 children were not given such drugs, which was due to the fact that different treatment protocols were used in these groups, depending on the type of the disease (ALL or AML).

Table 2. Patient characteristics by age group (7–10 and 11–13 years of age).

Variables	7–10 Years $n = 7$		11–13 Years $n = 14$	
	Mean	SD	Mean	SD
Determinant variables				
Age (years)	8.0	0.5	12.0	0.7
Height (cm)	128.0	6.0	152.0	12.0
Weight (kg)	30.13	5.156	46.86	13.46
Treatment duration (months)	6.429	1.512	6.071	1.73
HGB (g/dL) *	8.357	0.1902	8.329	0.1773
PLT (G/L) *	166	52.05	153	73.63
RBC (T/L) *	3.68	0.2312	3.409	0.2999
WBC (G/L) *	1.811	0.4956	2.245	1.118
HR at rest *	87.71	2.215	84.64	4.088
Outcome variables				
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) *	21.21	2.022	22.64	2.593
HR_{peak} *	151	6.325	152.5	12.97
VO_2 ($mL \cdot min^{-1}$) *	2667	3893	1108	331.6
VCO_2 ($mL \cdot min^{-1}$) *	1255	538.2	1068	412.3
VE ($L \cdot min^{-1}$) *	29.81	7.71	28.5	7.867
VE/VCO_2 *	25.63	5.56	28.77	4.525
RQ = $VCO_{2\,exhaled}/VO_{2\,uptake}$ *	0.891	0.3968	0.9465	0.1341
MET *	6.0	0.5715	6.414	0.742
Test duration (s)	458.4	35.59	476.8	33.95

* HGB, hemoglobin level; PLT, blood platelet count; RBC, red blood cell count; WBC, white blood cell count; HR (at rest), resting heart rate; VO_{2peak}, peak oxygen uptake; HR_{peak}, peak heart rate; VO_2-volume of O_2 uptake; VCO_2, volume of exhaled CO_2; VE, minute ventilation; VE/VCO_2, ventilatory equivalent of carbon dioxide; RQ, respiratory quotient; MET, metabolic equivalent of task.

2.2. *Research Methods*

2.2.1. Cardiorespiratory Fitness

In the initial stage of the study, anthropometric measurements were performed in each subject (height and weight). Cardiorespiratory fitness was assessed using the ergospirometry test (CPET). Progressive Godfrey protocol was performed [19]. The exercise stress test using the ergospirometer was initiated with a 3 min warm-up at 15 W (height of 120–150 cm) or 20 W (height > 150 cm). Body height >120 cm resulted in proper selection of the cycloergometer for a child.

– After a warm-up period, which prepared the body for greater effort, the test started. During the main part of the test, the load was increased at 1 min intervals by 15 or 20 W (depending on the height of the subject). During the exercise stress test, the pedal frequency was constant (60–80 rotations per minute; RPM). The peak value of exercise was defined as the moment when one of the three criteria was met and the test was then interrupted;

- The decrease in pedal frequency < 60 RPM despite the strong verbal encouragement of the researcher;
- HR_{peak} > 180 beats per minute (bpm);
- Peak respiratory exchange ratio (RER_{peak}) > 1.0.

Table 2 shows the mean peak values of HR and RQ. However, these values were not always the main criteria for the termination of the test. The level of RPM below 60 was often the criterion for terminating the test [20].

The VO_{2peak} value was adopted as the mean value from the last 30 s of the exercise stress test [20]. Due to safety reasons, the study did not assess the maximum oxygen uptake in children (VO_{2max}), but only the peak value of this parameter (VO_{2peak}). The measured VO_{2peak} values were compared with the predicted values for age and sex of the subjects [21].

The measurements of VO_2 and VCO_2 allowed the determination of the respiratory quotient (RQ) of the subjects and enabled the calculation of the physiological cost of physical exercise: $RQ = VCO_{2\,exhaled}/VO_{2\,uptake}$.

The enrollment was done by the attending physician. Moreover, each parent/legal guardian consented to the participation of the child in the study. The inclusion and exclusion criteria were defined (Table 3). Appropriate selection of the age group (7–13 years) resulted in the elimination of puberty-related factors, which could influence the examined parameters. During puberty, the exercise capacity parameters were significantly different between the groups of boys and girls.

Table 3. Inclusion and exclusion criteria in the study group.

Inclusion Criteria	Exclusion Criteria
- Diagnosed cancer disease: ALL or AML; - Hospital treatment; - Duration of hospitalization > 7 days; - Chemotherapy; - No physical disability, unassisted arrival at the examination; - Written informed consent of the parent/legal guardian for the participation in the study; - Age: 7–13 years, height > 120 cm.	- Platelet count < 20 G/L; - Hemoglobin concentration < 8 g /dL; - Infectious disease with fever > 38 °C; - Intellectual disability.

The ergospirometry system (K4b2; COSMED) was used to assess the exercise capacity parameters. This portable system is used for the measurement of pulmonary gas exchange and indirect calorimetry (VO2, VCO2, and RQ). Ergospirometer allows the measurement of O_2 and CO_2 concentrations during both inspiratory and expiratory phases.

Cycloergometer ASPEL CRG200 was used during the test. It allowed us to set the appropriate load at the programmed time intervals. The cycloergometer is designed for use with the CardioTEST stress test system and the AsTER cardiac rehabilitation system.

2.2.2. Subjective Assessment of the Physical Activity Level

Anonymous questionnaire surveys were conducted in the traditional paper form. Children who had problems with understanding the text due to age or those who could not assess the time properly were provided with the assistance of their parents or guardians to complete the survey.

The level of physical activity of the subjects was assessed by using the questions from the Health Behavior in School-Aged Children (HBSC 2018) questionnaire from the section connected with health behavior. The questions were related to the last seven days. In the beginning, we assessed what physical activity was and the characteristics of vigorous physical exercise that are the activities and tasks during which the subject experienced an increased heart rate, increased respiratory rate, or temporary breathlessness. Moderate-to-vigorous physical activity (MVPA) was assessed (i.e., the number of days a week during which children exercised for at least 60 min). Additionally, the frequency of undertaking vigorous physical activity was also assessed. The questionnaire included three questions related to sedentary behaviors, i.e., the time in a sitting position in front of a TV or computer screen, time devoted to computer/console stationary games except for movement-related games, time devoted to Internet use to contact the peers and to do homework, etc.

2.3. Ethics

The study was approved by the Local Bioethics Committee at the University of Physical Education in Wroclaw, Poland (consent no 22/2018).

2.4. Statistical Analysis

Statistical analysis was performed in the GraphPad Prism 7 (Institute of Immunology and Experimental Therapy, Wroclaw, Poland). Normality of the data distribution was assessed by using the Shapiro–Wilk test. The parameters determining the characteristics of the study group were presented by providing the descriptive statistics, including the arithmetic mean and the standard deviation. The Student's *t*-test for independent groups (unpaired *t*-test) was used to assess the statistical significance of the differences in the results between the study group and the predicted values for age and sex.

The assessment of the relationship between exercise capacity and the applied treatment protocol was checked by using the Student's *t*-test for independent variable pairs. A one-way ANOVA analysis of variance was used to assess the relationship between the level of physical capacity and the treatment regimen. It was used to compare the three regimens. The Bartlett test was applied to assess the homoscedasticity of the variables.

The assessment of the relationship between the level of exercise capacity and the risk group (to which each child included in a different treatment regimen was enrolled) was conducted. For this purpose, the Spearman's rank correlation was used. Moreover, the results of the exercise stress test were divided into subgroups according to the risk group and the Student's *t*-test for independent variable pairs was performed. Moreover, a non-parametric analysis of variance (ANOVA), i.e., the Kruskal–Wallis test for all three subvariables was performed.

The results of the HBSC surveys were presented as percentage data indicating the number of answers to particular questions. The values of the correlation of the survey results that assessed the level of physical activity and sedentary behaviors with the parameters of blood count and the heart rate were analyzed by means of the Spearman's rank correlation due to the lack of normality of the variable distribution. The significance level at $p < 0.05$ was used.

3. Results

3.1. Cardiorespiratory Fitness

The measured value of $VO_{2\,peak}$ in the group of children was, on average, 22.16 mL·kg^{-1}·min^{-1} (SD, 2.5). In the group of boys, this parameter was 22.67 mL·kg^{-1}·min^{-1} (SD, 2.7), whereas, in the study group of girls, it was 21.49 mL·kg^{-1}·min^{-1} (SD, 2.1) (Table 1). The mean value of the VO_{2peak} predicted for this age group was 45.48 mL·kg^{-1}·min^{-1} (SD, 3.8). The predicted value of VO_{2peak} in the group of healthy boys was 46.3 mL·kg^{-1}·min^{-1} (SD, 4.2), whereas in the group of healthy girls it was 44.7 mL·kg^{-1}·min^{-1} (SD, 3.4) (Figure 1).

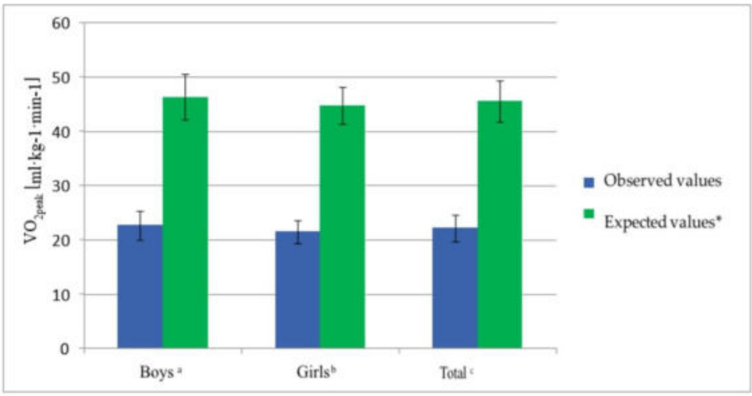

Figure 1. Measured values of VO_{2peak} compared to the predicted values for age and sex in boys, girls and the group in total. Unpaired *t*-test: [a] examined boys versus expected values $p < 0.0001$, [b] examined girls versus expected values $p < 0.0001$, and [c] general study group versus expected values $p < 0.0001$. * Based on age- and sex-predicted values [21].

The absolute difference between the measured and predicted VO_{2peak} between the groups was 23.32 mL·kg^{-1}·min^{-1}. In the groups of boys and girls, the difference was 23.63 and 23.21 mL·kg^{-1}·min^{-1}, respectively (Figure 1).

The measured value of VO_{2peak} in the study group with the division into age groups was, on average, 21.21 mL·kg^{-1}·min^{-1} (SD, 2.0) in children 7–10 years of age. In the group of children aged 11–13 years, this parameter was 22.64 mL·kg^{-1}·min^{-1} (SD, 2.6) (Table 2). The mean values of VO_{2peak} predicted for this age group were 45.48 mL·kg^{-1}·min^{-1} (SD, 3.8) (Figure 2).

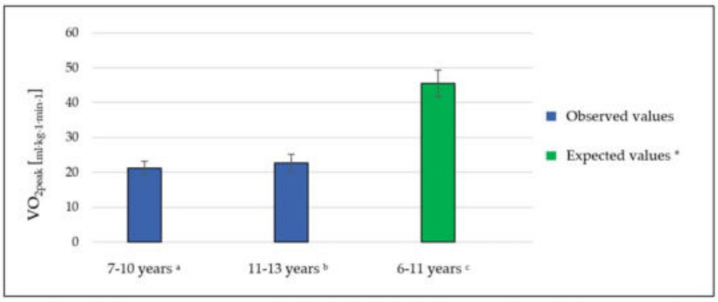

Figure 2. The values of VO_{2peak} in the study group with the division into age groups (children aged 7–10 and 11–13 years) compared to the values predicted in the relevant age group. Unpaired *t*-test: [a] examined boys versus expected values $p < 0.0001$, [b] examined girls versus expected values $p < 0.0001$, and [c] general study group versus expected values $p < 0.0001$. * Based on age- and sex-predicted values [21].

In the study group, 38% of children achieved above-average results. The value of VO_{2peak} below 20 mL·kg^{-1}·min^{-1} was obtained by 24% of the examined children (Figure 3).

