

# Frailty & Sarcopenia In Cirrhosis

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*NIH Beeson Scholar of Aging Research*

# Conflicts of Interest

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- Consultant, Third Rock Ventures

# Mr. D, a 57 year old man with NASH cirrhosis

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- History of HTN, DM with peripheral neuropathy, obesity

New onset ascites.

Controlled.

MELDNa 16.

**List for LT.**

Ascites, controlled.

New HE, mild.

MELDNa 16.

**Wait.**

Acute on chronic

liver failure.

MELDNa 35.

**Transplant?**

**9 mos ago**

**3 mos ago**

**Now**



# The Work-Up to Prepare for Transplant

- Diagnostic paracentesis – negative.
- Blood/urine cultures – no growth to date.
- No evidence of hemorrhage; hemoglobin stable.
- Abdominal ultrasound – no portal vein thrombosis; no new masses; normal appearing gallbladder.
- TTE – unremarkable.

Mr. D, a 57 year old man with NASH cirrhosis

**Too sick for transplant?**

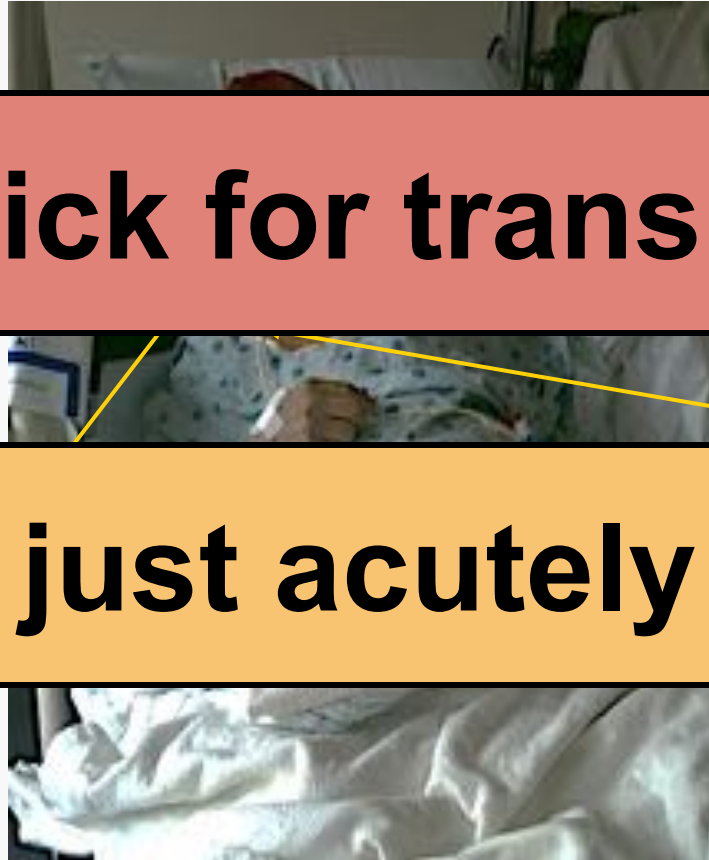
Requires  
mechanical  
bed to sit up

Inadequate  
e

**Or just acutely ill?**

Unable  
war  
maintain body  
temperature

(body tilted,  
arms stuck)



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Wait.

Acute hepatic  
decompensation.  
MELDNa 35.  
Transplant?

9 mos ago

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Now

Grip strength 29 kg  
(age-norm: 45 kg)

**FRAIL**

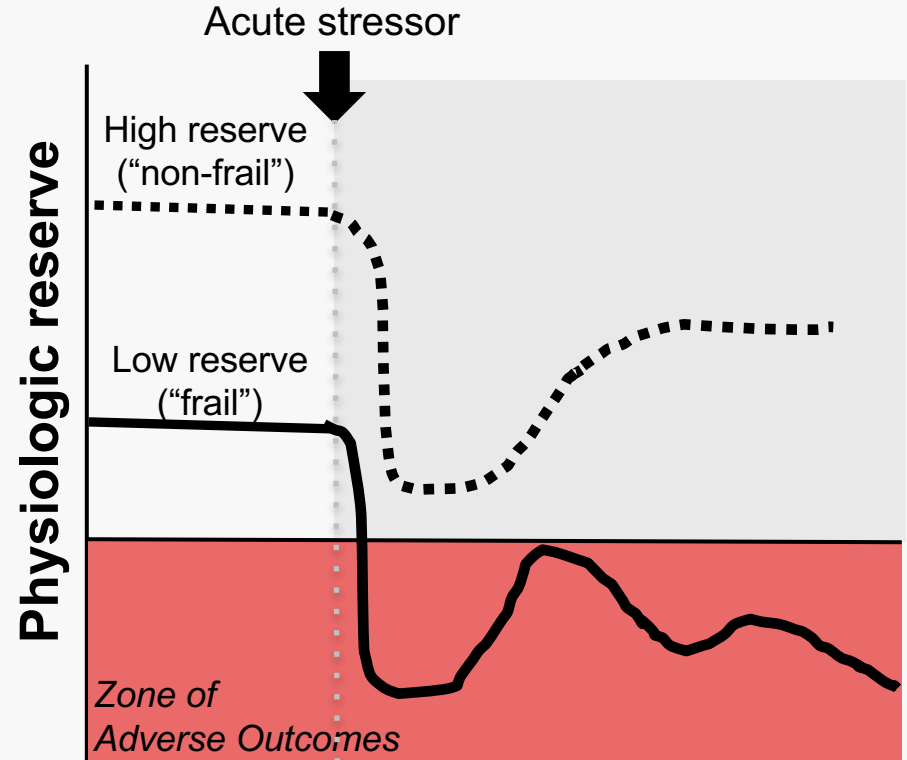
er.

help going  
bathroom.

