What's in this week's issue?
Week of January 17 - 21, 2022

SPOTLIGHT: Feed Me and Send Me Home - Early Oral Refeeding in Acute Pancreatitis

- The Short and Long of It: What is the Right Course of Antibiotic Therapy for Men with UTI?
- Do Probiotics Decrease Ventilator-Associated Pneumonia?
Immediate Oral Refeeding in Patients with Mild and Moderate Acute Pancreatitis: A Multicenter, Randomized Controlled Trial (PADI Trial)


**KEY TAKEAWAY:** Adult patients with mild to moderate acute pancreatitis who received immediate oral refeeding (IORF) had shorter hospital stays, lower costs, and less complications than those who received conventional oral refeeding (CORF).

**STUDY DESIGN:** Multi-center randomized controlled trial (RCT)

**LEVEL OF EVIDENCE:** STEP 2

**BRIEF BACKGROUND INFORMATION:** Acute pancreatitis is a common disease resulting in significant morbidity, mortality, and health care costs. Conventional oral refeeding includes fasting up to 48 hours and gradual intake based on clinical and analytical improvements. However, a growing body of evidence suggests that earlier enteral feeding in these patients can reduce hospital stays and pain. Despite these findings, controversy remains over the optimal timing and onset of oral refeeding.

**PATIENTS:** Adults with mild or moderate acute pancreatitis

**INTERVENTION:** Immediate oral refeeding (IORF)

**CONTROL:** Conventional oral refeeding (CORF)

**OUTCOME:** Hospital length of stay (LOS)

Secondary Outcomes: Abdominal pain relapse, diet intolerance, cost, complications, and laboratory findings

**METHODS (BRIEF DESCRIPTION):**

- 131 adult patients presenting to the emergency rooms at four secondary and tertiary care hospitals in Spain with mild to moderate pancreatitis were enrolled in the study.
- Enrolled patients met at least 2 or 3 acute pancreatitis (AP) criteria: AP on US or tomography, >3-fold elevation of serum amylase and/or lipase levels, and acute abdominal pain
- Patients were randomized within 12 hours of admission to IORF with a low-fat solid diet or CORF with a 24–48 hour fast followed by gradual advancement of their diet based on criteria met (no abdominal pain, decrease C-reactive protein, appropriate blood leukocyte and pancreatic enzyme levels) and diet tolerance.
- Other than diet, all patients received the same guideline-based treatment (IV fluid resuscitation, pain control, electrolyte repletion, etc.).
- Hospital LOS in days, abdominal pain based on standardized scale, diet intolerance, complications (peripancreatic fluid collections, necrosis, surgical interventions, ICU admissions, and deaths), and cost in euros were reported as the primary and secondary outcomes.

**INTERVENTION (# IN THE GROUP):** 71

**COMPARISON (# IN THE GROUP):** 60

**FOLLOW UP PERIOD:** 1 to 3 month clinical and analytical follow-up

**RESULTS:**

Primary Outcome –

- Compared to CORF, the mean hospital LOS was significantly shorter for the IORF group (3.4 vs 8.8 days, \( P < .001 \)).

Secondary Outcomes –

- Based on a 10-point standardized pain scale, the IORF group had significantly more abdominal pain on the refeeding day (6.2 vs 2, \( P < .001 \)), but they also received less pain medication.
- Diet intolerance, defined by relapse of pain, nausea, vomiting, and hyperoxia, was significantly less in the IORF group (1% vs 22%, \( P < .001 \)).
- Complications (peripancreatic fluid collections, necrosis) were significantly lower in the IORF group (4.2% vs 18%, \( P < .009 \)).
- There were significantly less ICU admissions in the IORF group (0% vs 6.6%, \( P = .03 \)).
- The healthcare costs were estimated to be approximately 50% lower in the IORF group (1,230 vs 2,556 euros).

**LIMITATIONS:**

- Small sample size
- Unblinded study
- Complication and intervention cost analyses were performed only at the coordinating hospital.
- Limited generalizability:
  - Predominantly European population with lower average BMI than U.S. population
Higher proportion of the study population had biliary pancreatitis (73%) compared to the U.S. population (40–70%).

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Effect of 7 vs 14 Days of Antibiotic Therapy on Resolution of Symptoms among Afebrile Men with Urinary Tract Infection: A Randomized Controlled Trial


**KEY TAKEAWAY:** This study demonstrated no inferiority of seven-day versus 14-day antibiotic treatment of afebrile male urinary tract infection (UTI).

