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ABSTRACT

Introduction: Hospitalized patients having feeding tubes are at constant risk for incidents; therefore, healthcare professionals need to routinely monitor risks and adopt strategies for patient safety and quality of care.

Aim: To evaluate the feeding tube-related incidents in hospitalized patients and associated factors.

Methods: This is a multicenter study, with quantitative, analytical, prospective design. Data will be collected at the general medical ward of seven Brazilian hospitals in the North, Northeast, Southeast, and South. The sample will consist of 391 patients that require feeding tube for enteral nutrition and/or medication during hospitalization. Three different methods will be used to identify the incidents: (1) healthcare professionals and patients/caregivers will be required to report any feeding tube-related incidents; (2) researchers will visit the wards to get information about the incidents with healthcare professionals and patients/caregivers; (3) the researchers will review the medical records looking for information on the occurrence of any feeding tube-related incidents. Demographic, clinical and therapeutic characteristics will be obtained from the medical records and will be registered in an electronic data collection tool developed for the purposes of this study. The complexity of patients will be assessed by the Patient Classification System, and the severity of comorbid diseases, through the Charlson Comorbidity Index.

Implication for practice: It is expected that the results encourage the use of evidence effectively to influence the scientific foundation for clinical practice and the development of evidence-based policies that will prevent, manage and eliminate complications caused by feeding tube-related incidents, and improve the quality and safety of care provided to hospitalized patients.

Strengths and limitations of this study

- Several single-centre studies have identified the prevalence of feeding-tube related incidents in general inpatients, however, there are no studies reporting on those incidents across multiple hospital sites and at national level.
- A multicentred study may ascertain better generalisability of the data.
- To our knowledge, this is the first large scale study in Brazil and in Latin America documenting the incidence of feeding-tube related incidents in internal medicine wards.
- Although voluntary reporting can detect a broad range of incidents, this system misses the vast majority of incidents and cannot provide stable estimates of the true underlying causes.

- It is difficult to demonstrate causality between feeding tube-related incidents and negative patient outcomes due to a number of confounding factors.

INTRODUCTION

During hospitalization, patients with advanced disease have caloric and protein malnutrition, and therefore require nutritional and drug interventions. Therefore, these patients often need enteral feeding to ensure that their daily nutritional and medical needs are met. [1] Data from the American Society for Enteral and Parenteral Nutrition (ASPEN) revealed that more than 245,000 patients per year require at least a temporary feeding tube during a hospital stay, along with another nearly 31,000 patients that are on enteral nutrition at home. [2] In the United States, about one million feeding tubes are introduced in adults and children each year [3] and the rate of complications is 2% to 36%. [4-6]

Although inserting an enteral feeding tube is a relatively innocuous procedure, improper positioning can cause severe and fatal complications. [7-9] One of the major incidents related to the enteral tube is the wrong connection. The design of these devices is such that it is possible to infuse enteral feeding and / or medications via an unwanted route, such as intravenous route. [10,11]

It is also common having inadvertent positioning of the tube in the respiratory tract, resulting in bronchoaspiration and pneumothorax. [8,12-14] Pulmonary aspiration occurs in 2% to 10% of patients receiving enteral feeding. The inadvertent insertion of the tube into the tracheal tree results in discomfort for the patient, delayed feeding, increased morbidity and mortality, and length of stay, resulting in onus for the institution and patients. [5,15] Therefore, health care professionals need to routinely monitor risks and adopt strategies aimed at patient safety.

Other incidents may occur during the insertion and / or progression of the feeding tube through the gastrointestinal tract, such as sinusitis, vomiting, nasopharyngeal discomfort, erosion of the nasal septum, epistaxis, and blood return by the tube during guidewire withdrawal. [16] In Brazil, this data is not available, however, it is observed that feeding tube is a common procedure in most Brazilian health institutions. [17]

Regarding medication administration, administering drugs with absorption at the intestinal level in patients using nasogastric tube is a challenge. As demonstrated in the literature, some drugs should never be crushed and administered through a nasogastric tube because they have enteric or controlled release protection coatings. [18] The grinding process of these drugs can destroy the coating film and result in incidents, exposing patients to unnecessary risks. [19] In this regard, experts argue that healthcare professionals should not assume that a drug formulated to be administered orally can be administered safely through a feeding tube because drug delivery mechanisms can be altered or destroyed, reducing effectiveness or increasing risk of toxicity. [20]

In order to achieve adequate clinical outcomes in hospitalized patients, it is essential that medication and enteral nutrition therapy be administered appropriately. However, nursing

guidelines on enteral feeding tube care are not based on scientific evidence, but in traditions, rituals and expert opinions, exposing patients to unnecessary harm. [21]

Although feeding tube-related incidents are common in hospitals settings with significant morbidity and mortality, the issue has not been extensively studied, especially in developing countries. Given that the number of patients with chronic conditions have increased significantly worldwide, as well as in Brazil, it is critical that health care professionals employ a repertoire of evidence based interventions in order to provide safe and high quality care. [22,23] However, there is a knowledge gap regarding the safe handling of enteral feeding tubes in Brazilian healthcare institutions. Studies that aim to identify the most frequent feeding tube-related incidents that occured during hospital stay, can reduce that gap and consequently reduce the risks of complications and lower overall cost of care.

The results of the study will contribute to the production of knowledge and its application in clinical practice for injury reduction towards a safer environment for patient care; will provide national and international data that reflect the problem of feeding tube-related incidents in acute care units; and will contribute to the use of the evidence in an efficient way to influence the development of national practices and policies aimed at managing the risks associated with the feedind tube.

Significance and theoretical framework

Enteral nutrition is administered through a nasogastric tube, a nasoenteric tube, or an ostomy. These devices are not exclusively used for administration of enteral nutrition. They are also frequently used for administering drugs. The consequence of this duo use is the increased risk of tube obstruction, physical-chemical incompatibilities, and potential drug-nutrient interactions. [24] In a previous study it was shown that 74% of nurses had employed wrong medication administration methods to deliver medicines through feeding tube and according to researchers, those errors could reduce the effects of drugs and lead to unsuccessful treatment. [25]

According to a study conducted in a Brazilian private hospital, the main reason for the loss of the feeding tubes was obstruction (36%) related to wrong medication preparation and administration techniques. [26] Estimates of incidence of clogged feeding tubes range widely from 12.5%-45%, but it is undisputed that they result in increased costs for patients and institutions. [27] Thus, health care practitioners, especially nurses, should not assume that a medication intended to be taken by mouth can be safely administered through a feeding tube, because this misconception can result in harm to patients and increase medical costs to society. [20]

Another incident related to improper medication administration via feeding tube is caused by drug interactions in elderly people due to polypharmacy, with a prevalence of 20-

40%. Polypharmacy increases the complexity of clinical management and contributes to medication adverse events. [28]

Therefore, the causes of the incidents are multifaceted and that the consequences are associated with increasing complexity of patients and treatments, intensifying the need for measures aimed at improving the quality of care. In this sense, opportunities to share knowledge are fundamental to patient safety. [29]

Efforts to overcome these problems have resulted in the development of international programs and policies. For instance, the WHO proposed the patient safety research cycle and the first step in improving care quality and safety is to measure the occurrence of incidents in order to know the magnitude of the problem. The WHO then suggests understanding the causes and identifying solutions. [30]

In Brazil, the Ministry of Health and the National Health Surveillance Agency (ANVISA), in line with WHO's global initiatives, launched the National Patient Safety Program in mid-April 2013 with the aim of promoting strategies aimed at prevention and reduction of risks associated with health care. Among the strategies, increasing patient safety research. [31,32]

Considering that patient safety is a global problem affecting countries at all levels of development; [33] that the production of knowledge and its application in clinical practice can promote a safe environment for the provision of care; that in Brazil, there is concern about the need to increase knowledge on this issue; that there are insufficient national data that reflect the problem of the incidents related to enteral feeding tube in hospitalized patients; thus the present study is necessary. We expect that the results of this study will provide high quality evidence that will support interventions designed to improve patient safety in use of feeding tubes.

The objective of this study is to evaluate the feeding tube-related incidents in hospitalized patients and the associated factors. The secondary objectives are:

1. To analyse the association between the feeding tube-related incidents and the complexity of the patients;
2. To analyse the association between the feeding tube-related incidents and the severity of comorbid diseases;
3. To examine the predictive role of Charlson Comorbidity Index (CCI) on mortality of patients having feeding tube;
4. To assess potential drug interactions (pDDI) and its association with patient complexity and comorbid diseases.

METHODS

Research Design

This is a multicenter study, with quantitative design, prospective and analytical.

Setting

Seven centers across Brazil will participate in this study; the centers include a mix of community and university hospitals, hospitals with and without residency programs, and public and private hospitals; they also vary in size. The hospitals will be as follows: Acre Hospital of Clinics - HCA, General Hospital of Fortaleza - HGF, Hospital of Clinics of the Medical School of Ribeirão Preto of the University of São Paulo - HCFMRP-USP, Américo Brasiliense State Hospital - HEAB, Sumaré State Hospital - HES, São Vicente de Paulo Hospital - HSVP, and Santa Cruz Hospital - HSCRGS.

