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Study of the Effect of Early Versus Delayed Enteral Nutrition in Critically Ill Mechanically Ventilated Medical Patients

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Abstract

Background: At the present time, the optimal timing and use of enteral nutrition for mechanically ventilated medical patients is unknown. The current study will focus on the effect of early versus delayed enteral nutrition in critically ill mechanically ventilated medical patients.

Aim of Study: To compare between early versus delayed enteral feeding in Invasive Mechanical Ventilation (IMV) patients. To assess association linking early nutrition (<48 hours after intubation), feeding route and calorie intake to mortality and risk of Ventilator Associated Pneumonia (VAP) in patient with Invasive Mechanical Ventilation (IMV) .

Patients and Methods: Patients will be scheduled to received their estimated total daily enteral nutritional requirements on either day 1 (early-feeding group) or day 5 (late-feeding group) of mechanical ventilation. Patients in the late-feeding group will be also scheduled to receive 20% of their estimated daily enteral nutritional requirements during the first 4 days of mechanical ventilation. Thirty (50%) consecutive eligible patients will be entered into the early-feeding group and thirty (50%) patients will be enrolled in the late-feeding group. All patients will be received enteral nutrition via continuous infusion by a feeding pump. Eligible patients will be followed in ICU for a maximum of 12 days or until death or discharge from ICU.

Results: Logistic regression analysis shows that; after applying (forward method) and entering some predictor variables; the increase in BMI and late feeding technique; had an independent effect on increasing the probability of mortality occurrence; with significant statistical difference (p <0.05 respectively). The increase in BMI and late feeding technique; had an independent effect on increasing the probability of VAP occurrence; with significant statistical difference (p <0.05 respectively). By using ROC-curve analysis, early enteral feeding predicted shortening of hospital stay, with failed (64%) accuracy, sensitivity=63% and specificity=63% (p $<^{0}.^{05}$).

Conclusion: Evidence shows improvement in patient outcomes associated with the use of EEN in a diverse population of critically ill patients. The results of our study strengthen our understanding of the benefits of EEN. These were evident even though <50% of the patients in each group reached a goal rate of EN. Given the potential ease of consistent implementation of EEN, the minimal cost associated with such a practice, and the potentially substantial.

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Key Words: *Acute lung injury – Acute respiratory distress syndrome – Intensive care units.*

Introduction

ACCORDING to different studies, one of the most important entities in Intensive Care Units (ICUs) is Acute Lung Injury (ALI) or Acute Respiratory Distress Syndrome (ARDS). In this subpopulation of patients, persistent hypoxemia may entail additional treatments, such as mechanical ventilation in the ICUs. Mechanical ventilation was, first recommended in 1976 can be readily implemented in any ICU and has been shown to improve respiratory mechanics and arterial oxygenation in patients with ARDS **[1]**. Patients admitted to ICUs who need MV are expected to have higher mortality rates compared with those who do not require respiratory support **[2]**.

Critically ill patients are at particular risk of malnutrition, which occurs in up to 40% of the cases. The metabolic changes that occur in response to stress lead to an increase in protein catabolism, resulting in a significant loss of lean body mass, which in turn results in a higher incidence of complications, especially infectious ones, in an increase in wound dehiscence and in unfavorable outcomes **[3]**. Nutritional support in critically ill patients was considered as an adjunctive care to provide exogenous fuels to support the patient during the period of stress. This support had 3 main goals:

1- To preserve the lean body mass.

2- To maintain the immune function.

3- To avoid metabolic complications.

Feeding an ICU patient now extends beyond choosing the right feeding route, the rate and the caloric density. In modern critical care, the concept of 'therapeutic nutrition' is replacing traditional ' supportive nutrition [4].

Enteral feeding is considered to be more cost-effective than Total Parenteral Nutrition (TPN), but TPN remains a common therapeutic intervention in the ICU and represents a significant burden on health care budgets. Although it is generally accepted that early enteral nutrition is of benefit to critically ill patients, there is little conclusive evidence to support this assertion among medical or nonsurgical patients. Enteral alimentation is currently the most widely used modality for providing nutrition support in the ICU. However, infectious hazards, tissue injury, and aspiration associated with placement and maintenance of orogastric and nasogastric tubes used for the delivery of enteral nutrition suggest that not all patients benefit from this treatment [5].

At the present time, the optimal timing and use of enteral nutrition for mechanically ventilated medical patients is unknown [6]. Unnecessary enteral feeding potentially subjects patients to the risks of aspiration and nosocomial pneumonia, but the avoidance of enteral feeding may delay tissue and organ repair, resulting in prolonged hospitalization [7].

Aim of the work:

The present study aims to compare between early versus delayed enteral feeding in Invasive Mechanical Ventilation (IMV) patients. To assess association linking early nutrition (<48 hours after intubation), feeding route and calorie intake to mortality and risk of Ventilator Associated Pneumonia (VAP) in patient with Invasive Mechanical Ventilation (IMV).

