

Frailty, Psychoactive Medications, and Cognitive Dysfunction are Associated with Poor Quality of Life and Sleep in Cirrhosis

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SF-8 Health Survey

1. Overall, how would you rate your health during the **past 4 weeks**?

Excellent	Very good	Good	Fair	Poor	Very poor
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. During the **past 4 weeks**, how much did physical health problems limit your usual physical activities (such as walking or climbing stairs)?

Not at all	Very little	Somewhat	Quite a lot	Could not do physical activities
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. During the **past 4 weeks**, how much difficulty did you have doing your daily work, both at home and away from home, because of your physical health?

None at all	A little bit	Some	Quite a lot	Could not do daily work
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. How much **bodily pain** have you had during the **past 4 weeks**?

None	Very mild	Mild	Moderate	Severe	Very Severe
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. During the **past 4 weeks**, how much energy did you have?

Very much	Quite a lot	Some	A little	None
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

6. During the **past 4 weeks**, how much did your physical health or emotional problems limit your usual social activities with family or friends?

Not at all	Very little	Somewhat	Quite a lot	Could not do social activities
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7. During the **past 4 weeks**, how much have you been bothered by **emotional problems** (such as feeling anxious, depressed or irritable)?

Not at all

Slightly

Moderately

Quite a lot

Extremely



8. During the **past 4 weeks**, how much did personal or emotional problems keep you from doing your usual work, school or other daily activities?

Not at all

Very little

Somewhat

Quite a lot

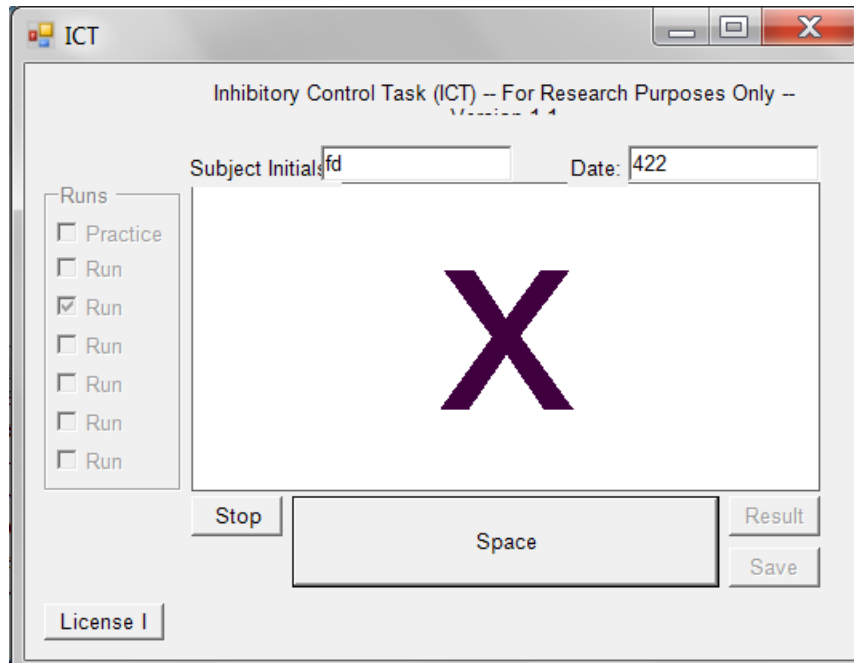
**Could not do
daily activities**



Katz ADL Scale

Activities	Independence (1 Point) NO supervision, direction or personal assistance	Dependence (0 Points) WITH supervision, direction, personal assistance or total care
Bathing ____ points	(1 POINT) Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity	(0 POINTS) Need help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing
Dressing ____ points	(1 POINT) Get clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.	(0 POINTS) Needs help with dressing self or needs to be completely dressed.
Toileting ____ points	(1 POINT) Goes to toilet, gets on and off, arranges clothes, cleans genital area without help.	(0 POINTS) Needs help transferring to the toilet, cleaning self or uses bedpan or commode.
Transferring ____ points	(1 POINT) Moves in and out of bed or chair unassisted. Mechanical transfer aids are acceptable	(0 POINTS) Needs help in moving from bed to chair or requires a complete transfer.
Continence ____ points	(1 POINT) Exercises complete self control over urination and defecation	(0 POINTS) Is partially or totally incontinent of bowel or bladder
Feeding ____ points	(1 POINT) Gets food from plate into mouth without help. Preparation of food may be done by another person.	(0 POINTS) Needs partial or total help with feeding or requires parenteral feeding.

