UNIVERSITY OF MEDICINE AND PHARMACY

„CAROL DAVILA", BUCHAREST

DOCTORAL SCHOOL

AREA MEDICINE

THE PROGNOSTIC VALUE OF THE EVALUATION OF FRAILTY AND SARCOPENIA IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE

DOCTORAL THESIS SUMMARY

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YEAR

2024

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II. PERSONAL CONTRIBUTIONS

1. INTRODUCTION

The world population is rapidly expanding, the life expectancy growing as there is enormous progress in the medical field. The data from WHO foresee that the adult population over 65 years will be greater than 3.1 billion by the year 2100, and will reach to 0.9 billion for the persons over 80 (1,2). This is promising data, considering that the life expectancy in Romania is of 76.6 year, a third place for the lowest life expectancy in Europe. With age, the number of health problems increases, among other chronic disease is the appearance of frailty and sarcopenia. The biggest impact of these two is over the quality of life, by lowering independence and needing more health assistance. This puts a big pressure over the Health system, by raising the costs. It is highly important that these ailments be recognized as early as possible so that the patients receive optimal care, so that their life quality is not affected. Both frailty and sarcopenia need a multidisciplinary management, that involves the gastroenterolog, the internal medicine specialist, and a psychologist, which may lead not only to the slowing of the progression of these two, but also to a potential reversibility. For this reason, it is imperative that some test should be standardized.

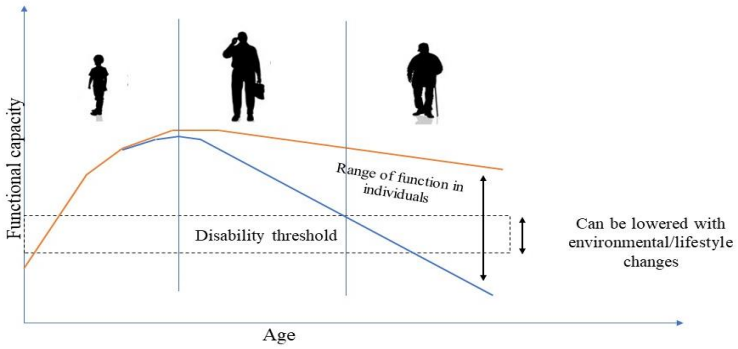
Over 2 million deaths per year are caused by the advanced hepatic liver disease all over the world. These deaths are preventable by the prevention of trigger risk factors. There is also a possibility that this data is underestimated because of the lack of data(3,4).

There is a 2023 study on the Romanian population that showed that the prevalence of the chronic advanced liver disease is 17.9%, which translates that every1 in 5 patients has it(5). At a national level, the number of studies that evaluate sarcopenia is fairly small, especially in patients with advanced chronic liver disease. Globally and at the european level, the interest for this evaluation grew exponentially in the last 10 years, as both sarcopenia and frailty are predictor factors for mortality. Taking into consideration the novelty of out theme, the fact that there is a great interest in the subject only from 10 years ago, we consider it to be actual.we found only 113 studies in a small research from 2014-2023 (6).

The origin of the term of sarcopenia is Greek, from the words `sarx` - meat and `penia` - loss, translating to muscle loss. At first, sarcopenia was described as an elderly disease, and

the term was introduced by doctor Irwin Rosenberg, in the year 1989. It was he who mentioned for the first time `frail elderly` and the wonderful capacity of muscle strength regeneration (7–9)

WHO recognized in the year 2000 that sarcopenia is a risk factor that is important both for a diminished grade of independency as well as for the apparition of multiple diseases at the elderly. At the same time, it targeted sarcopenia as a modifiable factor by lifestyle changes (7,8,10).



Figură 1. Functional capacity variability- adapted from WHO, Geneva 2000

In the year 1968 the term of frailty appeared for the first time; its first definition being given in the year 1988 by Winograd and co. They observed that the elderly patients over 65 years that were frail have from 3 up to 5 comorbidities in common and a longer hospital stay (11,12).

Frailty was defined as a clinical syndrome in 2001 by Fried and co, in thei cardiovascular Health study. For diagnosis it would require at least 3 of 5 criteria (13).

We learned from systematic reviews that the prevalence of frailty in patients that are diagnosed with advanced chronic liver disease is of 27%, and that of sarcopenia of 33%, this meaning that 1 in 3 patients have either sarcopenia or frailty or both (14,15).

A multidisciplinary approach is as important as necessary for the early diagnosis of these 2 syndromes, not only to establish an optimal treatment plan, but also in order to improve the life quality of elderly patients and assuring them a successful ageing.

In this thesis, we choose to verify what is the prognostic value of the evaluation of frailty and sarcopenia in patients that are already diagnosed with advanced chronic liver disease, in a tertiary center from Romania. Our motivation was that both frailty and sarcopenia can become national health problems. The identification and evaluation of these patients in the early stages bringing benefits for slowing the progression and raising the quality of life, and also, hopefully reducing the costs for the healthcare system. Another motivation was that the number of patients that are diagnosed with advanced chronic liver disease is continually growing.

The thesis has a general part, that has 3 chapters that present information from the specialty literature and the special part, that is comprised of 5 chapters that include the study motivation, research methodology, results, discussions and conclusions regarding the study.