# Frailty: a state of chronically low physiologic reserve

“...the aggregate expression of risk resulting from age- and disease-related subthreshold decrements of multiple physiologic systems”

Fried L. J Gerontol A Biol Sci Med Sci 2004.





# Frailty matters in patients with cirrhosis

- ~20% frail
  - ~40% physically impaired
- =
- 85 yo  
(without liver disease)

- **2X** increased risk of mortality among outpatients

- Predicts:
  - Hospitalized days
  - Annual inpatient costs
  - Rehabilitation needs
  - 90-day mortality after hospitalization


# The “Frailty” Toolbox

*For frailty screening in patients with cirrhosis in the clinic*

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## Tested in patients with cirrhosis

- Fried Frailty Index
- Short Physical Performance Battery
- Karnofsky Performance Status (KPS)
- ECOG
- Braden Scale
- Clinical Frailty Scale
- Short gait speed (single measure)
- Activities of Daily Living (ADL)
- Liver Frailty Index



Karnofsky Performance Status  
Activities of Daily Living (ADLs)  
Liver Frailty Index

# Karnofsky Performance Status

Assessed by the clinical provider or patient.

100	Normal; no evidence of disease	High
90	Able to perform normal activities with only minor symptoms	
80	Normal activity with effort; some symptoms	
70	Able to care for self but unable to do normal activities	Inter-mediate
60	Requires occasional assistance; cares for most needs	
50	Requires considerable assistance	
40	Disabled; requires special assistance	Low
30	Severely disabled	
20	Very sick; requires active supportive treatment	
10	Moribund	

- Predicts 3-month mortality after hospitalization (better than MELD + age alone)
- Predicts 30-day mortality after liver transplantation

# Activities of Daily Living (ADL)

Assessed by the patient.



Eating



Bathing



Dressing



Transferring



Toileting



Walking or  
moving around

Acronym for clinical  
practice:

## **DEATTH**

- **D**ressing
- **E**ating
- **A**mbulating
- **T**ransferring
- **T**oileting
- **H**ygine

- Predicts 90-day mortality after hospitalization
- Predicts overall waitlist mortality

# Mortality Impact: Disability Assessment Tools

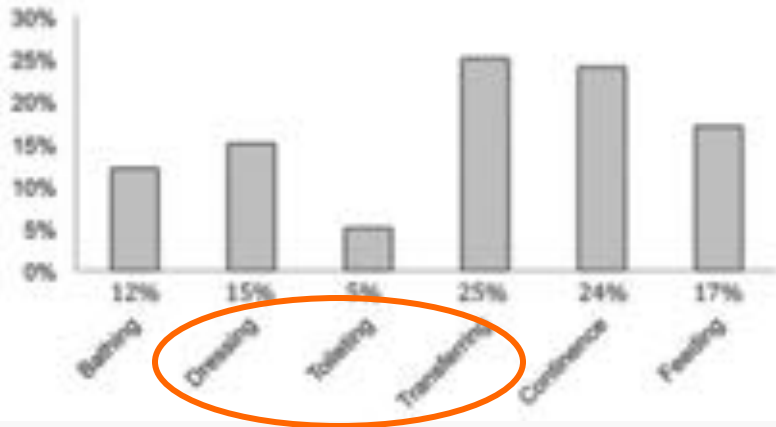
## Activities of Daily Living (ADLs)

- Necessary for basic living within one's space

## Instrumental ADLs

- Necessary to live within a community

First ADL disability



First IADL disability





# The Liver Frailty Index

[liverfrailtyindex.ucsf.edu](http://liverfrailtyindex.ucsf.edu)



