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RESEARCH ARTICLE

FALL RISK, POSTURAL CONTROL, MUSCLE STRENGTH AND COGNITIVE FUNCTION IN PATIENTS WITH LIVER CIRRHOSIS

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ABSTRACT

Purpose: Falls are common in liver cirrhosis. Our aim was to investigate fall risk, postural control, muscle strength and cognitive function in cirrhosis, compare the results to healthy controls and investigate the inter-relationships.
Materials and Methods: Twenty-four patients (12 males, 12 females) and 24 healthy controls (11 males, 13 females) were enrolled. Fall risk was assessed with Falls Efficacy Scale (FES) and Timed Up and Go Test (TUGT). Postural control was assessed using posturography. Quadriceps Femoris and Tibialis Anterior strength were assessed with dynamometer. Cognitive function was evaluated with Stroop test. Disease severity was assessed with Child-Pugh and Model for End-Stage Liver Disease scores.
Results: Postural sway velocity (PSV) on foam surface eyes open (FSEO), FES score and TUGT duration were higher in patients (p<0.05). TUGT duration was correlated with disease severity. Lower extremity muscle strength was lower in patients (p<0.05). Dynamic postural control was deteriorated in patients (p<0.05). Lower extremity muscle strength was correlated with PSV-FSEO and FES score (p<0.05).
Conclusion: Patients with liver cirrhosis present significant decrease in muscle strength independent from disease severity, associated with static postural control on an unstable surface and fear of falling. Dynamic postural control is significantly deteriorated in liver cirrhosis, not in relation to muscle strength.

Keywords: Fall risk, postural control, muscle strength, cognitive function, liver cirrhosis

INTRODUCTION

The World Health Organization defines a fall as “an event which results in a person coming to rest inadvertently on the ground or floor or other lower level” (1). These inadvertent events mainly occur due to impairments in postural control, which is the ability to maintain the body position in space during static and dynamic conditions dependent on the interaction between visual, vestibular and somatosensory systems (2). Falls are common in patients with liver cirrhosis, a diffuse hepatic process characterized by fibrosis and structurally abnormal nodules (3,4)

Previous studies presented postural control problems in liver cirrhosis (5-7). The majority of these studies mostly focused on minimal hepatic encephalopathy (HE), clinically manifested as cognitive impairment (5-7). HE is a brain dysfunction caused by liver insufficiency and/or portosystemic shunts. Hyperammonaemia, systemic inflammation and oxidative stress are the critical factors in the pathophysiology of HE. It has a broad spectrum of neuro-psychiatric manifestations ranging in severity from subclinical alterations to coma (8).

There are many other factors possibly affecting postural instability in liver diseases such as muscle mass loss, hyponatremia, psychoactive drugs and sleep problems (9). However, most of the studies investigated only HE as a predictor of postural instability and falls in patients with liver cirrhosis (5-7, 10). Only in one study by Frith et al., decreased lower extremity muscle strength was associated with increased fall risk in a subgroup of patients including primary biliary cirrhosis (3).

Protein-energy malnutrition due to dietary restrictions, malabsorption, intestinal protein loss and hypermetabolism leads to loss of muscle mass in cirrhosis (13). Muscle strength also decreases as a result of skeletal muscle mass loss and mitochondrial dysfunction including reduced number of mitochondria and diminished mitochondrial oxidative capacity (14). The strength of different muscle groups decrease in patients with liver cirrhosis including respiratory, upper and lower extremity muscles (15-17).

In spite of the studies exploring fall risk, postural control problems and their relation to cognitive dysfunction, no studies have investigated the relationship between muscle strength and these parameters in patients with liver cirrhosis. Therefore, our study was designed to assess fall risk, postural control, muscle strength and cognitive function in patients with liver cirrhosis, to compare the results to healthy controls and to investigate the relationships between these parameters.

