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Impact of a natural versus commercial enteral-feeding on the occurrence of diarrhea in critically ill cardiac surgery patients. A retrospective cohort study

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A R T I C L E I N F O

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A B S T R A C T

Background: Diarrhea is an important complication in critically ill patients undergoing enteral feeding. The occurrence of diarrhea may lead to systemic and local complications and negatively impacts on nursing workload and patient's wellbeing. An enteral feeding based on blenderized natural food could be beneficial in reducing the risk of diarrhea. No study has compared natural and commercial enteral feedings in critically ill cardiac surgery patients.

Objective: The aim of this study was to compare the risk of diarrhea occurrence in two cohorts of patients fed a blenderized natural food diet or commercial enteral feeding preparations, respectively.

Design: Retrospective cohort study.

Setting: Cardiac-Surgery Intensive Care Unit of a University Hospital.

Participants: Two-hundred and fifteen patients admitted to the postoperative cardiac surgery intensive care unit were included, 103 fed blenderized natural enteral feeding and 112 fed commercial formulas.

Methods: Commercial enteral formulas were delivered by continuous pump administration, while natural enteral feeding by bolus 3 times per day. Diarrhea was documented in the presence of three or more evacuations of loose or watery stool (or an amount above 250 ml) per day. The presence of diarrhea was recorded daily from the beginning to the end of the enteral feeding, up to a maximum of 8 days. The unadjusted time to the first event of diarrhea between the two enteral feeding groups was compared. Adjusted comparison was then performed by fitting a multivariable Cox Proportional-Hazards model, adjusted for potential confounders for diarrhea occurrence (i.e. administration of inotropes, vasopressors, prokinetics, antibiotics, oral nutritional supplements, antifungal agents, sedatives, opioids, probiotics, laxatives).

Results: In unadjusted survival analysis the probability of diarrhea was significantly lower in the natural enteral feeding group (log rank test: $p = 0.023$). In the multivariable model patients in natural enteral feeding cohort showed a non-significant trend towards an almost halved risk of experiencing diarrhea (hazard ratio: 0.584; 95% confidence interval: 0.335–1.018; $p = 0.058$) compared to those fed commercial enteral feeding.

Conclusions: Administration of a blenderized diet based on natural food for enteral feeding can reduce the incidence of diarrhea in cardiac surgery critically ill patients. This strategy may reduce the risk of diarrhea-associated malnutrition and systemic and local complications, also having a positive impact on nursing workload and patient wellbeing.

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What is already known about the topic?

- The administration of enteral feeding in critically ill patients is burdened by the risk of diarrhea.
- The occurrence of diarrhea may hamper the delivery of an adequate calorie provision in critically ill patients.

What this paper adds

- Patients receiving a blenderized natural enteral feeding have a reduced risk of diarrhea compared to those fed commercial formulas.
- Although preparation and administration of natural food is more time-consuming, the related reduced risk of diarrhea occurrence can have a positive impact on nursing workload and patient wellbeing.

1. Introduction

Critically ill patients requiring mechanical ventilation are at high risk of malnutrition, which can lead to infections, muscle wasting, delayed recovery and increased mortality. In the subgroup of cardiac surgery patients–which are characterized by additional distinguishing features, including systemic inflammatory response, ischemia and reperfusion injury–malnutrition aggravates the risk of complications related to the surgical trauma and to anesthesia (Hill et al., 2018). Recent guidelines recommend starting enteral feeding by 24–48 h after intensive care unit admission (Blaser et al., 2017; Singer et al., 2019; Taylor et al., 2016). Unfortunately, this strategy is often burdened by early complications precluding the achievement of satisfactory calorie delivery (Blaser et al., 2014). Feeding intolerance is particularly relevant among enteral feeding complications being characterized by three main features: (1) large gastric residual volumes; (2) inadequate delivery of enteral feeding; and (3) intolerance symptoms, such as vomiting, abdominal distension, ileus, or diarrhea (Blaser et al., 2014). The pathophysiological mechanisms for the onset of diarrhea are related to reduced water absorption due to the presence of osmotically active substances in the bowel lumen, shortened bowel transit time, or imbalance between gut absorption and secretion of electrolytes leading to increased water secretion (Blaser et al., 2015; Silk and Bowling, 2017).

