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# Quality of life and menopausal symptoms in women with liver transplants

Qualidade de vida e sintomas da menopausa em mulheres transplantadas hepáticas

### Artigo Original

# Abstract

## Keywords

Hot flashes Liver transplantation Menopause Quality of life

#### Palavras-chave

Fogachos Transplante de fígado Menopausa Qualidade de vida

PURPOSE: To assess quality of life and climacteric symptoms in women with and without liver transplants. METHODS: This was a cross-sectional study of 52 women undergoing follow-up at a university hospital in southeastern Brazil from February 4th, 2009 to January 5th, 2011. Twenty-four of these women were 35 years old or older and had undergone liver transplantation at least one year before study entry. The remaining 28 women had no liver disease and were matched by age and menstrual patterns to the patients with transplants. The abbreviated version of the World Health Organization (WHOQOL-BREF) questionnaire was used to assess quality of life. Menopausal symptoms were assessed using the Menopause Rating Scale (MRS). Statistical analysis was carried out by Student's t-test, Mann-Whitney test and analysis of variance. Correlations between MRS and the WHOQOL-BREF were established by correlation coefficients. RESULTS: The mean age of the women included in the study was 52.2 (±10.4) years and the mean time since transplantation was 6.1 (±3.3) years. Women with liver transplants had better quality of life scores in the environment domain (p=0.01). No difference was noted between the two groups in any domain of the MRS. For women in the comparison group, there was a strongly negative correlation between somatic symptoms in the MRS and the physical domain of the WHOQOL-BREF (p<0.01; r=-0.8). In contrast, there was only a moderate association for women with liver transplants (p<0.01; r=-0.5). CONCLUSIONS: Women with liver transplants had better quality of life scores in the domain related to environment and did not exhibit more intense climacteric symptoms than did those with no liver disease. Climacteric symptoms negatively influenced quality of life in liver transplant recipients, although less intensely than in women without a history of liver disease.

#### Resumo

OBJETIVO: Avaliar a qualidade de vida e os sintomas do climatério em mulheres com e sem transplante de fígado. MÉTODOS: Estudo de corte transversal com 52 mulheres em acompanhamento ambulatorial em um hospital universitário na região sudeste do Brasil no período de 04/02/09 a 05/01/11. Dessas mulheres, 24 tinham 35 anos ou mais e haviam sido submetidas a transplante de fígado a pelo menos um ano antes do início do estudo. As outras 28 mulheres não tinham doença hepática e suas idades e padrões menstruais eram similares ao das transplantadas hepáticas. Para avaliação da qualidade de vida foi usada a versão abreviada do questionário da Organização Mundial da Saúde (WHOQOL-bref). Os sintomas da menopausa foram avaliados através do Menopause Rating Scale (MRS). A análise estatística foi realizada através dos testes t de Student, Mann-Whitney e ANOVA. As correlações entre o MRS e o WHOQOL-bref foram realizadas através de coeficientes de correlação. RESULTADOS: A idade média das mulheres incluídas no estudo foi de 52,2 (±10,4) anos e o tempo médio desde a realização do transplante foi de 6,1 (±3,3) anos. As mulheres transplantadas hepáticas tiveram melhores escores de qualidade de vida no domínio relacionado ao meio ambiente (p=0,01). Não houve diferença entre os dois grupos em nenhum domínio do MRS. As mulheres no grupo de comparação tiveram uma correlação fortemente negativa entre os sintomas somáticos do MRS e o domínio físico do WHOQOL-bref (p<0,01; r=0,8), diferentemente das mulheres com transplante de fígado que tiveram uma

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Study carried out at Departament of Tocogynecology, Hospital da Mulher Professor José Aristodemo Pinotti, Centro de Atenção Integral à Saúde da Mulher, Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil.

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correlação apenas moderada (p<0,01; r=-0,5). **CONCLUSÕES**: As mulheres com transplante de figado tiveram melhores escores de qualidade de vida no domínio relacionado ao meio ambiente e não tiveram sintomas climatéricos mais intensos. Os sintomas do climatério influenciaram negativamente a qualidade de vida nas transplantadas hepáticas, porém com menor intensidade do que nas mulheres sem antecedentes de doença hepática.

