Nutrition approaches to ARDS (Acute Respiratory Distress Syndrome)

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Clinical Nutrition Service
St. Luke’s Medical Center, Quezon City
Philippines
# ARDS definition

<table>
<thead>
<tr>
<th>The Berlin definition of acute respiratory distress syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing</strong></td>
</tr>
<tr>
<td><strong>Chest imaging</strong></td>
</tr>
<tr>
<td><strong>Origin of edema</strong></td>
</tr>
<tr>
<td><strong>Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present</strong></td>
</tr>
<tr>
<td><strong>Oxygenation</strong></td>
</tr>
<tr>
<td><strong>Mild</strong></td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
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<tr>
<td><strong>Severe</strong></td>
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</tbody>
</table>

Abbreviations: CPAP, continuous positive airway pressure; \( \text{FiO}_2 \), fraction of inspired oxygen; \( \text{PaO}_2 \), partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure; \(^a\) Chest radiograph or computed tomography scan; \(^b\) If altitude is higher than 1,000 m, the correction factor should be calculated as follows: \[ \text{PaO}_2/\text{FiO}_2 \times (\text{barometric pressure}/760) \]; \(^c\) This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

ARDS management

- Protective mechanical ventilation
- Non conventional therapies in severe ARDS
  - prone positioning,
  - high frequency oscillatory ventilation
  - extracorporeal membrane oxygenation
- Therapies other than mechanical ventilation
  - conservative fluid strategy
  - neuromuscular blocking agents
- Future non-ventilatory therapeutic options
  - gene therapy for ALI/ARDS

Immunopathophysiology

- **Alveolar macrophages** – APC, cytokines
- **Granulocytes** – proteases, cytokines, chemotaxis
- **Complement** – MACs
- **MALT activation** – cloning
- **Lymphocyte activation** – circulation, cellular and humoral defense activation, cytokines
- **Endothelial changes** – chemokines,
- **Edema, hyaline membrane**
- **Coagulation changes**
- **Fibroblasts** – procollagen, fibrosis
- **Alveolar collapse**

Google Images
http://www.studyblue.com/notes/note/n/w-ards--sepsis/deck/1264727
Inflammation phases of injury

Moore FA. Presidential address: imagination trumps knowledge.
Immunopathology approach

**PNEUMONIA**

\[ \text{Antibiotics/Others} \]

**INFLAMMATORY PROCESS**

\[ \uparrow \text{Neutrophils} \]
\[ \uparrow \text{Lymphocytes} \]
\[ \uparrow \text{Complement} \]
\[ \text{Coagulation factors} \]

\[ \text{IMMUNOMODULATORS} \]

\[ \uparrow \text{Energy + nutrient needs} \]
1. Cell proliferation
2. Cytokine production
3. Factors for cell repair
4. Microcirculation maintenance
5. Wound healing

\[ \text{FLUIDS/COLOIDS} \]
\[ \text{NUTRITION} \]
Nutrition management approaches

• Management phases
  – Acute setting (critical care)
    • Malnutrition assessment: Lean body mass management e.g. respiratory muscles, gas exchange
    • Macronutrient and micronutrient manipulations
    • Adequacy of intake
    • Pharmaconutrients e.g. inflammation modulation, protein synthesis
    • Pulmonary rehabilitation
  – Chronic setting (long term follow up)
    • Lean body mass management e.g. respiratory muscle improvement
    • Adequacy of intake
    • Pharmaconutrients e.g. inflammation modulation, protein synthesis
    • Pulmonary rehabilitation
    • Exercise
ACUTE SETTING
Nutrition management approach

Nutrition Assessment

High Risk of developing complications

Assess Lean Body Mass Loss (% weight loss)
  - Gas exchange
  - Acid base balance
  - Respiratory muscles

Plan Lean Body Mass maintenance / build up
  - Diet plan
  - Pharmaconutrition
  - Adequate intake
  - Pulmonary rehab
Nutrition assessment

