PUNIVERSIDADE FEDERAL DA BAHIA
FACULDADE DE MEDICINA DA BAHIA

PROGRAMA DE PÓS-GRADUAÇÃO
EM MEDICINA E SAÚDE

Mychelle Morais de Jesus

CARACTERÍSTICAS COMPORTAMENTAIS E PSIQUIÁTRICAS DE PACIENTES EM LISTA DE ESPERA PARA TRANSPLANTE HEPÁTICO

TESE DE DOUTORADO

Salvador
2018

Morais de Jesus, M.

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v.1

> Tese apresentada ao Programa de Pós-graduação em Medicina e Saúde da Faculdade de Medicina da Bahia da Universidade Federal da Bahia, como requisito parcial para a obtenção do título de Doutor em Medicina e Saúde.

> Orientador: Dr. Lucas C. Quarantini

Salvador
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MYCHELLE MORAIS DE JESUS

CARACTERÍSTICAS COMPORTAMENTAIS E PSIQUIÁTRICAS DE PACIENTES EM LISTA DE ESPERA PARA TRANSPLANTE HEPÁTICO

> **Tese de autoria de Mychelle Morais de Jesus intitulada Características comportamentais e psiquiátricas de pacientes em lista de espera para transplante hepático, apresentada a Universidade Federal da Bahia, como requisito parcial para obtenção de título de Doutor em Medicina e Saúde.**

BANCA EXAMINADORA

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Dedico este trabalho, a alguém que se desenvolveu junto com ele e, portanto, precisou mesmo que sem saber e/ou escolher, dividir tempo, atenção, cuidado, memórias.

A minha filha Lanna Morais Flach

RESUMO

O presente estudo objetivou investigar o impacto do diagnóstico psiquiátrico durante o pré-transplante sobre o desfecho de morte no pós-transplante hepático. Para tanto, foi conduzido um estudo de coorte, ao avaliar longitudinalmente 93 indivíduos expostos e não expostos a transtornos mentais ainda no pré-transplante transplante e acompanhados por pelo menos dois anos após o transplante. Os instrumentos utilizados foram, além de entrevista semi-estruturada, o M.I.N.I. PLUS (*Mini International Neuropsychiatric Interview-BrazilianVersion*5.0.0), *Short-Form* 36 e Bis 11 (*Barrat Impulsiviness Scale*). Todos os instrumentos foram aplicados em pacientes elegíveis para o transplante de fígado durante o período de 2010 a 2015 no Complexo Hospitalar Professor Edgard Santos (Com-HUPES)–Universidade Federal da Bahia (UFBA). Resultaram da presente tese, artigos que descreveram o perfil psiquiátrico destes sujeitos em lista de espera de transplante, comportamentos de risco de contágio do VHC e, o principal achado da tese, o papel dos transtornos mentais no prognóstico pós-transplante. Os trabalhos demonstraram alta prevalência de comorbidades psiquiátricas, evidências de comportamentos de risco como o compartilhamento de equipamentos de manicure, e a falta de diretriz para avaliação psiquiátrica nos pacientes em fila de espera. Prospectivamente observou-se que comorbidades psiquiátricas no pré-transplante não confeririam risco para morte no pós-transplante. Conclui-se através dos trabalhos realizados que apesar da elevada prevalência de comorbidades psiquiátricas em pacientes em lista de espera esta prevalência não foi associada a desfecho negativo no pós-transplante, além disso, ressalta a necessidade de diretrizes para avaliação e acompanhamento destes pacientes em todo o processo do transplante hepático.

Palavras-Chave: transplante, fígado, comorbidade psiquiátrica

ABSTRACT

The study aimed to investigate the impact of pre-transplant psychiatric diagnosis on the outcome of death after liver transplantation. We conducted a cohort study with 93 individuals exposed and not exposed to mental disorders in the pretransplant accompanied during at least two years after transplantation. The instruments used were a semi-structured interview, the M.I.N.I. PLUS (Mini International Neuropsychiatric Interview-Brazilian Version 5.0.0), Short-Form 3 and BIS 11 (Barrat Impulsiviness Scale). All instruments were applied in patients eligible for liver transplantation during the period from 2010 to 2016 at the Hospital Edgar Santos Edgard Santos (Com-HUPES) - Federal University of Bahia (UFBA). The present paper presents articles describing the psychiatric profile of these subjects on the transplant waiting list, risk behaviors of HCV infection and the main finding of the production, the mental disorder role for post-transplant prognosis. The studies show a high prevalence of psychiatric comorbidities, evidence of risk behaviors such as sharing of manicure equipment, and lack of guidelines for psychiatric evaluation to the waiting patients. It was prospectively observed that it is not an association between pre-transplant psychiatric comorbidities and post-transplant negative clinical outcome, such as death. It is concluded through the studies carried out that despite the high prevalence of psychiatric comorbidities in patients on the waiting list; this prevalence was not associated with a negative outcome in the post-transplantation. The results highlight the need of guidelines for the evaluation and the caring to these patients during the process of liver transplantation.

Keywords: transplant, liver, psychiatric comorbidity

LISTA DE ABREVIATURAS E SIGLAS

ALC *Alcoholic Liver Cirrhosis*

ALD *Alcoholic liver disease*

BAI *Beck Anxiety Inventory*

BDI *Beck depression inventory*

BDI-FS *Beck Depression Inventory-Fast Screen*

BIS *Barrat Impulsiviness Scale*

CCI *Charlson Comorbidity Index*

CES-D *Center for Epidemiologic Studies Depression Scale*

CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico

Com-HUPES Complexo Hospitalar Professor Edgard Santos

DAF Doença alcoólica do fígado

DSM *Diagnostic and statistical manual of mental disorders*

HADS *Hospital anxiety and depression scale*

HCC Hepatocellular carcinoma

HCV *Hepatitis C Virus*

INTERMED *Interdisciplinary Medicine Instrument*

M.I.N.I *Mini International Neuropsychiatric Interview*

MADRS *Montgomery Asberg Depression Rating Scale*

MDE *Mood disorder episode*

MMPI-2 *Minnesota Multiphasic Personality Inventory—2, 370-item version*

MMSE *Mini-Mental State Examination*

NASH *Nonalcoholic fatty liver disease*

NEO-FFI *NEO Five-Factor Inventory*

PAS *Psychogeriatric Assessment Scales*

PHQ-4 *Patient Health Questionnaire-4*

PSS *Perceived Stress Scale*

PTSD *Post-traumatic stress disorder*

QoL *Quality of life*

SCL-90-R *Checklist-90-Revised*

SF-36 *Medical Outcomes Study 36 – Item Short – Form Health Survey*

SIPAT *Stanford Integrated Psychosocial Assessment for Transplant*

TDAH Transtorno de déficit de atenção e hiperatividade

UFBA Universidade Federal da Bahia

SUMÁRIO

1 INTRODUÇÃO

O transplante de fígado é a única opção para pacientes em estágio avançado da doença hepática[1]. De acordo com dados divulgados pelo Ministério da Saúde, houve em 2016, 1880 transplantes de fígado apenas no Brasil[2]. A quantidade de fígados a serem doados é muito limitada frente ao número de pessoas aguardando o transplante, o que produz grandes filas de espera. Em julho de 2017 a lista de espera para fazer transplante de fígado no Brasil foi de 1279 pessoas [3].

Estudos anteriores já observaram a prevalência de comorbidades psiquiátricas nesta população[4, 5], por exemplo, abuso e dependência de álcool, abuso de opióides, transtornos de ansiedade e depressão [6]. No Brasil, este é um tema pouco explorado[6]. Entretanto, algumas variáveis como aspectos psicossociais podem afetar a probabilidade de sucesso no pós-transplante [7]. Pode-se citar o diagnóstico de doença alcoólica do fígado (DAF) que foi associado a baixos índices de sobrevivência no pós-transplante [8, 9], também a depressão que pode aumentar o risco de mortalidade após o transplante [10].

Apesar de já haver o relato da prevalência de comorbidades psiquiátricas em paciente em lista de espera para transplante de fígado, ainda são necessários estudos que explanem a prevalência de diferentes comorbidades psiquiátricas de forma mais aprofundada. Além disso, também são escassos os estudos que observem o impacto deste fator no prognóstico pós-transplante.

Pesquisas apontam a necessidade de avaliações psiquiátricas prévias ao transplante para os pacientes [11-13]. Apesar da importância da avaliação médica para inserção na lista de transplante, a qual, diante da limitação de recursos, busca maior chance de sucesso no pós-transplante, não há uma diretriz padronizada para avaliação da saúde mental assim como de que forma proceder diante de dificuldades relacionadas à saúde psicológica nesta população.

Importante ressaltar que além do estresse causado pelo declínio da saúde, existe o estresse, para o paciente, provocado pelo receio de não ser aprovado para transplante através da avaliação médica[14]. O alto nível de estresse nestes pacientes pode afetar tanto a qualidade de vida como também o sucesso desta modalidade terapêutica complexa, requerida para o transplante[15].

Diante da relevância e necessidade de aprofundamento sobre o tema, este estudo pretende investigar o valor preditivo de transtornos mentais, impulsividade e qualidade de vida durante o pré-transplante para o prognóstico pós-transplante. Ampliar o entendimento sobre a situação psicológica e psiquiátrica de pacientes que esperam o transplante de fígado pode viabilizar a construção de estratégias de intervenção que preparem melhor o indivíduo para a experiência de transplante e, portanto, contribuindo para melhor prognóstico da doença hepática. Adicionalmente, esperamos que o presente trabalho contribua para novas equipes em formação, direcionadas ao cuidado destes sujeitos em situação de transplante.

2 OBJETIVOS

Principal

Investigar o impacto da presença de diagnóstico psiquiátrico no pré-transplante sobre o desfecho de morte no pós-transplante hepático.

Secundários

Revisar artigos científicos que observaram comorbidades psiquiátricas em sujeitos a espera para transplante de fígado.

Realizar avaliação psiquiátrica em indivíduos na fila de espera para transplante de fígado.

Descrever as características sócio-demográficas, comportamentais (qualidade de vida e impulsividade) e psiquiátricas dos indivíduos em lista de espera para transplante hepático.

3 REVISÃO DE LITERATURA

Psychiatric Issues in patients awaiting liver transplantation: an original cross-sectional study followed by systematic review of existing evidence.

Summary

Objective This study aimed to investigate pre-transplant psychiatric variables in patients waiting liver transplantation. Also, it aimed analyze psychiatric variables in different diagnosis etiology.

Design Cross-sectional study and systematic review of published evidence

Measurement Psychiatric comorbidity, quality of life variants and systematic review of literature using the Pubmed search engine. The systematic review included studies which investigated psychiatric comorbidity and diagnosis of liver disease in individuals waiting liver transplantation.

Results Data obtained from 215 liver transplant candidates presented high prevalence of psychiatric comorbidities (53%). The mental health wasn't significantly different at the groups Hepatitis C Virus (HCV), Alcoholic Liver Cirrhosis (ALC), HCV and ALC, and Other indications. However, HCV patients presented higher percentage of psychiatric diagnosis on five from the nine psychiatric diagnoses presented at the study – Current Mood disorder episode (MDE), Past MDE, Anxiety Disorders, Abuse of illicit substances and Post-Traumatic Stress Disorder (PTSD). The systematic review identified 28 studies addressing psychiatric comorbidity in patients waiting liver transplantation. None of the studies analyzed whether there was a difference in the prevalence of psychiatric comorbidities in the different etiologies of clinical diseases. The studies methodologies varied considerably, they used different instruments to access psychiatric comorbidity: Hospital Anxiety & Depression Scale (HADS) (32%), Beck's Depression Inventory (BDI) (14%), MINI MENTAL (7%), Semi

structured Psychiatric Interview (7%) and Others instruments (39%). The review showed high psychiatric comorbidity prevalence (27%).

INTRODUCTION

Liver transplantation is the main therapeutic alternative for patients with terminal chronic liver disease [1]. The waiting process, when the patient awaits the moment of being transplanted, is marked by intense mental suffering and presence of psychiatric symptoms, particularly anxiety and depression [2]. In this sense, individuals list waiting experience decreased quality of life itself [3-5] even compared to kidney transplantation [6] and own post - liver transplant [3].

HCV, ALD and nonalcoholic steatohepatitis are the most clinical conditions associated with the indication to liver transplantation [7]. Individuals with Hepatitis C often experience increased six fold risk of suicide and the emergence of depressive symptoms and anxiety that result in decreased quality of life, compared to the general population [8]. Studies have indicated that the individual with hepatitis C tends to have a lower quality of life (QoL) than the general population and to have a high presence of psychiatric symptoms associated with their own course [8-12].

Alcoholic liver cirrhosis is a major cause of chronic liver disease worldwide and has become a public health problem. This disease can range from simple steatosis, alcoholic hepatitis or steatohepatitis, progressive fibrosis and, finally, cirrhosis and / or hepatocellular carcinoma [13]. Alcohol consumption corresponds to 3.8% of global mortality and 4.6% of disability adjusted life years lost due to premature death [14].

Literature indicates high prevalence of psychiatric comorbidity in waiting list for liver transplantation [2, 15-17]. It is observed that 40% or more of the individuals enrolled in the liver transplant list have comorbid psychiatric disorders, which may negatively affect the outcome of the procedure and, consequently, post-transplant quality of life [18]. Solid organ is a limited resource, the number of potential transplant recipients and available donors result in a long waiting. Patients "who would be most likely a successful recipient" are selected. Individuals who need transplantation face severe transformation of their usual lives and stressful medical evaluations. The apprehension of don´t pass at transplant evaluation could declines the own patient health [19].

Mental health specialists should then contribute understanding this population better in order to improve care. Aiming to help minimize bias of team member decision about listing patients

with psychiatric illnesses, this study describes clinical, psychiatric and socio demographic characteristics of individual candidates for liver transplantation with HCV (Hepatitis C Virus), ALC (Alcoholic Liver Cirrhosis), HCV and ALC, and with other indications. Also compare quality of life among individuals infected groups. These investigative studies have been put into context by conducting a systematic review of previous studies addressing psychiatric comorbidities in liver transplant candidates in different etiology of diagnosis.

