# 1. enteral nutrition vs standard diet

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of follow-up</th>
<th>Outcome measures</th>
<th>Source of funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>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</td>
<td>RCT 1+ Randomisation and treatment allocation – no details ITT Power analysis (underpowered) Blinding – encephalopathy assessed blind</td>
<td>N=32 Drop-outs N=6 (3 per group)</td>
<td>Patients with alcoholic liver disease Inclusion criteria: serum bilirubin &gt;51μmol/L and one of the following: albumin &lt;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 &gt; 221 μmol/L</td>
<td>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</td>
<td>Normal diet N=12</td>
<td>9 weeks</td>
<td>Mortality Weight change Diarrhea</td>
<td>None reported</td>
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**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
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)


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<tr>
<th>RCT 1+</th>
<th>N=35</th>
<th>Patients with advanced cirrhosis and severe PEM</th>
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<tbody>
<tr>
<td>Randomisation and treatment allocation – no details</td>
<td></td>
<td></td>
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<tr>
<td>No power analysis</td>
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<td></td>
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<tr>
<td>Blinding – no details</td>
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<tr>
<td>No ITT</td>
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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

Mortality
TEN 23.3 (+/- 3) days
Control 25.3 (+/- 3.2) days

Adverse events
UNIASA, Spain
2. enteral nutrition vs steroids

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<tbody>
<tr>
<td>N=71 Randomized by computer generated random lists. ITT. Blinding unclear.</td>
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<tr>
<td>Inclusion criteria: Patients with severe alcoholic hepatitis= Maddrey’s Index (MI) &gt;32 and/or hepatic encephalopathy. With jaundice, hepatomegaly, anorexia, transaminase levels &gt;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</td>
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<tr>
<td>40mg/ day prednisolone (for 28 days) (encouraged to eat 2,000 kcal/day, low sodium diet)</td>
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<tr>
<td>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 elements. (for 28 days)</td>
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<td>N=35 1 year or until death Treatment related adverse events, mortality, development of infections and survival.</td>
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**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
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

<table>
<thead>
<tr>
<th>Mendenhall CL, Mortz TE, Roselle GA et al.</th>
<th>RCT 1++</th>
<th>N=273</th>
<th>Male adults with alcohol-related hepatitis</th>
<th>Oxandrolone 80 mg/day for 30 days accompanied by a high-calorie, high-protein food supplement</th>
</tr>
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<tbody>
<tr>
<td>Study of oral nutritional support with oxandrolone in malnourished patients with alcoholic hepatitis: results of a Department of Veterans Affairs cooperative study.</td>
<td>Double blind Central randomisation balanced for severity of liver disease (and therefore malnutrition) ITT analysis</td>
<td></td>
<td>60 gm protein and 1600 kcal/day</td>
<td>Placebo plus food supplement 6.8 gm/day protein and 264 kcal/day</td>
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<tr>
<td>Hepatology. 1993; 17(4):564-576. Ref ID: 2541</td>
<td></td>
<td></td>
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<td>Outpatient therapy 5.1 gm protein and 198 kcal/day</td>
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<tr>
<td></td>
<td></td>
<td>N=137</td>
<td></td>
<td>N=136</td>
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<td></td>
<td></td>
<td></td>
<td>6 months</td>
<td>6 months</td>
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<tr>
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<td>Patient population: Active treatment Mean age 50 yrs, daily caloric intake 2830 kcal/day, alcohol aetiology 50%, duration of alcohol intake 25</td>
<td></td>
<td>Mortality Adverse events</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oxandrolone 40 mg/day for 60 days accompanied by 1200 kcal/day and 45 gm protein</td>
<td></td>
<td>McGaw Inc, Merck, Sharpe and Dohme, Grand Forks Human Nutrition Centre and GRAND Food Description Master Coding Manual</td>
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DRAFT FOR CONSULTATION

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