The feasibility of electromagnetic sensing aided post pyloric feeding tube placement (CORTRAK) in patients with thrombocytopenia with or without anticoagulation on the intensive care unit

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Abstract

Background: The successful initiation of enteral nutrition is frequently hampered by various complications occurring in patients treated in the intensive care unit (ICU). Successful placement of a nasojejunal tube by CORTRAK enteral access system (CEAS) has been reported to be a simple bedside tool for placing the postpyloric (PP) feeding tube.

Methods: We evaluated the efficacy and side effects using CEAS to establish EN in patients with critical illness, thrombocytopenia, and/or anticoagulation.

Results: Fifty-six mechanically ventilated patients were analyzed. Twenty-four of them underwent prior hematopoietic stem cell transplantation (SCT). Sixteen patients received extracorporeal membrane oxygenation treatment because of acute respiratory distress syndrome. The median platelet count at PP placement was 26 g/L (range, 4–106 g/L); 16 patients received therapeutic anticoagulation (activated partial thromboplastin time, 50–70 s). CEAS-assisted placement of a PP nasojejunal tube was performed successfully in all patients. The most frequent adverse event was epistaxis in 27 patients (48.2%), which was mostly mild (Common Terminology Criteria for Adverse Events grade 1, n = 21 [77.8%], and grade 2, n = 6). A significant association between a low platelet count and bleeding complications was observed (P < 0.001).

Conclusion: Performed by an experienced operator, CEAS is a simple, rapidly available, and effective bedside tool for safely placing PP feeding tubes for EN in patients with thrombocytopenia, even when showing an otherwise-caused coagulopathy in the ICU. Higher-grade bleeding complications were not observed despite their obvious correlation to thrombocytopenia. A prospective study is in preparation.
CLINICAL RELEVANCY STATEMENT

Enteral nutrition via a postpyloric tube reduces several risks like nosocomial pneumonia and aspiration but necessitates endoscopy for reliable placement. Endoscopic insertion carries implications on patient safety issues, which are of importance, particularly in patients compromised by thrombocytopenia and/or receiving anticoagulants or in patients experiencing severe mucositis because of antineoplastic treatments. CORTRAK enteral access system (CEAS) has been reported to be a promising bedside tool for placing a PP feeding tube. Our data showed that CEAS is safe and successful also in thrombocytopenic and simultaneously anticoagulated critically ill patients, not bearing the risk of severe complications when performed by an experienced operator.

INTRODUCTION

The ESIICM (European Society of Intensive Care Medicine) Working Group on gastrointestinal (GI) function provided clinical practice guidelines on early enteral nutrition (EEN) and suggested to initiate it as soon as possible at a low rate, as beneficial effects regarding infection prevention have been demonstrated in critically ill patients.1 Postponed EN was suggested only in patients with uncontrollable shock, uncontrollable hypoxemia and acidosis, uncontrolled GI bleeding, gastric aspiration rate >500 ml per 6 h, and various intra-abdominal problems.2 EN is also recommended as first-line nutrition support for patients diagnosed with hematological disorders, especially after allogeneic hematopoietic stem cell transplantation (SCT).3 However, its prompt onset is often hampered by severe thrombocytopenia and/or high-grade mucositis, implicating potentially severe complications. Considering the emerging evidence regarding the association between gut microbiota dysbiosis and acute graft-vs-host disease (GVHD) occurrence, a protective effect of nutrition was also attributed to the improved gut eubiosis observed in enterally fed patients.3 Therefore, EEN should be initiated soon in those patients, with the latest opportunity being at intensive care unit (ICU) admission.

Initiating EN via a gastric tube is technically easier and may decrease the time to initiation of EN. Gastric access should, therefore, be used as the standard approach to initiate EN.4,5 Although postpyloric (PP) alimentation may be associated with a reduction in pneumonia in critically ill patients, there is no difference in mortality between PP and gastric EN.4,5 Current guidelines recommend PP feeding in patients with an increased risk for aspiration; yet positioning of enteral feeding tubes necessitates endoscopy for reliable PP placement. Endoscopic insertion is so far considered the gold standard for insertion of PP feeding tubes with high success rate; however, it involves manpower and carries implications on patient safety issues.7 The latter may be of importance, particularly in hematological/oncological patients compromised by thrombocytopenia and/or receiving anticoagulants and in patients experiencing mucositis, in addition to the presence of life-threatening complications such as septic shock, including disseminated intravascular coagulation (DIC), severe pneumonia, and other organ failures that warranted admission to the ICU.