METHODS

Cross-sectional study

Patients were older than 18, eligible for liver transplantation, enrolled in the Hepatology Service of the University Hospital Professor Edgar Santos, between 2010 and 2014. This study was approved by the Institutional Review Board. All participants provided written informed consent to participate in the sectional study.

Patients eligible for liver transplantation were grouped into four distinct groups according to their clinical indication for transplantation. The first group - HCV - was formed by individuals infected with Hepatitis C, including individuals with Hepatitis B co - infection. The second group - ALC – individuals with alcoholic liver cirrhosis. Third group – HCV and ALC – patients with both diagnoses. And fourth group - OTHER INDICATIONS - was formed by individuals indicated to the transplant due to other diseases such as autoimmune hepatitis, NASH, alcoholic liver disease, Wilson's disease, hepatitis B and hepatocarcinoma.

QoL was assessed using the self-assessment scale SF-36 (Medical Outcomes Study 36 – Item Short – Form Health Survey). It features eight quality of life domains: physical functioning, role limitations due to physical aspects, pain, general health, vitality, social Functioning, emotional aspects and mental health. Each domain ranges from 0 to 100 [20].

When the data follow standard compatible with the normal distribution, continuous variables were compared using the Student t test or the Mann-Whitney test. Categorical variables were compared using the chi-square test and Fisher's exact test (when required) and were evaluated the powers of association between independent variables and the outcomes studied. Statistical analyses were performed using Statistical Package for Social Sciences software (version 16.0). Significance was defined as a value of $p<0.05$.

The Mini International Neuropsychiatric Interview in its extended version - M.I.N.I. PLUS.5.0 [21] was used to standardize the diagnostic method during the research according to DSM– IV-R criteria [22]. The structural organization of M.I.N.I. is made up of modules, represented by letters of the alphabet and corresponding to each diagnostic category. There is at the beginning of each module, key question (s) that represent the mandatory criterion (s) of

each diagnosis. The questions were answered with a simple "yes" or "no", property that streamlined the interview.

Systematic review

The systematic review was performed using an electronic search in the Medline-PubMed database. The survey took place in June, 2017. The Medline search was performed through PubMed (www.ncbi.nlm.nih.gov/pubmed) using the Mesh-terms: ("Liver Transplantations" OR "Transplantation, Liver" OR "Transplantation, Hepatic" OR "Grafting, Liver" OR "Graftings, Liver" OR "Liver Grafting" OR "Liver Graftings" OR "Hepatic Transplantation" OR "Hepatic Transplantations" OR "Transplantations, Hepatic") AND (("psychiatric Comorbidities" OR "psychiatric Comorbidity" OR "psychiatric Multimorbidity" OR "psychiatric Multimorbidities") OR ("Health, Mental" OR "Mental Hygiene" OR "Hygiene, Mental")). The search was not limited by language of publication. The authors selected 51 relevant studies using as inclusion criteria that the article described psychiatric comorbidity and also described the disease etiology. The review studies were excluded as well as the studies which their pdf. File were not available, leaving 28 studies for a more detailed evaluation.

RESULTS

Sistematic review

Psychiatric comorbidities on different disease etiology

The systematic review found publications from 1992 to 2016, most of the studies were conducted in USA (12) and Germany (4). The studies used different instruments to access psychiatric comorbidity: HADS (32%), Beck's Depression Inventory (14%), MINI MENTAL (7%), Semi structured Psychiatric Interview (7%), Others instruments (39%). 11 studies investigated three or more psychiatric diagnosis, 10 studies analyzed only anxiety and depression, 4 only one psychiatric comorbidity and 3 wasn't clear about which psychiatric comorbidity were analyzed. All studies investigated anxiety and/or depression disorders, only nine described that investigated others mental disorders. Four studies presented others mental disorders prevalence (Adjustment Disorder and Personality Disorder).

13 from the 28 selected studies presented prevalence data to the readers. The total number of subjects, including the original study, was 1864 individuals, 508 (about 27%) of individuals presented at least one psychiatric comorbidity. Although the most of papers had investigated psychiatric comorbidities, few differentiated the prevalence of psychiatric comorbidity in different etiologies; none crossed the data from these two variables: psychiatry comorbidity and etiology disease.

The methodology varied considerably, such that meta-analysis was not feasible.

Original study

Socio demographic and psychiatric comorbidities among patients with ALC, HCV and other indications

The authors examined the pre transplant prevalence of comorbid psychological disorders in 215 liver disease patients waiting liver transplantation, the total conventional population, 114 (53%) individuals had at least one psychiatric comorbidity. Excluding individuals who only had "alcohol abuse/dependence" as psychiatric comorbidity, the prevalence was 68 individuals (31.6%). Among the 215 individuals surveyed, the majority were male (78.6%),

equal or older than 40 years old (85.5%), married or in a stable relationship (71.6%) and professionally active (56.3%).

Table 2 shows that, even was not statistically significant, HCV patients had higher psychiatric comorbidity prevalence in five from nine prevalence related on the sample: Current MDE, Past MDE, Anxiety Disorders, Abuse of illicit substances and PTSD. ALC patients had higher prevalence only on Alcohol Abuse and/or Dependence (Life time). None individual had psychotic disorder diagnosis.

Quality of life in different etiologies

There was also no significant difference in quality of life scores between the four groups. Table 3.

DISCUSSION

The present study corroborate the specialized scientific literature that already indicated the high prevalence of mental disorders among individuals indicated for liver transplantation [23]. According to original data, 114 (53%) patients on the waiting list are diagnosed with at least one mental disorder, at the moment or throughout life, even excluding "Alcohol abuse/dependence" it was high (31.6%). These data are considered high when compared to those referring to the prevalence of mental disorders in the world population. A systematic review and meta-analysis of the literature revealed that 17.6% out of 650,000 people in 59 countries surveyed experienced a mental disorder during the 12 months prior to the survey and 29.2% out of 450,000 individuals surveyed in 38 Countries have experienced at least one mental disorder throughout their lives [24].

Table 2 shows that the only psychiatric comorbidity which ALC had higher prevalence was "Alcohol Abuse and/or Dependence (Life time)". This one was expected due the disease course. On the other hand, although not significant, HCV patients were most affected in the majority of psychiatric disorders (Table 2). Others papers related already the high prevalence of psychiatric comorbidity in hepatitis C infected patients [25]. It's expected that the no significance is due the small sample size.

It is known that the main route of transmission of Hepatitis C is the use of injecting drugs (syringe sharing) [1]. However, the rates of abuse and dependence of psychoactive substances in individuals with Hepatitis C were not significant, 4 patients (5.5% from the total HCV group). In view of this, we believe that there is a selection bias among the individuals who are candidates for transplantation, corroborated by the low coverage and poor health support services and by the exclusion and low demand of some segments of society to the Health System.

There was no diagnosis of psychotic disorder in the sample studied. We believe that is also due a selection bias ratified by the widespread belief among health professionals, especially those with no mental health training, that such patients would be poorly adherent to treatment.

Contrary to expectations, there were no differences in quality of life scores between groups of different etiologies. This result could be related to the sample size, since we divide it into four groups. However similar quality of life scores was perceived when compared each group

scores with total population scores. Given the high prevalence of psychiatric comorbidities, low scores were expected in the quality of life domains of the studied population, but only the "physical role functioning" domain showed low scores. This domain should be associated with the individual difficult clinical situation [26].

Although a meta-analysis with the review data was not possible, it is important to highlight the high prevalence of psychiatric comorbidity on the transplant waiting list patients (27%), greatly detected in several different studies, including this study. Once the others studies didn´t crossed the data of psychiatric comorbidity and different etiology, we don´t know through review if one diagnose disease could be more conduce to psychiatric comorbidity than the other. It still needs to be better understood. It is also necessary to look for ways to detect and address this issue with more homogeneity, decreasing bias.

Within the criteria chosen for this review only nine studies investigated others mental disorders, others than anxiety and depression, and four studies from them demonstrated prevalence data. Usually not many different psychiatric disorders were investigated in one study. Since there are not much data about this issue, this factor points to important negligence related to the mental health of the patients, or even maybe the exclusion without parameters of patients suffering from mental illness for the waiting list for liver transplantation.

CONCLUSION

From the original study and review is perceived the need of better understanding around psychiatric comorbidity facing its high prevalence in liver transplant candidates. This knowledge is necessary to build evaluations about mental health with less bias and improve the assistance to the patients before liver transplantation.

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TABLE 1 – Pre-transplant socio-demographic and psychiatric comorbidities

Variables	Total	Psychiatric comorbidities		
		Absence N (%)	Presence N (%)	*p value*
Gender				**0.014
Female	46	29 (63.0)	17 (37.0)	
Male	169	72 (42.6)	97 (57.4)	
Age				**0.865
< 40	31	15 (48.4)	16 (51.6)	
≥ 40	184	86 (46.7)	98 (53.3)	
Marital status				**0.003
Single	25	11 (44.0)	14 (56.0)	
Married / Stable relationship	154	81 (52.6)	73 (47.4)	
Divorced/ Windower	34	7 (20.6)	27 (79.4)	
Occupation				***0.661
Unemployed	8	3 (37.5)	5 (62.5)	
Professionally active	122	58 (47.5)	64 (52.5)	
Retired by age	32	15 (46.9)	17 (53.1)	
Retired due to illness	51	24 (47.1)	27 (52.9)	
Diagnosis etiology*				**0.678
HCV	72	50(69.4)	22(30.6)	
ALC	71	49(69.0)	22(31.0)	
HCV and ALC	18	14 (77.8)	4(22.2)	
Others	54	34 (63.0)	20 (37.0)	

* Alcohol abuse/dependence was excluded from this analysis. ** Analyzed through Pearson Chi-Square. *** Exact Fisher

TABLE 2- Diagnosis etiology and psychiatric comorbidity through MINI

Psychiatric Comorbidity	Total	Diagnosis Etiology N (%)				p value
		HCV	ALC	HCV and ALC	Others	
Current MDE	11	5 (45.5)	2 (18.2)	1 (9.1)	3 (27.3)	**0.684
Past MDE	19	9 (47.4)	5 (26.3)	0 (0.0)	5 (26.3)	**0.425
Bipolar disorder	3	0 (0.0)	1 (33.3)	0 (0.0)	2 (66.7)	**0.381
Risk of suicide (Moderate / High)	6	1 (16.7)	1 (16.7)	0 (0.0)	4 (66.7)	**0.271
Anxiety Disorders	20	8 (40.0)	4 (20.0)	1 (5.0)	7 (35.0)	**0.478
Alcohol abuse/dependence	74	21 (28.4)	40 (54.1)	9 (12.2)	4 (5.4)	*0.000
Other substance abuse/dependence	6	4 (66.7)	1 (16.7)	1 (16.7)	0 (0.0)	**0.167
Adjustment Disorder	25	7 (28.0)	7 (28.0)	1 (4.0)	10 (40.0)	**0.367
PTSD	19	8 (42.1)	4 (21.1)	2 (10.5)	5 (26.3)	**0.658

* Analyzed through Pearson Chi-Square, **Exact Fisher

TABLE 3 - Etiology diagnosis and Quality of Life

SF-36 Domains	Total	HCV	ALC	HCV and ALC	Others	*p value
			Mean (95% Confidence Interval for Mean)			
Physical functioning	68.66(64.58-72.74)	69.42(62.59-76.25)	66.71(58.64-74.78)	69.72(55.91-83.54)	69.90(62.27-77.54)	0.930
physical role functioning	34.57(29.00-40.14)	40.58(29.01-52.15)	28.93(20.40-37.46)	31.94(14.46-49.43)	35.10(24.40-45.80)	0.408
Bodily pain	67.78(64.15-71.40)	66.75(60.66-72.85)	69.01(62.46-75.56)	65.28(50.90-79.66)	68.33(60.87-75.78)	0.934
General health	59.49(56.62-62.37)	62.87(58.13-67.61)	60.50(55.90-65.10)	62.22(51.86-72.58)	52.71(46.03-59.40)	0.053
Vitality	64.32(59.62-69.03)	66.91(55.11-78.71)	63.77(58.46-69.08)	71.11(58.02-84.20)	59.33(51.97-66.68)	0.532
Social role functioning	70.93(66.98-74.88)	70.11(63.01-77.21)	69.29(62.39-76.18)	76.39(62.92-89.85)	72.36(64.16-80.55)	0.793
Emotional role functioning	80.86(72.72-89.00)	83.09(75.49-90.69)	82.86(61.18-104.54)	83.33(66.04-100.63)	74.36(63.39-85.33)	0.846
Mental health	81.76(77.69-85.83)	79.88(75.21-84.56)	84.00(74.99-93.01)	86.89(79.61-94.17)	79.69(70.06-89.33)	0.694