The medical ward of these hospitals was chosen for this study because it provides care for adult patients in various medical specialties and most of the patients have chronic conditions, thus many require enteral nutrition and medications through a feeding tube.

Subjects

The study population will be the patients admitted to the medical ward of the seven Brazilian hospitals that require a feeding tube during hospitalization. The inclusion criteria are: patients older than 18 years; who are admitted to the medical ward with a nasogastric or a nasoenteric feeding tube (or patients who require the insertion of a nasogastric or nasoenteric feeding tube during hospitalization); and patients that have been hospitalized for at least 24 hours. The exclusion criteria is: patients having feeding tube who are readmitted to the medical wards / units during data collection period.

Sampling size was determined by a stratified random sampling with proportional allocation by strata, where each stratum is formed by the floors / units of each hospital (Table 1):

Table 1. Determination of sample size, 2018

Hospital / Strata	Number of inpatients	Prevalence of patients with feeding tube	Estimated size of each stratum
HCA	980	0.1908	58
HGF	192	0.1563	11
HCFMRP-USP	2247	0.0788	134
HEAB	783	0.1073	47
HES	1991	0.1828	119
HSVP	323	0.0650	19
HSCRGS	48	0.0324	3

The formula for the calculation of the sample size is given by:

$$n = \frac{z^2_{\alpha/2} N(1-P)}{\varepsilon^2 P(N-1) + z^2_{\alpha/2}(1-P)} \quad (1)$$

,where P represents the prevalence of the event of interest

(column 4 of table 1), $z_{\alpha/2}$ represents the level of significance adopted and o ε is the relative sampling error. If the sample size calculated by the expression given in (1) is greater than 20% of the population the following finite correction procedure is adopted:

$nc = \frac{n}{\left(1 + {}^{n}/_{N}\right)}$ (2), where N is the total size of the study population and n is the value obtained in (1). The sample was allocated proportionally among the H strata according to the formula:

$n_h = n\frac{N_h}{N}$, where N is the total population of hospitalized patients (N = 6,564), and N_h is the total of each stratum H. Population totals are found in the second column of table 1. Adopting the parameters of relative error of 20%, level of significance of 5% and the total population of 6,564, a total sample size of 391 patients was calculated. The required sample sizes of each strata are found in the last column of Table 1.

Instruments

Data collection tools will be composed of three virtual forms which will be developed by the research team, and assessed for face and content validity by a panel of experts. The forms will be developed in Portuguese language and using an online platform (Survey Monkey®).

The experts will be selected through the analysis of existing curricula in the database of the Brazilian National Council for Scientific and Technological Development (CNPq) and will be invited to participate in the study, by invitation letter sent by electronic mail. Then the access links to the electronic forms will be made available for the experts to carry out their analysis; the experts will have up to 30 days to evaluate the electronic forms and give their feedback to the researchers. The modified forms will be tested through a pre-test, where the forms will be applied to five hospitalized patients from the first day of use of a feeding tube until patient discharge.

At admission, demographic, clinical, and therapeutical information will be recorded in the first electronic data collection form, including:

- ✓ *Demographic data*: registration number; date of admission to the ward / unit; date of birth; city / state of origin; gender; skin color; marital status; education level; profession; origin of the referral.
- ✓ *Clinical data:* principal and secondary International Classification of Dieases (ICD); comorbidities; the final score of the Patient Classification System (PCS). [34]

- ✓ *Therapeutic data:* data related to the feeding tube (type; gauge; location; tests performed to confirm the correct positioning and results of the tests); data related to the enteral nutrition (type, total volume in 24 hours, frequency of administration); data related to the medications prescribed (drug name; dosage form; dose; route of administration; frequency of administration; and planned / scheduled administration time).

The second electronic data collection form will include variables related to the incidents:

- ✓ *Incident:* date and time of occurrence; type of incident (mechanic; metabolic; gastrointestinal; infectious; and others); [4] consequence of the incident for the patient, according to the WHO (none; mild; moderate; severe; and fatal); [35] measures adopted after the incident; sources of information on the occurrence of the incident; and means of obtaining information about the incident.
- ✓ *Clinical:* principal and secondary ICD; comorbidities; the final score of the PCS. [34].
- ✓ *Therapeutic:* data related to the enteral nutrition (type, total volume in 24 hours, frequency of administration); data related to the medications prescribed (drug name; dosage form; dose; route of administration; frequency of administration; and planned / scheduled administration time).

The third electronic data collection form will include variables related to the start of feeding tube and patient follow-up:

- ✓ *Clinical:* date of the start of the feeding tube use; principal and secondary ICD; comorbidities; the final score of the PCS. [34]
- ✓ *Therapeutic:* data related to the medications prescribed 24 hours after feeding tube insertion (or 24 hours after admission if the patient is admitted at the unit with a feeding tube); medications prescribed 120 hours after feeding tube insertion (or 120 hours after admission if the patient is admitted at the unit with a feeding tube); and medications prescribed 24 hours before patient discharge.
- ✓ Date of programmed feeding tube removal and the main reason; date and time of patient discharge; reason for patient discharge.

Procedures

At each center, a registered nurse in the medical ward and a research assistant will serve as a liaison to the study investigators; a designated nurse coordinator will ensure that the collection of data will be carried out completely and correctly. The liaison nurse and the research assistant at each center will attend a total of 16 hours of theoretical and practical formal training sessions led by the regional study coordinator, at which the overall study design will be presented and each electronic data collection forms will be explained. The study

protocol will neither mandate nor direct any element of patient care, and thus will pose no risk to patients.

In addition, a data collection guideline will be developed with the purpose of standardizing data recording in the eight hospitals participating in the study. This guideline will consist of general information related to the research project; general instructions on how to access the electronic data collection forms using mobile devices; definition of each variable and additional information for completing the variables that make up the three electronic data collection forms. The guideline will be available on printed version and by e-mail to assist all the research team on data collection.

Before data collection starts, the researchers will identify the patients who will start the use of a feeding tube (nasogastric or nasoenteric) during hospitalization, according to the inclusion criterias proposed for this study. Researchers will explain the research objectives and will ask patients, or their legal guardian's, to voluntarily sign the Informed Consent Form.

For purposes of confidentiality, each patient will be identified by a unique identifying number; data will be collected from the moment a patient starts using a feeding tube until the patient is discharged (due to death or non-death).

Using a mobile device, research assistants will collect demographic data at patient admission, and prospectively record clinical and therapeutic data from the patients' medical record. Considering that four hospitals participating in this study have present electronic medical records, these will be accessed in the computers available in the medical wards / units. In both situations, the researchers will request permission from the nurse responsible for the unit to access the computers, and to record the information in the electronic data collection forms. The consultation of the medical records will occur in the afternoon or at night, because these are the periods with the least movement of people.

Assessment of the complexity of patients having feeding tubes

Patient complexity will be assessed by an experienced nurse, member of the research team, on the first day of feeding tube use, on the day of the incident, and weekly until patient discharge. Nurses will have up to 24 hours to complete their evaluation.

For this purpose, the PCS proposed by Fugulin [34] will be used. The PCS is recommended by the Federal Nursing Council, Brazil, [36] and it was developed to classify patients according to the degree of dependence of the nursing team. This instrument has nine critical indicators: mental state, oxygenation, vital signs, motility, ambulation, feeding, body care, elimination and therapeutics. Therefore, the scores are distributed in five categories that correspond to the complexity of the assistance: minimum (scores of 9-14), intermediate (scores of 15-20), high-dependency (scores of 21-26), semi-intensive (scores of 27-31), and intensive care (scores > 31).

Assessment of the severity of comorbid diseases of patients having feeding tubes

Regarding the severity of comorbid diseases, this will be evaluated on admission at the medical ward / unit; on the first day of use of the feeding tube; on the day of the incident; and weekly until patient discharge. For this purpose, the Charlson Comorbidity Index (CCI) [37] will be used. The CCI is the most widely used comorbidity, which is a method of categorizing patients' comorbidities, according to the ICD. The aim of the CCI is to measure the severity of the patient, regardless of the main diagnosis, and therefore, to predict the one-year mortality of patients. The final score is the result of the sum of the weights assigned to the comorbidities recorded as secondary diagnoses; the higher the score, the greater the risk of the patient dying. It should be noted that the CCI will be adjusted according to the patient's age, so that, from the age of 50, a point will be added to the final score for every decade of life. [37]

Based on the final CCI score, patients will be divided into three groups: mild (with CCI scores of 1–2); moderate (with CCI scores of 3–4); and severe (with CCI scores ≥5). In addition, survival time in days will be calculated from the first day patient start using a feeding tube during hospital stay to the death of a patient. [38]

Assessment of the feeding tube-related incidents

In this study, incident was defined as an event or circumstance that could have resulted, or did result, in unnecessary harm to a patient. [35] The feeding tube-related incidents considerate in this study are:

- ✓ Mechanical incident (unplanned / accidental removal; obstruction; displacement / migration; epistaxis; nasal mucosa edema; perforation or stenosis of the esophagus; perforation of the brain; penumothorax; various attempts to introduce the tube).
- ✓ Metabolic incident (hypernatremia; hyponatremia; hyperglycemia; hypoglycemia).
- ✓ Gastrointestinal incident (nausea / vomiting; diarrhea; constipation; colic / abdominal distension / flatulence).
- ✓ Infectious incident (aspiration pneumonia; gastroenterocolitis).
- ✓ Other incidents (skin lesion associated with the feeding tube insertion; bronchoaspiration; wrong connection; quality of the tube material).

