



# Sarcopenia, Frailty in End-Stage Liver Disease

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No disclosure

# Definitions

**Sarcopenia:** A generalized reduction in muscle mass and function due to aging (primary sarcopenia), acute or chronic illness (secondary sarcopenia), including chronic liver disease

## Cirrhosis-related

Synthetic dysfunction, anabolic resistance...

## Other systems

Inflammation, insulin resistance, metabolic/endocrin dysfunction

Physical inactivity

Environmental/Organizational factors

**MALNUTRITION**

**Frailty:** Loss of functional, cognitive, and physiologic reserve leading to a vulnerable state

# Malnutrition in cirrhosis

- Prevalence
  - 20 to 50%
  - Correlation to the severity of cirrhosis
  - Alcohol-PBC >>> HBV or HCV
- Mechanisms
  - Decreased intakes, anorexia
  - Maldigestion, malabsorption
  - Changes in glucose metabolism
  - insulin resistance
  - Increase in resting energy expenditure
  - ...



**The Child–Turcotte score**

Group	A	B	C
Bilirubin (μmol/l)	< 34	34–51	> 51
Albumin (g/l)	> 35	30–35	< 30
Ascites	Absent	Controlled	Refractory
Encephalopathy	None	Minimal	Advanced (coma)
Nutritional status	Good	fair	poor

*Jeremiah Turcotte and Charles Gardner Child. Assessment of post operative risk after surgical portosystemic shunt. 1964*

# How to assess malnutrition?

## Subjective tools

- Subjective Global Assessment

*Poorly accurate*

- RFH Global Assessment

*Accurate, time-consuming, not validated outside UK*

## Objective tools

### Many biases during cirrhosis

- Water and salt retention
  - ✓ Ascites
  - ✓ Edema
- Reduced protein synthesis
- Protein leak
  - ✓ Ascites

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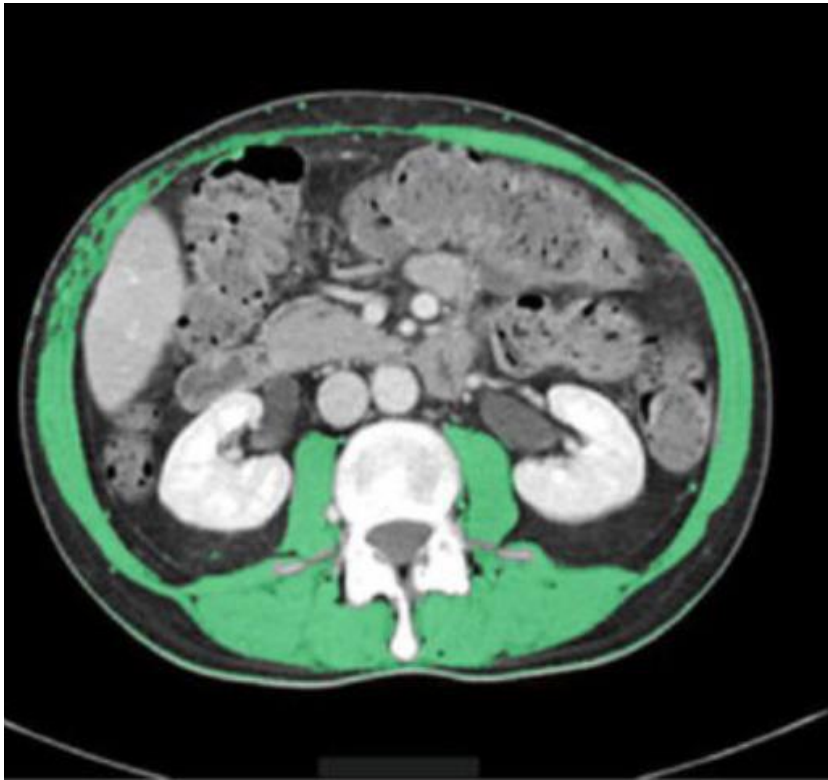
Physical inactivity

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# Assessment of sarcopenia: muscle measure



Cross sectional area on CT scan: reference  
(specific imaging software)