MATERIALS AND METHODS

Participants

Twenty-four outpatients were recruited from Department of Gastroenterology, Dokuz Eylul University Hospital, diagnosed as liver cirrhosis by clinical, analytical, and ultrasonographic findings or by liver biopsy (18). Exclusion criteria were: ≥ 65 years of age, severe neurologic or vestibular disease that can affect postural control, history of severe lower extremity musculoskeletal injury and/or surgery, alcoholic liver cirrhosis, diabetes mellitus, active alcohol consumption (in previous three months), severe co-morbidities (e.g., cardiac, pulmonary, renal, psychiatric). We also recruited 24 healthy controls with similar age and gender without any known chronic diseases and previous lower extremity injury and/or surgery. Subjects with active alcohol intake were also excluded from the control group.

The study was approved by Non-invasive Research Ethics Board of Dokuz Eylul University (Date: 01.03.2012, Decision No: 2012/08-06) and performed following the ethical guidelines of 1975 Declaration of Helsinki. All patients and healthy controls gave written consent before participation.

Data Collection

Demographic and clinical features of the patients had been collected from the patients and patient records. Age, gender, body weight and height were recorded as demographic features while etiology of liver cirrhosis, Child-Pugh score, Model for End-Stage Liver Disease (MELD) score and time since diagnosis were recorded as clinical features (19).

Assessment of fall risk

Turkish version of Falls Efficacy Scale (FES) was used to measure fear of falling and fall risk based on the patient's perceived self-efficacy at avoiding falls during activities of daily living (20). The scale consists of 10 items. Each item is scored from 1 (very confident) to 10 (not confident at all). Total score is between 10 and 100, higher scores indicating higher fall risk. Timed Up and Go Test (TUGT) was used to assess dynamic balance function and functional mobility. The patient was asked to rise from a standard arm chair, walk 3 meters away, return and sit down again. The time in seconds was recorded by a chronometer. The test was repeated for three times and mean duration of three measurements was used for the analysis. Scores more than 13.5 seconds were interpreted as high fall risk (21). Mean durations to complete the test were compared between the groups, as higher durations indicating higher fall risk. History of falls including the number of falls in the previous one year, hospital admissions due to falls and fall-related injuries were also recorded for each subject in the groups.

Postural control assessment

Postural control was objectively assessed using the Balance Master system continuously monitoring the position and movement of the center of gravity (CoG). During assessments subjects stand on the force platform measuring the vertical forces. The computer analyses the data from the force platform and prints a graphical and a numerical report (22).

"Modified Clinical Test of Sensory Interaction on Balance" (mCTSIB) was performed to assess

Figure 1. Modified Clinical Test of Sensory Interaction on Balance

Figure 2. Limits of stability Test

postural control under different sensory conditions and "Limits of Stability" (LoS) test was performed to assess dynamic postural control. mCTSIB quantifies the position of CoG in the upright position under four different conditions including firm and foam surfaces with eyes open (EO) and eyes closed (EC). Postural control was assessed as the sway velocity of the CoG and indicated by postural sway velocity (Fig 1).

LoS, quantifies the maximum distance that a patient can displace his CoG in a given direction. It involves shifting the weight to target points. The measurements include reaction time, CoG movement velocity, directional control, end point excursion and maximum excursion (Fig 2).

Reaction time is the time between the command to move and the initial movement, expressed in seconds. Movement velocity is the average speed of CoG movement (degrees/second). End point excursion is the distance of the first movement toward the target which is the point at which the first movement stops. Maximum excursion is the maximum distance achieved during the trial. Directional control is the comparison of the amount of intended movement to the extraneous movement.

Lower extremity muscle strength

The maximal isometric muscle strength for Quadriceps Femoris and Tibialis Anterior of each leg were assessed using a hand-held dynamometer (Powertrack II, J-Tech Medical, USA). Quadriceps Femoris strength was measured in sitting position with 90 degrees knee flexion by applying the force on full knee extension. Tibialis Anterior strength was measured in supine position with ankles slightly hanging out of bed by applying the force to the end point of ankle dorsi-flexion. The testing procedures were repeated for three times for each muscle with 90 second-intervals and the best value was recorded for the analysis (23).