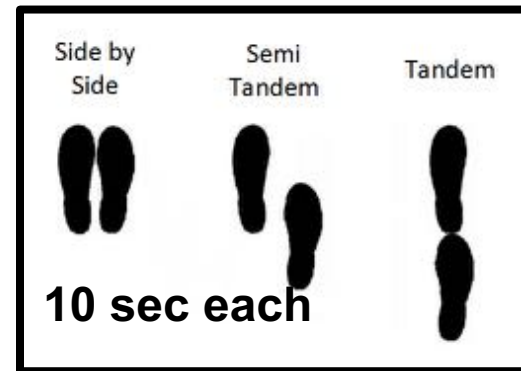
**Grip**

+

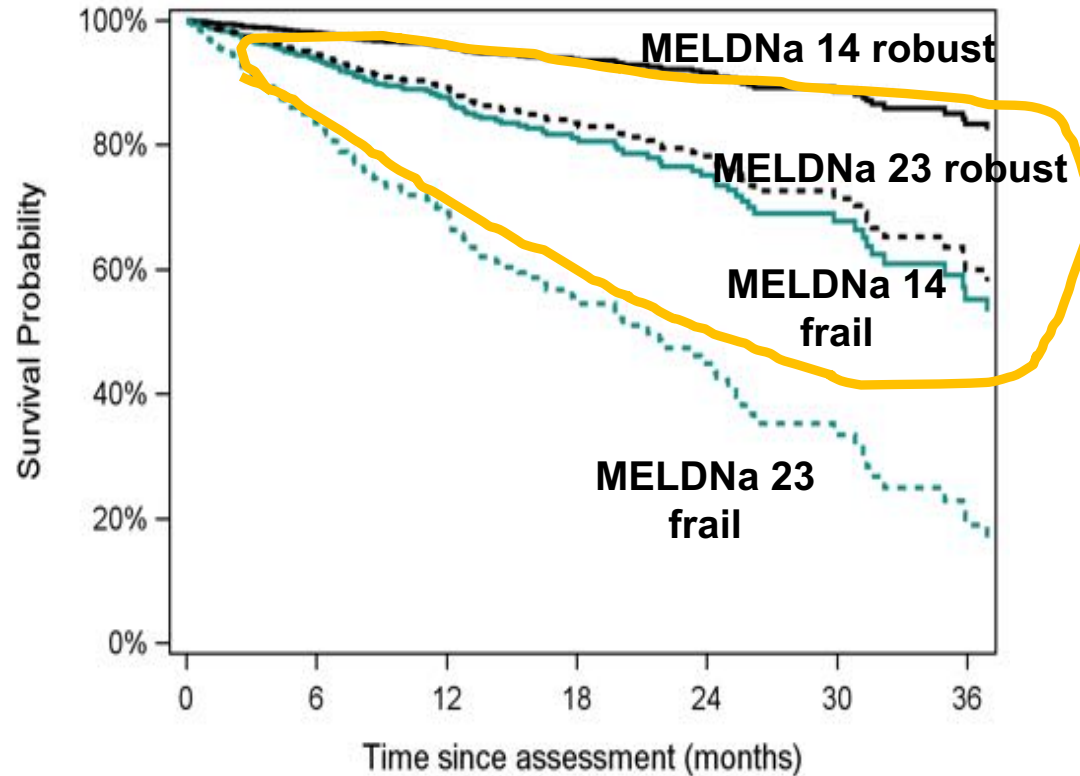
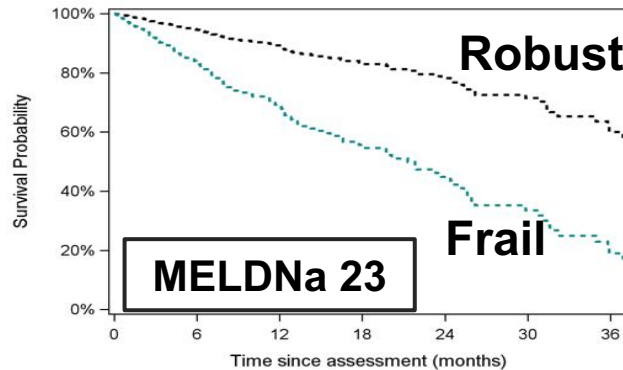
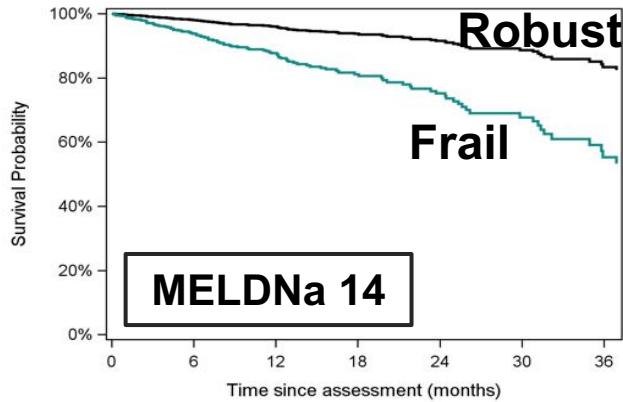
**Chair  
stands**

+

**Balance**



# Frailty adds 9 MELDNa points to mortality risk



\* Robust / Frailty defined as the 20% / 80%ile Liver Frailty Index values.

# Back to the bedside: Mr. D, MELD 35, ICU

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Mr. D, I want you to  
stand up and sit  
down from a chair  
5 times.





# Back to the bedside: Mr. D, MELD 35, ICU

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Mr. D, I want you to  
balance in 3 different  
positions for 10  
seconds each.



# Back to the bedside: Mr. D, MELD 35, ICU

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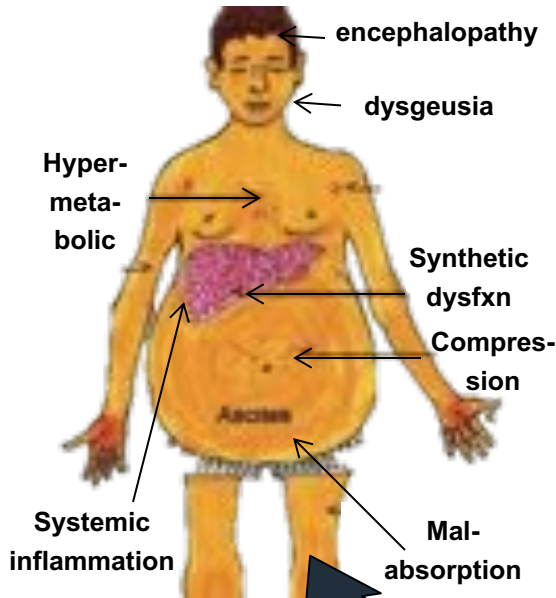


Can you squeeze this  
3 times with your  
dominant hand?



