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Impact of Physical Activity on Health-Related Quality of Life in Post Liver Transplant Patients

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Original Research Article

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Abstract: Liver transplant is the corner for patients with end stage liver diseases. Post-transplant patients face many challenges including poor general health, physical inactivity and emotional problem. This article reviews studies that explored the impact of physical activity on health related quality of life (HRQOL) for post liver transplant patients. To collect evidence to supporting the relationship between physical activity and HRQOL for post liver transplant patients, a search of the PubMed, CINAHL, Psych Info, EbscoHost, Medline, and ProQuest Dissertations and Theses databases was conducted using key phrases, including chronic liver disease, liver transplant, post liver transplant, liver transplant and physical activity, liver transplant and health-related quality of life. The main search parameters were studies written in English and those conducted between 2005 and 2014. The initial search resulted in 957 records. There were 246 duplicate records. These records were removed. Records were excluded if patients were pediatric, second-time transplant recipients or receiving more than one organ transplant or if they had active infections. First records were excluded by screening the record titles; 453 records were excluded using this method. Next, records were excluded by screening the abstracts; 214 records were excluded using this method. Finally, records were excluded by screening the entire record text; an additional 37 records were excluded using this method.
Keywords: Chronic liver disease, liver transplant, post liver transplant, liver transplant and physical activity, liver transplant and health-related quality of life.

INTRODUCTION

Liver Transplantation

Treatment for chronic liver disease may take many forms. Some patients with chronic liver disease manage their disease with multiple drug regimens [1]. Others manage their disease by consuming a low sodium diet, avoiding alcohol, and medically managing disease-related symptoms [2]. Lifestyle interventions are prescribed for sustained weight loss and physical activity [1]. Weight reduction does not need to be significant in order to produce observable improvements in liver function, especially among patients with hepatitis C and NAFLD [1]. Although nonsurgical options for treating chronic liver disease may slow the progression of the disease, liver transplantation is "the only effective method of treatment for end-stage and acute liver failure" [3].

A significant challenge to liver transplantation is the shortage of viable organs for transplantation [4]. According to [5], lack of program resources including "organ shortage, quality of organ harvested, inability to meet the growing national need, increased demand of resource to meet the need of the program, and lack of a collaborative national strategy in organ donation and transplantation" affect the survival outcomes of people with liver disease [5]. suggested that national level collaborative efforts to speed up and simplify the liver donation process could significantly help improve survival outcomes for people with liver disease.

Liver transplants may be whole or partial transplants [6]. When a whole or orthotopic transplant is performed, the entire diseased liver is replaced with a heathy liver [6]. Orthotopic liver transplants occur using a whole liver from a deceased donor [4]. When a partial, or heterotopic, transplant is performed, healthy liver tissue is attached to the disease liver, which remains in place [6]. Heterotopic liver transplants occur using a partial liver from a living donor [4].

Complications of Liver Transplantation

Outcomes of liver transplantation may be impacted by multiple factors. Common factors include gender, level of education [7], diet, adherence to prescription regimens, and engagement in physical activity [4]. While post liver transplant patients may experience a variety of complications post-transplant, the two most common complications are rejection and infection [4].

Rejection of the whole or partially transplanted liver refers to the body's reaction to the new liver tissue as a foreign object [4]. The body's immune system attacks the new liver tissue [4] by generating antibodies to the transplanted liver tissue [8]. To keep the body's immune system from attacking the new liver tissue, patients take immunosuppressive medications such as calcineurin inhibitors and corticosteroids as well as other adjunctive agents such as Mycophenolate Mofetil and Sirolimus [9]. Use of immunosuppressive medications has decreased the incidence of rejection for post liver transplant patients in the United States [4], who have an 86% chance of survival after 1 year and a 78% survival rate after 3 years [10]. However, immunosuppressive medications may negatively impact blood pressure and cause headaches, diarrhea, and nausea [4]. They tend to interfere with the body's capacity to fight infections [4] as well.

Infections may be local, incidental, or opportunistic. Local infections occur in the area of the transplant, as is the case with biliary tract infections [11]. Incidental infections occur secondary to blood transfusions [11]. Opportunistic infections are typically hospital acquired and include pneumonia or encephalitis [11]. They also can also occur post operatively [11]. The use of immunosuppressive drugs increases the chance of infection from a variety of bacteria, viruses, and fungi [13]. Due to infection and other intra and perioperative causes, the risk of post liver transplantation mortality and graft losses is 60% in the first year following transplantation [12].