Patients and Methods

Design: Prospective comparative study.

Setting: The present study will be carried out at General Intensive Care Unit (ICU), Ain Shams University Hospitals, Egypt.

Study period: From September 2019 to November 2019.

Patients: A total of 60 adult patients (older than 18 years old) intubated and mechanically ventilated within 48 hours of ICU admission, stayed in ICU for >_72 hours, will be enrolled in the study.

Eligible patients will be selected according to the following inclusion and exclusion criteria:

Inclusion criteria: Any adult patient with an age >_18 years who is received IMV within 48 hours.

Exclusion criteria: Patients transferred to the medical ICU temporarily because of a lack of available beds in 1 of the other hospital ICUs. Patients who will be expected to die or be extubated within 24 hours of ICU admission; if they had received prior mechanical patients will be received prior mechanical ventilation during the same hospitalization. Contraindication to enteral feeding (e.g.: Pancreatitis, short gut syndrome, or malabsorption syndrome). Surgical patients. Malnourished patients by the ICU.

Methods:

Eligible patients will be followed in ICU for a maximum of 12 days or until death or discharge from ICU.

All patients will be subjected to: Different laboratory parameters will be monitored to each patient on enteral nutrition daily until patient becomes stable, then 1-2 times/week. Labs these include: Renal function test and serum electrolytes. Blood glucose. Calcium and albumin. Magnesium and phosphorous.

The primary outcome measured will be the occurrence of Ventilator Associated Pneumonia (VAP).

Secondary outcome measures will be included duration of mechanical ventilation, ICU and hospital lengths of stay (LOS), hospital mortality, diarrhea, and total number of antibiotic days in the ICU.

Ethical consideration: The study protocol will be approved by the Ethics Committee of Faculty of Medicine, Ain Shams University. Written informed consent will be obtained from all the participants.

Statistical methodology:

Sample size justification:

Using STATA program, version 10, setting alpha error at 5% and power at 90%, results from a previous study Woo et al. [8] showed that pneumonia among early group was present in 5.5% of cases while among delayed group, it was present in 44% of cases. Based on these results, the needed sample will be 30 cases per group (total 60). Data entry, processing and statistical analysis was carried out using MedCalc ver. 18.2.1 (MedCalc, Ostend, Belgium). Tests of significance (Mann-Whitney's, Chi square, logistic regression analysis, Spearman's correlation, and ROC curve analysis) were used. Data were presented and suitable analysis was done according to the type of data (parametric and non-parametric) obtained for each variable. *p*-values less than 0.05 (5%) was considered to be statistically significant.

p-value: Level of significance: $p>0.05$: Non-Significant (NS). $p<0.05$: Significant (S). $p<0.01$: Highly Significant (HS).

Descriptive statistics: Mean, Standard Deviation (± SD) and range for parametric numerical data, while median and Inter-Quartile Range (IQR) for non-parametric numerical data. Frequency and percentage of non-numerical data.

Analytical statistics: Mann-Whitney's Test (U-test) was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. Chi-Square test was used to examine the relationship between two qualitative variables. Correlation analysis (using Spearman's method): To assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "*r*" defines the strength and direction of the linear relationship between two variables. Logistic regression: Useful in the prediction of the presence or absence of an outcome based on a set of independent variables. It is similar to a linear regression model but is suited when the dependent variable is qualitative (categorical). The ROC curve (receiver operating characteristic) provides a useful way to evaluate the sensitivity and specificity for quantitative diagnostic measures that categorize cases into one of two groups.

Statistical analysis:

Data entry, processing and statistical analysis was carried out using MedCalc ver. 18.2.1 (MedCalc, Ostend, Belgium). Tests of significance (Mann-Whitney's, Chi square, logistic regression analysis, Spearman's correlation, and ROC curve analysis) were used. Data were presented and suitable analysis was done according to the type of data (parametric and non-parametric) obtained for each variable. *p*-values less than 0.05 (5%) was considered to be statistically significant.

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Results

This was a prospective comparative study conducted on 60 adult patients (older than 18 years old) intubated and mechanically ventilated within 48 hours of ICU admission, stayed in ICU for ≥72 hours will be enrolled in the study; to compare between early versus delayed enteral feeding in Invasive Mechanical Ventilation (IMV) patients. To assess association linking early nutrition (<48 hours after intubation), feeding route and calorie intake to mortality and risk of Ventilator Associated Pneumonia (VAP) in patient with Invasive Mechanical Ventilation (IMV) and shock.

Table (1): Socio-demographic data among 60 patients.

Variables	Frequency (%)
Age (years)	55.4±9.8*
Gender:	
Female	27 (45%)
Male	33 (55%)

*: Mean ± SD.