The occurrence of diarrhea may lead to systemic (e.g., hydroelectrolyte imbalance) and local complications (e.g., dermatitis, pressure ulcers), to increased risk for healthcare-associated infections (Beeckman, 2017; Binks et al., 2015; García et al., 2013), thus increasing intensive care unit length of stay and mortality (Jakob et al., 2017; Tirlapur et al., 2016). Furthermore, diarrhea has a deep impact on nursing workload (Heidegger et al., 2016) and on the quality of life and dignity of both patients and relatives (García et al., 2013). Accordingly, minimizing the occurrence of diarrhea should be a key aim for the multiprofessional team.

The incidence of enteral feeding-related diarrhea is highly variable, ranging from 13% to 70% depending on feed composition (e.g., high energy, high osmolarity, low fiber content) and method of administration (e.g., bolus feeding or continuous administration, flow rate, temperature) (Atasever et al., 2018; Blaser et al., 2015, 2014; Gungabissoon et al., 2015; Jakob et al., 2017; Kadamani et al., 2014; Kim et al., 2017; Schmidt et al., 2018; Thibault et al., 2013). The impact of enteral feeding composition on gut physiology (digestion, absorption, gut enzymes, hormones, gut microbiota, often affected by antibiotics administration) and the related risk for diarrhea are still debated issues. When comparing natural with industrially prepared foods, an interesting concept to refer to is the food matrix. The food matrix is related to the microstructure of foods, which may explain the different behavior exhibited by a component or a nutrient in the setting of a whole food as compared with its isolated form (e.g., in a solution). In food matrix, composition and structure of food products have an effect on the interaction between nutrients, their absorption and functionality, explaining specific health effects that cannot be explained by individual nutrients (Aguilera, 2018). Although the relationship between food matrix and digestion, nutrition and human health is not completely understood, it's reasonable to think that food matrix may be different in commercial and in natural foods. With the sole exception of vegetable oils, in almost all commercial enteral feeding preparations nutrients (e.g., milk protein) are extracted from food, isolated and concentrated in powder form, thus being devoid of the natural food matrix (Schmidt et al., 2018). In addition, enteral formulas do not contain specific nutrients which could cause intestinal problems (e.g., lactose, cholesterol, purines, gluten). Since human gut physiology and intestinal microbiota are intended to process natural food, thus including the food matrix, administration of natural or industrially prepared food may have a different impact on gastrointestinal complications (Jacobs and Tapsell, 2007).

In recent years, new insights have been provided about the potential beneficial effects of natural enteral feeding. Although encouraging, evidence in the field is available mainly for outpatients suffering from chronic conditions, while literature about the use of natural enteral feeding in critically ill patients is still very limited (Gallagher et al., 2018; Schmidt et al., 2018). Furthermore, no study has compared natural versus commercial formulas in adult critically ill cardiac surgery patients.

The aim of this study was therefore to compare the impact of a blenderized natural food diet versus commercial enteral feeding preparations on diarrhea occurrence in adult postoperative critically ill cardiac surgery patients.

2. Materials and methods

2.1. Study design and setting

The INTERLINEAR Study (Impact of Natural Versus Commercial Enteral-feeding on Diarrhea in Critically Ill Cardiac Surgery Patients) was a retrospective cohort study conducted in the cardiac-surgery intensive care unit, University Hospital of Trieste (Italy).

The study was approved by the Regional Bioethics Committee (protocol number: 8566-2019) and was conducted according to the Declaration of Helsinki. At hospital admission, all enrolled patients or her/his legal representative authorized the use of their clinical data for study purposes.

2.2. Study population

All consecutive patients who were admitted postoperatively in the intensive care unit between 01/01/2012 and 31/05/2018 were considered in the study. Inclusion criteria were: (1) undergoing open-heart surgery; (2) age ≥18 years; (3) undergoing postoperative enteral feeding. Exclusion criteria included history of inflammatory bowel disease, documented Clostridium difficile colitis or bowel ischemia.

Two cohorts of patients were selected, one fed blenderized natural enteral feeding and the other one commercial enteral feeding formula. In the study setting, according to a new enteral feeding policy the administration of commercial enteral formulas was abandoned in favor of natural enteral feeding starting from 01/01/2015. Inclusion of patients in the commercial or natural enteral feeding cohort was determined based on above time criterion.