Based on previous studies, [39,40] three methods will be used for incidents detection:

(1) Prompted spontaneous reporting: healthcare professionals (nursing and medical staff) and patients / caregivers will be continuouslly prompted to report any feeding tube-related incident to the investigators. A pen and a booklet containing instructions on incident reporting will be available and remained at the bedside of each patient participating in the study;

(2) Researchers will visit the wards / units at least twice a week to request information about the incidents, along with healthcare professionals (nursing and medical staff) and patients / caregivers;
(3) Researchers will review the booklet and medical records at least twice a week to obtain information about feeding tube-related incident.

Using a mobile device, the research assistant will record data related to the incidents in the electronic data collection form developed for this purpose. More than one incident may occur on the same day and/or at the same time (eg. feeding tube obstruction and unplanned removel), thus each incident will be recorded on a different form, resulting in a form filled for each feeding tube related incident.

Assessment of potential drug interactions in patients having feeding tubes

Regarding the analysis of potential drug interactions, it will be performed only in patients with a residence time of at least five days, because longer hospital stays are associated with the likelihood of adverse drug events. [41]

The research assistants will record on electronic data collection forms all medications and enteral nutrition prescribed for patients, regardless of whether they were administered or not. Data related to the medications will be collected in the following moments of hospitalization: at admission; 24 hours and 120 hours after admission because it is the period of greatest therapeutic adjustment. [42-44]. Data related with medications will be also recorded 24 hours before patient discharge and on the day of the incident. Data related with enteral nutrition will be recorded on admission ando n the day of the incidente.

Medications will be classified according to the WHO Chemical Anatomical Therapeutic Classification (ATC), [45] and the analysis of drug interactions will be performed based on drug monographs from the DrugReax System database from Thomson Healthcare® because it is a highly reliable software. [46] The software is also available in the journal portal of the Coordination of Improvement of Higher Level Personnel - CAPES, Brazil. Potential drug interactions will be classified according to the speed of action, documentation and severity, as recommended by DrugReax®.

Data analysis

Data will be downloaded from the Survey Monkey® to a computer file and analysed using the Statistical Package for the Social Program Sciences® (SPSS) version 22.0. In the statistical analysis, we will apply: calculation of proportions and measures of central tendency and variability. Quantitative variables will be assessed for normal distribution using the Kolmogorov-Smirnov test. The importance of the normal distribution evaluation is justified, among others, by the subsequent indication of parametric and non-parametric statistical tests.

Pearson's Chi-square (χ^2) and Fisher's exact tests will be used to compare the response variables with the categorical explanatory variables, when indicated. For the comparison of the variable responses with the quantitative explanatory variables, t or Mann-Whitney tests will be performed, when indicated.

To examine the predictive role of Charlson Comorbidity Index (CCI) on mortality of patients having feeding tube, a one-way analysis of variance (ANOVA) will be used to compare group differences stratified by CCI, and otherwise Chi-square tests will be applied. All analyzes will be carried out considering a significance level of 5% (α= 0,05).

Patient and Public Involvement

Patients will be informed of possible risks which are: discomfort or embarrassment to answer questions about feeding tube-related incidents, thus patients will be able to refuse to answer any question that he/she feels inconvenient or inappropriate, without causing harm to their care. In addition, participants will be informed that the results will be used for possible publications. We will guarantee their confidentiality and anonymity.

Contributors

FREG and MCAP initiated the project and are the chief investigators on the project. PRP, REFLC, JK, LMF, TCAT, and AIMi, are associate investigators and all made significant contributions to the protocol in their specific areas of expertise. FREG prepared the first draft of this manuscript and all authors have reviewed and provided input.

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Competing interests

None declared.

Ethics approval

The study was approved by the Research Ethics Committee of the University of São Paulo at Ribeirão Preto College of Nursing (CAAE: 56166016.1001.5393) and written informed consent will be obtained from each patient, or their guardian, prior to enrollment in the study.

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Feeding tube-related incidents in hospitalized patients: a study protocol of a multicenter prospective cohort study

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Feeding tube-related incidents in hospitalized patients: a study protocol of a multicenter prospective cohort study

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ABSTRACT

Introduction: Hospitalized patients with feeding tube are at constant risk of incidents; therefore, health professionals need to routinely monitor risks and adopt strategies for patient safety and quality of care.

Aim: To evaluate the feeding tube-related incidents in hospitalized patients and associated factors.

Methods: This is a multicenter study, with a multicenter prospective cohort design. Data will be collected at the general medical ward of seven Brazilian hospitals in the North, Northeast, Southeast, and South. The sample will consist of 391 patients that require a feeding tube during hospitalization. Three different methods will be used to identify the incidents: (1) healthcare professionals and patients/caregivers will be required to report any feeding tube-related incidents; (2) researchers will visit the wards to get information about the incidents with healthcare professionals and patients/caregivers; (3) the researchers will review the medical records looking for information on the occurrence of any feeding tube-related incidents. Demographic, clinical and therapeutic details will be obtained from the medical records and will be registered in an electronic data collection tool developed for the purposes of this study. The complexity of patients will be assessed by the Patient Classification System, and the severity of comorbid diseases, through the Charlson Comorbidity Index.

Implication for practice: The results may encourage the use of evidence effectively to influence the scientific foundation for clinical practice and the development of evidence-based policies that will prevent, manage and eliminate complications caused by feeding tube-related incidents, and improve the quality and safety of care provided to hospitalized patients.

Ethics and dissemination: The study has been approved by the Research Ethics Committee. Detailed information about the study can be provided by the principal investigator. The findings will be reported through academic journals, seminar and conference presentations, social media, print media, the internet, and community/stakeholder engagement activities.

Strengths and limitations of this study

- Several single-center studies have identified the prevalence of feeding-tube related incidents in general inpatients, however, there are no studies reporting on those incidents across multiple hospital sites and at a national level.
- A multicenter study may ascertain better generalizability of the data.
- To our knowledge, this is the first large scale study in Brazil and in Latin America documenting the incidence of feeding-tube related incidents in internal medicine wards.

- Although voluntary reporting can detect a broad range of incidents, this system misses the vast majority of incidents and cannot provide stable estimates of the true underlying causes.
- It is difficult to demonstrate causality between feeding tube-related incidents and negative patient outcomes due to a number of confounding factors.

INTRODUCTION

During hospitalization, patients with advanced disease have caloric and protein malnutrition, and require nutritional and drug interventions. Therefore, these patients often need feeding tube to ensure that their daily nutritional and medical needs are met. [1] Data from the American Society for Enteral and Parenteral Nutrition (ASPEN) revealed that more than 245,000 patients per year require at least a temporary feeding tube during a hospital stay, along with another nearly 31,000 patients that are on enteral nutrition at home. [2] In the United States, about one million feeding tubes are introduced in adults and children each year [3] and the rate of complications is 2% to 36%. [4-6]

Although inserting a feeding tube is a relatively innocuous procedure, improper positioning can cause severe and fatal complications. [7-9] One of the major incidents related to feeding tube is the wrong connection. The design of these devices is such that it is possible to infuse enteral feeding and/or medications via an unwanted route, such as intravenous route. [10,11]

It is also common to have inadvertent positioning of the tube in the respiratory tract, resulting in bronchoaspiration and pneumothorax. [8,12-14] Pulmonary aspiration occurs in 2% to 10% of patients receiving enteral feeding. The inadvertent insertion of the tube into the tracheal tree results in discomfort for the patient, delayed feeding, increased morbidity and mortality, and length of hospital stay, resulting in added burdens for the institution and patients. [5,15] Therefore, health care professionals need to routinely monitor risks and adopt strategies aimed at patient safety.

