Frailty in Patients with Cirrhosis: From Recognition to Reversal

NCSCG Liver Symposium 2021

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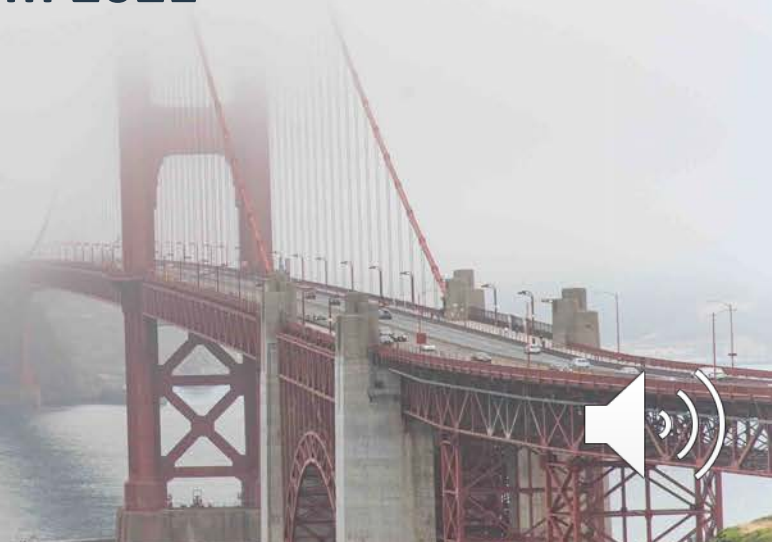
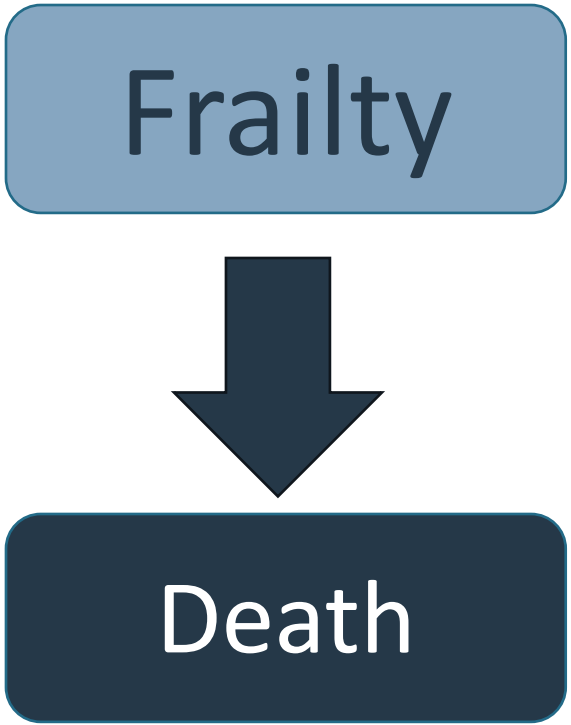


Financial Conflicts of Interest

Consultant: Axcella Health, Inc
(terminated 12/31/2019)

In patients with cirrhosis



Frailty → adverse outcomes

In patients with cirrhosis

Frailty is associated with:

- 2-fold increased risk of waitlist mortality

  Carey, Liver Transpl 2010. Lai, Hepatology 2016. Lai, Gastroenterol 2019.

- Greater risk of hospitalizations and mortality after hospitalization

  Dunn, AJG 2016. Sinclair, WJG 2017. Tandon, AJG 2016. Tapper. Hepatology 2015.