Cognitive function

We used a color-word version of the Stroop test to evaluate cognitive function. This test has been used previously in patients with cirrhosis in order to evaluate particularly "anterior attention system" which was hypothesized to be more sensitive to early stages of minimal HE compared to posterior attention system (24). The test is based on assessing the abilities of selective selection, response inhibition, and executive control under congruent and incongruent conditions. Congruent stimuli consisted of the words displayed in the same color indicated by the word. Incongruent stimuli consisted of the words naming colors displayed in a different color from that indicated by the word. Our test included four tasks: (1) Naming the colors printed in black, (2) Naming the colors printed in a rectangular shape (neutral condition), (3) Reading the colors printed in incongruous colors, (4) Naming the colors printed in incongruous colors (incongruent condition).

"Stroop Effect" was calculated (Forth task duration-Second task duration) for the interpretation of the test results. We also recorded the number of errors during the incongruent condition in order to use for analysis (25).

Table 1. Demographic features of the groups

	Patient Group	Control Group	p
Age *(years)*	39 (35-46)	38 (35-44.75)	0.620
Gender, *male/female (%)*	12 (50) / 12 (50)	11 (45.8) / 13 (54.2)	0.773
Height *(cm)*	167 (158-170)	168 (164.25-180)	0.098
Body Weight *(kg)*	70 (62.50-74)	73.5 (64.25-83-75)	0.297
BMI* *(kg/m²)*	24.63 (22.25-27.45)	25.95 (23.19-27.08)	0.797

**BMI: Body Mass Index; Mann Whitney U Test, Chi-Square Test*
Values expressed as median (interquartile ranges) or number of patients (%)

Table 2. Disease characteristics of liver cirrhosis

Etiology of cirrhosis	Number of patients	%
Viral Hepatitis	9	37
Cryptogenic	4	17
Autoimmune Hepatitis	3	13
Wilson Disease	3	13
Budd-Chiari Syndrome	2	8
Primary Biliary Cirrhosis	1	4
Primary Sclerosing Cholangitis	1	4
Overlap Syndrome	1	4
Clinical Scores	**Median**	**25^{th} -75^{th}**
Child-Pugh	7	5-9
Model for End-Stage Liver Disease	13	8.25-16
Time since diagnosis *(years)*	5	2-9.50

Values expressed as median and interquartile ranges or number of patients (%)

Table 3. Comparison of fall risk assessments between the groups

	Patient Group	Control Group	p
Falls Efficacy Scale Score *(10-100)*	13 (10-35.75)	10 (10-12.50)	**0.027**
Timed Up and Go Test Duration *(sec)*	8.5 (7-10.75)	6 (5-6)	**0.001**

Mann-Whitney U Test, Values expressed as median and interquartile ranges (25^{th}-75^{th})

Table 4. Comparison of postural control measurements between the groups

	Patient Group	Control Group	p
mCTSIB *(°/sec)*			
EO firm surface	0.30 (0.26-0.30)	0.30 (0.30-0.30)	0.769
EC firm surface	0.30 (0.30-0.40)	0.35 (0.30-0.40)	0.877
EO foam surface	0.70 (0.52-0.70)	0.55 (0.50-0.60)	**0.047**
EC foam surface	1.25 (1-1.47)	1.10 (1-1.37)	0.334
LOS			
Reaction Time *(sec)*	1.03 (0.93-1.24)	0.72 (0.59-0.90)	**0.001**
Movement Velocity *(°/sec)*	2.80 (2.37-3.37)	4.15 (3.10-5.62)	**0.001**
Maximum Excursion *(%)*	76.63 (68.28-81.75)	86.62 (76.10-91.50)	**0.005**
End point Excursion *(%)*	96.37 (89.03-99.87)	101.31 (96.15-103.65)	**0.006**
Directional Control *(%)*	81.50 (77-84.75)	84 (82.25-87.00)	**0.014**

mCTSIB: Modified Clinical Test of Sensory Interaction on Balance, EO: Eyes Open, EC: Eyes Closed; LOS: Limits of Stability, Mann-Whitney U Test, Values expressed as median and interquartile ranges (25^{th}-75^{th})

