

Sarcopenia in Cirrhosis

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Sarcopenia is associated with poor prognosis

Sarcopenia	Kim PlosOne 2017	Sarcopenia indicates poor prognosis independent of MELD and Child Pugh
MELD-sarcopenia score	Montano-Loza CGH 2012	MELD-sarcopenia score (MELD and psoas muscle area) is superior to MELD score alone
MELD <15	Tandon Liver Transpl 2012	sarcopenia improved prognostic accuracy in patients with MELD <15
CTP A/B	Merli Metab Brain Dis 2013	Muscle loss is a predictor of mortality in class A/B but not in CTP C patients

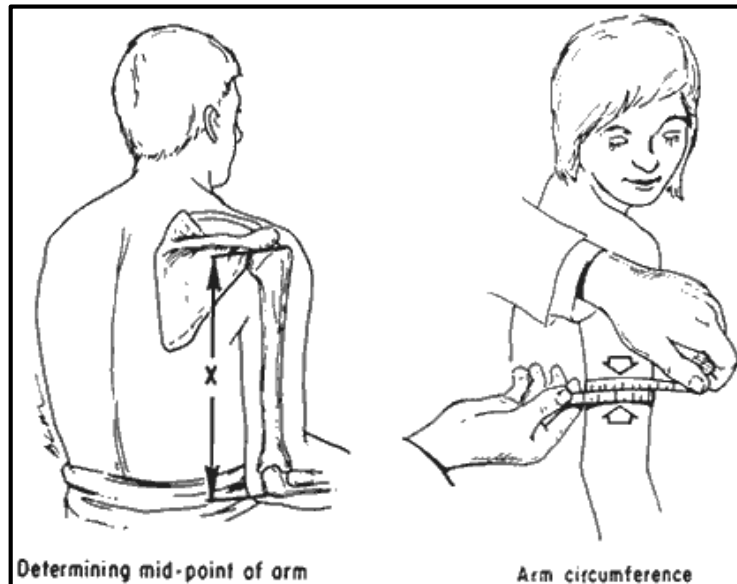
Assessment of Sarcopenia



Prevalence of Sarcopenia and association with HE

First author	Study population	Assessment of Sarcopenia	Prevalence of Sarcopenia	Prevalence of Hepatic Encephalopathy
Kalaitzakis 2007	128 cirrhosis	Anthropometry	40%	HE in 46% with malnutrition vs. 27% without malnutrition

Anthropometry



Midarm Circumference



*TSF, triceps skinfold thickness

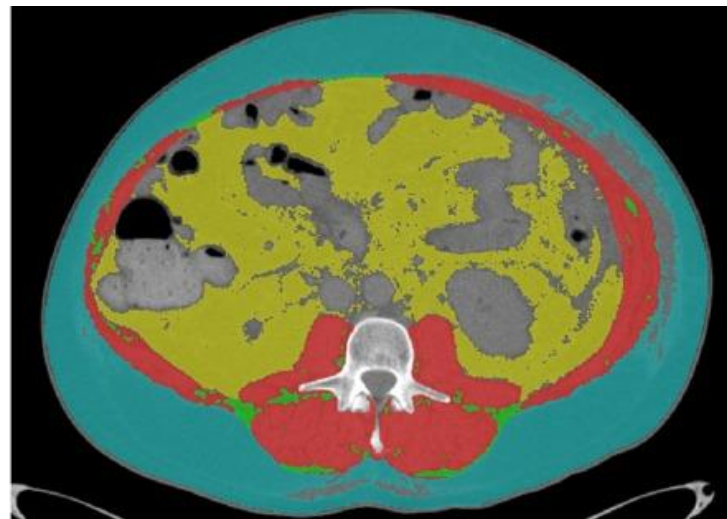
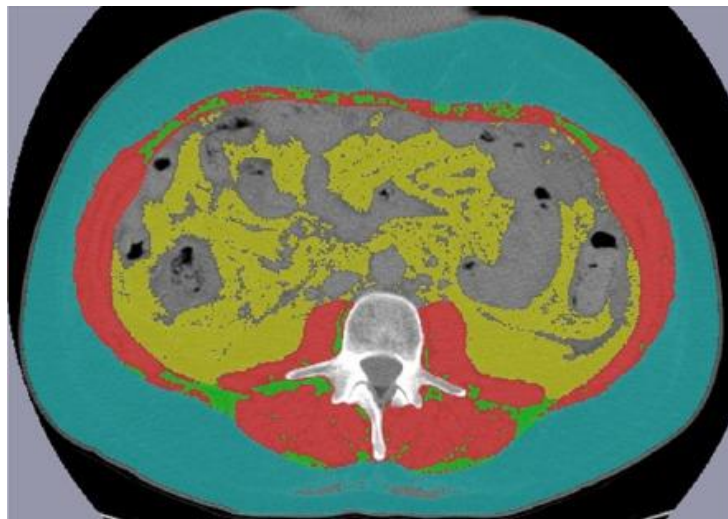
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Huisman 2011	84 cirrhosis	Jamar hand grip strength	67%	HE in 29% with malnutrition vs. 0% without malnutrition