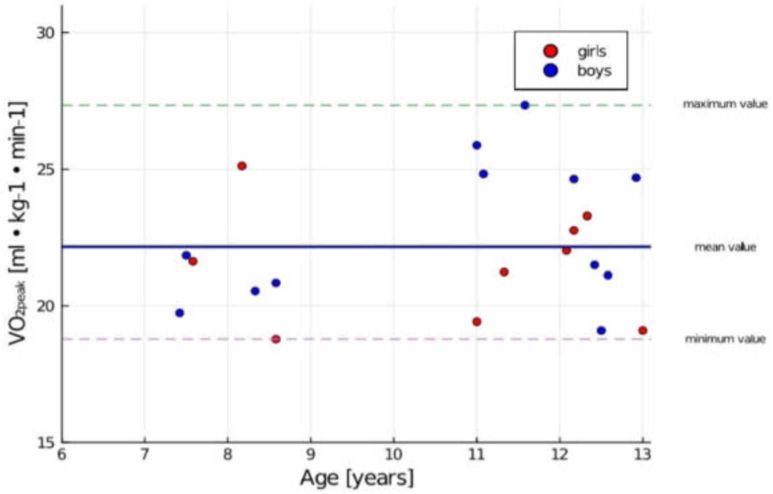

Figure 3. Distribution of measurement results of VO_{2peak} in the group with the division into sex.

The assessment of the relationships between VO_{2peak} levels of the children and the treatment protocol (ALL-AIEOP-BFM ALL 2017 protocol; AML-AML-BFM-2012 protocol) did not show statistical significance (Table 4).

Table 4. The relationship between the level of exercise capacity (VO_{2peak}) and the treatment protocol (AIEOP-BFM ALL 2017; 1-AML-BFM-2012).

Variables	VO_{2peak} Treatment Protocol (AIEOP-BFM ALL 2017), $n = 13$	VO_{2peak} Treatment Protocol (AML-BFM-2012), $n = 8$
VO_{2peak} treatment protocol (AIEOP-BFM ALL 2017)	-	-
vs.	-	-
VO_{2peak} treatment protocol (AML-BFM-2012)	-	-
Unpaired *t*-test		
p-value		0.5149
p-value summary	Ns	
Significantly different ($p < 0.05$)?		No
One-or two-tailed *p*-value?	Two-tailed	

The assessment of the relationships between the level of exercise capacity (VO_{2peak}) and the treatment regimen (B-ALL, T-ALL, and AML-BFM) showed no statistically significant correlations (Table 5).

Table 5. Relationship between the level of exercise capacity (VO_{2peak}) and the treatment regimen (B-ALL, T-ALL, and AML-BFM).

Variables	Statistical Values
VO_{2peak} treatment regimen (B-ALL), $n = 7$	
vs.	
VO_{2peak} treatment regimen (T-ALL), $n = 6$	
vs.	
VO_{2peak} treatment regimen (AML-BFM), $n = 8$	
One-way ANOVA	
F	0.1775
p-value	0.8388
p-value summary	Ns
Significant difference among means ($p < 0.05$)?	No
R square	0.01934
Bartlett's test for homoscedasticity	
Bartlett's statistic (corrected)	0.1198
p-value	0.9419
p-value summary	Ns
Are SDs significantly different ($p < 0.05$)?	No

The assessment of the relationship between the level of exercise capacity (VO_{2peak}) and the risk group, including each child (SR, standard risk; IR, intermediate risk; and HR, high risk) who underwent a different treatment regimen, did not show statistically significant values (B-ALL, T-ALL, and AML-BFM) (Table 6).

Table 6. The relationship between the level of exercise capacity (VO_{2peak}) and the risk group (SR, standard risk; IR, intermediate risk; and HR, high risk).

Variables	Treatment Regimen	Risk Group SR: $n = 6$, HR: $n = 3$, IR: $n = 12$	VO_{2peak}
Spearman Rho	Treatment regimen	Risk group	VO_{2peak}
Treatment regimen		−0.388	−0.268
Risk group	−0.388		−0.011
VO_{2peak}	−0.268	−0.011	
p-values	Treatment regimen	Risk group	VO_{2peak}
Treatment regimen		0.082	0.241
Risk group	0.082		0.962
VO_{2peak}	0.241	0.962	
VO_{2peak} _risk group–high risk			
vs.			
VO_{2peak}_risk group-standard risk			
Unpaired *t*-test			
p-value	0.9881		

Table 6. *Cont.*

Variables	Treatment Regimen	Risk Group SR: $n = 6$, HR: $n = 3$, IR: $n = 12$	VO_{2peak}
p-value summary	Ns		
Significantly different ($p < 0.05$)?	No		
One-or two-tailed p-value?	Two-tailed		
t, DF	t = 0.01521 DF = 16		
Kruskal–Wallis test of VO_{2peak}_risk group (SR, IR, HR)			
p-value	0.6766		
Exact or approximate p-value?	Exact		
p-value summary	Ns		
Do the medians vary significantly ($p < 0.05$)?	No		
Number of groups	3		
Kruskal–Wallis statistic	0.8447		

The study showed that physical exercise at the end of the exercise stress test was vigorous. This is evidenced by the high respiratory quotient (RQ) achieved in the last 30 s of the test. The mean RQ in the study group was 0.93 (SD, 0.24) (Table 1). The study results also showed that children had low blood counts, including hemoglobin (Hb) level (mean 8.34, SD 0.18) (Table 1). High RQ correlated with low hemoglobin levels (Table 7).

Table 7. Correlation of the results of the exercise stress test with the parameters of blood count and heart rate in the study group of children in total. Values of $p < 0.05$ were considered statistically significant.

Spearman Rho	Hb (mg/dL)	PLT (G/L)	RBC (T/L)	WBC (G/L)	HR at Rest	Exercise HR
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	−0.22	−0.15	−0.09	−0.02	0.22	0.25
VO_2 ($mL \cdot min^{-1}$)	0.11	−0.12	−0.09	0.01	0.16	−0.02
VCO_2 ($mL \cdot min^{-1}$)	−0.01	−0.18	−0.10	−0.03	0.09	−0.09
RER	−0.28	−0.01	−0.09	−0.20	0.23	−0.27
VE ($L \cdot min^{-1}$)	0.12	−0.03	−0.22	0.14	0.11	0.08
VE/VCO_2	−0.06	0.25	−0.15	0.24	0.09	0.11
RQ = $VCO_{2\ exhaled}/VO_{2\ uptake}$	−0.45 *	−0.12	−0.14	−0.24	0.13	−0.30
MET	−0.21	−0.16	−0.11	−0.03	0.21	0.23

* Results showing the correlation.

The analysis of the relationship of the results of the exercise stress test with the division into age groups showed a positive relationship between the level of the minute ventilation (VE) and the number of WBC in children aged 11–13 years. An inversely proportional relationship was observed in the correlation between high RER values and low RBC in the group of children aged 7–10 years. The same relationship was observed in the correlation between high values of exhaled carbon dioxide (VCO_2) and VE and low WBC in children aged 11–13 years (Table 8).

Table 8. Correlation between the exercise stress test results and blood count parameters and heart rate with the division into age groups (7–10 and 11–13 years). Values of $p < 0.05$ were considered statistically significant.

Spearman Rho	Hb (mg/dL)		PLT (G/L)		RBC (T/L)		WBC (G/L)		HR at Rest		Exercise HR	
	I	II	I	II	I	II	I	II	I	II	I	II
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	−0.44	−0.13	−0.32	−0.15	−0.20	0.01	−0.25	−0.05	0.64	0.20	−0.36	0.39
VO_2 ($mL \cdot min^{-1}$)	0.44	−0.03	0.36	−0.45	−0.61	−0.15	−0.61	0.41	0.15	0.14	0.34	−0.11
VCO_2 ($mL \cdot min^{-1}$)	0.00	0.01	0.14	−0.40	−0.68	−0.06	−0.93 *	0.46	0.13	0.10	0.07	−0.12
RER	−0.44	−0.36	0.24	−0.25	−0.93 *	0.17	−0.73	0.18	−0.18	0.37	−0.23	−0.36
VE ($L \cdot min^{-1}$)	0.16	0.08	0.00	−0.28	−0.68	−0.19	−0.79 *	0.56 *	0.11	0.11	−0.02	0.04
VE/VCO_2	0.16	−0.14	−0.14	0.39	0.47	−0.21	0.75	−0.03	0.20	0.19	−0.18	0.09
RQ = $VCO_{2\,exhaled}/VO_{2\,uptake}$	−0.76	−0.35	−0.14	−0.26	−0.58	0.19	−0.57	0.17	−0.25	0.36	−0.45	−0.36
MET	−0.44	−0.11	−0.32	−0.15	−0.20	−0.02	−0.25	−0.06	0.64	0.19	−0.36	0.37

* Results showing the correlation. Group I = children aged 7–10; group II = children aged 11–13.

3.2. *Physical Activity Level*

None of the children met the standards for the recommended level of weekly physical activity. All subjects declared that during the previous week they did not undertake any form of physical activity longer than 60 min per day (MVPA index). None of the children underwent any moderate or vigorous physical activity in the previous week, i.e., the one that would influence the values of exercise capacity parameters. The percentage of children treated for cancer who declared spending at least 5 h per day in the week in front of a computer or TV screen was 95.24. On days off, all children spent at least 5 h daily in front of the screen. All the children declared playing stationary games daily which did not require physical activity (computer, console, smartphone, or tablet games). These games were only stationary, not active, such as Kinect. On days off, the amount of time spent on games increased. All children declared that they had used the Internet every day and spent at least 4 h daily on it (Table 9).

Table 10 shows the relationship between the level of physical activity (HBSC questionnaire) and morphotic parameters of blood and heart rate. No statistically significant results were observed that could indicate the effect of insufficient level of morphotic parameters of blood on exercise frequency, exercise time, or sedentary behaviors (Table 10).

A positive relationship was found between the amount of time spent using a computer and mobile devices and low WBC in the group of children aged 11–13 years (Table 11).

Table 12 shows the relationship between the level of exercise capacity parameters obtained in the ergospirometry test and the levels of physical activity and sedentary behaviors. There was no effect of reduced physical activity or increased sedentary behaviors on the exercise capacity on children treated for leukemia (Table 12).

Table 9. Level of physical activity and sedentary behaviors. Percentage data on the number of people answering questions from the HBSC survey (%).

Response *	The Number of Days Per Week in Which the Child Performed the Physical Activity of at Least 60 min (MVPA)—HBSC 1	Frequency of Undertaking Vigorous Physical Activity—HBSC 2	The Number of Hours in Front of a Screen Per Week—HBSC 4.1	The Number of Hours in Front of a Screen at the Weekend—HBSC 4.2	The Number of Hours Spent Playing Games Per Week—HBSC 5.1	The Number of Hours Spent Playing Games at the Weekend—HBSC 5.2	The Number of hours Spent Using a Computer, Tablet or Smartphone Per Week—HBSC 6.1	The Number of Hours Spent Using a Computer, Tablet or Smartphone at the Weekend—HBSC 6.2
0	100	-	-	-	-	-	-	-
1	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-
4	-	-	4.76	-	9.52	9.52	-	-
5	-	-	38.10	23.81	38.10	14.29	38.10	14.29
6	-	100	33.33	42.86	52.38	52.38	61.90	38.10
7	-	-	23.81	33.33	-	23.81	-	47.62

* Content of the response included in the previous paper [22]. The third question was not considered in the current study since the new HBSC 2018 questionnaire was formed with the exclusion of question 3.

Table 10. Correlation between the survey results that assessed the level of physical activity and sedentary behaviors and blood count parameters and heart rate in the study group of children in total. Values of $p < 0.05$ were considered statistically significant. [a] The question content of the HBSC questionnaire is given in Table 7.

Spearman Rho	Hb (mg/dL)	PLT (G/L)	RBC (T/L)	WBC (G/L)	HR at Rest	Exercise HR
HBSC 1 [a]	-	-	-	-	-	-
HBSC 2 [a]	-	-	-	-	-	-
HBSC 4.1 [a]	0.01	−0.25	0.31	0.15	0.20	−0.01
HBSC 4.2 [a]	0.11	0.07	−0.04	0.32	0.27	0.25
HBSC 5.1 [a]	−0.08	−0.08	0.10	−0.30	0.21	0.04
HBSC 5.2 [a]	−0.06	−0.29	0.13	−0.10	0.01	−0.04
HBSC 6.1 [a]	−0.18	−0.06	0.09	−0.25	-0.15	−0.03
HBSC 6.2 [a]	−0.02	0.28	0.12	−0.46 *	0.31	−0.08

* Results showing the correlation.

