Pediatric Buried Bumper Syndrome: Diagnostic Validity of Transabdominal Ultrasound and Artificial Intelligence

Buried-Bumper-Syndrom in der Pädiatrie: Diagnostische Wertigkeit des transabdominalen Ultraschalls und künstlicher Intelligenz

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ABSTRACT

Purpose Buried bumper syndrome (BBS) is a severe complication of percutaneous endoscopic gastrostomy (PEG) resulting from overgrowth of gastric mucosa and penetration of the inner holding plate into the gastric wall. The aim of this study was to evaluate the diagnostic value of transabdominal ultrasound (US) in comparison to an artificial intelligence (AI) model for the diagnosis of BBS in children.

Materials and Methods In this monocentric retrospective study, pediatric US data concerning BBS from a ten-year period (2009–2019) were analyzed. US findings were compared to a clinical multiparameter-based AI model and reference standard endoscopy. Clinical risk factors for the occurrence of pediatric BBS were determined.

Results In n = 121 independent examinations of n = 82 patients, the placement of the inner holding plate of the PEG was assessed by US. In n = 18 cases BBS was confirmed. Recall and precision rates were 100 % for US and 88 % for the AI-based assessment. Risk factors for the occurrence of BBS were mobilization problems of the PEG (rs = 0.66, p < 0.001), secretion/exudation (rs = 0.29, p = 0.002), time between 1st PEG placement and US (rs = 0.38, p < 0.001), and elevated leukocyte count (rs = 0.24, p = 0.016).

Conclusion Transabdominal US enables correct, rapid, and noninvasive diagnosis of BBS in pediatric patients. Preceding AI models could aid during diagnostic workup. To avoid unnecessary invasive procedures, US could be considered as a primary diagnostic procedure in suspected BBS.

ZUSAMMENFASSUNG

Ziel Das Buried-Bumper-Syndrom (BBS) ist eine schwerwiegende Komplikation der perkutanen endoskopischen Gastrostomie (PEG) und beschreibt eine Schleimhautüberwucherung der inneren PEG-Halteplatte. Ziel dieser Studie war es, die Wertigkeit des transabdominalen Ultraschalls (US) mit einem Modell der künstlichen Intelligenz (KI) zur Diagnose eines BBS zu vergleichen.


Ergebnisse Die Position der inneren PEG-Halteplatte wurde bei n = 82 pädiatrischen Patienten in n = 121 unabhängigen US-Untersuchungen bewertet. Alle n = 18 Fälle mit BBS wurden mittels US korrekt diagnostiziert (Sensitivität/positiver Prädiktionswert von 100 %). Das KI-basierte Modell zeigte...
Introduction

Percutaneous endoscopic gastrostomy (PEG) is a well-established and safe long-term feeding method for pediatric patients suffering from malnutrition and inability to swallow [1–3]. A PEG consists of a polyurethane probe that is inserted through the abdominal wall into the gastric lumen providing direct access for enteral nutrition. The probe is held in position by an external fixation plate and an inner holding plate, adjacent to the inner gastric wall. Besides acute procedural complications, a major long-term complication is the development of a buried bumper syndrome (BBS) [4]. BBS describes the overgrowth of gastric mucosa and penetration of the inner holding plate of the PEG into the gastric wall or beyond [1, 5]. With a prevalence of 2.0–2.9 % in adults [1, 6, 7], BBS can cause peritonitis, heavy bleeding, and even gastric perforation [8, 9]. Therefore, timely diagnosis and rapid endoscopic or surgical PEG replacement are necessary [8, 10]. The current recommendations for the diagnosis of BBS include contrast studies via the PEG or upper endoscopy [11]. Computed tomography (CT) may provide additional detailed imaging information [12, 13], but the risk of ionizing radiation needs to be considered for pediatric patients. As an alternative approach, endosonography (EUS) represents a radiation-free, but invasive [6, 14] modality, which is not yet accessible for pediatric patients in routine diagnostics [15, 16]. Conventional B-mode ultrasound is commonly used in various clinical scenarios as the standard of care in pediatric medicine. High-resolution US imaging is capable of differentiating the individual wall layers of the stomach and bowel segments [17]. While the identification of the mucosa (hyperechoic), submucosa (hyperechoic), and muscularis propria (hypoechoic) has already been helpful in the assessment of bowel diseases [17–20], it may also allow the exact location of the inner holding plate in BBS [10]. However, imaging approaches are time-consuming [21], while the clinical routine is characterized by time and medical staff shortage. Therefore, AI-supported methods, which offer the possibility to aid clinical symptom-based decision making in real time, are becoming increasingly important. In adults, AI implementation for diagnostic support in gastroenterological diseases is expanding [22, 23] and the trend to integrate these systems in pediatric routine care is imminent [24, 25]. The primary objective of this retrospective study was to evaluate the feasibility of transabdominal ultrasound to visualize the inner holding plate of a PEG and its relation to the gastric wall for the diagnosis of BBS in children. Furthermore, we compared the value of transabdominal US for the diagnosis of BBS to a novel symptom-based AI approach.