#### Introduction

Liver transplantation aims to prolong the survival of patients with end-stage liver disease. Five- and ten-year survival rates are around 70 and 60%, respectively<sup>1</sup>. Increasing survival has led to a greater concern with quality of life after transplantation<sup>2</sup>. Previous studies have shown that patients undergoing liver transplantation have alterations in quality of life, with increased fatigue, physical problems and a higher prevalence of depression and anxiety after transplantation than before it<sup>3-6</sup>. However, despite resulting in some negative changes, liver transplantation leads to an overall improved quality of life for patients and their caregivers and companions<sup>7,8</sup>. This improvement often becomes apparent three to five years after transplantation, by which time patients typically achieve a new level of psychosocial stability<sup>9</sup>.

Women account for approximately one-third of patients undergoing liver transplantation. The major causes of liver failure indicating liver transplantation in these women are primary biliary cirrhosis and cirrhosis secondary to post-viral hepatitis and autoimmune hepatitis<sup>10</sup>. In Brazil, alcohol abuse and chronic hepatitis C are also important indications for liver transplantation<sup>11</sup>. The liver is an essential organ to sex hormone metabolism. It conjugates estrogens to form glucuronides and sulfates. About one-fifth of these products are excreted in bile, while most of the remainder is excreted in urine. Furthermore, liver converts the estrogens estradiol and estrone into estriol, which is a less potent estrogen<sup>12</sup>. Women with severe liver disease have alterations in liver function which may compromise the metabolism of sex hormones and sex hormone-binding globulin (SHBG), leading to clinical repercussions. Studies on hypogonadism in liver transplant recipients have largely assessed only men. The few studies that have evaluated women undergoing transplantation have determined that the main gynecologic repercussions are abnormalities in the menstrual cycle. Following transplantation, 80 to 90% of women recover menstrual function<sup>13-15</sup>.

Climacteric is defined as a group of physiological events manifested as a decline in ovarian function, both before and after the last menstrual period<sup>16</sup>. It is a universal phenomenon and includes other aspects, such as the end of a woman's childbearing years and the so-called "empty-nest syndrome" when children leave home<sup>17</sup>.

The manner in which each woman reacts to this period in her life varies greatly according to cultural/psychosocial/biological factors and social relationships<sup>18</sup>. There is currently no consensus on the impact of menopausal status on quality of life. Some studies have demonstrated that menopause has a negative influence on quality of life scores<sup>19,20</sup>, whereas others have not shown this<sup>18</sup>. In addition, several studies have shown that menopausal transition-associated symptoms such as hot flashes and those caused by genital atrophy have a greater negative influence on quality of life than do cultural and psychosocial factors<sup>21–23</sup>.

In the near future, an increasing number of women with liver transplants will experience menopausal transitions. However, there are few studies evaluating menopausal transitions in this particular female subgroup. We postulated that variations in serum concentrations of sex hormones and long-term use of immunosuppressive agents would result in worse quality of life and more intense climacteric symptoms in women with liver transplants than in those without them. We therefore conducted a study in women with and without a history of liver transplantation attending outpatient clinics of a university hospital in southeastern Brazil. The aims of this study were to assess the influence of liver transplants and climacteric symptoms on quality of life in these subjects.

#### **Methods**

This cross-sectional study included women who had undergone liver transplantation and were attending the Liver Transplant Outpatient Unit of the Clinics Hospital at the State University of Campinas (UNICAMP) School of Medicine and women with no history of liver disease undergoing follow-up at the Menopause Outpatient Clinic of the Professor Dr. José Aristodemo Pinotti Women's Hospital (CAISM/ UNICAMP) from 4<sup>th</sup> February 2009 to 5<sup>th</sup> January 2011. All women aged 35 years or older who had received a liver transplant at least one year prior to the study were included. For each liver transplant recipient, a woman of similar age (within three years) and menstrual pattern was selected for comparison. Women were considered postmenopausal if they had been amenorrheic for at least 12 months. Women who had menstrual irregularity without an identified anatomic cause were classified as perimenopausal. Women who had regular menstrual

cycles were considered premenopausal<sup>24</sup>. Women with debilitating clinical conditions that precluded them from participating in the study, those with a history of bilateral oophorectomy, and those who had taken hormones for treatment of menopausal symptoms or as contraception in the three months before the study were excluded. Thirty-three (33) women with liver transplants who met the inclusion criteria were identified. Of these, five could not be contacted by telephone and four declined to participate in the study. Therefore, the final number of participating transplant recipients was 24. The comparison group consisted of 28 women without a history of liver disease who were matched by age (within 3 years) and menstrual pattern with the transplant recipients. Therefore, the final number of women in the study was 52.

