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Short Communication

Detection of gastroesophageal reflux by multichannel intraluminal impedance technology during mechanical ventilation: the first case series

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SUMMARY

Background & Aims: Gastroesophageal reflux (GER) is a common event among mechanically ventilated and tube-fed critically ill patients and it is associated with an increased risk of ventilator-associated pneumonia. Most of the available tools for the detection of GER are experimental and not available bedside. Intraluminal impedance was suggested as a technique for real-time detection and quantification of GER. This study aimed to evaluate the frequency and duration of GER events in mechanically ventilated and tube-fed patients and to determine their correlation with routine procedures performed during patient care.
Methods: This was a prospective observational study of 20 critically ill patients hospitalized in a university hospital general intensive care unit. We included adult, mechanically ventilated patients receiving continuous enteral feeding by feeding tube (FT). A FT with multichannel intraluminal impedance sensors capable of detecting movement of gastro-esophageal content above the lower esophageal sphincter was used for GER detection. The frequency, duration, and association with routine procedures (position change, suction, and fluid bolus administration) were evaluated.
Results: During the median monitoring time of 2.9 days (IQR 2.8–3) per patient, a median number of 2.7 (IQR 2.1–3.8) GER events were detected every hour. 61% of GERs lasted 10–30 seconds.

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Position changes, endotracheal suctions, and fluid bolus administrations were associated with a high frequency of GERs.
Conclusions: Multichannel impedance sensors embedded on a FT enable real-time bedside detection of GER. This technology provides an opportunity for the development of new strategies aimed to decrease GER prevalence and prevent aspiration.
Registration: The study was registered at http://www.clinicaltrials.gov (NCT02705781).

Introduction

Aspiration of gastric content in mechanically ventilated, critically ill, and tube-fed patients is associated with an increased risk for the development of ventilator-associated pneumonia (VAP). [1] Gastroesophageal reflux (GER) is a common event in these patients, and its incidence, frequency, and duration are associated with an increased risk of aspiration and VAP. [2] However, the exact timing and extent of GER are difficult to determine bedside.

Most of the available diagnostic tools for GER detection are experimental and include esophageal pH-metry, scintigraphy, and pepsin detection. [1,2] Recently, intraluminal impedance was suggested as a promising technique for real-time detection and quantification of GER. [3–5].

This study aimed to assess the frequency and duration of GER events in a cohort of mechanically ventilated patients receiving enteral nutrition via a feeding tube (FT) and to determine its correlation with procedures performed during routine patient care.

Materials and methods

The study was approved by the Institutional Review Board of Rambam Health Care Campus (RHCC) (approval number 0392-11-TLV) and registered at http://www.clinicaltrials.gov (NCT02705781). Informed consent was given by a next of kin and approved by an independent physician.

This prospective pilot study included 20 consecutive adult critically ill and mechanically ventilated patients hospitalized in the general 18-bed intensive care unit (ICU) of RHCC, Haifa, Israel. RHCC is a 1000-bed tertiary academic medical center serving more than two million residents.

We included adult patients (≥18-year-old), expected to be mechanically ventilated and to receive enteral feeding by FT for at least 72 hours. Patients with recent abdominal surgery or any known disease of the esophagus or stomach (including GER disease) were excluded.

The smARTrack™ FT (ART MEDICAL, Netanya, Israel) was used for GER detection and enteral feeding (single tube). The system uses multichannel intraluminal impedance sensors capable of detecting the movement of gastroesophageal content above the lower esophageal sphincter (LES). There are nine sensing points within the FT wall, located above and below the LES. After insertion, the positioning of the FT is reaffirmed by an upper abdominal x-ray and the location of the LES, relative to the sensing points, is integrated into the algorithm of the smARTrack™ FT. The algorithm is capable of detecting the movement of gastric content above the LES as well as displacement of the FT relative to the LES. Only GERs lasting more than 3 seconds are recorded. The multichannel impedance technology was previously described and found to be accurate in detecting GER as identified by manometry, pH-metry, videofluoroscopy, and barium swallows (r^2=0.79–0.89, P<0.001). [5–7] Briefly, the multichannel intraluminal impedance sensors detect GER by measuring the change in resistance of intraluminal content to alternating current. Only a few ions are present in an empty esophagus; when a GER appears above the LES, the ionic load increases, allowing better electrical conductivity, which is recorded by the algorithm. [7] The smARTrack™ FT platform has received the CE Mark and FDA clearance.