Table 11. Correlation between the survey results that assessed the level of physical activity and sedentary behaviors and blood count parameters and heart rate with the division into age groups (7–10 and 11–13 years of age). Values of $p < 0.05$ were considered statistically significant. [a] The question content of the HBSC questionnaire is presented in Table 7.

Spearman Rho	Hb (mg/dL)		PLT (G/L)		RBC (T/L)		WBC (G/L)		HR at Rest		Exercise HR	
	I	II	I	II	I	II	I	II	I	II	I	II
HBSC 1 [a]	-	-	-	-	-	-	-	-	-	-	-	-
HBSC 2 [a]	-	-	-	-	-	-	-	-	-	-	-	-
HBSC 4.1 [a]	−0.27	−0.42	0.30	0.02	0.21	0.02	0.00	−0.27	0.33	0.10	−0.36	−0.42
HBSC 4.2 [a]	−0.58	−0.69 *	−0.19	−0.10	0.10	0.00	−0.19	−0.42	0.53	0.24	−0.81 *	−0.25
HBSC 5.1 [a]	0.24	−0.15	0.39	0.02	−0.12	0.14	0.23	0.33	−0.53	−0.07	0.78	−0.21
HBSC 5.2 [a]	0.48	−0.27	0.61	−0.03	0.00	−0.16	−0.04	0.55 *	−0.24	0.27	0.87 *	−0.13
HBSC 6.1 [a]	0.31	−0.45	−0.61	−0.16	0.41	−0.18	0.41	−0.18	0.21	0.16	−0.21	−0.37
HBSC 6.2 [a]	0.00	−0.45	−0.29	−0.21	−0.22	0.13	−0.58	−0.21	0.29	0.15	−0.51	−0.53

* Results showing correlation. Group I = children aged 7–10; group II = children aged 11–13.

The analysis of the relationships between the level of physical activity and the results obtained in the exercise stress test with the division into age groups (7–10 and 11–13 years of age) did not show statistically significant observations (Table 13).

Table 12. Correlation between the survey results that assessed the level of physical activity and sedentary behaviors and the results of the exercise stress test in the study group of children in total. Values of $p < 0.05$ were considered statistically significant. [a] The question content of the HBSC questionnaire is presented in Table 7.

Spearman Rho	VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	VO_2 ($mL \cdot min^{-1}$)	VCO_2 ($mL \cdot min^{-1}$)	RER	VE ($L \cdot min^{-1}$)	VE/VCO_2	$RQ = VCO_{2\,exhaled}/VO_{2\,uptake}$	HR_{peak}	MET
HBSC 1 [a]	-	-	-	-	-	-	-		-
HBSC 2 [a]	-	-	-	-	-	-	-	-	-
HBSC 4.1 [a]	0.21	−0.04	−0.05	−0.24	−0.09	0.03	−0.26	−0.26	0.19
HBSC 4.2 [a]	0.31	0.14	0.02	−0.08	0.15	0.13	−0.21	−0.11	0.30
HBSC 5.1 [a]	−0.11	0.21	0.26	0.30	0.15	−0.44 *	0.39	0.00	−0.10
HBSC 5.2 [a]	−0.05	0.30	0.30	0.19	0.11	−0.48 *	0.20	−0.08	−0.04
HBSC 6.1 [a]	0.36	−0.15	−0.20	−0.10	−0.17	0.18	−0.17	−0.01	0.34
HBSC 6.2 [a]	0.27	−0.22	−0.30	−0.10	−0.36	0.11	−0.21	−0.01	0.26

* Results showing correlation.

Table 13. Correlation between the results of the questionnaire that assessed the level of physical activity and sedentary behaviors and the results of the exercise stress test with the division into age groups (7–10 and 11–13 years of age). Values of $p < 0.05$ were considered statistically significant. [a] The question content of the HBSC questionnaire is presented in Table 7.

Spearman Rho	VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)		VO_2 ($mL \cdot min^{-1}$)		VCO_2 ($mL \cdot min^{-1}$)		RER		VE ($L \cdot min^{-1}$)		VE/VCO_2		$RQ = VCO_{2\,exhaled}/VO_{2\,uptake}$		HR_{peak}		MET	
	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II
HBSC 1 [a]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HBSC 2 [a]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HBSC 4.1 [a]	0.00	−0.39	−0.42	−0.12	−0.30	−0.10	−0.27	0.13	−0.54	−0.08	0.18	0.20	−0.12	0.11	−0.24	0.28	0.00	−0.45
HBSC 4.2 [a]	0.28	0.12	−0.47	−0.19	−0.19	−0.24	−0.10	−0.02	−0.28	−0.25	0.19	0.18	0.19	−0.03	0.00	−0.23	0.28	0.06
HBSC 5.1 [a]	−0.08	0.04	0.31	0.20	0.08	0.26	0.20	0.22	−0.04	0.10	−0.19	−0.25	−0.08	0.22	0.18	0.37	−0.08	0.05
HBSC 5.2 [a]	−0.29	−0.07	0.42	0.42	0.26	0.46	0.03	0.16	0.00	0.31	−0.39	−0.21	−0.26	0.15	−0.08	0.28	−0.29	−0.09
HBSC 6.1 [a]	0.00	−0.18	−0.20	−0.14	−0.41	−0.18	−0.52	−0.14	0.00	−0.28	0.61	0.19	−0.41	−0.14	−0.51	−0.16	0.00	−0.23
HBSC 6.2 [a]	−0.14	−0.16	0.14	0.07	0.43	0.09	0.15	0.51	0.58	−0.10	−0.29	−0.10	0.29	0.51	0.07	0.27	−0.14	−0.20

* Results showing the correlation. Group I = children aged 7–10; group II = children aged 11–13.

4. Discussion

The results of the study showed reduced peak oxygen uptake, which indicates reduced exercise capacity in children during leukemia treatment. The VO_{2peak} parameter was assessed in the study because, in the group of children, it is particularly difficult to examine the effort at the maximum level. Moreover, reaching the plateau is often impossible despite the increase in exercise load. In children, the values of oxygen uptake before reaching the plateau are assumed to be the maximum values. In addition, cancer itself and its sequelae are contraindications for performing maximum tests [23,24]. The evaluated VO_{2peak} values were lower, on average, by 23.32 $mL \cdot kg^{-1} \cdot min^{-1}$, compared to healthy children in a similar age group [21].

Children achieved high RQ values during the measurement, which indicates that the level of physical effort was high. Relatively low HR peak values were also observed when the children completed the test (139.5 bpm; SD, 21.32) (Table 1). The duration of the test was relatively short (mean time, 470.67 s; SD, 33.91), and children often interrupted the test prematurely and showed the signs of heavy exercise load. High RQ values correlated with low hemoglobin levels (Table 7), which indicates impaired oxygen transport to muscles. These results suggest that children prematurely felt the symptoms of fatigue, confirming the reduced exercise tolerance of the study subjects.

Unexpectedly, the results of our study also showed that the VO_{2peak} values were significantly lower compared to the results of other researchers who evaluated the level of exercise capacity in children with cancer. The difference was 9.54 $mL \cdot kg^{-1} \cdot min^{-1}$ (SD, 9.2). One of the possible reasons for such a difference may be related to a different age group. Braam et al., in their study, assessed the level of exercise capacity in the group of children aged 8–18 years. A large group included children in the puberty period [17]. Intensive changes occur at puberty, and the exercise capacity parameters show significantly different values in boys and girls. Our study results were related to a narrow age group of children who were mostly before puberty (mean age, 10.7; SD, 2.0). This allowed the elimination of the influence of puberty-related factors on the VO_{2peak} parameter [25].

Another reason for such a large discrepancy in the results obtained may be related to the different stage of cancer treatment. The study subjects were at the initial stage of cancer treatment. The mean treatment time was 6.0 months (SD, 2.0) in the study group. In the early stage of cancer disease, the therapy is very aggressive and is aimed at the fastest destruction of a large number of cancer cells. One of the adverse effects of the first stage of cancer treatment is related to the adverse effect on morphotic parameters of blood. Anemia is a particularly common symptom. A decreased hemoglobin level is the cause of insufficient oxygen transport to muscles. As a result, it is manifested by a decrease in exercise capacity in children [26]. Our study included only children treated for leukemia (ALL $n = 13$; AML $n = 8$). This disease of the hematopoietic system also directly adversely affects the morphotic parameters of blood and determines the exercise capacity [27].

Cancer treatment is also the cause of adverse changes that affect the circulatory system. Chemotherapy often has a cardiotoxic effect and can cause heart failure. It was also a limiting factor for children to undertake full-time physical activity. Our exercise stress tests were conducted in a group of children without circulatory disorders. Symptoms such as dyspnea, coughing, and fainting may indicate cardiorespiratory abnormalities resulting from the adverse effects of chemotherapy [28].

Cachexia is a common sequela of cancer, which is manifested by weight loss and muscle atrophy. It has a negative effect on the exercise capacity in children undergoing treatment for cancer [29,30]. This reduces the exercise capacity level, which is still insufficient in the group of childhood cancer survivors. Low muscle mass and the deficiency of energy substrates are also important factors that have a direct impact on the reduction in exercise capacity [31].

Low blood counts and insufficient oxygen uptake are also manifested by general malaise and excessive fatigue in children. This increases the reluctance to undertake physical exercise and sometimes even the fear of the occurrence of fatigue symptoms, such as fainting, increased sweating, and headaches. Lack of contact with peers and being surrounded only by adults affect children's motivation to be active and their bad mental state. Most children declared that they had not undertaken any form of physical activity in the previous week (Table 9).

One of the important factors influencing the final result of the cardiopulmonary exercise test is the level of motivation of the examined subjects. Children with cancer disease have a low level of motivation. It is not only due to the disease and the related procedures, which often cause fear and anxiety. Additionally, psychosocial problems resulting from cancer treatment adversely influence motivation in children. Parental attitude and excessive care are the reasons for low motivation in children to undertake physical activity out of their own will. This may result in a worse perception of the child's ability to undertake physical activity. As a result, it causes a premature termination of the stress test despite the absence of fatigue symptoms [32].

None of the children reported any form of physical activity in the previous week; nor did they meet the MVPA recommendations (Table 9). It is also a possible cause of achieving low VO_{2peak} values.

It can be assumed that one of the reasons for the lack of interest in sports and physical activity is the lack of attractive forms of physical activity dedicated to children during hospitalization.

Children with no functional deficits who do not require special rehabilitation are not offered any form of physical activity. Promoting attractive forms of physical effort (e.g., exercise using virtual reality technology or interactive games) as part of cancer therapy may prevent a significant decrease in exercise capacity. Such forms of exercise would positively influence improving and maintaining exercise capacity parameters [33].

Habits acquired during treatment often become permanent and remain even after treatment. Reduced VO_{2peak} is an important predictor of premature mortality. Therefore, it is important that children treated for cancer should undertake physical activity and maintain high values of VO_{2peak} [10,34,35].

In conclusion, it is important to prevent excessive exercise capacity deficits and to maintain physical activity at a level adapted to the current abilities of the treated children from the onset of cancer treatment. Lack of physical activity during cancer treatment remains a habit and a factor predisposing this group of patients to the occurrence of diseases of affluence in adult life. Rehabilitation of children with cancer is particularly significant at the hospital stage. However, a frequent problem is related to the selection of appropriate forms of exercise for these children and the selection of appropriate exercise intensity in particular. The results of the exercise stress test are a very useful tool to help plan an individual rehabilitation program for a child with cancer. The comparison of the results of the exercise stress test in the group of affected children with the results of healthy children is a strong motivator to undertake action to increase the level of physical activity of these children, which in turn will improve their level of exercise capacity.