## NUTRITION CARE PLAN

<table>
<thead>
<tr>
<th>Date Admitted</th>
<th>Room / Bed No.</th>
<th>File No.</th>
<th>PIN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient’s Name (Last, First, Middle Name)</th>
<th>FM</th>
<th>Weight (kg)</th>
<th>Age</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>46 kg</td>
<td>68 y/o</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Attending Physician</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Actual Body Weight</th>
<th>46 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ideal Body Weight</td>
<td></td>
</tr>
<tr>
<td>Corrected Body Weight</td>
<td></td>
</tr>
</tbody>
</table>

### PARAMETERS

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>DATA</th>
<th>REMARKS / DETAILS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Calorie Requirement</strong></td>
<td>46 ( \times ) 25 = 1150 kcal/day</td>
<td>NPC=874 kcal; Carbo=50% = 874 x 0.5 = 437 kcal / 4 kcal/g (=109 g); Fat = 437/9 (=49g)</td>
</tr>
<tr>
<td><strong>Total Protein Requirement</strong></td>
<td>46 ( \times ) 1.5 g = 69 gm/day</td>
<td>Add sodium due to Na=130 Add potassium due to K=3.2</td>
</tr>
<tr>
<td><strong>Electrolytes</strong></td>
<td></td>
<td>water + fat soluble</td>
</tr>
<tr>
<td><strong>Vitamins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Trace Elements</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pharmaco Nutrition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>Standard dose</td>
<td>glutamine=0.3g x 46 kg = 14g/day</td>
</tr>
<tr>
<td>Omega-3 Fatty Acid</td>
<td>Specific</td>
<td>EPA/DHA=0.1 x 46 kg = 4.6g/day</td>
</tr>
<tr>
<td>Antioxidants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nutrition care plan

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Specifics</th>
<th>1. Full diet + Prosure 2 servings a day 2. If not ok with full regular diet - Nepro or Glucerna + Prosure (=2 servings a day) 3. If inadequate with enteral add Nutriflex Lipid 1 bag for 24 to 36 hours (with micronutrient supplements)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Access/Route</td>
<td></td>
<td>1. oral intake with commercial preparation 2. supplemental peripheral parenteral nutrition</td>
</tr>
<tr>
<td>Standard Diet Specifics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delivery Method</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitorng</td>
<td></td>
<td>Frequency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>daily</td>
</tr>
</tbody>
</table>

Lean body mass loss and mortality

Decision Box

Maastricht trial 1992
Veterans trial 1990
Nottingham trial 1983
Lincoping trial 1990
Studley 1930
Keys 1953
Warsaw Ghetto 1942

>60% Mortality*
30% Mortality

Lean body mass loss and mortality

<table>
<thead>
<tr>
<th>Loss of Total LBM</th>
<th>Complications</th>
<th>Associated Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>Decreased immunity</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>Increased infections</td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td>Decrease in healing, increase in weakness, infection</td>
<td>30%</td>
</tr>
<tr>
<td>30%</td>
<td>Too weak to sit, pressure ulcers, Pneumonia, lack of healing</td>
<td>50%</td>
</tr>
<tr>
<td>40%</td>
<td>Death, usually from pneumonia</td>
<td>100%</td>
</tr>
</tbody>
</table>

LBM=Lean Body Mass

Lean body mass changes in elderly

Sarcopenia: Vandewoude M. Abbott Symposium, ESPEN 2011, Goteborg, Sweden
Lean body mass enhancers

• Acute phase
  – High protein intake
    • Branched chain AA
  – Pharmaconutrients
    • Fish oil (EPA/DHA)
    • Glutamine
    • HMB, glutamine, arginine combinations
  – Adequate intake
    • Pulse feeding
  – Insulin

• Long term
  – High protein intake
  – Pharmaconutrients
  – Adequate intake
  – Insulin
  – Exercise
    • Impact of free radicals
    • Not too much anti-oxidants
# Nutrition management in ARDS