Survival Rates Following Liver Transplantation

In the United States, the overall 5-year survival rate post-transplant is approximately 75% [4]. At King Faisal Specialist Hospital (KFSH), the overall survival rates are higher. For Saudi Arabian and Egyptian KFSH post-transplant patients, 1- and 3-year survival rates between 2003-2007 have been reported to be 92% and 84%, respectively [11]. Between 2001-2012, the 1-year survival rate for adult and pediatric patients at KFSH was more than 90%, and the 5-year survival rate for this mixed population was more than 80% [5]. Post-transplant, patients may experience a recurrence of liver disease and again need some form of ongoing treatment or a second liver transplant [4].

The Sources of Evidence

A summary of the six studies providing evidence of the impact of physical activity on HRQOL in liver transplant patients is presented in Appendix B. The six studies varied in a variety of ways. The most notable were the general study characteristics and either the implemented intervention or means of measuring physical activity, depending on what method was used. In all six studies, HRQOL was measured in the same way.

General Study Characteristics

Only one study was conducted in the United States. The other six studies were conducted in countries in Europe. Numbers of liver transplant patients ranged from 8 to 119. Total numbers of participants ranged from 16 to 162. Not all studies included both age ranges and mean ages of participants. However, the age ranges of participants were most similar in the studies 13-15]. Mean ages were relatively similar among the studies in which the means were provided and ranged from 48.0 to 56.8 years. The time lapse since transplant varied greatly and ranged from less than 1 month to 8 years. In the three studies in which interventions were implemented, one intervention lasted 3 months and the other two interventions lasted 12 months each. Both [16, 13] in addition to HRQOL, also measured exercise capacity, muscle strength, and body composition [14]. also measured severity of fatigue. Only [15] also measured daily functioning, participation, anxiety, and depression. These study characteristics are summarized in Table-1.

Interventions

Studies also varied depending on whether or not a physical activity intervention was implemented. Three of the six studies included an intervention: [16, 13, 15]. In each case, the physical activity was a cardiovascular exercise. The major differences in the activities are identified on the evidence table in Appendix B. In addition to the cardiovascular exercise [16], included a diet plan as part of the intervention [13, 15] also include strength training.

Reporting of Physical Activity

When a physical activity intervention was implemented, physical activity was reported in one of two ways. Patients in the [16] study reported their perceived level of exhaustion on the Borg Category Scale for Rating of Perceived Exhaustion. [13] recorded patients' heart rates using heart rate monitors [15] did not report levels of physical activity.

When a physical activity intervention was not included in a study, physical activity was reported in several ways. Patients in the [17] study completed a brief questionnaire about their weekly recreational physical activity. Patients in the [14] study wore an activity monitor [18]. Measured physical activity using the short version of the International Physical Activity Questionnaire (IPAQ).

Table-1: Summary of Study Characteristics

Study	Setting	Transplant patients *N/n*	Patient age in years	Time lapse since transplant	Length of study	Additional outcomes measured
Krasnoff *et al.*, [16]	California, US	119	*M* = 49.5	2 months	12 months	Exercise capacity Muscle strength Body composition
Masala *et al.*, [18]	Rome, Italy	54 (plus 108 controls)	41-73 *M* = 55	1-8 years	NA	None
Roi *et al.*, [13]	Italy	69 (results for 26; plus 34 controls: results for 26)	18-70	<1 month	12 months	Exercise capacity Muscle strength and power Body composition
Rongies *et al.*, [17]	Poland	26	Group A *M* = 55.2 Group B *M* = 56.8	> 5 years	NA	None
van den Berg-Emons [14]	Netherlands	8 (plus 8 controls)	18-65	6-36 months	NA	Severity of fatigue
van Ginneken *et al.*, [15]	Netherlands	18	*M* =51	< 1 year	3 months	Daily functioning Participation Anxiety Depression

The IPAQ was developed to fill the need for a measure of self-reported physical activity that could be used internationally with comparable outcomes [19]. The IPAQ can be used with diverse international populations of young and middle-aged adults ranging from 15 to 69 years of age [20]. The full length version of the IPAQ is made up of 27 questions broken into five categories: (a) job-related physical activity; (b) transportation physical activity; (c) housework, house maintenance, and caring for family; (d) recreation, sport, and leisure-time physical activity; and (e) time spent sitting [21]. The short form is made up of seven questions broken up by level of vigor of the physical activities included in the questions: (a) vigorous, (b) moderate, (c) walking, and (d) sitting [21]. Both versions include instructions for patients to report their physical activity for the 7 days prior to completing the questionnaire. There also is a version of the instrument for use during telephone interviews that includes directions and prompts to aid the interview process [21]. The IPAQ can be used with diverse international populations of young and middle-aged adults ranging from 15 to 69 years of age [20]. Various versions of the IPAQ have been translated into at least 25 different languages [21].