# Why is Mr. D sick? The Cycle of Frailty in Cirrhosis

## Contributing factors



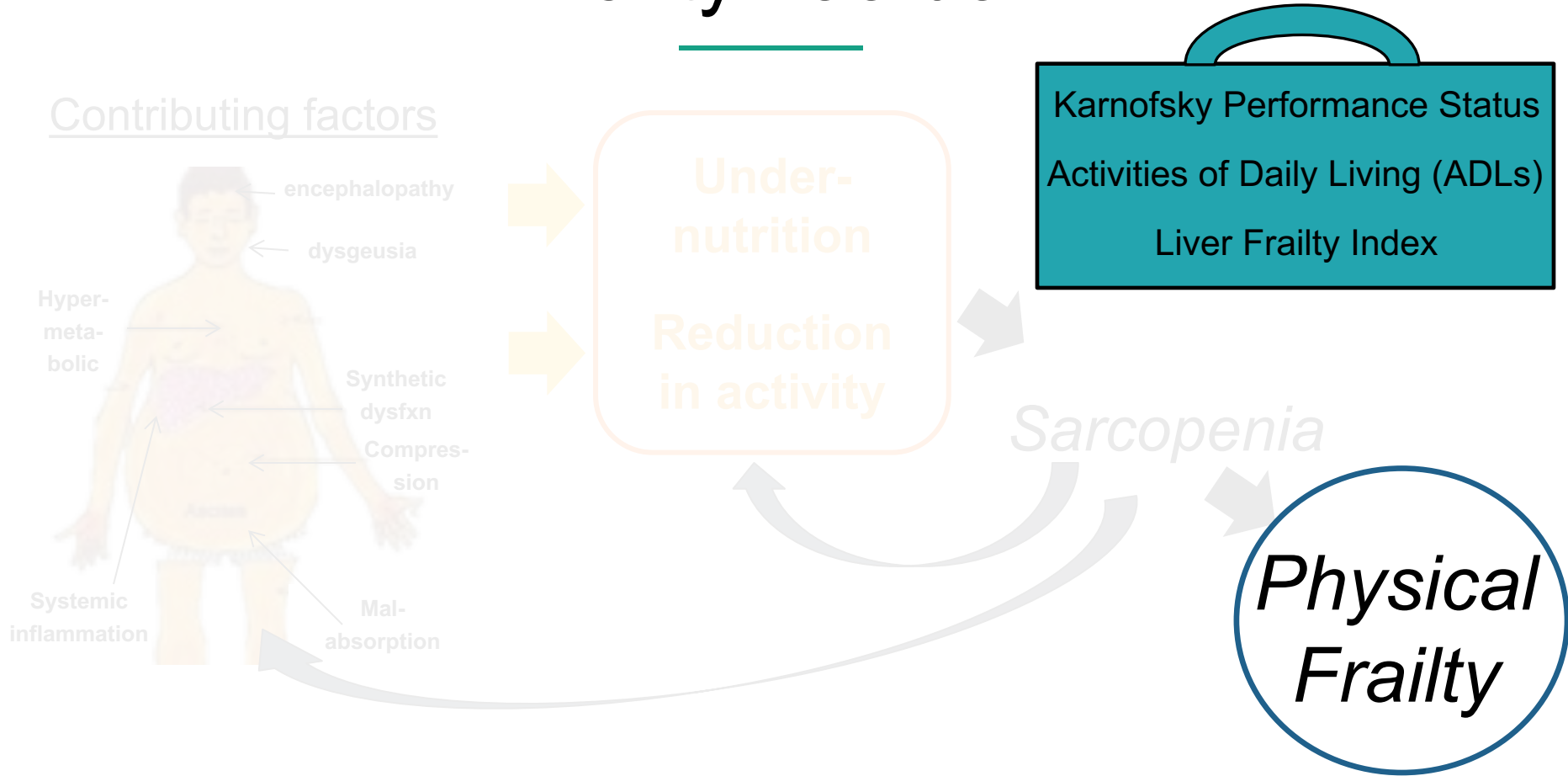
*Sarcopenia*



*Physical Frailty*



# Frailty Toolbox

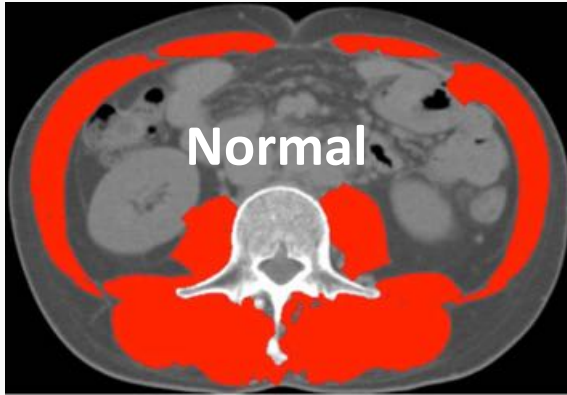