2.3. Enteral nutrition composition

Natural enteral feeding consisted of a standard balanced diet prepared by the hospital kitchen and subdivided into three main meals: (1) a breakfast with coffee milk or tea, biscuits and a modular commercial protein supplement; (2) a lunch comprising a first course (e.g., a soup), a second course of meat or fish, a side dish of vegetables, grated cheese and olive oil, and a dessert (yogurt or fruit juice); (3) a dinner similar to lunch. The solid foods were blenderized and diluted with an appropriate amount of water to allow tube administration. Overall, this diet provided daily: energy: 1700 Kcal; protein: 68.5 g (15%); lipids: 52 g (27%); and carbohydrates: 268 g (58%).

Commercial enteral feeding consisted of a commercially available formula, which was chosen according to the patient's conditions or comorbidities (list in Supplementary Table S1).

For both patients fed natural or commercial enteral feeding, daily caloric target was individually calculated using a simple weight-based-equation (25–30 kcal/kg/day) (Atasever et al., 2018; Taylor et al., 2016). Accordingly, in order to cover the individual daily requirement natural enteral feeding was integrated with oral nutritional supplements (list in Supplementary Table S1) or the amount of food was proportionally reduced, as appropriate.

2.4. Enteral feeding administration protocol

In both cohorts, enteral feeding was started 48–72 h after intensive care unit admission in patients needing prolonged mechanical ventilation, unless the following conditions were present: expected new surgery, severe hemodynamic instability, excessive gastric residual volume, digestive hemorrhage or ileus. All administrations were carried out via naso-gastric feeding tubes.

The modality of administration was different for natural and commercial enteral feeding:

- commercial enteral feeding was administered by continuous pump infusion for approximately 15 h a day, starting at 20–30 ml/h and gradually increasing to reach the target rate in order to provide the calculated energy and protein requirements.
- natural enteral feeding was administered by bolus 3 times per day (breakfast, lunch, dinner), to respect the normal mealtime. Bolus administration was chosen because natural food should be administered within one hour from its preparation. In addition, the characteristics of the blenderized food entailed a greater risk of tube obstruction, better controlled through administration through a syringe.

When nutritional support via the enteral route was unable to cover individual energy and protein requirements because of feeding intolerance, the patient was switched to parenteral nutrition.

2.5. Collected variables

The following data were collected from the clinical documentation in order to compare the baseline characteristics of the natural and commercial enteral feeding cohorts:

- sociodemographic characteristics (gender and age)
- Charlson Comorbidity Index, to describe the comorbility condition (Charlson et al., 1987)
- EuroSCORE II, calculated at patient's hospital admission to predict the cardiac surgery-related risk of death (Noyez et al., 2012)
- duration (from incision to skin closure time) and type of the surgery
- duration of extra corporeal circulation
- presence of intra-aortic balloon pump
- adoption of veno-arterial extra corporeal membrane oxygenation
- need for new surgery due to immediate postoperative complications (e.g. bleeding).

Moreover, drugs and oral nutritional supplements administered in intensive care unit before and during the observation period were collected for their potential impact on development of diarrhea (García et al., 2013).

2.6. Study outcome

Diarrhea was defined as the presence of loose or watery stool (Bristol Stool Chart type 7) (Jakob et al., 2017; Kadamani et al., 2014) with three or more bowel evacuations per day or with an amount above 250 ml per day, depending on whether a stool collection system was used or not (Blaser et al., 2015; Kim et al., 2017; Lewis and Heaton, 1997; Schmidt et al., 2018). Since studies documented that in intensive care unit patients diarrhea occurs mostly within three days from enteral feeding starting and lasts for a median of 2 days (interquartile range [IQR] 1–3) (Wang et al., 2018), the presence of diarrhea was recorded every day during enteral feeding administration for a maximum of 8 days. The time (day) when the first event of diarrhea occurred during this observation period in the commercial and natural enteral feeding cohorts was used as main outcome measure.

2.7. Sample size

Sample size estimation was performed using a Monte-Carlo simulation approach. The procedure is summarized below:

1. A time to event database was generated using the flexible-hazard method simulation procedure described by Harden and Kropko (2018). A Cox regression coefficient of $\beta_{trt} = -0.59$ was assumed, corresponding to an HR for natural enteral feeding of 0.55 compared to commercial enteral feeding.
2. A Cox proportional hazard model was estimated, checking whether the null hypothesis (no treatment effect) could be rejected with 95% confidence.
3. Steps 1 and 2 underwent 1000 replications.
4. The empirical power was calculated considering the proportion of replications in which type II error did not occur.