Enteral nutrition was delivered continuously by a feeding pump (Alcore Sentinel, Smithfield, USA). The prescribed formula and dose were at the attending physician's discretion after daily consultation with a clinical dietitian.

During the study period, patients' care and feeding processes were video recorded, and the timing of the following clinical events was registered:

1. Regular body position change - movement from back to both sides (performed at least every two hours). All the position changes were performed when the patient is transiently moved to a flat position;
2. Endotracheal suctioning via a closed suction system;
3. Fluid/drug bolus-these were used to administer enteral medications using a 50-cc syringe. The syringe was attached to the tube port and the diluted medication instilled into the FT by slowly and steadily pushing on the plunger (the exact time was not defined by the protocol).

We assessed the association between these events and the GER episodes that were recorded by the smARTrack™ system.

All the included patients were ventilated using Pressure Regulated Volume Control (PRVC) + Pressure Support mode (Servo-i Ventilator, Getinge, Inc., Wayne, NJ). A lung protective ventilation strategy was used (i.e. tidal volume was set between 6-8 ml/kg of ideal body weight and plateau pressure was kept below 30 cm of water). Sedation level was titrated to a Richmond Agitation-Sedation Scale (RAAS) score of 0 to -2. In patients experiencing ventilator dyssynchrony or requiring aggressive ventilator settings (e.g. ARDS) deeper sedation (RASS -3 to -4) was applied. The head of the bed was elevated at 30-45^o. None of the patients was pronned during the study period.

Patients' characteristics were summarized with descriptive statistics. Median (interquartile range, IQR) was used for the description of quantitative variables. Spearman rank correlation coefficient (r) was used to assess the correlation between GER events and time after position changes, endotracheal suctions, and fluid/drug boluses. Data analysis was conducted with Statistical Package for the Social Sciences, version 23.0 (IBM SPSS Statistics for Windows; IBM Corporation, Armonk, NY, USA).

Results

The demographic and clinical characteristics of the patients included in the study are presented in Table 1. The median monitoring time was 2.9 days (IQR 2.8–3) per patient with a cumulative time of 57.2 days. The smARTrack™ FT was successfully placed in all the patients recruited for the study. No adverse events related to the device were recorded during the study period.

During the study period, a total of 4,072 GER events were documented. The median number of GERs per patient was 183 (IQR 139–228), translated to 2.7 (IQR 2.1–3.8) events per hour per patient. In our

Table 1
Clinical and demographic characteristics of 20 patients included in the study

Age, median (IQR), years	50 (36–68)
Male gender, n (%)	18 (90%)
Body mass index, median (IQR), kg/m^2	27.77 (23.27–33.96)
Obese (BMI>30 kg/m^2)	7 (35%)
APACHE-II score on admission, median (IQR)	14 (11–17)
Trauma, n (%)	6 (30%)
Sepsis, n (%)	10 (50%)
Vasopressors, n (%)	6 (30%)
Opiates, n (%)	19 (95%)
Propofol, n (%)	9 (45%)
Benzodiazepines, n (%)	8 (40%)
Muscle relaxants, n (%)	0 (0%)
Prokinetic agents (metoclopramide and/or erythromycin), n (%)	2 (10%)
Proton-pump inhibitors, n (%)	10 (50%)
Enteral nutrition administration rate, median (IQR), ml/h	73 (50–78)

IQR- Interquartile range; APACHE- Acute physiology and chronic health evaluation.

cohort, the number of GERs per hour, per patient ranged from 0.6 to 8.6. Of the GERs, 31% lasted 3–10 seconds, 61% lasted 10–30 seconds, and 8% lasted more than 30 seconds (Fig. 1).