Interviews with the participants were conducted in the Menopause Outpatient Clinic of CAISM at UNICAMP. The same researcher interviewed all participants and obtained data on age, skin color, level of school education, marital status, date of transplantation, time since transplantation, disease causing liver failure, type of current immunosuppressive medication, presence of arterial hypertension or diabetes mellitus, smoking habits, date of menarche, date of last menstruation, menstrual pattern and if the woman was sexually active. Weight (kg), height (m) and arterial pressure (mmHg) were also measured. Women then responded to questionnaires that assessed menopausal symptoms and quality of life. All women signed free and informed written consents before their interviews. The study was approved by the Research Ethics Committee of UNICAMP under number 721/2008 and financed by FAPESP under number 2008/09726-6.

#### Menopause rating scale

Menopausal symptoms were assessed using a scale that has been formally validated according to the requirements for quality of life instruments and translated into Portuguese, namely the Menopause Rating Scale (MRS)<sup>25</sup>. This questionnaire consists of 11 questions covering 3 dimensions of symptoms: psychological, somatic and urogenital. For each item, women could choose between five categories, namely no symptoms, less severe, moderate, severe and very severe symptoms. The total MRS score can vary from 0 (no symptoms) to 44 (maximum symptomatology). MRS scoring can also be analyzed in relation to the 3 domains of psychological symptoms (depression, irritability, anxiety, physical and mental fatigue, accounting for 0-16 points); somatic (sweating/hot flashes, cardiac symptoms, sleep disturbances, and muscular and joint problems, accounting for 0-16 points); and urogenital symptoms (sexual issues, bladder disorders,; and vaginal dryness, accounting for 0–12 points)<sup>25</sup>.

#### Quality of life assessment

For assessment of quality of life, the abbreviated version of the World Health Organization (WHOQOL-BREF) questionnaire was used. This questionnaire is a generic instrument used to assess quality of life that had already been validated and translated into Portuguese<sup>26</sup>. It contains 26 questions in four domains: physical, psychological, social relationships, and environment. There are an additional two questions about quality of life and general health. Higher scores indicate a better quality of life. The questionnaire was administered directly to subjects by the researcher in face-to-face interviews<sup>26</sup>.

#### Statistical analysis

Sample characteristics were compared between the transplantation group and non-transplantation group by  $\chi^2$  or Fisher's exact tests. Neither the WHOQOL-BREF (physical, psychological and social) nor the MRS domains (psychological, somatic and urogenital) had normal distributions. Data transformation was used (quadratic, cubic and square root) to apply parametric tests. For the quality of life and health domains, data normalization was not possible. Comparisons were made between transplant recipients and non-transplant patients according to menopausal status by Student's t-test or the Mann-Whitney test. For each group studied, the quality of life domains (normal data) were assessed after eliminating the effect of control variables by analysis of variance. Correlations between WHOQOL-BREF domains and MRS domains were established by Pearson's (normal data) or Spearman's (non-normal data) correlation coefficients. A classification proposed by Santos in 2007 was used to classify linear correlations<sup>27</sup>. The level of significance was set at 5% and SAS version 9.2 was the software used for analysis.

#### Results

Relevant clinical and sociodemographic data on the women studied are shown in Table 1. Their mean age was 52.2±10.4 years (median 49.02, range 35.0-72.2). Mean patient age at liver transplantation was 46.0±12.3 years (median 43.4, range 25.7-63.9). The mean time since transplantation was 6.1±3.3 years (median 5.8, range 1-12.5). The mean body mass index (BMI) was 27.6±4.8 (median 26.7, range 18.8–40.9). Of the 52 women studied, 14 (26.9%) were premenopausal, 13 (25%) perimenopausal, and 25 (48.1%) postmenopausal. There were no significant differences between the groups of women regarding age, level of education, marital status, menopausal status, presence of diabetes mellitus, age at menarche, BMI, sexual activity, number of births (deliveries), estradiol concentrations, and smoking habits. There was a significant difference in terms of skin color; 83.3% of women in the liver transplant group were white, whereas only 53.6% were white in the comparison group (p=0.02). Fewer women with liver transplants had chronic arterial hypertension than in the comparison group (p=0.04). However, at the time of the interviews there were no significant differences between the groups in systolic or diastolic arterial blood pressures. As expected, there was a difference in the use of immunosuppressive drugs, because none of the women in the comparison group were taking this type of medication (p<0.01) (Table 1).