*ANOVA

Table 4 – Studies reviewed

Study	Country	N	Instruments used	Categories of psychiatric diagnosis investigated	Categories of clinical diagnosis investigated
Teixeira, Marques et al. 2016 [27]	Brazil	52	psychiatric interview and MADRS	Mood disorders, anxiety disorders, personality disorders, psychotic disorders, substance abuse, alcohol abuse, alcohol and substance abuse	Alcoholic etiology, viral etiology, viral and alcoholic etiology, other etiologies
Benzing, Krezdorn et al. 2016 [28]	Germany	235	PHQ-4	Anxiety, depression	Alcoholic etiology , cryptogenic liver cirrhosis , cholestatic bile duct diseases, viral hepatitis, cystic liver disease, autoimmune hepatitis, not specified
Benzing, Krezdorn et al. 2016 [29]	Germany	57	HADS	Anxiety, depression	Alcoholic etiology, cryptogenic liver cirrhosis, cholestatic bile duct diseases, viral hepatitis, cystic liver disease, autoimmune hepatitis, not specified
El-Meteini, Montasser et al. 2015 [30]	Egypt	35	Checklist-90-Revised (SCL-90-R)	Obsessive–compulsive, depression, anxiety, phobic anxiety, paranoid ideation, psychoticism	HCV-related ESLD, HCC on top of HCV-related liver cirrhosis, ESLD accompanied by portal vein thrombosis
Madan, Borckardt et al. 2015 [31]	USA	45	PAS, BDI-FS, SAAST, psychiatric assessment and diagnosis	Depression, alcool abuse, personality	cirrhosis secondary HCV, alcoholic cirrhosis only, both HCV and alcohol-related cirrhosis, and cirrhosis secondary to nonalcoholic steatohepatitis (NASH)
Ludwig, Dobe-Tauchert et al. 2015) [32]	Germany	21	TERS	Uninformed	Uninformed
López-Navas A 2013 [33]	USA	63	MMPI-2	Personality	Ethanol cirrhosis, hepatitis C virus cirrhosis, ethanol with hepatocellular cirrhosis, hepatocarcinoma with hepatitis C in virus, other etiologies
Miller, Paulson et al. 2013 [34]	USA	82	BAI and CES-D	Anxiety, depression	Hepatitis C, Hepatitis C and alcoholic cirrhosis, Alcoholic cirrhosis, cryptogenic cirrhosis, primary biliary cirrhosis, primary sclerosing cholangitis, nonalcoholic steatohepatitis, others
Ludwig, Dobe-Tauchert et al. 2014 [35]	Multicentric	60	HADS	Anxiety, depression	Uninformed
Baranyi, Krauseneck et al. 2013 [36]	Germany	42	STAI short version and PSS	Anxiety	Alcoholic liver disease, infectious hepatitis, primary biliary cirrhosis, malignancy, miscellaneousc
Santos, Goncalves et al. 2012 [37]	USA	100	HADS (Portuguese version), (NEO-FFI) (Portuguese	Depression, anxiety, personality traits	Uninformed

			version)		
Schneekloth, Jowsey et al. 2012 [38]	USA	143	Psychiatric interview	Major depressive disorder, anxiety disorder, schizophrenia and severe personality disorders	Colangio carcinoma and no colangio carcinoma
Zaydfudim, Feurer et al. 2012 [39]	USA	186	standardised psychiatric interview, and the MMSE	Uninformed	Noncolestatic, colestatic and others
Rogal, Landsittel et al. 2011 [40]	USA	179	Chart by treating physician	Anxiety, depression, PTSD and others	Hepatitis C, alcohol, hepatitis C and alcohol, acute liver failure, hepatitis B, NAFLD, alpha-1-antitrypsin deficiency, cryptogenic, primary sclerosing cholangitis, autoimmune hepatitis, others
Telles-Correia, Barbosa et al. 2011 [41]	Portugal	45	CES-D, and BAI	Anxiety, depression	ALD
Telles-Correia, Barbosa et al. 2011 [42]	Portugal	84	HADS	Anxiety, depression	Familial amyloid polyneuropathy (FAP) and chronic liver disease (CLD)
Dominguez-Cabello, Martin-Rodriguez et al. 2010 [43]	Spain	51	HADS	Anxiety	Hepatitis C infection, alpha-1 antitrypsin deficiency, hemochromatosis and primary biliary cirrhosis. Diagnosis of hepatocellular carcinoma in their explanted livers
Karim, Intaraprasong et al. 2010 [44]	Canada	80	BDI	Anxiety, depression	Liver cirrhosis
Day, Best et al. 2009 [45]	United Kingdom	155	HADS	Anxiety, depression	ALD, primary biliary cirrhosis, cryptogenic cirrhosis, primary sclerosing cholangitis (PSC), HCV, metabolic, autoimmune hepatitis, polycystic liver, malignancy, hepatitis B infection
Goetzmann, Ruegg et al. 2008 [46]	Switzerland	69	Mini-Mental State exam scores,	DSM-III criteria for a psychiatric diagnosis	Liver cirrhosis (due to hepatitis C), post-alcoholic cirrhosis, liver cirrhosis (due to hepatitis B), primary biliary cirrhosis, primary sclerosing cholangitis, other diagnoses
Silva, Ferrara et al. 2008 [47]	Italy	553	HADS, Prior psychiatric history Axis I and II disorder according to DSM-III-R	Uninformed	HCV, HBV, HIV, alcohol cirrhosis
Russell, Feurer et al. 2008 [48]	USA	107	HADS portuguese version	Anxiety, depression	Noncholestatic cirrhosis (hepatitis B, C, or alcoholic cirrhosis), metabolic liver disease, cryptogenic cirrhosis, nonalcoholic steatohepatitis, or autoimmune hepatitis, cholestatic cirrhosis (primary biliary cirrhosis or primary sclerosing cholangitis) and other indications
Estraviz, Quintana et al. 2007 [49]	Spain	60	Psychiatric interview	Adjustment disorder, depression, substance abuse, organic mental disorders, anxiety, other	Alcoholic liver disease, comorbid HCV or HBV, HCV, HBV, hemochromatosis, autoimmune, antitrypsin deficiency, and others

DiMartini A, Dew DA et al. 2004 [50]	USA	112	BDI	Depression	Alcohol, HBV, HCV, hepatocarcinoma, cholestatic disease
Weinrieb, Barnett et al. 2004 [51]	USA	27	Psychiatric interview	Ethanol abuse/dependence	Hepatocellular carcinoma, HCV, cryptogenic
Chacko, Harper et al. 1996 [52]	USA	22	INTERMED, MADRS, HADS.	Anxiety, depression	Uninformed
Collis, Burroughs et al. 1995 [53]	Ingland	11	SA-45 questionnaire	Somatizations, obsessions-compulsions, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.	Uninformed
Trzepacz and DiMartini 1992 [54]	USA	247	Psychiatric interview	Alcohol diagnosis, alcohol consumption patterns, length of sobriety, other substance use diagnoses, and alcohol rehabilitation experience	Uninformed

4 CASUÍSTICA E MÉTODOS

Foi conduzido um estudo prospectivo no período de 2010 a 2016 com pacientes eleitos para transplante hepático acompanhados no Complexo Hospitalar Professor Edgard Santos (Com-HUPES) – Universidade Federal da Bahia (UFBA). Até junho de 2015 foram incluídos 215 sujeitos com idade igual ou maior que 18 anos avaliados em ordem consecutiva após a indicação médica para o transplante. Foram excluídos os pacientes com hepatite fulminante, os que não tinham condições físicas para participar e os que não aceitaram participar, após a leitura do termo de consentimento. Todos os sujeitos foram acompanhados por, pelo menos, um ano a partir da primeira avaliação.

No pré-transplante foi utilizado, além de um questionário sócio-demográfico e clínico, o M.I.N.I. PLUS (*Mini International Neuropsychiatric Interview-Brazilian Version* 5.0.0) [16] - um instrumento estruturado de diagnóstico, compatível com os critérios do DSM-IV e CID-10 [17, 18], para avaliar a saúde mental. *SF*-36 [19] foi o instrumento escolhido para analisar qualidade de vida. Foram utilizados os oito domínios da escala para fazer a avaliação: Funcionamento físico, Desempenho físico, Dor corporal, Desempenho Emocional, Saúde Geral, Vitalidade, Funcionamento Social e Saúde mental. Os escores de cada domínio varia de 0 (pior qualidade de vida) a 100 (melhor qualidade de vida). Para avaliar a impulsividade, a escala BIS 11 [20] foi usada, ela é composta por 30 itens que produzem um escore total de impulsividade. Para esta escala foram adotados os seguintes pontos de corte: até 52 (baixa impulsividade), 52 a 71 (impulsividade normal ou limite) e acima de 71 (alta impulsividade).

A fim de evitar vieses de compreensão pelos entrevistados, todas as avaliações foram conduzidas por um profissional de saúde mental treinado.

Além das avaliações realizadas diretamente com os pacientes, informações complementares foram obtidas através de prontuários, de familiares, e de profissionais especialistas que acompanhavam o desenvolvimento clínico dos pacientes. Foi utilizada a melhor informação obtida.

Esta pesquisa segue as Diretrizes e Normas da Resolução 466/12 como também da declaração de Helsinki de 1989 sobre pesquisas envolvendo seres humanos. Os sujeitos participaram da pesquisa somente após estar cientes sobre os objetivos e procedimentos a ser realizados, após concordar voluntariamente a participar do estudo e assinar o termo de consentimento já

submetido ao Comitê de Ética em Pesquisa da Maternidade Climério de Oliveira situada no Com-HUPES (vide Anexo A).

5 RESULTADOS

Artigo n° 1

Mental disorders as a risk factor for death after liver transplantation:

A 2-year observational cohort study

Liver International

Submetido

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Mental disorders as a risk factor for death after liver transplantation: A 2-year observational cohort study

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ABBREVIATIONS:

BIS: Barratt Impulsiveness Scale

HCV: Hepatitis C virus

HCC: Hepatocellular carcinoma

ALD: Alcoholic liver disease

SIPAT: Stanford Integrated Psychosocial Assessment for Transplant

CCI: Charlson Comorbidity Index

Conflict of interest: none

ABSTRACT

Background & aims

Psychosocial aspects may affect the liver transplant survival rates and outcomes. The present study aimed to investigate the impact of mental disorders and impulsivity on the prognosis after liver transplantation.

Methods

We performed a prospective cohort study assessing end-stage liver disease individuals with and without psychiatric comorbidities during the two years' post-transplant. Psychiatric diagnosis was carried out through Mini-Plus 5.0.0 and impulsivity by using BIS-11 Scale in the pre-transplant phase. The end point data collection of the data was death after transplantation. The mortality outcome was observed during two years post-transplant. Kaplan-Meier was used for survival analysis.

Results

Between June 2010 and July 2014, 93 out of 191 transplant candidates received transplants. From the total of 93 patients given transplants, 21 had psychiatric comorbidities and 72 did not. By the end of the study, 25 people died. The presence of psychiatric comorbidity ($p = 0.160$) and impulsivity ($p = 0.245$) were not significantly associated with the outcome of death.

Conclusion

This study found no evidence that the presence of mental disorders and impulsivity worsened prognosis in post-liver transplantation.

Key points:

1. Psychiatry comorbidity is frequent in liver transplant candidates.

2. Psychiatry comorbidity and Impulsivity are not associated to death during two years after liver transplantation.

3. Most deaths occurred during the first year after transplantation.

INTRODUCTION

Liver transplantation is the only treatment for decompensated end-stage liver disease.[1] Hepatitis C virus (HCV), hepatocellular carcinoma (HCC) and alcohol abuse are the clinical conditions most associated with disease that leads to liver transplantation.[2, 3]

Key points among psychosocial aspects, affects the probability of success after transplant. [4, 5] Consequently, identifying the behavioral variables related to post transplant prognosis is essential, given the limited availability of organs. Diagnosis of alcoholic liver disease (ALD) and alcohol abuse were associated to poorer survival rates,[6, 7] especially in the absence of formal alcohol abuse programs.[8] In spite of this, favorable results have been obtained in patients undergoing liver transplantation for ALD.[9-11] There are some issues regarding the establishment of a guideline to the pre-transplant screening process. Most studies have shown that prognosis is one of the most important criteria that clinicians should use in distributing organs, despite the decision being related to moral ground in some instances. [12, 13]

Psychiatric diagnosis is one of the most controversial characteristics among transplant providers. [1] In some cases, psychiatrists are unable to recommend liver transplantation for individuals with psychiatric comorbidities even without a formal contraindication. [14] Few behavioral variables had been investigated as predictors of good or bad prognosis in liver post-transplant, including endophenotypes such as impulsiveness. One of the few available instruments to screen psychosocial and medical outcomes among candidates for liver transplantations is the SIPAT (Stanford Integrated Psychosocial Assessment for Transplant), which was created after verify information of 58 candidates for liver transplantation after only 1 year of follow-up. [4]

The present study aimed to assess decompensated end-stage liver disease patients. They were prospectively evaluated during two years after liver transplant comparing two groups: with or without psychiatric comorbidities. The study also intended to assess whether impulsive behaviors have a prognostic effect. The hypothesis is that both psychiatric aspects and impulsive behaviors have no effect on the patient's prognosis if the patient is well attended.

METHODS

Participants

Between June 2010 and July 2014, every patient with chronic liver disease referred to Hospital Universitário Professor Edgard Santos, Salvador, Brazil, was assessed for liver transplantation and invited to participate in the study. Those who agreed to participate underwent psychological assessment by a trained psychologist. The study included subjects aged 18 years or older. All the subjects were followed prospectively for two years. Reasons for exclusion were patients in fulminant hepatic failure, unable to participate in pre-transplantation psychological assessment and patients declining participation.

This study was approved by the Institutional Review Board. It is in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki declaration of 1975, as revised in 1983.

Measures

The subjects were evaluated for the diagnosis of mental disorders through the M.I.N.I. PLUS.5.0. [15] They were separated into two groups: unimpaired (there were no psychiatric comorbidities during pre-transplant) and mentally impaired (there was at least one psychiatric comorbidity during pre-transplant). Pre-transplantation diagnosis of `Lifelong abuse or alcohol dependence´ was analyzed separately from others psychiatric comorbidities since this one is highlighted in the scientific literature on its possible impact on post-transplant prognosis. Clinical diagnosis were categorized into 4 groups: ALD, HCV, others (others diagnosis) and "HCV and ALD".

In order to evaluate impulsivity, a self-administered scale, BIS-11, was used. It consists of 30 items that provide a total score of impulsivity in three second-order factors: attentional (lack

of focus), motor (acting without thinking), and non-planning (guidance for the present and not the future). Cutoff values were established for low, normal and high impulsivity (min.-51; 52-71; 72-max.) according to literature.[16]

In addition to the self-report, information was also obtained from medical records, experts who accompanied the patients, as well as through family members. The best available information was used.

The main outcome was mortality within 2 years. We report survival analysis for 2 years of follow-up.

Statistical analysis

For bivariate comparisons, we used chi-squared-test or Fisher test for categorical variables and Student's *t*-test or Mann-Whitney for continuous variables. We used Kaplan-Meier for survival analysis between the two groups: mentally unimpaired and mentally impaired. Time zero for the Kaplan-Meier survival curves was time of transplant. Logistic regression and Cox regression were used for multivariate analysis.

We considered a significance threshold (α) of 5%.