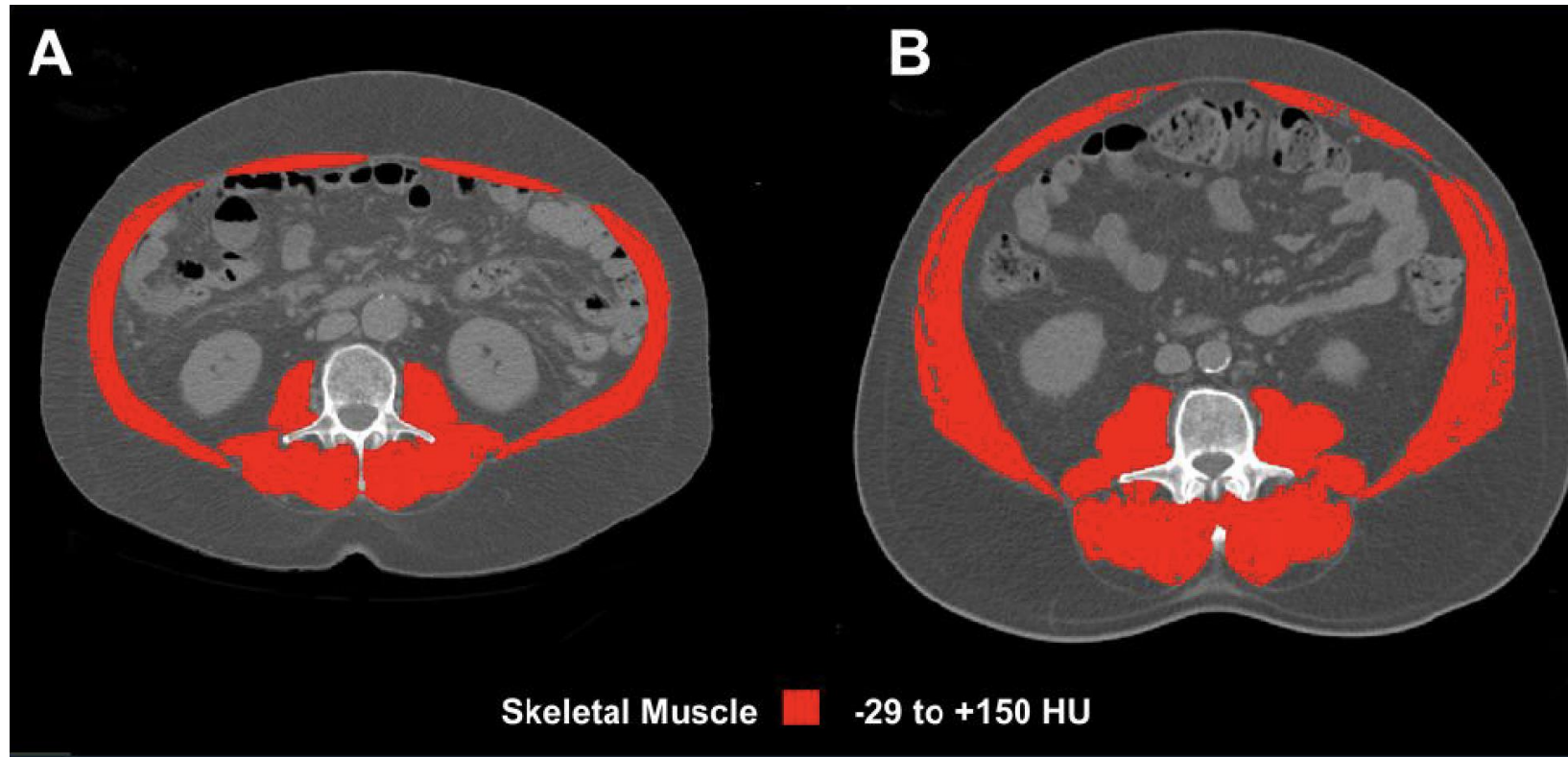
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Meza-Junco 2013	116 HCC & LT evaluation	Skeletal muscle mass at the third lumbar spine	35%	HE in 23% with sarcopenia vs. 12% without sarcopenia