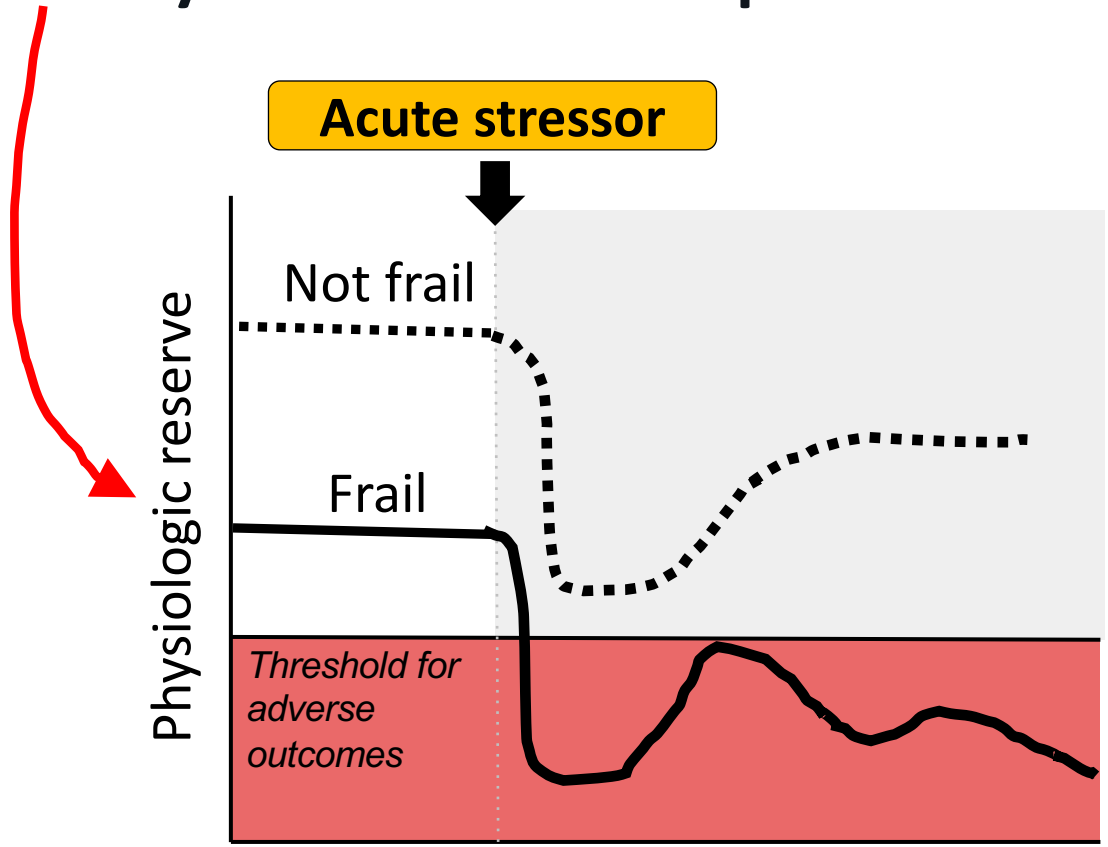
- Poor QOL and subsequent disability

  Tapper, Hepatology 2019. Lai, Hep Comm 2019.

- Higher risk of mortality and poor functional recovery after liver transplantation

  Lai, AJT 2019. Thuluvath, J Hep 2018. Lai, AASLD abstract 2020.

Frailty : A Conceptual Model



Frailty : Formal Definition

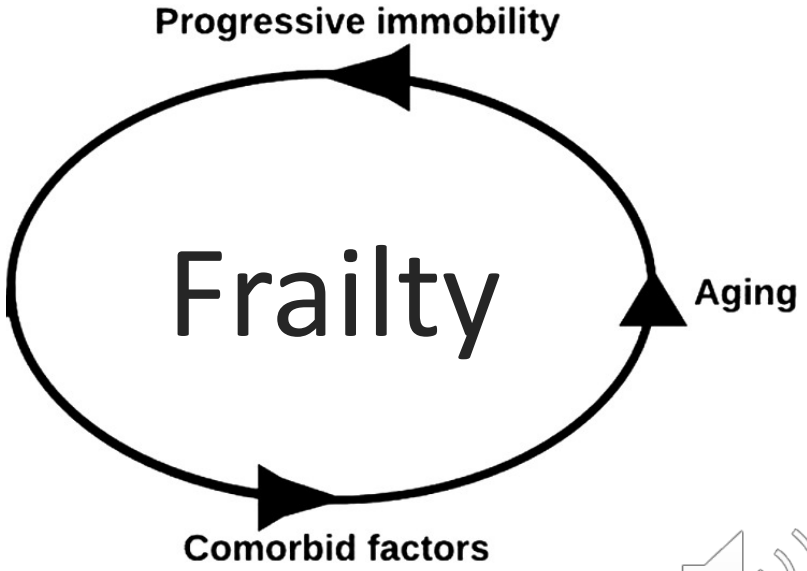
From the field of geriatrics

"A distinct biologic syndrome of decreasing physiologic reserve and increasing vulnerability to health stressors"

Fried L. J Gerontol A Biol Sci Med Sci 2001.