# Measuring Risk in Inpatients: Sarcopenia



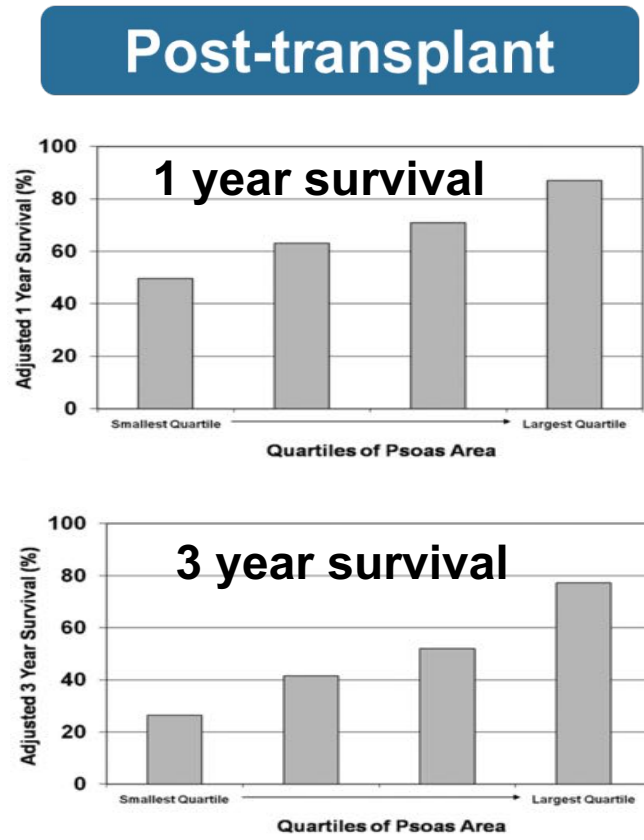
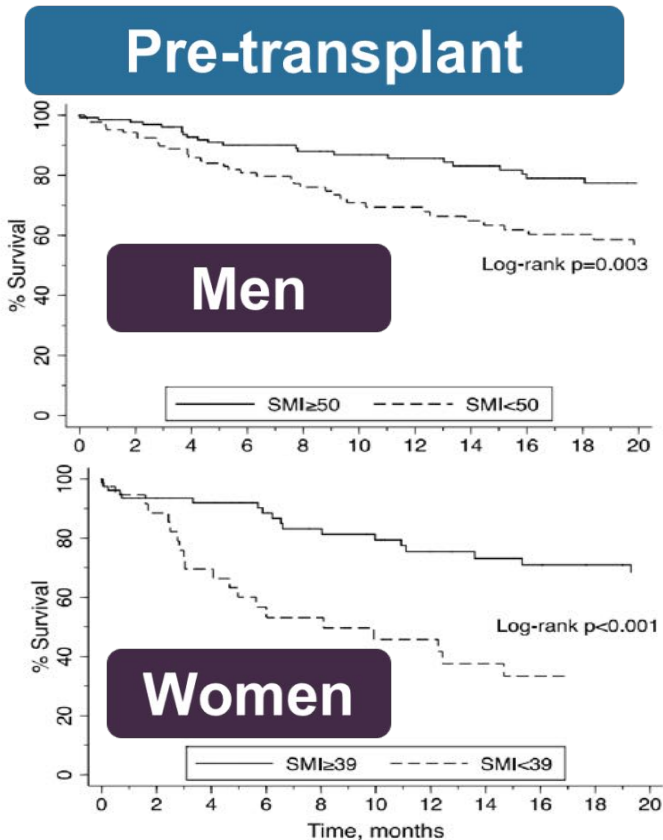
# Quantifying muscle mass

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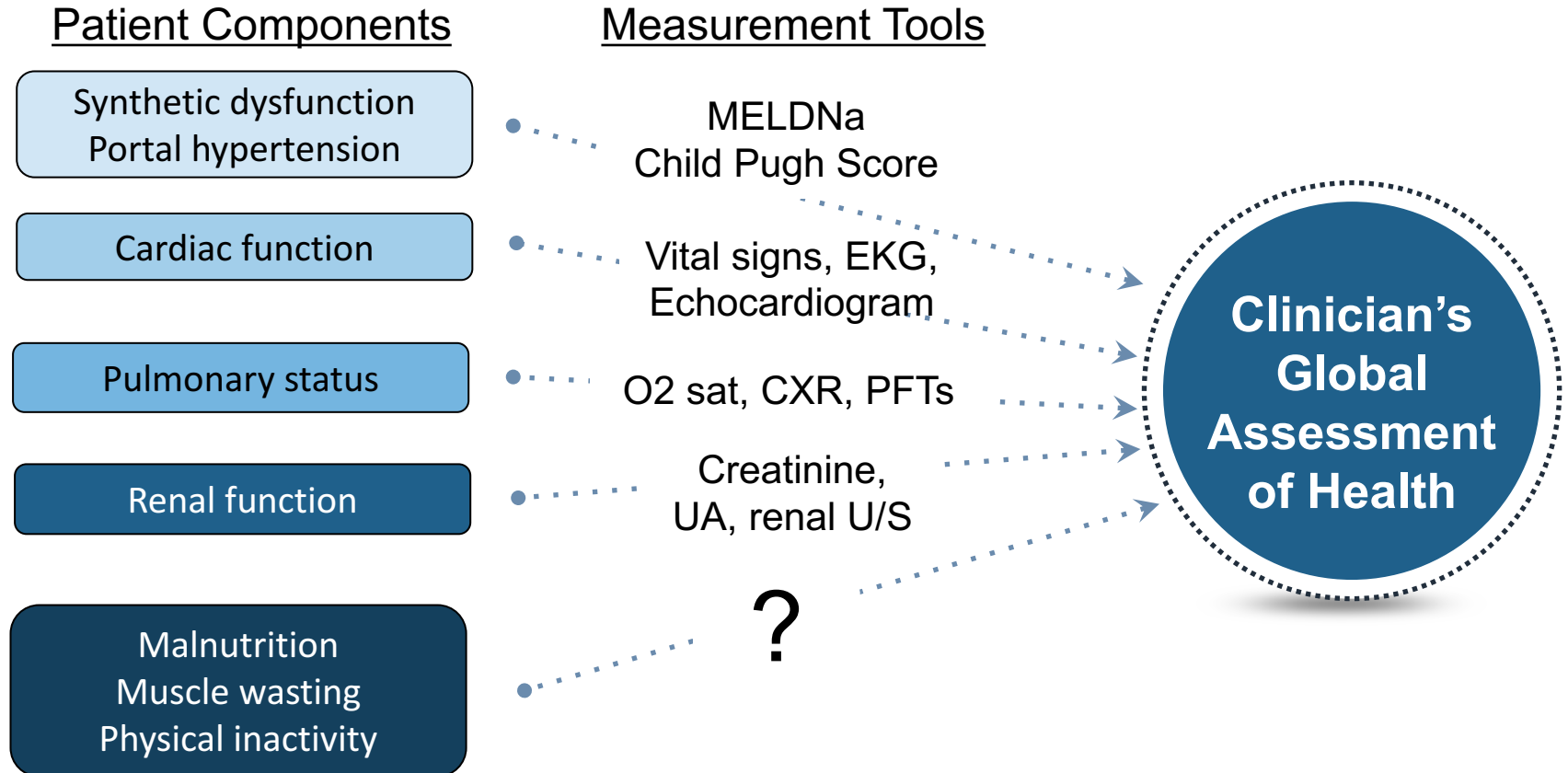