Quantification of Muscle Mass – Sarcopenic Obesity

3rd lumbar vertebral level skeletal muscle index SMI (muscle area corrected for height)
Reference: Men <50 cm²/m² / Women <39 cm²/m²



Male, BMI 32.3 kg/m², SMI 49.5 cm²/m²

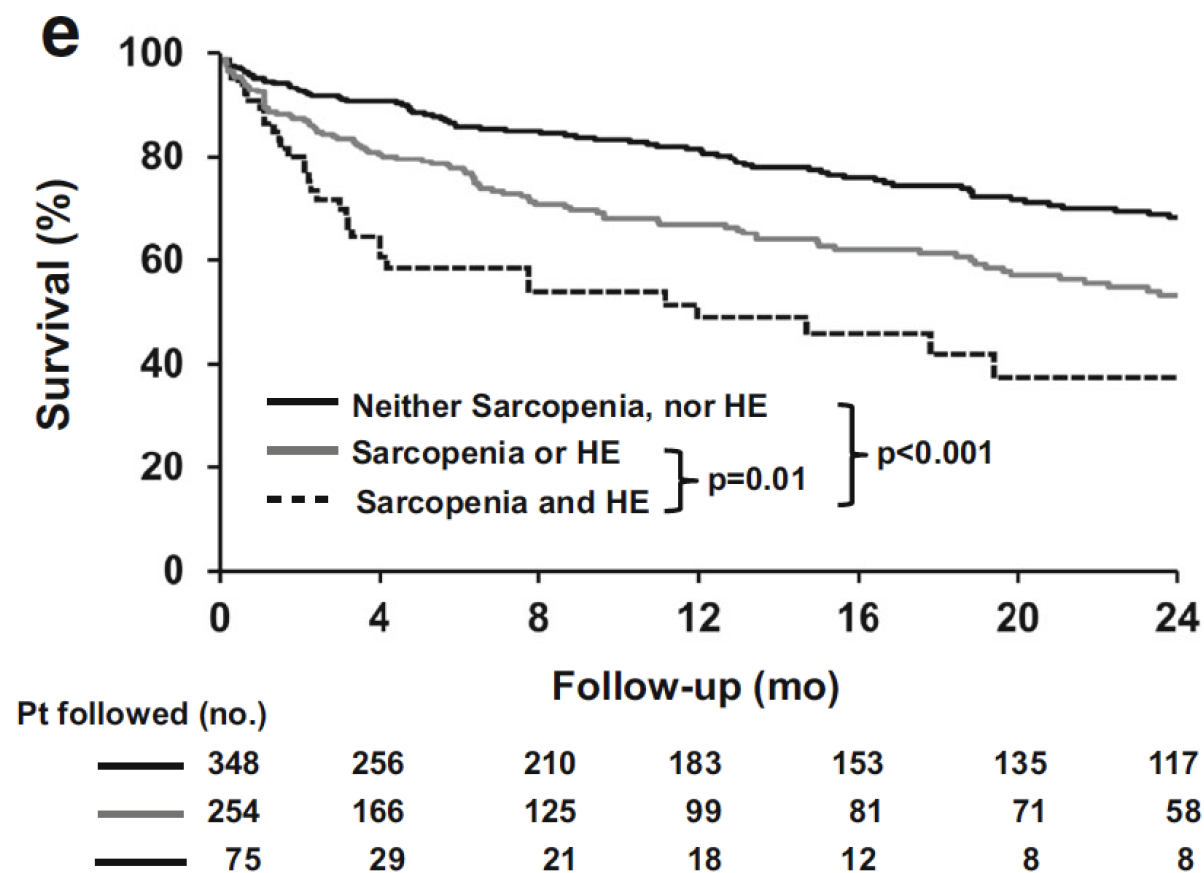
Male, BMI 31.7 kg/m², SMI 66.9 cm²/m²

Prevalence of Sarcopenia and association with HE

First author	Study population	Assessment of Sarcopenia	Prevalence of Sarcopenia	Prevalence of Hepatic Encephalopathy