Considering such a framework, the enrollment of 100 patients per group was necessary to achieve an empirical power of 0.8.

2.8. Statistical analysis

Descriptive statistics were reported as median (IQR) for continuous variables. Percentage (absolute number) was used for categorical variables. Differences of patient characteristics between groups were assessed by using Kruskal–Wallis test for continuous variables, and Pearson χ^2 test or Fisher's exact test for categorical variables, depending on at least five observations in each cell were present, respectively. *P*-values were adjusted using Benjamini–Yekutieli correction since individuals were not randomized to nutritional groups.

"Survival" analysis was adopted to separate patients with longer from those with shorter diarrhea-free times within the 8-days observation window. Accordingly, observations were right-censored after 8 days of NE administration. Observations containing missing entries were removed. A normalized variable to describe diarrhea incidence was created by reporting the relative incidence of days with diarrhea for 100 days of observation.

Both unadjusted and adjusted analyses were performed to compare time to the first event of diarrhea between commercial and

Table 1
Descriptive characteristics of natural enteral feeding (NEF) and commercial enteral feeding (CEF) cohorts at baseline.

Variable	N	Combined	CEF	NEF	p^*
Age	214	72 (66–78)	72 (66–77)	72 (65–78)	1
Sex	212				1
Female		31% (65)	31% (34)	31% (31)	
Male		69% (147)	69% (77)	69% (70)	
EuroScore II (%)	215	9.0 (4.0–26.5)	9.0 (4.0–26.3)	8.0 (3.5–27.0)	1
Charlson comorbidity index	215	6.0 (4.0–8.0)	6.0 (4.0–8.0)	5.0 (4.0–7.5)	1
Need for immediate new surgery (complications)	215				1
No		89% (192)	89% (100)	89% (92)	
Yes		11% (23)	11% (12)	11% (11)	
IABP	215				1
No		62% (134)	59% (66)	66% (68)	
Yes		38% (81)	41% (46)	34% (35)	
ECMO	215				1
No		94% (203)	93% (104)	96% (99)	
Yes		6% (12)	7% (8)	4% (4)	
Length of ECC (minutes)	214	163 (111–211)	158 (111–220)	164 (111–206)	1
Length of surgery (minutes)	215	338 (266–405)	344 (267–417)	335 (261–385)	1
Complexity of surgery	215				1
Single non CABG		19% (41)	18% (20)	20% (21)	
Isolated CABG		34% (73)	36% (40)	32% (33)	
Two procedures		29% (63)	28% (31)	31% (32)	
Three procedures		18% (38)	19% (21)	17% (17)	

Continuous variables are reported as median (interquartile range), categorical variables as percentage (frequency).
* adjusted using Benjamini–Yekutieli correction. ECC: extra corporeal circulation; IABP: intra-aortic balloon pump (IABP); ECMO: extra corporeal membrane oxygenation (V-A ECMO); CABG: Coronary Artery Bypass Graft surgery.

Table 2
Comparisons between potential confounders in natural enteral feeding (NEF) and commercial enteral feeding (CEF) cohorts based on 850 observation days.

Variable	CEF ($n = 449$)	NEF ($n = 401$)	p-value*
Length of enteral feeding (days)[§]	3 (2–4)	3 (1–4)	1
Antibiotics/antifungals	82% (367)	67% (268)	<0.001
Colchicin	2% (10)	20% (79)	<0.001
Laxatives	3% (13)	7% (29)	0.021
Oral nutritional supplements	13% (60)	48% (194)	<0.001
Opioids	11% (48)	13% (53)	1
Probiotics	19% (87)	22% (90)	1
Prokinetics	14% (64)	6% (25)	0.001
Sedative agents[¥]	42% (190)	42% (169)	1
Adrenaline (*mean daily* γ/Kg/min)[†]	0.00 (0.00–0.00)	0.00 (0.00–0.00)	<0.001
Dobutamine (*mean daily* γ/Kg/min)	0.00 (0.00–2.65)	0.00 (0.00–0.81)	0.011
Noradrenaline (*mean daily* γ/Kg/min)	0.00 (0.00–0.07)	0.00 (0.00–0.05)	1

Continuous variables are reported as median (interquartile range), categorical variables as percentage (frequency).
* adjusted using Benjamini–Yekutieli correction. ¥: benzodiazepine, propofol; †: higher in the CEF cohort.

natural enteral feeding groups. Crude evaluation was carried out comparing Kaplan–Meier curves and differences in survival rates between groups were assessed with Log-Rank test. Adjusted comparison was performed by fitting a multivariable Cox proportional-hazards model; results were reported as hazard ratios (HRs) with relative 95% confidence intervals (CI) and p-values (Nieto and Coresh, 1996).