Contributors to Frailty

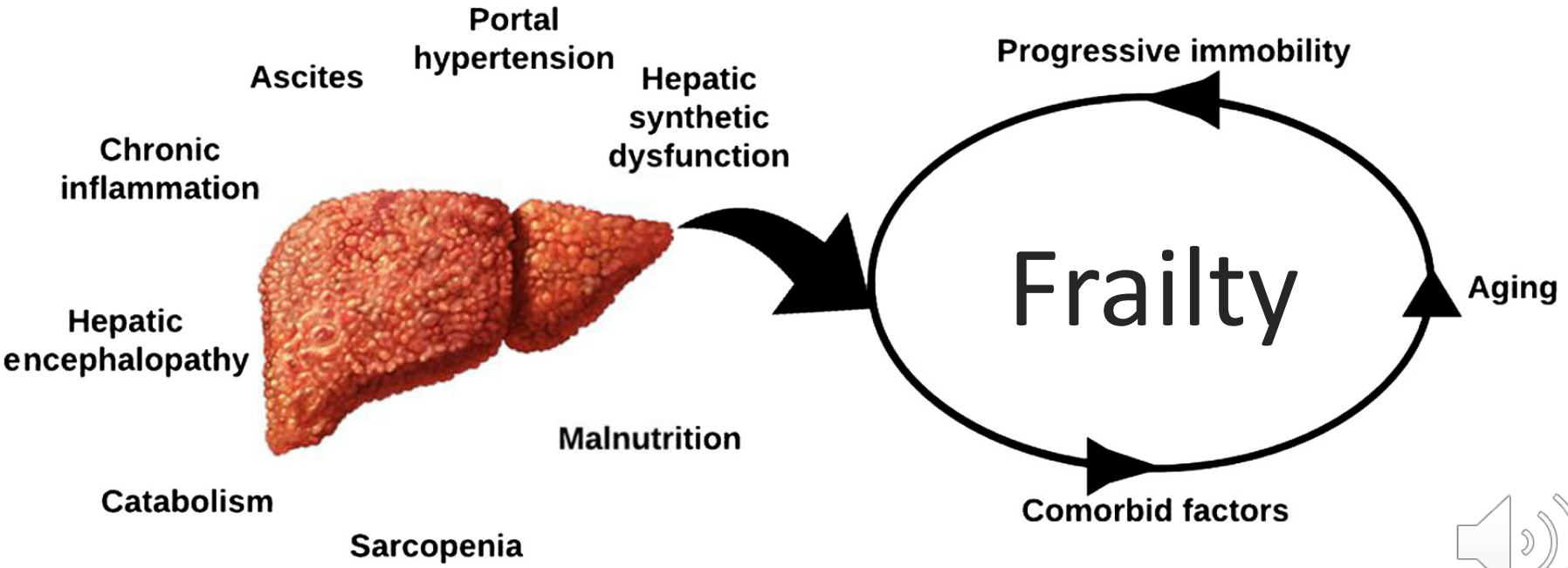
In the general geriatric population



Expert opinion statement on frailty in liver transplantation. AJT 2019.

Contributors to Frailty

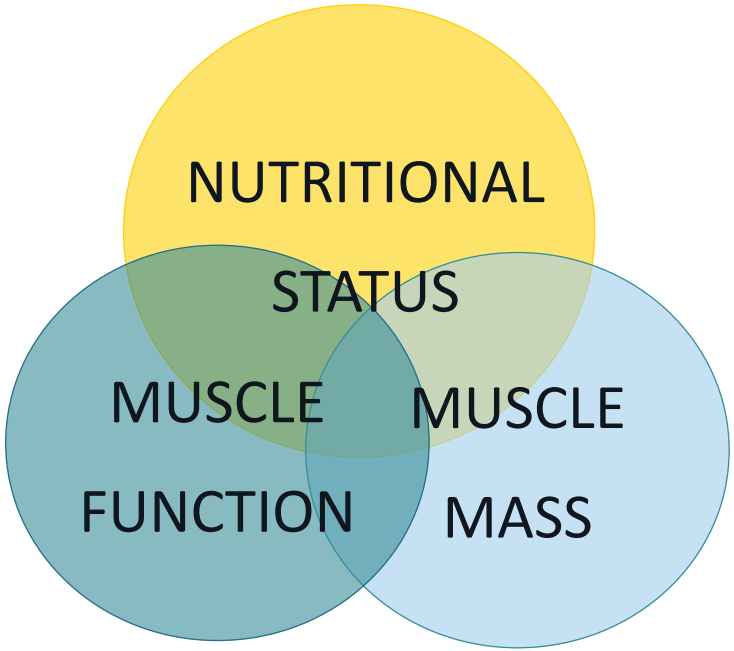
In patients with cirrhosis



Expert opinion statement on frailty in liver transplantation. AJT 2019.