Domain scores for the WHOQOL-BREF are shown in Table 2. Comparing the group of women with liver transplants and those without a history of liver disease, statistically significant differences were observed in the domain related to environment, with values of 65.6 ( $\pm 12.7$ ) for liver transplant recipients and 57.5 ( $\pm 14.7$ ) for women without a history of liver disease, both by bivariate analysis (p=0.03) and multivariate analysis adjusted for age, color, school education, marital status, sexual activity and comorbid conditions such as chronic arterial hypertension, diabetes mellitus and smoking (p=0.01) (Table 2).

A comparison between women according to history of liver transplantation can be seen in Table 3, which shows WHOQOL-BREF scores for premenopausal and peri/postmenopausal women. In the liver transplant group, no difference between peri/postmenopausal and premenopausal women in quality of life was observed. In the comparison group, there was a significant difference in the physical domain, with values of 80.1 (±9.6) for premenopausal and 64.1 (±19.3) for peri/postmenopausal women (p=0.04). Again, in the comparison group, for the question on general health, values of 85.7 (±13.4) for premenopausal and 60.7 (±29.1) for peri/postmenopausal women (p=0.04) were found (Table 3).

For statistical analysis of MRS scores, different approaches were used. First, total scores and domain scores from the questionnaires were compared according to history of liver transplantation. No significant difference was noted in any domain of the questionnaire. Second, MRS scores were compared in premenopausal women only; again, no significant difference was noted in any domain. Finally, peri/postmenopausal women alone were compared; again, no significant difference was observed (Table 4).

To assess the influence of menopausal symptoms on quality of life scores both in the liver transplant and comparison groups, correlation coefficients were applied between domain scores for the MRS and WHOQOL-BREF. In the transplantation group, there were moderately negative correlations (i.e. higher MRS scores corresponding to worse quality of life) between psychological symptoms on the MRS and the physical domain

of the WHOQOL-BREF (p<0.01, r=-0.6), between somatic symptoms of the MRS and the physical (p<0.01, r= 0.5) and general health (p<0.01, r=-0.6) domains of the WHOQOL-BREF, and between the total MRS score and the physical (p<0.01, r=-0.6) and general health (p<0.01, r=-0.5) domains of the WHOQOL-BREF. There were weakly negative correlations between psychological

Table 1. Clinical and sociodemographic data according to liver transplantation status (n=52)

	Liver		Control		
	transplantation				p-value
Ano	n	(%)	n	(%)	1.0
Age	12	(E0.0)	14	(E0.0)	1.0
≤49 years	12	(50.0)	14	(50.0)	
>49 years Color	12	(50.0)	14	(50.0)	0.02
White	20	(02.2)	1.5	(52.7)	0.02
Non-white	20 4	(83.3)	15 13	(53.6)	
	4	(16.7)	13	(46.4)	0.0/*
Schooling	0	(22.2)	1/	(57.1)	0.06*
0-7 years	8	(33.3)	16	(57.1)	
8-12 years	13	(54.2)	12	(42.9)	
>12 years	3	(12.5)	0	(0.0)	
Relationship status					0.1
With partner	14	(58.3)	22	(78.6)	
Without partner	10	(41.7)	6	(21.4)	
Hypertension					0.04
Yes	4	(16.7)	12	(42.9)	
Diabetes mellitus					0.2*
Yes	5	(20.8)	2	(7.1)	
Menopausal status					0.4
Premenopausal	7	(29.2)	7	(25.0)	
Perimenopausal	4	(16.7)	9	(32.1)	
Menopausal	13	(54.2)	12	(42.9)	
Menarche					0.6
≤13 years	13	(54.2)	17	(60.7)	
>13 years	11	(45.8)	11	(39.3)	
Sexually active					0.9
Yes	16	(66.7)	19	(67.9)	
BMI					0.7
≤27	12	(50.0)	15	(53.6)	
>27	12	(50.0)	13	(46.4)	
Immunosuppression					< 0.01
No corticosteroids	16	(66.7)	28	(100.0)	
With corticosteroids	8	(33.3)	0	(0.0)	
Parity					0.2*
0	3	(12.5)	3	(10.7)	
1	9	(37.5)	5	(17.9)	
≥2	12	(50.0)	20	(71.4)	
Serum estradiol concentration					0.7
<44.5 pg/mL	14	(58.3)	17	(63.0)	
≥44.5 pg/mL	10	(41.7)	10	(37.0)	
Smoking				•	0.3*
Yes	1	(4.2)	4	(14.3)	
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Unasterisked p-values,  $\chi^2$  test; \*Fisher's exact test; BMI: Body Mass Index.