Other incidents may occur during the insertion and/or progression of a feeding tube through the gastrointestinal tract, such as sinusitis, vomiting, nasopharyngeal discomfort, erosion of the nasal septum, epistaxis, and blood return by the tube during guidewire withdrawal. [16] In Brazil, this data is not available, however, it is observed that feeding tube is a common procedure in most Brazilian health institutions. [17]

Regarding medication administration, administering drugs with absorption at the intestinal level in patients using a feeding tube is a challenge. As demonstrated in the literature, some drugs should never be crushed and administered through a feeding tube because they have enteric or controlled release protection coatings. [18] The grinding process of these drugs can destroy the coating film and result in incidents, exposing patients to unnecessary risks. [19] In this regard, experts argue that healthcare professionals should not assume that a drug formulated to be administered orally can be administered safely through a feeding tube because drug delivery mechanisms can be altered or destroyed, reducing effectiveness or increasing risk of toxicity. [20]

In order to achieve adequate clinical outcomes in hospitalized patients, it is essential that medication and enteral nutrition be administered appropriately. However, nursing

guidelines on enteral feeding tube care are not based on scientific evidence, but on traditions, rituals and expert opinions, exposing patients to unnecessary harm. [21]

Although feeding tube-related incidents are common in hospital settings with significant morbidity and mortality, the issue has not been extensively studied, especially in developing countries. Given that the number of patients with chronic conditions have increased significantly worldwide, as well as in Brazil, it is critical that health care professionals employ a repertoire of evidence based on interventions in order to provide safe and high quality care. [22,23] However, there is a knowledge gap regarding the safe handling of feeding tubes in Brazilian healthcare institutions. Studies that aim to identify the most frequent feeding tube-related incidents that occurred during hospital stays, can reduce that gap and the risks of complications and lower overall cost of care.

The results of the study will contribute to the production of knowledge and its application in clinical practice for harm reduction towards a safer environment for patient care; will provide national and international data that reflect the problem of feeding tube-related incidents in acute care units; and will contribute to the use of the evidence in an efficient way to influence the development of national practices and policies aimed at managing the risks associated with the feeding tube.

Significance and theoretical framework

Feeding tubes may be used long-term (ie., gastrostomy or jejunostomy) or short-term with distal tips positioned in the stomach (ie., nasally placed gastric tube) or small intestine (ie., nasally placed small-bowel feeding tube). [24] Long-term feeding tubes are not part of the scope of this study and, therefore these enteral access devices will not be addressed.

These devices are not exclusively used for administration of enteral nutrition. They are also frequently used for administering drugs. The consequence of this duo use is the increased risk of tube obstructions, physical-chemical incompatibilities, and potential drug-nutrient interactions. [25] In a previous study, researchers found that 74% of nurses employed wrong medication administration methods to deliver medicines through feeding tubes and those errors could reduce the effects of drugs and lead to unsuccessful treatments. [26]

According to a study conducted in a Brazilian private hospital, the main reason for the loss of a feeding tube was obstruction (36%) related to wrong medication preparation and administration techniques. [27] Estimates of incidence of clogged feeding tubes range widely from 12.5%-45%, but it is undisputed that they result in increased costs for patients and institutions. [28] Thus, health care practitioners, especially nurses, should not assume that a medication intended to be taken by mouth can be safely administered through a feeding tube, because this misconception can result in harm to patients and increase medical costs to society. [21]

Another incident related to improper medication administration via a feeding tube is caused by drug-drug interactions in older people due to polypharmacy, with a prevalence of 20-40%. Polypharmacy increases the complexity of clinical management and contributes to medication adverse events. [29]

Therefore, the causes of the incidents are multifaceted and the consequences are associated with increasing complexity of patients and treatments, intensifying the need for measures aimed at improving the quality of care. For this reason, opportunities to share knowledge are fundamental to patient safety. [30]

Efforts to overcome these problems have resulted in the development of international programs and policies. For instance, the WHO proposed the patient safety research cycle and the first step in improving care quality and safety is to measure the occurrence of incidents in order to know the magnitude of the problem. The WHO then suggests understanding the causes and identifying solutions. [31]

In Brazil, the Ministry of Health and the National Health Surveillance Agency (ANVISA), in line with WHO's global initiatives, launched the National Patient Safety Program in mid-April 2013 with the aim of promoting strategies aimed at prevention and reduction of risks associated with health care. Among the strategies were increasing patient safety research. [32,33]

The present study is necessary when considering the fact that patient safety is a global problem affecting countries at all levels of development; [34] the production of knowledge and its application in clinical practice can promote a safe environment for the provision of care, and in Brazil, there is concern about the need to increase knowledge on this issue and there are insufficient national data that reflect the problem of the incidents related to feeding tubes in hospitalized patients. We expect that the results of this study will provide high quality evidence that will support interventions designed to improve patient safety.

The objective of this study is to evaluate the feeding tube-related incidents in hospitalized patients and associated factors. The secondary objectives are:

1. To analyse the association between the feeding tube-related incidents and the complexity of the patients;
2. To analyze the association between the feeding tube-related incidents and the severity of comorbid diseases;
3. To examine the predictive role of Charlson Comorbidity Index (CCI) on mortality of patients with a feeding tube;
4. To assess potential drug-drug interactions (pDDI) in patients with a feeding tube and its association with patient complexity and comorbid diseases.

METHODS

Research Design

This is a multicenter study, with a prospective cohort design.

Setting

Seven centers across Brazil will participate in this study; the centers include a mix of community and university hospitals, hospitals with and without residency programs, and public and private hospitals; they also vary in size. The hospitals will be as follows: Acre Hospital of Clinics - HCA, General Hospital of Fortaleza - HGF, Hospital of Clinics of the Medical School of Ribeirão Preto of the University of São Paulo - HCFMRP-USP, Américo Brasiliense State Hospital - HEAB, Sumaré State Hospital - HES, São Vicente de Paulo Hospital - HSVP, and Santa Cruz Hospital - HSCRGS.

The medical wards of these hospitals were chosen for this study because many adult patients in these wards have chronic conditions and require enteral nutrition and medications through a feeding tube.

Subjects

The study population will be the patients admitted to the medical ward of the seven Brazilian hospitals that require a feeding tube during hospitalization. The inclusion criteria are: patients older than 18 years; who are admitted to the medical ward with a short-term feeding tube (nasally placed gastric tube or a nasally placed small-bowel feeding tube); patients who required the insertion of a short-term feeding tube during hospitalization; and patients that have been hospitalized for at least 24 hours. Patients meeting the above inclusion criteria who are re-admitted during the study period will be only counted for their first admission. Patients with nasogastric aspiration will be also excluded from this study.

Sampling size was determined by a stratified random sampling with proportional allocation by strata, where each stratum is formed by the floors / units of each hospital (Table 1):

Table 1. Determination of sample size, 2018

Hospital / Strata	Number of inpatients	Prevalence of patients with feeding tube	Estimated size of each stratum
HCA	980	0.1908	58
HGF	192	0.1563	11
HCFMRP-USP	2247	0.0788	134
HEAB	783	0.1073	47
HES	1991	0.1828	119
HSVP	323	0.0650	19

HSCRGS	48	0.0324	3

The formula for the calculation of the sample size is given by:

$$n = \frac{z^2_{\alpha/2} N(1-P)}{\varepsilon^2 P(N-1) + z^2_{\alpha/2}(1-P)} \quad (1)$$

,where P represents the prevalence of the event of interest

(column 4 of table 1), $z_{\alpha/2}$ represents the level of significance adopted and o ε is the relative sampling error. If the sample size calculated by the expression given in (1) is greater than 20% of the population the following finite correction procedure is adopted:

$nc = \frac{n}{\left(1 + {}^{n}/_{N}\right)}$ (2), where N is the total size of the study population and n is the value obtained in (1). The sample was allocated proportionally among the H strata according to the formula:

$n_h = n\frac{N_h}{N}$, where N is the total population of hospitalized patients (N = 6,564), and N_h is the total of each stratum H. Population totals are found in the second column of Table 1. Adopting the parameters of relative error of 20%, level of significance of 5% and the total population of 6,564, a total sample size of 391 patients was calculated. The required sample sizes of each strata are found in the last column of Table 1.

Instruments

Data collection tools will be composed of three virtual forms which will be developed by the research team and assessed for face and content validity by a panel of experts. The forms will be developed in Portuguese and an online platform (Survey Monkey®) will be used.

The experts will be selected through the analysis of existing curricula in the database of the Brazilian National Council for Scientific and Technological Development (CNPq) and will be invited to participate in the study, by invitation letter sent by electronic mail. Then the access links to the electronic forms will be made available for the experts to carry out their analysis; the experts will have up to 30 days to evaluate the electronic forms and give their feedback to the researchers. The modified forms will be tested through a pre-test, where the forms will be applied to five hospitalized patients from the first day of use of a feeding tube until patient discharge.

At admission, demographic, clinical, and therapeutic information will be recorded in the first electronic data collection form, including:

- ✓ *Demographic data*: registration number; date of admission to the ward / unit; date of birth; city / state of origin; gender; race; marital status; education level; profession; origin of the referral.

- ✓ *Clinical data:* principal and secondary International Classification of Diseases (ICD); comorbidities; the final score of the Patient Classification System (PCS); [35] level of consciousness measured by Glasgow Coma Scale (GCS).
- ✓ *Therapeutic data:* data related to the short-term feeding tube (time to insertion; type; gauge; location [gastric or small-bowel]; methods used to confirm feeding tube placement and the results of the methods used); data related to the enteral nutrition (type, total volume in 24 hours, frequency of administration); data related to the medications prescribed (drug name; dosage form; dose; route of administration; frequency of administration; and planned / scheduled administration time).