Frailty : Modified Definition

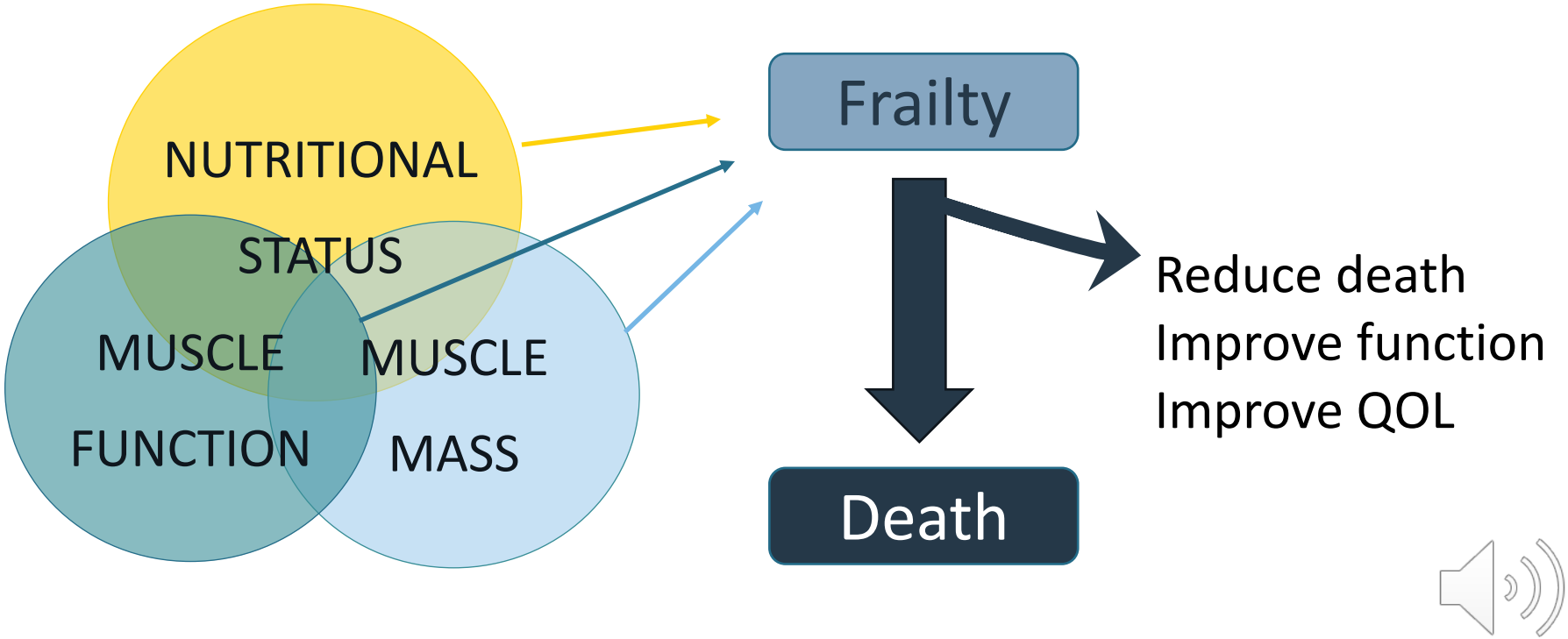
For consideration in patients with cirrhosis



The phenotypic presentation of the intersection between nutritional status, muscle function, and muscle mass

Roadmap for Reversal : “Prehabilitation”

In patients with cirrhosis



Objective

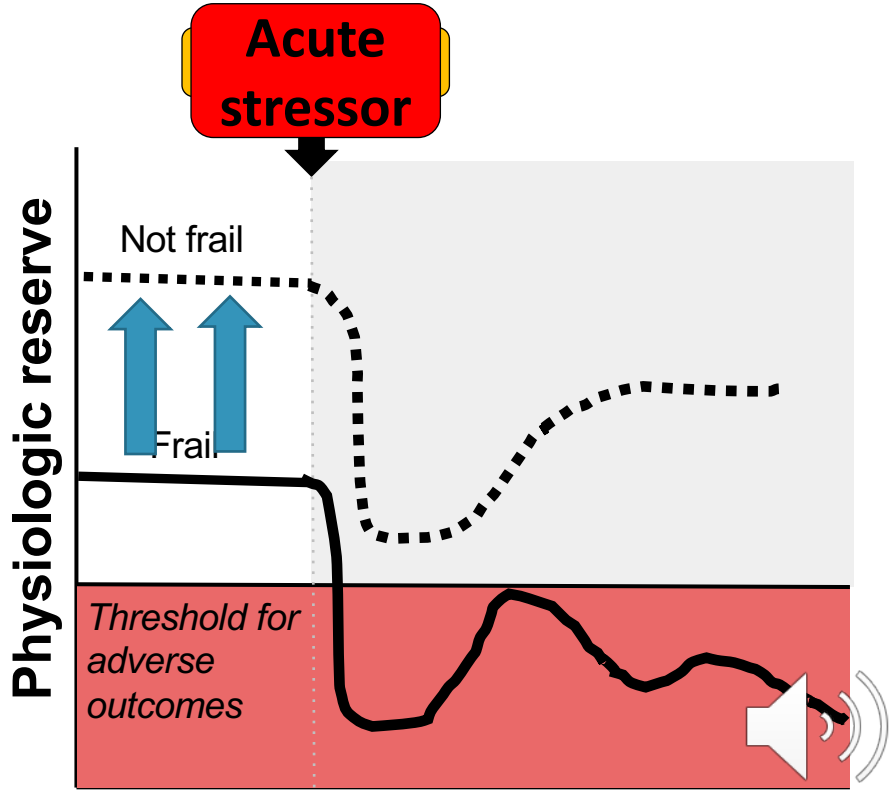
An approach to prehabilitation

To acquire pragmatic skills to prehabilitate your patient with cirrhosis that you can implement in your practice *today*.