This table shows that; the mean age of all patients was (55.4±9.8) years. Regarding gender of the patients, the majority (55%) of patients were males; while (45%) were females.

Table (2): Basic clinical data among 60 patients.

Variables	Frequency (%)
BMI	29.8±6.5
HTN	14 (23.3%)
DM	15 (25%)
IHD	9 (15%)
Feeding route (Nasogastric tube)	60 (100%)

BMI : Body Mass Index. DM : Diabetes Mellitus.
HTN : Hypertension. IHD : Ischemic Heart Disease.

This table shows that; the mean BMI of all patients was (29.8±6.5), with (23.3%) had HTN, (25%) had DM, and (15%) had IHD. Regarding feeding route, all patients had nasogastric tube.

Table (3): Laboratory data among 60 patients.

Variables	Mean	SD
Creat. (mg/dL)	0.72 2.	0.22
Alb. (g/dL)	75 109.	0.73
FBS (mg/dL)	08	15.54
Ca (mg/dL)	9.3	1.04
Mg (mEq/dL)	1.87	0.19
Ph (mEq/dL)	3.86	0.53

Alb : Albumin. Ca : Calcium.
Creat. : Creatinine. Mg : Magnesium.
FBS : Fasting Blood Sugar. Ph : Phosphorus.

This table shows that; the mean value of each baseline laboratory variable.

Table (4): Outcome data among 60 patients.

Variables	Frequency (%)
Total number of antibiotic days	10.3±2.4
Hospital stay (days)	16.1±5.3
ICU stay (days)	6.7±3.9
Diarrhea: +ve	8 (13.3%)
VAP: +ve	11 (18.3%)
Mortality rate: +ve	10 (16.7%)

VAP: ventilator associated pneumonia. ICU: Intensive Care Unit.

Regarding outcome data, (13.3%) of patients had diarrhea, (18.3%) had VAP, and (16.7%) suffered mortality. The average antibiotic days was (10.3±2.4) days, the average hospital stay was (16.1±5.3) days, and the average ICU stay was (6.7±3.9) days.

Table (5): Comparison between the 2 groups as regards socio-demographic data using Mann-Whitney's U and Chi square tests.

Variable	Early feeding group (30) Median (IQR)	Late feeding group (30) Median (IQR)	Mann-Whitney's U-test *p*-value
Age (years)	52.5 (45-63)	57.5 (47-66)	=0.5197
Variable	**Early feeding group (30)**	**Late feeding group (30)**	**Chi square test *p*-value**
Gender:			
Female	12 (40%)	15 (50%)	=0.4401
Male	18 (60%)	15 (50%)	

IQR: Inter-Quartile Range. *: Percentage of column total.

Comparative study between the 2 groups revealed non-significant difference as regards age and sex of the patients (*p*>0.05).

Table (6): Comparison between the 2 groups as regards basic clinical data using Mann-Whitney's U and Chi square tests.

Variable	Early feeding group (30) Median (IQR)	Late feeding group (30) Median (IQR)	Mann-Whitney's U-test *p*-value
BMI	26.7 (23.8-32.9)	31.8 (25.9-35.3)	=0.1392
Variable	**Early feeding group (30)**	**Late feeding group (30)**	**Chi square test *p*-value**
HTN: +ve	8 (26.7%)	6 (20%) 6	=0.5449
DM: +ve	9 (30%)	(20%) 5 (	=0.3751
IHD: +ve	4 (13.3%)	16.7%)	=0.7200

*: Percentage of column total.

Comparative study between the 2 groups revealed non-significant difference as regards all basic clinical data (*p*>0.05).

Table (7): Comparison between the 2 groups as regards laboratory data using Mann-Whitney's U-test.

Variable	Early feeding group (30) Median (IQR)	Late feeding group (30) Median (IQR)	Mann-Whitney's U-test *p*-value
Creat. (mg/dL)	0.7 (0.6-0.8)	0.7 (0.6-1)	=0.8401
Alb. (g/dL)	2.75 (2-3.3)	2.7 (2.3-3.2)	=0.9881
FBS (mg/dL)	106.5 (96-119)	107.5 (100-114)	=0.7503
Ca (mg/dL)	9.5 (8.5-10.2)	9.4 (8.7-9.9)	=0.6894
Mg (mEq/dL)	1.9 (1.7-2.1)	1.8 (1.7-2)	=0.6695
Ph (mEq/dL)	3.9 (3.5-4.1)	3.8 (3.4-4.3)	=0.8997

Comparative study between the 2 groups revealed non-significant difference as regards all baseline laboratory data (*p*>0.05).

Table (8): Comparison between the 2 groups as regards outcome data using Mann-Whitney's U and Chi square tests.

