Clinical repercussions of game therapy in the management of individuals with cystic fibrosis

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SUMMARY

Game therapy (GT) has been used as a method to encourage the practice of physical activity in individuals with cystic fibrosis (CF), which may provide improvement in the cardiorespiratory system and treatment adherence. Objective: analyze the clinical repercussions of game therapy in the management of patients with CF. Methods: A systematic review of the literature was carried out in the following databases: PubMed, Embase, Scopus and MEDLINE via Ovid, using the descriptors: "Cystic fibrosis", "video games" and their cognates, through which they included Studies describing the repercussions of the use of GT in individuals with CF were sought. Results: 293 studies were identified, seven of which were selected at the end. In six studies, the heart rate reached during the TG was within the recommended standards for training. The assessment of maximum oxygen consumption (VO2max) was performed in three publications, and this parameter showed higher levels compared to that identified in the six-minute walk test. The most used consoles were Nintendo WiiTM and Xbox 360™ and the intensity in carrying out the exercises with the TG was moderate and intense. The individuals' adherence to this resource was also verified, and the GT was more acceptable than others and was considered playful. Conclusion: TG proves to be an intervention capable of generating physiological responses that correspond to training needs and greater adherence and satisfaction of individuals with CF in its performance.

Keywords: Cystic fibrosis, Physiotherapy, Games, Virtual reality, Rehabilitation.

INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disease caused by a mutation of the CFTR (Transmembrane Conductance Regulator) gene^{3,10}. Because it is a systemic disease, it can affect several body systems, especially the respiratory, gastrointestinal, and reproductive systems⁴¹; pulmonary impairment is the main reason for greater morbidity and mortality in individuals with CF, since, as a consequence of the genetic mutation, there is a production of a large amount of thick mucus⁴. The main symptoms of the disease are shortness of breath, chronic cough, bronchiectasis, and pulmonary exacerbations - due to recurrent infections-, malnutrition, and pancreatitis³⁸.

Due to the manifestations of CF, the importance of multidisciplinary work (doctors, specialized nurses, pharmacists, social workers, psychologists, nutritionists, and physiotherapists) in the management of individuals with the disease is justified^{19,31}. In this context, physiotherapy is

part of several rehabilitation scenarios for these patients, with emphasis on the reduction of pulmonary complications through the application of techniques and resources for secretion removal, aerobic exercise programs to improve cardiorespiratory capacity, interventions to increase ventilation lung and, consequently, benefits for lung function and activities of daily living¹⁷.

Within the physiotherapeutic action in individuals with CF, physical activity should be stimulated as early as possible, thus helping to improve cardiorespiratory fitness and lung function, which affects the quality of life and self-esteem of these individuals⁴⁸. However, most patients with CF do not perform the daily physical activity recommendations, with very low adherence, justified by the tedious routine of this practice^{23,26}.

With a consensus on the positive effects of physical activity in the treatment of CF, studies have presented more attractive alternatives to encourage physical activity and, among them, the

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use of video games – through game therapy (GT) – has been presented as a possibility. GT seems to arouse greater interest in this target audience and, consequently, lead to greater adherence to the physical exercises involved in games^{4,8}.

In this line of studies with GT and CF, there is a study by CAMPOS⁴ initiated on physiological and cardiorespiratory responses in patients with CF undergoing training with GT and, so far, the results are favorable concerning heart rate variability (HRV) and maximum oxygen volume (V02max), since, according to Kuys²³ et al., exercises performed with TG present a cardiovascular demand similar to conventional exercise modalities already practiced by individuals with CF²³.

In this context, there is a need to verify the effects of GT on HR. Therefore, this systematic review aims to analyze the clinical repercussions of GT in the management of individuals with this disease.

METHOD

This is a review that uses systematic methods for the identification and selection of studies, which uses eligibility criteria predefined by the authors of the study, data extraction, and then data analysis. The search was conducted on the following data platforms: Embase, PubMed, and Medical Literature and Retrieval System Online (MEDLINE) via Ovid and Scopus, according to the PRISMA checklist, which represents the entire process of searching and selecting articles, from the beginning to the end. Using the descriptors: Medical Subject Headings (MeSH), Health Sciences Descriptors (DeCS), and Embase Subject Headings (Emtree): "Cystic Fibrosis" and "Video Game" and their cognates ("Mucoviscidosis", "Pulmonary cystic fibrosis", "Kinect Xbox", "Nintendo Wii", "Gaming console", "Active videogame", "Xbox Wii therapy", "Interactive games", "Gaming system"). There was no restriction on dates due to the few studies on the subject, and studies in the following languages were considered: English, Portuguese, and Spanish. The search process was carried out until November 2022. The PICO strategy was used to select the studies (participants, intervention, comparator, results), as follows: P: individuals with CF; I: GT; C: usual care; O: lung function, clinical parameters, exercise capacity, ventilatory demand, and treatment adherence. Studies that did not show

the repercussions of GT in individuals with CF were excluded, as well as those that did not address the aforementioned outcomes (O).