Prehabilitation

Reducing vulnerability by increasing reserve

"The process of enhancing functional capacity prior to surgery to improve tolerance for the upcoming physiologic stressor"



McAdams DeMarco *et al*, Clin Transpl 2019.

3-Step Approach to Prehabilitation

For real-life clinical practice

Measure

Muscle Health

Motivate

3-Step Approach to Prehabilitation

For real-life clinical practice

Measure

The universal frailty assessment tool

In real-life clinical practice

Limitations

- Subjective
- Variably applied
- Does not offer granularity
- Limited ability to follow longitudinally

Anchor your frailty assessment

THE FRAILTY TOOL KIT

Tailor the measure to the setting

- Karnofsky Performance Status
- Activities of Daily Living (ADLs) / Instrumental ADLs
- 6-minute walk test
- Liver Frailty Index

American Society of Transplantation Expert Opinion Statement on Frailty in Liver Transplantation. AJT 2019.

The Frailty Tool Kit

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
- Mortality after liver transplantation
- Waitlist mortality in children

Karnofsky, Cancer 1948. Tandon, Hepatology 2016. Perito, AJT 2018. Thuluvath, J Hep 2018.

The Frailty Tool Kit

ACTIVITIES OF DAILY LIVING

Assessed by the patient/caregiver

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

Graphic from: www.elderneedslaw.com

Katz, JAMA 1963. Samoylova, Liver Transpl 2016. Tapper, Hepatology 2016.

The Frailty Tool Kit

SIX MINUTE WALK TEST

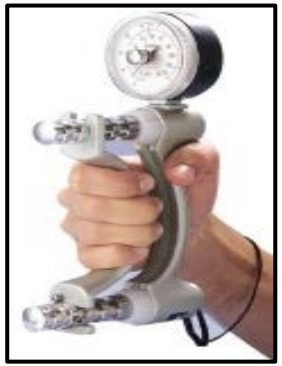
Distance walked in 6 minutes

- Predicts waitlist mortality
- Correlated with QOL post-transplant

Carey E, *et al*. Liver Transpl 2010. Van Wagner L, *et al*. Phys Ther 2016.

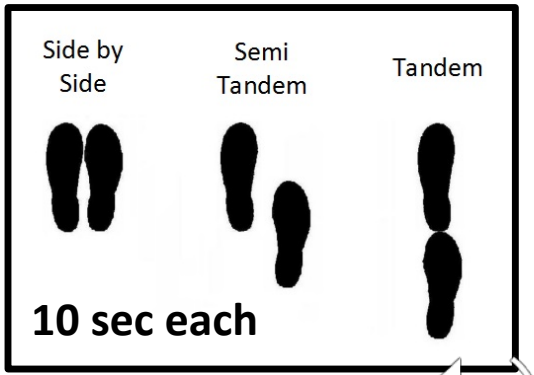
The Liver Frailty Index
liverfrailtyindex.ucsf.edu

Grip + **Chair stands** + **Balance**



Nutrition

Muscle strength



Neuromotor coordination

Lai *et al*. Hepatology 2017.

The Liver Frailty Index

Associated with adverse outcomes

In patients with cirrhosis

Frailty = 9 MELDNa points of mortality risk

- Enhances clinician prediction of death
- Is associated with current and subsequent patient-reported disability
- Predicts death after liver transplantation
- Is the single predictor of functional robustness after liver transplantation

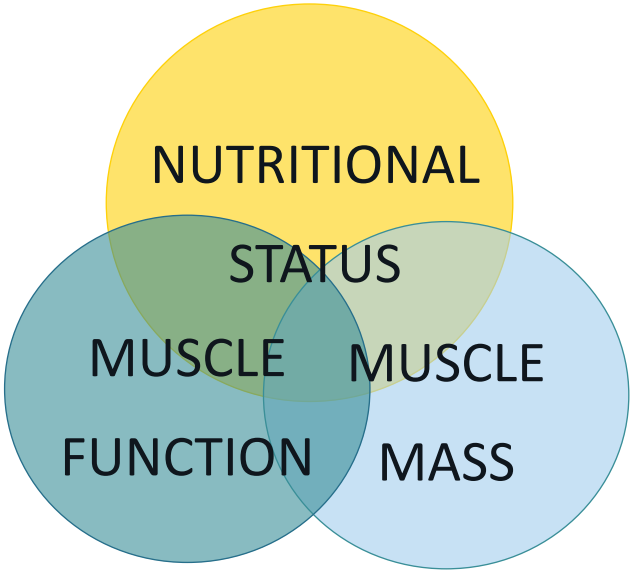
Lai, AJG 2016. Lai, Hep Comm 2019. Lai AASLD abstract 2020. Lai AJT 2018.