Merli 2013	300 cirrhosis	Anthropometry	48%	Overt HE in 30% with sarcopenia vs. 15% without sarcopenia Minimal HE in 49% with sarcopenia vs. 30% without sarcopenia
Verna 2014	82 LT wait list	Fried Frailty Instrument	38%	HE in 65% of frail patients vs. 46% who were not frail
Lai 2014	294 LT wait list	Fried Frailty Instrument	17%	HE in 26% of frail patients vs. 17% who were not frail

Shrinking
Physical Inactivity
Energy level
Weakness
Slow walking speed

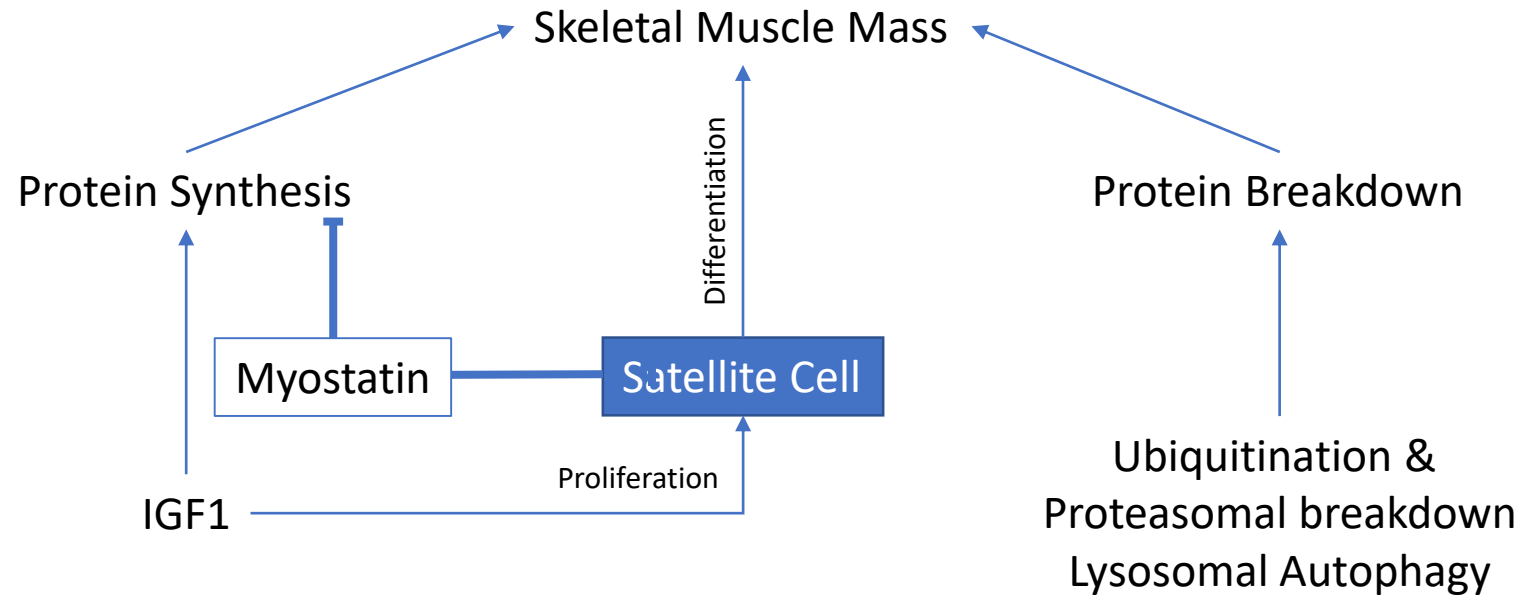
Association between Sarcopenia and Encephalopathy



