

Critical Care Guidelines: Aggressive Application



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Introduction



- Value of enteral nutrition (EN) – Need for aggressive strategies
- Changing physician behavior
- Re-defining tolerance – Changing perceptions
- Importance of bed-side EN protocols in changing practice

JPEN 2009;33:277

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient:

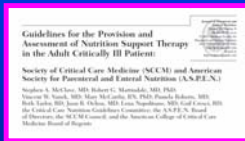
Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave, MD, Robert G. Martindale, MD, PhD, Vincent W. Yank, MD, Mary McCarthy, RN, PhD, Pamela Roberts, MD, Beth Taylor, RD, Juan E. Dubois, MD, Lena Napolitano, MD, Gail Cress, RD, the Critical Care Nutrition Guidelines Committee, the A.S.P.E.N. Board of Directors, the SCCM Council, and the American College of Critical Care Medicine Board of Regents
CCM 2009;37(5):1757

- Disclosure: Consultant, Speaker – Nestle, Abbott, Kimberly-Clark

Value of Enteral Nutrition

Is early enteral feeding really that important for the critically ill ICU patient?



- A3: EN is preferred over PN. (Grade B)
- A4a: Start EN within first 24-48 hours. (Grade C)
- A4b: Advance to goal next 48-72 hours. (Grade E)

Value of Enteral Nutrition

- Early (<36 hrs) vs delayed (>36 hrs) EN
Infection ↓ 55%, hosp LOS by 2.2 days *¹
Mortality ↓ 35% (p=0.06)²
- EN vs Standard (do nothing) Rx
Elective surgery and surgery critical care³
Infections ↓ by 28%, hosp LOS by 0.84 days *³ p<0.05
Severe acute pancreatitis post-op after complications⁴
Mortality ↓ by 74% (p=0.06)
- Cumulative Caloric Deficit⁵
Greater deficit = worse outcome
- Efficacy of EN protocols⁶
More EN earlier = better outcome



¹ Marik (GCM 2001) ² Heyland (JPEN 2003) ³ Lewis (BMJ 2001)
⁴ McClave (JPEN 2006) ⁵ Villet (Clin Nutr 2005) ⁶ Martin (GMAJ 2004)

Value of Early EN: Mechanisms



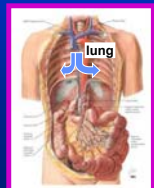
Gut Integrity



Innate Immunity



Acquired Immunity



Gut-Lung Conduit for Inflammation

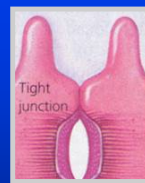
Kudsk (Am J Surg 2002;183:390)



Commensal Orgs

Value of EN: Dose-Dependent Effect

Maintaining Gut Integrity in Burn Patients



Gut Integrity Maintained



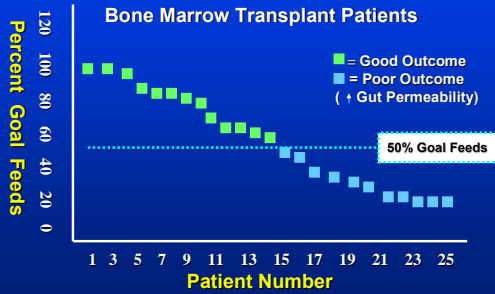
Loss of Gut Integrity

(*urine lactulose, p<0.05)	Controls	Uninfected	Infected
% Caloric provision	100%	64%	40%
Permeability increased	no	no	yes *

Ziegler (Arch Surg 1988;123:1313-1319)

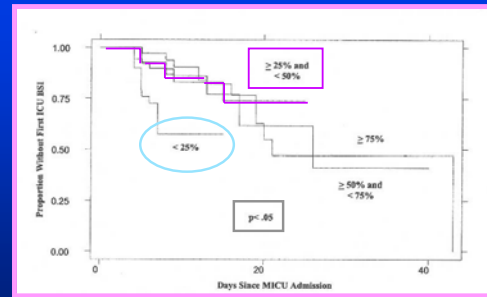
Value of EN: Dose-Dependant Effect

Maintaining Gut Integrity



Value of EN: Dose-Dependant Effect

Achieving Sufficient Volume of EN



- Low caloric intake correlated with nosocomial bloodstream infection Rubinson (CCM 2004;32:350)