3-Step Approach to Prehabilitation

For real-life clinical practice

Measure

- Frailty Toolkit



NUTRITION

General recommendations for patients with cirrhosis

Recommended energy intake: ≥35 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

EASL Clinical Practice Guidelines: Nutrition in Chronic Liver Disease 2018.

Amodio, Hepatology 2013.

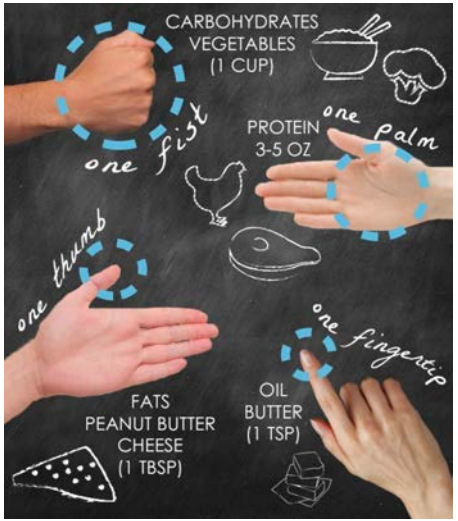
NUTRITION

General recommendations for patients with cirrhosis

Recommended energy intake: ≥35 kcal/kg body weight/day

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

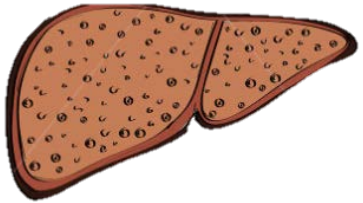
Food	Serving	Protein
Chicken	6 oz	36 g
Salmon	6 oz	34 g
Egg	1	6 g
Peanuts	6 oz	12 g



www.fitfluential.com

Optimal timing of energy intake:

LATE EVENING SNACK / NOCTURNAL FEEDS



↓gluconeo-genesis → ↑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**

Give before bedtime to "break the fast"

Owen OE, J Clin Invest 1981.

Late Evening Snack

OPTIMAL COMPOSITION

≥210 kcal Late Evening Snack

Glucose solution

Rice Ball

Regular food

Supplemental shake

BCAA-enriched supplement

<u>Consider these foods</u>:

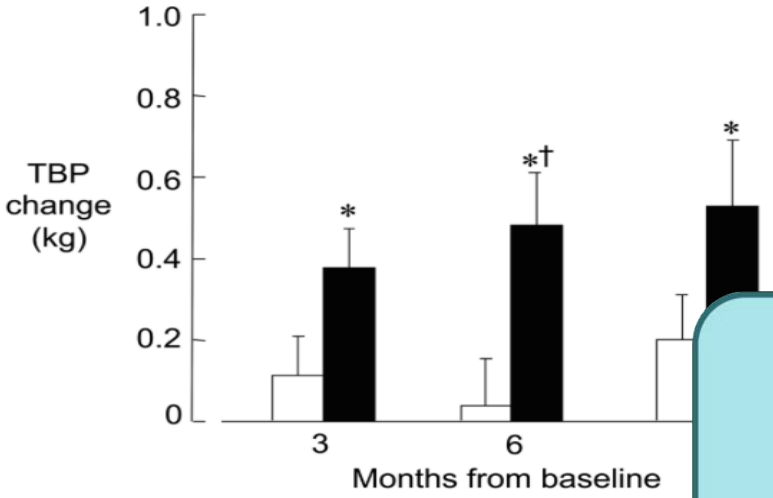
Greek yogurt + a handful of nuts

2 slices of toast with low-salt peanut butter

Owen OE, J Clin Invest 1981. Tsien C, J Gastro Hep 2012.

RCT Evidence

NOCTURNAL FEEDS IMPROVE BODY PROTEIN



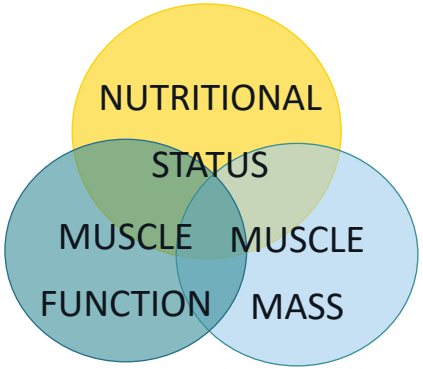
Daytime feeding (between 7am-7pm), n=52

Nighttime feeding (between 9pm-7am), n=51

Used in the study:

2 cans of an over-the-counter supplemental shake (710 kcal extra per day)

Plank L, Hepatology 2008.



EXERCISE

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

Dictionary.com

BE SPECIFIC!

