1. enteral nutrition vs standard diet

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kearns PJ, Young H, Garcia G et al. Accelerated improvement of alcoholic liver disease with enteral nutrition. *Gastroenterology.* 1992; 102(1):200-205. Ref ID: 66	RCT 1+ Randomisation and treatment allocation – no details ITT Power analysis (underpowered) Blinding – encephalopathy assessed blind	N=32 Drop-outs N=6 (3 per group	Patients with alcoholic liver disease Inclusion criteria: serum bilirubin >51µmol/L and one of the following: albumin <30 g/L, prothrombin time prolonged ≥ 4 seconds over control, pr presence of ascites on physical examination Exclusion criteria included: continuous GI bleeding, elevated serum creatinine level > 221 µmol/L Patient population EN: mean age 42 yrs, male:female 9:7, encephalopathy (stage 1-2) 10/16, ascites 12/16 Control: mean age 46 yrs, male:female 12:3, encephalopathy (stage 1-2) 7/15, ascites 13/15 The groups were well matched at baseline	Enteral nutritional (EN) supplementation + normal diet N=13 EN 167 kj/kg and 1.5 g/kg of ideal body weight protein delivered through ND tube	Normal diet N=12	9 weeks	Mortality Weight change Diarrhea	None reported
Mortality EN vs control Two weeks 0 vs 13% (ns); EN 0/16; control 2/15, RR 0.19 [0.01, 3.63], P=0.27 Four weeks								

13 vs 27% (ns); EN 2/16; control 4/15, RR 0.47 [0.10, 2.20], P=0.34 **Length of stay** 11 vs 12 days Diarrhea 5/16 vs 6/15, RR 0.78 [0.30, 2.03], P=0.61 **Weight change (during study 2 weeks)** EN 74 to 72 kg (ns) Control 78 to 72 (p<0.05)								
Cabre E, Gonzalez HF, Abad LA et al. Effect of total enteral nutrition on the short-term outcome of severely malnourished cirrhotics. A randomized controlled trial. *Gastroenterology.* 1990; 98(3):715-720. Ref ID: 2542	RCT 1+ Randomisation and treatment allocation – no details No power analysis Blinding – no details No ITT	N=35	Patients with advanced cirrhosis and severe PEM Exclusion criteria: upper GI bleeding on admission Diagnosis was based on histology 12/35. In remaining 23 the clinical and biological findings were 'unequivocally diagnostic of cirrhosis' Patient population TEN group Mean age 48 yrs, male:female 6:10, alcohol aetiology 11/16, ascites on admission 13/16, modified Child's score 11.9, serum creatinine 83.6 mM Control Mean age 53 yrs, male:female 9:10, alcohol aetiology 12/19, ascites on admission 16/19, modified Child's score 11.1, serum creatinine 87.5 mM	Total enteral nutrition (TEN) N=16 2115 kcal/day giving 71 g protein delivered through NG tube	Control N=19 Standard low-sodium hospital diet. 2200 kcal giving 70 to 80 g protein per day	TEN 23.3 (+/- 3) days Control 25.3 (+/- 3.2) days	Mortality Adverse events	UNIASA, Spain

			The groups were well matched at baseline					
Mortality TEN vs Control 2./16 (12%) vs 9/19 (47%) RR 0.26 [0.07, 1.05] P=0.06 **Adverse events** There were no cases of hepatic encephalopathy associated with TEN. No patient developed diarrhoea								

2. enteral nutrition vs steroids

Cabre E, Rodriguez IP, Caballeria J et al. Short- and long-term outcome of severe alcohol-induced hepatitis treated with steroids or enteral nutrition: a multicenter randomized trial. *Hepatology.* 2000; 32(1):36-42. Ref ID: 53	RCT 1+ Randomized by computer generated random lists. ITT. Blinding unclear.	N=71 No patient in the steroid group dropped out, however 8 patients in the enteral group dropped out during the treatment period (vomiting 1; epitaxis 1, variceal bleeding 1, 4 voluntary removal of tube, 1 psychological	Inclusion criteria: Patients with severe alcoholic hepatitis= Maddrey's Index (MI) >32 and/or hepatic enecephalopathy. With jaundice, hepatomegaly, anorexia, transaminase levels >2, increased leukocyte count in the setting of recent heavy drinking and histologically confirmed. Exclusion criteria: under 18 years, active GI bleeding not ceasing in 48 hrs, clinical and microbiological evidence of bacterial or fungal infection, insulin dependant diabetes mellitus, active peptic ulcer or acute pancreatitis, severe underlying diseases including cancer, refractory cardiac or respiratory insufficiency, and organic renal failure; hepatitis B or	40mg/ day prednisolone (for 28 days) (encouraged to eat 2,000 kcal/day, low sodium diet) N=36	Continuously infused, pump assisted, polymeric TEN (2000 Kcal/day)- 72 g protein, 345g carbohydrate, 36g fat, 40mmol sodium, 1,000ml water, recommended dietary allowances x 2 of vitamins and trace elemnts. (for 28 days) N=35	1 year or until death	Treatment related adverse events, mortality, development of infections and survival.	Not reported

