Abstract

Background Delayed gastric emptying (DGE) is a frequent complication after pancreaticoduodenectomy (PD). The diagnosis of DGE is based on International Study Group for Pancreatic Surgery (ISGPS) clinical criteria and objective assessments of DGE are infrequently used. The present literature review aimed to identify objective measures of DGE following PD and determine whether these measures correlate with the clinical definition of DGE.

Methods A systematic search was performed using the MEDLINE Ovid, EMBASE, Google Scholar and CINAHL databases for studies including pancreatic surgery, delayed gastric emptying and gastric motility until June 2022. The primary outcome was modalities undertaken for the objective measurement of DGE following PD and correlation between objective measurements and clinical diagnosis of DGE. Relevant risk of bias analysis was performed.

Results The search revealed 4881 records, of which 46 studies were included in the final analysis. There were four objective modalities of DGE assessment including gastric scintigraphy (n = 28), acetaminophen/paracetamol absorption test (n = 10), fluoroscopy (n = 6) and the 13C-acetate breath test (n = 3). Protocols were inconsistent, and reported correlations between clinical and objective measures of DGE were variable; however, amongst these measures, at least one study directly or indirectly inferred a correlation, with the greatest evidence accumulated for gastric scintigraphy.

Conclusion Several objective modalities to assess DGE following PD have been identified and evaluated, however are infrequently used. Substantial variability exists in the literature regarding indications and interpretation of these tests, and there is a need for a real-time objective modality which correlates with ISGPS DGE definition after PD.

Introduction

Delayed gastric emptying (DGE) is one of the most common complications following pancreaticoduodenectomy (PD), with postoperative DGE rates ranging between 10 and 45% [1, 2]. DGE can significantly increase postoperative morbidity, prolong hospital stay and increase healthcare costs [3, 4].

Historically, there have been several definitions of DGE, with studies using different definitions leading to significant challenges in interpreting findings across studies. In 2007, the International Study Group for Pancreatic Surgery (ISGPS) consensus statement standardized the definition of
DGE [4]. While allowing for a standardized measure of DGE, this definition is reliant on subjective clinical judgement based on the duration of nasogastric (NG) tube intubation and reinsertion. The DGE grade can also only be established at the end of the patient’s clinical course. Nevertheless, there have been several publications validating the ISGPS definition of DGE [1, 5, 6]. Furthermore, DGE can be classified into those relating to the surgical procedure itself (primary DGE) or to postoperative complications, e.g., pancreatic fistulas, hemorrhages or intra-abdominal abscess (secondary DGE) [7]. A more objective measure of DGE after PD may allow a real-time and impartial assessment to guide clinical management and develop strategies to prevent or treat DGE.

The aim of this systematic review was to identify the objective assessment modalities of DGE used in the literature following PD. This study also aimed to identify correlations between current clinical definitions of DGE and objective DGE assessments, along with correlations between postoperative symptoms and the objective assessment of DGE.

Materials and methods

This systematic review was completed in accordance with the PRISMA 2020 statement [8] and was prospectively registered with PROSPERO (ID: CRD42021260141).

Literature search

A systematic literature review of MEDLINE (OVID) (1946-June 2022), EMBASE (1980-June 2022), Google Scholar and CINAHL (1982-June 2022) databases was performed in June 2022.

In brief, the search was conducted using the following Medical Subject Heading (MeSH) terms and text words: “pancreaticoduodenectomy”, “pancreatectomy”, “Whipples” AND “gastroparesis”, “postgastrectomy syndrome”, “gastric emptying”, “delayed gastric emptying”, “DGE”, “gastrointestinal motility”, “gastrointestinal transit”, limiting to human studies in English. Reference lists of relevant records were also manually searched for additional eligible publications.

Inclusion and exclusion criteria

This literature search included studies involving pancreaticoduodenectomy (classical, pylorus-preserving or other variations) and excluded other forms of pancreatic resections such as distal, total and central pancreatectomy. The search only included studies that assessed DGE using a non-clinical and objective measure. Meta-analyses, review articles, case reports (with n ≤ 5), letters to the editors, conference proceedings and abstracts were excluded.