The second electronic data collection form will include variables related to the incidents:

- ✓ *Incident:* date and time of occurrence; type of incident (mechanic; gastrointestinal; infectious; and others); [4] consequence of the incident for the patient, according to the WHO (none; mild; moderate; severe; and fatal); [36] measures adopted after the incident; sources of information on the occurrence of the incident; and means of obtaining information about the incident.
- ✓ *Clinical:* principal and secondary ICD; comorbidities; the final score of the PCS; [35] level of consciousness measured by GCS.
- ✓ *Therapeutic:* data related to the enteral nutrition (type, total volume in 24 hours, frequency of administration); data related to the medications prescribed (drug name; dosage form; dose; route of administration; frequency of administration; and planned / scheduled administration time).

The third electronic data collection form will include variables related to the start of feeding tube and patient follow-up:

- ✓ *Clinical:* date of the start of the feeding tube use; principal and secondary ICD; comorbidities; the final score of the PCS; [35] level of consciousness measured by GCS.
- ✓ *Therapeutic:* data related to the medications prescribed 24 hours after feeding tube insertion (or 24 hours after admission if the patient is admitted at the unit with a feeding tube); medications prescribed 120 hours after feeding tube insertion (or 120 hours after admission if the patient is admitted at the unit with a feeding tube); and medications prescribed 24 hours before patient discharge.
- ✓ Date of programmed feeding tube removal and the main reason; date and time of patient discharge; reason for patient discharge.

Procedures

This study will be completed in 24 months. At each center, a registered nurse in the medical ward and a research assistant will serve as a liaison to the study investigators; a designated

nurse coordinator will ensure that the collection of data will be carried out completely and correctly. The liaison nurse and the research assistant at each center will attend a total of 16 hours of theoretical and practical formal training sessions led by the regional study coordinator, at which the overall study design will be presented and each electronic data collection forms will be explained. The study protocol will neither mandate nor direct any element of patient care, and thus will pose no risk to patients.

A data collection guideline will be developed with the purpose of standardizing data recording in the seven hospitals participating in the study. This guideline will consist of general information related to the research project; general instructions on how to access the electronic data collection forms using mobile devices; definition of each variable and additional information for completing the variables that make up the three electronic data collection forms. The guideline will be available on printed version and by e-mail to assist all the research team on data collection.

Before data collection starts, the researchers will identify the patients who will start the use of a short-term feeding tube during hospitalization, according to the inclusion criteria proposed for this study. In Brazilian hospitals, short-term feeding tubes are performed by registered nurses.

Researchers will explain the research objectives and will ask patients, or their legal guardians, to voluntarily sign the Informed Consent Form.

For purposes of confidentiality, each patient will be identified by a unique identifying number; data will be collected from the moment a patient starts using a short-term feeding tube until the patient is discharged (due to death or non-death).

Using a mobile device, research assistants will collect demographic data at patient admission, and prospectively record clinical and therapeutic data from the patients' medical record. Considering that four hospitals participating in this study have present electronic medical records, these will be accessed in the computers available in the medical wards / units. In both situations, the researchers will request permission from the nurse responsible for the unit to access the computers, and to record the information in the electronic data collection forms. The consultation of the medical records will occur in the afternoon or at night, because these are the periods with the least movement of people.

Assessment of the complexity of patients with feeding tube

Patient complexity will be assessed by an experienced nurse, member of the research team, on the first day of feeding tube use, on the day of the incident, and weekly until patient discharges. Nurses will have up to 24 hours to complete their evaluation.

For this purpose, the PCS proposed by Fugulin [35] will be used. The PCS is recommended by the Federal Nursing Council, Brazil, [37] and it was developed to classify

patients according to the degree of dependence of the nursing team. This instrument has nine critical indicators: mental state, oxygenation, vital signs, motility, ambulation, feeding, body care, elimination and therapeutics. Therefore, the scores are distributed in five categories that correspond to the complexity of the assistance: minimum (scores of 9-14), intermediate (scores of 15-20), high-dependency (scores of 21-26), semi-intensive (scores of 27-31), and intensive care (scores > 31).

Assessment of the severity of comorbid diseases of patients with feeding tube

Regarding the severity of comorbid diseases, this will be evaluated on admission at the medical ward / unit; on the first day of use of the short-term feeding tube; on the day of the incident; and weekly until patient discharges. For this purpose, the Charlson Comorbidity Index (CCI) [38] will be used. The CCI is the most widely used comorbidity, which is a method of categorizing patients' comorbidities, according to the ICD. The aim of the CCI is to measure the severity of the patient, regardless of the main diagnosis, and therefore, to predict the one-year mortality of patients. The final score is the result of the sum of the weights assigned to the comorbidities recorded as secondary diagnoses; the higher the score, the greater the risk of the patient dying. It should be noted that the CCI will be adjusted according to the patient's age, so that, from the age of 50, a point will be added to the final score for every decade of life. [38]

Based on the final CCI score, patients will be divided into three groups: mild (with CCI scores of 1–2); moderate (with CCI scores of 3–4); and severe (with CCI scores ≥5). In addition, survival time in days will be calculated from the first day patient start using a feeding tube during hospital stay to the death of a patient. [39]

Assessment of the feeding tube-related incidents

In this study, incident was defined as an event or circumstance that could have resulted, or did result, in unnecessary harm to a patient. [36] The feeding tube-related incidents considered in this study are:

- ✓ Mechanical incident (unplanned / accidental removal; obstruction; displacement / migration; epistaxis; nasal mucosa edema; perforation or stenosis of the esophagus; perforation of the brain; pneumothorax; various attempts to introduce the tube).
- ✓ Gastrointestinal incident (nausea / vomiting; diarrhea; constipation; colic / abdominal distension / flatulence).
- ✓ Infection (aspiration pneumonia; gastroenterocolitis).
- ✓ Other incidents (skin lesion associated with the feeding tube insertion; bronchoaspiration; wrong connection; quality of the tube material).

Based on previous studies, [40,41] three methods will be used for incidents detection:

(1) Prompted spontaneous reporting: healthcare professionals (nursing and medical staff) and patients / caregivers will be continuously prompted to report any feeding tube-related incidents to the investigators. A pen and a booklet containing instructions on incident reporting will be available and remain at the bedside of each patient participating in the study;
(2) Researchers will visit the wards / units at least twice a week to request information about the incidents, along with healthcare professionals (nursing and medical staff) and patients / caregivers;
(3) Researchers will review the booklet and medical records at least twice a week to obtain information about feeding tube-related incident.

Using a mobile device, the research assistant will record data related to the incidents in the electronic data collection form developed for this purpose. More than one incident may occur on the same day and/or at the same time (eg. tube obstruction and unplanned removal), thus each incident will be recorded on a different form, resulting in a form filled for each incident.

Assessment of potential drug-drug interactions in patients with feeding tube

Regarding the analysis of potential drug-drug interactions, it will be performed only in patients with a hospital stay of at least five days, because longer hospital stays are associated with the likelihood of adverse drug events. [42]

The research assistants will record on electronic data collection forms all medications and enteral nutrition prescribed for patients, regardless of whether they were administered or not. Data related to the medications will be collected in the following moments of hospitalization: at admission; 24 hours and 120 hours after admission because it is the period of greatest therapeutic adjustment [43-45]. Data related to medications will also be recorded 24 hours before patient discharge and on the day of the incident. Data related to enteral nutrition will be recorded on admission and on the day of the incident.

Medications will be classified according to the WHO Chemical Anatomical Therapeutic Classification (ATC), [46] and the analysis of drug interactions will be performed based on drug monographs from the Drug Reax System database from Thomson Healthcare® because it is a highly reliable software. [47] The software is also available in the journal portal of the Coordination of Improvement of Higher-Level Personnel - CAPES, Brazil. Potential drug-drug interactions will be classified according to the speed of action, documentation and severity, as recommended by Drug Reax®.

Data analysis

Data will be downloaded from the Survey Monkey® to a computer file and analyzed using the Statistical Package for the Social Program Sciences® (SPSS) version 25.0. In the statistical analysis, we will apply: calculation of proportions and measures of central tendency and variability. Quantitative variables will be assessed for normal distribution using the Kolmogorov-Smirnov test. The importance of the normal distribution evaluation is justified, among others, by the subsequent indication of parametric and non-parametric statistical tests. Pearson's Chi-square (χ^2) and Fisher's exact tests will be used to compare the response variables with the categorical explanatory variables, when indicated. For the comparison of the variable responses with the quantitative explanatory variables, t or Mann-Whitney tests will be performed, when indicated.

To examine the predictive role of Charlson Comorbidity Index (CCI) on mortality of patients having feeding tubes, a one-way analysis of variance (ANOVA) will be used to compare group differences stratified by CCI, and otherwise Chi-square tests will be applied. All analysis will be carried out considering a significance level of 5% (α= 0,05).