Table 5. Comparisons of lower extremity muscle strength between the groups

	Patient Group	Control Group	p
Quadriceps Femoris *(R)*	18.25 (16.12-27.16)	34 (27.87-44.5)	**0.001**
Quadriceps Femoris *(L)*	18.08 (14.58-25.20)	30.66 (25.16-41)	**0.001**
Tibialis Anterior *(R)*	13.83 (10.95-15.62)	20.75 (16.20-26)	**0.001**
Tibialis Anterior *(L)*	11.83 (9.75-15.50)	19.50 (14.70-23.91)	**0.001**

R: Right, L: Left; Mann-Whitney U Test; Values expressed as median and interquartile ranges (25^{th}-75^{th})

Statistical Analysis

SPSS software version 22 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Descriptive statistics and frequencies were used for demographic and clinical features. Normality of the data distribution was tested by Shapiro–Wilk test. Medians and interquartile ranges (25th–75th percentile) were used for descriptive analyses of quantitative variables. Fall risk assessments, posturographic measurements, lower extremity muscle strength and cognitive function of the groups were compared with Mann-Whitney U Test.

Spearman's rank correlation coefficient rho (r) was used to identify the relationships between fall risk (FES scores and TUGT duration), posturographic measurements (mCTSIB and LoS), lower extremity muscle strength (Quadriceps Femoris and Tibialis Anterior) and cognitive function (Stroop effect and number of errors during incongruent condition). The strength of correlations was classified as very weak (r=0–0.19), weak (r=0.2–0.39), moderate (r=0.40–0.59), strong (r=0.6–0.79), and very strong (r=0.8–1). p values <0.05 were considered as statistically significant.

RESULTS

No significant difference was found in terms of the demographic features between the groups (Table 1). Table 2 shows the clinical characteristics of liver cirrhosis including etiology of the disease, Child-Pugh score, MELD score and time since diagnosis.

FES score and TUGT duration were significantly higher in patients with liver cirrhosis compared to healthy controls (p=0.027 and p=0.001, respectively) (Table 3). There were no subjects within the two groups having TUGT score >13.5 seconds indicating high fall risk. Four subjects in patient group and one subject in control group declared one or more times of falls in the previous one year (p=0.156). One subject in patient group was admitted to hospital having a fracture due to a fall.

Postural sway velocity for EO condition on foam surface assessed by mCTSIB was significantly higher in patients with cirrhosis compared to healthy controls (p=0.047) (Table 4).

Patient group showed slower reaction times in comparison to control group during LoS test (p=0.001). Movement velocity was also significantly slower in-patient group (p=0.001) whereas the percentages of directional control, maximum excursion and end point excursion were significantly lower than the control group (p=0.014, p=0.005 and p=0.006, respectively) (Table 4).

Quadriceps Femoris and Tibialis Anterior muscle strength were significantly lower for both left and right sides in patient group compared to the control group (p<0.01) (Table 5).

There was a significant difference in terms of Stroop effect between the groups (p=0.004). The time to complete the task was 33 seconds (27-47) in the patient group, whereas it was 26 seconds (21-31) in the control group. No significant difference was found in terms of number of errors during incongruent condition between the groups (p=0.063).

Correlations between the parameters in patients with liver cirrhosis are shown in Table 6.

There was no significant correlations between muscle strength and LoS test parameters.

Cognitive function assessed by Stroop effect and number of errors did not correlate with any of the postural control measurements, fall risk assessments and lower extremity muscle strength (p>0.05).

Clinical disease scores (MELD and Child-Pugh) and time since diagnosis were not significantly correlated with postural control and lower extremity muscle strength. TUGT duration was moderately and positively correlated with MELD score (r=0.414, p=0.044) and with Child-Pugh score (r=0.471, p=0.020).