Table 2. Scores for the World Health Organization quality of life questionnaire — abbreviated version (liver transplant recipients and con trols) (n=52)

	Liver transplant	recipients (n=24)	Control (n=28)			
Domain	Mean	SD	Mean	SD	p-value <sup>a</sup>	p-value <sup>b</sup>
Physical	66.2	15.0	68.1	18.6	0.6	0.44
Psychological	66.5	17.1	67.4	16.6	0.8	0.84
Social relationships	64.2	28.5	59.5	24.1	0.2	0.27
Environment	65.6	12.7	57.5	14.7	0.03	0.01
Overall QOL	79.2	17.6	72.3	14.2	0.1*	**
General health	76.0	20.2	67.0	28.1	0.3*	**

<sup>&</sup>quot;Student's Hest. "Analysis of variance with adjustment for age, race, education, marital status, sexual activity, comorbidities. \*Mann-Whitney test. \*\*Not assessed. QOL: quality of life.

Table 3. Scores for the World Health Organization quality of life questionnaire — abbreviated version according to history of liver transplantation (premenopausal versus peri/postmenopausal) (n=52)

Domain	Premenopausal (n=7)		Peri/postmeno			
(Liver transplantation)	Mean	SD	Mean	SD	p-value	
Physical	72.5	13.9	63.7	15.1	0.1	
Psychological	72.0	16.8	64.2	17.1	0.2	
Social relationships	72.6	20.3	60.8	31.2	0.4	
Environment	67.0	12.5	65.1	13.1	0.7	
Overall QOL	89.3	13.4	75.0	17.7	0.08*	
General health	85.7	19.7	72.1	19.5	0.1*	
Domain	Premenopo	Premenopausal (n=7) Peri/postmenopausal (n=21)				
(Control)	Mean	SD	Mean	SD	p-value	
Physical	80.1	9.6	64.1	19.3	0.04	
Psychological	76.8	7.9	64.3	17.7	0.1	
Social relationships	64.3	13.4	57.9	26.8	0.8	
Environment	62.5	4.0	55.8	16.6	0.3	
Overall QOL	75.0	0.0	71.4	16.4	0.6*	
General health	85.7	13.4	60.7	29.1	0.04*	

QOL: quality of life; WHOQOL:BREF: World Health Organization quality of life questionnaire – abbreviated version. Unasterisked p-values, Student's Hest; \*Mann-Whitney test.

Table 4. Scores for the Menopause Rating Scale (liver transplantation versus controls) (n=52)

Total group	Liver transplantation (n=24)		Control		
	Mean	SD	Mean	SD	p-value
Psychological	5.1	3.6	4.9	3.6	0.6
Somatic	3.5	2.8	4.2	3.5	0.8
Urogenital	2.0	1.9	2.0	2.2	0.9
Total score	10.7	6.0	11.1	7.8	0.8
Premenopausal	Liver transplantation (n=7)		Contro	p-value	
	Mean	SD	Mean	SD	p-value
Psychological	4.6	2.6	2.3	2.1	0.1
Somatic	1.9	1.6	1.3	1.3	0.4
Urogenital	1.9	2.0	0.3	0.8	0.07
Total score	8.3	4.7	3.9	3.0	0.06
Peri/postmenopausal	Liver transplantation (n=17)		Control	p-value	
	Mean	SD	Mean	SD	p-value
Psychological	5.4	4.0	5.8	3.6	0.8
Somatic	4.2	2.9	5.2	3.5	0.5
Urogenital	2.1	1.9	2.5	2.3	0.7
Total score	11.7	6.4	13.5	7.4	0.4

p-values: Student's t-test; SD: standard deviation.