Value of Enteral Nutrition

Characteristics of Increased Gut Permeability



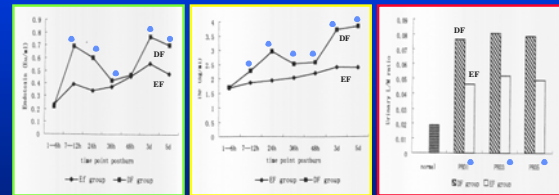
Characteristics : Time dependent
 Correlation to disease severity

Value of EN

Time Dependent Effect



22 Burn Pts (61% TBSA) Early < 24 hrs (n=13) Delayed > 48 hrs (n=9)



Endotoxin TNF Lact/Mann Ratio

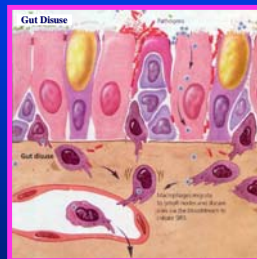
Peng (Burns 2001;27:145) (* p < 0.05)

Value of EN

Correlation to Disease Severity

Intestinal Permeability
 (% Urinary Excretion PEG 3350)

Controls	0.009
Mild	0.008
Severe	
No MOFS	0.040 *
MOFS	0.160 *



Ammori (J Gastrointest Surg 1999;3:252) * p<0.001

Value of EN: When to Add Supplemental PN

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient:

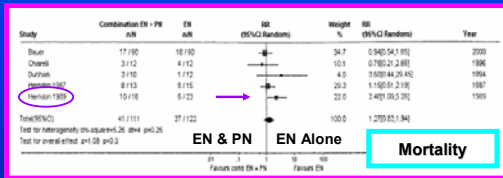
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- Add supplemental PN if unable to meet target goal calorie requirements only **after 7-10 days** by EN alone. (Grade: E)
- Adding PN prior to 7-10 days does not improve outcome and may increase risk to patient. (Grade: C)

Value of EN: Risk of Supplemental PN



- Meta-Analysis ¹: Greater cost, no Δ infect, hosp LOS, vent days
- Herndon Study ² (39 Burn patients, TBSA >50%)
Ratio helper/suppressor T-cells \downarrow EN/PN (days 7-14)
 \uparrow Mortality - EN/PN 63% vs EN alone 26% (p<0.05)

¹ Heyland (JPEN 2003;27:355) ² Herndon (J Burn Care Rehab 1989;10:309)

Value of EN Cumulative Caloric Balance



- Retrospective Study – Bartlett (1982) ¹

Positive EB (n=15) 26.6% Mortality
Negative EB* (n=17) 76.4% Mortality

- Prospective Multicenter Study – Mault (2000) ²

Duration Mech Vent ICU LOS
Positive EB (n=57) 10.6d ++ 15.9d ++
Negative EB* (n=16) 19.9d 24.6d

¹ Surg 1982;92:771 ² JPEN 2000;24:S4
* Negative EB > 10,000 kcal ++ p<0.05

Value of EN

Cumulative Caloric Balance



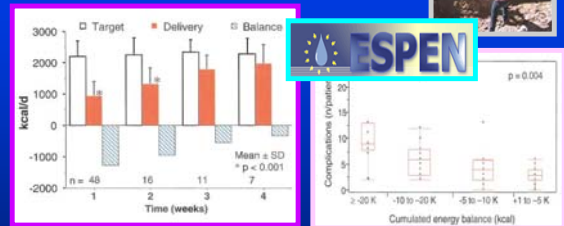
Pierre Singer, MD

- Dvir Study: 4000 Kcal Deficit
50 Med Surg ICU pts, APACHE II 23.1
- Cumulative deficit >4000 kcal associated with:
ARDS (p=0.0003)
Renal failure (p=0.0001)
Sepsis (p=0.003)
Need for surgery (p=0.0001)
Total complications (0.0001)

Dvir, Cohen, Singer (Clin Nutr 2006;25:37)

Value of EN

Cumulative Caloric Balance



- Cumulative energy deficit correlated to:
Hosp LOS (p=0.0001) Complications (p=0.0003)
Infections (p=0.004) Durat mech vent (p=0.0002)

Villet, Chiolero (CCM in press)