Materials and Methods

Study design

This single-center retrospective study was performed in accordance with the declaration of Helsinki and approved by the local ethics committee (No. 110_20 Bc).

To identify relevant cases, the hospital data warehouse was screened for ultrasound reports containing the keywords “BBS” or “PEG tube” in the years between 2009–2019. Regardless of age, gender or primary disease, all US reports of children with PEG or PEG with jejunal extension (PEG-J) and description of positioning of the inner holding plate (bumper), were included in the study.

The exclusion criteria were the lack of time-related (within 4 weeks) endoscopic or CT-guided validation in the case of US reports indicating the presence of a BBS (BBS+), and patients with a PEG button device or US reports where the same diagnoses was repeatedly given within a 4-week interval.

Transabdominal US acted as a binary classifier (US positive = diagnosis BBS+ = inner holding plate not luminal to the gastric mucosa/US negative = diagnosis BBS- = inner holding plate luminal to the gastric mucosa) dividing the study population into two groups. The accuracy of the group assignment to the diagnosis was subsequently verified by the gold standard of endoscopic or CT control. BBS+ was proven by negative endoscopic assessment within 4 weeks or assumed if the inner holding plate was clearly visible on US without sonographic and clinical signs or evidence of a BBS and by the absence of any clinical evidence for BBS+ within 4 weeks leading to further diagnostics.

Data acquisition

Relevant patient data were extracted from electronic patient records or written/printed documents. Data collection included demographic characteristics (e.g., sex, age, and BMI), patient history (e.g., primary disease and gastroenterological characteristics), and laboratory parameters (e.g., hemoglobin level and c-reactive protein (C-reactive protein)). The time interval between laboratory results, clinical symptoms, medications, and the US examination should not exceed seven days in order to be considered.

Ultrasound acquisition

US examinations were performed by n = 11 pediatricians with varying degrees of US qualification. Images were acquired with seven different US systems (six high-end US devices and one mid-range device) and probes with frequencies ranging from 5 to 17 Megahertz (MHz). The US probe was positioned at the area of the PEG entry point (for further details please see ▶ Supplementary Table 1).
Statistical Analysis

Categorical variables are given as number and percentage. Metric variables are given as mean and standard deviation. Non-parametric Kolmogorov-Smirnov and Mann-Whitney-U test were used for statistical evaluation. Precision rate, recall rate, and f1 score (harmonic mean between precision and recall) were calculated in order to predict the accuracy of ultrasound as a diagnostic tool. A correlation matrix was created in order to describe the strength of the correlation between the collected data. Spearman’s coefficient ($r_s$) was applied. Missing data points were excluded from the final analysis. P-values < 0.05 were considered statistically significant. All statistical analyses were performed by the Python programming language (version 3.7 released in June 2018 by Python Software Foundation Wilmington, Delaware, United States) and its corresponding libraries (SciPy, Pandas, Seaborn, Matplotlib and Scikit-learn).