- Quantify muscle area at L3 or L4 vertebral levels on cross-sectional imaging
  - Psoas
  - Psoas + abdominal wall + lumbar
- Can be done by your radiologist
- Requires specialized software (that your radiologist may already have)
  - [www.coreslicer.com](http://www.coreslicer.com)\* (free!)

# Sarcopenia is strongly predictive of outcomes

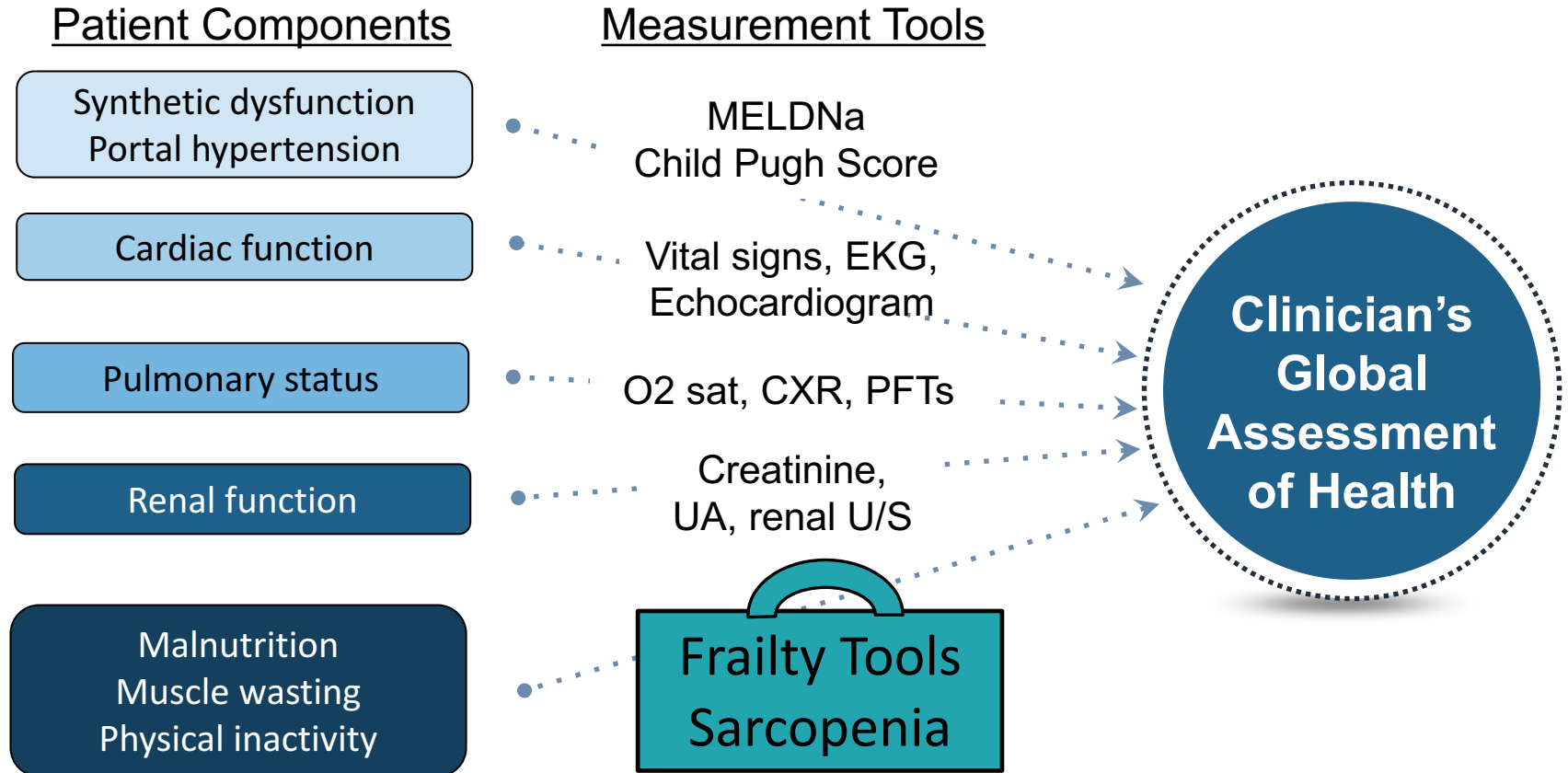


# A Framework for Incorporating Frailty into Practice





# A Framework for Incorporating Frailty into Practice



# Frailty & Sarcopenia: Key Points

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- Frailty = low physiologic reserve → vulnerability
- Impacts clinical outcomes in patients with cirrhosis



- The Frailty Toolbox provides us with a range of tools to systematically and routinely screen for frailty in the clinic
  - Use sarcopenia for the inpatient
- Frailty tools can and should be incorporated into clinical practice to anchor our judgments and decision-making



# There's more!

- There is more to frailty and sarcopenia than just measurement.
- Objective assessments of frailty/sarcopenia can identify those in need of therapeutic interventions.