Variables that were supposed to act as potential confounders for diarrhea occurrence (i.e. administration of inotropes, vasopressors, prokinetics, antibiotics, oral nutritional supplements, antifungal agents, sedatives, opioids, probiotics, laxatives) were included in the model. Given the low number of events per variable, a ridge penalty factor was applied to all the regression coefficients of the model but the one of the compared groups, i.e. natural vs. commercial enteral feeding (Gray, 1992). This procedure was implemented to minimize both overfitting and bias of the estimator's effect of natural enteral feeding with respect to commercial enteral feeding (Chen et al., 2016). Penalty factor was chosen such that the Akaike information criterion (AIC) of the model was minimized. Proportional hazard assumptions were tested by evaluating correlation coefficients between transformed survival times and scaled Schoenfeld residuals (Grambsch and Therneau, 1994). Statistical significance was accepted at p-value < 0.05.

Statistical analysis was performed with R software for statistical computing (version 3.5.1). Cox-proportional hazard model was fitted using *survival* R package (version 2.43-1).

3. Results

During the study period, 3395 patients were admitted to the intensive care unit and were assessed for inclusion. According to eligibility requirements, 3180 (93.7%) patients were excluded (3133: not undergoing enteral feeding; 27: no open-heart surgery; 2: bowel ischemia; 2: clostridium difficile colitis; 36: lack of clinical data), resulting in the inclusion of 215 patients. Table 1 presents the baseline characteristics of the two cohorts. No significant differences were identified.

During the 8-days observation window, 54 patients (48.2%) developed diarrhea in the commercial enteral feeding group and 28 (27.2%) in the natural enteral feeding group ($p = 0.002$). The relative incidence of days with diarrhea was 18.4/100 observation days for commercial enteral feeding and 6.7/100 observation days for natural enteral feeding. The probability of developing diar-