"FITT" RECOMMENDATIONS FOR EXERCISE

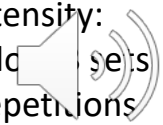
FREQUENCY | INTENSITY | TIME | TYPE

AEROBIC ACTIVITY
3-5 days/week
150 minutes total per week
5-6/10 intensity

RESISTANCE TRAINING
≥2 days/wk
upper and lower body days

The "talk test" to guide intensity:
be short of breath but still able to talk

The "rep test" to guide intensity:
Be able to do [illegible] sets of 10-15 repetitions

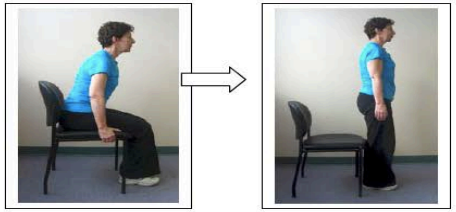


Adapted from American College of Sports Medicine. Tandon P, J Hep 2018.

London Health Sciences Centre
Multi-Organ Transplant Program

Exercise Program #2

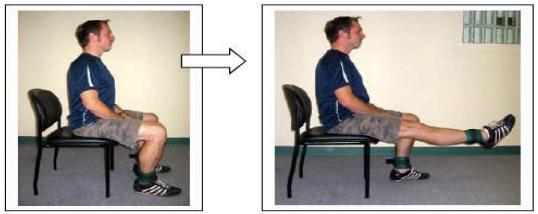
1> Sit to Stand



Go from sit to stand.
Use hands if necessary.
Slowly return to sitting position.

Repetitions:

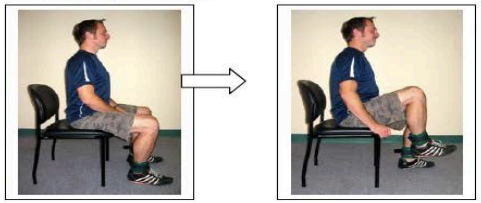
2> Sitting Knee Extension



Wrap weight around ankle.
Sit with feet flat on floor.
Lift foot off floor by straightening knee in front. Slowly return foot to floor.

Weight:
Repetitions:

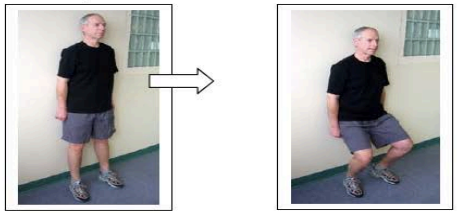
3> Sitting Hip Flexion



Wrap weight around ankle.
Lift knee toward chest.
Slowly lower leg back to floor.

Weight:
Repetitions:

4> Wall Squat



Stand with feet shoulder width apart.
Lean slightly against wall.
Squat down a small amount.
Return to standing position.

Weight:
Repetitions:

Do these with the patient in clinic!

Slide courtesy of Nancy Howes, Physical Therapist, London Canada

EXERCISE RESOURCES

Embed these into patient handouts

www.wellnesstoolbox.ca

Cirrhosis is a chronic condition caused by scarring of the liver.
It is caused by many things like fatty liver disease, viral infections , and alcohol use.

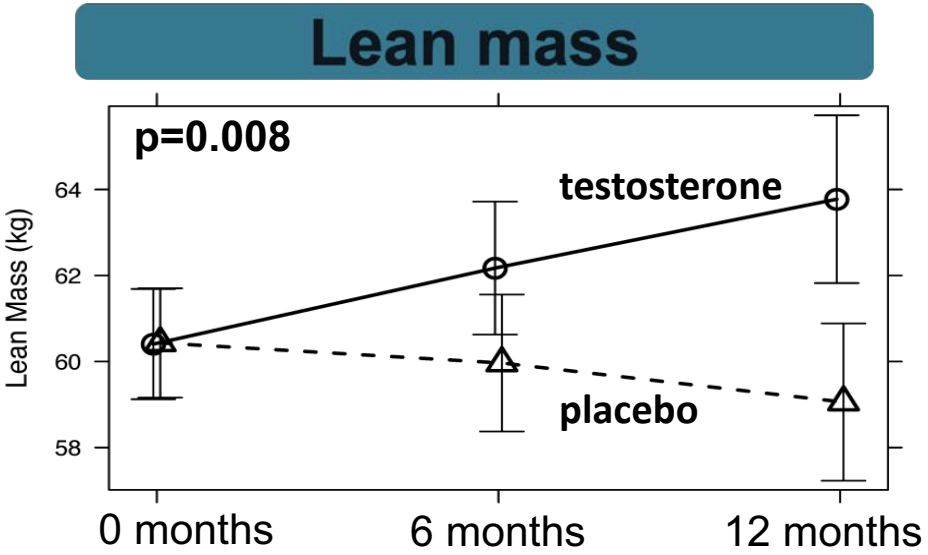
There are many ways to help you stay healthy when living with cirrhosis, such as nutrition & exercising.