# ESPEN Guidelines on Enteral Nutrition : Liver Disease

Recommended energy intake: 35-40 kcal/kg body weight/day

Recommended protein intake: 1.2-1.5 g/kg body weight/day

Body weight	Energy intake	Protein intake
60 kg / 132 lbs	2,100-2400 kcal	72-90 g
75 kg / 165 lbs	2,625-3,000 kcal	90-113 g
95 kg / 209 lbs	3,325-3,800 kcal	114-143 g
110 kg / 243 lbs	3,850-4,400 kcal	132-165 g

## Consider BMI-modified:

- BMI 30-40:
  - 25-35 kcal/kg/day
- BMI>40:
  - 20-25 kcal/kg/day

# What type of protein? Branched-chain amino acids

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- Altered amino acid metabolism → low BCAA

BCAA  
37 kcal

n=59

Lactoalbumin  
34 kcal  
(equal kcal,  
equal nitrogen)

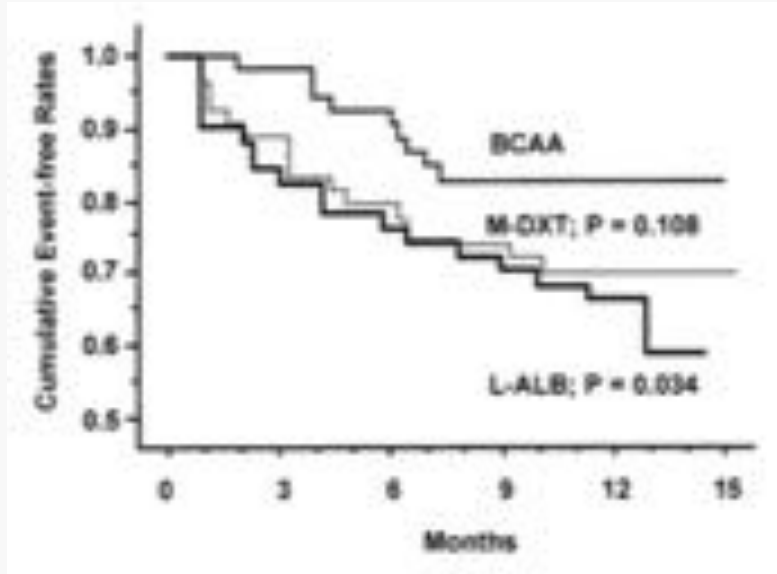
n=56

Maltodextrin  
35 kcal  
(equal kcal,  
no protein)

n=59

# BCAA (modestly) improved event-free survival

Event-free = death + decompensation



## BCAA arm:

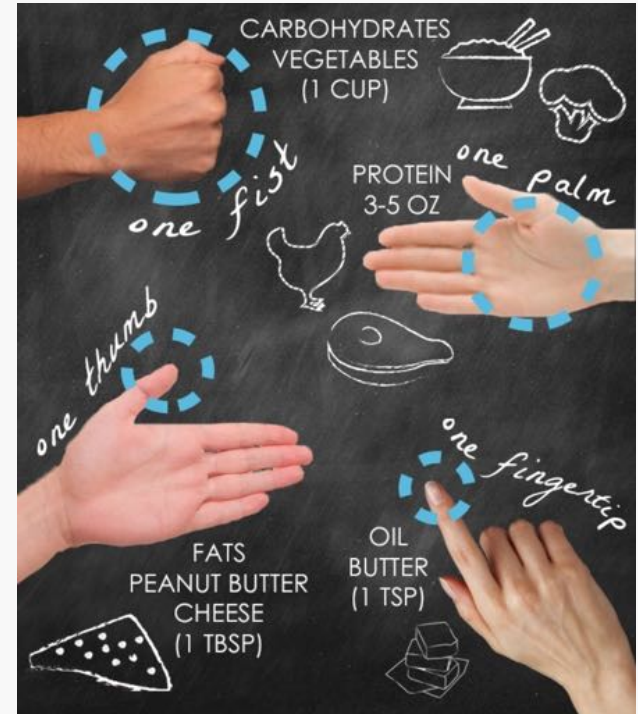
- Decreased hospitalizations
- Decreased # hospital days
- No difference in nutritional parameters / health-related QoL

**Limitation: unpalatable**

# BCAA in real-life practice

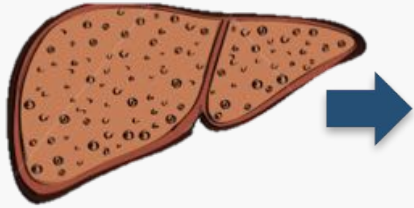
- Studies used 12-14 grams / day
- Recommend high protein foods

Food	Serving	Protein	BCAA
Chicken	6 oz	36 g	6.6 g
Salmon	6 oz	34 g	5.9 g
Egg	1	6.3 g	1.3 g
Peanuts	6 oz	12 g	6.8 g