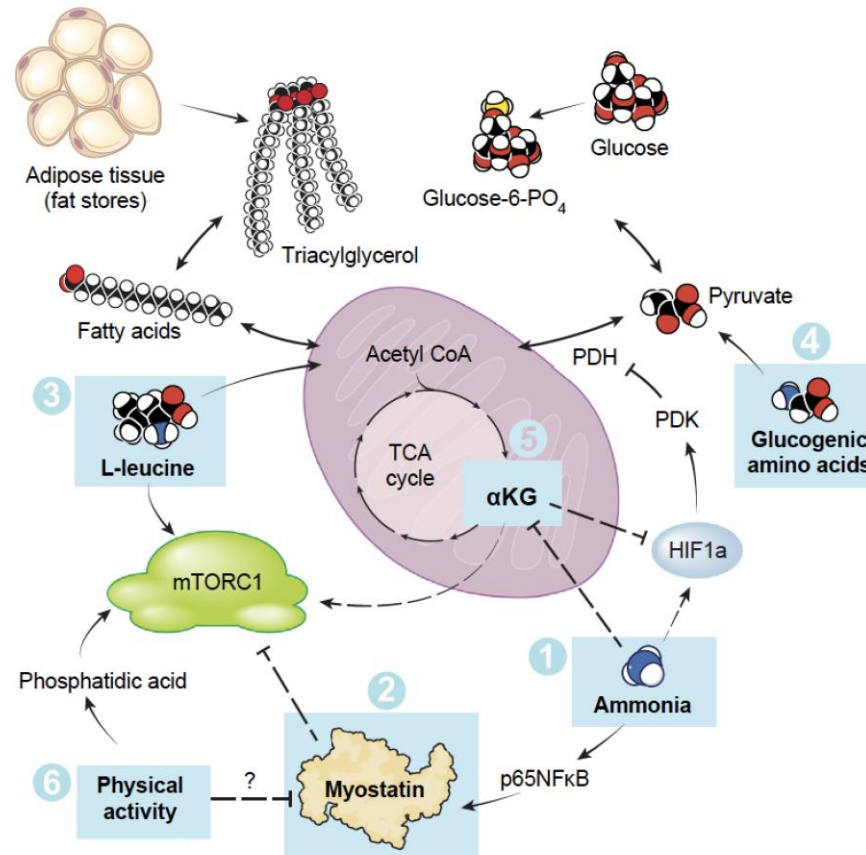
Bhanji RA et al Myosteatorsis and sarcopenia are associated with hepatic encephalopathy in patients with cirrhosis. Hepatology International <https://doi.org/10.1007/s12072-018-9875-9>