During the study, every patient underwent 39 position changes (IQR 32–48). 36% of the position changes were followed by GER within 5 minutes. The median number of GERs recorded in a single patient within 5 minutes after position change was 15 (IQR 8–20). The frequency of GERs decreased over the 10 minutes after position change (r=-0.92, 95% CI -0.98, -0.7, P<0.001). The median number of GERs after position change is presented in Fig. 2.

Three hundred and seven endotracheal suctions events (16 suctions per patient, IQR 10–23) were evaluated. 64.5% of suctions were followed by at least one GER within 5 minutes. The median number of GERs recorded in a single patient within 5 minutes after tracheal suction was 10 (IQR 2–15) (r=-0.98, 95% CI -0.99, -0.66, P=0.005). The median number of GERs after endotracheal suctions is presented in Fig. 2.

During the study, 151 fluid/drug boluses were administered via FT to 18 patients, translated to a median of 8 (IQR 5–11) boluses per patient. GER was recorded within 5 minutes after 24% of boluses. The median number of GERs recorded in a single patient within 5 minutes after bolus administration was 2 (IQR 1–3). Due to the small number of events per minute per patient, the Spearman rank correlation coefficient could not be calculated.

Discussion

In this pilot study, we present a new method of real-time bedside detection of GER in mechanically ventilated ICU patients receiving enteral nutrition by FT. Using multichannel intraluminal impedance sensors, we found that GER is a universal phenomenon in these patients, taking place, on average, every 22 minutes. Routine clinical procedures such as position change, fluid/drug bolus, and tracheal suction may serve as a trigger for GER.

One of the most important risk factors for VAP is the bacterial colonization of the gastric content with subsequent GER and aspiration into the airways. [1] Cumulative GER time was found to be a strong predictor of developing VAP. [2] Mechanical ventilation, sedation, shock, sepsis, FT, straining or coughing, and supine body position are all associated with lower LES pressure and increased risk of GER. [8] Balihar *et al.* found, using high-resolution impedance manometry, that critically ill mechanically ventilated patients suffer from major esophageal motility abnormalities and that GER is extremely common in this population. GER was most commonly associated with transient LES relaxation. The authors found an association between GER episodes and cough, ventilator interference, and agitation. [5].

Although the association between GER and VAP is well known, currently, there is no means to detect GER and prevent the consequential aspiration in real-time. FTs incorporating an inflatable esophageal balloon were shown to decrease GER as well as broncho aspiration of gastric contents. However, the method was found safe for only limited periods of time, making it less suitable for ICU patients requiring prolonged FT feeding. [9] Intermittent inflation of esophageal balloon guided by a real-time GER detection may prevent aspiration and decrease the risk of VAP without causing esophageal ischemia.

Further, our study provides some additional insights into possible strategies for GER prevention in this unique population. First, routine body position changes of mechanically ventilated patients, especially when accompanied by recumbent position, coughing, or straining, may serve as a significant risk factor for GER and aspiration. Efforts should be done to prevent even short periods of supine position, and when these are essential, such as during central vein catheterization, withholding enteral nutrition (with appropriate compensation of daily caloric intake) should be considered. Second, tracheal suction should be performed on ‘as needed’ basis (compared with routine suctioning) while patient's straining and agitation are minimized. [10] Third, previous studies found that bolus gastric feeding is safe, feasible, and associated with a comparable number of GER events in healthy volunteers. [11] However, we found that a fast bolus delivery of approximately 50cc of fluids/drugs was followed by GER in 23% of cases making it a possible trigger for aspiration in critically ill patients. Slow delivery of diluted drugs over several minutes may decrease the risk of reflux.

The main limitation of our study is that the clinical significance, as well as the correlation between the detected events of GER and bronchial aspiration events, were not evaluated in this pilot study.