CORTRAK enteral access system (CEAS) (CORPAK MedSystems, Buffalo Grove, IL, USA) is an electromagnetic sensing device that tracks and displays the path of feeding tubes during the placement procedure. Because of real-time tracking of the tube-tip position, this approach may improve successful tube placement quota, reduce overall placement time, and might even diminish the need for confirmatory x-rays after intervention. Aside from in a cohort of patients with thrombocytopenia and/or anticoagulation, CEAS has proven efficacy and safety in numerous studies when performed by an experienced operator, minimizing operator pitfalls and patient risks.7–15 Yet there are few data available on feasibility and complications in critically ill patients, in particular when focusing on patients with coagulopathies caused by, for example, chemotherapy-induced thrombocytopenia, application of heparin, DIC, hepatic failure, or other causes.16,17 This retrospective analysis was conducted to evaluate the feasibility, safety, and effectiveness of the CEAS in establishing nasojejunal nutrition after admission to the ICU in a patient cohort with thrombocytopenia and/or anticoagulation experiencing predominantly hematological/oncological disease.

MATERIALS AND METHODS

We retrospectively analyzed the use of CEAS for insertion of a feeding tube in a patient cohort with thrombocytopenia and/or anticoagulation between 2017 and 2019 at the Haematology/Oncology and Gastroenterology ICU of the University Hospital of the Ludwig Maximilian University of Munich, Campus Grosshadern. Necessity for PP feeding resulted from insufficient nutrition via a gastric tube because of high reflux.

The study was conducted in accordance with the Declaration of Helsinki. The Ethics Committee of the Ludwig Maximilian University of Munich recognized the retrospective evaluation and waived the need for informed consent because of the noninterventional design of the investigation.

We evaluated the success rate, number of attempts, time requirement, and the adverse events (AEs) of using the CEAS for PP feeding tube placement. Age, gender, characteristics of hematological/oncological disease, platelet count at placement, platelet transfusion, therapeutic anticoagulation (activated partial thromboplastin time [aPTT], 50–70 s), as well as treatment and the reason for ICU admission, were recorded.

Nasojejunal feeding tube was placed using the CEAS. The tube was watered for a few minutes for better lubrication, and placement time

KEYWORDS
anticoagulation, cancer patients, CEAS, enteral nutrition, feeding tube, thrombocytopenia
FIGURE 1 Confirmation of correct placement by portable abdominal x-ray with contrast material (10 ml of Gastrografin 76%, Bayer Vital). Patient no. 35, 65-year-old female, acute myeloid leukemia (AML), sepsis, pneumonia, metapneumovirus was recorded starting with the beginning of the tube insertion. Time for preparation procedures was not included. The PP position of the tube tip was confirmed by abdominal x-ray, using 10 ml of water-soluble contrast agent given immediately prior to x-ray via tube (Gastrografin 76%, 100 ml N1; Bayer). When the trace shown by the electromagnetic sensing device showed typical and highly suggestive placement in the small bowel at the end of the placement procedure, confirmation by x-ray was omitted (Figures 1 and 2).

All nasojejunal tube placements were performed by the same experienced operator (>500 successful placements). In patients experiencing chemotherapy-induced severe mucositis, higher-grade, mucosal acute GVHD; severe thrombocytopenia; and preexisting epistaxis events prior to the procedure, platelet concentrates were transfused in preemptive intention prior to placement.

Definitions (grading of preexisting conditions and AEs)

Because of the fact that the majority of the patients were diagnosed with a hematological/oncological disease, grading of preexisting conditions, such as epistaxis, mucositis, and low platelet number, was according to the National Cancer Institute common terminology criteria for AEs. It is a descriptive terminology that can be used for AE reporting (https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf).

- Platelet count

The majority of the hematological patients experienced treatment-induced thrombocytopenia. The platelet count at the time of CEAS insertion was graded according to the CTCAE v5.0 criteria. According to these criteria, a decreased platelet count is defined as follows: grade 1 (lower limit of reference to 75 g/L), grade 2 (75–50 g/L), grade 3 (50–25 g/L), and grade 4 (<25 g/L).

- Oral mucositis

Twenty-two patients who underwent prior hematopoietic SCT experienced higher-grade mucositis. According to the CTCAE v5.0 criteria, oral mucositis is defined as follows: grade 1 (asymptomatic or mild symptoms, intervention not indicated), grade 2 (moderate pain or ulcer that does not interfere with oral intake, modified diet indicated), grade 3 (severe pain, interfering with oral intake), and grade 4 (life-threatening consequences, urgent intervention indicated).