5. Strengths and Limitations of This Study

The examined group of children was very homogeneous in terms of age, treatment time, the type of disease, and treatment procedures. The methods used to measure respiratory parameters, including the parameter assessing exercise capacity in children (VO_{2peak}), were objective. However, these methods are rarely used in the group of children during cancer therapy. This is probably due to the difficult access to a homogeneous study group and frequently aggressive medical procedures applied to children. Consequently, the duration of the entire research period and the time of data collection are often very long. A large number of children who could be included in the study group did not agree to participate in the study, due to the high intensity of chemotherapy and fatigue or malaise symptoms. Sometimes low PLT is a contraindication for cardiopulmonary stress testing. Taking these factors into account, we assert that the study group is relatively large. In terms of statistical analysis, the study group was small ($n = 21$), which could increase the risk of statistical error and undermine the inference.

In some cases, CPET could have lasted longer and the achieved VO_{2peak} values could have been higher. A frequent reason for interrupting the cardiopulmonary exercise test was the lack of motivation among children. The subjects undergoing cancer treatment showed a premature desire to terminate the test despite low heart rate and RQ values. Despite the researcher's encouragement, the subjects significantly reduced the pedaling frequency. Moreover, the study coincided with the COVID-19 pandemic, which resulted in the suspension of the study. The study group included the patients from the high-risk group of infection, which made it impossible to conduct the study in its complete scope. In the future, the study period should be prolonged, and the study should be conducted on a larger group of children with cancer. Moreover, the methods used for the assessment of the level of physical activity were not objective. These methods only estimated the weekly level of physical activity of children. Therefore, the use of devices such as Sport Tester or ActiGraph would certainly provide objective data.

6. Future Research Directions

The assessment of the baseline level of the exercise capacity should be the starting point for the whole process of rehabilitation of a child with cancer. In the future, the test results will serve as a prognostic element enabling individual selection of the intensity of the exercise/rehabilitation program. This will enable the maintenance of exercise-capacity parameters and prevent an excessive decrease in the child's exercise capacity during the long-term process of cancer treatment. Rehabilitation focused on increasing the level of daily physical activity and preventing sedentary behaviors is of crucial importance. However, it is not always properly selected.

7. Conclusions

The study results showed that children undergoing treatment for leukemia were characterized by a reduced level of exercise capacity. Their level was much lower compared to healthy children of the same age. The low levels of exercise capacity parameters were probably caused by the medical procedures and many circles of chemotherapy that children underwent. Cancer and its aggressive treatment result in a decrease in the level of morphotic parameters of blood, which results in tissue hypoxia and a significant decrease in exercise capacity parameters. Lack of physical activity and failure to meet the standards for the minimum level of weekly physical activity (MVPA) probably contributed to the deterioration in exercise capacity in children treated for cancer.

Psychosocial factors, such as lack of contact with peers, feeling of isolation, and awareness of a life-threatening disease, contributed to physical inactivity.

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Article

Interactive Video Games as a Method to Increase Physical Activity Levels in Children Treated for Leukemia

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Abstract: Despite the beneficial effect of exercise, children treated for cancer do not engage in sufficient physical activity. It is necessary to search for attractive forms of physical activity, including interactive video games (IVGs). The aim of this study was to verify the effectiveness of the rehabilitation model developed by the authors based on the use of IVGs in children undergoing leukemia treatment. The study included a group of 21 children aged 7–13 years (12 boys, 9 girls) undergoing treatment for acute lymphoblastic leukemia (ALL) (n = 13) and acute myeloid leukemia (AML) (n = 8). The children were randomly assigned to an intervention group and a control group. To assess the level of cardiorespiratory fitness (CRF), each child participated in a Cardiopulmonary Exercise Test. Daily physical activity was assessed using the HBSC questionnaire. The study also used the Children's Effort Rating Table Scale (CERT) to assess the intensity of physical effort. The children in the intervention group participated in 12 sessions of. The study participants managed to complete all stages of a progressive training program, which confirmed the feasibility of such physical effort by patients with cancer. Pediatric patients reported that the IVG training required a light to moderate physical effort despite high values of energy expenditure (EE).

Keywords: childhood cancer; children; cardiorespiratory fitness; physical activity; energy expenditure; interactive video games; Children's Effort Rating Table

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1. Introduction

The use of modern treatment methods in pediatric oncology has resulted in an increase in the survival rates of pediatric patients. Even 85% of children treated for cancer are permanently cured [1,2]. Therefore, it is necessary to identify factors that directly affect the loss of overall psychophysical fitness in pediatric patients [3,4]. Oncological treatment may cause a significant deterioration of physical and mental health. Children most often complain of fatigue, pain, anxiety, stress, social isolation [5,6], or deterioration of cardiorespiratory fitness (CRF) and physical fitness [4,7]. Such deficits persist even after treatment completion [8]. Many studies have confirmed that prolonged hospitalization and related procedures (i.e., chemotherapy, radiotherapy, surgical treatment) significantly reduce the quality of life of children and discourage them from undertaking spontaneous physical activity (PA) [9]. Studies have shown that exercise programs had a beneficial effect on the well-being and mood of pediatric patients and improved CRF and PA [10,11]. Fiuza-Luces et al. (study group, n = 24) proved that an intrahospital exercise program in pediatric cancer patients could be safely applied to improved muscle strength [12]. Studies have also shown that exercise interventions in this group of patients are beneficial during and after treatment [13]. Despite the beneficial effect of exercise, children treated for cancer do not engage in sufficient physical activity. Rehorst-Kleinlugtenbelt et al. (study group, n = 25) proved that children undergoing cancer treatment, both in hospital and in home settings, showed a reduced PA level and did not comply with the general recommendations for PA in children [14]. As a result, it is necessary to search for modern forms of physical activity attractive for children, including interactive video games (IVGs) [15].

To date, IVGs used to increase physical activity levels have been widely used in healthy children and young adults, overweight and obese children, as well as adults [16–21]. IVGs have also been applied in a group of children with developmental disorders and abnormal motor patterns. Interactive games positively influenced the improvement of the examined parameters: small and large motor skills, balance, coordination, natural forms of movement and locomotion (running, walking, jumping) [22]. IVGs have also been used as part of a rehabilitation program for children with cerebral palsy and in the case of amputation [23–25]. IVGs have not been commonly used in children undergoing treatment for malignant tumors [15,26].

The aim of this study was to verify the effectiveness and feasibility of the rehabilitation model developed by the authors with the use of IVGs in children undergoing leukemia treatment. In addition, the levels of cardiorespiratory fitness, physical activity, and sedentary behavior were assessed, during hospitalization and in a follow-up study.

2. Study Design

2.1. Participants and Recruitment

The selected sample included children diagnosed with acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) during hospitalization; the disease period did not exceed 6 months from the diagnosis. Patients were included from January 2019 until January 2020. The study participants comprised children undergoing treatment for cancer (cycles of chemotherapy in hospital settings) at the Department of Pediatric Bone Marrow Transplantation, Oncology and Hematology at the Wroclaw University Clinical Hospital, Poland. We recruited a group of 21 children aged 7–13 years (12 boys, 9 girls) undergoing treatment for ALL (n = 13) and AML (n = 8). The children were randomly assigned to the intervention and the control groups. The subjects from the intervention group participated in IVGs in the intrahospital intervention program. The children from the control group were not included in any rehabilitation program. The children from the control group reported no possession of any interactive video game kit. Not all of the recruited children completed the research program (Figure 1). The distribution of the recruited children into the intervention and the control groups allowed for checking whether the participation in the IVGs program improved their health behavior and regular physical activity level. Additionally, it was possible to assess whether the acquired health habits were permanent and whether they significantly improved the efficiency parameters of the children.

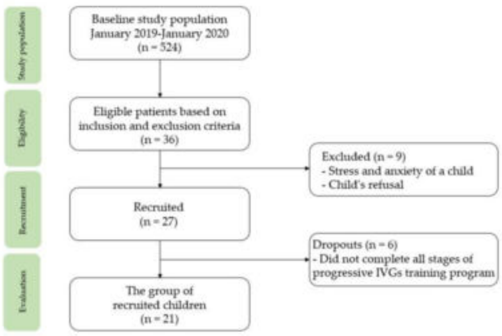

Figure 1. Participants recruitment.

2.2. Intervention Group

The intervention group included 10 children (5 boys, 5 girls) undergoing treatment for ALL (n = 8) and AML (n = 2). The pediatric patients were aged 7–13 years (mean age 11.3, SD 2.0 years; mean body height 149.1, SD 13.76 cm; mean body weight 46.59, SD 16.0 kg) (Table 1).

Table 1. Patient characteristics according to sex and group.

	Intervention Group $n = 10$			Control Group $n = 11$			p-Values Intervention Group vs. Control Group
Determinant Variables	**Mean ± SD**	**Boys Mean ± SD $n = 5$**	**Girls Mean ± SD $n = 5$**	**Mean ± SD**	**Boys Mean ± SD $n = 7$**	**Girls Mean ± SD $n = 4$**	
Age (years)	11.3 ± 1.9	11.4 ± 2.2	11.2 ± 2.0	10.08 ± 1.9	10.15 ± 2.0	9.9 ± 2.2	0.38
Height (cm)	149.1 ± 13.76	154 ± 15.36	144.2 ± 11.39	140 ± 16.5	141.7 ± 18.42	137 ± 14.51	0.51
Weight (kg)	46.59 ± 16.01	49.6 ± 17.8	43.5 ± 15.4	36.45 ± 9.9	36.57 ± 10.86	36.25 ± 9.43	0.24
Treatment Duration (months)	6.4 ± 1.6	6.0 ± 2.0	6.8 ± 1.3	6.3 ± 1.7	6.4 ± 2.1	6.0 ± 1.15	0.87
HGB (mg/dL)	8.35 ± 0.2	8.44 ± 0.15	8.26 ± 0.18	8.33 ± 0.17	8.24 ± 0.15	8.47 ± 0.12	0.78
PLT (G/L)	173.9 ± 57.26	162.6 ± 60.97	185.2 ± 57.8	142.3 ± 72.6	116.7 ± 76.78	187 ± 40.11	0.28
RBC (T/L)	3.143 ± 0.36	3.0 ± 0.29	3.29 ± 0.4	3.52 ± 0.29	3.46 ± 0.3	3.62 ± 0.22	0.02
WBC (G/L)	1.91 ± 0.8	2.16 ± 0.9	1.67 ± 0.57	2.27 ± 1.1	2.39 ± 1.42	2.06 ± 0.31	0.92
HR at rest	86.5 ± 3.4	86.2 ± 4.2	86.8 ± 2.9	84.9 ± 4.16	85.1 ± 4.95	84.5 ± 2.89	0.35

Note: HGB—hemoglobin level, PLT—blood platelet count, RBC—red blood cell count, WBC—white blood cell count, HR (at rest)—resting heart rate.

2.3. Control Group

The control group included 11 children (7 boys, 4 girls) undergoing treatment for ALL (n = 5) and AML (n = 6). The patients were aged 7–13 years (mean age, 10.08, SD 1.9 years; mean body height, 140.0, SD 16.5 cm; mean body weight, 36.45, SD 9.9 kg) (Table 1).

2.4. Participants Characteristics

Height and weight were measured in each participant prior to the study. The subjects were enrolled by a physician and a physiotherapist. Both inclusion and exclusion criteria were defined. The inclusion criteria in the study group were as follows: diagnosed cancer (ALL or AML), 7–13 years of age, hospital treatment, duration of hospital stay >7 days, chemotherapy, lack of physical disability, unassisted arrival at the examination, written consent of a parent/legal guardian to participate in the study, height >120 cm. The exclusion criteria were as follows: platelet count <20,000/mm^3, hemoglobin level <8 g/dL, infectious disease with fever >38 °C, intellectual disability. The children underwent the cycles of chemotherapy in the hospital settings. The mean time of treatment was 6.22 months (SD 1.64). None of the subjects presented with comorbidities.

The subjects treated for ALL were included in the International collaborative treatment protocol for children and adolescents with acute lymphoblastic leukemia (AIEOP-BFM ALL 2017 protocol) [27] (n = 13), whereas those treated for AML were included in the International therapeutic protocol for children with acute myeloid leukemia (AML-BFM 2012 protocol) [28] (n = 8). Depending on the type of ALL, the treatment was different, according to the B-ALL regimen (n = 8) or the T-ALL (n = 5) regimen. After the first stage of treatment (i.e., after induction), all children were classified into three risk groups based on the following criteria: age, leukocyte count, type of leukemia, response rate to treatment, remission, and cytogenetic results. Three children were enrolled in the standard-risk group, one child in the intermediate-risk group, and five children in the high-risk group.