Value of EN: Supplemental PN Increases Infection, Mortality

- Large multicenter trial including severely injured trauma patients studying “Inflammation and the Host Response to Injury” (Glue Grant)
- Prospectively collected data 1000 patients
Retrospectively reviewed: 567 enrolled
17% PN only
87% EN only
13 % EN and supplemental PN
- Results:
Infection higher with PN alone, early supplemental PN (p<0.05)
Mortality higher in the EN + PN than in the EN alone (p<0.06)



Sena MJ JACS 2008

EN vs EN/Supp PN



Claude Pichard

- Four international study groups (PIs)
Have designed PRCTs
Benefit early EN vs early EN/Supp PN
Results coming in 2-3 yrs
Positive findings would change practice



Greet Van Den Berghe



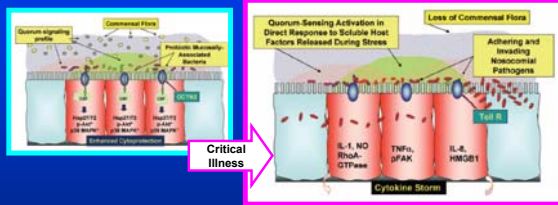
Daren Heyland
“Top Up Study”



Gordon Doig

Value of EN

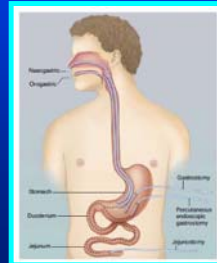
Timing of Early Gut Resuscitation



- As patient is admitted to ICU, critical illness is progressing
- SIRs pts vs controls: ↓Protective orgs, ↑virulent orgs, ↓SCFAs
Loss of HSPs, ↑permeability, cytokine storm
- What can be done during resuscitation to improve EN delivery?

Alverdy (J Leuko Biol 2008;83:461)

Value of EN: Promoting Tolerance Utilizing Gut Prior to Feeding



- McQuiggan Moore Study
Trauma pts on admission (n=20)
Start glutamine day 0, EN day 1
Results Gln Controls
%Goal Cal (7d) 75% 46% *
Intol episodes 8 42 *
- Separate Pharmaconutrients + formula
ARDSNET EdenOmega – Bolus FO,
borage oil, antioxidants
Stapleton - Bolus FO
McQuiggan Moore (JPEN 2008;32:28)

Changing Physician Behavior

“Are you nuts or just hard-headed?”



Changing Behavior: Volume-Based Feeding

	Study Pts (n=37)	Controls (n=20)
%Goal kcals	92.9%	80.9% *
Cum balance	-776.0 kcal	-1933.8 kcal *
%Goal kcal/d	Study Days	Control Days
Uninterrupted	103.5%(n=88)	102.1%(n=60)
Interrupted	77.6%(n=82)	61.5%(n=50) *

(Compliance in a third of pts – 95.3%)



EN Vol	Rate for hours remaining
Gastric Enteral Feeding Guidelines to Provide Goal Rate Ordered	
Esterle, McClave	
Louisville Study	

(*p<0.05)

Changing Physician Behavior: Top-Down Therapy

- Come out of gate at full throttle

Rapid advancement (start at goal)
Initiate prokinetics
Volume-based feeds
Chart cumulative caloric balance
Small peptide formula
Protein supplements
Small bowel feeds
Elevate head of bed

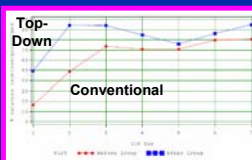


- Back off as tolerance develops

- Example: Canadian Pep-Up Study

	Goal Cal	Goal Prot
Controls (n=20)	58.8%	61.2%
Study pts (n=30)	67.9%	73.6%
Compliant pts (n=18)	83.2%*	89.4%*

Heyland, McClave (Crit Care 2010) *p<0.02



Changing Physician Behavior: Glucose Control

- Intensive insulin therapy (IIT) results (mortality) conflicting

	#Pts	IIT	Conventional	Signif
Leuven I (SICU)	(n=1548)	4.6% *	8.0%	p<0.04
Leuven II (MICU)	(n=1200)	24.2%	26.8%	p=0.31
VISEP	(n=536)	24.7%	26.0%	p=0.74
NICE-SUGAR	(n=6022)	27.5%	24.9% *	p=0.02