- Epistaxis

Epistaxis, as an AE due to the procedure, was graded according to CTCAE v5.0. According to these criteria, bleeding from the nose is defined as follows: grade 1 (mild symptoms, intervention not indicated), grade 2 (moderate symptoms, medical intervention indicated [eg, nasal packing, cauterization, and topical vasoconstrictors]), grade 3 (transfusion, invasive intervention indicated [eg, hemostasis of bleeding site]), and grade 4 (life-threatening consequences, urgent intervention indicated).

- Anticoagulation

Anticoagulation means aPTT with use of intravenous heparin and a targeted aPTT of 50–70 s.

Statistical analysis

Median values and ranges were used for continuous variables and percentages for categorical variables. Subgroup analysis on occurrence of side effects was performed using the chi-squared test or Fisher exact test for categorical variables and the Wilcoxon or Kruskal-Wallis test for continuous variables, depending on compared samples. All statistical tests were two-sided, and a P-value of <0.05 was considered statistically significant. Data were analyzed using R 3.2.0 statistical software (http://www.R-project.org).

RESULTS

Baseline characteristics

Fifty-six patients (female, n = 26; male, n = 30) were analyzed who were admitted and treated at the ICU over 3 years (years 2017–2019) and at high-risk for AEs related to PP tube placement because of treatment-induced thrombocytopenia, therapeutic anticoagulation (aPTT, 50–70 s), and treatment-associated oral mucositis.
Median age was 54.5 (20–76) years. All patients were analgesedated (Richmond Agitation Sedation Scale score >2), intubated, and mechanically ventilated.

Patients with preexisting oral mucositis (grade 1, n = 13; grade 2, n = 4; grade 3, n = 3; and grade 4, n = 2), thrombocytopenia (n = 56), and preexisting epistaxis (n = 2) received one platelet concentrate prior to the procedure (n = 30). The median platelet count at placement was 26 g/L (range, 4–106 g/L).

Sixteen patients with severe acute respiratory distress syndrome (ARDS) were referred to venovenous extracorporeal membrane oxygenation (ECMO). Those patients were put on therapeutic intravenous anticoagulation with a targeted aPTT of 50–70 s. None of the patients received antiplatelet agents, warfarin, or direct-acting oral anticoagulants. One patient was diagnosed with von Willebrand disease. One patient with Child C liver cirrhosis and acute on chronic liver failure was diagnosed with an international normalized ratio of >5.0.

Hematology and oncology
Forty-four patients were diagnosed with a hematological/oncological disease. Acute leukemia was diagnosed in 22 patients (three with acute lymphatic leukemia and 19 with acute myeloid leukemia), lymphoma in eight patients (two with Hodgkin lymphoma, four with diffuse large B-cell lymphoma, three with T-cell non-Hodgkin lymphoma, and one with mantle cell lymphoma), multiple myelomas in three patients, and chronic myelocytic leukemia and chronic myelomonocytic leukemia in one patient each. The remaining patients were diagnosed with solid tumors.

Twenty-four patients underwent prior hematopoietic SCT (allogeneic, n = 20; autologous, n = 4), 22 of whom (92%) experienced a higher-grade mucositis. According to the European Organization for Research and Treatment of Cancer CTCAE v5.0 criteria, mucositis was graduated severe (CTCAE grade 3 and 4) in five patients (23%), whereas 17 patients experienced mild and moderate mucositis.

Causes for ICU admission
The main cause for ICU admission was ARDS, most likely originating from pneumonia. Severe ARDS was found in 28 patients, of whom 16 were referred to venovenous ECMO. Prior to ECMO, all 16 patients underwent prone position maneuver. In these patients, PP tube placement took place prior to prone position. Nineteen patients fulfilled the criteria of severe sepsis. Microbiological analysis found pathogens in 39 patients. In the remaining patients, fever remained of unknown origin.

CEAS procedure: Number of attempts, position monitoring, and time requirement
Positioning of the nasojejunal tube was successfully performed in all of our high-risk patients in mean after 1.3 attempts (first run in 44 patients, second run in 9, third run in 2, and fourth run in 1). In addition to a typical sigmoidal curve on the CORTRAK monitor, placement was confirmed by portable abdominal x-ray in 44 patients (Figures 1 and 2A and 2B). An x-ray was omitted in the remaining eight patients because of a typical CORTRAK curve and ability of bile aspiration. Particularly in patients mechanically ventilated in prone position, x-ray guaranteed the successful PP position. The duration of successful EN varied from 2 to 48 days postplacement (median, 16.5 days).
FIGURE 3 Subgroup analysis on time to pass the pylorus (A, B) and on attempts required for successful placement (C, D). P-values are (A) .39, (B) .71, (C) .39, and (D) .25. Coagulopathy is defined as heparin-induced prolongation of the activated partial thromboplastin time. *statistical outlier

Excluding all preparation procedures, such as logistics, the recording of patients’ data, and watering of the tube, the time required to pass the pylorus and place the feeding tube took a median of 8:30 min (1:34–23:10 min). When patients were stratified for mucositis or therapeutic anticoagulation, no differences were found regarding the placement time (mucositis yes vs no [P = 0.39]; anticoagulation yes vs no [P = 0.71]) (Figure 3). Further subgroup analysis revealed no significant difference between the groups in terms of number of attempts necessary for successful placement, with a median of 1 (1–4) attempts (Figure 3). No patient necessitated endoscopic PP repositioning.