3. Research Methods

3.1. Cardiorespiratory Fitness

Among the methods for the assessment of exercise tolerance which show the level of cardiorespiratory fitness, the most reliable and commonly used is the measurement of peak oxygen uptake (VO_{2peak}) by means of respiratory gas analysis performed during the gradually increasing the load, known as the Cardio Pulmonary Exercise Test (CPET) [29]. According to the World Health Organization, this measurement is considered the gold standard to assess aerobic exercise capacity [30].

To assess the baseline level of cardiorespiratory fitness, each child (from intervention and control groups) participated in a CPET. The test was repeated after 14 months and not immediately after the intervention, as planned. The study was discontinued due to restrictions in the initial period of the SARS-CoV-2 pandemic. The test was initiated with a 3 min warm-up at 15 W (height of 120–150 cm) or 20 W (height > 150 cm). After the warm-up period, the test began. The load was increased at one-minute intervals by 15 or 20 W (depending on the patient's height) according to the progressive Godfrey protocol [31,32]. The pedal frequency was at the constant level of 60–80 rotations per minute (RPM). The peak value of exercise was defined as the moment when one of the three following criteria was met: decrease in pedal frequency below 60 RPM, despite the strong verbal encouragement given by the investigator; $HR_{peak} > 180$ beats per minute; peak respiratory exchange ratio (RER_{peak}) > 1.0. The peak oxygen uptake (VO_{2peak}) was adopted as the mean value and was obtained during the last 30 s of the test [33]. Due to safety reasons, the children were not subjected to vigorous exercise. Additionally, the maximum oxygen uptake (VO_{2max}) was not assessed, as opposed to the peak value of this parameter. The VO_{2peak} results were compared with predicted values for age and sex of the study participants [34]. A portable ergospirometry system (K4b2; COSMED) was used in the study. This system is used to measure metabolic parameters, i.e., pulmonary gas exchange and indirect calorimetry—volume of O_2 uptake (VO_2), volume of exhaled CO_2 (VCO_2), respiratory quotient (RQ), minute ventilation, heart rate (HR), and energy expenditure (EE). The ergospirometer allows the measurement of O_2 and CO_2 concentrations during the inspiratory and expiratory phases. The cycle ergometer ASPEL CRG200 was also used, which enabled to set the appropriate load at scheduled intervals. The cycle ergometer is designed to work with the CardioTEST stress test system and the AsTER cardiac rehabilitation system (Figure 2).

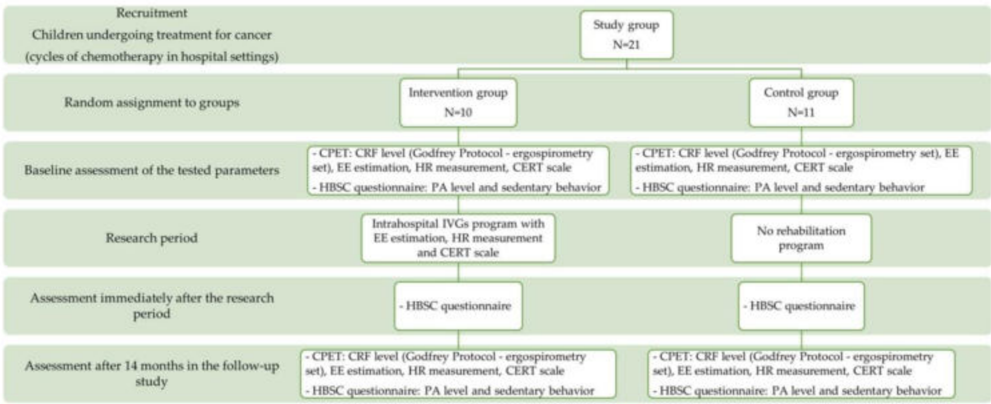

Figure 2. Flow chart diagram showing the scheme of the intervention carried out, with time and instruments.

3.2. Children's Effort Rating Table (CERT) Scale

The study also used a scale to assess the intensity of physical effort during the IVGs sessions (Figure 2). It is a scale that graphically depicts the level of physical effort experienced by the participants. The CERT scale is recommended for children due to reproducibility and a simple and understandable graphic design [35]. Moreover, other stages of the scale adequately represent the level of physical effort, and the results adequately correlate with heart rate and oxygen uptake [35,36].

3.3. Energy Expenditure during the IVGs Intervention

Energy expenditure during CPET and IVGs training was assessed by Keytel equation [37] used to estimate the amount of energy expenditure in children during the intervention (Figure 2). The following factors were considered: sex, weight, age, and heart rate.

3.4. Health Behavior Based on the School-Aged Children (HBSC 2018) Questionnaire

The level of physical activity in the intervention and control groups was assessed using the questions in the Health Behavior in School-Aged Children (HBSC 2018) questionnaire, in the section regarding health behavior (Figure 2). The questions were related to the last seven days [32]. The survey questions concerned the following: number of days per week in which the child performed physical activity for at least 60 min (Moderate to Vigorous Physical Activity—MVPA) (HBSC 1); frequency of undertaking vigorous physical activity (HBSC 2); number of hours in front of a screen per week (HBSC 4.1); number of hours in front of a screen in the weekend (HBSC 4.2); number of hours spent playing games per week (HBSC 5.1); number of hours spent playing games in the weekend (HBSC 5.2); number of hours spent using a computer, tablet, or smartphone per week (HBSC 6.1); number of hours spent using a computer, tablet, or smartphone in the weekend (HBSC 6.2).

4. Training with IVGs—Intervention Group

Children from the intervention group participated in 12 sessions of IVGs during hospitalization (Xbox 360 console, Microsoft), while the control group children received no intervention. Such IVGs sessions were held three times per week for four weeks (Figure 2). The intervention consisted of intervals and began with a 3 min introductory session during which each participant played any game to learn how the console worked. The sessions consisted in playing four different IVGs, each lasting 5 min. Between the games, the participant could rest for 1 min. The type of physical effort during the selected games was most similar to a continuous effort. The amount of exercise load during IVGs training was determined by the results of the baseline CPET. The intensity of the training (moderate level) was chosen considering the relationship between oxygen uptake and heart rate in children. The training was characterized by increasing intensity, which was adjusted by a gradual introduction of more advanced game levels to reach the target HR for each session. Strong verbal encouragement given by the researcher and the parents during the games was crucial to achieve the expected HR values [38]. Each game had three levels of difficulty that were gradually introduced during subsequent IVGs sessions. The difficulty level of the game depended on the pace of the game, the sensitivity of the console to movement, and the number of obstacles that occurred in the game. A gradual increase in these parameters required the player to increase the frequency of the motor response.

The IVGs kit included a motion sensor gaming console and a TV screen. The Kinect Xbox motion sensor is an input device that allows the user to interact with the console, without the need for a controller, through an interface using body gestures and voice commands.

During the game, the level of effort (intensity) was monitored using a physical activity monitor (Polar M 430). It was an additional tool that allowed the real-time monitoring of HR and assessed the effort intensity in children. The HR value was checked in real time using the Polar Flow App compatible with the PA monitor. In addition, the researcher asked each child to control the HR and report the achievement of the planned HR values. The following games were selected: Kinect Sports, Kinect Sports Season Two, and Kinect

Adventures. The intervention regimen using IVGs (5 min exercise, 1 min break) resulted in interval effort. We distinguished three levels of difficulty (Table 2). First level—70% HR_{peak} (1–4 IVG session), second level—75% HR_{peak} (5–8 IVG session), third level—80% HR_{peak} (9–12 IVG session). The game types during each selected categories were: Beach volleyball, Tennis, River rush, Reflex ridge. Every game lasted 5 min, and every break between game periods lasted 1 min.

Table 2. Interactive video game intervention—selected games.

Level of Difficulty	IVG Session Number	Game Type	Game Duration/Break Duration in Each Session
First level—70% HR_{peak}	1–4	Beach volleyball	5 min/1 min
		Tennis	5 min/1 min
		River rush	5 min/1 min
		Reflex ridge	5 min/end of the game
Second level—75% HR_{peak}	5–8	Beach volleyball	5 min/1 min
		Tennis	5 min/1 min
		River rush	5 min/1 min
		Reflex ridge	5 min/end of the game
Third level—80% HR_{peak}	9–12	Beach volleyball	5 min/1 min
		Tennis	5 min/1 min
		River rush	5 min/1 min
		Reflex ridge	5 min/end of the game

IVGs interventions were performed by a clinical physiotherapist–researcher qualified to work with children with cancer disease. During each IVGs session, the child's parent was also present.

5. Ethics

The study was approved by the Local Bioethics Committee of Wroclaw University of Health and Sport Sciences, al. Ignacego Jana Paderewskiego 35, 51-612 Wrocław. Approval Code: 22/2018; Approval Date: 3 July 2018.

6. Statistical Analysis

Statistical analysis was performed using GraphPad Prism 7 software (Institute of Immunology and Experimental Therapy, Wroclaw, Poland). The normality of data distribution was assessed using the Shapiro–Wilk test. The parameters describing the group characteristics were given by descriptive statistics, such as arithmetic mean and standard deviation (SD). The ANOVA test with Brown–Forsythe correction for inequality of variance was used for the global analysis of differences between the groups, followed by Dunnett's post-hoc tests to test the significance of the differences between the selected variables. Next, the Student's *t*-test for independent groups with Welch correction was used to assess the statistical significance of the differences in the results between the examined groups and age- and sex-predicted values.

To demonstrate the statistical significance of differences in CPET test results before and after the intervention in both groups (intervention and control groups), we used the ANOVA test with Brown–Forsythe correction for inequality of variance for the global analysis of differences between the groups and then Dunnett's post-hoc tests to test the significance of differences between selected variables. Depending on the data distribution, the Student's *t*-test with Welch's correction was used for data with a normal distribution. When the distribution was different from normal, the Dunn's test was used.

The Student's *t*-test with Welch's correction was used to assess the statistical significance of differences in the results of energy expenditure between the groups of boys and girls.

To verify the statistical significance of the differences in the HBSC survey results between the intervention and the control groups, the Kruskal Wallis test was used for a global analysis of differences between the groups and then Dunn's post-hoc tests to test the significance of differences between the selected variables.

The Wilcoxon test was used to verify the differences in the level of physical activity (before the examination vs. immediately after the intervention; after the intervention and in the follow-up study after 14 months) within the groups. The level of significance was adopted at $p < 0.05$.

7. Results

7.1. Cardiorespiratory Fitness before the IVGs Intervention—CPET Results

The mean value of VO_{2peak}, which was measured during CPET, was 22.5 mL kg^{-1} min^{-1} (SD 2.6) in the intervention group of children. The mean value of this parameter was 23.3 mL kg^{-1} min^{-1} (SD 2.7) in the group of boys and 21.69 mL kg^{-1} min^{-1} (SD 2.5) the group of girls (Table 3). In the control group, the mean value of VO_{2peak} was 21.86 mL kg^{-1} min^{-1} (SD 2.44). In the control group of boys, the mean value of this parameter was 22.22 mL kg^{-1} min^{-1} (SD 2.8), and in the control group of girls it was 21.24 mL kg^{-1} min^{-1} (SD 1.9) (Table 3). The mean VO_{2peak} predicted for this age group was 45.48 mL kg^{-1} min^{-1} (SD 3.8). The predicted value of the VO_{2peak} parameter in the group of healthy boys was 46.3 (SD 4.2), while in the group of healthy girls it was 44.7 (SD 3.4) (Figure 3) [34]. The absolute difference of the measured and predicted VO_{2peak} in the group of childhood cancer patients and the predicted values in healthy children was 23.32 mL kg^{-1} min^{-1}. In the groups of boys and girls, the difference was 23.3 mL kg^{-1} min^{-1} and 23.22 mL kg^{-1} min^{-1}, respectively (Figure 3).

Table 3. Cardiorespiratory test results (CPET) before the IVGs intervention in the study and control groups.