DISCUSSION

In our study, in which we have investigated fall risk, postural control, muscle strength and cognitive function in patients with liver cirrhosis, we found impairments in postural control under the conditions in which the somatosensory system had been compromised. Dynamic control of posture was deteriorated which had been considered as an indicator for fall risk. Our patients showed increased fear of falling and a clinically assessed fall risk associated with disease severity. Lower extremity muscle strength bilaterally decreased and was correlated with both fear of falling and postural control on an unstable surface in patients with cirrhosis. Cognitive function of patients with cirrhosis was also impaired in comparison to healthy controls, but did not show any correlations with fall risk, postural control and muscle strength.

Previous studies demonstrated deterioration in postural control using posturographic measurements in patients with liver cirrhosis (5-7). Aref et al. investigated postural control using dynamic posturography and found significantly weaker performances in cirrhotics compared to healthy controls (5). In another posturographic study, Schmid et al. found deterioration in postural control in alcohol induced and non-alcohol induced cirrhosis (6). In both of these studies, patients with cirrhosis showed impairments in sensory organization tests indicating the inability to organize sensory information appropriately to maintain balance (5,6). In a recent study, Urios et al. performed mCTSIB and LoS tests similar to our study and found lower stability on foam surface in eyes open condition (7). Patients with minimal HE in that study showed lower global scores in eyes open condition while the deterioration was higher on foam surface compared to patients without minimal HE (7). Aforementioned studies indicated an association between postural control disturbances and cognitive impairment in cirrhosis. Although we have detected a significant decrease in cognitive function evaluated with Stroop test, which had been commonly used for patients with chronic liver diseases, we did not find a relationship between cognitive function and neither postural control nor fall risk.

Postural sway velocity of our patients and the controls were similar, while all sensory systems were available for maintenance of balance. However, on foam surface with eyes open, postural control of the patients significantly deteriorated suggesting the difficulty in integrating somatosensory information in the presence of visual information. Interestingly, when the eyes were closed, the deterioration in postural control disappeared. Oppositely, maintenance of balance is expected to be hindered in the absence of visual information. Contrary to Aref et al.'s and Schmid et al.'s findings, indicating the increase in postural instability parallel to the progression of liver disease (5,6), we did not find any relationships between postural control and clinical disease scores. However, disease scores were positively correlated with TUGT duration suggesting a disease severity-dependence in clinically assessed fall risk. Although there were not any recurrent fallers in our patient group, the duration to complete TUGT was significantly higher in patients than the controls. FES score was also significantly higher in our patients than healthy controls indicating an increased fear of falling and fall risk based on the patient's perceived self-efficacy at avoiding falls during daily life.

Postural sway velocity during standing on a foam surface with eyes open was significantly correlated with all lower extremity muscle strength values except left side Tibialis Anterior in patient group. Although the relationship between postural control and lower extremity muscle strength has been shown in different populations (26, 27), no data exists in liver cirrhosis. Only in one study, Frith et al. recorded the duration of 5 times sit-to-stand test in order to

Table 6. Correlations between the parameters in patients with liver cirrhosis

	QF-L		QF-R		TA-L		FES Score		TUG		PSV-foam EO		Child-Pugh		MELD	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
QF-L			.951	**<.001**	.809	**<.001**	-.634	**.001**	-.307	.145	-.518	**.009**	.133	.535	.257	.225
QF-R	.951	**<.001**			.785	**<.001**	-.603	**.002**	-.403	.051	-.574	**.003**	.004	.987	.111	.607
TA-L	.785	**<.001**	.809	**<.001**			-.563	**.004**	-.801	.707	-.425	**.039**	.021	.923	.146	.496
FES	-.634	**.001**	-.603	**.002**	-.563	**.004**			.082	.703	.148	.491	-.209	.328	-.250	.239
TUG	-.307	.145	-.403	.051	-.081	.707	.082	.703			.599	**.002**	.471	**.020**	.414	**.044**
PSV-foam EO	-.518	**.009**	-.574	**.003**	-.425	**.039**	.148	.491	.599	**.002**			.029	.893	-.100	.642
CP	.133	.535	.004	.987	.021	.923	-.209	.328	.471	**.020**	.029	.893			.896	**<.001**
MELD	.257	.225	.111	.607	.146	.496	-.250	.239	.414	**.044**	-.100	.642	.896	**<.001**		