Alternative tool: Transversal psoas muscle  
thickness (no software)

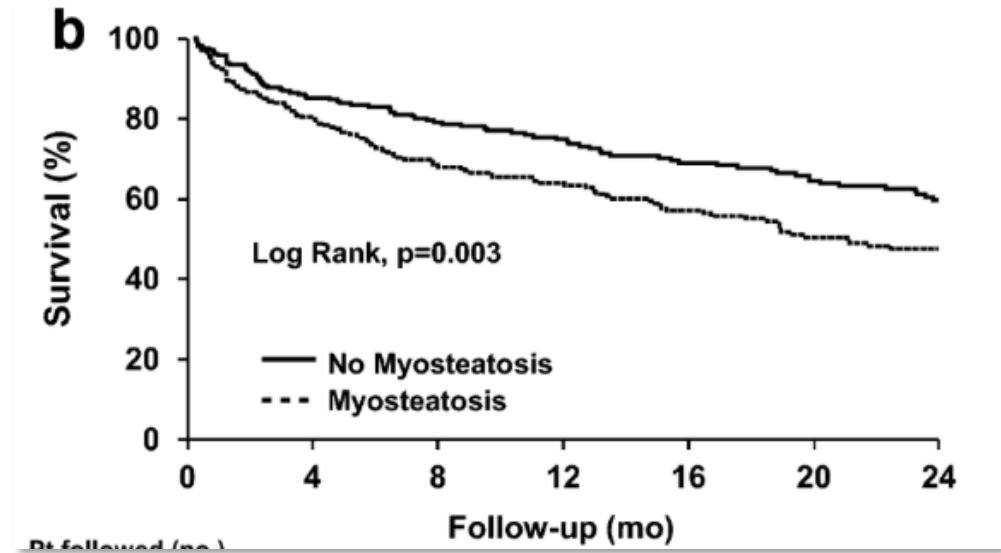
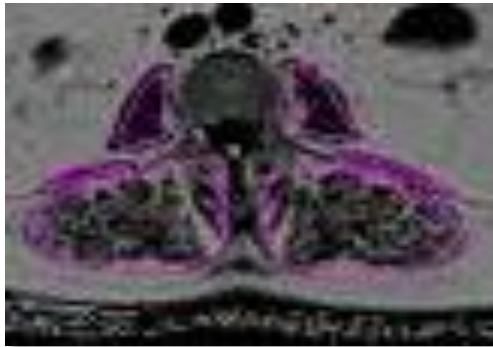
# Sarcopenia: prognostic impact

Author	n	Measurement	Prognostic value
Durand F. 2014	376	TPMT/height	WL mortality
Huguet A. 2018	173	TPMT/height	WL mortality
Meza-Junco J, 2013	116	SMA/Height , L3 level (SMI)	HCC/cirrhosis mortality

- Muscle measurement accurates to predict outcome
  - Which tool?
  - Which cut-off values? (extrapolated from oncology)
- No validation in large multicentric cohort



# Qualitative changes in muscle: myosteatorsis



- Prognostic impact in patients with HCC, in patients with NASH (non obese)
- Differences male/female? Differences across ethnicity?

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**Frailty:** Impaired muscle contractile function

# Tools to assess frailty

Test	Description	Time (Minutes)	Limitations
FFI	Single 5-point score based on subjective (exhaustion, unintentional weight loss, low physical activity) and objective (walk speed, HGS) measures	<10	Complex and time-consuming compared with other frailty measures; omits other consideration such as comorbidities, age, malnutrition, and HE; limited use in measuring change to interventions such as prehabilitation
CFS	Subjective clinical assessment of stability/presence of comorbidities, level of daily physical activity, dependence on ADLs, and presence of terminal illness*	<1	Only a snapshot of frailty and not able to identify specific areas of frailty; not specific enough to monitor change in therapeutic intervention
LFI	Composite metric of three performance-based measures (HGS, balance, chair stands)	<5	Not validated outside of the United States; not validated in hospitalized inpatients or acutely unwell

# Liver frailty index

536 patients (FrAILT Study)