Artificial intelligence (AI)-based model for BBS prediction

Logistic regression, a supervised learning classification AI algorithm, was used. The aim was to extract patterns out of raw data and compute, based on the clinical parameter data sets and their occurrences, an automated, accurate AI model capable of predicting and identifying children with BBS (+). The initial data set was randomly divided into two sub-data sets SDS1 (clinical data for 2/3 of the patients) and SDS2 (clinical data for 1/3 of the patients). The SDS1 set was used to perform the training of the AI model and compute the learning process. The SDS2 set was used to verify the results and test the accuracy of automated BBS (+) prediction. Subsequently, the whole data set (SDS1 + SDS2) was subjected to a second analysis of the AI model. Precision rate, recall rate, and f1 score for the developed AI model were calculated and compared to the findings by ultrasonography.

Results

Patient characteristics

Between 2009 and 2019, n = 82 biologically independent pediatric patients with US of the PEG/PEG-J were identified according to the study inclusion and exclusion criteria. The patient cohort included n = 40 female (48.8 %) and n = 42 (51.2 %) male children with a mean age ± standard deviation (SD) of 5.9 ± 5.6 years at first presentation (Table 1). Relevant comorbidities included neurological (n = 42, 51.2 %) and metabolic, cardiological, gastroenterological, oncological, nephrological, neurological and metabolic, cardiological, oncological, gastroenterological, nephrological, and oncological disorders (range 6.1–13.4 %, Table 1).

Distribution of ultrasound examinations among the patient cohort

In total n = 82 pediatric patients underwent n = 124 transabdominal US examinations. Of those, n = 3 cases with sonographic diagnosis of a BBS+ were excluded due to missing endoscopic or CT control after US, resulting in n = 121 independent sonographic cases for further analysis. Of n = 82 patients, n = 55 patients underwent a single sonographic examination and n = 27 patients had multiple examinations performed within 4 weeks to 6 years. The US equipment that was used (devices, probes, and image settings) is summarized in Supplementary Table 1.

Ultrasonographic examinations, imaging precision, and recall rate

The position of the inner holding plate was determined in n = 121 independent sonographic cases (please see exemplary images in Fig. 1). In n = 101 cases the inner holding plate was correctly positioned in the child’s stomach (intragastral, Fig. 1a), whereas in n = 2 cases the inner holding plate was not in its original gastric position but had slipped into the jejunum (intrajejunal). Thus, in n = 103 cases the inner holding plate had not grown into the mucous membrane and a BBS was sonographically excluded (BBS-), which was verified in n = 20 cases by endoscopy and in n = 83 cases based on the further clinical course. In n = 18 cases a BBS was sonographically diagnosed (n = 16 intragastral and n = 2 extragastral) with n = 17 being endoscopically (Fig. 1b, c) confirmed and n = 1 being confirmed by CT (Fig. 1d). Therefore, false positives and false negatives were n = 0, true positives were n = 18 and true negatives were n = 103. The recall and precision rates were 100 % and an f1 score of 1 was achieved. In addition, the expertise of the investigator (pediatricians trained in US and/or DEGUM (Deutsche Gesellschaft für Ultraschall in der Medizin) level I-III-certified pediatricians) did not appear to affect the accuracy of BBS diagnosis (Supplementary Table 2).

Table 1 Demographic and clinical patient characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>n = 82 patients</th>
<th>mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>sex (female, n)</td>
<td>40 (48.8)</td>
<td></td>
</tr>
<tr>
<td>age (years)</td>
<td>82 (100)</td>
<td>5.9 ± 5.6</td>
</tr>
<tr>
<td>weight (kg)</td>
<td>70 (85.4)</td>
<td>17.4 ± 12.0</td>
</tr>
<tr>
<td>height (cm)</td>
<td>62 (75.6)</td>
<td>97.3 ± 27.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>61 (74.4)</td>
<td>16.4 ± 3.1</td>
</tr>
<tr>
<td>primary disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>neurological</td>
<td>42 (51.2)</td>
<td></td>
</tr>
<tr>
<td>cardiological</td>
<td>11 (13.4)</td>
<td></td>
</tr>
<tr>
<td>metabolic</td>
<td>9 (11.0)</td>
<td></td>
</tr>
<tr>
<td>gastroenterological</td>
<td>7 (8.5)</td>
<td></td>
</tr>
<tr>
<td>oncological</td>
<td>6 (7.3)</td>
<td></td>
</tr>
<tr>
<td>nephrological</td>
<td>5 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Ø documentation</td>
<td>2 (2.4)</td>
<td></td>
</tr>
</tbody>
</table>

n = 82 independent pediatric patients. Categorical variables are given as n (%), continuous variables as mean ± standard deviation (SD).
Clinical and gastroenterological findings of n = 121 independent sonographic cases