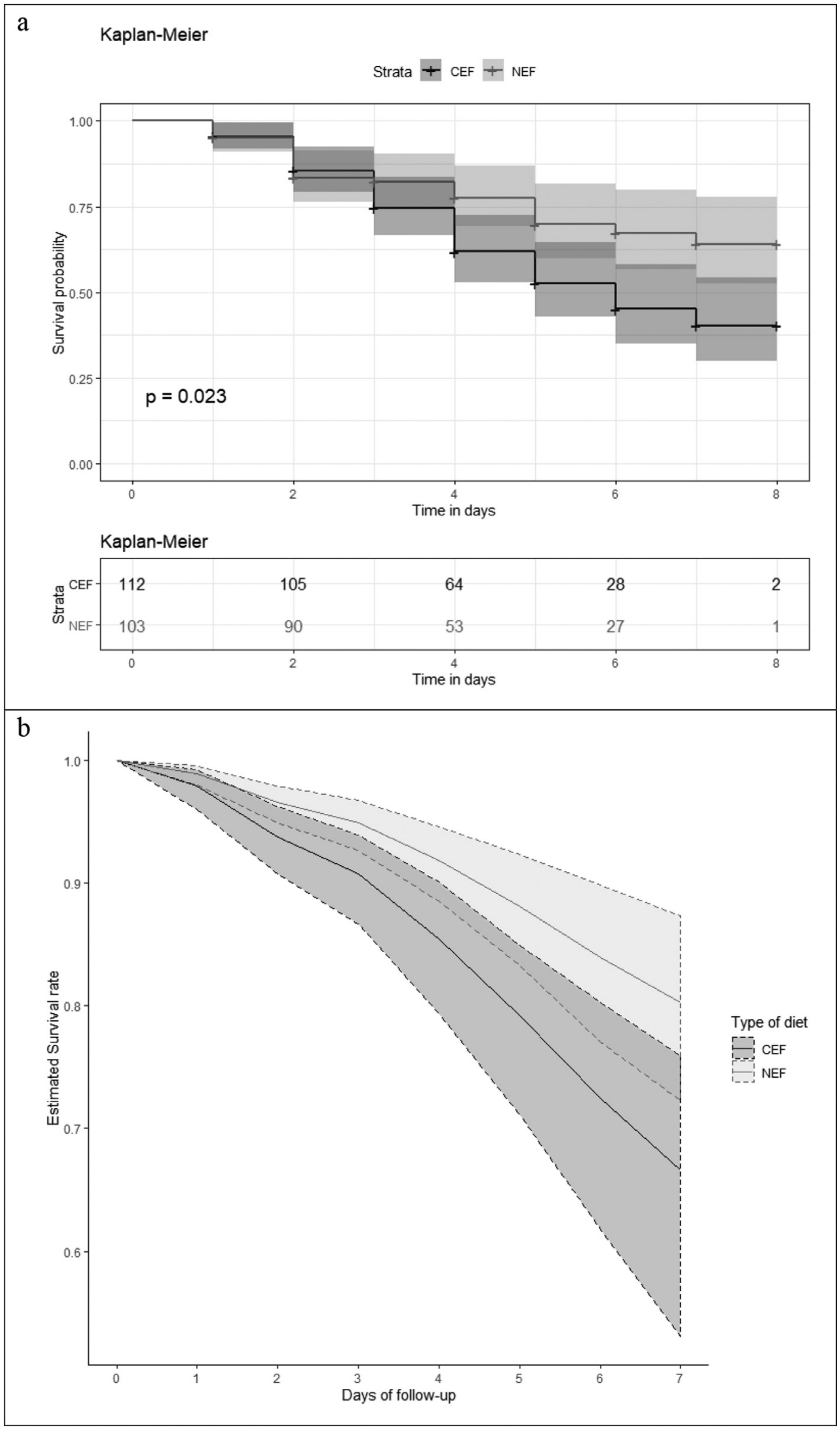

Fig. 1. Crude Kaplan–Meier (a) and adjusted (b) survival curves with relative 95% CI for commercial enteral feeding (CEF) and natural enteral feeding (NEF) groups.

rhea in the natural enteral feeding group was lower than that in the commercial enteral feeding group (log-rank test: $p = 0.023$) (Fig. 1(a)).

Patients in the natural enteral feeding group received significantly more ($p<0.03$) oral nutritional supplements, laxative drugs and colchicine, while those in the commercial enteral feeding cohort received more antibiotics, prokinetics, and inotropic/vasoactive drugs ($p<0.02$) (Table 2).

According to the multivariable Cox model (Table 3), patients in the natural enteral feeding cohort showed a non-significant trend toward a reduced risk of experiencing diarrhea (HR 0.584; 95% CI 0.335–1.018; $p = 0.058$).

Adjusted survival curves estimated with multivariable Cox Proportional-Hazards model for each compared group with relative 95% CI are reported in Fig. 1(b).

Table 3
Results of the multivariable Cox-proportional hazard model (partial log-likelihood = −432.568, $p = 0.007$; AIC = 875.263).

Variable	HR (95% CI)	p-values
Natural enteral feeding	0.584 (0.335–1.018)	***0.058***
Adrenaline	1.192 (0.896–1.587)	0.228
Antibiotics/antifungals	1.091 (0.886–1.343)	0.413
Colchicin	0.919 (0.668–1.263)	0.601
Dobutamine	1.015 (0.978–1.054)	0.424
Laxatives	0.626 (0.446–0.880)	**0.006**
Noradrenaline	1.067 (0.776–1.467)	0.690
Opioids	0.847 (0.660–1.086)	0.191
Oral nutritional supplements	0.961 (0.764–1.209)	0.734
Probiotics	1.195 (0.927–1.541)	0.168
Prokinetics	0.722 (0.559–0.932)	**0.012**
Sedative agents	0.983 (0.810–1.191)	0.858

HR: hazard ratio; CI: confidence interval.

Table 4
Test for proportional hazard assumptions.

Variable	ρ	χ^2	p-value
Natural enteral feeding	−0.154	2.337	0.126
Oral nutritional supplements	0.059	0.073	0.787
Sedatives	0.062	0.069	0.792
Opioids	0.095	0.086	0.770
Probiotics	0.091	0.209	0.647
Laxatives	−0.110	0.062	0.803
Norepinephrine	0.064	0.085	0.771
Adrenaline	0.125	0.286	0.593
Dobutamine	0.146	0.297	0.586
Colchicin	−0.010	0.002	0.966
Prokinetics	0.106	0.056	0.813
Antibiotics/antifungals	0.015	0.003	0.955
Global	/	*3.684*	*0.988*

No variable seemed to violate the proportional hazard assumptions, with correlation coefficients always statistically different from 0 (Table 4).