Test	Evaluation	Unit of measure
Gait speed	Measured	m/sec
Grip strength	Measured	kg
Chair stands (n/ 30 sec)	Measured	n/30 sec
Balance time	Measured	sec

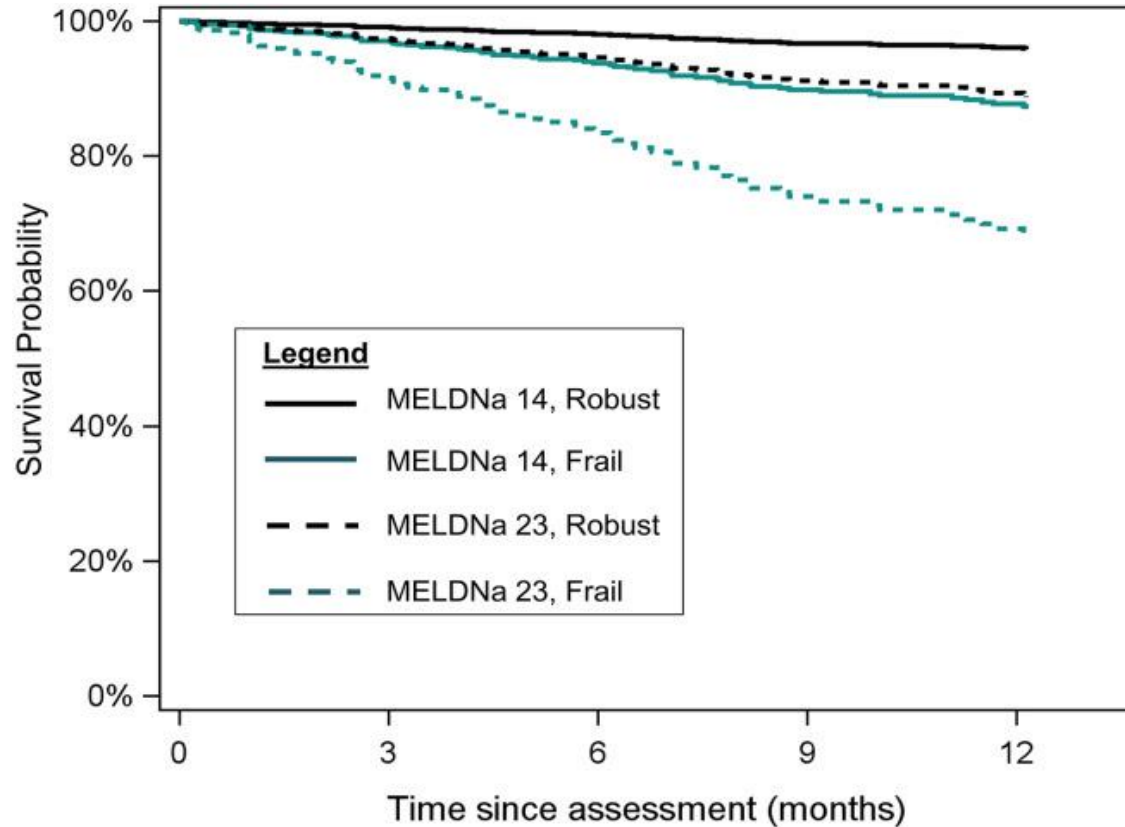
**Frailty index = (-0.33 x grip strength adjusted to gender) + (-2.529 x number of chair stands) + (-0.040 x balance time) + 6**