Measures of Health-Related Quality of Life

In all six studies, the researchers reported HRQOL using the SF-36. SF-36 stands for Short Form 36 and is a shortened version of a core survey developed for the Medical Outcomes Study, a 2-year-long study of patients with chronic health issues [22]. The 36 items on the SF-36 were designed to measure "eight health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions" [22]. One single item measures patients' perceived change in health [22, 16, 18, 17] also calculated a physical component summary (PCS) score and a mental component summary (MCS) score. The SF-36 is available in Arabic from Rand Health. [14] and [15] both used a validated Dutch version of the SF-36 and [17] used a Polish version of the SF-36. Although both the [18] and the [13] studies were conducted in Italy, neither group of researchers specified the language of the SF-36 they used.

RESULTS

Of the original 957 records, seven records were retained for synthesis. A preferred reporting items for systematic reviews and meta-analysis (PRISMA) flowchart of the search process is presented in Appendix A.

To determine levels of evidence, I used [23] rating system for the hierarchy of evidence for intervention/treatment questions, which they developed using multiple sources. There are seven levels of evidence:

- Evidence from a systematic review or meta-analysis of all relevant random control trials.

- Evidence obtained from well-designed random control trials.
- Evidence obtained from well-designed controlled trials without randomization.
- Evidence from well-designed case-control and cohort studies.
- Evidence from systematic reviews of descriptive and qualitative studies.
- Evidence from single descriptive or qualitative studies.
- Evidence from the opinion or authorities and/or reports of expert committees [23].

Of the six studies retained for synthesis, one was a Level II randomized control trial, two were Level III prospective nonrandomized studies, two were Level IV case-control studies, and one was a Level VI cross sectional study. The studies and their corresponding levels of evidence are provided in Table-2.

Table-2: Level of Evidence for Selected Studies

Level of evidence	*n*	Study
Level II Randomized control trial	1	Krasnoff *et al.*, [16]
Level III Prospective nonrandomized control	2	Roi *et al.*, [13] van Ginneken *et al.*, [15]
Level IV Case-control	2	Masala *et al.*, [18] van den Berg-Emons *et al.*, [14]
Level VI Cross section	1	Rongies *et al.*, [17]

Generally speaking, all studies reviewed for this project showed that physical activity impacted HRQOL. However, results varied from study to study with regard to the specific health concepts. The HRQOL outcomes found to be associated with physical activity are identified in Table-3.

Table-3: SF-36 Health-Related Quality of Life Concepts Found to be Related to Physical Activity