Pathophysiology & Interventions

Proteostasis

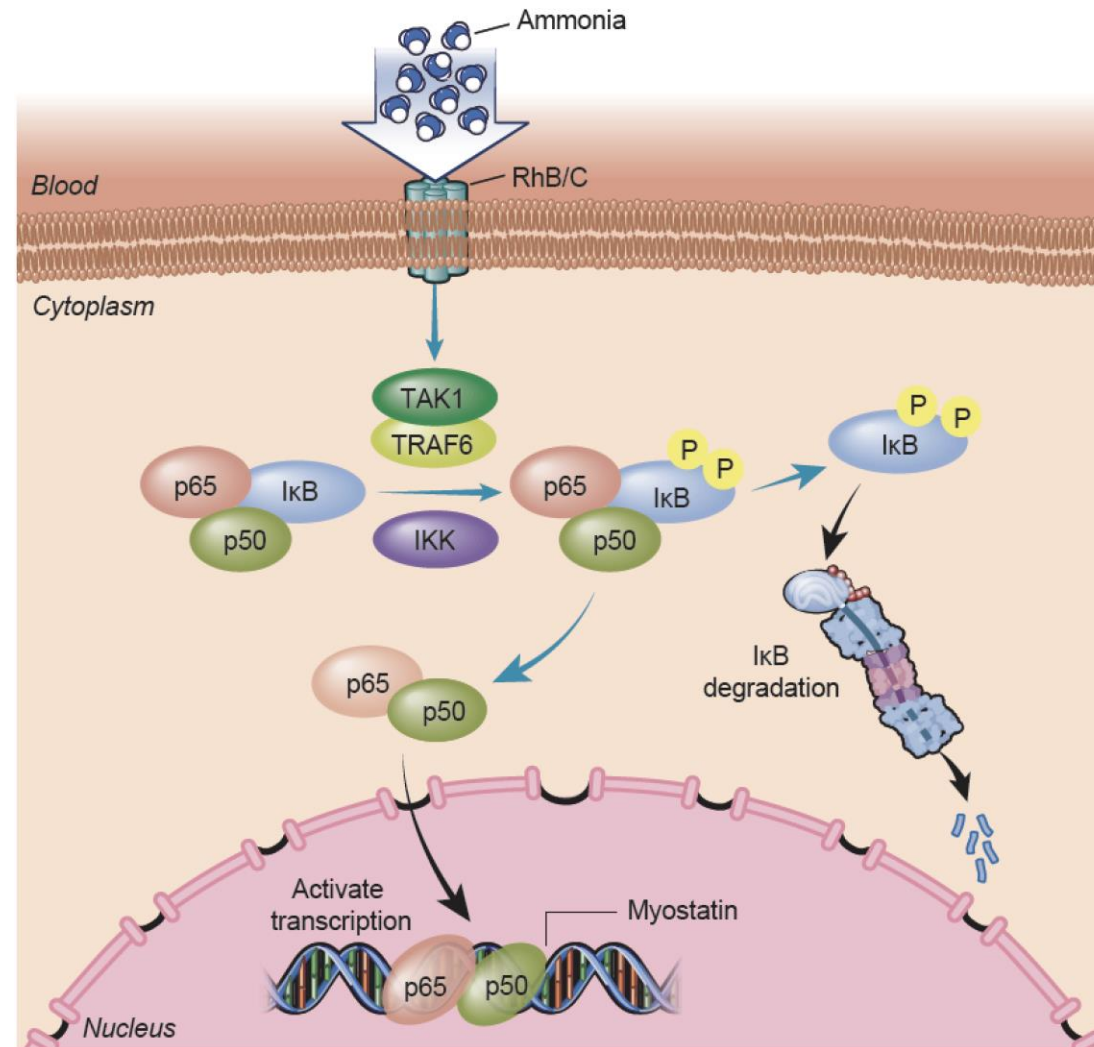


Potential Biochemical Strategies to Block Myostatin Activation



Dasarathy S and Meli M Sarcopenia from mechanism to diagnosis and treatment in liver disease.
J Hep 2016; 65: 1232–1244