QF: Quadriceps Femoris, L: Left, R: Right, TA: Tibialis Anterior, FES: Falls Efficacy Scale, TUG: Timed Up and Go, PSV: Postural Sway Velocity, EO: Eyes Open, CP: Child-Pugh, MELD: Model for End stage Liver Disease estimate lower extremity muscle strength indirectly and concluded that lower limb strength was associated with number of falls in patients with primary biliary cirrhosis (3). However, the authors included only one etiology of cirrhosis and interpreted a functional test's results rather than measuring muscle strength using direct methods. Similar results have been shown in previous studies indicating diminished lower extremity muscle strength in patients with alcoholic liver cirrhosis, which was an exclusion criteria in our study (28,29). However, there is no study addressing the relationship between muscle strength, postural control and fall risk in this patient group. Our results showed a correlation between lower extremity muscle strength, static postural control and fear of falling.

The inability to voluntarily shift the body toward LoS may lead to instability during dynamic daily living activities such as reaching for objects and walking (30). Therefore, it is important to test this ability in order to measure dynamic postural control and determine fall risk during daily life among populations with higher fall incidence. Our patient group presented impairments in overall performance on LoS test compared to control group which was not in association with cognitive function. Similar to our findings, not only patients with minimal HE but also without minimal HE got lower global LoS scores indicating high risk for falls independent from cognitive impairment in Urios et al.'s study (7). Reaction time was significantly longer in our patient group suggesting the possible psychomotor slowing (31). End point excursion, representing the distance of the first movement toward the target, was smaller in our patient group indicating that patients with cirrhosis could not stop their initial movement as far as the healthy controls possibly suggesting the disturbances in the perception of safety limits. Movement velocity was also slower in our patient group showing the insecure in CoG displacement in order to maintain balance during dynamic activities. Not surprisingly, the maximum distance achieved during the trials defined as maximum excursion was also smaller in our patients. The percentage of directional control was also smaller in patients than the controls indicating the inability to control the movement of CoG through the targeted directions. These findings suggest that special attention is necessary to restore the dynamic balance abilities in patients with cirrhosis in order to prevent fall risk.

We have some limitations in this current study. Although, we have assessed fall history including number of falls during the last one year, hospital admissions and fall related injuries, we could not detect any important differences between the patients and the controls. Therefore, we could not divide our patients into groups such as non-fallers and recurrent fallers. Indeed, this point is much more important for elderly patients with cirrhosis. However, we believe that relatively younger patient population in our study, contrary to other studies investigating postural control in cirrhosis, is the strength of our study as postural control, muscle strength and cognitive function possibly deteriorate with older age. In spite of the exclusion of elderly patients and the absence of recurrent fallers, our findings indicated higher fall risk, impaired postural control and decreased muscle strength not dependent on the deterioration of cognitive function in patients with liver cirrhosis. Our findings should be considered in future studies

CONCLUSION

Patients with liver cirrhosis presented significant increase in fall risk represented by the deterioration in dynamic postural control independent from muscle strength loss. The decrease in lower extremity muscle strength was associated with postural control on an unstable surface and fear of falling. Contrary to the general findings, cognitive function did not affect postural control and fall risk in our patient group who presented significant decline compared to healthy controls. Therefore, we believe that individually planned exercise programs to increase lower extremity muscle strength and functional activities including standing or walking, especially on irregular surfaces or under challenging conditions, would help to restore static and dynamic postural control strategies in patients with liver cirrhosis, no matter if they clinically present higher fall incidence or not.

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