symptoms of the MRS and the psychological (p=0.04, r=-0.4) and environmental (p=0.01, r=-0.4) domains of the WHOQOL-BREF, and between the total MRS score and the psychological domain (p=0.03, r=-0.4) of the WHOQOL-BREF. In the comparison group, there was a strongly negative correlation between somatic symptoms on the MRS and the physical domain of the WHOQOL-BREF (p<0.01; r=-0.8). There were moderately negative correlations between psychological symptoms of the MRS and the physical domain of the WHOQOL-BREF (p<0.01; r=-0.5), between somatic symptoms of the MRS and general health (p<0.01; r = -0.5) domain of the WHOQOL-BREF, and between the total MRS score and the physical (p<0.01, r=-0.7) and general health (p<0.01, r=-0.5) domains of the WHOQOL-BREF. There were weakly negative correlations between psychological symptoms of the MRS and the environmental (p=0.03, r=-0.4) and general health (p=0.01, r=-0.4) domains of the WHOQOL-BREF, between somatic symptoms of the MRS and the environmental domain (p=0.01, r=-0.4) of the WHOQOL-BREF, and between the total MRS score and psychological (p=0.01, r=-0.4) and environmental (p=0.01, r=-0.4) domains of the WHOQOL-BREF.

#### Discussion

The aim of this study was to obtain an accurate understanding of how liver transplantation influences quality of life and menopausal symptoms in women. Furthermore, we correlated menopausal symptoms with quality of life scores to measure the effect of these symptoms on quality of life in liver transplant recipients.

Women with a history of liver transplantation had better quality of life scores in the domain related to environment than did women with no history of liver disease, even after adjusting for the remaining variables such as age, color, school education, marital status, sexual activity, chronic arterial hypertension, diabetes mellitus and smoking. This result is in agreement with previously reported data. Telles-Correia et al. reported that one month after liver transplantation, patients with end-stage liver disease have significant improvements in quality of life in the physical and mental domains<sup>28</sup>. There is significant improvement in quality of life in the physical domain<sup>28</sup> six months after transplantation, and after three to five years there is an even greater improvement in quality of life because by this stage transplant recipients have achieved greater psychosocial stability9. In our study, it is noteworthy that liver transplant recipients not only had good quality of life but indeed superior values than did women with no history of liver transplantation. We believe that several factors may have contributed to this finding.

First, in this study the mean time since transplantation was approximately six years. As previously reported, the more time has elapsed since transplantation, the higher the quality of life scores are. Furthermore, women with a history of liver transplantation receive multidisciplinary follow-up care. It is likely that women feel strongly supported by this type of management and that it therefore has a beneficial effect on quality of life scores. Another factor that may explain this finding is that transplant recipients have already experienced periods of severely debilitated health. After going through the stressful experience of organ transplantation, recipients cherish their subsequent stability in health and tend to complain less about various aspects of their lives. Some authors suggest that surviving a potentially lethal disease may change internal values and moral concepts, altering the manner in which survivors cope with anxiety, depression and fatigue<sup>29-31</sup>.

Various studies have explored the influence of menopausal status and climacteric symptoms on quality of life. Some authors have found no difference in overall quality of life between premenopausal and postmenopausal women<sup>18,32-34</sup>, although some note that vasomotor symptoms have a negative effect on it 18. In 2009, a study entitled "Study of Women's Health across the Nation" found that, after final adjustment for all variables, the only independent relationship between menopausal status and quality of life indicators was with physical limitations. The same study showed that impaired quality of life during menopausal transition is most strongly related to symptoms such as vasomotor symptoms, urinary incontinence, sleep disturbances, and those caused by genital atrophy and morbid conditions associated with aging, such as rheumatoid arthritis, depression and stress<sup>23</sup>.

In 2012, a study entitled "Do Stage Transitions Result in Detectable Effects?" showed that the transition from premenopausal to postmenopausal status is associated with impaired quality of life, irrespective of the symptoms experienced<sup>17</sup>. In this study, negative impacts were more intense in the physical, pain and general health domains, as well as in energy levels and fatigue. One important finding of this study was that impaired quality of life did not impose limitations on daily living. It was suggested that, despite feeling worse, women did not let menopause interfere in their lives. Symptoms such as hot flashes and vaginal dryness in particular resulted in deterioration in quality of life, negatively interfering with social activities with friends and family<sup>17</sup>. In the present study, we analyzed the influence of menopausal status on quality of life scores in the liver transplant comparison groups separately. Being peri/postmenopausal did not influence quality of life in the liver transplant group. However, in the comparison group, peri/postmenopausal women had worse quality of life scores in the physical and general health domains.

Liver transplant recipients did not have more intense climacteric symptoms than women in the comparison group. We found no significant differences between the groups in total or domain scores from either questionnaire, regardless of menopausal status. There is still no published data about menopausal symptoms in liver transplant recipients. Previous studies have reported only that the main gynecologic symptom of premenopausal women with end-stage liver disease is secondary amenorrhea. After transplantation, most women resume having regular menstrual cycles<sup>13-15</sup>. Our results are in agreement with these data: we did not find more severe menopausal symptoms in liver transplant recipients than in comparison patients without liver disease. We therefore believe that when liver transplantation is successful, hormone metabolism reverts to normal and transplants have no influence on menopausal symptoms.