CEAS procedure: AE

Epistaxis was the most frequent AE due to the procedure and was mostly mild (CTCAE grade 1, n = 27). Medical intervention, including nasal packing, was indicated in six patients (CTCAE grade 2). Lower platelet count was significantly associated with occurrence of epistaxis (P < 0.001) (Figure 4). However, neither the use of therapeutic anticoagulation with heparin (P = 0.49) nor mucositis (P = 0.45) nor duration (P = 0.75) or number of attempts for successful tube placement (P = 0.77) had an impact of the occurrence of bleeding complications. One patient developed self-limiting gastric hemorrhage (CTCAE grade 1). No further GI bleeding was seen. Gastric or bowel perforation did not occur. Neither pulmonary misplacement, accidental extubation, nor other pulmonary complications (eg, aspiration), including pneumothorax or pneumonitis, as well as hypoxemia and arrhythmia, were observed. No lethal complication was seen.

CEAS data are summarized in Table 1.

DISCUSSION

So far, endoscopy is the gold standard for insertion of PP feeding tubes. However, particularly in ICU patients compromised by severe thrombocytopenia, therapeutic anticoagulation, and chemotherapy-induced severe mucositis, endoscopy bears the risk of bleeding and
of the MAUDE database, 54 AEs between the years 2006 and 2016

Death occurred in 17% of pulmonal placements. Unfortunately, clinicians require specialized training and experience to develop
trauma, resulting in perforation during the procedure. Furthermore, transport of ICU patients to another department for the intervention may compromise patients safety, ultimately resulting in more operation time to be required and postponement of the intervention.24,25

With this analysis, we are the first to show that the use of electromagnetic-guided CEAS for PP feeding tube placement is feasible, safe, and effective in patients with a low platelet count and receiving therapeutic anticoagulation in the ICU. Beside this high selected study population, CEAS has proven efficacy and safety in numerous studies when performed by an experienced operator.7–15

A recently published study has shown that once routine has been built up, half or more patients requiring a nasoduodenal feeding tube would qualify for CORTRAK placement, and in the same way, ICU patients could be considered.8 Despite promising results, researchers in recent studies have expressed concern that a higher level of user expertise may be required for safe use. A retrospective study showing the results of >6000 PP feeding tube placements in mostly critically ill patients (83%) stressed out that the continuous training of the staff is required to avoid serious complications; they reported on 2% pulmonary deviation complications, whereas we induced none in our high-risk cohort.25 Further, in a retrospective, secondary analysis of the MAUDE database, 54 AEs between the years 2006 and 2016 were identified and reviewed related to CORTRAK.5,9 Most events (98%) involved erroneous pulmonary feeding tube placement. Pulmonary complications included pneumothorax (77%) and pneumonitis (21%). Death occurred in 17% of pulmonal placements. Unfortunately, clinicians failed to recognize placement in 89% of CORTRAK insertion tracings reviewed. The authors conclude that pulmonal placement is not unique to CORTRAK and is an inherent risk of all feeding tube insertions. Therefore, clinicians must observe closely for lung placement and discriminate lung from gastric placement on insertion tracings. Moreover, clinicians require specialized training and experience to develop competency in using the CORTRAK device.9 Another prospective, observational pilot study has shown that confidence with the CORTRAK tracing was estimated to require ≥10 feeding tube insertions.

The authors concluded that interpretation of correct positioning can be challenging and, therefore, requires multiple successful attempts to gain enough competency and confidence for this intricate skillset.10 In our study, cohort pulmonal misplacement and consecutive pulmonal complications could be totally avoided, and no gut perforation occurred when performed by an experienced operator.

Recent data show that electromagnetic-guided PP feeding tube placement can be conducted successfully in a high proportion of patients (70%–91%) taking in mean 11–42 min and 1.2 attempts. It is of note that despite the high-risk profile of our patient cohort, the success rate was 100%, taking in mean 8:30 min, whereas the number of attempts was similar to the previously reported. Once again, this finding emphasizes the argument of experience and, consequently, staff training to place PP tubes quickly, successfully, and safely in critically ill patients with coagulopathies.