Variable	Early feeding group (30) Median (IQR)	Late feeding group (30) Median (IQR)	Mann-Whitney's U-test *p*-value
• Total number of antibiotic days	10 (7-12)	10 (8-13)	=0.2382
• Hospital stay(days)	15 (9-19)	17 (14-22)	=0.0559
• ICU stay (days)	4 (3-5)	7.5 (5-11)	=0.000048**
Variable	**Early feeding group (30)**	**Late feeding group (30)**	**Chi square test *p*-value**
Diarrhea: +ve	5 (16.7%)	3 (10%)	=0.4513
VAP: +ve	2 (6.7%)	9 (30%)	=0.02*
Mortality rate: +ve	2 (6.7%)	8 (26.7%)	=0.039*

*: Percentage of column total.

Comparative study between the 2 groups revealed; highly significant decrease in ICU stay in early feeding group; compared to late feeding group; with highly significant statistical difference ($p < 0.01$). Comparative study between the 2 groups revealed; significant decrease in VAP and mortality in early feeding group; compared to late feeding group; with significant statistical difference ($p<0.05$ respectively). Comparative study between the 2 groups revealed non-significant difference as regards antibiotic days, hospital stay and diarrhea ($p >0.05$).

Table (9): Spearman's correlation analysis for baseline clinical/ laboratory factors associated with ICU stay.

Associated factor	ICU stay	
	rho	p
Age (years)	–0.156	=0.2333
BMI	0.379	=0.0028**
Creat. (mg/dL)	–0.0511	=0.6980
Alb. (g/dL)	–0.0990	=0.4517
FBS (mg/dL)	–0.0422	=0.7491
Ca (mg/dL)	–0.0378	=0.7742
Mg (mEq/dL)	0.191	=0.1435
Ph (mEq/dL)	–0.0978	=0.4574

rho: Spearman's rho (correlation coefficient).

Spearman's correlation analysis shows that; BMI had a highly significant positive correlation with ICU stay; with highly significant statistical difference (p=0.0028).

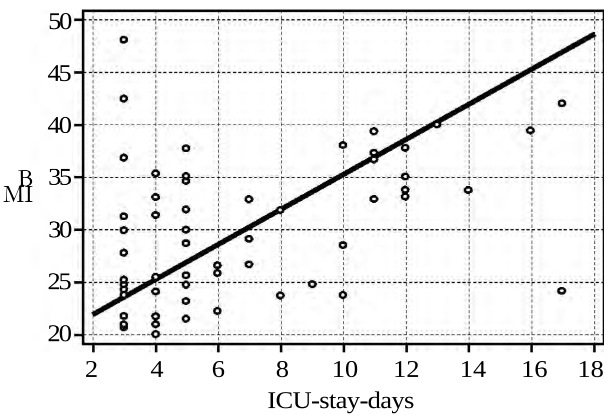

Fig. (1): Correlation between ICU stay and BMI.

Table (10): Logistic regression model for the factors affecting mortality occurrence using forward method.

Predictor factor	Coefficient	OR	p-value
(Constant)	–5.78462		
BMI	0.14895	1.1606	0.018*
Late feeding	1.64833	1.1924	0.007**

Other factors excluded from the model as (p-value >0.1).
OR: Odds Ratio.

Logistic regression analysis shows that; after applying (forward method) and entering some predictor variables; the increase in BMI and late feeding technique; had an independent effect on increasing the probability of mortality occurrence; with significant statistical difference ($p<0.05$ respectively).

Table (11): Logistic regression model for the factors affecting VAP occurrence using forward method.

Predictor factor	Coefficient	OR	p-value
(Constant)	–6.16314		
BMI	0.16619	1.1808	0.0099**
Late feeding	1.88660	1.1516	0.042*

Other factors excluded from the model as (p-value >0.1).
OR: Odds Ratio.

Logistic regression analysis shows that; after applying (forward method) and entering some predictor variables; the increase in BMI and late feeding technique; had an independent effect on increasing the probability of VAP occurrence; with significant statistical difference ($p<0.05$ respectively).

Table (12): Roc-curve of early enteral feeding to predict patients' stay outcomes.

Variable	AUC	SE	Criterion "Cut off point"	Sensitivity (%)	Specificity (%)	p-value
Antibiotic days	0.588	0.0739	≤7	30	93.33	0.2350
Hospital stay	0.643	0.0713	≤16	63.33	63.33	0.044*
ICU stay	0.802	0.0573	≤4	63.33	86.67	<0.0001**

ROC: Receiver Operating Characteristic.
AUC: Area Under Curve. SE: Standard Error.

By using ROC-curve analysis, early enteral feeding predicted shortening of ICU stay, with good (80%) accuracy, sensitivity=63% and specificity=87% ($p<0.01$). By using ROC-curve analysis, early enteral feeding predicted shortening of hospital stay, with failed (64%) accuracy, sensitivity= 63% and specificity=63% ($p<0.05$). By using ROC-curve analysis, early enteral feeding showed non-significant predictive values in shortening antibiotic days ($p>0.05$).