Patient and Public Involvement

Although patients were not involved in the setting of the research questions or the outcome measures, participants will be informed of the project aims and asked to voluntarily sign the consent form. They will be informed of possible risks which are: discomfort or embarrassment when answering questions about feeding tube-related incidents, thus participants will be able to refuse to answer any question that he/she feels inconvenient or inappropriate, without causing harm to their care. In addition, participants will be informed that the results will be used for possible publications and we will guarantee their confidentiality and anonymity.

Ethics and Dissemination

The study was approved by the Research Ethics Committee of the University of São Paulo at Ribeirão Preto College of Nursing, according to the Resolution No. 466/2012, of the National Council of Ethics in Research of the Brazilian Ministry of Health, which addresses research ethics with humans (CAAE: 56166016.1001.5393). Written informed consent will be obtained from each patient, or their guardian, prior to enrollment in the study. No personally identifiable information will be collected in order to maintain the anonymity of the participants and they will be informed that the results will be used for possible publications.

The results will be reported to the hospitals and the findings may contribute to the hospital's policies and procedures to reduce the risks for feeding tube related incidents and to improve the quality of care and patient safety. There is very little information about feeding tube related incidents in developing countries, so this study will provide important information about risk levels. Results will also be reported through academic journals and conference

presentations, social media (ie, Facebook, Twitter), print media (ie,. Patient Safety Alert), the internet (ie, links to study reports on the Patient Safety Research Group website), and community/stakeholder engagement activities (ie, community forums, stakeholder meetings). The project team includes academic researchers, hospital clinicians and experts involved in patient safety. This provides the project with access to a range of other conduits through which to disseminate results to, for example, policymakers and system implementers.

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Competing interests

None declared.

Patient Consent

Obtained.

Ethics approval

The study was approved by the Research Ethics Committee of the University of São Paulo at Ribeirão Preto College of Nursing (CAAE: 56166016.1001.5393).

Provenance and peer review

Not commissioned; externally peer reviewed.

Contributorship statement: FREG and MCAP initiated the project and are the chief investigators on the project; they made substantial contributions to the conception and design of the work. PRP, REFLC, JK, LMF, TCAT, and AIM, are associate investigators and all made significant contributions to the protocol in their specific areas of expertise. FREG prepared the first draft of this protocol and all authors have reviewed, provided input and gave final approval of the version published.

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Nasogastric/Nasoenteric tube-related incidents in hospitalized patients: a study protocol of a multicenter prospective cohort study

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Nasogastric/Nasoenteric tube-related incidents in hospitalized patients: a study protocol of a multicenter prospective cohort study

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ABSTRACT

Introduction: Hospitalized patients with nasogastric/nasoenteric tube (NGT/NET) are at constant risk of incidents; therefore, healthcare professionals need to routinely monitor risks and adopt strategies for patient safety and quality of care.

Aim: To evaluate the NGT/NET related incidents in hospitalized patients and associated factors.

Methods: This is a multicenter study, with a multicenter prospective cohort design. Data will be collected at the general medical ward of seven Brazilian hospitals in the North, Northeast, Southeast, and South. The sample will consist of 391 patients that require a NGT/NET during hospitalization. Three different methods will be used to identify the incidents: (1) healthcare professionals and patients/caregivers will be required to report any NGT/NET related incidents; (2) researchers will visit the wards to get information about the incidents with healthcare professionals and patients/caregivers; (3) the researchers will review the medical records looking for information on the occurrence of any NGT/NET related incidents. Demographic, clinical and therapeutic details will be obtained from the medical records and will be registered in an electronic data collection tool developed for the purposes of this study. The complexity of patients will be assessed by the Patient Classification System, and the severity of comorbid diseases, through the Charlson Comorbidity Index.

Implication for practice: The results may encourage the use of evidence effectively to influence the scientific foundation for clinical practice and the development of evidence-based policies that will prevent, manage and eliminate complications caused by NGT/NET related incidents, and improve the quality and safety of care provided to hospitalized patients.

Ethics and dissemination: The study has been approved by the Research Ethics Committee. Detailed information about the study can be provided by the principal investigator. The findings will be reported through academic journals, seminar and conference presentations, social media, print media, the internet, and community/stakeholder engagement activities.

Strengths and limitations of this study

- Several single-center studies have identified the prevalence of NGT/NET related incidents in general inpatients, however, there are no studies reporting on those incidents across multiple hospital sites and at a national level.
- A multicenter study may ascertain better generalizability of the data.
- To our knowledge, this is the first large scale study in Brazil and in Latin America documenting the incidence of NGT/NET related incidents in internal medicine wards.

- Although voluntary reporting can detect a broad range of incidents, this system misses the vast majority of incidents and cannot provide stable estimates of the true underlying causes.
- It is difficult to demonstrate causality between NGT/NET related incidents and negative patient outcomes due to a number of confounding factors.

INTRODUCTION

During hospitalization, patients with advanced disease have caloric and protein malnutrition, and require nutritional and drug interventions. Therefore, these patients often need a nasogastric/nasoenteric tube (NGT/NET) to ensure that their daily nutritional and medical needs are met. [1] Data from the American Society for Enteral and Parenteral Nutrition (ASPEN) revealed that more than 245,000 patients per year require at least a temporary feeding tube during a hospital stay, along with another nearly 31,000 patients that are on enteral nutrition at home. [2] In the United States, about one million NGT/NET are introduced in adults and children each year [3] and the rate of complications is 2% to 36%. [4-6]

Although inserting a NGT/NET is a relatively innocuous procedure, improper positioning can cause severe and fatal complications. [7-9] One of the major incidents related to NGT/NET is the wrong connection. The design of these devices is such that it is possible to infuse enteral feeding and/or medications via an unwanted route, such as intravenous route. [10,11]

It is also common to have inadvertent positioning of the tube in the respiratory tract, resulting in bronchoaspiration and pneumothorax. [8,12-14] Pulmonary aspiration occurs in 2% to 10% of patients receiving enteral feeding. The inadvertent insertion of the tube into the tracheal tree results in discomfort for the patient, delayed feeding, increased morbidity and mortality, and length of hospital stay, resulting in added burdens for the institution and patients. [5,15] Therefore, health care professionals need to routinely monitor risks and adopt strategies aimed at patient safety.

Other incidents may occur during the insertion and/or progression of a NGT/NET through the gastrointestinal tract, such as sinusitis, vomiting, nasopharyngeal discomfort, erosion of the nasal septum, epistaxis, and blood return by the tube during guidewire withdrawal. [16] In Brazil, this data is not available, however, it is observed that NGT/NET are a common procedure in most Brazilian health institutions. [17]

Regarding medication administration, administering drugs with absorption at the intestinal level in patients using a NGT is a challenge. As demonstrated in the literature, some drugs should never be crushed and administered through a NGT because they have enteric or controlled release protection coatings. [18] The grinding process of these drugs can destroy the coating film and result in incidents, exposing patients to unnecessary risks. [19] In this regard, experts argue that healthcare professionals should not assume that a drug formulated to be administered orally can be administered safely through a NGT/NET because drug delivery mechanisms can be altered or destroyed, reducing effectiveness or increasing risk of toxicity. [20]

In order to achieve adequate clinical outcomes in hospitalized patients, it is essential that medication and enteral nutrition be administered appropriately. However, nursing

guidelines on enteral feeding tube care are not based on scientific evidence, but on traditions, rituals and expert opinions, exposing patients to unnecessary harm. [21]

Although NGT/NET related incidents are common in hospital settings with significant morbidity and mortality, the issue has not been extensively studied, especially in developing countries. Given that the number of patients with chronic conditions have increased significantly worldwide, as well as in Brazil, it is critical that health care professionals employ a repertoire of evidence based on interventions in order to provide safe and high quality care. [22,23] However, there is a knowledge gap regarding the safe handling of NGT/NET in Brazilian healthcare institutions. Studies that aim to identify the most frequent NGT/NET related incidents that occurred during hospital stays, can reduce that gap and the risks of complications and lower overall cost of care.

The results of the study will contribute to the production of knowledge and its application in clinical practice for harm reduction towards a safer environment for patient care; will provide national and international data that reflect the problem of NGT/NET related incidents in acute care units; and will contribute to the use of the evidence in an efficient way to influence the development of national practices and policies aimed at managing the risks associated with the NGT/NET.

Significance and theoretical framework

Feeding tubes may be used long-term (ie., gastrostomy or jejunostomy) or short-term with distal tips positioned in the stomach (ie., NGT) or small intestine (ie., NET). [24] Long-term feeding tubes are not part of the scope of this study and, therefore these enteral access devices will not be addressed.