The inclusion criteria were: clinical trials and observational studies - cross-sectional or longitudinal - were selected, and exclusion criteria were considered pilot studies, study protocols, abstracts, comments, editorials, letters, address materials or pages of electronic publications, literature reviews, systematic reviews, texts, and books, course conclusion works, dissertations, theses, and studies of a qualitative nature, publications of congress annals, presentations at congresses, symposiums, seminars, round tables, debates and studies not available.

The selection of studies was carried out by two independent evaluators, according to pre-established criteria. Initially, compatible titles were identified, then the abstracts were analyzed and, by consensus, the evaluators read the articles in full to select the studies included in the review. The methodological quality assessment for randomized clinical trials was conducted using the PEDro scale, which evaluates 11 criteria. Studies with scores equal to or greater than 7 are of high quality, and those below this score are of low methodological quality⁴². In our study, only 10 of the 11 PEDro scale criteria were used to score the articles included in the systematic review.

Non-observational randomized studies were performed by two independent evaluators, using the Cochrane Library risk of bias assessment (ROBINS – I). ROBINS – I is evaluated by 7 guiding questions for the judgment of each domain. These domains are classified by the time of occurrence.

Before the intervention: Confounding bias, Bias in participant selection. During the intervention: Bias in the classification of interventions; after intervention: bias due to deviation from intended interventions; Bias due to missing data; Bias in the measurement of outcomes; Bias in the selection of reported results.

The judgment domains are low risk of bias, moderate risk of bias, severe risk of bias, critical risk of bias, or no information.

The studies were analyzed to characterize the types of research, highlight the effects of TG for the individual with CF, what interventions were performed, whether there was an improvement compared to the individual's usual treatment, and, also, in what frequency or intensity the GT was applied.

RESULTS

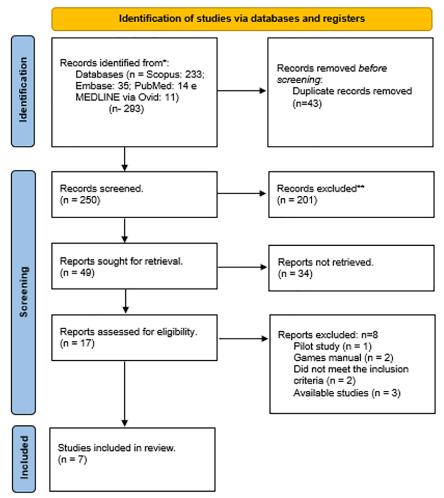
In the process of selecting studies, initially, 293 titles were identified in the consulted databases and, in the end, seven publications related to the use of GT in individuals with CF were selected for the presentation of results (Figure 1).

The main consoles used in GT were Nintendo Wii $_{\text{TM}}^{8,9,23}$, Xbox 360 $_{\text{TM}}^{39,21,32}$ and Nintendo Wii TM + Xbox One $_{\text{TM}}^{4}$.

Regarding outcomes, six studies assessed lung function using spirometry, including parameters such as forced vital capacity (FVC), forced expiratory volume in one second (FEV1), forced expiratory flow between 25-75% of vital capacity (FEF25-75%), and peak expiratory flow (PEF) 4,8,9,21 and only 1, plethysmography³². The clinical parameters of heart

rate (hr), maximum heart rate (hrmax), and oxygen saturation (SpO2) during TG were evaluated in all studies using a pulse oximeter^{4,39,9,21,23} and cardiac monitor^{4,8,39,32}, and the results are shown in Table 1.

Three studies evaluated the volume of oxygen (VO2) during the practice of TG through functional tests and cardiopulmonary tests^{21,9,32}, and the use of functional capacity assessment tests were observed in 5 studies^{4,8,9,21,32}, including the 6-minute walk test (6MWT)³², Cardiorespiratory Effort Test (CPET), Test of Modified Shuttle (MSWT)⁸, horizontal jump, and ball throwing test⁸. During the tests, the SpO2 variables, levels of dyspnea and muscle fatigue of the lower limbs (modified BORG scale), maximum heart rate (HRmax), and analysis of respiratory gases were observed. Another variable analyzed in the publications refers to energy expenditure during the TG and was found in 3 studies^{32,9,23}.