Considering n = 121 independent US examinations, in n = 92 cases a PEG tube, in n = 20 cases a PEG-J tube and in n = 9 cases no sufficient documentation was found (for details please see \ref{Supplementary Table 3}.). Documented complications during insertion were post-operative bleeding, abrasions of mucous membranes, and small rupture of the liver capsule. In n = 69 cases the children were treated with proton pump inhibitors (PPI) (\ref{Table 2}).
While in n = 16 BBS+ cases the inner holding plate had grown into the stomach wall, n = 2 BBS+ cases required surgical intervention due to extragastral positioning of the plate and/or gastric perforation. General complaints of the patient cohort were general/localized abdominal pain (n = 32, 26.4 %), mobilization problems of the PEG tube (n = 31, 25.6 %), inflammation signs (redness, overheating or swelling) (n = 35, 28.9 %), secretion/exudation (n = 22, 18.2 %), pus discharge (n = 10, 8.3 %), vomiting (n = 30, 24.8 %) and/or leakage of tube feed (n = 8, 6.6 %) (▶ Table 2).

In the BBS+ group (n = 18) the mobilization problem was the most common symptom (n = 17, 94.4 %). The main symptoms in the BBS- group (n = 103) were vomiting (n = 28, 27.2 %) and abdominal pain (n = 28, 27.2 %). The BBS+ group showed a significantly longer time interval between 1st PEG/PEG-J placement and US than the BBS- group (5.6 ± 3.0 years vs. 1.9 ± 3.0 years, p-value < 0.001). Within laboratory parameters only leucocytes showed a statistically significant difference between groups (27.5 ± 63.9 × 10^3/μl vs. 11.4 ± 6.9 × 10^3/μl, p = 0.027) (▶ Table 2).

### Correlation between BBS and clinical characteristics

To reveal potential correlations between BBS+, PEG-associated parameters, and clinical characteristics, a correlation matrix was created. A significantly positive correlation of the occurrence of BBS+ and mobilization problems of PEG (r_s = 0.66, p-value < 0.001), secretion/exudation of the PEG (r_s = 0.29, p = 0.002), longer time interval between 1st PEG placement and US examination (r_s = 0.38, p < 0.001), and white blood cell count (r_s = 0.24, p = 0.016) was observed. No statistically significant negative correlation between the occurrence of BBS+ and PEG-associated parameters and clinical symptoms was found (▶ Fig. 2).

### Table 2 Laboratory values and gastroenterological characteristics.

<table>
<thead>
<tr>
<th>laboratory values</th>
<th>cases</th>
<th>BBS(−)</th>
<th>n</th>
<th>BBS(+)</th>
<th>n</th>
<th>BBS(−)</th>
<th>n</th>
<th>BBS(+)</th>
<th>n</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (mmol/L)</td>
<td>103</td>
<td>88</td>
<td>15</td>
<td>15</td>
<td>7.4 ± 1.6</td>
<td>15</td>
<td>7.7 ± 1.2</td>
<td>0.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>101</td>
<td>87</td>
<td>14</td>
<td>14</td>
<td>39.4 ± 70.3</td>
<td>14</td>
<td>18.6 ± 34.6</td>
<td>0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC (10^9/μl)</td>
<td>103</td>
<td>88</td>
<td>15</td>
<td>15</td>
<td>11.4 ± 6.9</td>
<td>15</td>
<td>27.5 ± 63.9</td>
<td>0.027</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLT (10^9/μl)</td>
<td>103</td>
<td>88</td>
<td>15</td>
<td>15</td>
<td>272.4 ± 162.0</td>
<td>15</td>
<td>269.7 ± 150.7</td>
<td>0.95</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### gastroenterological characteristics and medication