These devices are not exclusively used for administration of enteral nutrition. They are also frequently used for administering drugs. The consequence of this duo use is the increased risk of tube obstructions, physical-chemical incompatibilities, and potential drug-nutrient interactions. [25] In a previous study, researchers found that 74% of nurses employed wrong medication administration methods to deliver medicines through NGT/NET and those errors could reduce the effects of drugs and lead to unsuccessful treatments. [26]

According to a study conducted in a Brazilian private hospital, the main reason for the loss of a NGT/NET was obstruction (36%) related to wrong medication preparation and administration techniques. [27] Estimates of incidence of clogged feeding tubes range widely from 12.5%-45%, but it is undisputed that they result in increased costs for patients and institutions. [28] Thus, health care practitioners, especially nurses, should not assume that a medication intended to be taken by mouth can be safely administered through a NGT/NET, because this misconception can result in harm to patients and increase medical costs to society. [21]

Another incident related to improper medication administration via a NGT/NET is caused by drug-drug interactions in older people due to polypharmacy, with a prevalence of 20-40%. Polypharmacy increases the complexity of clinical management and contributes to medication adverse events. [29]

Therefore, the causes of the incidents are multifaceted and the consequences are associated with increasing complexity of patients and treatments, intensifying the need for measures aimed at improving the quality of care. For this reason, opportunities to share knowledge are fundamental to patient safety. [30]

Efforts to overcome these problems have resulted in the development of international programs and policies. For instance, the WHO proposed the patient safety research cycle and the first step in improving care quality and safety is to measure the occurrence of incidents in order to know the magnitude of the problem. The WHO then suggests understanding the causes and identifying solutions. [31]

In Brazil, the Ministry of Health and the National Health Surveillance Agency (ANVISA), in line with WHO's global initiatives, launched the National Patient Safety Program in mid-April 2013 with the aim of promoting strategies aimed at prevention and reduction of risks associated with health care. Among the strategies were increasing patient safety research. [32,33]

The present study is necessary when considering the fact that patient safety is a global problem affecting countries at all levels of development; [34] the production of knowledge and its application in clinical practice can promote a safe environment for the provision of care, and in Brazil, there is concern about the need to increase knowledge on this issue and there are insufficient national data that reflect the problem of the incidents related to NGT/NET in hospitalized patients. We expect that the results of this study will provide high quality evidence that will support interventions designed to improve patient safety.

The objective of this study is to evaluate the NGT/NET related incidents in hospitalized patients and associated factors. The secondary objectives are:

1. To analyse the association between the NGT/NET related incidents and the complexity of the patients;
2. To analyze the association between the NGT/NET related incidents and the severity of comorbid diseases;
3. To examine the predictive role of Charlson Comorbidity Index (CCI) on mortality of patients with a NGT/NET;
4. To assess potential drug-drug interactions (pDDI) in patients with a NGT/NET and its association with patient complexity and comorbid diseases.

METHODS

Research Design

This is a multicenter study, with a prospective cohort design.

Setting

Seven centers across Brazil will participate in this study; the centers include a mix of community and university hospitals, hospitals with and without residency programs, and public and private hospitals; they also vary in size. The hospitals will be as follows: Acre Hospital of Clinics - HCA, General Hospital of Fortaleza - HGF, Hospital of Clinics of the Medical School of Ribeirão Preto of the University of São Paulo - HCFMRP-USP, Américo Brasiliense State Hospital - HEAB, Sumaré State Hospital - HES, São Vicente de Paulo Hospital - HSVP, and Santa Cruz Hospital - HSCRGS.

The medical wards of these hospitals were chosen for this study because many adult patients in these wards have chronic conditions and require enteral nutrition and medications through a NGT/NET.

Subjects

The study population will be the patients admitted to the medical ward of the seven Brazilian hospitals that require a feeding tube during hospitalization. The inclusion criteria are: patients older than 18 years; who are admitted to the medical ward with a short-term feeding tube (NGT or NET); patients who required the insertion of a NGT/NET; and patients that have been hospitalized for at least 24 hours. Patients meeting the above inclusion criteria who are re-admitted during the study period will be only counted for their first admission.

Sampling size was determined by a stratified random sampling with proportional allocation by strata, where each stratum is formed by the floors / units of each hospital (Table 1):

Table 1. Determination of sample size, 2018

Hospital / Strata	Number of inpatients	Prevalence of patients with NGT/NET	Estimated size of each stratum
HCA	980	0.1908	58
HGF	192	0.1563	11
HCFMRP-USP	2247	0.0788	134
HEAB	783	0.1073	47
HES	1991	0.1828	119
HSVP	323	0.0650	19
HSCRGS	48	0.0324	3

The formula for the calculation of the sample size is given by:

$$n = \frac{z^2_{\alpha/2} N(1-P)}{\varepsilon^2 P(N-1) + z^2_{\alpha/2}(1-P)} \quad (1)$$

,where P represents the prevalence of the event of interest

(column 4 of table 1), $z_{\alpha/2}$ represents the level of significance adopted and o ε is the relative sampling error. If the sample size calculated by the expression given in (1) is greater than 20% of the population the following finite correction procedure is adopted:

$nc = \frac{n}{\left(1 + {}^{n}/_{N}\right)}$ (2), where N is the total size of the study population and n is the value obtained in (1). The sample was allocated proportionally among the H strata according to the formula:

$n_h = n\frac{N_h}{N}$, where N is the total population of hospitalized patients (N = 6,564), and N_h is the total of each stratum H. Population totals are found in the second column of Table 1. Adopting the parameters of relative error of 20%, level of significance of 5% and the total population of 6,564, a total sample size of 391 patients was calculated. The required sample sizes of each strata are found in the last column of Table 1.

Instruments

Data collection tools will be composed of three virtual forms which will be developed by the research team and assessed for face and content validity by a panel of experts. The forms will be developed in Portuguese and an online platform (Survey Monkey®) will be used.

The experts will be selected through the analysis of existing curricula in the database of the Brazilian National Council for Scientific and Technological Development (CNPq) and will be invited to participate in the study, by invitation letter sent by electronic mail. Then the access links to the electronic forms will be made available for the experts to carry out their analysis; the experts will have up to 30 days to evaluate the electronic forms and give their feedback to the researchers. The modified forms will be tested through a pre-test, where the forms will be applied to five hospitalized patients from the first day of use of a NGT/NET until patient discharge.

At admission, demographic, clinical, and therapeutic information will be recorded in the first electronic data collection form, including:

- ✓ *Demographic data*: registration number; date of admission to the ward / unit; date of birth; city / state of origin; gender; race; marital status; education level; profession; origin of the referral.

- ✓ *Clinical data:* principal and secondary International Classification of Diseases (ICD); comorbidities; the final score of the Patient Classification System (PCS); [35] level of consciousness measured by Glasgow Coma Scale (GCS).
- ✓ *Therapeutic data:* data related to the NGT/NET (time to insertion; type; gauge; location [gastric or small-bowel]; methods used to confirm feeding tube placement and the results of the methods used); data related to the enteral nutrition (type, total volume in 24 hours, frequency of administration); data related to the medications prescribed (drug name; dosage form; dose; route of administration; frequency of administration; and planned / scheduled administration time).

The second electronic data collection form will include variables related to the incidents:

- ✓ *Incident:* date and time of occurrence; type of incident (mechanic; gastrointestinal; infectious; and others); [4] consequence of the incident for the patient, according to the WHO (none; mild; moderate; severe; and fatal); [36] measures adopted after the incident; sources of information on the occurrence of the incident; and means of obtaining information about the incident.
- ✓ *Clinical:* principal and secondary ICD; comorbidities; the final score of the PCS; [35] level of consciousness measured by GCS.
- ✓ *Therapeutic:* data related to the enteral nutrition (type, total volume in 24 hours, frequency of administration); data related to the medications prescribed (drug name; dosage form; dose; route of administration; frequency of administration; and planned / scheduled administration time).

The third electronic data collection form will include variables related to the start of feeding tube and patient follow-up:

- ✓ *Clinical:* date of the start of the feeding tube use; principal and secondary ICD; comorbidities; the final score of the PCS; [35] level of consciousness measured by GCS.
- ✓ *Therapeutic:* data related to the medications prescribed 24 hours after feeding tube insertion (or 24 hours after admission if the patient is admitted at the unit with a NGT/NET); medications prescribed 120 hours after feeding tube insertion (or 120 hours after admission if the patient is admitted at the unit with a NGT/NET); and medications prescribed 24 hours before patient discharge.
- ✓ Date of programmed feeding tube removal and the main reason; date and time of patient discharge; reason for patient discharge.

Procedures

Data collection started on February 2019 and will be completed in 24 months. At each center, a registered nurse in the medical ward and a research assistant will serve as a liaison to the

study investigators; a designated nurse coordinator will ensure that the collection of data will be carried out completely and correctly. The liaison nurse and the research assistant at each center will attend a total of 16 hours of theoretical and practical formal training sessions led by the regional study coordinator, at which the overall study design will be presented and each electronic data collection forms will be explained. The study protocol will neither mandate nor direct any element of patient care, and thus will pose no risk to patients.

A data collection guideline will be developed with the purpose of standardizing data recording in the seven hospitals participating in the study. This guideline will consist of general information related to the research project; general instructions on how to access the electronic data collection forms using mobile devices; definition of each variable and additional information for completing the variables that make up the three electronic data collection forms. The guideline will be available on printed version and by e-mail to assist all the research team on data collection.