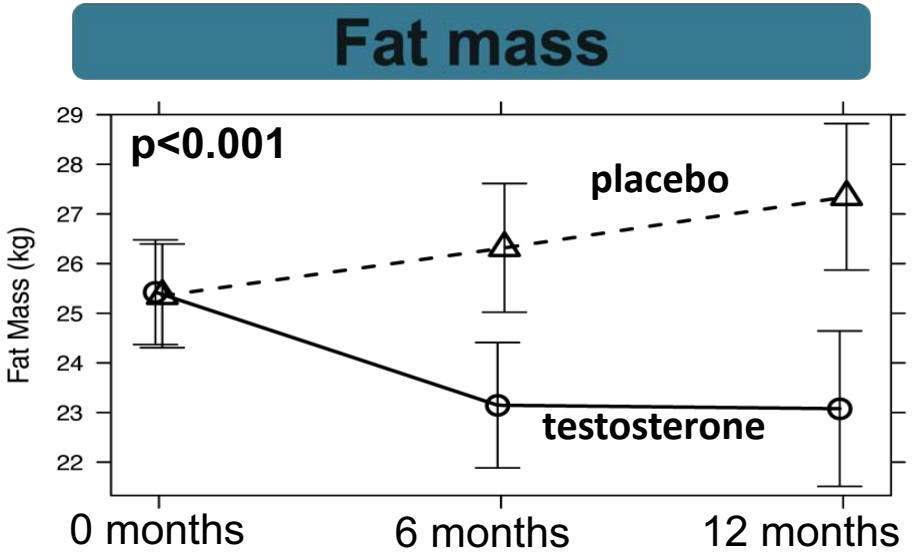
Work-out videos from the National Institute on Aging Go4Life campaign:
Go4Life.nia.nih.gov
--> Go to “See Workout Videos”

Otago Exercise Program
- Evidence-based fall prevention program for frail older adults
- 12 strengthening exercises

INTRAMUSCULAR TESTOSTERONE FOR MEN

Doubled-blinded/placebo-controlled RCT in men with cirrhosis and low testosterone





O = testosterone n=50

Δ = placebo n=50

Sinclair M, J Hep 2016.

3-Step Approach to Prehabilitation

For real-life clinical practice

Measure

- Frailty Toolkit

Muscle Health

- Prehabilitation Toolkit

Motivate

"NUDGE" BEHAVIORAL THEORY

Recommendations from the UK meeting on Exercise in Solid Organ Transplantation

... Encourages interventions that focus on changing the environment, including both social and physical aspects, in such a way to increase the probability of people performing a desired behavior without requiring those people to think very reflectively about it.

Neuberger J, *et al*. Transplantation 2019. Framework developed by the UK Behavioral Insights Team.

TOOLKIT: MINDSPACE

9 NON-COERCIVE MECHANISMS TO INFLUENCE BEHAVIOR

M

MESSENGER

We are influenced by who communicates information.

I

INCENTIVES

We are easily motivated to avoid losses, favor immediate payoffs, overweight small probabilities.

N

NORMS

We are strongly influenced by what others do.

D

DEFAULTS

We “go with the flow” with default options (options in which we don’t have to make an active choice).

S

SALIENCE

We are influenced by what draws our attention.

P

PRIMING

Our acts are influenced by subconscious cues.

A

AFFECT

Our emotional associations can powerfully shape our actions.

C

COMMITMENTS

We seek to be consistent with our public promises. Commitments become more effective as the costs of failure increase.

E

EGO

We active in ways that make us feel better about ourselves.

Neuberger J, *et al*. Transplantation 2019. Framework developed by the UK Behavioral Insights Team.

TOOLKIT: MINDSPACE

9 NON-COERCIVE MECHANISMS TO INFLUENCE BEHAVIOR

M

MESSENGER

We are influenced by who communicates information.

Primary gastroenterologist and/or hepatologist (working alongside dietician, physical therapist)

I

INCENTIVES

We are easily motivated to avoid losses, favor immediate payoffs, overweight small probabilities.

"Don't eat too much salt"
"Too much protein → HE"
"Be careful not to fall"

Add spice for palatability
Set min/max protein targets
Use a chair for balance

N

NORMS

We are strongly influenced by what others do.

Standard treatment for all patients with cirrhosis (akin to antibiotics for SBP prophylaxis or Q6month liver imaging for HCC screening)

Neuberger J, *et al*. Transplantation 2019. Framework developed by the UK Behavioral Insights Team.

3-Step Approach to Prehabilitation

For real-life clinical practice

Measure

- Frailty Toolkit

Muscle Health

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Motivate

- MINDSET Toolkit

Thank you!

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