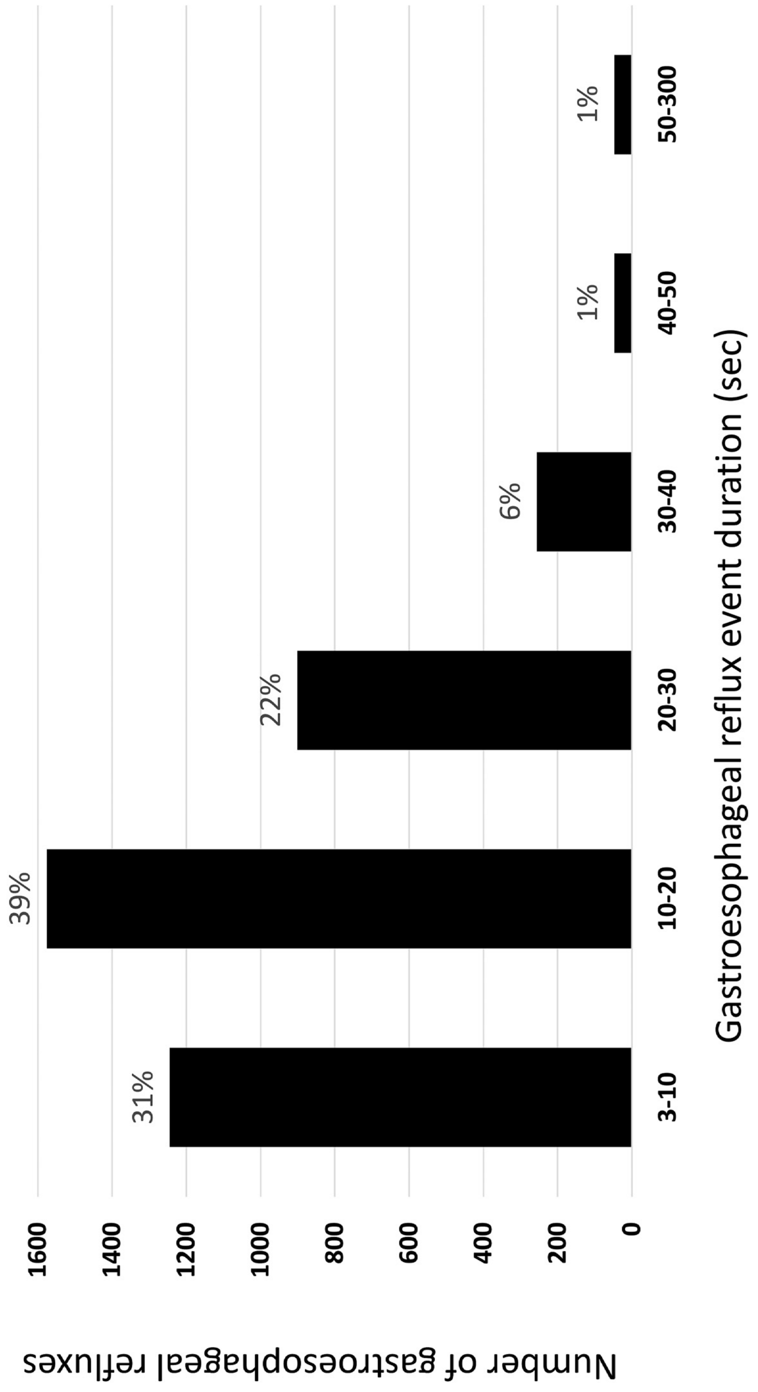

Fig. 1. Distribution of gastroesophageal reflux durations.