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<td></td>
</tr>
<tr>
<td>Pulmonary support/fluid management/rehabilitation</td>
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<td></td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Protein synthesis

Leucine (branched chain AA)

mTOR pathway

Hydroxy-methyl-butyric acid (HMB)

PROTEIN SYNTHESIS

Slows down protein degradation

PROTEIN BUILD UP (LBM enhanced)

BCAA (enteral and/or parenteral)

Fish Oil (EPA/DHA) (enteral and/or parenteral)
Feeding approaches

Enteral nutrition

Adequate intake
• EPA/DHA
• GLA
• Glutamine
• HMB
• Antioxidants

Assess outcome

Inadequate intake
Enteral nutrition
• EPA/DHA
• GLA
• Glutamine
• Antioxidants
• Pulse feed

Supplemental PN

Assess outcome

Assess outcome

Guidelines:
• ASPEN 2009 (critical care) Guideline E2, E3, E4, H1
• ESPEN 2006 (critical care) Guideline 1, 2
• ESPEN 2009 (critical care) Guideline 1, 2, 6-17
Vitamin D3: immune-competence

GIT

M-cells: Antigen Presenting Cells (APC)

Peyer’s Patches - GALT

Lymphocyte activation

VITAMIN D3

T-Cells upregulate gut homing receptors

PULMONARY

Alveolar macrophage (APC)

Respiratory LN - MALT

The role of the gut in immune competence

Pharmaconutrition

- HMB, glutamine, arginine combination
  - HMB (β-hydroxy-β-methyl-butyric acid)
    - reduces inflammation
    - Improves protein synthesis
    - Improves ventilatory capacity
  - Glutamine
    - Improves WBC function
    - Anti-oxidant precursor
  - Arginine
    - Improves microcirculation
    - Enhances T-cell function
  - Fish Oil (EPA/DHA)
    - Immunomodulation
    - Protein synthesis
  - Antioxidants
    - Metabolism enhancement

- Ventilator improvement
- Pressure ulcer healing
- Organ function improvement
- Immune modulation
IMD (Inflammation modulating diet)

Table 5: ICU Stay.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Group (Standard Feeding, SF) N=19</th>
<th>Study Group (Supportan, SP) N=18</th>
<th>P value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU stay</td>
<td>10.84 ±7.08</td>
<td>7.05 ±2.89</td>
<td>0.04</td>
<td>0.19 to 7.48</td>
</tr>
</tbody>
</table>

Figure 3: Mean ICU Stay.

Glutamine

Animal study, sepsis model (cecal ligation)


* P < 0.05
Glutamine

Legend:
HV = acid aspiration, high volume
HVG = acid aspiration, high volume + GLN
LV = acid aspiration, low volume
LVG = acid aspiration, low volume + GLN

* P < 0.05

* animal study

Nutrient modification

• CO2 load can be reduced through lipids
  – Non-protein calorie ratio of 60%-70% lipid and 40%-30% carbohydrate
  – Modified through modular feeding: enteral or parenteral
    • ESPEN 2009 guideline 2.6 (Grade B)
  – Usually done when patient is already in stable status in the acute and long term setting

• Increased protein through pulse feeding
Pulse feeding

Adequate intake and survival in the ICU

Nutrition team and adequate intake

Nutrient intake in ICU patients (n=80)

- TCR_kcal_x10
- CalorieInt_x10
- %_AdeqCalorie
- TPR_gm
- Prot_Int_gm
- %_AdeqProt

* p < 0.05
Mann-Whitney U

http://www.dpsys120991.com/POJ_0001.html
EN/PN GUIDELINES
ASPEN 2009 guideline

• E. Selection of Appropriate Enteral Formula
  – E2. Patients with ARDS and severe acute lung injury (ALI) should be placed on an enteral formulation characterized by an anti-inflammatory lipid profile (ie, ω-3 fish oils, borage oil) and antioxidants. (Grade: A)
  – E3. To receive optimal therapeutic benefit from the immune-modulating formulations, at least 50%-65% of goal energy requirements should be delivered. (Grade: C)
ASPEN 2009 guideline