- Arguments

Failure of IIT responsible for difference EN >> TPN
SICU pts benefit from insulin Rx (cardiac, dysrhythmias)
Insulin rescue from high glucose loads gave benefit
Advanced glycolytic endproducts (AGEs) in hypo/hyperglycemia
Combination sufficient nutrition Rx plus IIT = best outcome
Insufficient nutrition plus IIT = poor outcome (hypoglycemia)
Take home point: Have protocols for moderate glucose control

Egi (J Diab Sci Tech 2009;3:1302)

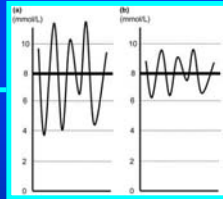
Changing Physician Behavior: Glucose Variability

Independent Risk Factor for Mortality

- Mean glucose range (mortality)

70-99 mg/dL	18.1%
180 mg/dL	35.9%
- Glucose variability (mortality)

	Lowest Quartile	Highest Quartile
70-99 mg/dL	5.9%	30.1% *
100-119 mg/dL	9.7%	31.0% *



- Mechanism
 - Reflects nursing care, use of protocols
 - Reflects disease severity
 - Reflects toxic effect and oxidative stress

Krinsley (CCM 2008;36:3008)

Redefining Tolerance



- Redefining how we assess tolerance

Redefining Tolerance: Feed an Ileus

Physician Interpretation of Ileus *Flawed*



- Bowel sounds don't correlate to SB functl status¹
Borborygmy, abd pain, distention, flatus, stool
Surrogate markers, no correlation to manometry
- Return of bowel function same open vs laparoscopic surgery²
- Surgical factors little effect on duration of colonic ileus³

Length time operation	Degree bowel handling
Amt post-op analgesia	Duration bowel exposure
- Aggressive early feeding vs post-op fasting⁴

↓ Hosp LOS	↓ Risk of anastomotic leaks
↓ Infections	(↑ Vomiting)

¹ Schippers (Dig Dis Sci 1991;36:621)

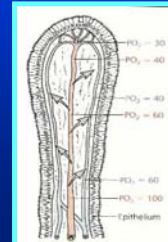
² Jeffrey (Am Surg 1996;62:167)

³ Wilson (Gut 1975;16:689)

⁴ Lewis (BMJ 2001;323:773)

Redefining Tolerance Ischemic Bowel

- Ischemic bowel rare complication of EN
- SB at risk due to countercurrent mechanism
- Villous tips affected first – Absorption



Redefining Tolerance

Process of Intestinal
Ischemia/Infarction

- Mucosal then transmural ischemia
- Capillary sludging, ↓ mucosal perfusion
- Gas formation, bowel distention
- ↓ Contractility, SBO, fermentation
- Osmotic effect pulls fluid into lumen
- Formula sits in lumen of gut
- Absorption in SB stops
- Ischemic injury to tips of villi



Scaife (J Trauma 1999;47:859)

Schunn (J Amer Coll Surg 1995;180:410)

Redefining Tolerance

Recommendations
for EN in Hypotension

- Hold feeds in hypotension :
 - Initiating pressor Rx
 - Increasing dose of pressors
 - Adding second or third agent
- OK to feed in hypotension on pressors :
 - Stable (24-36 hrs) or decreasing doses
 - Confirm resuscitation
 - Avoid fiber, stomach may be better (safer) than SB
- Hold feeds (on pressors) for any sign of intolerance :


NG output increases	New abdominal pain
Abdominal distention	Cessation of flatus, stool



Redefining Tolerance

Effect of Changing GRVs

British Study¹	Complications	%Goal Kcal
200cc GRV (n=41)	37% *	59% *
150cc GRV (n=41)	61%	36%



Canadian Study²	Vomitting	Intolerance
250cc GRV (n=44)	7%	45%
150cc GRV (n=36)	6%	58%

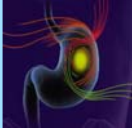
Louisville Study³	Regurgitation	Aspiration
400cc GRV (n=20)	27.8%	22.6%
200cc GRV (n=20)	35.0%	21.6%

Spanish Study⁴	GI Complications	%Goal Feeds
500cc GRV (n=160)	47.8% *	89% *
200cc GRV (n=169)	63.6%	83%

¹ Taylor (CCM 1999;27:2525) ² Pinilla (JPEN 2001;29:1955)
³ McClave (CCM 2005;33:324) ⁴ Montejo (ESICM 2007) *p<0.05

