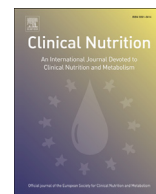




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Original article

Comparison of different definitions of feeding intolerance: A retrospective observational study

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SUMMARY

Background & aims: While feeding intolerance (FI) is clinically important in the critically ill it is inconsistently defined. By evaluating definitions of FI based on relationships between symptoms and signs of gastrointestinal (GI) dysfunction and mortality the objective was to define FI using the definition that was most strongly associated with subsequent mortality.

Methods: Data from all adult patients admitted to a single ICU between 2004 and 2011, and who were receiving enteral nutrition (EN), were analysed. The amount of EN administered, presence of absent bowel sounds (BS), vomiting and/or regurgitation, diarrhoea, bowel distension, and large gastric residual volumes (GRVs) were documented daily. A GRV ≥ 500 ml/day was considered as large and the sum of gastrointestinal (GI) symptoms including large GRV was calculated daily. Various definitions of FI were modelled. Definitions using only GRV, or GRV with other GI symptoms, or GRV and failure to reach preset EN targets were evaluated. The predictive power of FI on mortality was tested by adding the presence of FI (different definitions were tested one-by-one) into multiple regression analyses together with admission day demographic and severity of illness variables.

Results: Of the 1712 patients included, 221 (12.9%) died in ICU and 495 (28.9%) had died within 90 days after ICU admission. The definition of FI based on the presence of at least three out of five GI symptoms was most strongly related to ICU-mortality (6.3% prevalence in survivors vs. 23.5% in non-survivors, $p < 0.001$, odds ratio (95%CI) 3.39 (2.23–5.14)), whereas EN $< 23\%$ of caloric target was the strongest predictor for mortality 90 days after admission (50.7% prevalence among survivors vs 75.2% in non-survivors, $p < 0.001$, odds ratio (95% CI) 2.34 (1.80–3.04)).

Conclusions: FI is associated with increased mortality but the strength of this relationship depends on the definition used. The 'best' definition of FI for prediction of ICU-mortality is based on a complex assessment of GI symptoms (including large GRV), whereas enteral underfeeding is the definition of FI that is the strongest predictor of death within 90 days of admission. Our 'best' definitions are not immediately generalizable, but should help building up future studies.

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1. Introduction

The expression „feeding intolerance“ (FI) is frequently used in daily clinical practice, but there is no consensus definition. While FI is associated with unfavourable outcomes [1–5] it is uncertain as to whether this is because FI *per se* is a marker of gastrointestinal (GI) dysfunction, or because of harm from inadequate enteral nutrition and/or the use of parenteral nutrition [6], or FI simply represents an epi-phenomenon of severity of illness.

Abbreviations

APACHE	acute physiology and chronic health evaluation
BS	bowel sounds
CI	confidence interval
EN	enteral nutrition
FI	feeding intolerance
GI	gastrointestinal
GRV	gastric residual volume
ICU	intensive care unit
OR	odds ratio
ROC	receiver operating characteristic
SOFA	sequential organ failure assessment

Whereas the exact role of FI in definition of GI dysfunction remains to be clarified, the importance of GI function in intensive care patients is increasingly recognized. There is substantial interest in having an accepted definition for GI dysfunction in the critically ill, particularly a definition that is associated with important patient-centred outcomes and can be used when evaluating specific GI therapies [7]. Observational data are consistent with the concept that GI dysfunction is clinically important, but the absence of an agreed definition of FI limits generalizability of research undertaken in this area [7]. The most frequently used definition of FI is as based on aspiration of the gastric residual volume (GRV) during enteral feeding, but the threshold volume chosen varies considerably between studies and investigators [8]. Other investigators have focused on the inability to reach a threshold amount of energy that is administered to a patient [9,10].

The aims of this study were to evaluate various definitions of FI and the relationship with mortality; and identify the definition that was most strongly associated with mortality. The hypothesis was that FI is related to adverse outcomes and it is therefore possible to evaluate definitions of FI based on the association with mortality. To achieve the objectives various definitions of FI were used and their association with ICU- and 90-day mortality was evaluated using an existing database.