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Table 1 Synthesis and analysis of selected publications.

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Author and year	Study objectives and number of subjects	Groups and description of the intervention	Variables and results	Conclusion
Campos <i>et</i> <i>al.</i> , (2020)⁴	Evaluate the use of GT and the cardiorespiratory demand response for aerobic physical training in healthy individuals and patients with CF.	Random sequence of 6 games, for 10 minutes, with a 10-minute break between sets (25 healthy children and 30 with CF)	Analyses were performed on perceived exertion, spirometry, physical activity level (IPAQ-C and IPAQ-A), gas analysis and level of satisfaction. Differences were found in lung function in GC and EG and SpO2 at rest and peak exercise.	The use of GT generated the necessary cardiorespiratory demand for aerobic physical training of moderate intensity, high levels of satisfaction.
del Corral <i>et</i> <i>al.</i> , (2017) ⁸	Evaluate the effectiveness of a home exercise program using VGAs as a training modality for children and adolescents with CF. N: 40	Sessions: held 5 days a week, in 6 weeks Duration: 30 to 60 min Post-intervention follow-up: 12 months (20 healthy children and 20 with CF)	The variables analyzed were: 6MWT, MSWD, horizontal jump and medicine ball throwing test, spirometry. There was a significant difference: between the TG and CG groups and in the 3 evaluation moments (before, after and after 12 months) in the 6MWT and MSWD; Adherence was higher during the 6 weeks of intervention (95%), and 35% after 12 months	The VGAs home program shows improvement in exercise capacity in individuals with CF, producing a significant and sustained improvement in exercise capacity and muscle strength.
Salomini <i>et</i> <i>al.</i> , (2015)³³	Evaluate the cardiovascular demand produced and the perceptions of dyspnea, fatigue and pleasure in children and adolescents with CF when using the TG and compare traditional stationary cycle training. N: 30 (only with FC)	Intervention time: On two alternate days after 72 hours of hospital discharge GI: played Xbox Kinect GC: Aerobic exercises Duration: 20 min of intervention both groups	Dyspnea, perceived exertion (OMNI Scale - Children's Step), SpO2 and HR, spirometry were evaluated. There was no significant difference in the FrCmax achieved over time between the Xbox Kinect and the steady cycle. * Xbox Kinect tm provided a lower level of dyspnoea and fatigue and it was more pleasant than stationary cycling.	GT induced a significant increase in FrCmax. Individuals expressed greater pleasure when performing GT and less perception of dyspnea and muscle fatigue.
del Corral <i>et</i> <i>al.</i> , (2014)³	Evaluate the physiological response during three TG modes to be used as physical training modalities in CF patients.	Wii-Fit mode: exercise on a platform that requires aerobic work, balance and coordination. Duration: 5 min at each difficulty level. Duration: 5 min (only with FC)	The following were analyzed: HR, VO2 and SpO2, spirometry, 6MWT, fatigue and dyspnea Wii-Act and Wii-Train showed a higher metabolic demand (VO2) than the 6MWT while Wii-Fit had the lowest intensity Wii-Fit resulted in less leg fatigue than all other activities and the 6MWT'	GT exercises produced high physiological demands similar to conventional exercises

Author and year	Study objectives and number of subjects	Groups and description of the intervention	Variables and results	Conclusion
Holmes <i>et</i> <i>al.</i> , (2013) ²¹	Evaluate the exercise intensity achieved with TG compared to CPET in adult patients with CF.	It started with a 10-minute warm-up, then they played on the Xbox Kinect for 20 minutes.	Perceived exertion (modified Borg Scale), Perceived exertion (RPE Scale), electrocardiogram, VO2 and spirometry Exercise intensity with Xbox Kinect was 6.1METs	
	N: 10	(adults with CF)	Higher values were achieved during CPET for: FrC, dyspnea, perceived exertion, fatigue in lower limbs and desaturation compared to Xbox Kinect	
			Analyzed variables: 6MWT, calorimetry, HR, pedometer, SpO2, plethysmography and VO2	
O'Donovan <i>et al.</i> , (2013)³²	Evaluate energy expenditure and exercise intensity in TG in children with CF. N: 60	Participants played each game for 15 min with 5 min of rest (30 healthy children and 30 with CF)	There was a statistically significant difference for the distance covered in the 6MWT between the groups, being greater in the CG	Wii Fit Free Jogging can be recommended as a moderate form of aerobic exercise
			Mean levels of METs were significantly lower than those recommended for individuals with CF	
-	Evaluate the use of exercises in TG and relate according everying everying in	GI: Played GT for 15 on Nintendo Wii		
Kuys <i>et al.,</i> (2011) ²³	patients with CF.	CG: exercise bike or treadmill Duration: 15 min in both adults hospitalized with CF)	Variables analyzed: spirometry	

