Figure 1. The flow of clusters (ICUs) and participants (patients) through the trial.

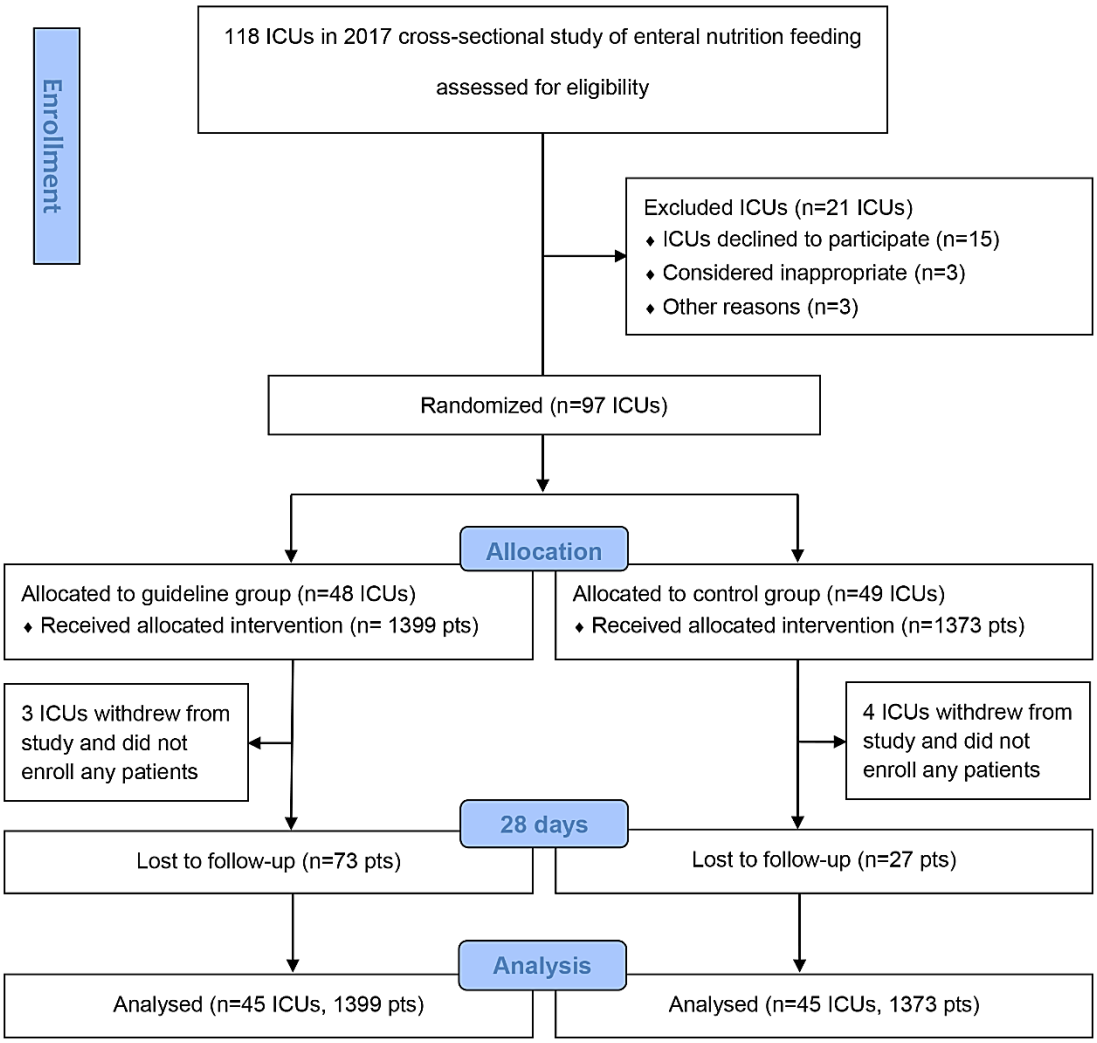

Table 1. Baseline ICU and Patient-Level Characteristics

Characteristics	Feeding guideline 48 ICUs, 1399 pts	Control 49 ICU, 1373 pts	P-value
ICU-level characteristics			
Tertiary, No. (%)	34 (70.8)	37 (75.5)	0.61
ICU type, No. (%)			0.97
Emergency	2 (4.2)	2 (4.1)	
Medical	1 (2.1)	1 (2)	
Neuro	1 (2.1)	1 (2)	
Surgical	2 (4.2)	2 (4.1)	
General	42 (87.5)	43 (87.8)	
Geographical region, No. (%)			0.623
Western	8 (16.7)	10 (20.4)	
Eastern	25 (52.1)	25 (51)	
Central Region	12 (25)	12 (24.5)	
Northeast	3 (6.2)	2 (4.1)	
Patient-level characteristics			
Age, mean±SD, y	61.0 ±17.6	60.1 ±17.7	0.98
Male, No. (%)	938(67.0%)	928(67.6%)	0.56
Weight, mean±SD, kg	63.6 ±11.1	65.1 ±11.2	0.16
BMI, mean±SD, kg/m^2	22.8 ±3.2	23.1 ±3.2	0.27
APACHE II score, mean±SD	18.3 ± 6.8	18.6 ±7.6	0.63
NUTRIC score, mean±SD	4.7 ±2.2	4.7 ±2.3	0.80
SOFA score, mean±SD	7.5 ±3.4	8.1 ±3.7	0.07
SOFA score for individual organ systems, mean±SD			
Respiration	2.2 ±1.2	2.3 ±1.1	0.15
Renal	0.8 ±1.3	0.9 ±1.4	0.29
Cardiovascular	1.1 ±1.7	1.4 ±1.7	0.31
Gastrointestinal function, No. (%)			0.09
AGI-I	1019 (75.9%)	888 (66.5%)	
AGI-II	236 (17.6%)	290 (21.7%)	
AGI-III	50 (3.7%)	126 (9.4%)	
AGI-IV	37 (2.8%)	31 (2.3%)	

ICU denotes intensive care unit; BMI denotes body mass index; APACHE, acute physiology and chronic health evaluation; NUTRIC denotes nutrition risk in the