Redefining Tolerance

Effect of Changing GRVs



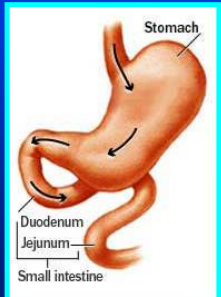
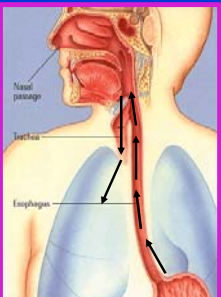
Powell Study (PRCT)¹	GRVs Used (n=15)	No GRVs (n=13)
Aspirat pneumonia	6.7%	15.4%
Tube clogging	66.7%	7.7% *

Reignier Study (Prospective before-after study)²	GRV Used (n=102)	No GRVs (103)
Intolerance	46.1%	26.2% *
Vol EN infused	1381 ml/d	1489 ml/d *
Vomitting	24.5%	26.2%
VAP pneumonia	19.6%	18.4%

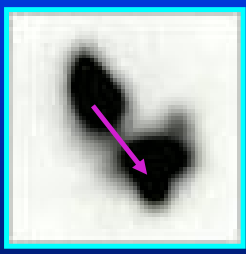

¹ Powell (JPEN 1993;17:243) ² Reignier(JPEN in Press)

Redefining Tolerance: What Are We Trying to Measure?

Tolerance (Gastric Emptying) vs Risk of Aspiration (Pneumonia)





Redefining Tolerance: To Study Gastric Emptying Requires a Label

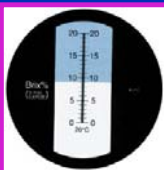




Radioisotope Formula

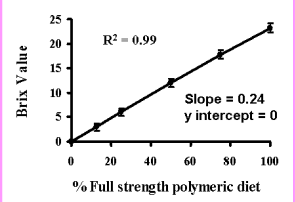

Using Refractometry to Determine Formula Volume



Michael Chang, MD

Brix Value: A Physical Constant

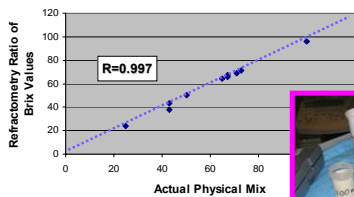
Total formula BV = 18.8 (sum of components)
 Fat BV = 6.4
 Carb BV = 5.8
 Prot BV = 6.3

Tight correlation with concentration
 100% Conc BV=18.8 25% Conc BV=4.7
 50% Conc BV=9.4 0% Conc BV=0.0 (water)

Determining Volume of Formula

(Concentration Based on $BV_{\text{Measured}} / BV_{\text{Full Formula}}$)

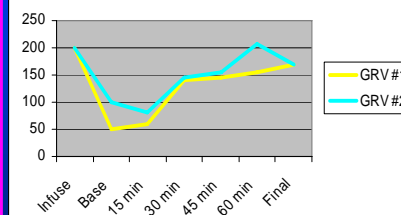
Determining Concentration



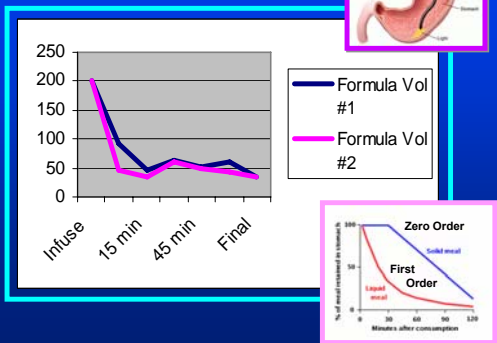
150ml
Conc
(% formula)