**STUDY DESIGN:** Double-blind, placebo-controlled randomized trial

**LEVEL OF EVIDENCE:** STEP 3

**BRIEF BACKGROUND INFORMATION:** Antimicrobial stewardship remains an important influencer when prescribing antibiotics, and UTIs remain one of the most common reasons for antimicrobial use. Evidence suggests that shorter antibiotic treatments may be as successful as longer courses in many infections and may reduce costs and the risk for adverse events. Optimal antibiotic treatment in men with UTIs is still undefined, and this study evaluated whether seven days of antibiotic treatment is noninferior to the standard 14-day antibiotic treatment.

**PATIENTS:** Adult afebrile males with UTI symptoms

**INTERVENTION:** Seven days ciprofloxacin or trimethoprim/sulfamethoxazole followed by seven days placebo

**CONTROL:** 14 days ciprofloxacin or trimethoprim/sulfamethoxazole

**OUTCOME:** Resolution of UTI symptoms by 14 days after stopping treatment

**METHODS (BRIEF DESCRIPTION):**
- Conducted at two U.S. Veterans Affairs (VA) centers (Minnesota and Texas).
- Enrolled patients were adult, afebrile men with UTI symptoms (at least one of dysuria, urination frequency or urgency, hematuria, costovertebral angle [CVA] tenderness, or perineal/suprapubic pain) initially prescribed ciprofloxacin or trimethoprim/sulfamethoxazole.

**RESULTS:**

**Primary Outcome –**
- UTI symptom resolution at 14 days after antibiotic treatment was not different for the patients treated with seven days or 14 days of antimicrobial therapy (93% vs 90%; absolute difference 2.9%; 1-sided 97.5% CI, –5.2 to ∞).

**Secondary Outcomes –**
- No difference in UTI symptom recurrence within 28 days in either the seven- or 14-day antimicrobial group.
  - As randomized: 10% vs 17% (absolute difference 6.6%; 95% CI, –16 to 2.2)
  - As treated: 9.9% vs 13% (absolute difference 3.0%; 95% CI, –11 to 6.2)
- Adverse Events: Similar rates of adverse events reported (20% in the 7-day group, 24% in the 14-day group).

**LIMITATIONS:**
- Underpowered due to non-adherence and recruitment
- Subjective assessment of UTI symptoms
• Population was limited to VA. Possible issues of generalizability to other care systems and patients.
• Inferiority margin was not evidence-based.
• Length of study (5 years).

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Do Probiotics Decrease Ventilator-Associated Pneumonia?

**Effect of Probiotics on Incident Ventilator-Associated Pneumonia in Critically Ill Patients**


**KEY TAKEAWAY:** Probiotics do not appear to offer significant benefit in reducing ventilator-associated pneumonia (VAP) in critically ill patients.

**STUDY DESIGN:** Randomized placebo-controlled trial with duplicate blinding central adjudication

**LEVEL OF EVIDENCE:** STEP 2

**BRIEF BACKGROUND INFORMATION:** Probiotics have been studied to see effects on antibiotic associated diarrhea, *Clostridioides difficile* infections, and gut health. Research thus far has shown that in critically ill patients probiotics may have some benefit in preventing infection. However, studies have been inconsistent with results.

**PATIENTS:** Adults expected to need mechanical ventilation for at least 72 hours

**INTERVENTION:** Enteral *Lactobacillus rhamnosus* GG (1x10^10 colony-forming units)

**CONTROL:** Placebo of microcrystalline cellulose twice a day

**OUTCOME:** Rates of VAP

Secondary Outcomes: Other infections, length of stay, adverse events

**METHODS (BRIEF DESCRIPTION):**

- Patients were monitored for signs of VAP and other infections using objective measures such as chest X-ray, fever or hypothermia, leukocytosis or leukocytopenia, purulent sputum, and cultures.

**INTERVENTION (# IN THE GROUP):** 1,321

**COMPARISON (# IN THE GROUP):** 1,332

**FOLLOW UP PERIOD:** Maximum of 60 days, until discharged from the ICU, or until *L rhamnosus* was isolated from a sterile site

**RESULTS:**

Primary Outcome –

- There was no difference in the VAP infection rate in probiotic treated group vs control (22% vs 21%, respectively; HR 1.0; 95% CI, 0.9–1.2).

Secondary Outcomes –

- There was no difference in other infections in probiotic treated group vs control (31% vs 31%, respectively; HR 1.0; 95% CI, 0.8–1.1).
- Length of hospital stay was the same between probiotic and control (22% vs 22%, *P*=.4).
- 16 patients had adverse events of which 12 isolated *L rhamnosus* as primary organism. All 12 were in the intervention group.

**LIMITATIONS:**

- *L rhamnosus* was used in this study due to initial promise in previous studies, however, there may be variations in dose, genus, species, or strain when compared to other studies.
- This study was also not able to examine pulmonary or gastrointestinal microbiota over time.
- There are differences in each definition of VAP and no universal reference standard when comparing different studies.

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