<table>
<thead>
<tr>
<th>n = 121 cases with multiple items possible</th>
<th>n = 121 cases (n %)</th>
<th>n = 103 BBS (−) cases (n %)</th>
<th>n = 18 BBS (+) cases (n %)</th>
<th>n-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>abdominal pain</td>
<td>32 (26.4)</td>
<td>28 (27.2)</td>
<td>4 (22.2)</td>
<td></td>
</tr>
<tr>
<td>mobilization problems</td>
<td>31 (25.6)</td>
<td>14 (13.6)</td>
<td>17 (94.4)</td>
<td></td>
</tr>
<tr>
<td>inflammation signs</td>
<td>35 (28.9)</td>
<td>27 (26.2)</td>
<td>8 (44.4)</td>
<td></td>
</tr>
<tr>
<td>secretion/exudation</td>
<td>22 (18.2)</td>
<td>14 (13.6)</td>
<td>8 (44.4)</td>
<td></td>
</tr>
<tr>
<td>pus discharge</td>
<td>10 (8.3)</td>
<td>8 (7.8)</td>
<td>2 (11.1)</td>
<td></td>
</tr>
<tr>
<td>vomiting</td>
<td>30 (24.8)</td>
<td>28 (27.2)</td>
<td>2 (11.1)</td>
<td></td>
</tr>
<tr>
<td>leakage of tube feed</td>
<td>8 (6.6)</td>
<td>7 (6.8)</td>
<td>1 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Ø documentation</td>
<td>22 (18.2)</td>
<td>22 (21.4)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

### proton-pump inhibitors

| n = 121 independent ultrasound cases. For gastroenterological symptoms, multiple entry of items was possible. Categorical variables are presented as n (%), continuous variables are given as mean ± SD. P-values < 0.05 were considered statistically significant. Ø Documentation: cases in which the requested data was too old (> 7 days older than the ultrasound examination) or not documented. Hb = hemoglobin, in mmol/L, CRP = C-reactive protein, in mg/L, WBC = white blood cells in 10^3/μl, PLT = platelets/thrombocytes in 10^3/μl. |

*Omeprazole* | 60 (49.6) | 50 (48.5) | 10 (55.6) | | |
*Esomeprazole* | 9 (7.4) | 8 (7.8) | 1 (5.6) | | |
*no medication* | 32 (26.4) | 28 (27.2) | 4 (22.2) | | |
*Ø documentation* | 20 (16.5) | 17 (16.5) | 3 (16.7) | | |
Precision and recall rate of AI-based model in comparison to US

In order to assess precision, recall rate, and f1 score for the AI-based model, the same clinical characteristics as described above in the correlation matrix were weighted according to the logistic regression algorithm for the diagnosis of BBS (+). The two most important identifying characteristics were mobilization problems of the PEG (logistic regression coefficient value $r = 5.36$) and time between 1st PEG placement and US examination (logistic regression coefficient value $r = 3.03$) (for individual rating please see ▶ Supplementary Table 4). Applying the AI prediction model to the SDS2 data set (clinical data for 1/3 of patients) 3 out of 5 BBS (+) children were predicted (▶ Fig. 3) and a precision, recall rate, and f1 score of 0.6 were achieved. Applying the same model to the integral data set (SDS1 + SDS2), 16 of 18 BBS (+) children were predicted (▶ Fig. 3). The AI model achieved a precision, recall rate, and f1 score of 0.88, which turned out to be inferior to the US examination with a precision, recall rate, and f1 score of 1. The confusion matrices (AI-based model vs. US) and the experimental setup for creating the AI model are shown in ▶ Fig. 3.