4. Discussion

The main finding of the present study is that, in a population of postoperative critically ill cardiac surgery patients, the use of a blenderized natural enteral feeding was associated with a significantly lower probability of diarrhea occurrence as compared to commercial enteral feeding preparations. According to the adjusted survival analysis, an almost halved risk of diarrhea was showed in the natural enteral feeding group, although without reaching statistical significance, perhaps because of the reduced size of the study population. Among the considered confounders, the administration of prokinetic and laxative agents (prescribed in the presence of gastroplegia, ileus and constipation) independently reduced the risk of diarrhea. Literature data showed that prokinetic agents reduced feeding intolerance in critically ill patients, while a significant impact on the risk of diarrhea was not previously demonstrated (Lewis et al., 2016).

Optimal nutrition therapy is a cornerstone to improve survival and recovery in critically ill patients (Stoppe et al., 2017). However, complications associated with tolerance to enteral nutrition by tube feeding may hamper the delivery of adequate nutritional requirement to these patients. Diarrhea is one of the most common complications in intensive care units (Elpern et al., 2004), potentially representing a marker of intestinal malabsorption and of energy/nutrient loss when occurring in amounts >250–350 g/day (van Schijndel et al., 2006; Wierdsma et al., 2011). Although some studies have suggested that natural diets contain less nutrients than commercial enteral nutrition formulas (Jolfaie et al., 2017), avoiding diarrhea may reduce the occurrence of malnutrition.

Underlying mechanisms of diarrhea include enhanced exudation as a result of local and systemic inflammation, hypersecretion related to enterotoxins as in the case of bacterial bowel colonization secondary to the use of antibiotics, increased intestinal osmotic pressure and motor dysfunction such as during enteral feeding, mainly related to the type of formula and method of administration (Tatsumi, 2019). For the above reasons, the present investigation excluded patients with documented intestinal Clostridium difficile infection and considered inotropes and vasopressors, prokinetics, laxatives, antibiotics, antifungal agents and oral nutritional supplements as confounding factors.

In the present study, the mode of administration was different in the natural and commercial enteral feeding groups, being represented by bolus in the former group and by continuous infusion in the latter. Robust literature data are lacking to definitely support a continuous or intermittent enteral feeding method, although some studies showed that intermittent enteral feeding (as in the natural enteral feeding group) allows to achieve better nutritional results in less time, also reducing the risk of aspiration pneumonia (Aguilera-Martinez et al., 2014), while continuous administration (as in the commercial enteral feeding group) has been associated with better tolerance to enteral feeding as compared to bolus intermittent enteral feeding (MacLeod et al., 2007). Despite this evidence, in the present investigation bolus natural enteral feeding administration resulted in lower incidence of diarrhea, suggesting that mechanisms other than medications and mode of enteral feeding administration play a role in this type of patients. We speculate that the natural enteral feeding composition may have played an independent role in lowering the incidence of diarrhea.

Content and composition of administered diet, particularly lack of dietary fibers and increased amounts of some carbohydrates (fermentable oligosaccharides, disaccharides, monosaccharides and polyols – FODMAPs) have been related to the development of diarrhea. Antidiarrheal effects of natural foods rich in resistant starch and acidic oligosaccharides have been previously documented (Qi and Tester, 2018) and have been attributed both to their anti-adhesive effects against enteric pathogens (Guggenbichler et al., 1997) as well as to their prebiotic action (Zaman and Sarbini, 2016). This effect has been ascribed both to the generation of short chain fatty acids and to the improvement of small bowel mucosal permeability. Although we do not have the precise composition of natural enteral feeding, it is likely to be different from that of commercial enteral feeding in terms of amount and types of fibers and FODMAPs. It has been demonstrated that in a population of tube-fed critically ill neurological patients, administration of a commercially available product based on natural foods such as milk, meat and carrots was associated with a statistically significant reduction of the number of watery defecations and diarrhea (minus 61%) as compared with a standard formula for enteral feeding made of powdered raw materials (Schmidt et al., 2018). In another study natural enteral feeding resulted in higher micronutrient content, lower prevalence of vomiting and use of acid-suppressive agents in a medically complex pediatric population while no difference was shown in stool consistency and frequency (Gallagher et al., 2018). Finally, in tube-fed critically ill patients 7-day administration of banana flakes alleviated diarrhea as compared with patients on routine enteral feeding (Emery et al., 1997). Changes in intestinal microbiota composition in patients fed commercial enteral feeding formulas have been described (Whelan, 2007) as well as during refeeding of pediatric patients affected by enteritis using selected natural foods (Heine et al., 1993) and during transition from commercial enteral feeding to plant-based enteral nutrition in chronically ill children (McClanahan et al., 2019). The novelty of the present study lies on the fact that these observations were extended to a cohort of critically ill postoperative cardiac surgery patients, which have not been previously investigated in terms of enteral nutrition support and tolerance.