RESULTS

Pre-transplant data from 191 patients of a possible 240 patients considered for transplantation was assessed. Of the remaining patients, 93 received transplants and were monitored for two years, and 14 received transplants and did not complete a follow-up. Of the monitored patients, 25 died; 21 deaths occurred within the first year after transplantation.

Most of the subjects presented a score of 0 in the Charlson Comorbidity Index (CCI) (94%), were male (80%), in stable relationship (72%) and had a normal limit of impulsivity (65%). The two groups, mentally unimpaired and mentally impaired, had a difference in impulsivity (p= 0.033). Descriptive statistics and p-values from bivariate analysis are displayed in Table 1.

Most mortality outcomes were caused by primary graft dysfunction, acute cellular rejection, hepatic failure, sepsis, pulmonary infection, hepatocellular carcinoma and others cause of death. No socio-demographic or mental health variables showed significant association to the outcome of death under bivariate analysis, including impulsivity ($p = 0.245$) and lifelong abuse or alcohol dependence ($p = 0.515$).

In the logistic regression analysis, impulsiveness was associated with psychiatric comorbidity ($p = 0.043$) but not with mortality ($p = 0.287$). Impulsivity, psychiatric comorbidity ($p = 0.586$) and lifelong abuse or alcohol dependence ($p = 0.994$) were not associated with mortality.

The survival analysis confirmed that psychiatric comorbidity was not associated with mortality. There was no statistically significant difference between the mentally unimpaired and mentally impaired groups, at two years follow-up (93 subjects; $p = 0.419$).

DISCUSSION

The main result of this study was that transplanted end-staged liver subjects with mental disorders had similar clinical prognosis to those without mental disorder. The data corroborates previous studies, excluding delirium which presented higher mortality rate.[17] Corbett C et. al. (2013) endorses the idea that patients with mental health disorders have outcomes similar to the general transplant population when they are adequately controlled and socially supported.[18]

A similar situation occurred in individuals with a lifetime of alcoholic dependence: the diagnosis was not associated with post-transplant death. This data extended the discussion on the impact of the diagnosis of alcoholic dependence in the prognosis of transplanted patients. Despite many positive outcomes after a liver transplant, this treatment for ALD patients remains controversial. [19-21] According to Ubel PA (1997) not transplanting livers into patients with alcoholic cirrhosis, reflects social prejudice against alcoholism when resources are scarce.[12] Once the alcoholic candidate is carefully selected and has a prognosis as positive as the average person receiving a liver transplant, these criteria should not be supported.

Most death (21) occurred during the first year after transplant, and many of them occurred due to primary graft dysfunction (24%). This data supports the results found in this study, which suggest that the presence of psychiatric comorbidity does not interfere with post-transplant prognosis.

Hepatitis C diagnosis is highly associated with worse quality of life impulsive behaviors and risk behaviors.[22,23] Even knowing that 38% of the sample had hepatitis C, the disease and impulsivity were not associated to mortality post-transplant.

The present study has limitations. An example is the impossibility to predict when the transplantation candidate will be receiving the organ. It imposes a wide variation of time between pre-transplant and post-transplant assessment. Although patients were accompanied

for 2 years and 84% of the deaths within the first year after surgery, perhaps more years of monitoring would be needed to perceive differences in survival rates between patients with and without psychiatric comorbidities.

Another limitation is the absence of assessment for personality disorders. A study done by Yates et. al. (1998), however, assessed personality disorder comorbidity in alcoholic cirrose candidates for liver transplantation and did not find differences between individuals with this comorbidity.[24] A possible critical limitation in this study is that the most severe psychiatric patients are not even able to get on the waiting list for liver transplantation, promoting interpretation bias. Organ transplant in individuals with comorbid psychiatric illness already has been exposed as a current ethical dilemma.[25] The exclusion from transplantation based on the psychiatric diagnosis were considered unethical and not medically justified, unless, despite full support, the individual has an unacceptable quality of life, likely to be noncompliant with treatment or follow-up.[18] Still, anxiety, depression, resilience, self-efficacy, social support and coping are variables that must be considered for psychological interventions.[26]

In conclusion, in at least two years of subject follow-ups, the data does not show differences in survival rates between patients with and without psychiatric comorbidities. This issue, however, should be better explored in order to promote better psychosocial support to patients waiting for liver transplantation. To better understand liver transplant prognosis, longer follow up periods and the assessment of personality disorders, schizophrenia and bipolar disorder are necessary.

CONFLICT OF INTEREST

The authors do not have any disclosures to report.

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FIGURE LEGEND

Figure 1. Survival rates between groups with and without at least one psychiatry comorbidity. Two years of follow-up.

Table 1 - Sample descriptive characteristics.

Variables	Total (n = 93)	Unimpaired (72)	Mentally impaired (21)	*p* Value
Age	93	53 (11.75)	48 (12.44)	0.064
Gender				0.114
Female	18	12 (16.66)	6 (28.57)	
Male	75	60 (83.33)	15 (71.42)	
CCI				0.241
0	88	69 (95.83)	19 (90.47)	
1	5	3 (4.16)	2 (9.52)	
2	0	0 (0.00)	0 (0.00)	
Marital status				0.146
Stable relationship	67	54 (75.00)	13(61.90)	
Divorced	13	9 (12.50)	4 (19.04)	
Single	10	7 (9.72)	3 (14.28)	
Widow	3	2 (2.77)	1 (4.76)	
Occupation				0.091
Away by disease	15	12 (16.66)	3 (14.28)	
Retired by age	26	23 (31.94)	3 (14.28)	
With occupancy	48	35 (48.61)	13 (61.90)	
Student	2	1 (1.38)	1 (4.76)	
Unemployed	2	1 (1.38)	1 (4.76)	
Initial diagnosis				0.066
ALD	30	23 (31.94)	7 (33.33)	
Others	28	20 (27.77)	8 (38.09)	
HCV	30	24 (33.33)	6 (28.57)	
HCV and ALD	5	5 (6.94)	0 (0.0)	
Death				0.160
No	68	54 (75.00)	14 (66.66)	
Yes	25	18 (25.00)	7 (33.33)	
Lifelong abuse or alcohol dependence				0.073
No	61	50 (69.44)	11 (52.38)	
Yes	32	22 (30.55)	10 (47.61)	
Impulsivity				0.033
Low impulsivity	21	17 (23.61)	4 (19.04)	
Normal limit impulsivity	61	50 (69.44)	11 (52.38)	
High impulsivity	11	5 (6.9)	6 (28.57)	

Values reported as Mean (± Std. Dev) or Frequency (%).

Survival Functions
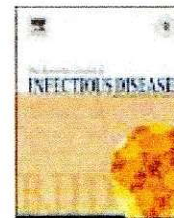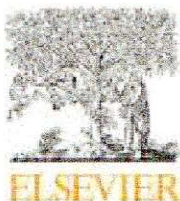

Follow-up time after surgery (days)
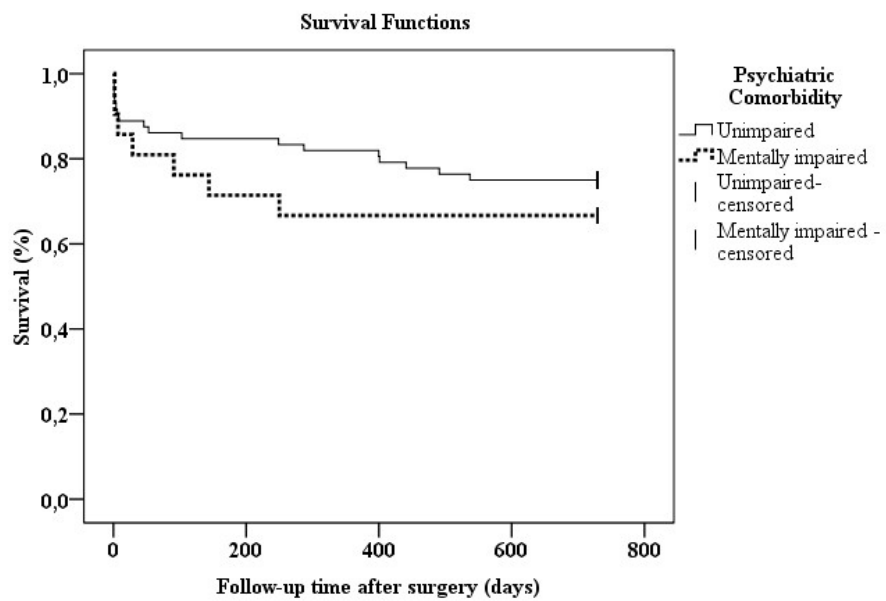
Artigo n° 2

Brazilian manicure: a potential dangerous behavior

The Brazilian Journal of Infectious Diseases

2016; Jan-Feb; 20(1): 109-10

Letter to the Editor

Brazilian manicure: a potential dangerous behavior

Dear Editor,

Hepatitis C virus (HCV) is a public health issue that affects about 150 million people worldwide. Transmission most commonly occurs through sharing of injection equipment for injecting drug use, transfusion of unscreened blood and blood products, and reuse or inadequate sterilization of medical equipment, such as syringes and needles.[1] Surprisingly, under these circumstances, it is customary and a cultural phenomenon in Brazil to visit beauty salons and remove the cuticles of the nails in the hands and feet.[2] Manicurists have little knowledge about transmission routes and prevention of infectious agents, despite the underlying risk from an invasive procedure which involves handling of biological material.[3]

We conducted an observational study, at the University Hospital of the Federal University in Salvador, Bahia, from 2010 to 2014, including 95 individuals with hepatitis C on a waiting list for liver transplantation, with the objective of determining the proportion of these subjects aware of their status who had shared sharp objects when receiving the service of a manicure, which is considered a risk behavior for infection. Median age was 57.9 years and the majority were men (81%) who were married or in a stable relationship. The subjects knew about their viral status and were asked whether they were using or had used someone else's manicure equipment; 55.3% gave a positive reply (Fig. 1).

This study found that more than half of the participants, at some point in their lives had shared manicure equipment, including after knowing about their viral infection status. This behavior may be due to belief that correct sterilization by beauty salons reduces the risk of transmission. Manicures can generate trauma or microtrauma on the skin surface, incurring an elevated risk of infection when blades or nail scissors are shared, without proper sterilization, with an asymptomatic infected family member who visits a barbershop or beauty salon.[4]

This scenario may be more serious if we consider previous studies conducted in Brazil that showed a low risk perception of contamination and few biosecurity precautions for manicures and pedicures. In a study with 100 professionals in the Southeastern region of Brazil, the majority (54%) related that they did not perform any procedures when in contact with customer's biological material, 80% declared that they did not use gloves, 85% did not know how the transmission
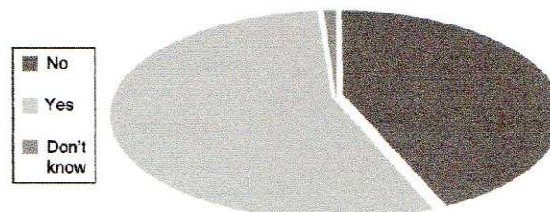
Fig. 1 – Distribution of shared use of manicure equipment among patients diagnosed with HCV in the municipality of Salvador, 2010–2014.

occurs, and 95% did not know how to prevent it.[3] Therefore, the low level of knowledge about transmission routes, prevention, biosafety, basic care, and risk perception elevates the risk of viral hepatitis infection.[2]

The hepatitis C virus infection can be minimized by changes in behavior, educational interventions, such as information materials and health education in beauty salons.[5] It is also recommended to use one's own equipment for procedures done in beauty salons in order to prevent contamination. Given the risks to which customers and salon professionals are exposed through the shared use of manicure equipment, there is a need to focus increasing knowledge about modes of transmission of the virus and its prevention. Moreover, public health authorities must ensure oversight of commercial establishments.

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Conflicts of interest

The authors declare no conflicts of interest.

59

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6 DISCUSSÕES

Foram avaliados durante o período pré-transplante191 sujeitos. Foi possível seguir prospectivamente 93 sujeitos durante pelo menos 2 anos. As perdas de seguimento deveram-se principalmente a morte não notificada pela família, desistência do paciente do tratamento e inviabilidade operacional de seguimento mais prolongado.

Dados importantes surgiram ao longo do percurso planejado para o estudo. Foi relatada alta prevalência de comorbidades psiquiátricas na amostra estudada. Este fator já foi freqüentemente relatado em outros estudos [21] de outros países, no Brasil, ainda pouco descrito. De acordo com a revisão sistemática que foi realizada durante este trabalho, não há homogeneidade entre os estudos ao investigar e descrever estes dados. Portanto, também não há diretrizes respaldadas para lidar com tal aspecto. A pouca informação, falta de consenso em investigar, avaliar, interpretar os dados, traz abertura para avaliações criteriosas no momento de decidir se o paciente tem condições ou não para passar por todo o processo de transplante e cuidados requeridos no pós-transplante. Inclusive, outro dado extremamente importante relatado neste estudo, é a não associação entre comorbidades psiquiátricas no pré-transplante e o desfecho morte durante o pós-transplante. A hipótese nula apresentada poderia estar relacionada ao grande percentual de mortes no primeiro ano pós o transplante (84%). A maioria das mortes foi causada pela disfunção primária do enxerto, choque circulatório, falência do fígado e rejeição do transplante. De acordo com especialistas da área, no Brasil, neste período em que a pesquisa foi realizada, houve baixo índice de doação na Bahia [2]. Estes fatores poderiam influenciar nos desfechos descritos deste estudo.

A impulsividade já foi citada como um componente de inúmeros transtornos psiquiátricos déficit de atenção e hiperatividade (TDAH), mania, abuso de substâncias e transtorno de personalidade [22]. Assim, como comorbidades psiquiátricas, poderia ser esperado que pudesse haver alguma relação desta variável com o desfecho. Mas também não apresentou associação. Por outro lado, surpreendentemente foi observado um comportamento de risco importante que é frequentemente emitido por esta população – mais da metade dos sujeitos com hepatite C, mesmo sabendo dos riscos de contaminar e ser re-contaminado, tem o hábito de compartilhar equipamentos de manicure. Esta é uma informação nova que precisa ter continuidade de observação, através deste estudo e de pesquisas futuras.