To test the hypothesis that menopausal symptoms have a greater influence on quality of life scores in liver transplant recipients than in comparison patients without liver disease, we measured correlation coefficients between various domains of the MRS and WHOQOL-BREF. We used both sets of coefficients to assess correlations between findings for women in the post transplantation and comparison groups and found that menopausal symptoms negatively influenced quality of life in both groups. Climacteric symptoms had greater influences on the physical and general health domains than they did on the environmental and psychological domains. For women in the comparison group, there was a strongly negative correlation between somatic symptoms in the MRS and the physical domain of the WHOQOL-BREF.

In contrast, there was only a moderate association for women with liver transplants. We believe that the same explanation accounts for the higher quality of life scores and the smaller influence of somatic menopausal symptoms on quality of life in women with liver transplants.

A limitation of this study was the small number of cases and the fact that they were in two subgroups, which made it difficult to perform analyses and reach definitive conclusions. However, we did include all eligible liver transplant patients attending our institution and available for study during the study period. Because this is the first study on quality of life and menopause symptoms in liver transplant recipients, we believe that, despite the limitation of few participants, our findings broaden knowledge about the needs of women undergoing liver transplantation, particularly during the climacteric years. Further studies are needed to enable the reaching of definitive conclusions.

Women with liver transplants had better quality of life scores in the environment domain and did not report more intense climacteric symptoms than did comparison patients without liver disease. Climacteric symptoms negatively influence quality of life in liver transplant recipients, although less intensely than in women without a history of liver disease.

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#### References

- Saab S, Ng V, Landaverde C, Lee SJ, Comulada WS, Arevalo J, et al. Development of a disease-specific questionnaire to measure health-related quality of life in liver transplant recipients. Liver Transpl. 2011;17(5):567-79.
- Lim KB, Schiano TD. Long-term outcome after liver transplantation. Mt Sinai J Med. 2012;79(2):169-89.
- van Ginneken BT, van den Berg-Emons RJ, van der Windt A, Tilanus HW, Metselaar HJ, Stam HJ, et al. Persistent fatigue in liver transplant recipients: a two-year follow-up study. Clin Transplant. 2010;24(1):E10-6.
- Bryan S, Ratcliffe J, Neuberger JM, Burroughs AK, Gunson BK, Buxton MJ. Health-related quality of life following liver transplantation. Qual Life Res. 1998;7(2):115-20.
- Nickel R, Wunsch A, Egle UT, Lohse AW, Otto G. The relevance of anxiety, depression, and coping in patients after liver transplantation. Liver Transpl. 2002;8(1):63-71.
- Masala D, Mannocci A, Unim B, Del Cimmuto A, Turchetta F, Gatto G, et al. Quality of life and physical activity in liver transplantation patients: results of a case-control study in Italy. Transplant Proc. 2012;44(5):1346-50.

- Sirivatanauksorn Y, Dumronggittigule W, Limsrichamrern S, Iramaneerat C, Kolladarungkri T, Kositamongkol P, et al. Quality of life among liver transplantation patients. Transplant Proc. 2012;44(2):532-8.
- Wang GS, Yang Y, Li H, Jiang N, Fu BS, Jin H, et al. Health-related quality of life after liver transplantation: the experience from a single Chinese center. Hepatobiliary Pancreat Dis Int. 2012;11(3): 262-6.
- De Bona M, Ponton P, Ermani M, Iemmolo RM, Feltrin A, Boccagni P, et al. The impact of liver disease and medical complications on quality of life and psychological distress before and after liver transplantation. J Hepatol. 2000;33(4):609-15.
- Jabiry-Zienjewicz Z, Kaminski P, Bobrowska K, Pietrzak B, Wielgos M, Zieniewicz K, et al. Menstrual cycle and sex hormone profile in perimenopausal women after liver transplantation. Transplant Proc. 2006;38(9):2909-12.
- Boin IF, Ataide EC, Leonardi MI, Stucchi R, Sevá-Pereira T, Pereira IW, et al. Elderly donors for HCV(+) versus non-HCV recipients: patient survival following liver transplantation. Transplant Proc. 2008;40(3):792-6.