Inhibitory Control Test



The ICT is lap-top based computer program that involves following instructions; pressing space bar in response to specific letters flashing on the screen. A target is achieved when the user presses the space-bar when an X follows a Y (or vice-versa); a lure is marked when the user presses space when X follows X or Y follows Y.

30 second Chair-Stand Test

Instructions to the patient:

1. Sit in the middle of the chair.
2. Place your hands on the opposite shoulder crossed at the wrists.
3. Keep your feet flat on the floor.
4. Keep your back straight and keep your arms against your chest.
5. On **"Go,"** rise to a full standing position and then sit back down again.
6. Repeat this for 30 seconds.



Source: <http://www.cdc.gov/steady/index.html>

Hand Grip Strength

Procedures: Using a hand-held dynamometer, patients will be asked to squeeze the device three times with their dominant hand in front of their body. The force of each squeeze is recorded, keeping the best trial as their value. Abnormal results are defined below.

Males

BMI	Males (kg)
Low ≤ 24	≤ 29
Average 24.1-28	≤ 30
High > 28.0	≤ 32

Females

BMI	Females (kg)
Low ≤ 23	≤ 17
Average 23.1-26	≤ 17.3
High $> 26-29$	≤ 18
Very High ≥ 29	≤ 21

Source: Lai JC, Feng S, Terrault N, Lizaola B, Hayssen H, Covinsky K. Frailty predicts waitlist mortality in liver transplant candidates. American Journal of Transplantation 2014;14:1870-9.

Medication inventory

Class	Medications
Benzodiazepines	Chlordiazepoxide, Diazepam, Lorazepam, Oxazepam, Alprazolam, Clonazepam, Eszopiclone, Zolpidem, Temazepam, Triazolam
GABAergic	Gabapentin, Pregabalin
Opiate	Oxycodone, Morphine, Hydromorphone, Codeine, Hydrocodone, Fentanyl Methadone, Buprenorphine, Tramadol
Antidepressant	Citalopram, Bupropion, Venlafaxine, Desvenlafaxine, Escitalopram, Fluoxetine Paroxetine, Vilazodone, Sertraline, Duloxetine, Fluvoxamine, Mirtazapine Nefazodone
Antipsychotic	Aripiprazole, Chlorpromazine, Clozapine, Fluphenazine, Haloperidol Lurasidone, Olanzapine, Quetiapine, Risperidal, Thioridazine, Ziprasidone
Diuretics	Furosemide, Spironolactone, Amiloride, Epleronone, Torsemide
Beta-blockers, non-selective	Nadolol, Carvedilol, Propranolol

Supplementary Table 1: Associations with Poor Health-Related Quality of Life (SF-8 < 50)

	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% Confidence Interval)	P-Value	Odds Ratio (95% Confidence Interval)	P-value
Education (per year)	1.18 (1.04 – 1.35)	0.009	1.18 (0.99 – 1.42)	0.06
Body Mass Index (per point)	0.97 (0.93 – 1.00)	0.09		
Alcohol-related liver disease	1.08 (0.55 – 2.14)	0.82		
Child class B	1.86 (1.04 – 3.31)	0.04	1.33 (0.50 – 3.49)	0.57
MELD-Na (per point)	1.07 (1.01 – 1.12)	0.02	0.97 (0.90 – 1.06)	0.53
Albumin (per mg/dL)	0.37 (0.23 – 0.59)	<0.0001	2.00 (0.90 – 4.41)	0.08
Falls	4.32 (2.35 – 7.94)	<0.0001	1.82 (0.79 – 3.47)	0.16
Chair stands (per 10 stands)	0.17 (0.09 – 0.31)	<0.0001	0.24 (0.11 – 0.56)	0.0005
ADL dependence	4.92 (2.18 – 11.1)	0.0001	1.39 (0.40 – 4.87)	0.61
Proton Pump Inhibitor	1.94 (1.10 – 3.39)	0.02	1.65 (0.29 – 1.27)	0.18
Benzodiazepine	2.41 (1.27 – 4.5())	0.007	1.97 (0.78 – 4.94)	0.15
Gabapentin	1.66 (0.81 – 3.39)	0.17		
Opiate	3.36 (1.84 – 6.15)	<0.0001	1.39 (0.58 – 3.32)	0.47
Tricyclic Antidepressant	1.97 (0.90 – 4.29)	0.09		
Antidepressant	2.78 (1.46 – 5.28)	0.002	1.65 (0.63 – 4.29)	0.31
Weighted lures (per point)	1.02 (1.01 – 1.04)	0.002	1.01 (1.00 – 1.03)	0.04