Before data collection starts, the researchers will identify the patients who will start the use of a NGT/NET during hospitalization, according to the inclusion criteria proposed for this study. In Brazilian hospitals, NGT/NET are inserted by registered nurses.

Researchers will explain the research objectives and will ask patients, or their legal guardians, to voluntarily sign the Informed Consent Form.

For purposes of confidentiality, each patient will be identified by a unique identifying number; data will be collected from the moment a patient starts using a NGT/NET until the patient is discharged (due to death or non-death).

Using a mobile device, research assistants will collect demographic data at patient admission, and prospectively record clinical and therapeutic data from the patients' medical record. Considering that four hospitals participating in this study have present electronic medical records, these will be accessed in the computers available in the medical wards / units. In both situations, the researchers will request permission from the nurse responsible for the unit to access the computers, and to record the information in the electronic data collection forms. The consultation of the medical records will occur in the afternoon or at night, because these are the periods with the least movement of people.

Assessment of the complexity of patients with NGT/NET

Patient complexity will be assessed by an experienced nurse, member of the research team, on the first day of feeding tube use, on the day of the incident, and weekly until patient discharges. Nurses will have up to 24 hours to complete their evaluation.

For this purpose, the PCS proposed by Fugulin [35] will be used. The PCS is recommended by the Federal Nursing Council, Brazil, [37] and it was developed to classify patients according to the degree of dependence of the nursing team. This instrument has nine

critical indicators: mental state, oxygenation, vital signs, motility, ambulation, feeding, body care, elimination and therapeutics. Therefore, the scores are distributed in five categories that correspond to the complexity of the assistance: minimum care (scores of 9-14), intermediate care (scores of 15-20), high-dependency (scores of 21-26), semi-intensive (scores of 27-31), and intensive care (scores > 31).

Assessment of the severity of comorbid diseases of patients with NGT/NET

Regarding the severity of comorbid diseases, this will be evaluated on admission at the medical ward / unit; on the first day of use of the short-term feeding tube; on the day of the incident; and weekly until patient discharges. For this purpose, the Charlson Comorbidity Index (CCI) [38] will be used. The CCI is the most widely used comorbidity, which is a method of categorizing patients' comorbidities, according to the ICD. The aim of the CCI is to measure the severity of the patient, regardless of the main diagnosis, and therefore, to predict the one-year mortality of patients. The final score is the result of the sum of the weights assigned to the comorbidities recorded as secondary diagnoses; the higher the score, the greater the risk of the patient dying. It should be noted that the CCI will be adjusted according to the patient's age, so that, from the age of 50, a point will be added to the final score for every decade of life. [38]

Based on the final CCI score, patients will be divided into three groups: mild (with CCI scores of 1–2); moderate (with CCI scores of 3–4); and severe (with CCI scores ≥5). In addition, survival time in days will be calculated from the first day patient start using a feeding tube during hospital stay to the death of a patient. [39]

Assessment of the NGT/NET related incidents

In this study, incident was defined as an event or circumstance that could have resulted, or did result, in unnecessary harm to a patient. [36] The NGT/NET related incidents considered in this study are:

- ✓ Mechanical incident (unplanned / accidental removal; obstruction; displacement / migration; epistaxis; nasal mucosa edema; perforation or stenosis of the esophagus; perforation of the brain; pneumothorax; various attempts to introduce the tube).
- ✓ Gastrointestinal incident (nausea / vomiting; diarrhea; constipation; colic / abdominal distension / flatulence).
- ✓ Infection (aspiration pneumonia; gastroenterocolitis).
- ✓ Other incidents (skin lesion associated with the NGT/NET insertion; bronchoaspiration; wrong connection; quality of the tube material).

Based on previous studies, [40,41] three methods will be used for incidents detection:

(1) Prompted spontaneous reporting: healthcare professionals (nursing and medical staff) and patients / caregivers will be continuously prompted to report any NGT/NET related incidents to the investigators. A pen and a booklet containing instructions on incident reporting will be available and remain at the bedside of each patient participating in the study;

(2) Researchers will visit the wards / units at least twice a week to request information about the incidents, along with healthcare professionals (nursing and medical staff) and patients / caregivers;

(3) Researchers will review the booklet and medical records at least twice a week to obtain information about NGT/NET related incident.

Using a mobile device, the research assistant will record data related to the incidents in the electronic data collection form developed for this purpose. More than one incident may occur on the same day and/or at the same time (eg. tube obstruction and unplanned removal), thus each incident will be recorded on a different form, resulting in a form filled for each incident.

Assessment of potential drug-drug interactions in patients with NGT/NET

Regarding the analysis of potential drug-drug interactions, it will be performed only in patients with a hospital stay of at least five days, because longer hospital stays are associated with the likelihood of adverse drug events. [42]

The research assistants will record on electronic data collection forms all medications and enteral nutrition prescribed for patients, regardless of whether they were administered or not. Data related to the medications will be collected in the following moments of hospitalization: at admission; 24 hours and 120 hours after admission because it is the period of greatest therapeutic adjustment [43-45]. Data related to medications will also be recorded 24 hours before patient discharge and on the day of the incident. Data related to enteral nutrition will be recorded on admission and on the day of the incident.

Medications will be classified according to the WHO Chemical Anatomical Therapeutic Classification (ATC), [46] and the analysis of drug interactions will be performed based on drug monographs from the Drug Reax System database from Thomson Healthcare® because it is a highly reliable software. [47] The software is also available in the journal portal of the Coordination of Improvement of Higher-Level Personnel - CAPES, Brazil. Potential drug-drug interactions will be classified according to the speed of action, documentation and severity, as recommended by Drug Reax®.

Data analysis

Data will be downloaded from the Survey Monkey® to a computer file and analyzed using the Statistical Package for the Social Program Sciences® (SPSS) version 25.0. In the statistical analysis, we will apply: calculation of proportions and measures of central tendency and variability. Quantitative variables will be assessed for normal distribution using the Kolmogorov-Smirnov test. The importance of the normal distribution evaluation is justified, among others, by the subsequent indication of parametric and non-parametric statistical tests. Pearson's Chi-square (χ^2) and Fisher's exact tests will be used to compare the response variables with the categorical explanatory variables, when indicated. For the comparison of the variable responses with the quantitative explanatory variables, t or Mann-Whitney tests will be performed, when indicated.

To examine the predictive role of Charlson Comorbidity Index (CCI) on mortality of patients having a NGT/NET, a one-way analysis of variance (ANOVA) will be used to compare group differences stratified by CCI, and otherwise Chi-square tests will be applied. All analysis will be carried out considering a significance level of 5% (α= 0,05).

Patient and Public Involvement

Patients were not involved in the setting of the research questions or the outcome measures. However, we have specific plans to disseminate the results of the research to the patient community through social media (ie, Facebook, Twitter), print media (ie,. Patient Safety Alert), the internet (ie, links to study reports on the Patient Safety Research Group website), and community/stakeholder engagement activities (ie, community forums, stakeholder meetings).

Ethics and Dissemination

The study was approved by the Research Ethics Committee of the University of São Paulo at Ribeirão Preto College of Nursing, according to the Resolution No. 466/2012, of the National Council of Ethics in Research of the Brazilian Ministry of Health, which addresses research ethics with humans (CAAE: 56166016.1001.5393). Written informed consent will be obtained from each patient, or their guardian, prior to enrollment in the study. Participants will be informed of the project aims and asked to voluntarily sign the consent form. They will be informed of possible risks which are: discomfort or embarrassment when answering questions about NGT/NET related incidents, thus participants will be able to refuse to answer any question that he/she feels inconvenient or inappropriate, without causing harm to their care. No personally identifiable information will be collected in order to maintain the anonymity of the participants and they will be informed that the results will be used for possible publications.

The results will be reported to the hospitals and the findings may contribute to the hospital's policies and procedures to reduce the risks for NGT/NET related incidents and to improve the quality of care and patient safety. There is very little information about NGT/NET

related incidents in developing countries, so this study will provide important information about risk levels. Results will also be reported through academic journals and conference presentations, social media (ie, Facebook, Twitter), print media (ie,. Patient Safety Alert), the internet (ie, links to study reports on the Patient Safety Research Group website), and community/stakeholder engagement activities (ie, community forums, stakeholder meetings). The project team includes academic researchers, hospital clinicians and experts involved in patient safety. This provides the project with access to a range of other conduits through which to disseminate results to, for example, policymakers and system implementers.

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Competing interests

None declared.

Patient Consent

Obtained.

Ethics approval

The study was approved by the Research Ethics Committee of the University of São Paulo at Ribeirão Preto College of Nursing (CAAE: 56166016.1001.5393).

Provenance and peer review

Not commissioned; externally peer reviewed.

Contributorship statement: FREG and MCAP initiated the project and are the chief investigators on the project; they made substantial contributions to the conception and design of the work. PRP, REFLC, JK, LMF, TCAT, and AIM, are associate investigators and all made significant contributions to the protocol in their specific areas of expertise. FREG prepared the first draft of this protocol and all authors have reviewed, provided input and gave final approval of the version published.

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