- Supplement if unable to meet these targets

# When to give protein: Late evening / overnight



↓ gluconeogenesis



↑ breakdown of skeletal muscle to meet amino acid needs



protein-energy malnutrition

Metabolic profile of a *patient with cirrhosis* after an **overnight fast**

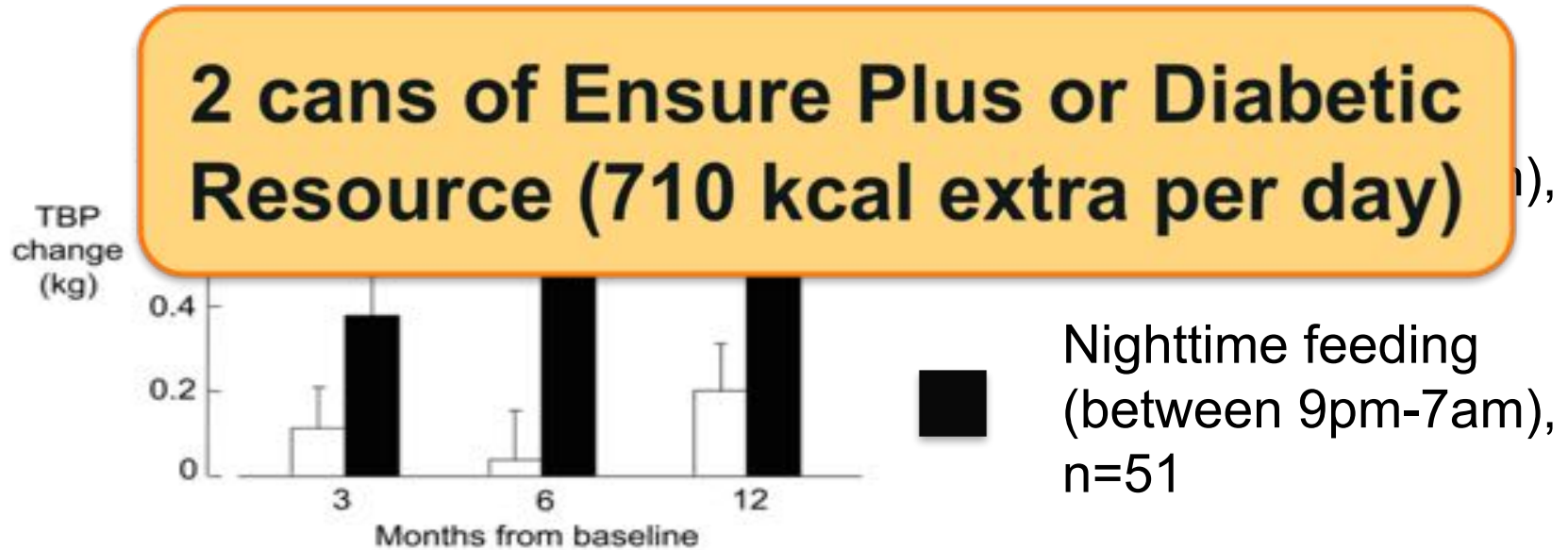
=

Metabolic profile of a *healthy person* after **3 days starvation**

**200 kcal snack: 20-30% protein  
Given before bedtime to “break the fast”**



# Nocturnal feeding improves total body protein



# EXERCISE

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“Activity requiring physical effort, carried out especially to sustain or improve health and fitness.”

**Aerobic**

**Resistance**

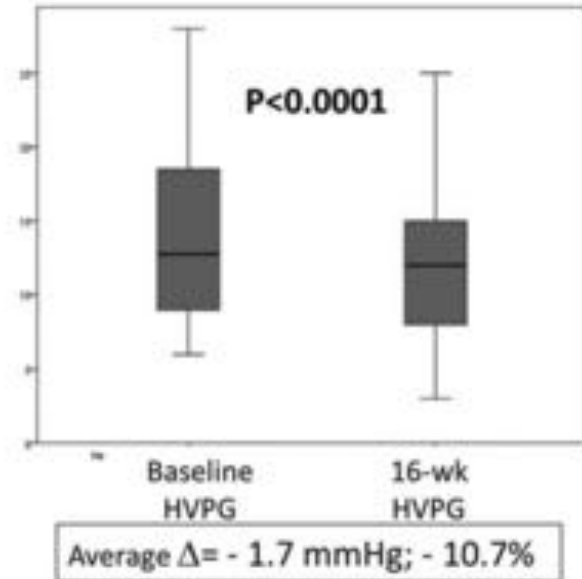
# Exercise studies in cirrhosis

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- Sample sizes small : n= 17 to 50
- Majority Child Pugh A cirrhosis : 64% to 92%
- Duration : 8-16 weeks
- Exercise : supervised cycle-based exercise 3 x/week
- **↑**Peak  $VO_2$ , 6 minute walk, muscle mass, quality of life

# Exercise reduces HVPG

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Among 50 patients with compensated cirrhosis who underwent 16 weeks of supervised exercise, HVPG *decreased* by ~11%

# Therapeutic Interventions: Key Points

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- Recommended energy intake : 35-40 kcal/kg per day
- Recommended protein intake: 1.2-1.5 g/kg per day
  - 12-14 grams BCAA
- Use the “hand” tool to help communicate portion sizes
- Late evening snack / nocturnal feeding is CRITICAL
- Exercise should consist of BOTH aerobic and resistance activities