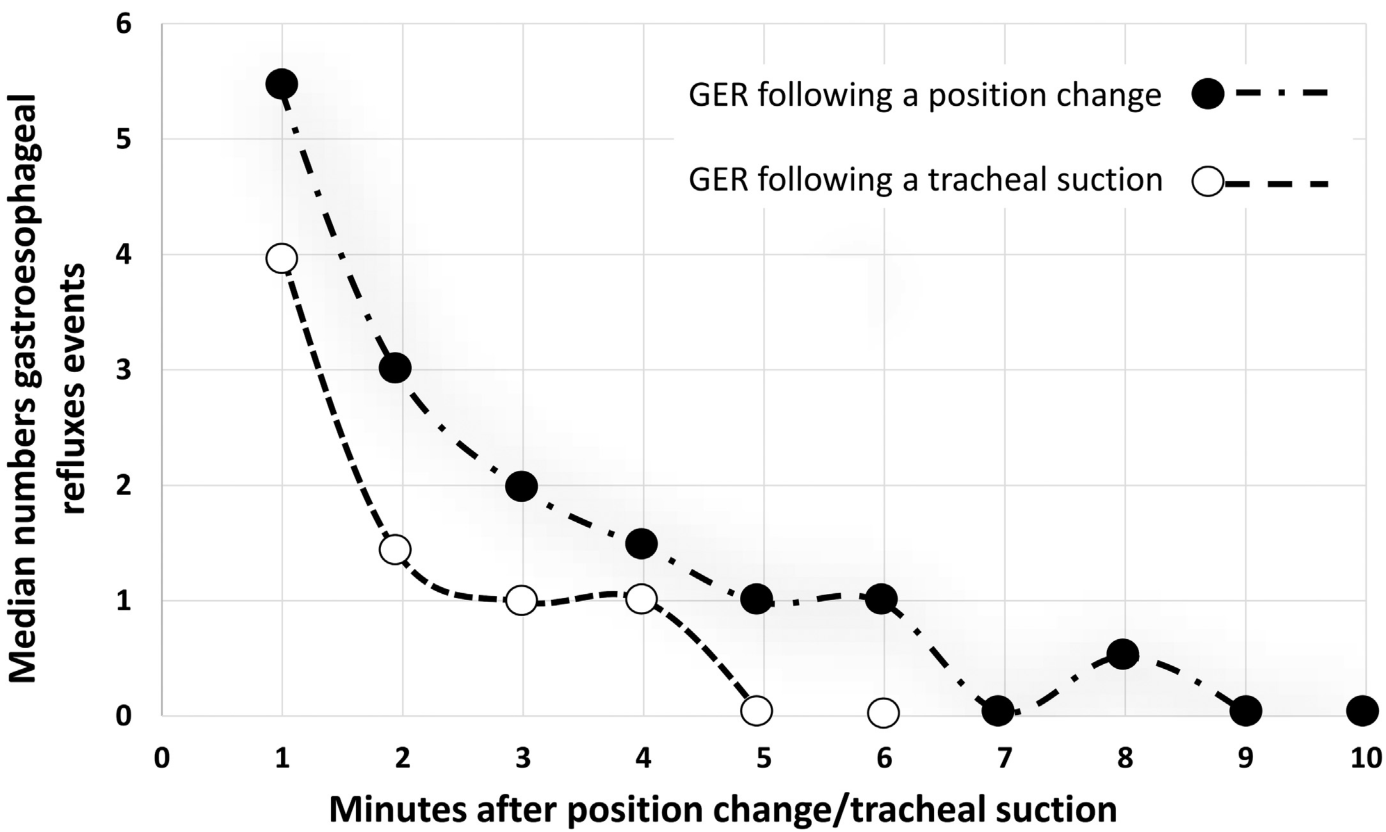

Fig. 2. Median number of gastroesophageal reflux events after position change and tracheal suction. GER- Gastro-esophageal reflux.

Although prolonged and higher elevation of gastric content along the esophagus may possess a higher risk of aspiration, it should be evaluated in further studies. Additionally, some parameters, such as ventilation pressures, rate of enteral feeding, height of the refluxate, agitation or cough during suction or position change, may be associated with an increased risk for GER. These parameters were not evaluated in this study. Due to the small number of GERs after fluid bolus, this association could not be tested statistically and therefore generalization of this finding should be made cautiously.

In conclusion, GER is common among mechanically ventilated critically ill patients receiving enteral nutrition. It may be spontaneous or triggered by some routine clinical tasks. Multichannel impedance sensors embedded on a FT enable real-time bedside detection of GER among these patients. This technology provides an opportunity for the development of new strategies aimed to decrease the incidence of GER and to prevent gastric content aspiration when GER has already occurred.