Hyperammonemia Increases Myostatin Transcription via NF κ B Activation



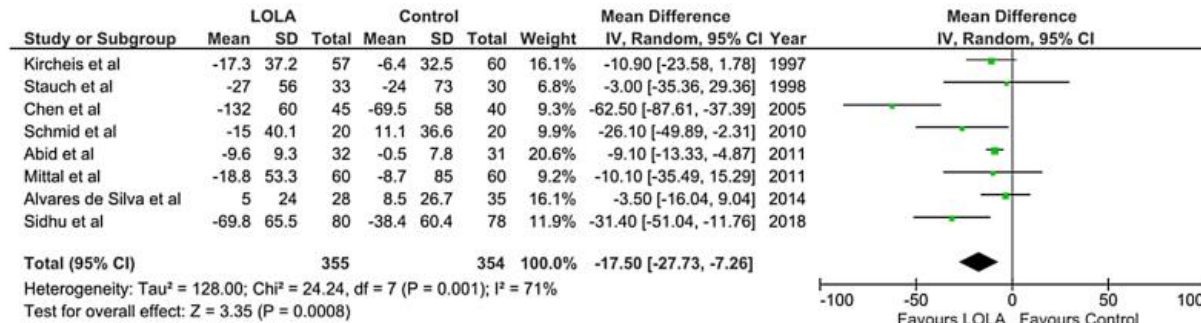
Qiu J et al Hyperammonemia in cirrhosis induces transcriptional regulation of myostatin by an NF- κ B-mediated mechanism. *Proc Natl Acad Sci* 2013; 110 (45): 18162–18167

Dasarathy S and Meli M Sarcopenia from mechanism to diagnosis and treatment in liver disease.