Discussion

This retrospective single-center study provides systematically collected pediatric data demonstrating that transabdominal US is suitable to exactly assess the intra- or extra-gastral position of the inner PEG holding plate for the diagnosis of BBS in children. To date, endoscopy is used as the reference standard for the diagnostic and therapeutic workup in most cases of suspected BBS [10, 11, 26]. However, invasive endoscopic procedures are risky in children and multimorbid patients with PEG tubes [7]—especially when considering the need for sedation and its potential associated complications. In addition, the time resources required for preparation and performing of an endoscopy examination are considerably higher than for US. Moreover, for endoscopic procedures an experienced pediatric gastroenterologist is needed while US is widely accessible and commonly performed by pediatricians and radiologists. In this study, all investigators, regardless of their professional training level, were able to correctly identify the position of the inner PEG holding plate. However, cases with extragastral positioning of the PEG holding plate were scarce. Furthermore, in the clinical routine BBS is relatively easy to assess by verification of proper mobilization of the inner holding plate in its intra-gastral position during dynamic US. To reduce the occurrence of BBS, it is generally recommended for trained nursing staff to regularly mobilize and maintain the PEG [8, 10].

From a clinical perspective, subjects with mobilization problems, increased secretion, longer time interval between 1st PEG placement and US as well as elevated leucocytes showed the highest positive correlation with the occurrence of pediatric BBS. Similar to our findings, Blumenstein et al. [4] ranked mobilization problems or blockage of the PEG tube, peritubular leakage, and abdominal pain among the most frequent symptoms in patients with BBS. Other studies considered the insertion of PEG-J tubes and the number of gastrostomies as potential risk factors for the development of BBS [8]. While white blood cell count correlated with the occurrence of BBS, C-reactive protein (CRP) was insignificant.

To increase cost-efficiency and save time, symptom-based AI models could aid clinical decision making [27, 28]. Although the
The initial implementation of a structured electronic database is also time-consuming, the basic concept is to integrate automated algorithms without further expenditure of time afterwards. Furthermore, as previously shown in pediatric patients with appendicitis, routine parameters could be used in AI models to improve diagnostics [29]. Oelen et al. described that deep learning-based algorithms could even be superior to physicians for measuring hip angles [25]. In this study, clinical diagnosis supported by AI was able to identify BBS cases, however, to a lower degree than conventional US. The inferior results of the AI approach might be attributed to the small data set and the general nonspecific clinical appearance of pediatric BBS. However, the AI approach could provide aid during differential diagnostic considerations and initiation of appropriate US diagnostics with subsequent specific therapy as far as clinical data sets are digitally explorable. A sequence of AI supported clinical diagnostics with point-of-care ultrasound (POCUS) [30, 31] could eventually display the right balance for future settings. While the results revealed perfect diagnostic accuracy for conventional US and good potential for AI-based decision support, the results are potentially limited by the lack of endoscopic validation in BBS+ cases. Therefore, especially early-stage BBS, classified as type II by Richter-Schrag [26], could be missed. To further increase the diagnostic validity of US for the diagnosis of BBS, a standard procedure and documentation could be implemented as follows: mobilization of the PEG in its intragastral position during the examination and documentation of local findings including complications like abscesses of the abdominal wall and/or retention. If the inner holding plate is not clearly detectable, the examination should be performed with an empty stomach followed by installation of fluids (water or tea).

In summary, this is, to the best of our knowledge, the first study evaluating the diagnostic value of transabdominal US and a clinical parameter-based AI approach for the diagnosis of BBS in children. Particularly the routine use of US in cases of suspected BBS enables rapid diagnosis and a personal encounter and could spare pediatric patients more invasive diagnostics. It should therefore be integrated in the routine clinical workup of suspected BBS.
Author contributions
A.H. and J.J. designed the study. Data were analyzed by C.A., A.H., and J.J. C.A. completed data entry. Statistical analysis were performed by D.R.. C.A., A.P.R. and F.K. wrote the first draft of the manuscript. A.L.W. performed language editing. G.S. contributed ultrasonic data. H.K. contributed endoscopic data. The manuscript was critically reviewed by all authors. CA and APR contributed equally as first authors. AH and J.J contributed equally as last authors.

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Conflict of Interest
The authors declare that they have no conflict of interest.

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