Statement of authorship

All authors contributed to the conception of the work, analysis, or interpretation of the data and drafting or revising the manuscript, gave final approval to submit, and accept accountabilities for all aspects of the work. The authors had full access to the data in the analysis.

Role of the funding source

ART MEDICAL has provided the gastric tubes used in the study as well as the capital equipment used in the study. The hospital research fund received compensation for administrative expenses and partial employment of a study coordinator. YBL, MR, and DE received no compensation or any financial support for this research study.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: YBL, MR, and DE have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript. SS works for ART MEDICAL in biomedical engineering at ART MEDICAL Company. As part of her position, she conducts research in the medical and marketing fields. As part of the current manuscript, SS was involved in the fields of development and outline of trial protocols, trained site staff, and managed trial materials. Shirly received a salary for this work.

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References

[1] Metheny NA, Clouse RE, Chang YH, Stewart BJ, Oliver DA, Kollef MH. Tracheobronchial aspiration of gastric contents in critically ill tube-fed patients: frequency, outcomes, and risk factors. Crit Care Med 2006;34:1007–15. https://doi.org/10.1097/01.CCM.0000206106.65220.59.

[2] Abdel-Gawad TA, El-Hodhod MA, Ibrahim HM, Michael YW. Gastroesophageal reflux in mechanically ventilated pediatric patients and its relation to ventilator-associated pneumonia. Crit Care 2009;13:R164. https://doi.org/10.1186/CC8134.

[3] Huerta-Franco MR, Vargas-Luna M, Montes-Frausto JB, Flores-Hernández C, Morales-Mata I. Electrical bioimpedance and other techniques for gastric emptying and motility evaluation. World J Gastrointest Pathophysiol 2012;3:10. https://doi.org/10.4291/WJGP.V3.I1.10. 8.

[4] Kagan I, Hellerman-Itzhaki M, Neuman I, Glass YD, Singer P. Reflux events detected by multichannel bioimpedance smart feeding tube during high flow nasal cannula oxygen therapy and enteral feeding: First case report. J Crit Care 2020;60: 226–9. https://doi.org/10.1016/J.JCRC.2020.08.005.

[5] Balihar K, Kotyza J, Zdrhova L, Kozeluhova J, Krcma M, Matejovic M. Characterization of esophageal motor activity, gastroesophageal reflux, and evaluation of prokinetic effectiveness in mechanically ventilated critically ill patients: a high-resolution impedance manometry study. Crit Care 2021;25:1–12. https://doi.org/10.1186/S13054-021-03479-8/TABLES/6.

[6] Shay SS, Bomeli S, Richter J. Multichannel intraluminal impedance accurately detects fasting, recumbent reflux events and their clearing. Am J Physiol Gastrointest Liver Physiol 2002;283:G376–83. https://doi.org/10.1152/AJPGI.00470.2001.

[7] Tutuian R, Castell DO. Clinical Applications of Esophageal Multichannel Intraluminal Impedance Testing. Gastroenterol Hepatol (N Y) 2006;2:250.
[8] Nind G, Chen WH, Protheroe R, Iwakiri K, Fraser R, Young R, et al. Mechanisms of gastroesophageal reflux in critically ill mechanically ventilated patients. Gastroenterology 2005;128:600–6. https://doi.org/10.1053/J.GASTRO.2004.12.034.
[9] Orozco-Levi M, Félez M, Martínez-Miralles E, Solsona JF, Blanco ML, Broquetas JM, et al. Gastro-oesophageal reflux in mechanically ventilated patients: effects of an oesophageal balloon. Eur Respir J 2003;22:348–53. https://doi.org/10.1183/09031936.03.00048902.
[10] Jelic S, Cunningham JA, Factor P. Clinical review: Airway hygiene in the intensive care unit. Crit Care 2008;12:209. https://doi.org/10.1186/CC6830.
[11] Pletschette Z, Preiser JC. Continuous versus intermittent feeding of the critically ill: have we made progress? Curr Opin Crit Care 2020;26:341–5. https://doi.org/10.1097/MCC.0000000000000733.