The use and the choice of fiber-enriched formulas in selected situations in general intensive care unit patients has been discussed by recent guidelines (Taylor et al., 2016), but not by others (Singer et al., 2019). However, there is a general consensus on avoiding both soluble and insoluble fiber in patients at high risk for bowel ischemia. In the present study cohorts patients were comparable in terms of demographic and comorbid conditions, complexity of surgery, postoperative risk and use of noradrenaline, while patients in commercial enteral feeding cohort received more inotropes and adrenaline (although this latter was seldom used). Nevertheless, neither the amount of administered dobutamine nor of total amines resulted significantly related to the diarrhea occurrence in the multivariable regression model.

Administration of natural preparations could present critical aspects, such as increased nursing workload related to enteral feeding preparation (blend the food, etc.) and bolus administration three times a day, as well as possible microbial contamination and inadequate nutritional support. Indeed, a recent study in a population of home-cared adult patients undergoing enteral nutrition showed that homemade blenderized and strained diets were characterized by lower contents of energy and macronutrients–ensuring less than 50% of the prescribed energy requirement and demonstrated high levels of bacterial contamination (Vieira et al., 2016). It is therefore extremely important that the preparation of the blenderized natural smoothie meal is structured and controlled in terms of calorie and nutritional intake and that the administration is carried out relatively quickly so as to reduce any microbial contamination.

4.1. Strengths and limitations

Although the present study provides new evidence in the prevention of diarrhea (assessed through rigorous criteria) through the adoption of natural feeding patterns in critically ill cardiac surgery patients, it is worth pointing out that it presents some limitations. The main one is its retrospective design, characterized by a convenience sample consisting in consecutive patients. This design does not allow a comparison of relevant clinical outcomes, such as mortality between the two study groups. In addition, individual energy requirements were calculated by simplistic weight-based equations instead of using indirect calorimetry (Singer et al., 2019). Data on nutritional quality of blenderized natural enteral diet as well as patients' nutritional status before and after enteral feeding were not available at the time of the study. It should however be pointed out that, in contrast with intermittent bolus enteral feeding as in the natural enteral feeding group, continuous administration, as in the commercial enteral feeding group, is more susceptible to frequent interruptions due to routine clinical care and diagnostic exams which may preclude the delivery of target energy requirement. Moreover, these different administration methods could have significantly affected gut motility. Finally, drug administration was considered only during the days of EFs delivery; some drug administered at higher doses in the days before starting enteral feeding (e.g., vasopressors) may have subsequently influenced the occurrence of diarrhea.

5. Conclusions

Diarrhea continues to be an important complication in critically ill patients undergoing enteral feeding. Adopting a blenderized natural food diet may be an effective strategy to reduce its incidence.

Strategies decreasing the likelihood of diarrhea occurrence in this population can have a favorable impact on patient outcomes by reducing the risk of diarrhea-related local and systemic complications, also reducing the impact on patients' psychological burden and nursing workload.

Further prospective clinical trials are needed to compare commercial and blenderized enteral feeding in order to determine the impact of the different nutritional strategies on diarrhea occurrence and on different outcomes.

Declaration of Competing Interest

None

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Credit author statement

A. Fabiani, G. Sanson and D. Gregori equally contributed to the conception and design of the research; M. Zanetti, M. Sacilotto, L. Dreas, G. Lorenzoni and A. Pappalardo contributed to the design of the research; A. Fabiani, G. Gatti, D. Bottigliengo, G. Lorenzoni and D. Gregori contributed to the acquisition and analysis of the data; A. Fabiani, G. Sanson, D. Bottigliengo and D. Gregori contributed to the interpretation of the data; and A. Fabiani, G. Sanson and M. Zanetti drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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