		intolerance to tube feeding)	HIV; active drug abuse; systemic steroid therapy within the previous month; pregnancy and lactation. Both groups were homogenous at inclusion. Steroid group: Age 48.8± 9.5, male gender 26 (72%), alcohol intake (g/d) 126.1± 32.8, biopsy proven AH 20 (56%), cirrhosis 28 (78%), encephalopathy 11 (31%), ascites 28 (78%), hepatomegaly 29 (81%), total bilirubin (mg/dl) 16.3 ± 10.8, creatinine (mg/dl) 0.9 ± 0.4 Enteral group: Age 46.6 ± 10.1, male gender 23 (65%), alcohol intake (g/d) 140.8 ± 50.1, biopsy proven AH 17 (46%), cirrhosis 29 (83%), encephalopathy 9 (26%), ascites 28 (80%), hepatomegaly 32 (91%), total bilirubin (mg/dl) 17.0 ± 9.3, creatinine (mg/dl) 1.0 ± 0.7					
Side effects • Steroid group: 5/36; enteral group: 10/35, RR 0.49 [0.18, 1.28], P=0.14 **Infections** • Steroid group: 14/36; enteral group: 15/35, RR 0.91 [0.52, 1.59], P=0.73 **Mortality (as per protocol)** • Treatment period: Steroid group: 9/36; enteral group: 10/27, RR 0.68 [0.32, 1.43], p=0.30								

- Follow up: Steroid group: 10/27; enteral group: 1/17, RR 6.30 [0.88, 44.88], p 0.07

Probability of survival

- 1 yr probability of survival as assessed by the Kaplan-Meier method was 39% with steroids and 62% with TEN, ITT P=0.26, per protocol p=0.45

No. of hospital days/patient

- Steroid group: 8.6 ± 13.6; enteral group: 5.3 ± 12.3, Mean difference 3.30 [-2.73, 9.33] p=0.28

Authors' Conclusion:

'1) TEN and steroids are equally effective in SAH in terms of short-term survival, although death occurs earlier with TEN. 2) However, steroid treatment is associated with higher mortality rate in the immediate weeks after therapy, mainly due to septic complications. 3) A possible synergistic effect of both treatments should be investigated.'

3. enteral nutrition in combination with corticosteroids vs enteral diet

Mendenhall CL, Moritz TE, Roselle GA et al. A study of oral nutritional support with oxandrolone in malnourished patients with alcoholic hepatitis: results of a Department of Veterans Affairs cooperative study. *Hepatology.* 1993; 17(4):564-576. Ref ID: 2541	RCT 1++ Double blind Central randomisation balanced for severity of liver disease (and therefore malnutrition) ITT analysis	N=273	Male adults with alcohol-related hepatitis Diagnosis based on a history of heavy alcohol intake and laboratory changes associated with alcohol-related liver injury. Histology was not essential (to avoid excluding more severely ill patients) but was required in findings of atypical alcohol-related injury Exclusion criteria: Atypical biochemical liver test result without histological proof of diagnosis, comorbid disease that may alter liver function, late identification > 15 days hospitalisation, women Patient population: Active treatment Mean age 50 yrs, daily caloric intake 2830 kcal/day, alcohol aetiology 50%, duration of alcohol intake 25	Oxandrolone 80 mg/day for 30 days accompanied by a high-calorie, high-protein food supplement 60 gm protein and 1600 kcal/day Outpatient therapy Oxandrolone 40 mg/day for 60 days accompanied by 1200 kcal/day and 45 gm protein N=137	Placebo plus food supplement 6.8 gm/day protein and 264 kcal/day Outpatient therapy 5.1 gm protein and 198 kcal/day N=136	6 months	Mortality Adverse events	McGaw Inc, Merck, Sharpe and Dohme, Grand Forks Human Nutrition Centre and GRAND Food Description Master Coding Manual

			yrs, Severity of liver disease DF mean 86.6, malnutrition (PCM score, % of normal) 59.8, ascites (% with moderate or severe 64%) Placebo: treatment Mean age 51 yrs, daily caloric intake 2637 kcal/day, alcohol aetiology 46%, duration of alcohol intake 26 yrs, Severity of liver disease DF mean 87.0, malnutrition (PCM score, % of normal) 60.0, ascites (% with moderate or severe 66.4%) The groups were well matched at baseline					
Effect **Mortality (6 months)** Active treatment vs placebo 35% vs 39% (p=0.455); active treatment 48/137; placebo 53/136, RR 0.90 [0.66, 1.23], P=0.50 **Complications** There were no significant differences in the proportion of complications reported: GI bleeding 29.9 vs 24.3% (ns); active treatment 41/137, placebo 33/136, RR 1.23 [0.83, 1.83], P=0.29 Ascites 29.2 vs 30.2 (ns); active treatment 40/137; placebo 41/136, RR 0.97 [0.67, 1.40], P=0.86 Encephalopathy 19.0 vs 21.3% (ns); active treatment 26/137; placebo 29/136; RR 0.89 [0.55, 1.43], P=0.63 Infection 48.9 vs 44.1% (ns); active treatment 67/137; placebo 60/136; RR 1.11 [0.86, 1.43], p=0.43								