- Guyton AC, Hall JE. Textbook of medical physiology. 9th ed. Philadelphia: Saunders; 1996.
- Parolin MB, Rabinovitch I, Urbanetz AA, Scheidemantel C, Cat ML, Coelho JC. Impact of successful liver transplantation on reproductive function and sexuality in women with advanced liver disease. Transplant Proc. 2004;36(4):943-4.
- Mass K, Quint EH, Punch MR, Merion RM. Gynecological and reproductive function after liver transplantation. Transplantation. 1996;62(4):476-9.
- Cundy TF, O'Grady JG, Williams R. Recovery of menstruation and pregnancy after liver transplantation. Gut. 1990;31(3): 337-8.
- Hickey M, Davis SR, Sturdee DW. Treatment of menopausal symptoms: what shall we do now? Lancet. 2005;366(9483): 409-21
- Hess R, Thurston RC, Hays RD, Chang CC, Dillon SN, Ness RB, et al. The impact of menopause on health-related quality of life: results from the STRIDE longitudinal study. Qual Life Res. 2012;21(3): 535-44.
- Ozkan S, Alatas ES, Zencir M. Women's quality of life in the premenopausal and postmenopausal periods. Qual Life Res. 2005;14(8):1795-801.
- Dennerstein L, Lehert P, Guthrie J. The effects of the menopausal transition and biopsychosocial factors on well-being. Arch Womens Ment Health. 2002;5(1):15-22.
- Mishra GD, Brown WJ, Dobson AJ. Physical and mental health: changes during menopause transition. Qual Life Res. 2003;12(4):405-12.
- Kumari M, Stafford M, Marmot M. The menopausal transition was associated in a prospective study with decreased health functioning in women who report menopausal symptoms. J Clin Epidemiol. 2005;58(7):719-27.
- 22. Cheng MH, Lee SJ, Wang SJ, Wang PH, Fuh JL. Does menopausal transition affect the quality of life? A longitudinal study of middle-aged women in Kinmen. Menopause. 2007;14(5):885-90.
- 23. Avis NE, Colvin A, Bromberger JT, Hess R, Matthews KA, Ory M, et al. Change in health-related quality of life over the menopausal

- transition in a multiethnic cohort of middle-aged women: Study of Women's Health Across the Nation. Menopause. 2009;16(5): 860-9
- Birkhauser MH, Barlow DH, Notelovitz M, Rees MC. Management handbook: health plan for the adult woman. London: Taylor & Francis; 2005.
- Heinemann LA, Potthoff P, Schneider HP. International versions of the Menopause Rating Scale (MRS). Health Qual Life Outcomes. 2003;1:28.
- Fleck MP, Louzada S, Xavier M, Chachamovich E, Vieira G, Santos L, et al. Aplicação da versão em português do instrumento abreviado de avaliação da qualidade de vida "WHOQOL-bref". Rev Saúde Pública.2000;34(2):178-83.
- Santos C. Estatística descritiva Manual de auto-aprendizagem. Lisboa: Edicões Sílabo; 2007.
- Telles-Correia D, Barbosa A, Mega I, Mateus E, Monteiro E. When does quality of life improve after liver transplantation? A longitudinal prospective study. Transplant Proc. 2009;41(3):904-5.
- 29. Aadahl M, Hansen BA, Kirkegaard P, Groenvold M. Fatigue and physical function after orthotopic liver transplantation. Liver Transpl. 2002;8(3):251-9.
- Goetzmann L, Klaghofer R, Wagner-Huber R, Halter J, Boehler A, Muellhaupt B, et al. Quality of life and psychosocial situation before and after a lung, liver or an allogeneic bone marrow transplant. Swiss Med Wkly. 2006;136(17-18):281-90.
- Schwartz CE, Rapkin BD. Reconsidering the psychometrics of quality of life assessment in light of response shift and appraisal. Health Qual Life Outcomes. 2004;2:16.
- Dennerstein L, Dudley E, Guthrie J, Barrett-Connor E. Life satisfaction, symptoms, and the menopausal transition. Medscape Womens Health. 2000;5(4): E4.
- Brzyski RG, Medrano MA, Hyatt-Santos JM, Ross JS. Quality of life in low-income menopausal women attending primary care clinics. Fertil Steril. 2001;76(1):44-50.
- 34. Ekström H, Hovelius B. Quality of life and hormone therapy in women before and after menopause. Scand J Prim Health Care. 2000;18(2):115-21.