	Intervention Group $n = 10$			Control Group $n = 11$			p-Values Intervention Group vs. Control Group
Outcome Variables	**Mean ± SD**	**Boys Mean ± SD $n = 5$**	**Girls Mean ± SD $n = 5$**	**Mean ± SD**	**Boys Mean ± SD $n = 7$**	**Girls Mean ± SD $n = 4$**	
VO_{2peak} (mL kg^{-1} min^{-1})	22.5 ± 2.6	23.3 ± 2.7	21.69 ± 2.5	21.86 ± 2.44	22.22 ± 2.8	21.24 ± 1.9	0.57
HR_{peak}	154.7 ± 12	159.6 ± 10.45	149.8 ± 12.4	149.5 ± 10.0	143.1 ± 5.8	160.8 ± 1.7	0.30
VO_2 (mL/min)	1068 ± 395.6	1247 ± 329.3	888. 4 ± 404.1	1228 ± 251.9	1241 ± 292.1	1205 ± 199.6	0.29
VCO_2 (mL/min)	1069 ± 517.8	1269 ± 495.6	868.2 ± 507.3	1179 ± 403.9	1284 ± 479.1	995.8 ± 119.9	0.59
VE (L/min)	28.33 ± 9.4	31.22 ± 6.5	25.44 ± 11.7	29.47 ± 6.0	30.13 ± 6.8	28.33 ± 4.9	0.75
VE/VCO_2	28.74 ± 6.02	26.18 ± 5.1	31.31 ± 6.3	26.8 ± 3.9	25.91 ± 4.5	28.35 ± 2.2	0.4
RQ = $VCO_{2exhaled}$ /$VO_{2uptake}$	0.97 ± 0.14	0.99 ± 0.16	0.94 ± 0.15	0.95 ± 0.2	1.0 ± 0.2	0.8 ± 0.06	0.93
MET	6.38 ± 0.7	6.62 ± 0.8	6.14 ± 0.7	6.2 ± 0.7	6.3 ± 0.8	6.0 ± 0.5	0.53
Test Duration (s)	481.1 ± 35.5	474.4 ± 41.1	487.8 ± 32.3	461.2 ± 32.7	469.4 ± 37.7	446.8 ± 17.2	0.95

Note: VO_{2peak}—peak oxygen uptake, HR_{peak}—peak heart rate, VO_2—volume of O_2 uptake, VCO_2—volume of exhaled CO_2, VE—minute ventilation, VE/VCO_2—ventilatory equivalent of carbon dioxide, RQ—respiratory quotient, MET—metabolic equivalent of task.

7.2. Assessment of the Feasibility of Training with IVGs in the Intervention Group

The assessment of heart rate in the different training phases showed that the assumed training heart rate values were achieved in the group of girls, which was particularly evident in the final stages of the consecutive IVGs training phases. The required heart rate values for each training phase (70% HR_{peak}, 75% HR_{peak}, and 80% HR_{peak}) were achieved, and in some cases these values were even exceeded, and the children achieved higher HR values than predicted. Then children reached the assumed HR values for each phase mostly during the second or third training of the series. In the final stage of the training, all girls achieved the assumed HR values, which means that the training was feasible in the group of girls (Figure 4).

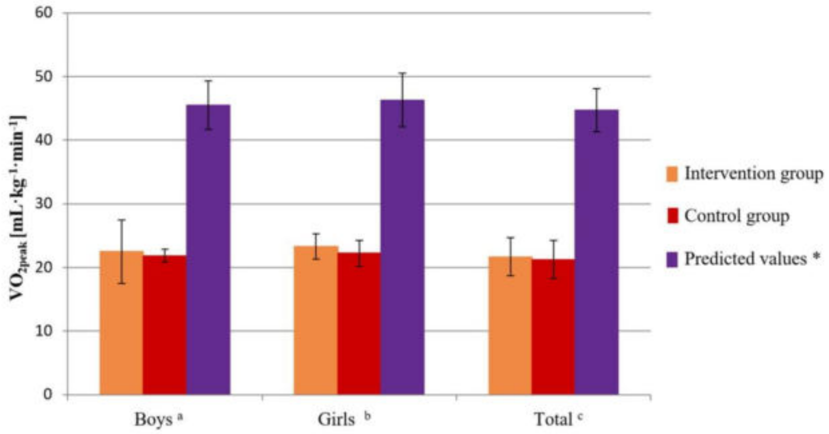

Figure 3. Baseline level of VO_{2peak} before the research period in the intervention and control groups compared to the predicted values for age and sex in boys, girls, and all children. Unpaired *t*-test: [a] boys from the intervention group vs. predicted values ($p < 0.0001$), boys from the control group vs. predicted values ($p < 0.0001$), [b] girls from the intervention group vs. predicted values ($p < 0.0001$), girls from the control group vs. predicted values ($p = 0.0001$), [c] intervention group vs. predicted values ($p < 0.0001$), control group vs. predicted values ($p < 0.0001$). * Based on age- and sex-predicted values [34].

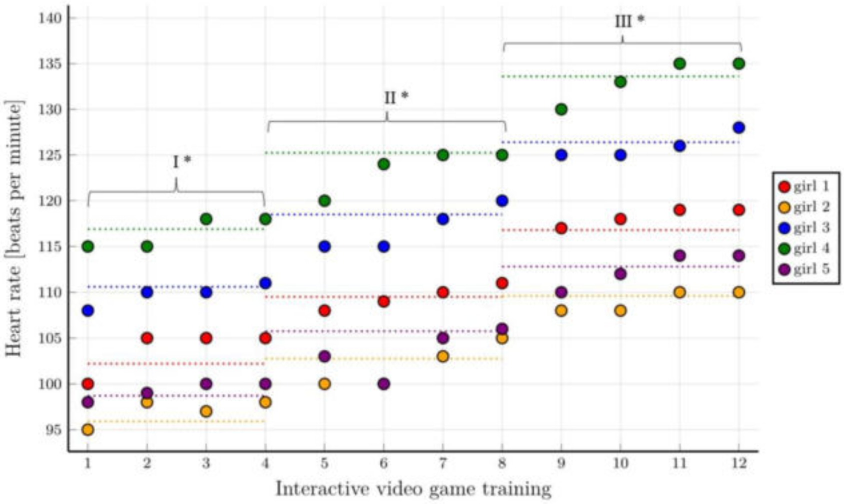

Figure 4. Heart rate values at different training stages in the group of girls with consideration given to individual training phases. * First level of difficulty of the game—70% HR_{peak}; second level of difficulty of the game—75% HR_{peak}; third level of difficulty of the game—80% HR_{peak}. The horizontal dotted lines show the range of heart rate values to be achieved for a given training phase.

The analysis of heart rate values in different training phases showed that in the group of boys, all subjects achieved the assumed HR values, or the results were close to the predicted values. The heart rate values required for each training phase (70% HR_{peak}, 75% HR_{peak} and 80% HR_{peak}) were achieved, particularly in the final phases of the individual training stages. In the final phase of training, all boys achieved the assumed HR values. One participant reached a value close to 80% HR_{peak}. The assumptions of the training using IVGs based on the heart rate analysis in the group of boys were met (Figure 5).

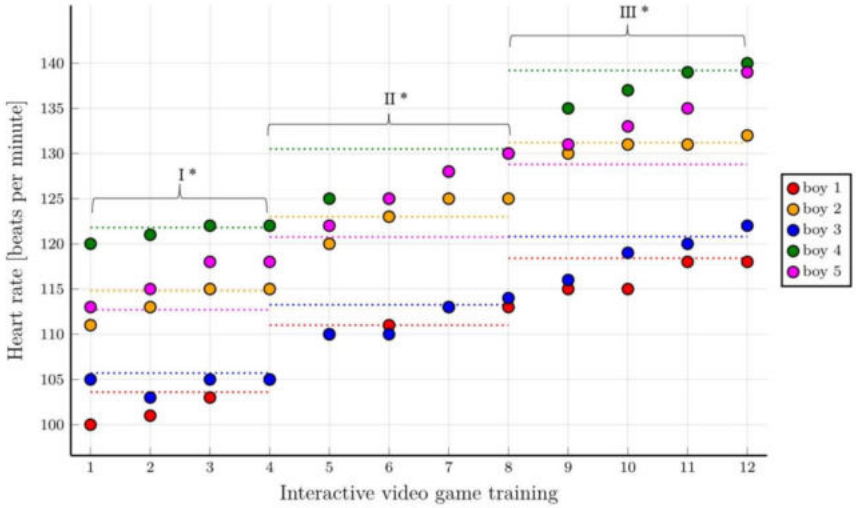

Figure 5. Heart rate values at different training stages in the group of boys with consideration given to individual training phases. * First level of difficulty of the game—70% HR_{peak}; second level of difficulty of the game—75% HR_{peak}; third level of difficulty of the game—80% HR_{peak}. The horizontal dotted lines show the range of heart rate values to be achieved for a given training phase.

The results of CERT during the training sessions with IVGs showed that physical effort was of a light to moderate level. The intervention group participants declared slight tension or light strain (Figure 6).

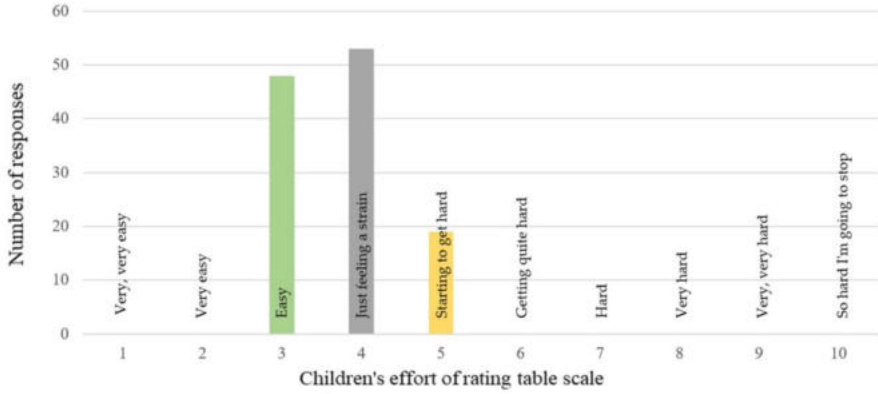

Figure 6. Overall assessment of the intensity of children's effort (CERT scale) during all training sessions with IVGs.

7.3. Assessment of Energy Expenditure during Training with the Use of IVGs

The assessment of energy expenditure achieved in the group of girls during the following phases of training with the use of IVGs showed the progressive nature of the intervention. In each subsequent training phase, the girls achieved higher values of energy expenditure. The values of energy expenditure reached in the initial phases of training showed a moderate intensity of physical effort (Figure 7).

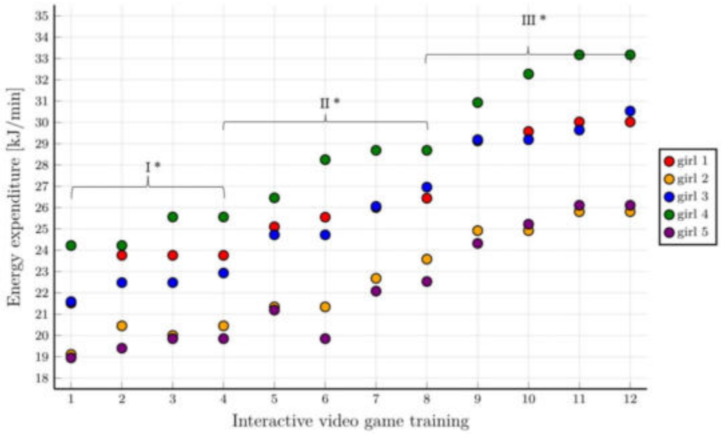

Figure 7. Energy expenditure in the following training stages for individual girls with consideration given to individual training phases. * First level of difficulty of the game—70% HR_{peak}; second level of difficulty of the game—75% HR_{peak}; third level of difficulty of the game—80% HR_{peak}.

Higher energy expenditure values were found in the group of boys in the early stages of training compared to the group of girls. In the final stages of training, the boys also achieved higher energy expenditure values compared to the girls (Figure 8).