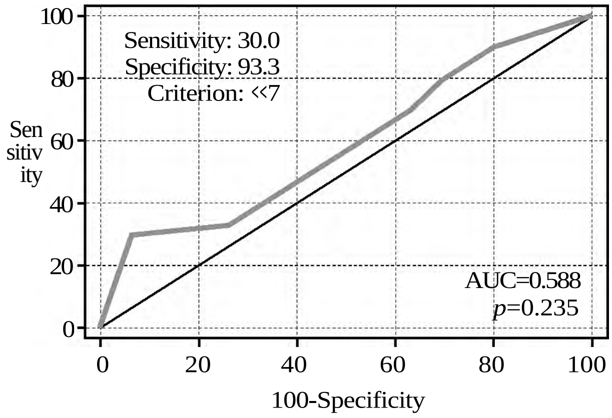

Fig. (2): ROC curve of early enteral feeding (antibiotic days).

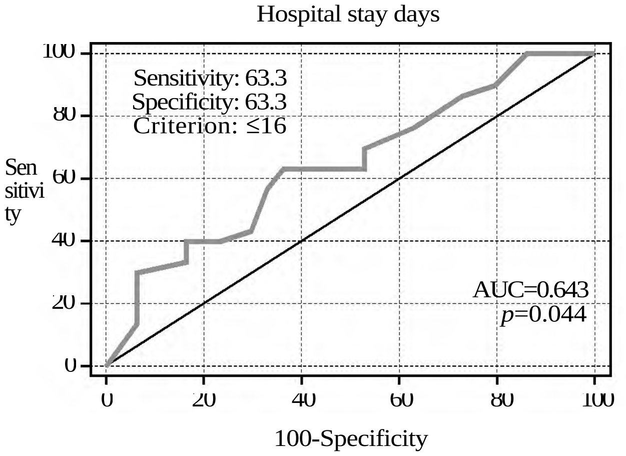

Fig. (3): ROC curve of early enteral feeding (hospital stay).

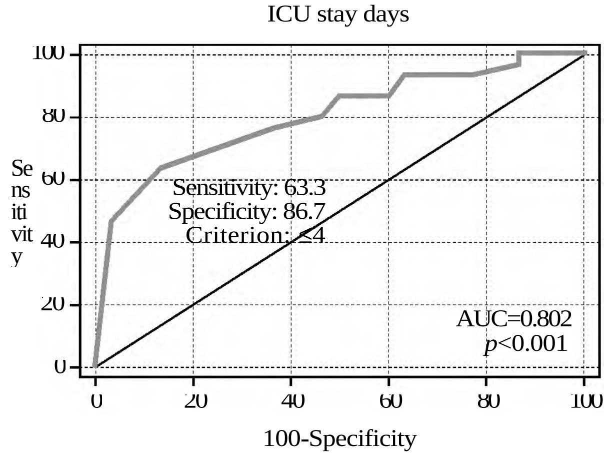

Fig. (4): ROC curve of early enteral feeding (short ICU stay).

Discussion

This was a prospective comparative study conducted on 60 adult patients (older than 18 years old) intubated and mechanically ventilated within 48 hours of ICU admission, stayed in ICU for ≥72 hours will be enrolled in the study; to compare between early versus delayed enteral feeding in Invasive Mechanical Ventilation (IMV) patients. To assess association linking early nutrition (<48 hours after intubation), feeding route and calorie intake to mortality and risk of Ventilator Associated Pneumonia (VAP) in patient with Invasive Mechanical Ventilation (IMV) and shock.

Patients will be scheduled to received their estimated total daily enteral nutritional requirements on either day 1 (early-feeding group) or day 5 (late-feeding group) of mechanical ventilation. Patients in the late-feeding group will be also scheduled to receive 20% of their estimated daily enteral nutritional requirements during the first 4 days of mechanical ventilation. Thirty (50%) consecutive eligible patients will be entered into the early-feeding group and thirty (50%) patients will be enrolled in the late-feeding group. All patients will be received enteral nutrition via continuous infusion by a feeding pump.

Eligible patients will be followed in ICU for a maximum of 12 days or until death or discharge from ICU.

The primary outcome measured will be the occurrence of ventilator-associated pneumonia. Secondary outcome measures will be included duration of mechanical ventilation, ICU and hospital Lengths of Stay (LOS), hospital mortality, diarrhea, and total number of antibiotic days in the ICU.

Different laboratory parameters will be monitored to each patient on enteral nutrition daily until patient becomes stable, then 1-2 times/week. These include:

Renal function test and serum electrolytes, blood glucose, Calcium, albumin, Magnesium and phosphorous.

We found that; the mean age of all patients was (55.4±9.8) years. Regarding gender of the patients, the majority (55%) of patients were males; while (45%) were females, which came in agreement with Mok et al. **[9]**, Mosier et al. **[10]**, Nguyen et al. **[11]**, Poulard et al. **[12]**, Wereszczynska-Siemiatkowska et al. **[13]** and Woo et al. **[8]**.