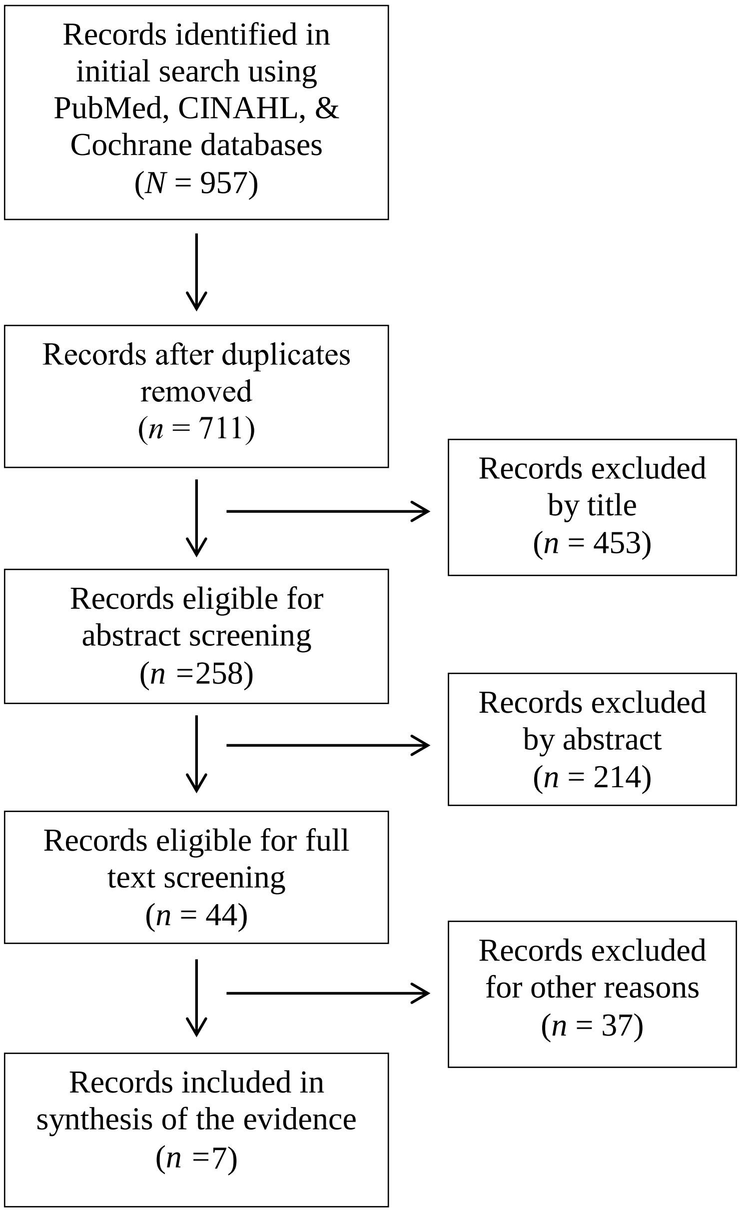
Health concept	Krasnoff *et al.*, [16]	Masala *et al.*, [18]	Roi *et al.*, [13]	Rongies *et al.*, [17]	van den Berg-Emons *et al.*, [14]	van Ginneken *et al.*, [15]
PF		X		X	X	X
RP		X				
RE		X	X	X	X	
GH	X		X	X		
BP			X	X		
SF			X	X		
VT			X			X
MH	X[a]	X			X	
PCS						
MCS		X				

Note. Health concept abbreviations from SF-36: PF = physical activity, RP = role limitations due to physical health, RE = role limitations due to emotional problems, GH = general health, BP = body pain, SF = social functioning, VT = vitality, MH = mental health, PCS = physical composite score for physical health, and MCS = mental composite score for mental health.

[a]Group by time interaction.

Of the six studies [18, 13, 17] all found an association between physical activity and five different measures of HRQOL, [14] found an association between physical activity and three different measures of HRQOL [15, 16] found an association for two; however, the association [16] found between physical activity and mental health was the result of a group by time interaction. More specifically [16], found that post liver transplant patients who participated in the exercise and diet intervention had significantly better mental health outcomes than patients who received only the usual post liver transplant care, but this difference was only recognized over time. The finding that there was no statistically significant difference between post liver transplant patients and patients without impairments with regard to reported levels of physical activity prompted [14] to hypothesize that fatigue and HRQOL may be more closely connected to HRQOL, when compared to physical activity, and the physical activity was a mediating factor as opposed to the final outcome.

Appendix A: PRISMA Flowchart



Appendix B: Table of Evidence

Author (Date)	Purpose	Design& Level of Evidence	Sample	Outcome Measures	Intervention	Results	Strengths/ Limitations
Krasnoff *et al.,* [16]	Effect of exercise and dietary counseling on HRQOL for post liver transplant patients.	RCT Level II	119 post liver transplant patients at 2, 6, and 12 months following liver transplant.	• HRQOL(measured using the SF-36) • Exercise capacity • Muscle strength • Body composition	Exercise Cardiovascular exercisemodeatleast 3 x's per week up to at least 30 min. per session; max. heart rate = 60–65% at start and 75–80% at end. Diet Caloric balance to attain and maintain ideal body weight and total fat intake ≤30% of total calories.	Exercise group showed greater increases in self-reported GH (*p*=0.038)and exercise capacity (*p*=0.036) compared to group receiving usual care. Both groups had similar increases in muscle strength, body weight, body fat, PF, RP, RE, BP, SF, VT, MH, PCS, and MCS.	Strengths: Large sample size, statistical rigor, prospective RCT Limitations: Drop-out rate 21.2%
Masala *et al.,* [18]	Effect of physical activity onHRQOL for post liver transplant patients.	Case control levelIV	108 controls and 54 post liver transplant patients between 1-8 years	• HRQOL (measured using the SF-36) • Physical activity (measured using the IPAQ)	None A control group was usedfor comparative purposes: engagement in physical activity versus no engagement in physical activity.	Positive correlation between metabolic equivalent andMCS(*p*=.043), PF (*p*=.001), RP (*p*=.006), RE (*p*=.006), and MH (*p*=.010).	Strength: Large sample size. Limitations:Opportunistic sample
Roi *et al.,* [13]	Effect of exercise on HRQOL for post liver transplant patients.	Multi-center controlled prospective nonrandomized Level III	26 post liver transplant patients	• HRQOL (measured using the SF-36) • Exercise capacity • Muscle strength and power • Body	Exercise Cardiovascular exercise (stationary bike) 3 x's per week for 30 min, per session. Strengthening 2 sets of 20 repetitions at	Significant improvement (*p*<.05) for BP, GH, VT, SF, and RE.Increased peak aerobic power (*t*=4.535;	Strengths:Model based on good cooperation of transplant specialists, sports medicine physicians and exercise specialists Limitations:Notrandomized. Small