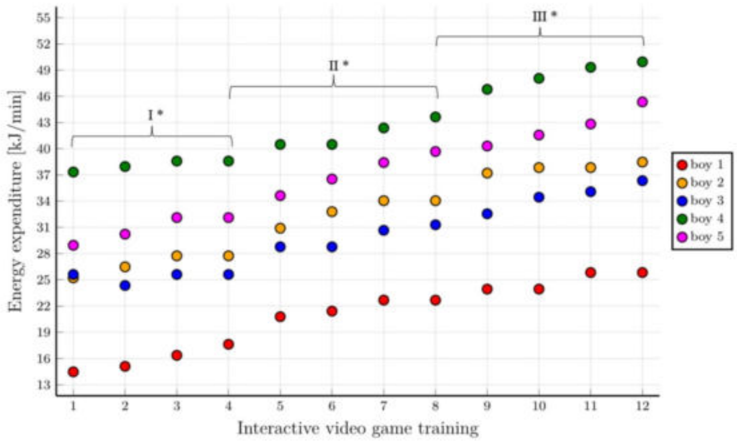

Figure 8. Energy expenditure in the following training stages for individual boys with consideration given to individual training phases. * First level of difficulty of the game—70% HR_{peak}; second level of difficulty of the game—75% HR_{peak}; third level of difficulty of the game—80% HR_{peak}.

The comparison of the mean values of energy expenditure achieved by the children during the pre-intervention CPET, post-intervention CPET (after 14 months), and subsequent IVGs training sessions showed that the boys reached higher values of energy expenditure compared to the girls. The values of energy expenditure achieved by the children in the CPET after 14 months showed that the children achieved much higher values of energy expenditure compared to the values measured in the baseline examination (Table 4).

Table 4. Mean values of energy expenditure during baseline CPET ($EE_{test\ I}$), CPET after 14 months ($EE_{test\ II}$), and subsequent IVGs training sessions in the intervention group and according to sex.

	$EE_{test\ I}$	$EE_{test\ II}$	EE_1	EE_2	EE_3	EE_4	EE_5	EE_6	EE_7	EE_8	EE_9	EE_{10}	EE_{11}	EE_{12}
Intervention group														
Mean (kJ/min)	49.83	54.59	23.7	24.44	25.21	25.42	27.44	27.97	29.37	29.95	31.93	32.7	33.57	34.16
Std. Deviation (kJ/min)	10.85	12.26	6.30	6.26	6.47	6.23	6.41	6.86	6.99	7.24	7.50	7.88	7.88	8.39
Girls														
Mean (kJ/min)	41.92	45.22	21.08	22.06	22.33	22.51	23.76	23.94	25.1	25.64	27.7	28.23	28.95	29.13
Std. Deviation (kJ/min)	4.04	3.97	2.16	2.09	2.45	2.36	2.37	3.36	2.72	2.53	2.91	3.12	3.06	3.13
Boys														
Mean (kJ/min)	57.74	63.96	26.32	26.82	28.09	28.34	31.11	32.0	33.64	34.27	36.16	37.17	38.18	39.19
Std. Deviation (kJ/min)	9.59	10.16	8.22	8.35	8.22	7.78	7.29	7.34	7.56	8.07	8.57	8.96	8.77	9.23
p-Values boys vs. girls	0.02 *	0.01 *	0.23	0.28	0.2	0.17	0.09	0.07	0.06	0.07	0.09	0.09	0.08	0.07

* Results showing the statistical significance.

7.4. Cardiorespiratory Fitness after 14 Months following the IVGs Intervention—CPET Results

The results of the examination conducted 14 months after the IVGs intervention indicated an improvement in the level of cardiovascular and respiratory efficiency in the intervention group. A statistically significant improvement of the following CPET parameters peak oxygen uptake and intensity of exercise determined by the size of MET and the test duration was observed. Statistically significant differences were also observed in the following morphotic parameters: HGB (hemoglobin level), PLT (blood platelet count), RBC (red blood cell count), WBC (white blood cell count). In the control group, an increase of the level of cardiovascular and respiratory efficiency was observed but it was not statistically significant. However, a statistically significant increase was observed in the parameters: HGB, PLT, RBC, WBC and in the test duration (Tables 5 and 6).

Table 5. Cardiorespiratory test results (CPET) after 14 months of intervention in the intervention and control groups.

	Intervention Group $n = 10$			Control Group $n = 11$			*p*-Values Intervention Group vs. Control Group
Outcome Variables	**Mean ± SD**	**Boys Mean ± SD $n = 5$**	**Girls Mean ± SD $n = 5$**	**Mean ± SD**	**Boys Mean ± SD $n = 7$**	**Girls Mean ± SD $n = 4$**	
VO_{2peak} (mL kg^{-1} min^{-1})	25.35 ± 2.3	25.59 ± 3.12	25.11 ± 1.4	22.84 ± 2.26	23.45 ± 2.24	21.78 ± 2.1	0.16
HR_{peak}	163.3 ± 13.2	168.8 ± 12.3	157.8 ± 12.8	147.5 ± 16.05	139.3 ± 11.04	162 ± 13.3	0.17
VO_2 (mL/min)	797.3 ± 250.2	830.6 ± 354.3	764 ± 111.9	1101 ± 384.1	1196 ± 441.2	936 ± 212.4	0.81

Table 5. *Cont.*

	Intervention Group $n = 10$			Control Group $n = 11$			*p*-Values Intervention Group vs. Control Group
Outcome Variables	**Mean ± SD**	**Boys Mean ± SD $n = 5$**	**Girls Mean ± SD $n = 5$**	**Mean ± SD**	**Boys Mean ± SD $n = 7$**	**Girls Mean ± SD $n = 4$**	
VCO_2 (mL/min)	739.3 ± 324.6	789 ± 454.1	689.6 ± 157.2	1025 ± 295.5	1088 ± 316.8	914.8 ± 254.7	0.77
VE (L/min)	32.86 ± 7.2	32.24 ± 10.0	33.48 ± 3.8	29.05 ± 7.12	27.74 ± 5.94	31.33 ± 9.3	0.88
VE/VCO_2	48.15 ± 14.17	45.16 ± 14.55	51.14 ± 14.8	29.16 ± 6.85	26.04 ± 2.4	34.63 ± 9.1	0.61
RQ = $VCO_{2exhaled}$/ $VO_{2uptake}$	0.9 ± 0.08	0.92 ± 0.1	0.89 ± 0.07	0.95 ± 0.099	0.94 ± 0.10	0.97 ± 0.1	0.90
MET	7.2 ± 0.65	7.26 ± 0.9	7.14 ± 0.4	6.58 ± 0.78	6.82 ± 0.81	6.2 ± 0.6	0.41
Test Duration (s)	591.6 ± 97.8	608.4 ± 112.9	574.8 ± 90	432.9 ± 71.7	439.14 ± 78.12	421.98 ± 84	0.62

Note: VO_{2peak}—peak oxygen uptake, HR_{peak}—peak heart rate, VO_2—volume of O_2 uptake, VCO_2—volume of exhaled CO_2, VE—minute ventilation, VE/VCO_2—ventilatory equivalent of carbon dioxide, RQ—respiratory quotient, MET—metabolic equivalent of task.

Table 6. Statistical significance of the differences in the CPET results between pre- and post- intervention values in the intervention group.

	VO_{2peak} [b] (mL kg^{-1} min^{-1})	VO_2 [a] (mL/min)	VCO_2 [a] (mL/min)	VE [b] (L/min)	VE/VCO_2 [a]	RQ = $VCO_{2exhaled}$ /$VO_{2\,uptake}$ [a]	HR_{peak} [b]	MET [b]	Test Duration [b] (s)
Mean Difference Between Pre- and Post-Intervention Results	2.86	−4.6	−8.8	4.53	7.6	−5.3	8.6	0.82	65.2
p-Value	0.02 *	0.72	0.5	0.24	0.56	0.68	0.14	0.02 *	0.03 *
		HGB [b]		**PLT** [b]		**RBC** [b]		**WBC** [b]	
Mean Difference Between Pre- and Post-Intervention Results		4.66		87,1		1.30		10.42	
p-Value		<0.0001 *		0.0013 *		<0.0001 *		<0.0001 *	

Note: [a] *p*-value of Dunn's test, [b] *p*-value of the Student's *t*-test with Welch correction, * results showing the statistical significance.

The results of the examination conducted 14 months after the IVGs intervention in the control group indicated a statistically significant improvement in the level of HGB, PLT, RBC, WBC and in the test duration (Table 7).

Table 7. Statistical significance of the differences in the CPET results between initial examination and follow-up after 14 months in the control group.

	VO_{2peak} [b] (mL·kg^{-1}·min^{-1})	VO_2 [b] (mL/min)	VCO_2 [b] (mL/min)	VE [b] (L/min)	VE/VCO_2 [a]	RQ = $VCO_{2exhaled}$/ $VO_{2uptake}$ [a]	HR_{peak} [b]	MET [b]	Test Duration [a] (s)
Mean Difference Between Pre- and Post-Intervention Results	0.98	−126.9	−153.7	0.43	4.41	3.09	−2	0.40	124.4
p-Value	0.34	0.37	0.32	0.88	0.91	0.94	0.73	0.21	0.005 *
		HGB [b]		**PLT** [b]		**RBC** [b]		**WBC** [a]	
Mean Difference Between Pre- and Post-Intervention Results		4.34		161		0.68		80.09	
p-Value		<0.0001 *		<0.0001 *		0.0012 *		0.049 *	

Note: [a] *p*-value of Dunn's test, [b] *p*-value of the Student's *t*-test with Welch correction, * results showing the statistical significance.

The analysis of peak oxygen consumption conducted in CPET after 14 months indicated an increase level of this parameter in both groups of examined children. The values achieved by children treated for leukemia still indicated considerable deviation from the expected values (observed in the healthy children group) (Figure 9).

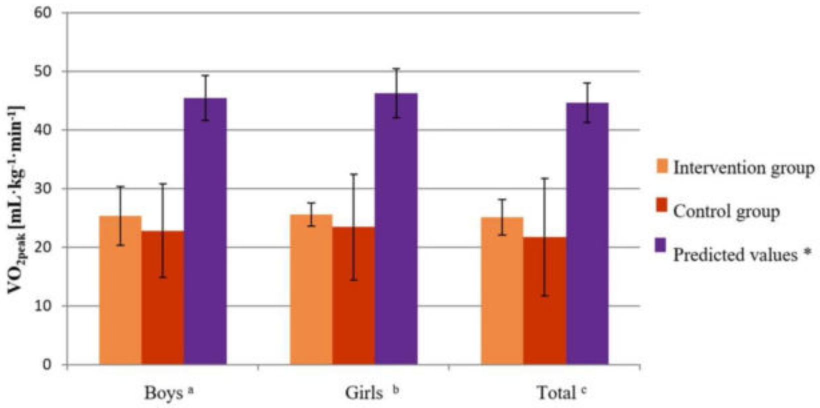

Figure 9. Baseline level of VO_{2peak} after the research period in the intervention and control groups compared to the predicted values for age and sex in boys, girls, and all children. Unpaired *t*-test: [a] values for boys in the intervention group vs. predicted values ($p = 0.0001$), values for boys in the control group vs. predicted values ($p < 0.0001$), [b] values for girls in the intervention group vs. predicted values ($p < 0.0001$), values for girls in the control group vs. predicted values ($p = 0.0002$), [c] values of the intervention group vs. predicted values ($p < 0.0001$), values of the control group vs. predicted values ($p < 0.0001$). * Based on age- and sex-predicted values [34].

7.5. Level of Physical Activity Immediately after the IVGs Intervention and in the Follow-Up Study

The results of our study assessing the level of physical activity in children after the IVGs intervention showed statistically significant differences. Children from the intervention group more often performed physical activity. Children included in the IVGs rehabilitation program fulfilled the recommendations to undertake physical activity at least 3 times a week. There was no statistically significant difference in the level of physical activity between the intervention and the control groups in the follow-up study 14 months after the IVG intervention (Table 8).

Table 8. Statistical significance of the differences in immediate HBSC post-intervention results and in follow-up study results conducted 14 months after the research period between the intervention and the control groups.

Kruskal-Wallis Test	Physical Activity Level Immediately after the IVGs Intervention in Intervention Group vs. Control Group							
	HBSC 1 *	HBSC 2 *	HBSC 4.1 *	HBSC 4.2 *	HBSC 5.1 *	HBSC 5.2 *	HBSC 6.1 *	HBSC 6.2 *
Difference Between Ranks	281	361.5	123	87.53	127	159.9	83.27	146.3
p-Value of Dunn's Test	0.0048 **	0.0003 **	0.22	0.38	0.20	0.11	0.40	0.14
	Physical Activity Level in Follow-Up Examination in Intervention Group vs. Control Group							
Difference Between Ranks	194.4	130	−63.49	−142.7	1.50	−72.93	65.4	−10.97
p-Value of Dunn's Test	0.12	0.28	0.6	0.24	0.99	0.54	0.59	0.93

Note: * The responses and questions were included in a previous paper [32]. The third question was not considered in the current study since the new HBSC 2018 questionnaire does not include question 3. ** Results showing statistical significance.