Apesar de não apresentar significância estatística, foi importante observar que os sujeitos diagnosticados com hepatite C apresentavam maior prevalência de comorbidades psiquiátricas em cinco dos nove tipos de comorbidades psiquiátricas relatadas neste estudo. Tais dados corroboram com estudos anteriores que também indicam altas prevalências de comorbidades psiquiátricas nesta população [23-25].

Houve limitações quanto ao recrutamento dos pacientes. Uma vez que os pacientes eram recrutados na medida em que eram atendidos nas consultas médicas, aqueles que não tinham boa adesão, que apresentavam um quadro clínico ou psiquiátrico mais grave, e até que foram a óbito e a família não informou, não foram contemplados. Portanto informações acerca destes pacientes não foram coletadas, o que leva um viés de seleção. Outra limitação é a falta de informações acerca do suporte social, especialmente no pós-transplante, visto que este é de extrema importância para os cuidados necessários do paciente.

Mesmo com limitações, os resultados apresentados foram expressivos quando comparados as amostras da maioria de estudos já realizados sobre comorbidades psiquiátricas no transplante de fígado. Além disso, como já exposto, ele também apresenta informações novas sobre o assunto. Pretende-se ainda realizar novas análises acerca da adesão dos pacientes, avaliando os aspectos comportamentais do pré-transplante e a adesão dos pacientes no pós-transplante. Esta análise não foi realizada até a conclusão da tese devido à restrição de tempo para apresentação do trabalho desenvolvido. É esperado que fatores como a impulsividade possam estar associados ao comportamento de adesão no pós-transplante.

Este estudo contribui com o entendimento mais aprofundado acerca da saúde mental destes pacientes. Todavia, mais estudos são necessários em vista de entender mais a saúde mental destes pacientes, como também o desenvolvimento de uma diretriz para avaliações e assistência a esta população.

7 CONCLUSÃO/ CONSIDERAÇÕES FINAIS

Esta tese demonstrou a alta prevalência de comorbidades psiquiátricas entre os pacientes na lista de espera para transplante hepático. Apesar de não demonstrar diferença estatisticamente significante, os pacientes com hepatite C obtiveram prevalência maior na maioria das categorias de transtornos psiquiátricos. Também expôs a heterogeneidade da literatura científica voltada a este tema, como também a escassez de estudos mais aprofundados e com amostras representativas.

O trabalho contribuiu especialmente demonstrando que a presença de transtornos psiquiátricos no paciente com indicação para transplante hepático não deve ser indicador de prognóstico negativo no pós-transplante. Além da presença de comorbidade psiquiátrica, a alta impulsividade também não foi associada ao desfecho.

Outro achado que deve ser contemplado não só pela equipe multidisciplinar que acompanha estes pacientes, mas também por políticas públicas, é a alta exposição dos pacientes infectados com hepatite C a comportamentos de risco como compartilhar equipamentos de manicure. Este comportamento pode resultar na transmissão do vírus a outros indivíduos como também a própria ré-infecção do paciente agravando o quadro clínico.

Diante do exposto é necessário entender melhor comportamentos de risco destes pacientes a fim de prevenir reinfecções, otimizar adesão e capacitá-los a boas estratégias comportamentais a fim de garantir uma boa resiliência no pré e pós transplante. A aquisição de conhecimento respaldado por uma adequada base científica deve ser prioritária na construção de ferramentas que auxiliem na identificação de sujeitos vulneráveis a uma evolução negativa no pós-transplante. Não devemos aceitar condutas baseadas em preconceitos, que rotulem sujeitos como incapazes de se tornarem receptores de enxertos somente baseados em diagnósticos psiquiátricos prévios; são obrigatórias evidências de que essas condições realmente se constituem em um obstáculo ao manejo clínico necessário no pós-transplante. Consequentemente, somente incluindo parâmetros de saúde mental podem ser elaboradas diretrizes consistentes para determinar candidatos adequados a transplante de fígado.

8 PERSPECTIVA DE ESTUDOS FUTUROS

Um número expressivo de sujeitos avaliados durante o pré-transplante não realizou a cirurgia até o final da pesquisa. A fim de continuar observar o impacto da presença de transtornos mentais no prognóstico destes pacientes, pretende-se dar continuidade as analises de dados encontrados neste trabalho avaliando o impacto da presença de transtornos mentais sobre permanência da lista de espera para transplante hepático. Muitas vezes o tempo de espera para o transplante é longo e requer considerável esforço dos pacientes para continuar atender, entre outras exigências, a adesão as consultas e atualização de exames solicitados. Portanto, conhecer melhor as variáveis que implicam sobre a continuidade ou exclusão dos pacientes da lista de espera para transplante hepático, é de grande valia para o desenvolvimento de conhecimentos sobre cuidados específicos a esta população.

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APÊNDICES

APÊNDICE A - The Portuguese Version of the Immunosuppressant Therapy Adherence Scale (ITAS) among Liver Transplant Recipient Patients: translation and psychometric properties

The Portuguese Version of the Immunosuppressant Therapy Adherence Scale (ITAS) among Liver Transplant Recipient Patients: Translation and Psychometric Properties

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ABSTRACT

Introduction and aim. Transplant recipients are chronically ill patients who rely on medical treatment throughout life to achieve positive results. Despite that, medication nonadherence after liver transplantation is extremely common. The self-report, one of several methods for measuring adherence, is easy to apply and lowcost. Thus, this study aims to translate and validate the Immunosuppressant Therapy Adherence Instrument (ITAS) in Brazilian Portuguese for liver transplant recipients. **Material and methods.** A total of 139 liver transplant recipients were selected from a general hospital, who were assessed by using the Portuguese version of ITAS. The scale was translated based on the model proposed by Wild, *et al*. and its psychometric properties were assessed. Results. The average Cronbach's α coefficient was 0.830. ITAS and Basel Assessment of Adherence with Immunosuppressive Medications Scale (BAASIS) presented significant correlation, with a Spearman's ρ coefficient = 0.300 (S = 309,580; p < 0.001). The area under the receiver operating characteristics (ROC) curve was 0.638 (95% CI: 0.557 - 0.715). Factor analysis results indicated that the carelessness factor model was the optimal model, and the factor "feeling worse" was the lowest. **Conclusion.** The Portuguese version of ITAS has adequate psychometric properties to measure adherence to immunosuppressant therapy.

Key words. Adherence. Liver Transplantation. Immunosuppression. Psychometrics.

INTRODUCTION

Adherence to a medical regimen is defined as the extent to which the patient's behavior coincides with the clinical prescriptions.[1] Among the greatest challenges to the success of transplants is to ensure regular adherence of immunosuppressive drugs. This is essential for the proper functioning of the graft.[2]

Immunosuppressant therapy nonadherence after liver transplantation is reported in 72.9% subjects who took less than 100% of the prescribed doses, tracked with electronic monitoring.[3] Therefore, almost half of transplant recipients have some non-adherent behavior, such as not using the medication regularly, nor taking the correct dose, nor the required timescales.[4,5] Despite the clinician's efforts to inform patients about the importance of immunosuppression to the maintenance of the graft, to avoid its rejection and other clinical outcomes negative, such consequences often occur.[6] In addition, nonadherence generates significant socioeconomic impacts on the health systems.[7]

There are several methods for measuring adherence. One of them, the self-report can measure adherence easily

and with very low cost, that being the most employed method in the clinical setting and research of medication nonadherence.[8,9] A validated self-report instrument is recommended for investigation of adherence behavior and can predict clinical outcomes. There is no gold standard to measuring adherence to immunosuppressive drugs,[10] so other objective methods and clinical outcomes can be used for correlation.[11] Adherence should be evaluated in the long term and strengthened through therapeutic strategies such as systematic education that may contribute to the adherence of medications.[12]

Brazil is the second country in the world in terms of numbers of liver transplantations.[13] Despite this fact there is no validated specific instrument to measure immunosuppressant therapy adherence for liver transplantations in Brazil. The aim of this study was to translate and assess the validation of the Immuno- suppressant Therapy Adherence Instrument (ITAS) to Brazilian Portuguese for patients submitted to liver transplantations.

MATERIAL AND METHODS

Design, sample and setting

This psychometric study was conducted in a general hospital (Hospital Português da Bahia) and in a Teaching Hospital (Universidade Federal da Bahia). Patients were recruited between September 01, 2014 and June 20, 2015. The assessments were applied to the participants who agreed to sign an informed consent form. The general sociodemographic survey was administered to all participants (n = 139). Patients were included in the study if they met the following criteria: received a liver transplant, able to understand the Portuguese language, and 18 years or older at the time of the study. Patients unable to read (illiteracy) and those who were submitted to retransplantation were excluded from the sample.

Demographic characteristics

Age, gender, marital status, and time post-transplant were assessed.

Variables and measurement

The ITAS is a self-report measure of immunosuppressant therapy adherence targeted to solid-organ transplant recipients, developed to be a reliable measure of adherence to immunosuppressant therapy in the three months prior to when research is conducted. The four items assess the behaviors of forgetfulness, carelessness, neglect and cessation due to feeling worse. Responses are designed for the patient to choose each behavior's frequency, in order to minimize patients' providing a positive adherence response of "yes". Response option levels are: 0 % of the time, 1-20 %', 21-50% and greater than 50%. Raw scores can range from 0 (greater than 50% for all items), indicating very poor adherence, to 12 (0% for all items), indicating perfect adherence. Scores below 80% indicate poor adhesion.[14]

A psychometric re-evaluation of the ITAS was performed and two theoretically linked psychosocial constructs were selected to design the construct validity analysis: social support and resilience. The results demon-

Table 1. The final version of the ITAS scale in Brazilian Portuguese.

ESCALA DE ADESÃO A TERAPIA IMUNOSSUPRESSORA (ITAS). Circule a letra da resposta que melhor estima a porcentagem de tempo descrita em cada uma das 4 questões.				
	0% (nenhuma)	1-20%	21-50%	Mais de 50% (Muito frequentemente)
1. Nos últimos 3 meses, com que frequência você esqueceu de tomar seu(s) medicamento(s) imunossupressor(es)?	A	B	C	D
2. Nos últimos 3 meses, com que frequência você foi descuidado ao tomar seu(s) medicamento(s) imunossupressor(es)?	A	B	C	D
3. Nos últimos 3 meses, com que frequência você parou de tomar seu(s) medicamento(s) imunossupressor(es) porque se sentiu pior?	A	B	C	D
4. Nos últimos 3 meses, com que frequência você deixou de tomar seu(s) medicamento(s) imunossupressor(es) por qualquer razão?	A	B	C	D

Legenda: 3 para "0% (nenhuma frequência) do tempo"; 2 para "1%-20% do tempo"; 1 para "21-50% do tempo"; 0 para "mais de 50% do tempo". Pontuação: Alta - baixa; sendo 0 baixa e 12 alta.

strated the ITAS statistical relationships with these constructs and confirmation that the ITAS is a valid and reliable measure of IST adherence.[15]

The Brazilian Portuguese version of the Basel Assessment of Adherence with Immunosuppressive Medications Scale (BAASIS), validated in kidney transplant patients was used as a standard for comparison. The BAASIS is a self-report instrument for measuring nonadherence (NA) in transplantations, that measures: taking adherence, drug holidays, timing adherence, and dose reduction in a four-week period. Responses are given a six-point scale: Never (0), once per month (1), every second week (2), every week (3), more than once per week (4), and every day (5).[16]

Translation

The ITAS was translated as according to the method proposed by Wild, et al.[17] The original questionnaire was translated independently by two fluent English speakers. This process resulted in two preliminary versions. A consensus among both translators resulted in a reconciled version. Next, a reverse translation from Portuguese to English was conducted.

The final version (Table 1) was applied to 30 liver transplant patients, who were asked about their understanding of the instrument.

Statistical analysis

Items were coded as 0, 1, 2, and 3 according to the Likert scale responses of "greater than 50%", "21-50%", "1-20%", and "0%", respectively.[14] Since ITAS and BAASIS present opposite punctuation directions, BAASIS raw score was inverted before analysis.

Cronbrach's α based on a polychoric correlation matrix was calculated to assess internal validity. Polychoric based α is considered to be more reliable in ordinal structured data.[18]

Convergent validity was assessed with Spearman's ρ correlation coefficient between ITAS and BAASIS (previously validated). ITAS accuracy considering BAASIS classification as a gold standard was evaluated by logistic regression. Individuals were labeled non-adherent if BAASIS items presented any answer different from "never".[19,20]

The Area Under the Receiver Operating Characteristic (AUROC) curve was calculated with respective confidence intervals estimated using bootstrap resampling. An optimal cut-point was determined using Youden criterion and used to determine accuracy, sensitivity, specificity, positive and negative predictive values.

Maximum-likelihood exploratory factor analysis with Varimax rotation was performed to analyze the optimal number of latent factors and to investigate factor loadings related to each item.

Analysis was performed using R programming language and environment.[21]

Ethic

This study was approved by the local Institutional Review Board (MCO-UFBA - process number 14/2002) and was carried out in accordance to Declaration of Helsinki (version dated 2013). The researchers ensured that the documents would be kept confidential.

RESULTS

Sample characteristics

Visual inspection (histogram) and normality tests (Shapiro-Wilk; p <0.001) suggested non-normality of the data. Descriptive analysis on the overall sample (n = 139) revealed that the majority of the participants were male (77%). The median age was 55.00 (Interquartile range [IQR]: 46.00-61.00). The participants were predominantly married (67.4%). The average time between transplant and collection was approximately 56.7 months IQR 30,00-79,00) (Table 2).

Psychometric properties

Internal consistency

Internal consistency measured by polychoric Cronbach's alpha coefficient value was high (a = 0.830; Standardized a = 0.800).

Table 2. Socio-demographic characteristics of liver transplant recipients who were assessed by using the Portuguese version of ITAS.