				composition, urinalysis	35%of the repetition maximum for each of the selected muscle groups of the upper and lower limbs.	*p*<.01) and decreased body mass index (*t*=1.966; *p*<.05).	sample size.Results for control group not discussed Included more kidney than liver transplant patients
Rongies *et al.*,[17]	Relationship between physical activity and HRQOL for post liver transplant patients.	Cross sectional Level IV	26 randomly selectedpost liver transplant patients> 5 years posttransplant divided into Group A = sedentary lifestyle and Group B= Involved in regular physical activity.	• HRQOL (measured using the SF-36)	None A control group was used for comparative purposes: engagement in physical activity versus no engagement in physical activity (sedentary).	Physical active participants hadhigher scores on PF (*p*=0.008), BP (*p*=0.04), GH (*p*=0.03), SF (*p*=0.03), and RE (*p*=0.0005) compared to sedentary participants.	Limitations: Small sample
van den Berg-Emons *et al.*, [14]	Determine activity levels between active and nonactivepost liver transplant patients. Assess the effect of physical activity on both severity of fatigue and HRQOL	Case control Level IV	8 post liver transplant patients between 3-36 months posttransplant + 8 patients without known impairments	• HRQOL (measured using the SF-36) • Fatigue	None A control group was used for comparative purposes: activity levels of liver transplant patients versus patients without impairments.	Strong positive correlation betweenPF, RE, and MH and both duration of dynamic activities ($p \leq 0.05$) and mean motility $p \leq 0.10$). Severity of fatigue was correlated (*p*=0.01) with both duration of dynamic activities (rs=-0.81) and intensity of everyday activity(-	Limitations: Small sample

						0.84). Both groups were equally active.	
van Ginneken *et al.*, [15]	Effects of fatigue-reducing physical rehabilitation on daily functioning, participation, HRQOL, anxiety, and depression for liver transplant recipients.	Uncontrolledpre/post intervention Level III	18 fatigued post liver transplant patients	HRQOL measured using the SF-36	Exercise & Strengthening 12 week program included aerobicactivitiesandstrength training1 hour 2 x's per week,and counseling sessions 1 time per week for 4 weeks.	Significant improvements in daily functioning, participation, PF (11.5%, *p*=0.007)and VT (21.5%, *p*=0.022).No effect noted on anxiety or depression.	Limitations: Lack of control group, lack of generalizability to general transplants population and small sample size

*Note.*RCT = randomized control trial. HRQOL = health related quality of life.HRQOL = quality of life. IPAQ = International Physical Activity Questionnaire. SF-36 =36-Item Short Form Health Survey. SF-36 scale abbreviations: PF = physical activity,RP = role limitations due to physical health, RE = role limitations due to emotional problems, GH = general health, BP = body pain, SF = social functioning, VT = vitality, MH = mental health, PCS = physical composite score for physical health, and MCS = mental composite score for mental health.

CONCLUSION

The evidence reviewed here shows that HRQOL for post liver transplant patients can be improved through engagement in a variety of physical activities. The implications for clinical practice are clear. In the post liver transplant clinical setting, physical activity programs can be implemented as a means of improving HRQOL for post liver transplant patients. The evidence showed that the physical activity need not be complicated or extensive. In this respect, local level considerations can drive the particular design of the intervention to be implemented so that the unique needs of each patient population can be addressed directly.

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