critically ill; SOFA denotes sequential organ failure assessment; AGI denotes acute gastrointestinal injury.

Table 2. Process measures of nutritional therapy

Process Measures	Feeding guideline 48 ICUs, 1399 pts	Controls 49 ICU, 1373 pts	Difference(95% CI)	P
Mean time to start EN, d, mean±SD	1.20 ±1.42	1.55 ±1.64	-0.40 [-0.71, -0.09]	0.01
Mean time to start PN, d, mean±SD	1.29 ±1.74	0.80 ±1.40	1.06 [0.44, 1.67]	0.001
Mean nutrition support days within first seven days after enrollment /10 patient-days, mean±SD				
EN and/or PN	8.29 ±2.26	8.34 ±2.43	0.10 [-0.44, 0.65]	0.71
EN	7.51 ±2.82	6.49 ±3.42	1.09 [0.46, 1.73]	0.001
PN	1.66 ±3.12	3.72 ±4.18	-1.68 [-2.86, -0.49]	0.006
Mean energy delivered for patients within first seven days after enrollment / fed patient*-days, kcal mean±SD				
EN	1070.8 ±500.6	1015.9 ±423.5	64.45 [-49.13,178.04]	0.26
PN	776.5 ±472.9	829.9 ±611.1	-43.21 [-245.8,159.41]	0.67
Patients never fed during first seven days, No. (%)	7(0.6%)	12(0.9%)	0.2% [-0.6%; 1.0%]	0.67
Patients received EN during first two days after enrollment, No. (%)	883(65.8%)	687(51.4%)	16.5% [7.0%; 25.9%]	<0.001
Patients received PN during first two days after enrollment, No. (%)	250(18.6%)	555(41.5%)	-19.5% [-33.1%; -5.9%]	0.005
Patients fed during first two days after enrollment, No. (%)	1036(77.2%)	1042(78.0%)	0.7% [-8.4%; 9.9%]	0.87
Patients received EN or PN first two days after enrollment, No. (%)	1022(76.2%)	1006(75.3%)	3.2 % [-6.0%; 12.5%]	0.49
EN tolerance score after enrollment, mean±SD				