Variable	Patients (n = 139)
Male gender (%)	108 (77.7)
Age (1st Qu. / Median / 3rd Qu.)	48.00 / 57.00 / 64.00
Education (years)	
	< 9 years 34 (24.5%)
	> 9 years 105 (75.5%)
Marital Status (%)	
Married	93 (67.4)
Single	24 (17.4)
Divorced	15 (10.9)
Widower	6 (4.3)
Post-transplant (mean, months)	56.7

ITAS: Immunosuppressant Therapy Adherence Instrument. SD: Standard deviation.
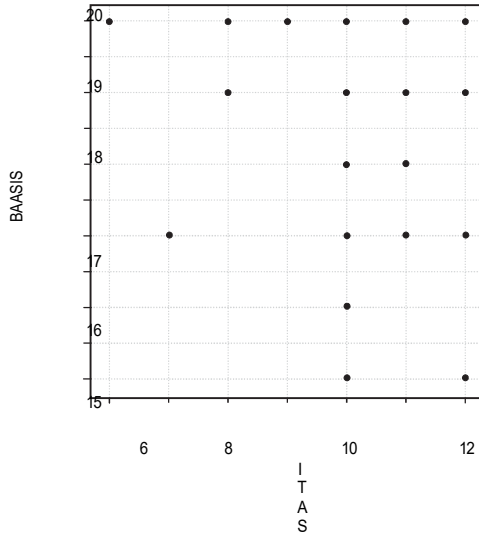
Figure 1. *Correlation plot. Opacity indicates frequency of overlaid points of the ITAS and BAASIS.*
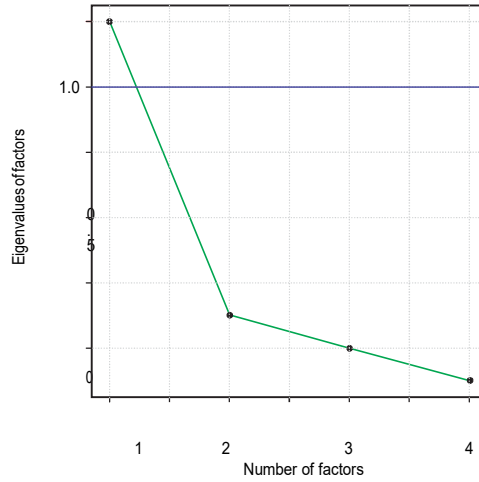

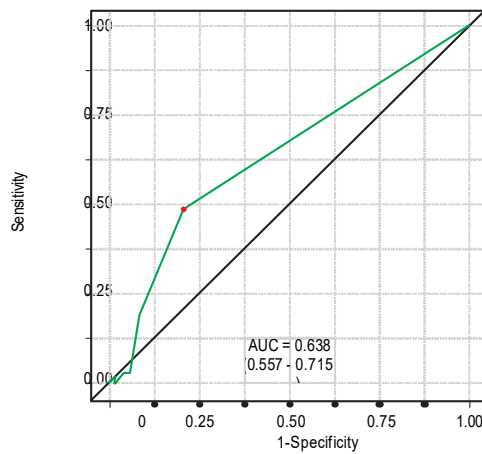**Figure 3.** *Scree plot of the ITAS.*

Figure 2. Area Under ROC curve. Red point indicates optimal cut-point value.

Table 3. Factor analysis of the ITAS, load values (Loading) for the first factor and sum of the squared factor loadings (Communalities).

Questions	Loading (F1)	Communalities
Forgetfulness	0.362	0.131
Carelessness	0.997	0.995
Feeling worse	-0.050	0.002
Neglect	0.358	0.128

The ITAS contributes as a valid instrument for immu- nosuppressant medication adherence in solid organ trans- plants[22] and several studies use the ITAS as an adherence

Convergent validity

ITAS and BAASIS (inverted) presented significant cor- relation, with a Spearman's coefficient = 0.302 (S = 312.500; p < 0.001) (Figure 1).

Classificatory performance and accuracy measures

ITAS discriminatory performance considering BAASIS classification as the outcome can be seen in figure 2 (AU- ROC = 0.638; 95% CI: 0.557 - 0.715). Reporting at least one negative response was the optimal cut-point (accuracy = 0.647; sensitivity = 0.492; specificity = 0.792; positive predictive value = 0.688; negative predictive value = 0.626).

Factor analysis

A single factor model was adequate to ITAS test data (χ^2 = 2.77; df = 2; p = 0.250). Carelessness presented higher loading (0.997), followed by Forgetfulness (0.362) and Ne- glect (0.358), in table 3. Factor analysis data is shown in ta- ble 4 and the scree plot with eigenvalues for different number of factors is displayed in figure 3.

DISCUSSION

Table 4. Polychoric correlation matrix of the ITAS.

	Forgetfulness	Carelessness	Feeling worse	Neglect
Forgetfulness	1,000	*	*	*
Carelessness	0,554	1,000	*	*
Feeling worse	0,449	0,512	1,000	*
Neglect	0,451	0,634	0,655	1,000

* $X_{ij} = X_{ji}$.

measure.[22-25] The aim of this study was to translate the ITAS to Brazilian Portuguese and to evaluate its psychometric properties in adult liver transplant recipients. The version of the ITAS - scale Brazilian Portuguese facilitates the measurement of immunosuppressant adherence in transplant patients, and reduces negative outcomes for example graft loss and death.

The ITAS is an instrument easy to apply that takes no longer than 5-10 min to complete. It is relatively inexpensive, simple, and can be conducted rapidly when compared with other methods of adherence assessment. In this study, we included patients from various parts of Brazil who had their transplants in the state of Bahia, therefore our study sample reflects a wider scale in Brazil. The answers (in percentage ranges) of this version were maintained to preserve continuality, but may present difficulties to patients presenting cognitive deficits, poor educational levels and low social support.[22]

Internal consistency provides an estimate of the equivalence of items from the same scale, and values between 0.70 and 0.95 are considered to be acceptable.[26,27] Our Brazilian Portuguese version of the scale presented good internal consistency and was similar to previously published studies - Cronbach's alpha = 0.81.[15] Items within the scale were correlated as expected.

Factor analysis solution with a single factor was adequate, indicating higher loading values for Carelessness (0.997), Forgetfulness (0.362), and Neglect (0.358). Feeling Worse (item 3) factor loading was close to zero (-0.050), since almost all patients included in the sample (98.6%) answered this item with option A: 0% (none). This behavior was not observed in the original ITAS validating studies[14] and might be due to regional differences. This hypothesis can be verified in further studies replicating the experiments in other regions.

Concerning convergent validity, our findings indicate that the translated ITAS correlates well with the translation of the BAASIS scale, an instrument validated in Brazil.[16] AUROC value of 0.5 should be considered a minimum.[28] Therefore, our results (AUROC = 0.638) indicate satisfactory discrimination for adherence.

The result of the psychometric properties analysis suggest that the Portuguese translated version of ITAS in Brazil is a psychometric scale internally consistent, with good convergent validity with BAASIS[a]. These findings need to be replicated in further studies. Altogether, these results require confirmation in larger samples with regional variance.

This study has some limitations. The sample may be subject to a bias recruitment due to convenience sampling, because the participants included in the study were those who attended routine consultations. Non-adherent patients may be more prone to miss consultations and, therefore, to not be included in the survey. Our sample covers only liver transplant patients and the results cannot be generalized to other types of transplants.

In conclusion, the ITAS instrument was successfully translated and an analysis of the data confirmed its consistency and convergent validity with a validated tool. The translation and validation of the ITAS instrument contributes to the applicability and relevance of the instrument for the Brazilian population.

ABBREVIATIONS

- **AUROC:** Area Under the Receiver Operating Characteristic.
- **BAASIS:** Basel Assessment of Adherence with Immunosuppressive Medications Scale.
- **ITAS:** Immunosuppressant Therapy Adherence Instrument.

SUPPORT

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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APENDICE B - Risk-taking behavior and impulsivity among HCV-infected patients

Risk-taking behavior and impulsivity among HCV-infected patients

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a r t i c l e i n f o

a b s t r a c t

The association between risk behaviors and hepatitis C virus (HCV) has been extensively studied. It is also proved that impulsivity is associated with risk behaviors. However, there is a lack of studies investigating the association between HCV and impulsivity, a characteristic that can contribute directly to these risk behaviors. This study aimed to investigate HCV-infected individuals' impulsivity and whether this feature mediates risk behavior. Adult patients with liver diseases (n ¼ 269) were divided into two groups: viral group (n ¼ 157) – patients with HCV and nonviral group (n ¼ 112). Risk behaviors were evaluated by a sociodemographic questionnaire. Impulsivity was assessed through Barratt Impulsiveness Scale – BIS-11. Psychiatric comorbidities were investigated by the Mini International Neuropsychiatric Interview 5.0.0. The viral group patients had higher impulsivity than the nonviral group in all domains: attentional impulsivity, motor impulsivity, and nonplanning. Risk behaviors were also shown to be associated with impulsivity levels. Our results suggest that HCV-infected patients are more impulsive than individuals with other liver diseases, even when analyses are controlled for the presence of comorbid mental disorders. In addition, at-risk behavior was signi?cantly mediated by impulsivity.

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1. Introduction

Hepatitis C virus (HCV) infection is a global public health problem. The disease makes progress gradually, becoming chronic in most cases. People who are chronically infected may develop cirrhosis or liver cancer (Rasi et al., 2014). Approximately 500,000 people worldwide annually die due to liver diseases related to HCV (World Health Organization, 2014).

In addition to complications from liver disease, it is necessary to pay attention to extrahepatic impairments such as cognitive de?cits and other neuropsychological disorders (Hilsabeck et al., 2002, 2003; Quarantini et al., 2008, 2009; Forton, 2011). It was believed that cognitive impairment was a consequence of hepatic encephalopathy associated with cirrhosis. However, recent studies have suggested that about one-third of patients with HCV have cognitive de?cits even in the absence of cirrhosis (Forton et al., 2001; Perry et al., 2008).

In addition to extensive associations shown between HCV and

psychiatric disorders in the literature, the disease is associated with risk behaviors: the use of shared needles for injection purposes, alcohol abuse, unprotected sex, promiscuity, prostitution, early sexual activity, and sexual abuse (Hagan and Des Jarlaiset al., 2000; Terrault, 2002; Chandra and Desai, 2005; Butt et al., 2006; Shuper et al., 2009). Several studies in HCV-free people have shown the importance of impulsivity in mediating these risk behaviors. That is, even in situations where impulsivity is unrelated to any disorder, an increased manifestation of this trait can lead to severe damage (Malloy-Diniz et al., 2010). Studies show that there is evidence of a relationship between risk behavior in traf?c and impulsivity (Araújo and Malloy-Diniz, 2009).

Impulsivity is a complex construct characterized by different cognitive and behavioral patterns that often lead to dysfunctional consequences (Malloy-Diniz et al., 2010). According to Moeller (2001), it can be de?ned as a "quick action without forethought or conscious judgment, a tendency to act with less caution than most individuals with equal ability and knowledge" (Moeller et al., 2001). It is worth noting that impulsivity is a trait usually formed in an early phase of human development (Bezdjian et al., 2011).

One of the self-report instruments most used in research to measure impulsivity is the Barratt Impulsiveness Scale, called BIS-11, whose validity was supported by studies conducted by Patton

(Patton et al., 1995). The current version of BIS-11 consists of 30 items designed to measure three dimensions: 1 – attentional: de?ned as lack of focus; 2 – motor: de?ned as acting without thinking, and 3 – nonplanning: de?ned as orientation to the present and not the future (Patton et al., 1995).

Although impulsivity can be seen as a normal dimension of personality (Eysenck and Eysenck, 1977), elevated levels can be associated with mental disorders such as attention-de?cit/hyperactivity disorder (ADHD), mania, substance abuse, and personality disorders (Winstanley et al., 2006).

Only two studies have assessed impulsivity as a primary aim (Huckans et al., 2011; Fabregas et al., 2013). Huckans and collaborators found through neuropsychological testing that adults with HCV were signi?cantly more likely to choose smaller immediate rewards than larger delayed rewards, which shows that these individuals are susceptible to impulsive behavior. However, this study assessed a small sample size of HCV-infected patients and involved exclusively armed forces veterans from the United States (Huckans et al., 2011). Fabregas et al. (2013) investigated a sample of chronic HCV patients and showed that impulsivity was associated with psychiatric comorbidity, such as ADHD and bipolar disorder, which are associated with impulsivity per se regardless of HCV infection. Thus, it does not provide clear evidence about impulsivity as an intrinsic characteristic of HCV-infected patients. In addition, it is not known how important is the apparent higher impulsivity in those individuals.

The aim of this study is to investigate whether HCV-infected patients show an association with impulsiveness and whether this characteristic mediates an association with at-risk behavior, such as drug use, unprotected sex, and alcohol abuse.

1. Methodology

Ethical aspects

This study was approved by the Institutional Review Board of MCO-UFBA (protocol 14/2002) and follows the Guidelines and Rules of Resolution 196/96 as well as the Declaration of Helsinki (1989) about human research.

Data collection

This is a cross-sectional study, whose participants were 418 years of age and provided an informed consent. The sample consisted of 269 outpatients with liver disease, whether indicated or not for a liver transplant, who have been monitored in the University Hospital Professor Edgard Santos Complex (ComHUPES) – Federal University of Bahia (UFBA), Brazil. The data were collected between 2010 and 2014.

Instruments

Patients were assessed through a clinical interview using a sociodemographic questionnaire. The Mini International Neuropsychiatric Interview Brazilian version 5.0.0 (MINI PLUS) (Amorim, 2000) was used to assess the occurrence of psychiatric disorders. In order to evaluate impulsivity, BIS 11 was used, which is a self-administered scale consisting of 30 items that provide a total score of impulsivity in three second-order factors: attentional (lack of focus), motor (acting without thinking), and nonplanning (guidance for the present and not the future). BIS-11 is the most widely used instrument to assess impulsivity in research and clinical practice. The total score was analyzed with regard to the following cutoff points: 052, low impulsivity; between 52 and 71, normal limit of impulsivity; and 4 71, high impulsivity (Stanford

et al., 2009). However, second-order factors of BIS-11 do not have established cutoffs; for this reason, our option was to analyze them by using tertiles.