2. Materials and methods

Data of all consecutive adult (≥ 18 years) patients admitted to a single centre general ICU of a university hospital between 2004 and 2011 were prospectively collected. This study involves retrospective analyses of these data. GI symptoms and feeding details were recorded. The GRV was documented as the sum of the residual contents in a 24 h period. In each patient with a gastric tube, GRV was measured every morning and additionally when considered needed (e.g. in case of vomiting, large GRV in last measurement). GRV was measured passively (by opening the tube and hanging collection bag on the bed-rack for 30 min) and evacuated contents were not returned.

Patients were stratified according to enteral feeding using the binary definitions of:

EN yes = the patient received EN (any amount) at least on one day during his/her ICU stay;

EN no = the patient did not receive EN during his/her ICU stay.

Initial analysis was performed to compare patients with and without EN. Only the patients receiving EN (i.e. EN yes) were included in subsequent comparative analysis.

The study was approved by the Ethics Review Committee on Human Research of the University of Tartu (Protocols no 191T-9 and 217/M-17). Informed consent was waived due to the retrospective and observational design of the study.

2.1. Definitions

The GI symptoms were predefined as follows: Absent bowel sounds (BS) = no BS detected by auscultation. Auscultation process was not protocolized, but auscultation was daily performed by a senior intensive care physician; Vomiting/regurgitation = any visible regurgitation of gastric contents; Diarrhoea = liquid stool ≥ 3 times/day; Bowel distension = suspected clinically or radiologically confirmed; Large gastric residual volume (GRV) = GRV ≥ 500 ml/24 h on a single calendar day.

Using a systematic review of the literature [8] the possible definitions of FI were extracted and grouped based on GRVs; percentage of EN delivered according to the calculated caloric requirements; or presence of GI symptoms related to EN.

In current study, the following definitions of feeding intolerance were tested:

1) Definitions based solely on GRVs. The thresholds were chosen from the literature [7,11,12], or derived as cut-off value from retrospective ROC (receiver operating characteristic) analysis of the current data-set, enabling to discriminate between the survivals and non-survivals of study population:

FI 1A = GRV ≥ 500 ml/24h for any day with EN [11];

FI 1B = GRV ≥ 250 ml/24 h for any day with EN [12];

FI 1C = GRV ≥ 1000 ml/24 h for any day with EN [7];

FI 1D = GRV ≥ 473 ml/24 h (according to the cut-off point in ROC curve analysis of data of present study)

2) Definitions based on percentage of EN delivered from daily caloric requirements. As per local protocol energy requirements were estimated as 20 kcal per kg of adjusted body weight (ABW) per day for the first 48 h after admission and 25 kcal/kgABW/day thereafter after this period [13]. The thresholds of EN from total caloric needs were set arbitrarily, extracted from the literature [3], or derived from ROC analysis of present data-set:

FI 2A = EN percentage of estimated caloric needs $< 20\%$ for any day with EN;

FI 2B = EN percentage of estimated caloric needs $< 50\%$ for any day with EN [3];

FI 2C = EN percentage of estimated needs $< 23\%$ for any day with EN (according to the cut-off point in ROC curve analysis of data of present study).

3) Definitions based on percentage of EN from caloric needs reached by day 3 or day 4 in ICU. Days 3 and 4 were chosen arbitrarily with the assumption that by this time development of FI should be evident in the majority of patients who would receive EN during their ICU admission. This approach is partly supported by our previous study investigating the impact of GI symptoms on ICU outcomes [3].

FI 3A = EN percentage of estimated caloric needs on day 3 was $< 80\%$ given that EN was started in any of these first days and the patient was still in ICU on day 3 [10];

FI 3B = EN percentage of estimated caloric needs on day 3 was $< 50\%$ given that EN was started in any of these first days and the patient was still in ICU on day 3;

FI 3C = EN percentage of estimated caloric needs on day 4 was $< 80\%$ given that EN was started within these first days and the patient was still in ICU on day 4;

FI 3D = EN percentage of estimated caloric needs on day 4 was $< 50\%$ given that EN was started in any of these first days and the patient was still in ICU on day 4;

FI 3E = EN percentage of estimated caloric needs on day 3 was $< 59\%$ (based on the cut-off point from ROC analysis of present data) given that EN was started in any of these first days and the patient was still in ICU on day 3;

FI 3F = EN percentage of estimated caloric needs on day 4 was $< 46\%$ (based on the cut-off point from ROC analysis of present data)

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