2. AIMS AND STUDY METHODOLOGY

The aims of the study were: the evaluation of the prevalence of sarcopenia and of frailty in a selected number of cases that have been diagnosed with liver disease, the relevance and the impact these two have over mortality and hospital readmission. We also wanted to evaluate the tests/scores that could be used in the hospital in order to establish easy, rapidly and precisely the diagnosis of these two syndromes.

Our study was an observational, prospective study that took place in the University Emergency Hospital of Bucharest and included 128 patients that had liver disease.

In order to diagnose the hepatic liver disease, we used clinical examination, abdominal ultrasound, upper GI endoscopy and CT. For the liver function evaluation, we used the Child-Pugh and Meld scores.

In order to be included in the study the patients had to be 18 or older in age, to sign the inform consent and to have a CT scan. The exclusion criteria were any disease that could influence sarcopenia by itself, including neoplasia.

We collected data like: age, sex, height, weight, biological parameters, the above-mentioned scores, and other infections and complications. We also included data about hospital stay, mortality and readmission.

The method of evaluation used for the evaluation of sarcopenia was the one suggested by the EWGSOP2 (European Working Group on Sarcopenia in Older People) from 2018, with the evaluation of hand grip strength and the SMAI. We wanted to evaluate if we could use HGS as a test for the evaluation of sarcopenia because it is a cheaper and easier way. We also applied o series of test in order to establish the prognostic value. Short Phyșical Performance Batery (SPPB) – which is formed from 3 tests – balance test, chair stand and gait speed. Frailty was calculated using the LFI, patients being divised into 3 groups: frail, prefrail, robust. These includes HGS, balance test and chair stand.

3. RESULTS

Our patients had a prevalence of sarcopenia of 44,53% , and a prevalence of frailty od 42% - higher numbers that those found in the literature.

Tabel 1. Prevalence of sarcopenia

Sarcopenie	Frecvență	Procent
Cu sarcopenie	57	44.53%
Fără sarcopenie	71	55.47%
Total	128	100.00%

Tabel 2. Prevalence of frailty

Fragilitate prezenta (>4.5-PERC 80)	Frecvență	Procent
Pacienți robuști / prefragili	86	67.19%
Pacienți fragili	42	32.81%
Total	128	100.00%

A univariable binary logistic regression was made for the next data in order to establish their prognostic value for mortality. In our study sarcopenia, LFI and SPPB haw statistical significance for predicting the 1-year mortality. Also, the MELD scores had predictive value, as well as other parameters showed in the bellow table.

Tabel 3. Predictors for 1 year mortality

Total deces– Univariable binary logistic regresșion					
Predictori	B	OR (Exp(B))	Interval de confidenta 95%		Valoare p
			Inferioara	Superioara	
Vârsta	0.024	1.024	0.994	1.056	0.122
Sex	-0.161	0.851	0.412	1.759	0.664
Etiologie etanolică	0.365	1.441	0.713	2.915	0.309
BMI	0.017	1.017	0.910	1.138	0.765
MELD	0.309	1.361	1.208	1.534	**<0.0001**
MELD-Na	0.240	1.271	1.168	1.382	**<0.0001**
Albumina	-1.271	0.281	0.132	0.598	**0.0001**
Ascita	0.740	2.096	1.398	3.142	**0.0003**
EH	1.212	3.360	1.732	6.516	**0.0003**
HCC	0.488	1.630	0.692	3.840	0.264
CRP	0.083	1.087	1.025	1.153	**0.0054**
Sarcopenie	3.143	23.164	8.134	65.963	**<0.0001**
LFI	5.476	238.780	34.371	1658.840	**<0.0001**
SPPB	-1.343	0.261	0.168	0.404	**<0.0001**

There is a significant statistical difference between the median values of SPPB in subject with or without hospital death.

Tabel 4. Valoarea scorului SPPB și decesul în spital

SPPB	Cu deces in spital	Fără deces in spital	Valoare p

Număr valori	13	115	**0,0002**
Valoare minimă	3.000	4.000	
25% Percentile	4.000	7.000	
Mediană	5.000	9.000	
75% Percentile	6.000	12.00	
Valoare maximă	12.00	12.00	
Medie	5.769	9.165	
Deviație standard	2.920	2.502	

There is significant statistical difference between the median values of LFI for the patients with hospital deaths.

Tabel 5. Valorile LFI și mortalitatea

LFI	Cu deces in spital	Fără deces in spital	Valoare p
Număr valori	13	115	**0,0005**
Valoare minimă	3.130	3.050	
25% Percentile	4.550	3.660	
Mediană	4.950	4.060	

75% Percentile	5.125	4.510	
Valoare maximă	5.360	5.410	
Medie	4.725	4.076	
Deviație standard	0.6459	0.5703	

4. Conclusions and personal contributions

The data in our study confirmed both sarcopenia and frailty as predictor factors for mortality, confirming that early diagnosis and treatment could slow down the progression of the disease and even mortality. It also confirmed that LFI and SPPB test are good predictors of mortality, bringing to our attention that the evaluation of the patients with advanced chronic liver disease with these tests is cheaper and easier.

The originality of the study is that, as to what we know, no national studies that evaluate the prognostic value of these tests.

The limitations of the present study were the small number of patients that were included and that it was unicentric. In the future, we propose to establish a protocol for the evaluation of sarcopenia and frailty in the patients that are chronically ill in order to increase their life quality. We consider the multidisciplinary approach in order to evaluate, diagnose and treat and the necessity for a task force.

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