expiratory time between 25-75%, CF= cystic fibrosis; FrC= Heart rate; FrCmax= Maximum heart rate; GC= Control group; GI= Intervention group; GT= Game therapy; IPAC-C= Physical activity questionnaire for children; IPAC-Q=Quizreadiness for physical activity; L=liters; METs= Energy Expenditure; MSWD= Modified walk test distance; OMNI= Perceived Exertion Scale; RPE=Rate of perceived exertion; SpO2=Oxygen saturation; TC6'= 6-minute walk test; CPET= Cardiopulmonary stress test; TM= Trademark VE=Expiratory volume; FEV1= Forced expiratory volume in the 1st minute; VGA= Active video games; VO2= Volume of oxygen. Subtitle: ATS= Health Technology Assessment; CFQ-R= Cystic fibrosis questionnaire-revised; FVC= forced expiratory vital capacity; VAS= Visual analog scale; FEF25-75%= Forced

These tests analyzed whether the participants are within the predicted values for their age group and sex, and are based on the comparison of physiological responses, such as measuring exercise capacity to compare patients before and after training with the GT^{8,9}. The samples were composed of children and adults - of both sexes - aged between 7 and 15 years.

Most studies also analyzed the perception of exertion of patients during the practice of conventional exercises and TG, using scales of perceived exertion for fatigue and dyspnea, as well as the degree of satisfaction^{4,39,9,21,23}. Only one publication evaluated the quality of life before and after the intervention⁸. (Chart 1).

The methodological quality of the three evaluated clinical trials presents a good score (Table 2).

DISCUSSION

This review presented the effects of GT in individuals with CF on outcomes such as aerobic

capacity^{8,4,39,9,21,32,23}, treatment adherence, in addition to levels of satisfaction, when compared to other conventional therapies^{4,39,23}, showing positive results in these parameters. Regarding lung function, studies have performed spirometry to obtain pre- and post-GT data^{8,4,9,21}. Studies such as CAMPOS⁴ observed in the analysis of spirometric data that there was a difference in lung function between the control and experimental groups: FEV1, FVC, FEV1/FVC, FEF25-75% in (L) and % predicted. According to the study by del CORRAL⁸, GT improved exercise capacity in individuals with CF.

In the selected studies, the criteria used to evaluate the participants are observed, namely, pulmonary function tests, parameters related to cardiorespiratory demand, functional tests, specific questionnaires, and participants' acceptance of TG. In the main assessments carried out in research, the pulmonary function test routinely used was spirometry^{34,43,29}.

Along these lines, it is recommended that lung function is used to verify different levels of functional

Table 2Methodological quality analysis of randomized studies. (PEDRo scale)

PEDro scale	1	two	3	4	5	6	7	8	9	10	11	Total
del Corral et al. (2017)	*	*	*	*	0	0	*	*	*	*	*	8/10
Salomini et al. (2015)	*	*	*	*	0	0	0	*	*	*	*	7/10
Kuys et al. (2011)	*	*	0	*	0	0	*	*	*	*	*	8/10

0: when the criterion is not correct; *: when the criterion is correct

1: eligibility; 2: randomness; 3: secret allocation; 4: similarities; 5: be blinded to the study (6: subjects, 7: therapists, and 8: evaluators); 9: measurement of key result; 10: intention to treat; 11: inter-group statistical comparison and precision measurement. The score ranges from 0 to 10 points.