The candidate variables for supplementary table 1 were those with univariate significance in Table 2. The multivariable analysis included all variables with p < 0.05 in the univariable analysis. Note that the multivariable model may be slightly over-fit because only 59 patients had low SF-8. ADL = activities of daily living, MELD = Model for endstage liver disease

Supplementary Table 2: Associations with Poor Sleep

	Univariate Analysis		Multivariate Analysis	
	Odds ratio (95% Confidence Interval)	P-Value	Odds Ratio (95% Confidence Interval)	P-value
Age (per year)	1.01 (0.99 – 1.03)	0.24		
Education (per year)	1.21 (0.89– 1.35)	0.20		
Male	0.89 (0.56 – 1.43)	0.63		
Body Mass Index (per point)	1.04 (1.00 – 1.08)	0.03	1.03 (0.98 – 1.08)	0.22
Charlson Comorbidity (per point)	0.99 (0.92 – 1.07)	0.78		
Alcohol-related cirrhosis	0.63 (0.35 – 1.15)	0.13		
Hepatocellular Carcinoma	1.04 (0.42 – 2.57)	0.93		
Child class B	1.83 (1.07 – 3.14)	0.03	1.39 (0.67 – 2.88)	0.38
Varices	1.09 (0.62 – 1.90)	0.76		
Ascites	1.19 (0.74 – 1.92)	0.47		
Platelet count < 80,000	1.23 (0.76 – 2.00)	0.40		
Alcohol abuse	1.30 (0.51 – 3.28)	0.59		
MELD-Na (per point)	0.97 (0.92 – 1.02)	0.17		
Bilirubin (per mg/dL)	0.83 (0.67 – 1.04)	0.11		
Creatinine (per mg/dL)	1.11 (0.84 – 1.48)	0.46		
INR (per point)	0.59 (0.22 – 1.57)	0.29		
Sodium (per meq/L)	1.08 (0.99 – 1.17)	0.06		
Albumin (per mg/dL)	0.50 (0.32 – 0.78)	0.002	0.64 (0.36 – 1.16)	0.15
Falls	3.18 (1.61 – 6.27)	0.0003	2.09 (0.87 – 5.04)	0.10
Chair stands (per 10 stands)	0.38 (0.23 – 0.62)	<0.0001	0.66 (0.38 – 1.16)	0.15
Hand grip (per 10 kilograms)	1.00 (0.84 – 1.20)	0.98		
ADL dependence	2.68 (0.98 – 7.32)	0.06		
Diuretics	1.02 (0.63 – 1.65)	0.94		
Nonselective Beta-blockers	1.15 (0.71 – 1.85)	0.57		
Proton Pump Inhibitor	0.78 (0.48 – 1.25)	0.30		
Benzodiazepine	3.59 (1.68 – 7.68)	0.0003		
Gabapentin	2.00 (0.97 – 4.13)	0.06		
Opiate	3.79 (1.89 – 7.61)	0.0002	2.85 (1.11 – 7.29)	0.03
Tricyclic Antidepressant	3.08 (1.23 – 7.69)	0.02	2.30 (0.74 – 7.14)	0.15
Antidepressant	2.17 (1.08 – 4.15)	0.03	1.59 (0.66 – 3.82)	0.30
Antipsychotic	2.68 (0.88 – 8.16)	0.08		
ICT Lures (per lure)	1.03 (1.01 – 1.06)	0.008	1.03 (1.00 – 1.05)	0.047
ICT Targets (per target)	1.00 (0.99 – 1.02)	0.76		
Weighted lures (per point)	1.01 (0.99 – 1.03)	0.07		

Poor sleep quality was defined as Pittsburgh Sleep Quality Index of > 5. ADL = activities of daily living, ICT = inhibitory control test; MELD-Na = Model for Endstage Liver Disease – Sodium,