• H. Pulmonary Failure
  – H1. Specialty high-lipid low-carbohydrate formulations designed to manipulate the respiratory quotient and reduce CO2 production are not recommended for routine use in ICU patients with acute respiratory failure. (Grade: E) (This is not to be confused with guideline E2 for ARDS/ALI).

JPEN J Parenter Enteral Nutr 2009 33: 277
## ESPEN 2009 Guidelines/Recommendation/Grade

<table>
<thead>
<tr>
<th>Macronutrient / Micronutrient</th>
<th>Type</th>
<th>Dose</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate</td>
<td>Minimum amount = 2 g/kg/day</td>
<td>Hyperglycemia = increased mortality</td>
<td>Grade B</td>
</tr>
<tr>
<td>Protein</td>
<td>balanced amino acid mixture</td>
<td>1.3–1.5 g/kg ideal body weight per day</td>
<td>Grade B</td>
</tr>
<tr>
<td>Glutamine</td>
<td></td>
<td>0.2–0.4 g/kg/day</td>
<td>Grade A</td>
</tr>
<tr>
<td>Lipid</td>
<td></td>
<td>To be provided daily</td>
<td>Grade B</td>
</tr>
<tr>
<td>LCT/MCT</td>
<td>Fish Oils</td>
<td></td>
<td>Grade C</td>
</tr>
<tr>
<td>Multivitamins</td>
<td>Water soluble</td>
<td>daily</td>
<td>Grade C</td>
</tr>
<tr>
<td>Fat soluble</td>
<td>daily</td>
<td></td>
<td>Grade C</td>
</tr>
<tr>
<td>Trace elements</td>
<td>daily</td>
<td></td>
<td>Grade C</td>
</tr>
</tbody>
</table>
LONG TERM SETTING (POST ARDS)
Long term outcome

• Survival statistics
  – Schmidt et al (1): Six months post-ICU discharge, 84 (60%) patients were still alive
  – Herridge et al: (2)
    • Most deaths occurred within 6 months after discharge
    • Mostly due to existing medical condition
    • Acute setting statistics:
      – Median 25 days in ICU; 48 days in the hospital
      – Lost 18% of baseline body weight

Philippine experience

Asian Hospital Nutrition Team

Dr. Liza Francisco, DPBCN
Long term outcome

<table>
<thead>
<tr>
<th>Type of care</th>
<th>% (of total)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Special Care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator (6)</td>
<td>17%</td>
<td>83% died within 21 days (n=5)</td>
</tr>
<tr>
<td>Ventilator + central PN (1)</td>
<td>3%</td>
<td>100% died within 21 days (n=1)</td>
</tr>
<tr>
<td>Ventilator + dialysis (1)</td>
<td>3%</td>
<td>100% died within 14 days (n=1)</td>
</tr>
<tr>
<td>Dialysis (3)</td>
<td>8%</td>
<td>33% died within 21 days (n=1)</td>
</tr>
<tr>
<td>Central PN (8)</td>
<td>22%</td>
<td>38% died within 21 days (n=3)</td>
</tr>
<tr>
<td>Standard Care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard care (21)</td>
<td>58%</td>
<td>5% died within 150 days (n=1)</td>
</tr>
</tbody>
</table>

Alive (n=28): pharmaconutrition given

Pharmaconutrition given:
- Fish oil = 50%
- Glutamine = 22%

Long term outcome (one year)

Long term outcome (five years)

Post-discharge program
- Self-instruction exercise manual
- Regular trainer visits
- Nurse-led follow up program
- ICU diary intervention
- Nutrition?