Table 3Analysis of the methodological quality of non-randomized studies (ROBINS Scale - I)

Study	D1	D2	D3	D4	D5	D6	D7
Campos et al. (2020)	low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias
Del Corral et al. (2014)	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate risk of bias
Holmes et al. (2013)	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Severe risk of bias	Moderate risk of bias	Low risk of bias
O'Donovan et al. (2013)	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Moderate risk of bias	

Domains:

D1:Confounding bias; D2: Bias in the selection of participants; D3: Bias in the classification of interventions; D4: Bias due to deviation from intended interventions; D5: Bias due to missing data D6: Bias in the measurement of outcomes; D7: bias in the selection of reported results. Classification: low risk of bias, moderate risk of bias, severe risk of bias, critical risk of bias or no information.

capacity and the degree of lung impairment, being able to monitor the dysfunction over time and the body's response to therapeutic strategies for its treatment³¹. In the case of GT, spirometry was performed in almost all selected studies^{39,4,9,32,21}, and its result was that video games raised FVC and FEV1 to levels close to those of the cardiopulmonary exercise test, translating that games bring a response to the level of exercise considered ideal for HR because they generated cardiorespiratory demand of moderate intensity, suitable for physical training⁴.

Another point highlighted in research related to the use of GT is the cardiorespiratory demand and cardiovascular response. According to Maddison²⁷ GT can significantly induce the physiological response in healthy individuals, which can also be observed in patients with CF, according to their results. Elevation of VO2max is considered an important clinical measure for physical assessment since its concentration in exercise capacity is reduced in individuals with CF, and this reduced capacity is considered a risk factor and a strong predictor of mortality.

VO2 is also related to training intensity. In the study by del Corral⁸, when using three game modes considered lighter on Wii-Fit, it was shown that VO2 consumption was lower when compared to two other moderate game modes, and concerning the 6-minute Walk Test (6MWT). Thus, the higher the intensity achieved in the TG, the more representative the cardiorespiratory changes are, which are similar to conventional physical activities - such as walking, jumping, and running - considered from light to moderate intensities regarding heart rate, VO2, and energy expenditure²⁷.

During the practice of physical activity provided by the TG, when compared to the practice of conventional exercises^{39,21}, lower levels of dyspnea and fatigue are evidenced, which corroborates studies of del Corral⁸ and Kuys²³. According to the authors, there were no reports of desaturation during the practice of TG in their studies, therefore, TG seems to be a viable and safe tool in the management of CF.

Three included studies showed that their participants were able to adhere more to therapy with the use of GT^{39,4,23}, and the adherence of individuals with CF to performing physical activities is still difficult, and it is up to the responsible professional to motivate these individuals for this routine practice, which can provide physiological benefits and also social effects on depression, anxiety and mood²⁴. These points were

highlighted in 4 studies^{8,4,39,23} in which the acceptability of individuals with CF to treatment is low when it comes to conventional therapies. It is noteworthy that, in some studies, some exercises were preferred by patients. Among them were interactive games, which involved rewards and scores, and games with dancing. These types of games generate greater interest for patients to continue performing physical therapy and, consequently, greater adherence compared to conventional exercises.

It is important to highlight that children and adolescents with CF have greater difficulty in adhering to physical therapy treatment when compared to adults with CF, as these are repetitive and tedious exercises, thus, it is suggested to also include fun activities, such as TG, whether supervised and individualized⁴⁵.

The scarcity of publications on the subject can be considered a limitation of this review - especially of controlled clinical trials -, as well as the small sample evaluated in the analyzed studies. Despite this, the clarifications in this article can help members of the multidisciplinary team in the management of CF in the indication of TG, since this presents itself as an alternative to the practice of physical activity for individuals with this disease. This is because TG seems to be a virtual reality game with a positive physiological impact and leads to a higher level of satisfaction and, consequently, adherence to physical activity, which deserves to be encouraged in the disease.

In short, virtual reality emerges as a new method that enables the performance of physical exercises with interactive games, in addition to being a pleasant way of interacting with its participants^{39,47}. More studies are still needed to demonstrate the effects of GT in individuals with CF, as well as to customize its prescription according to the severity and phenotype of each case.

However, in the studies included in this review, an increase in adherence to treatment was observed with the inclusion of TG, in the medium and long term, as well as benefits in increasing cardiorespiratory fitness, increasing metabolic load, and the level of satisfaction of individuals. Motivation increased with GT, with emphasis on individuals who were hospitalized.

CONCLUSION

The present review concludes that the use of GT as entertainment and a resource for performing

physical activity can have positive repercussions on the cardiorespiratory system, such as improving aerobic capacity and reducing fatigue and dyspnea, in addition to contributing to adherence to treatment. All these repercussions lead to a better quality of life and well-being for the individual with CF. Therefore, GT is suggested as an alternative to introducing the practice of physical activity in the management of individuals with this disease.

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