Data analysis

The patients were divided into two groups: "Viral," who are suffering from HCV and "nonviral," including all those with other hepatic diseases and without HCV. Comorbidities and impulsivity were compared between these groups. Comorbidities were analyzed as dichotomous variables, such as suicide risk, current alcohol abuse and dependence, past alcohol abuse and dependence, substance abuse and dependence, and risk behaviors. On the contrary, impulsivity was analyzed as a polytomous variable, such as attentional impulsivity, motor impulsivity, and lack of planning. Statistical analyses were performed using SPSS version 16.0 software. The following variables were selected for the groups' descriptive analysis: gender, age, marital status, occupation, and psychiatric comorbidities.

In order to verify the differences between the groups regarding impulsivity levels and comorbidities, bivariate analysis using Pearson's test was performed.

A multivariate analysis using a logistic regression model was used for dichotomous outcomes (suicide risk, dependence abuse and actual alcohol, dependence past abuse and alcohol, abuse and substance dependence, risk behaviors) and multinomial for polytomous outcome (attentional impulsivity, motor impulsivity, lack of planning) as well as for the odds ratio (OR) and con?dence intervals (CI) of 95% between the "viral" and "nonviral" Groups. The tests were performed with a signi?cance level of p 00.05.

2. Results

The groups analyzed predominantly involved male patients (66.24% viral and 75.89% nonviral), with the corresponding average ages 53.5 and 48.6 years. The groups had a different percentage of individuals with a stable partner (38.71% viral, 72.97% nonviral); most individuals in the viral group (57.14%) had paid employment, while in the nonviral group about 50.45% did. The presence of psychiatric comorbidity was observed in both groups. In the viral group, the highest prevalence was of current major depressive episode (MDE), with 13.38% (p ¼ 0.006) and past major depressive episode with 17.20% (p ¼0.017). In the nonviral group, the highest prevalence was of anxiety disorder 14.29% (p ¼0.342), although not statistically signi?cant, and the prevalence of adjustment disorder was 14.41% (p ¼ 0.064).

The total score of the BIS did not reveal any statistically signi?cant difference between the two groups when using the cutoff point presented in the literature; according to this cutoff, 15.13% and 11.43% in the viral and nonviral groups, respectively, presented higher impulsivity (471). On the contrary, when using the tertiles division to compare intensity domains of impulsivity areas, there was a relevant absolute difference with statistical signi?cance. The viral group showed a higher prevalence of impulsivity, and the highest score was in attentional impulsivity (45.16%), followed by nonplanning impulsivity (42.76%). The lowest levels (26.80%) were found for motor impulsivity.

The bivariate analysis showed signi?cance in the variable: abuse and dependence on psychoactive substances (p¼0.005) when comparing between viral and nonviral groups, the OR for abuse and dependence on psychoactive substances in viral group was 10.87 [CI 1.40; 83.90]. There was no signi?cant difference between the groups by bivariate analysis of the variable: risk of suicide (p¼0.385). We also found no signi?cant difference between the two groups in the bivariate analysis of the following

variables: current alcohol abuse (p ¼ 0.942) and past alcohol abuse (p¼ 0.194). In both groups, **⊿** 90% of the patients reported risky behavior – comparing between the nonviral and viral groups, the OR in viral group was 1.64 [CI 0.58; 4.69].

In multivariate analysis, the OR for abuse and dependence on psychoactive substances in the viral group remained high 10.13 [CI 1.29; 80.08] even after adjusting for comorbidities (current MDE, past MDE, and adjustment disorder). However, when it was adjusted for the impulsivity domains (attentional, motor, and nonplanning), the OR decreased to 8.15 [CI 0.99; 67.19]. After multivariate analysis of the variable, risk of suicide adjusted for psychiatric comorbidities, the OR in viral group decreased from 1.61 [0.54; 4.77] to 0.79 [CI 0.22; 2.70], which shows that higher probability of suicide risk is related to comorbidities. Multivariate analysis of the variable, risky behavior adjusted for comorbidities (current MDE, past MDE, and adjustment disorder), showed a reduction in the OR to 1.42 [0.50; 4.11]. When adjusted for impulsivity areas, the OR dropped to 0.42 [0.05; 0.80]; and after adjusting for total BIS, there was also a small reduction: the OR was 0.41 [0.05; 0.77] (Tables 1–3).

1. Discussion

This study shows that there is an association between impulsivity and HCV even after controlling these results for the presence of psychiatric comorbidities. To the best of the authors' knowledge, this is the ?rst study of its kind that shows that impulsivity may be a peculiar characteristic of patients with HCV and that it is more associated with risk behaviors. There has been a lack of studies investigating impulsivity in people infected with HCV. Although a previous study (Fabregas et al., 2013) has shown high scores of impulsivity in HCV patients, this ?nding has been best explained by the presence of psychiatric disorders such as ADHD, bipolar spectrum disorders, and anxiety symptoms.

In our analysis of the second-order factors of BIS-11 (attentional, motor, and nonplanning), a higher level of impulsivity was observed among patients with HCV than with other liver diseases, with a signi?cant difference in the attentional and nonplanning domains (45.16%, viral; 15.89%, between nonviral and viral; 42.76%, nonviral 19.05%). Although the motor domain had less difference than the other two, the viral group continued to have higher scores than the nonviral group (26.80% vs. 19.63%). Even after adjusting for the covariates: substance abuse and psychiatric

Table 1
Sociodemographic characteristics, clinical characteristics, and prevalence of psychiatric comorbidities according to the nonviral and viral groups.

Variables	Viral (157)	Nonviral (112)	
	N (%) or M (SD)	N (%) or M (SD)	p-value
Gender			
Male	104 (66.24)	85 (75.89)	
Female	53 (33.76)	27(24.11)	0.105[a]
Age (mean)	53.5 (8.8)	48.6 (12.9)	
Civil state			
Single	7 (4.52)	19 (17.12)	
With stable partner	60 (38.71)	81 (72.97)	
Divorced	33 (21.29)	11 (9.91)	
Widower	55 (35.48)	0 (0.00)	00.001[a]
Paid occupation			
Without	15 (9.74)	10 (9.01)	
With	88 (57.14)	56 (50.45)	
Retired by age	31 (20.13)	24 (21.62)	
Retired due to illness	19 (12.34)	18 (16.22)	
Student	1 (0.65)	3 (2.70)	0.553[a]
Psychiatry comorbidities			
Current major depressive disorder	21 (13.38)	4 (3.57)	0.006[a]
Last major depressive disorder	27 (17.20)	8 (7.14)	0.017[a]
Anxiety disorder	16 (10.19)	16 (14.29)	0.342[a]
Adjustment disorder	11 (7.01)	16 (14.41)	0.064[a]

[a] Fisher Exact Test.

Table 2
Prevailing levels of impulsivity in accordance with the groups.

Variables	Outcome Levels of Impulsivity	Main Viral (152)	Exhibition[a] Nonviral (105)		Multivariate Analysis
		N (%) or M (SD)	N (%) or M (SD)	p-value	OR [95% Conf. Interval]
BIS TOTAL					
4 71	More impulsivity	23 (15.13)	12 (11.43)		
52–71	Normal impulsivity	102 (67.11)	71 (67.62)		
o52	Low impulsivity[b]	27 (17.76)	22 (20.95)	0.619	
DOMAINS		Viral (155)	Nonviral (107)		
		N (%)	N (%)		
Attentional Impulsivity	More impulsivity	70 (45.16)	17 (15.89)		4.34 [2.22; 8.49][c]
	Averagely impulsive	38 (24.52)	31 (28.97)		4.09 [2.08; 8.03][d]
	Less impulsive[b]	47 (30.32)	59 (55.14)	0 0.001	
		Viral (153)	Nonviral (107)		
		N (%)	N (%)		
Motor Impulsivity	More impulsivity	60 (26.80)	21 (19.63)		3.34 [1.73; 6.44][c]
	Averagely impulsive	52 (33.99)	30 (28.04)		3.21 [1.65; 6.22][d]
	Less impulsive[b]	41 (26.80)	56 (52.34)	0 0.001	
		Viral (152)	Nonviral (105)		
		N (%)	N (%)		
Lack of Planning	More impulsivity	65 (42.76)	20 (19.05)		3.16 [1.63; 6.10][c]
	Averagely impulsive	40 (26.32)	29 (27.62)		3.00 [1.54; 5.82][d]
	Less impulsive[b]	47 (30.92)	56 (53.33)	0 0.001	

[a] Reference main exhibition.
[b] Reference outcome.
[c] Adjustment: current depressive episode, past depressive episode, and adjustment disorder.
[d] Adjustment: current depressive episode, past depressive episode, adjustment disorder, and substance abuse and dependence.

Table 3
Bivariate and multivariate analyses of comorbidities according to the groups.

Variables	Viral (157) N [%]	Nonviral (112) N [%]	p-value	Bivariate Analysis OR [95% Conf. Interval]	Multivariate Analysis OR [95% Conf. Interval]
Suicide risk	11 (7.01)	5 (4.46)	0.443[a]	1.61 [0.54; 4.77]	0.79 [0.22; 2.70][b]
Dependence abuse and current alcohol	13 (8.28)	9 (8.04)	1.000[a]	1.03 [0.42; 2.50]	0.88 [0.34; 2.20][b]
Dependence past abuse and alcohol	47 (29.94)	42 (37.50)	0.237[a]	0.71 [0.42; 1.18]	0.68 [0.40; 1.15][b]
Abuse and Substance Dependence	14 (8.92)	1 (0.89)	0.005[a]	10.87 [1.40; 83.90]	10.13 [1.29; 80.08][b] 8.15 [0.99; 67.19][c]
Risk behaviors[d]	150 (95.54)	104 (92.86)	0.422[a]	1.64 [0.58; 4.69]	1.42 [0.50; 4.11][b] 0.42 [0.05; 0.80][c] 0.41 [0.05; 0.77][e]

[a] Fisher Exact Test.
[b] Adjusted current depressive episode, past depressive episode, and adjustment disorder.
[c] Adjusted current depressive episode, past depressive episode, adjustment disorder, and by the areas of impulsivity: attentional, motor, and nonplanning.
[d] Risk behaviors: unprotected sex; promiscuity; drug use; unhygienic tattooing, body piercing, and acupuncture; sharing of razor and toothbrush; and manicure service.
[e] Adjusted current depressive episode, past depressive episode, adjustment disorder, and for total BIS.

disorders (past MDE, MDE current, and adjustment disorder), multivariate analysis showed that these values remained high. Previous studies suggest cognitive changes associated with HCV, especially in the following areas: attention, learning, psychomotor speed, and mental flexibility (Huckans et al., 2009). The most common complaints of HCV carriers related to cognitive impairment are characterized by impaired concentration and slow thinking. Attentional impulsivity refers to a lack of focus on activities and may be associated with mechanisms leading to cognitive dysfunction reported by HCV-positive patients. A study by Hilsabeck et al. (2002) examined the cognitive functioning of patients with HCV and other patients with chronic liver diseases, and the results showed that patients with HCV have a tendency toward lower cognitive performance than those with other chronic liver diseases. Furthermore, patients with HCV plus other medical comorbidities had an even worse performance. These cognitive difficulties may interfere with daily activities and with the ability to maintain independent functioning. Problems with attention and concentration can interfere with the ability to learn new information and may result in taking long durations to perform simple routine tasks. Because of these difficulties, such patients can become frustrated and may develop mood disorders such as depression and pathological anxiety. In addition, we should also consider the high comorbidity with other mental disorders in HCV-infected patients such as posttraumatic stress disorder (PTSD), which has, among its clinical aspects, attentional impair- ment (Forton et al., 2005; Morais-de-Jesus et al., 2014).

Although there is a higher incidence of depressive symptoms among patients with HCV, other psychiatric comorbidities are also reported frequently in this population, such as anxiety disorders, psychotic symptoms, drug abuse, and alcoholism (Quarantini et al., 2006; Schaefer et al., 2012). Our data indicate a history of alcohol abuse or dependence throughout life in one-third of the viral group. This was a lower prevalence than that found in other studies conducted in North America and Europe that have high prevalence rates of up 56% (Dwight et al., 2000; Golden et al., 2005; Perry et al., 2008; Novo-Veleiro et al., 2013). Verdejo-Garcia et al. (2008) found that there is an association between alcohol abuse and a more prominent trait of impulsivity. Our sample identified a low percentage of individuals with a history of abuse and dependence on alcohol (8.28% viral vs. 8.04% nonviral). Although there was no statistical significance (p ¼ 0.942), these results should be treated with caution, because when dealing with patients with liver disease, alcohol use can be extremely harmful and

contribute to a worsening of symptoms and consequently a worsening liver disease (Shoreibah et al., 2014).

Regarding substance use, abuse, and dependence, there was a statistical significance (p ¼ 0.005) in our sample and the prevalence in the viral group was higher than that in the nonviral group, confirming the literature data, which show that drug use is directly associated with HCV transmission, and a significant form of transmission by syringe sharing (Ministério da Saúde, 2011). Even after adjusting for psychiatric comorbidities and impulsivity levels using a multivariate analysis, drug use remained high: OR 8.15 [CI 0.99; 67.19]. This large CI may be explained by the fact that table cells with a value below 5 may have needed a larger sample to achieve significance. However, the expected direction is in agreement with the literature data, which associates substance abuse and dependence with contamination by the HCV. Considering previous evidence presented by Verdejo-Garcia et al. (2008), which supports the fact that impulsive behavior is associated with vulnerability to drug use, we can hypothesize that impulsivity may be highly prevalent in HCV-infected patients.

In our study, nonplanning impulsivity levels were also higher in the viral group than the nonviral group (42.76% vs. 19.05%). This characteristic encompasses behaviors oriented to the present and not the future. These data refer to a study by Huckans et al. (2011), which found that patients with HCV were significantly more likely to choose smaller immediate rewards than larger rewards later on.