In general, complications related to CEAS-guided feeding tube placement were reported in 3%–18%, with nose bleeding or GI bleeding occurring in 3.8%–18% or 0.3%, respectively.24 Preexisting epistaxis was considered as contraindication in those studies.25 In the light of the high-risk constellation for severe bleeding events in our cohort, the risk of severe bleeding was negligible to little when using CEAS for establishing nasojejunal EN. Clearly, a relatively high overall rate of epistaxis was noted in these high-risk patients but at a low grade (CTCAE grade 1, 37.5%). Medical intervention was indicated in only six patients (CTCAE grade 2, 10.7%), consisting solely of nasal packing while not requiring additional critical interventions. Taking into account the low-median thrombocyte count of 26 g/L and existing additional risk factors for bleeding due to mucositis or simultaneous intravenous anticoagulation in patients during ECMO, this AE is definitively manageable. Further bleeding reduction could be obtained by substitution of more than one platelet concentrate prior to the

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**TABLE 1**  Patient data and CEAS efficacy and AEs

<table>
<thead>
<tr>
<th>Group (subgroup)</th>
<th>n</th>
<th>Platelet count, median (range), g/L</th>
<th>PC transfusion, n</th>
<th>Therapeutic anticoagulation, n</th>
<th>CEAS trials, n</th>
<th>Median time, minutes</th>
<th>Duration of EN, days</th>
<th>AE epistaxis, grade</th>
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<tr>
<td>Study population</td>
<td>56</td>
<td>26 (4–106)</td>
<td>30</td>
<td>16</td>
<td>44 9 2 1</td>
<td>08:30</td>
<td>16.5</td>
<td>27 6 – –</td>
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<td>Hemato-oncology</td>
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<td>26 (4–106)</td>
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<td>21</td>
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<td>19 3 1 1</td>
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<td>vvECMO</td>
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Note: Whole study population n = 56; overlapping groups and subgroups. Therapeutic anticoagulation: heparin with activated partial thromboplastin time of 50–70 s. AE: epistaxis CTCAE grade.

Abbreviations: AE, adverse event; CEAS, CORTRAK enteral access system; EN, enteral nutrition; PC, platelet concentrate; SCT, stem cell transplantation; vvECMO, venovenous extracorporeal membrane oxygenation.

*aTime: exclusively all preparation procedures (in case of multiple trials, time of the successful trial).

*bCystic fibrosis (n = 2), interstitial lung disease, pulmonary thromboembolism, pancreatitis, and lymphangioleiomatosis.
start of the procedure. However, it is not surprising that bleeding complications were more frequently seen in our patients as compared with others, but it is remarkable that no severe bleeding complication was noted.\textsuperscript{16,24,25} The low rate of serious AEs and the complete absence of lung complications are probably due to the fact that all CEAS placements were undertaken without exception by one single intensivist with vast experience of CEAS placements. We therefore absolutely agree with the authors mentioned above that CEAS placements in such a high-risk population must be definitively reserved to an experienced operator.

Our analysis is hampered by low sample size, and its single-center and retrospective character. An unintended selection bias is an inherent risk of retrospective studies. We therefore reported on all patients matching the inclusion criteria treated in the above given period of time. Data quality is high, as patient charts give details regarding patients’ treatment course and their complications.

Considering operator pitfalls and patient risks, CEAS has proven efficacy and safety when placement is performed by such an experienced physician.\textsuperscript{7–15} Abdominal, contrast-enhanced x-ray is indicated in cases of uncertain tube positioning, particularly in patients ventilated mechanically in prone position. Moreover, our analysis shows that CEAS can safely be extended to patients with chemotherapy-induced mucositis, severe thrombocytopenia, and simultaneous therapeutic anticoagulation during ECMO.

CONCLUSION

This single institutional study allows the conclusion that CEAS performed by an experienced operator for many years seems to be a simple, safe, and rapidly available bedside tool for placing PP tubes also in thrombocytopenic and simultaneously anticoagulated critically ill patients not bearing the risk of severe complications. A prospective study is in preparation.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Stephanie Susanne Stecher, Hans Joachim Stemmler, and Alessia Fraccaroli equally contributed to the conception and design of the research and interpretation of the data; Michaela Barnikel, Heidrun Drolle, and Alexandra Pawlikowski contributed to the design of the research; Hans Joachim Stemmler, Joanna Tischer, Tobias Weiglein, Annabel Alig, and Sofia Anton contributed to the acquisition and analysis of the data; and Joanna Tischer, Alessia Fraccaroli, and Hans Joachim Stemmler drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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