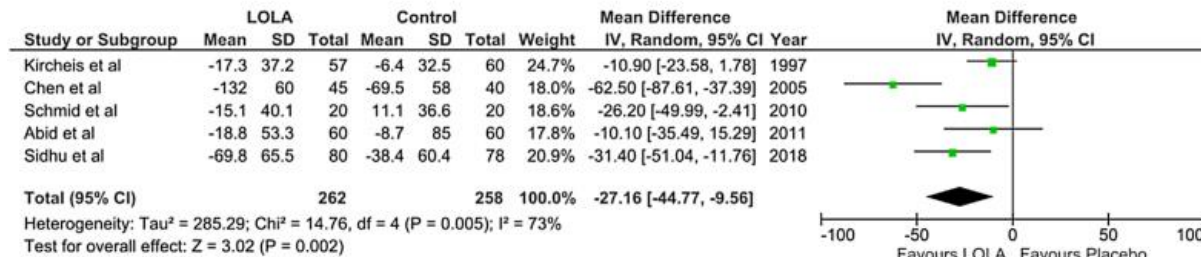
J Hep 2016; 65: 1232–1244

L-ornithine L-aspartate effectively lowers Ammonia

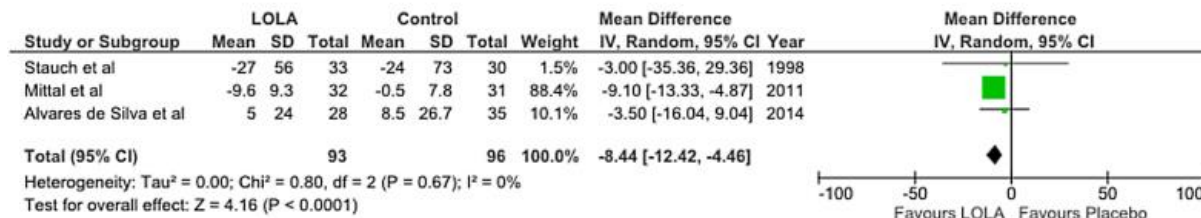
A. Ammonia lowering– all studies



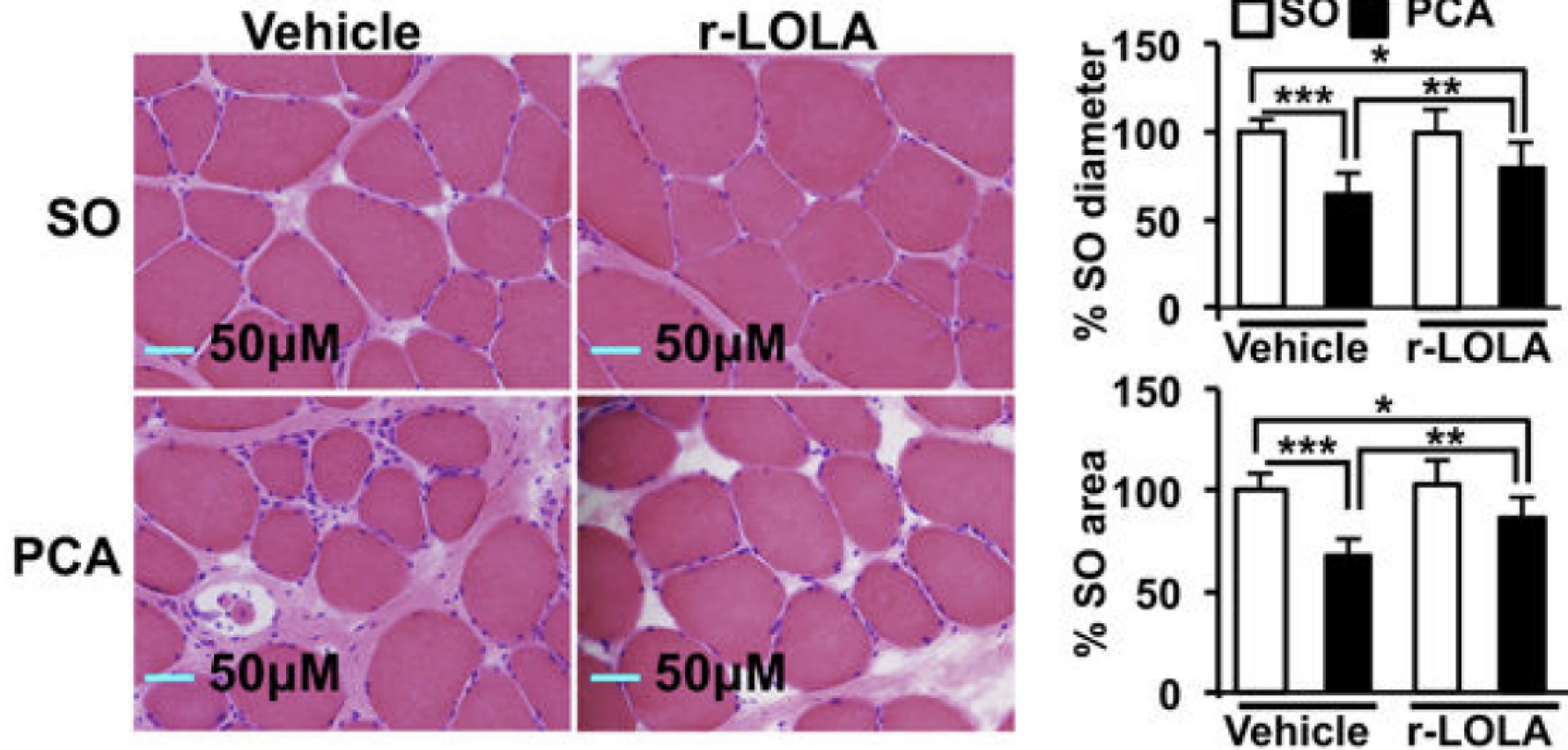
B. Ammonia lowering– IV LOLA



C. Ammonia lowering– PO LOLA



L-Ornithine L-Aspartate corrects sarcopenia in porto-caval anastomosis rats



Kumar A et al Ammonia lowering reverses sarcopenia of cirrhosis by restoring skeletal muscle proteostasis. Hepatology. 2017 June ; 65(6): 2045–2058. doi:10.1002/hep.29107

Summary and Conclusions

- Sarcopenia is independently associated with prognosis in patients with cirrhosis and after liver transplantation
- Sarcopenia = reduced muscle mass, function & myosteatosis
Skeletal Muscle Index (Men $<50 \text{ cm}^2/\text{m}^2$, Women $<39 \text{ cm}^2/\text{m}^2$)
- Nutritional interventions alone cannot correct sarcopenia but malnutrition can exacerbate it
- Exercise is partly effective
- Ammonia is a key mediator of sarcopenia in cirrhosis
- L-ornithine-L-aspartate lowers ammonia and could prevent sarcopenia