Day 1	0.2 ±0.8	0.2 ±0.8	-0.03 [-0.23, 0.16]	0.74
Day 2	0.3 ±0.9	0.3 ±1.0	-0.05 [-0.24, 0.14]	0.62
Day 3	0.4 ±1.0	0.4 ±1.0	-0.02 [-0.20, 0.16]	0.85
Day 4	0.3 ±0.9	0.4 ±1.1	-0.06 [-0.23, 0.11]	0.47
Day 5	0.3 ±0.9	0.4 ±1.1	-0.11 [-0.25, 0.04]	0.16
Day 6	0.3 ±0.9	0.4 ±1.0	-0.08 [-0.23, 0.07]	0.30
Day 7	0.3 ±0.9	0.4 ±1.0	-0.10 [-0.25, 0.05]	0.18
Days requiring prokinetic agents within first seven days enrollment /10 patient-days, mean±SD	1.1 ±2.7	1.0 ±2.5	0.37 [-0.29, 1.03]	0.26
Proportion of patients who received a post-pyloric feeding tube (patients receiving EN) within first seven days after enrollment, No. (%)	91(6.5%)	149(10.9%)	-3.1% [-9.3%; 3.1%]	0.32

EN denotes enteral nutrition, and PN denotes parenteral nutrition. *fed patients denotes patients who received oral intake, EN or PN, either alone or in combination

Table 3. Patient-centered outcomes and adverse events for all enrolled patients

Outcome Measure	Feeding guideline 48 ICUs, 1399 pts	Control 49 ICU, 1373 pts	Difference (95% CI)	P-value	ICC or Design Effect	
					Feeding guideline	Control
All-cause mortality at day 28, No (%)	188(14.2%)	205(15.2%)	-1.59% [-4.34%, 1.15%]	0.42	0.11	0.05
ICU-free days within 28 days, d	9.1 ±8.9	8.7 ±8.8	0.48 [-1.02, 1.98]	0.53	0.13	0.14
Incidence of new infections in ICU, No (%)	97(6.9%)	92(6.7%)	0.13% [-1.87%, 2.13%]	0.93	0.21	0.26

ICU denotes intensive care unit; CI denotes confidence interval; ICC denotes intraclass correlation coefficient.

Table 4. Organ failure-related outcomes

Outcome Measure	Feeding guideline 48 ICUs, 1399 pts	Control 49 ICU, 1373 pts	Difference (95% CI)	P-value
New-onset organ failure within first seven days after enrollment, patients/No. (%)				
New-onset respiratory failure	178(13.3%)	138(10.3%)	3.1% [-0.8%; 6.9%]	0.11
New-onset cardiovascular failure	88(6.6%)	97(7.3%)	-1.2% [-3.8%; 1.4%]	0.36
New-onset renal failure	75(5.6%)	82(6.2%)	-1.1% [-3.0%; 0.7%]	0.22
Organ support therapy within first seven days after enrollment, treatment days/10 patient-days				
Renal replacement therapy	0.97 ±2.50	1.46 ±3.05	-0.48 [-0.88, -0.08]	0.02
Vasoactive agents	2.19 ±3.39	2.98 ±3.75	-0.73 [-1.34, -0.12]	0.02
Mechanical ventilation[a]	7.18 ±3.85	7.28 ±3.80	-0.01 [-0.63, 0.61]	0.97

CI denotes confidence interval.

[a] non-invasive mechanical ventilation included