**LFI > 4.5 : frail**

**LFI < 3.2 : robust**

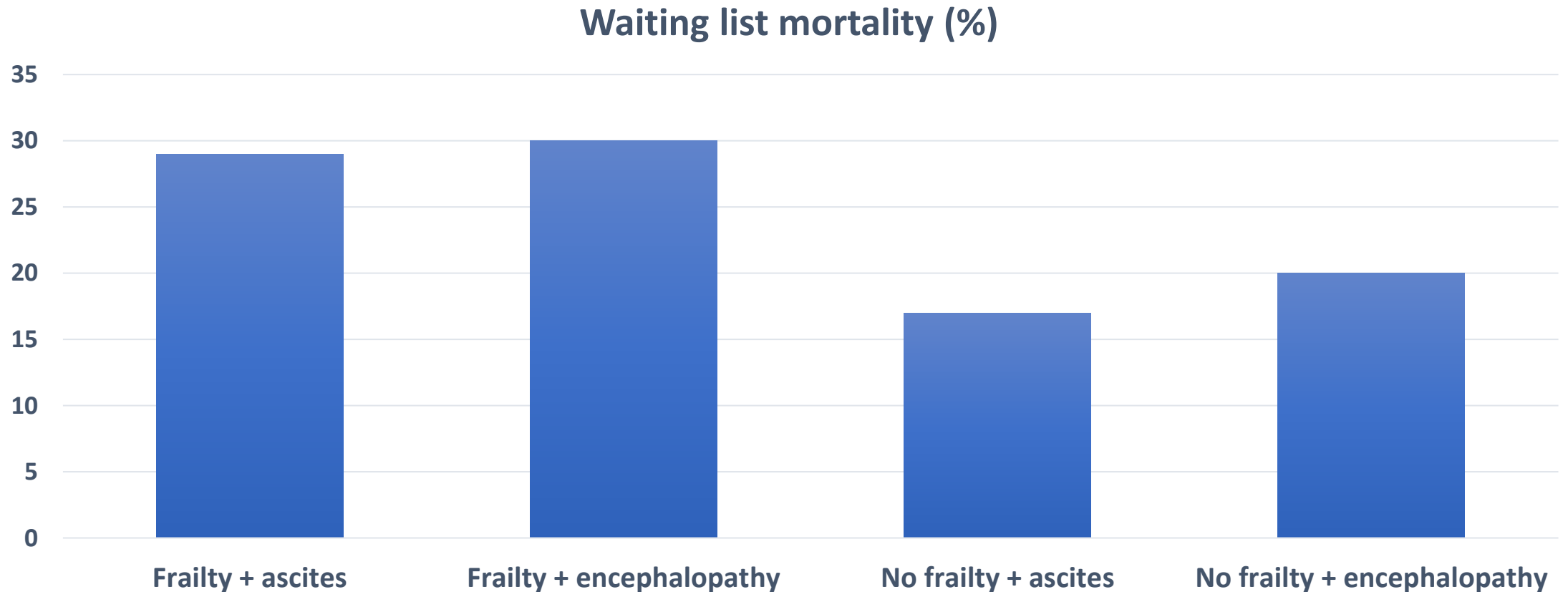
**3.2-4.5 : pre frail**

# Adding Frailty to the MELD score improves the prediction of death



536 candidates for LT

# Ascites and encephalopathy: higher mortality rate in frail patients



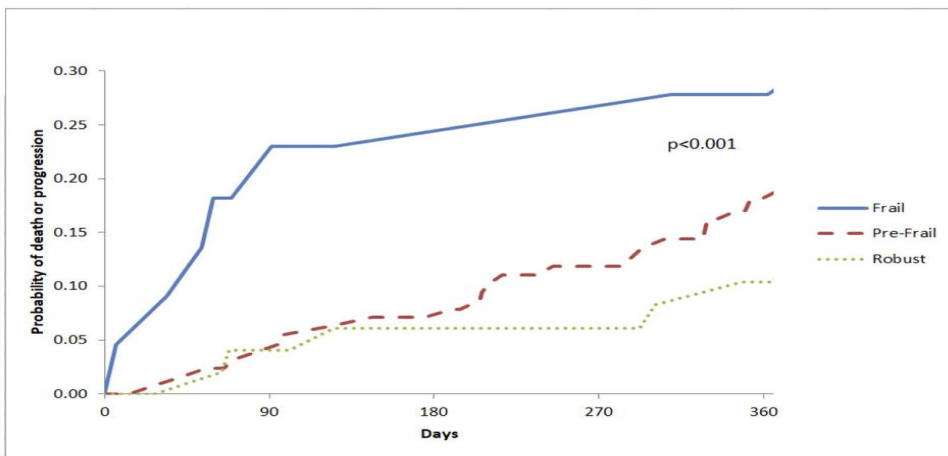
Multicentric study, 1044 patients

# Frailty associated with the risk of death, both in compensated and decompensated