Change in weight

Herridge MS et al. Functional Disability 5 Years after Acute Respiratory Distress Syndrome. NEJM 2011; 364 (14): 1293-1304
Long term outcome (five years)

Herridge MS et al. Functional Disability 5 Years after Acute Respiratory Distress Syndrome. NEJM 2011; 364 (14): 1293-1304
# Nutrition management approaches

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<tr>
<td>Exercise</td>
<td></td>
<td>✔️</td>
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</table>
Manner of feeding

Needham DM et al. One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial. BMJ 2013;346:
Inflammation modulating diets


N=143 (study)
129 (control)

* Trial stopped due to futility
Inflammation modulating diets

Study group:
- More sick (pneumonia, sepsis)
- Poorer lung function
- Very low protein/day (3.8g vs. 20g): lost lean body mass daily
- Very low carbo/day (4.2g vs. 31.8g): lost protein due to gluconeogenesis
- Higher fat (44.6g vs. 22g) and fish oil levels (EPA/DHA=10g; GLA=10g)
- Very high Vitamin C and E: leads to inefficient protein synthesis
- Bolus feeding (=diarrhea), reduced intake
- Became more malnourished at the end of the study

N=143 (study)
129 (control)

* Trial stopped due to futility

Fish oils and protein synthesis

Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial

Gordon I Smith, Philip Atherton, Dominic N Reeds, B Selma Mohammed, Debbie Rankin, Michael J Rennie, and Bettina Mittendorfer


8 weeks supplementation

1.86g EPA
1.50g DHA

Clamp = insulin + glucose + amino acid infusion
HMB: β-hydroxy-β-methyl-butyrate

- Stabilizes muscle cell membrane
- Upregulates protein synthesis
- Modulates protein degradation
HMB: Hydroxy-methyl-butyrate

Exercise after protein intake

Absolute values of CSA-q.f. pre- (■) and post-resistance training (□) for 12 weeks in the group ingesting protein immediately postexercise (P0, n = 7) and in the group ingesting protein 2 h postexercise (P2, n = 6). * Significantly different from pre-training ($P < 0.05$); § significantly larger relative increase in P0 than in P2 ($P < 0.01$). Bars are means ± S.E.M.

Cross-sectional area of m. quadriceps femoris

# Summary: long term setting

<table>
<thead>
<tr>
<th>Approach</th>
<th>Long Term</th>
<th>Details</th>
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<tbody>
<tr>
<td>Lean body mass management e.g. respiratory muscle improvement</td>
<td>✔</td>
<td>• 1.5 g/kg/day, BCAA, Pulse feeding, Fish oils, Insulin, HMB, Exercise</td>
</tr>
<tr>
<td>Adequacy of intake (macro and micronutrients)</td>
<td>✔</td>
<td>• Records</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nutrition team</td>
</tr>
<tr>
<td>Pharmaconutrients e.g. inflammation modulation, protein synthesis</td>
<td>✔</td>
<td>• EPA/DHA/GLA, Glutamine, Arginine, Antioxidants</td>
</tr>
<tr>
<td>Pulmonary support/rehabilitation</td>
<td>✔</td>
<td>• Lean body mass enhancers (HMB, Fish oils, pulse feeding, exercise)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Non-nutrition mgt</td>
</tr>
</tbody>
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## Summary: acute and long term mgt

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</tr>
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</table>
| Adequacy of intake (macro and micronutrients)      | ✔     | ✔         | • Records  
• Nutrition team                                                   |
| Pharmaconutrients e.g. inflammation modulation, protein synthesis | ✔     | ✔         | • EPA/DHA/GLA, Glutamine, Arginine, Antioxidants                        |
| Pulmonary support/fluid management/rehabilitation  | ✔     | ✔         | • Lean body mass enhancers (HMB, Fish oils, pulse feeding, exercise)   |
| Exercise                                           |       | ✔         | • Non-nutrition mgt                                                    |
THANK YOU