One hypothesis that we raised is that patients with HCV (and perhaps other chronic diseases) are more likely to regard the future as uncertain or believe they will be seriously ill or may soon die, which could lead them to behave with a higher focus on the present and poor planning. Moreover, impulsivity may precede the acquisition of viruses and contribute to risk behavior, which would favor one's own infection by HCV. This is supported by previous evidence that impulsivity is an early-acquired trait in neurodevelopmental models (Bezdjian et al., 2011). Furthermore, at-risk behaviors such as unprotected sex; promiscuity; drug use; unhygienic tattooing, body piercing, and acupuncture; sharing of razor and toothbrush; and manicure service were associated with impulsivity levels, as shown in bivariate and multivariate analyses.

The proportion of suicide risk was higher in the viral group, but adjusting for comorbidities in the multivariate analysis, the OR was not significant. On the contrary, a study conducted by Kristiansen et al. (2010) in Norway showed that total mortality in chronically infected HCV patients was 6.66 times higher than that in the general population. This increase was associated with liver

disease, alcohol dependence, drugs use, and suicide.

This study has some limitations. The cross-sectional design of this study limits the ability to determine whether impulsivity occurs before or after the interaction of the virus to the central nervous system. In our ?ndings, we did not observe a statistically signi?cant difference using the cutoff points for the total score of the BIS-11 available in the literature (Stanford et al., 2009). We believe that this proposed cutoff point is not suitable for this population, because we consistently found statistically signi?cant differences in the ?elds of impulsivity as measured on this scale by tertiles.

1. Conclusion

The results of this study suggest that HCV patients are more impulsive than those with other liver diseases, even when the analyses are adjusted for the presence of comorbid psychiatric disorders. In addition, we showed that impulsivity is signi?cantly associated with risk behaviors. Therefore, it may be considered as another extrahepatic manifestation, and it can be observed that HCV is not as mild as previously described. We stress the need for special attention to this behavioral aspect that may contribute to other lethal outcomes such as suicide and low adherence. Special attention should be paid to the approach toward drug users, because of higher vulnerability to acquiring HCV or reinfection after successful treatment (Grady et al., 2013). There is a crucial need for public policies of prevention and vigilance for the HCV population as well as a requirement for psychological/psychiatric support, not only during antiviral therapy.

Con?ict of interest

The authors declare that they have no competing interests.

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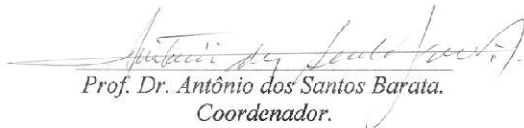
ANEXOS

Anexo A – Parecer do Comitê de Ética

Serviço Público Federal
Comitê de Ética em Pesquisa
Maternidade Climério de Oliveira -UFBA

RESOLUÇÃO 14/2002

O *Coordenador do Comitê de Ética em Pesquisa da Maternidade Climério de Oliveira, Universidade Federal da Bahia, tendo em vista a apreciação do Desenvolvimento Clínico sobre a* **"Incidência de Sintomas Psiquiátricos em Portadores de Hepatite C Crônica Tratados com Interferon Peguilado Alfa e Ribavirina"**, *protocolo versão 01 de 2002, e de conformidade com a regulamentação do mesmo e demais disposições oficiais em vigor, nacionais e internacionais, todas de pleno e formal conhecimento do* **Pesquisador Responsável**, *Doutor Lucas de Castro Quarantini, resolve considerar como ético o mesmo, inclusive o* **"Consentimento Livre e Pré-Esclarecido"** *a ele anexo, a ser realizado no Hospital Universitário Professor Edgar Santos , Serviço de Hepatologia da Faculdade de Medicina da Universidade Federal da Bahia,* **HUPES/FAMED/UFBA**. *O* **Parecer Consubstanciado** *aprovado na reunião deste CEP, nesta data e a ele referente, anexo, integra esta Resolução.*

Salvador, 28 de agosto de 2002.

Prof. Dr. Antônio dos Santos Barata.
Coordenador.

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Serviço Público Federal
Comitê de Ética em Pesquisa
Maternidade Climério de Oliveira -UFBA

Parecer Consubstanciado n.º 14/2002.

Identificação.

Estudo da **"Incidência de Sintomas Psiquiátricos em Portadores de Hapatite C Crônica tratados com Interferon Peguilado Alfa e Ribavirina"**, a ser realizado no Ambulatório de Hepatologia do Hospital Universitário Professor Edgar Santos, Faculdade de Medicina da Universidade Federal da Bahia. O **Pesquisador Responsável** será **Lucas de Castro Quarantini**, Médico Residente do terceiro ano de Psiquiatria nas mesmas entidades , cujo "Curriculum Vitae" encontra-se anexo. Projeto apresentado em 05 de agosto de 2002.

Objetivos.

Principal: a) determinar a incidência de transtornos psiquiátricos em indivíduos portadores de Hepatite C Crônica tratados com Interferon Peguilado Alfa associado a Ribavirina.

Secundários: a) comparar a incidência de transtornos psiquiátricos entre indivíduos portadores de Hepatite C Crônica tratados com Interferon Alfa Convencional associado com Ribavirina e aqueles tratados com Interferon Peguilado Alfa associado a Ribavirina;

b) Identificar pacientes de risco para o desenvolvimento de sintomas psiquiátricos ao longo do tratamento com Interferon Alfa;

c) avaliar a qualidade do sono da população em tratamento com os dois tipos de Interferon.

Sumário do Projeto.

Estudo coorte a ser realizado na vigência de um ensaio clínico para o tratamento de Hepatite C Crônica com o uso de Interferon Peguilado associado com Ribavirina e nos indivíduos em tratamento com Interferom Alfa Convencional e Ribavirina.

Maiores de 18 anos, ao iniciarem os tratamentos com Interferon Alfa-Peguilado ou não, constituirão a **População Alvo** destas observações.

Serão incluídos tantos indivíduos quanto necessário para a formação de dois grupos paralelos, abertos, de 50 cada. Psiquiatra ou psicólogo, em tempo estimado de 30 minutos, aplicarão, em cada investigando, 4 (quatro) escalas padronizadas para aferição das possíveis mudanças afetivas-cognitivas, além do questionário inicial para os dados demográficos.

Tratamentos estatísticos, quanti-qualitativos, além de análises gráficas para determinação dos tipos de parâmetros alcançados, definirão os resultados finais. Fluxograma operacional, com reavaliações ao 1.º, 3.º e 6.º mês, definirão quais os definidos portadores de algum distúrbio psiquiátrico que serão encaminhados para tratamento específico.

Comentários do Relator

Estudo observacional, aberto, sustentado financeiramente pelo Pesquisador. Pela própria ausência de qualquer intervenção não apresenta potencial de dano — maleficência — aos participantes. **A beneficência individual** está representada pelo diagnóstico e encaminhamento subsequente para tratamento especializado e a **coletiva** pelo acúmulo de conhecimentos médicos e seu posterior emprego na população usuária. O "Consentimento Livre e Pré-Esclarecido" encontra-se dentro dos padrões éticos vigentes. Opinamos pela sua aceitação.

PARECER/RESOLUÇÃO ADITIVA N.º 260/2009

Para análise e deliberação deste Institucional o Doutor **Lucas de Castro Quarantini**, Pesquisador Responsável pelo Projeto de Pesquisa "**Incidência de Sintomas Psiquiátricos em Portadores de Hepatite C Crônica tratados com Interferon Peguilado Alfa e Ribavirina**", aprovado em 28 de Agosto de 2002 por este Institucional através do Parecer/Resolução n° 14/2002, solicitou, em 23 de Novembro de 2009 deste Colegiado, a *"ampliação da amostra do estudo observacional para não somente os portadores de vírus B e C, mas também do HTLV e HIV que são atendidos nos Ambulatório do Complexo Hospitalar Universitário Professor Edgar Santos"*, com aplicação de "**Escala de Resiliência**" e de "**Religiosidade**" bem como a inclusão, no "Staff" investigatório, de mais 02 (duas) profissionais ora relacionadas — **Karine Miranda da Silva** e **Mychelle Morais de Jesus**, "Currícula Vitae" apensos.

Inexistindo na referida proposição conflito administrativo, processual e ético que contra-indique a conseqüente continuidade da pesquisa, fica a mesma **aprovada** por esta Instância.

Salvador, 01 de Dezembro de 2009

Professor, Doutor, Antônio dos Santos Barata
Coordenador – CEP/MCO/UFBA

Observações importantes. Toda a documentação anexa ao Protocolo proposto e rubricada pelo (a) Pesquisador (a), arquivada neste CEP, e também a outra devolvida com a rubrica da Secretária deste ao (à) mesmo (a), faz parte intrínseca deste Parecer/Resolução Aditiva e nas "Recomendações Adicionais" apensa, **bem como a impostergável entrega de relatórios parciais e final como consta nesta liberação** (Modelo de Redação para Relatório de Pesquisa, anexo).

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UNIVERSIDADE FEDERAL DA BAHIA
IORG0003460. Assurance FWA00002471, October 26, 2010
IRB00004123, October 5, 2007 - October 4, 2010

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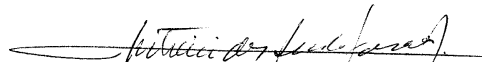
PARECER/RESOLUÇÃO ADITIVA N.º 274/2008

Para análise e deliberação deste Institucional o Doutor **Lucas de Castro Quarantini**, Pesquisador Responsável pelo Projeto de Pesquisa "**Incidência de Sintomas Psiquiátricos em Portadores de Hepatite C Crônica tratados com Interferon Peguilado Alfa e Ribavirina**", aprovado em 28 de Agosto de 2002 por este Institucional através do Parecer/Resolução nº 14/2002, solicitou, com a apresentação do "**Relatório Parcial**", em 28 de Novembro de 2008, a "*ampliação da amostra do estudo observacional para todos os portadores de vírus B e C que não foram tratados com antivirais e são atendidos no ambulatório de hepatologia do Ambulatório Magalhães Neto em um período de seis meses*", bem como a inclusão, no "staff" investigatório, de mais 11 (onze) profissionais ora relacionados e cujos "*Currícula Vitae*" vieram apensos.

Inexistindo na referida proposição conflito administrativo, processual e ético que contra-indique a conseqüente continuidade da pesquisa, fica a mesma **aprovada** por esta Instância.

APROVADO

Salvador, 03 de Dezembro de 2008

Professor, Doutor, Antônio dos Santos Barata
Coordenador – CEP/MCO/UFBA

Observações importantes. Toda a documentação anexa ao Protocolo proposto e rubricada pelo (a) Pesquisador (a), arquivada neste CEP, e também a outra devolvida com a rubrica da Secretária deste ao (à) mesmo (a), faz parte intrínseca deste Parecer/Resolução Aditiva e nas "Recomendações Adicionais" apensa, **bem como a impostergável entrega de relatórios parciais e final como consta nesta liberação** (Modelo de Redação para Relatório de Pesquisa, anexo).

Recebido em:
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82

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PARECER/RESOLUÇÃO ADITIVA N.º 123/2010

Para análise e deliberação deste Institucional o Doutor **Lucas de Castro Quarantini**, Pesquisador Responsável pelo Projeto de Pesquisa "**Incidência de Sintomas Psiquiátricos em Portadores de Hepatite C Crônica tratados com Interferon Peguilado Alfa e Ribavirina**", aprovado em 28 de Agosto de 2002 por este Colegiado através do Parecer/Resolução n° 14/2002, solicitou, em 19 de maio de 2010, a inclusão de "*portadores de hepatite auto-imune e colangite esclerosante e cirrose alcoólica*" com o intuito de ampliar o "*grupo controle de hepatopatas não portadores de hepatite C, visto a escassez de portadores com o vírus da hepatite B*". Para tanto, foi anexada a "**Escala de Experiência Sexual do Arizona (ASEX)**".

Inexistindo nas referidas proposições conflito administrativo, processual e ético que contra-indiquem a conseqüente continuidade da pesquisa, ficam as mesmas **aprovadas** por esta Instância.

Salvador, 21 de junho de 2010

Professor, Doutor, Eduardo Martins Netto
Coordenador em Exercício – CEP/MCO/UFBA

Observações importantes. Toda a documentação anexa ao Protocolo proposto e rubricada pelo (a) Pesquisador (a), arquivada neste CEP, e também a outra devolvida com a rubrica da Secretária deste ao (à) mesmo (a), faz parte intrínseca deste Parecer/Resolução Aditiva e nas "Recomendações Adicionais" apensa, **bem como a impostergável entrega de relatórios parciais e final como consta nesta liberação** (Modelo de Redação para Relatório de Pesquisa, anexo).

Anexo B – Termo de Consentimento Livre e Esclarecido

Projeto: Aspectos Comportamentais De Doenças Infecciosas (HCV, HBV, HIV, HTLV)

Você está sendo convidado (a) para participar voluntariamente de um estudo que investiga sintomas como fadiga, depressão e alterações de qualidade de vida, relacionados às diferentes hepatopatias. Antes de concordar em participar desta pesquisa é importante que você leia este documento.

Estas avaliações consistem somente de questionários, que têm duração aproximada de 60 minutos.

Algumas exigências para participar deste estudo são:

- Você deve ter idade maior que 18 anos.
- Deve ser portador de hepatopatias.

Você estará ajudando no estudo e compreensão de doenças virais, permitindo benefícios futuros para si próprio e para outras pessoas. Você poderá sair desse estudo a qualquer momento, caso decida. Os investigadores não são remunerados para a realização dessa pesquisa, assim como os pacientes voluntários não receberão benefícios financeiros para sua participação no mesmo.

Dúvidas poderão ser esclarecidas com Dr. Lucas Quarantini, no Hospital Universitário Edgard Santos, terceiro andar, Serviço de Psiquiatria. Você pode ainda falar com o Prof. Dr. Antônio dos Santos Barata, presidente do Comitê de Ética em Pesquisa no endereço Rua Augusto Viana, s/nº, 1º andar – Canela, Hospital Universitário Professor Edgard Santos, Canela, Salvador- Bahia, que é membro de um grupo independente que analisou este estudo.

Suas informações clínicas são totalmente confidenciais.

Para participar deste estudo, você precisa assinar esta página.

Nome do indivíduo

_____   _____

Assinatura do indivíduo   Data

_____   _____

Assinatura do investigador   Data