cirrhosis

4 centres (Canada, California, India), 822 patients

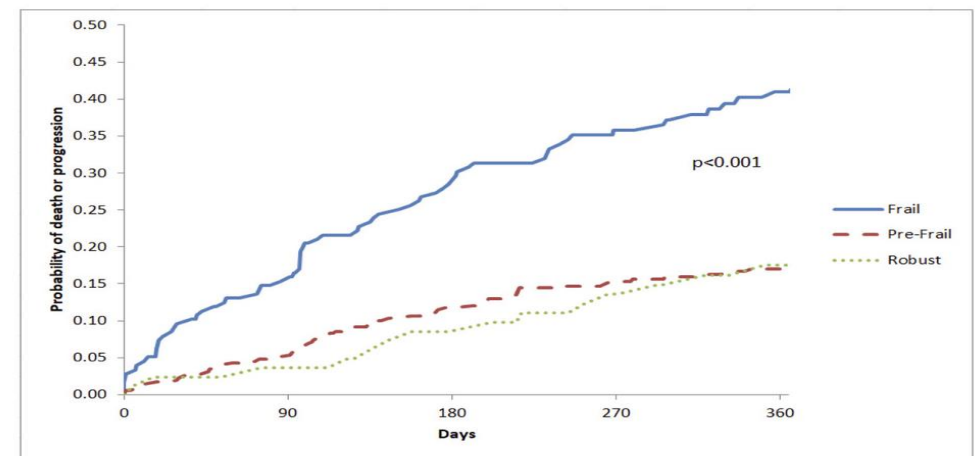
LFI > 4.5 : fail  
 LFI < 3.2 : robust  
 3.2-4.5 : pre frail

## Compensated



No. at risk	Start	90 days	180 days	270 days	360 days
Frail	22 (100%)	17 (77.3%)	14 (63.6%)	14 (63.6%)	12 (54.5%)
Pre-Frail	131 (100%)	118 (90.1%)	112 (85.5%)	97 (74.0%)	77 (58.8%)
Robust	50 (100%)	44 (88.0%)	42 (84.0%)	41 (82.0%)	36 (72.0%)