After the IVGs intervention, the children from the intervention group were more physically active compared to the pre-intervention period. The level of physical activity in the intervention group assessed 14 months after the end of the intervention was comparable to the level of physical activity immediately after the end of the IVGs program, and the difference was not statistically significant. Children reduced the time spent in front of the screen and the time devoted to using modern technologies (internet, computer, stationary games) (Table 9).

Table 9. Statistical significance of the differences between immediate HBSC post- intervention results and results after 14 months in the intervention group.

Wilcoxon's Test	Physical Activity Level before IVGs Intervention vs. Immediately after the IVGs Intervention							
	HBSC 1 *	HBSC 2 *	HBSC 4.1 *	HBSC 4.2 *	HBSC 5.1 *	HBSC 5.2 *	HBSC 6.1 *	HBSC 6.2 *
Median of Differences	3	4	1.5	1	1	1.5	0.5	1.5
p-Value Two Side Test	0.002 **	0.002 **	0.0039 **	0.0469 **	0.0156 **	0.0078 **	0.0625	0.002 **
	Physical Activity Level Immediately after the IVGs Intervention vs. in Follow-Up Study after 14 Months							
Median of Differences	0	0	2	3	2	2	1	1
p-Value Two Side Test	>0.9999	>0.9999	0.002 **	0.002 **	0.002 **	0.0039 **	0.0313 **	0.0156 **

Note: * The responses were included in the previous Table 7, and the questions in a previous paper [32]. The third question was not considered in the current study since the new HBSC 2018 questionnaire does not include question 3. ** Results showing statistical significance.

Children in the control group in the comparative study (at the beginning of the study and after 1 month in the re-examination) did not increase their physical activity level during the hospitalization period. After hospitalization, the children in the control group increased their daily physical activity, as it was shown by the results of the follow-up examination after 14 months (Table 10).

Table 10. Statistical significance of the differences between immediate HBSC post- intervention results and results after 14 months in the control group.

Wilcoxon's Test	Physical Activity Level before Examination vs. after 1 Month in the Re-Examination Study							
	HBSC 1 *	HBSC 2 *	HBSC 4.1 *	HBSC 4.2 *	HBSC 5.1 *	HBSC 5.2 *	HBSC 6.1 *	HBSC 6.2
Median of Differences	0	0	0	0	0	0	0	0
p-Value Two Side Test	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999	0.5	>0.9999	>0.9999
	Physical Activity Level Immediately after the IVGs Intervention vs. in Follow-Up Study after 14 Months							
Median of Differences	1	3	3	3	4	3	2	2
p-Value Two Side Test	0.0039 **	0.001 **	0.001 **	0.001 **	0.001 **	0.001 **	0.002 **	0.001 **

Note: * The responses were included in the previous Table 7, and the questions in a previous paper [32]. The third question was not considered in the current study since the new HBSC 2018 questionnaire does not include question 3. ** Results showing statistical significance.

8. Discussion

The physiological assessment of the cardiovascular function, during which respiratory gases and heart rate were analyzed, showed that children treated for cancer presented with significantly reduced cardiorespiratory fitness compared to healthy peers [34], which was confirmed by the low VO_{2peak} values during CPET (Tables 3 and 5). The mean value of VO_{2peak}, which was measured during baseline CPET, was 22.5 mL kg^{-1} min^{-1} (SD 2.6) in the intervention group and 21.86 mL kg^{-1} min^{-1} (SD 2.44) in the control group. After 14 months, the absolute difference of the measured and predicted VO_{2peak} values was 20.13 mL kg^{-1} min^{-1} in the intervention group and 22.68 mL kg^{-1} min^{-1} in the control group. The VO_{2peak} values were still significantly low (Figures 3 and 9).

The decreased level of baseline CPET was due to low blood count values, especially in terms of hemoglobin (Table 1). These values allow physical effort but to a limited extent. As a result, the children experienced fatigue more quickly due to insufficient oxygen delivery to muscles [39,40].

VE/VCO_2 is another important limiting factor when undertaking a great physical effort. The assessment of the relationship between ventilation and carbon dioxide (VE/VCO_2) is recommended and has a particular prognostic value in heart failure, which is a relatively common adverse effect of cancer treatment. Children treated for leukemia often develop cardiac disorders related to chemotherapy [41,42]. The results of the baseline CPET showed high values of this parameter in both groups. Another assessment conducted after 14 months also showed high values of the VE/VCO_2 ratio in the group of children treated for leukemia. The assessment of the VE/VCO_2 ratio in this group of patients may be an important prognostic factor. Additionally, special attention should be paid to the applied form of physical activity and rehabilitation, depending on the stage of cancer treatment.

The results of the baseline CPET assessment allowed for selecting individual IVGs training parameters for each participant in the intervention group. This is an innovative method for the rehabilitation of children during cancer treatment and ensures safe IVGs training programs. Individually tailored training programs are particularly beneficial [43]. Based on the peak heart rate value achieved during the CPET, training heart rate values were calculated individually for each participant. Although IVGs are not always effective in increasing the level of physical activity in healthy children [44], they have been shown to be more effective in children during cancer therapy [15,45]. Due to isolation and a high risk of infection, hospitalized children have limited opportunities to enjoy widely available forms of physical activity [46]. Hospitalized children willingly participate in IVGs activities as they provide interesting entertainment and a temporary distraction from painful and uncomfortable medical procedures [47]. Furthermore, children's playability increases their motivation and enjoyment [48]. Our results confirmed that most children treated for leukemia achieved the heart rate values (70% HR_{peak}, 75% HR_{peak}, and 80% HR_{peak}) required in each subsequent training phase. In some cases, the assumed values were even exceeded. This is particularly noticeable in the final stages of the individual IVG training phases, which means that the training was feasible, and the participants only needed time to adapt (Figures 4 and 5).

Our assessment of the intensity of physical effort using the CERT scale showed that the participants made a light to moderate physical effort during the IVG training. This type of physical effort is particularly recommended for children treated for cancer [22]. Although the participants did not subjectively feel a high level of fatigue during the IVG training sessions, as evidenced by the CERT scores (Figure 6), they achieved significant values of energy expenditure (Table 4). Biddiss et al. and Barnett et al. also found that children achieved a mild to moderate level of physical activity during IVGs [17,49], which is in line with recommendations during treatment [50]. Additionally, studies showed that real-time controlled and monitored interventions offered significantly more favorable results compared to simulated free play [51]. Therefore, it seems reasonable to apply individually tailored and real-time controlled training sessions using IVGs for children undergoing hospitalization and cancer treatment.

The attractive form of exercise during IVGs meant that our study participants treated the training task as fun and did not want to terminate the effort too early, which was a problem during the initial CPET. Of note, the duration of the CPET in the intervention and control groups was relatively short, and the test was completed when moderate heart rate values were achieved (Tables 3 and 5). In the follow-up study 14 months after the IVGs intervention, the test duration was prolonged, and the peak heart rate was higher (Tables 5–7). The results of the HBSC study carried out immediately after the IVGs intervention and in the follow-up studies showed no statistically significant differences in PA level. This was due to the fact that the level of PA of the examined children was comparable in these two periods (Tables 8–10). Parents who accompanied their children in IVGs training learnt that PA was possible for their child during cancer treatment. Parents were familiarized with the MVPA guidelines and probably motivated their children to practice PA regularly even during cancer treatment.

The level of children's motivation to undertake physical exercise in the form of a test and their fear of adverse effects were important at the beginning of the study. Children undergoing cancer treatment experience significantly reduced self-esteem [52]. Any form of assessment, including CPET, is an unpleasant and even stressful experience for them. All these limitations seem to be an obstacle to the performance of physical activity by children treated for cancer. Our research showed that the children were initially afraid to undertake an increased physical effort (Figures 4 and 5), but during the IVGs training period, they found that they were able to undertake PA. The results of many researchers, including our results, confirm that IVGs training is safe and feasible in this group of patients [53].

The rehabilitation of children with cancer is essential, especially during the hospitalization period. However, the selection of appropriate forms of exercise is problematic. The study results confirmed that individually tailored exercise programs using IVGs and based on the CPET results are feasible and provide significant benefits in terms of the psychophysical health of pediatric patients.

9. Strengths and Limitations of This Study

The study was conducted in a relatively small group of children. However, considering the intensity of the treatment process and related complications, the group was still large in terms of size, also due to the prevalence of cancer in children, which is generally low. Statistics on cancer incidence in Poland related to children show that the group of children we assessed was large. In Poland, about 1200 new cases of cancer are diagnosed annually among children. From this group, about 360 children are diagnosed with leukemia. There are about 500,000 children in the province where our center is located. The incidence rate of leukemia is 4 children per 100,000. The analysis of the data showed that there are 20 new cases of childhood leukemia per year in the Lower Silesia Province.

All children who were finally included in the study managed to complete a 4-week training program with IVGs. Cardiorespiratory fitness testing in children undergoing chemotherapy due to leukemia is difficult to perform because of the adverse treatment-related sequelae (i.e., anemia, musculoskeletal complications, and circulatory failure resulting from the cardiotoxic effect of the drugs). However, it was conducted on a group of 10 children. The research plan assumed the use of many research tools, including ergospirometry, CERT scale, HBSC questionnaire, heart rate measurements, and the estimation of energy expenditure during the IVG intervention. to the study period was performed during the SARS-CoV-2 pandemic, the researchers were deprived of the possibility of re-testing the cardiorespiratory efficiency of the children immediately after the IVG intervention. Another study conducted 14 months after the end of the IVG intervention could not be useful in assessing the direct impact of IVG training on the improvement of the cardiovascular and respiratory parameters. The results only proved that another stage of cancer treatment (maintenance therapy) had a significant impact on improving the level of cardiorespiratory efficiency.

10. Future Research Directions

Future investigation is needed. Studies with a larger group of children should be performed. Additionally, it would be essential to assess the extent to which improvement in terms of increased daily physical activity is a permanent result of the interventions. It would also be useful to assess whether the IVG intervention contributed to the change in habits related to undertaking regular physical activity. Future research should focus on the use of new virtual technologies with total immersion. Studies could compare the results of the interventions and assess which intervention (either IVGs or virtual reality games) is more effective to increase the physical activity levels and improve the quality of life of pediatric patients.

11. Conclusions

IVGs training at an intensity determined based on the baseline cardiorespiratory fitness test is safe and could become part of the rehabilitation program of children treated for leukemia. The subjects from the intervention group completed all stages of the progressive training program, which proved the feasibility of such physical effort during cancer disease treatment and even during hospitalization. Moreover, the children's subjective assessment of the severity of the required effort during IVGs showed that IVG training required a light or moderate effort, despite reaching high energy expenditure values.

In the early stage of cancer treatment, the children from the intervention group undertook physical activity during the IVGs interventions and fulfilled the MVPA recommendations. The results of the follow-up study, conducted 14 months after the IVGs program, showed that the children continued to perform regular physical activity, and their PA level was even comparable to that during the training intervention (no statistically significant difference in PA level between post-intervention and follow-up study). After 14 months of the IVGs intervention, the children were not cured as intensively as during the first stage of cancer treatment, and their fitness parameters were better, as shown by the CPET (the test duration was prolonged, and the peak heart rate was higher). As a result, the children treated for cancer had the opportunity to be much more active during this relative recovery period. This may indicate the necessity of sustained rehabilitation programs for children for the entire duration of their cancer treatment.

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Informed Consent Statement: Informed consent was obtained from all parents/legal guardians for the participation of their children in the study.

Data Availability Statement: The data are available upon reasonable request from the corresponding author.

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Oświadczenie o współautorstwie publikacji

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- [ ] koncepcja pracy
- [√] zaplanowanie badań wybór metodyki
- [√] prowadzenie badań
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- [√] korekta pracy przed złożeniem do druku
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