Mok et al., reported that, the early group and delayed group were similar in age (median 62.0 years vs. 64.2 years; p=0.17) and sex (males 64.6% vs. 63.4%; p=0.91) **[9]**.

Mosier et al., reported that, eligible subjects included all mechanically ventilated adults with complete outcome data enrolled in the burn arm of the "inflammation and host response to injury" program from March 2004 to September 2009, with age was 41 **[15]** in all groups **[10]**.

Nguyen et al., reported that, the demographics, disease severity, admission diagnosis, and the use of medications that potentially affect gastrointestinal function were comparable between patients who received early and delayed feeding. The age was 54.9±3.3 in early feeding group and was 56. 3±3.4 in delayed group **[11]**.

Poulard et al., reported that, this prospective before-after study was performed from July 2004 to July 2006 in the 15-bed adult medical-surgical Intensive Care Unit (ICU) of the District Hospital

Center in La Roche-sur-Yon, France. The age was 62±16 [12].

Wereszczynska-Siemiatkowska et al., reported that, of the 420 patients with AP, 197 patients (47%) met the inclusion and exclusion criteria and were considered for the final analysis. Of the 197 patients with severe AP, 97 patients (49%) were allocated to group A ("early" EN) and 100 patients (51 %) were allocated to group B ("delayed" EN). The age was 49 (39-56) [13].

Woo et al., reported that, throughout the study timeframe, 146 patients were evaluated for inclusion. Of the 146 patients, 110 patients met 1 or more exclusion criteria, leaving 36 patients eligible for inclusion. The age was 66.1±17.1 in early group and was 60.4±15.6 in delayed group [8].

We found that; the mean BMI of all patients was (29.8±6.5), with (23.3%) had HTN, (25%) had DM, and (15%) had IHD. Which came in agreement with Yin et al. [14], Woo et al. [8], Nguyen et al. [11] and Chouillard et al. [15].

Yin et al., reported that, of the 88 patients, 28 (31.8%) received early enteral feeding within 72 h of SICU admission. These patients were allocated to the early-initiation group, whereas the remaining 60 patients who received enteral feeding after 72h of admission were allocated to the delayed-initiation group. BMI (kg/m^2), mean ± SD was 22.1±2.4 in early group and 22.7±2.2 in delayed group with *p*=.022 [14].

Woo et al., reported that, 146 patients were evaluated for inclusion. Of the 146 patients, 110 patients met 1 or more exclusion criteria, leaving 36 patients eligible for inclusion, with mean BMI, kg/m^2 was 29.4±13.9 in early group and was 26.3 ±6.8 in delayed one [8].

Nguyen et al., reported that, the demographics, disease severity, admission diagnosis, and the use of medications that potentially affect gastrointestinal function were comparable between patients who received early and delayed feeding. Body mass index (kg/m^2) 28.3±1.7 in early group and 27.4±1.9 in delayed group [11].

Chouillard et al., reported that, fifty-nine patients admitted to the ICU were included in the study. The flow diagram presents enrollment, allocation, losses to follow-up, and number of patients per treatment group. BMI, kg/m^2, mean ± SD was 25.18±1.97 in delayed group and 24.86±2.06 in early group [15].

Regarding outcome data, (13.3%) of patients had diarrhea, (18.3%) had VAP, and (16.7%) suffered mortality. Which came in agreement with Mok et al. [9] and Woo et al. [8].

Mok et al., reported that, both groups spent a median of 5 calendar days (whole and part calendar days) in intensive care (*p*=0.88). Intensive care mortality was 13.1 % in the early group and 15.4% in the late group (*p*=0.65) [9].

Woo et al., reported that, 4 patients in the early group and 2 patients in the delayed group experienced diarrhea during the ICU admission [8].

The average antibiotic days was (10.3±2.4) days, the average hospital stay was (16.1±5.3) days, and the average ICU stay was (6.7±3.9) days, which came in agreement with Poulard et al. [12], Wereszczynska-Siemiatkowska et al. [13].

Poulard et al., reported that, the mean cumulative erythromycin dose over the 7-day study period was higher in the control group (1593±1775mg) than in the intervention group (888±1515mg) (p <.05) [12].

Wereszczynska-Siemiatkowska et al., reported that, of the 420 patients with AP, 197 patients (47%) met the inclusion and exclusion criteria and were considered for the final analysis. Of the 197 patients with severe AP, 97 patients (49%) were allocated to group A ("early" EN) and 100 patients (51%) were allocated to group B ("delayed" EN). Antibiotic prophylaxis, n (%) was 84 (87) in delayed group and 94 (94) in early one with *p*=0.078 [13].