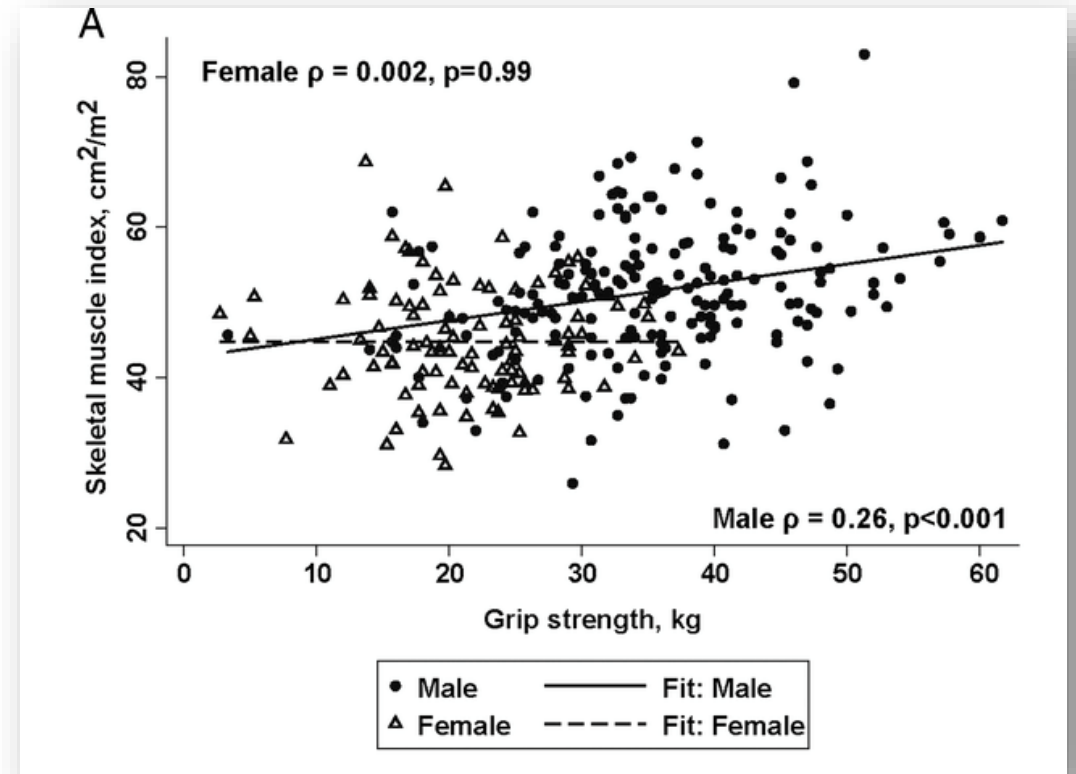
## Decompensated



No. at risk	Start	90 days	180 days	270 days	360 days
Frail	179 (100%)	141 (78.8%)	109 (60.9%)	82 (45.8%)	57 (31.8%)
Pre-Frail	357 (100%)	318 (89.1%)	267 (74.8%)	225 (63.0%)	187 (52.4%)
Robust	83 (100%)	74 (89.2%)	59 (71.1%)	50 (60.2%)	40 (48.2%)

# Limitations of Liver Frailty Index

- LFI proposed for outpatients, difficult to apply in hospitalized patients (refractory ascites, overt encephalopathy, ICU)
- Poor correlation between sarcopenia and frailty
- Only few studies published, more investigations are needed

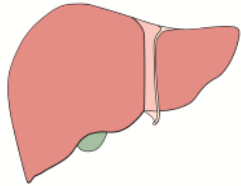


292 candidates for LT



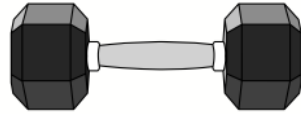
# Malnutrition, sarcopenia, frailty: management

## Management Toolbox



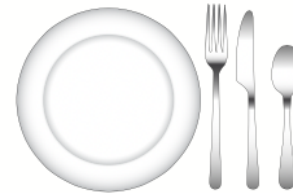
Liver specific

- Management of disease etiology
- Management of ascites
- Management of hepatic encephalopathy



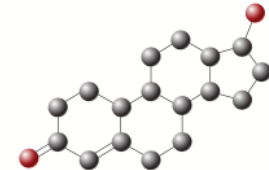
Physical activity

- **Personalized activity prescription (guided by FITT):**
  - **F**requency – Aerobic (4-7 d/week); Resistance (2-3 d/week)
  - **I**ntensity – Use the talk test (be short of breath but can still speak a full sentence); 3 sets of 10-15 repetitions at a time
  - **T**ime – Start slow and build up
    - Aerobic: 150 min per week
    - Resistance:  $\geq 1$  days per week
  - **T**ype – aerobic, resistance, flexibility and balance



Intake/Uptake

- Calorie intake of at least 35 kcal/kg (non-obese)
- Protein intake of 1.2 to 1.5 g/kg body weight/d
- Micronutrient repletion
- Frequent, small meals and minimize fasting (e.g. late evening snack)
- Address barriers to intake (e.g. liberalize sodium restrictions as needed)
- Consult a registered dietitian



Other systems

- Testosterone replacement (men)
- Refer to health behavior specialist
- Diabetes control

- **TIPS?**
- **Best therapeutic option: liver transplantation**

# Take Home messages

- Malnutrition, sarcopenia and frailty are common in the most severe forms
- Pathophysiology is complex and not fully understood
- Sarcopenia and frailty are risk factors for complications of cirrhosis, independently of MELD
- Muscle measurement (CT, area or thickness) is the most validated tool to assess sarcopenia
- LFI is the most studied tool to assess frailty but needs further investigations
- Whether sarcopenia or frailty or both should be used is still a matter of debate
- Sarcopenia and/or frailty should be integrated in grafts allocation systems
- Liver transplantation is the only definitive treatment