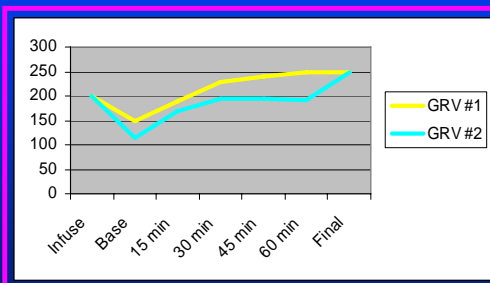
Patient #1



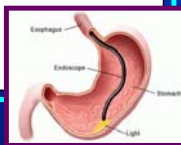
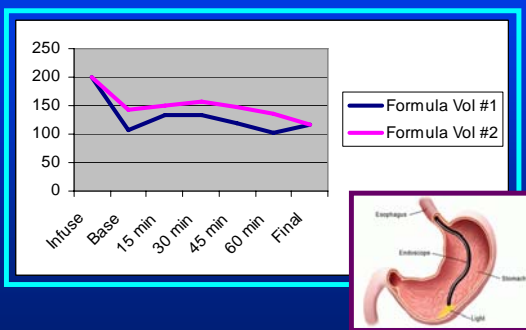
Patient #1 18% at 75 min



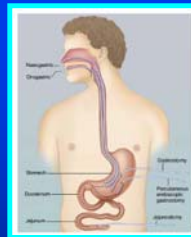
Patient #2



Patient #2 59% at 80 min



Redefining Tolerance: Formula Volume vs Total GRV



Questionnaire on Interpretation:

Patients (n=16)
(2 graphs each)

GI staff (n=18)

Question	GRV	Formula
• Delayed Gastric Emptying ?	52% yes	13% yes *
• Tolerating EN ?	36% yes	85% yes *
• Continue EN ?	34% yes	80% yes *

McClave (JPEN 2009 CNW Abstract) *p<0.05

Importance of Bedside (Nurse-Driven) Protocols

- Elements
 - Access
 - Elevate HOB
 - Oral care
 - Calorie balance
 - Rate ramp-up
 - GRVs
 - Prokinetics
- Enforcement
 - Orders to get EN
 - Incident report (nurses)
 - Buy in from leaders
 - Education
- Impact on outcome



Importance of Bedside Protocol for GRVs

- Check Gastric Residual Volume (GRV) q 4 hrs
Return contents < 500 mL to the patient
Determine Vol Formula by refractometry
- If **first** GRV > 400 mL initiate the following :
Continue EN at current rate
Turn patient to RLD position if possible for 30 min
Begin Reglan 10 mg IV q 6 hrs
Begin Narcan 8 mg in 10 mL saline per tube q 6 hrs
Recheck GRV in 4 hrs
- If **second** consecutive GRV 4 hrs later > 400 mL - Hold EN
Recheck GRV q 2 hrs, restart EN when GRV is <400 mL
If no signs of intolerance, restart at same rate
If evidence of intolerance present, consider reducing rate by 25 mL/hr (or to baseline 25 mL/hr if significant)



Importance of Bedside Protocols

Efficacy of EN Protocols:
Louisville Experience



	Control (n = 44)	Noncompliant (n = 13)	Compliant (n = 18)
% Goal Vol Ordered	66%	68%	82% *
% Goal Vol Delivered	52%	55%	68% *
Infusion time lost	16%	19%	11%

(* p < 0.05) Spain, McClave (JPEN 1999;23:288-92)



Efficacy of EN Protocols

PRCT in Head-Injured Trauma Patients

Consrv Protocol (n=41)	Aggr Protocol (n=41)
37 % Caloric goals	59 % Caloric goals

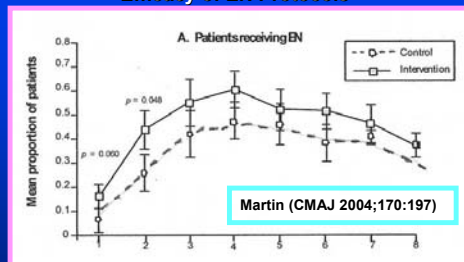
Infections	85%	61% *
Complications	61%	37% *
Good neuro outcome (3 mos)	39%	61% *
Good neuro outcome (6 mos)	61%	68% *
Hosp LOS (>20d)	46d	30d *

Conservative protocol: GRVs 50/150ml, slow ramp-up, gastric feeds
Aggressive protocol: GRVs 200ml, start at goal, post-pyloric feeds

Taylor (Crit Care Med 1999;27:2525) * p<0.04

Importance of Bedside Protocols

Efficacy of EN Protocols



	Intervention Centers	Control Centers	Signif
EN days/10d	6.7 days	5.4 days	p=0.042
Hosp LOS	25 days	35days	p=0.003
Mortality	27%	37%	p=0.058

Looking Out for Our Patients



- Paradigm shift in perspective promotes more aggressive delivery of early enteral nutrition