Woo et al., reported that, median hospital stay appeared shorter in the EEN group (10.4 days) compared with the delayed group (16.9 days) [8].

Comparative study between the 2 groups revealed non-significant difference as regards age and sex of the patients (*p*>0.05), which came in agreement with Poulard et al. [12].

Poulard et al., reported that, age, sex, McCabe score, weight, SAPS II, SOFA score, admission diagnosis, and risk factors for enteral feeding intolerance did not differ between the 2 groups [12].

Comparative study between the 2 groups revealed non-significant difference as regards all basic clinical data (*p*>0.05), which came in agreement with Wereszczynska-Siemiatkowska et al., [13], Woo et al., [8] and Mok et al., [9].

Wereszczynska-Siemiatkowska et al., reported that, there were no differences between the study groups in the BISAP score, the Ranson score, the Panc 3 score, the APACHE II score, and the SOFA score on day 1. In both groups, a gradual decrease in APACHE II scores over the study days was observed, with no significant difference between groups A and B on any of the measured days **[13]**.

Woo et al., reported that, there were no significant differences in the baseline characteristics of the 36 included patients **[8]**.

Mok et al., reported that, there were no statistically significant differences between the groups in intensive care diagnosis (categorized by organ system and surgical status), there was a weak trend toward fewer cardiovascular non-surgical diagnoses in the early group (10.9% vs. 17.1%; p =0.12) **[9]**.

Comparative study between the 2 groups revealed; significant decrease in VAP and mortality in early feeding group; compared to late feeding group; with significant statistical difference ($p<0.05$ respectively), which came in agreement with Tian et al. **[16]**, Mosier et al. **[10]** and Wereszczynska-Siemiatkowska et al., **[13]**.

Tian et al., reported that, analysis within subgroups revealed that early EN reduced pneumonia compared with delayed enteral intake (OR, 0.27; 95% CI, 0.10-0.70; p=0.0071; I^2=0%), and there was a strong trend toward a reduction in pneumonia when early EN was compared with PN (OR, 0.80; 95% CI, 0.63-1.00; p=0.052) **[16]**.

Mosier et al., reported that, they evaluated the influence of early EN on time to ventilator-associated pneumonia development and found that early EN was not a significant predictor (adjusted Hazard Ratio [HR]=1.23, p=.41, 95% Confidence Interval [CI] 0.74-2.04) **[10]**.

Wereszczynska-Siemiatkowska et al., reported that, overall, pulmonary complications occurred in 91 patients (46.2%): 42 patients (43.3%) in group A and 49 patients in group B (49%) **[13]**.

Our result came in disagreement with Yin et al., **[14]**.

Yin et al., reported that, there were no differences in the incidence of pneumonia, intra-abdominal abscess, wound infection, and bacteremia between the two groups **[14]**.

Comparative study between the 2 groups revealed non-significant difference as regards antibiotic days, hospital stay and diarrhea ($p>0.05$), which came in agreement with Poulard et al., **[12]**.

Poulard et al., reported that, no differences found regarding mean duration of mechanical ventilation (13±9 vs. 14±12 days, respectively; p=.65), mean length of stay in the ICU (18±14 vs. 17±15 days; p=.59), mean length of stay in hospital (27±22 vs. 27±22 days; p=.98), ICU mortality (24.5% vs. 35%; p=.13), or hospital mortality (35.3% vs. 42.7%; p=.32) **[12]**.

Logistic regression analysis shows that; after applying (forward method) and entering some predictor variables; the increase in BMI and late feeding technique; had an independent effect on increasing the probability of mortality occurrence; with significant statistical difference ($p<0.05$ respectively), which came in agreement with Woo et al., **[8]**, Tian et al., **[16]** and Koretz and Lipman, **[17]**.

Woo et al., reported that, total hospital mortality was higher in those patients who received delayed vs. EEN **[8]**.

Tian et al., reported that, Analysis within subgroups revealed that early EN reduced mortality compared with delayed enteral intake (OR, 0.45; p =0.038; I^2=0%), whereas a mortality difference was not detected when early EN was compared with PN (OR, 1.04; p=0.58; I^2=30%) **[16]**.

Koretz and Lipman reported that, when all trials were combined with meta-analysis, early enteral nutrition had a favorable effect on mortality (RR 0. 61, 95% CI 0.41, 0.89) and infectious morbidity (RR 0.80, 95% CI 0.72, 0.89), but not on non-infectious morbidity or any secondary outcome **[17]**.

Logistic regression analysis shows that; after applying (forward method) and entering some predictor variables; the increase in BMI and late feeding technique; had an independent effect on increasing the probability of VAP occurrence; with significant statistical difference ($p<0.05$ respectively), which came in agreement with Nguyen et al., **[11]**, Woo et al., **[8]**, Tian et al., **[16]** and Heighes et al., **[18]**.

Nguyen et al., reported that, there were fewer ventilator-free days in the delayed feeding groups as compared to the early feeding groups (15.60 ± 1.6 days vs. 20.30±1.1 days; p=.03). Although the number of patients (n=6) who had ventilator-associated pneumonia in the delayed feeding group was twice the number of patients who received early feeding (n=3), the difference did not reach statistical significance (p=.22) **[11]**.

Woo et al., reported that, incidence of new pneumonia was significantly higher in the delayed group compared with the EEN group (44% vs. 55.5%, p=.02) **[8]**.

Tian et al., reported that, analysis within subgroups revealed that early EN reduced pneumonia compared with delayed enteral intake (OR, 0.27; 95% CI, 0.10-0.70; p=0.0071; I^2=0%), and there was a strong trend toward a reduction in pneumonia when early EN was compared with PN (OR, 0.80; 95% CI, 0.63-1.00; p=0.052) **[16]**.

Heighes et al., reported that, in elective intestinal surgery, meta-analysis demonstrated a statistically significant reduction in mortality associated with early EN (Relative Risk [RR] 0.41, 95% Confidence Interval [CI] 0.18 to 0.93, p=0.03, I^2=0.0%) **[18]**.

By using ROC-curve analysis, early enteral feeding predicted shortening of ICU stay, with good (80%) accuracy, sensitivity=63% and specificity=87% (p<0.01), which came in agreement with Heighes et al., **[18]**.

Heighes et al., reported that, two systematic reviews reported a reduction in length of stay associated with early EN: Elective intestinal surgery (length of stay weighted mean difference –0.60 days, 95% CI –0.66 to –0.54, heterogeneity p=0.09) and acutely ill hospitalized patients (length of stay weighted mean difference –2.2 days, 95% CI –3.63 to –0.81, p=0.004, heterogeneity p=0.0012 **[18]**.

Conclusion:

Evidence shows improvement in patient outcomes associated with the use of EEN in a diverse population of critically ill patients. The results of our study strengthen our understanding of the benefits of EEN. These benefits were evident even though <50% of the patients in each group reached a goal rate of EN. Given the potential ease of consistent implementation of EEN, the minimal cost associated with such a practice, and the potentially substantial.

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دراسة تآثير التغذية المعوية المبكرة مقابل المتآخرة لدى مرضى الحالات الحرجة الخاضعين للتنفس الصناعى

الهدف من الدراسة: دراسة تآثير التغذية المعوية المبكرة مقابل المتآخرة لدى مرضى الحالات الحرجة الخاضعين للتنفس الصناعى.

المرضى وطرق العلاج: سيتم جدولة المرضى لتلقى إجمالى الإحتياجات الغذائية المعوية اليومية المقدرة فى اليوم الأول (مجموعة التغذية المبكرة) أو اليوم الخامس (مجموعة التغذية المتآخرة) من التهوية الميكانيكية. ومن المقرر أيضاً أن يتلقى المرضى فى مجموعة التغذية المتآخرة ٢٠٪ من إحتياجاتهم الغذائية اليومية المقدرة خلال الآيام الآربعة الآولى من التهوية الميكانيكية. سيتم إدخال ثلاثين (٥٠٪) من المرضى المؤهلين على التوالى فى مجموعة التغذية المبكرة وسيتم تسجيل ثلاثين (٥٠٪) مريضاً فى مجموعة التغذية المتآخرة. سيتلقى جميع المرضى تغذية معوية عن طريق التسريب المستمر بواسطة مضخة التغذية. سيتم متابعة المرضى المؤهلين فى وحدة العناية المركزة لمدة آقصاها ١٢ يوماً آو حتى الوفاة آو الخروج من وحدة العناية المركزة.

النتائج: عدم وجود فروق ذات إحصائية فيما يتعلق بعمر وجنس المرضى. عدم وجود فروق ذات دلالة إحصائية فيما يتعلق بجميع البيانات السريرية الآساسية. إختلاف غير مهم فيما يتعلق بجميع بيانات المختبر الآساسية. إنخفاض كبير فى البقاء فى وحدة العناية المركزة فى مجموعة التغذية المبكرة، مقارنة بمجموعة التغذية المتآخرة، مع فرق إحصائى كبير.

الإستنتاج: زيادة مؤشر كتلة الجسم وتقنية التغذية المتآخرة. كان لها تآثير مستقل على زيادة إحتمالية حدوث الوفيات، مع وجود فرق إحصائى كبير. زيادة مؤشر كتلة الجسم وتقنية التغذية المتآخرة. كان له تآثير مستقل على زيادة إحتمالية حدوث VAP، مع وجود فرق إحصائى كبير. بإستخدام تحليل منحنى ROC، تنبآت التغذية المعوية المبكرة بقصر مدة الإقامة فى المستشفى ، بدقة فاشلة (٦٤٪)، حساسية=٦٣٪ ونوعية=٦٣٪.