Data extraction

Two independent reviewers (THHW, AL) screened and assessed each article for inclusion and extracted data. A title and abstract screen were first performed, followed by a full-text review. Discrepancies were resolved by the senior author (SP). Data on the type of objective measure of DGE, how it was performed, whether there was any correlation between clinical and objective measures of DGE or between symptoms (not otherwise included in the clinical DGE definitions) and the objective measure of DGE were extracted. Data on routine exclusion of mechanical obstruction at the gastrojejunal anastomosis, whether primary and secondary DGE was clearly differentiated and whether the objective DGE results altered management were also extracted. Three risk of bias tools were used, including the revised Cochrane risk-of-bias tool for randomized trials (ROB 2), the Newcastle–Ottawa Scale (NOS) for cohort studies, and the Methodological Index for Non-Randomized Studies (MINORS) for case–control and case series [9–11].

Results

Included studies

In total, 4881 articles were identified from the initial search, of which 46 articles met the inclusion criteria and formed the basis of the systematic review (PRISMA diagram shown in Fig. 1). There were 7 randomized control trials (RCT), 16 cohort studies, 8 case–control studies and 15 case series. These studies encompassed 4 different objective measures of DGE: 28 studies used gastric scintigraphy (Table 1), 10 studies used acceaminophen/paracetamol absorption test, 6 studies used fluoroscopy, and 3 studies used 13C-acetate breath test (Table 2). One study used both the acetaminophen/paracetamol absorption and fluoroscopy in the early and late postoperative phase, respectively [12]. Only one study specified the routine exclusion of mechanical obstruction as a cause of DGE [13], though several studies performed endoscopy or barium radiography but not specifically to assess for mechanical obstruction. No study clearly specified a subgroup analysis on primary or secondary DGE, however, several studies compared the rates of postoperative complications in the DGE and non-DGE cohorts [14–20]. No study used the results of the objective measure of DGE to alter patient management. Relevant results are presented in Tables 1 and 2.
Gastric scintigraphy

28 studies used gastric scintigraphy to diagnose DGE following PD [13–15, 21–45], involving serial imaging to track the transit of isotopes ingested with a meal. Heterogeneous protocols were identified, including the use of different isotopes (\(^{99m}\text{Tc}\) or \(^{111m}\text{In}\)), test meals, serial imaging time intervals and definitions of DGE. Several studies also differentiated between liquid and solid phase gastric emptying [13, 23, 24, 27–29, 35, 40–42]. Additionally, one study used \(^{170}\text{Er}\)-labelled enteric-coated pancreatic microspheres along with \(^{99m}\text{Tc}\) to assess gastric emptying [31]. More recent studies used the standardized technique of gastric scintigraphy based on consensus definition, using a \(^{99m}\text{Tc}\)-labelled scrambled egg meal to assess solid gastric emptying, followed by serial imaging with a gamma camera at 1, 2 and 4 h following meal ingestion [58]. Residual gastric activity greater than 60% at 2 h was considered DGE [43, 44].

Acetaminophen/paracetamol absorption test

10 studies used the acetaminophen (also known as paracetamol) absorption test to define DGE following PD. This technique involves ingesting a standard dose of acetaminophen/paracetamol with regular serum acetaminophen/paracetamol concentration monitoring in the subsequent hours [59]. Any elevation in serum concentration indicates the passage of the ‘meal’ out of the stomach, indirectly assessing gastric emptying [53, 60]. Variable dosing was found between studies. Only one study by Strommer et al. [51] defined a numerical threshold for DGE, assessing maximal plasma concentration (< 25 \(\mu\text{M}\)) and time to reach this value (> 240 min). No other studies provided a quantitative definition for DGE.
| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition (s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|--------------|----------------|-------------------------|------|-------------------|---------|----------------------------------------------------------|-----------------------------------------------|--------------------------------------------------|------------------|
| 1986 | Braasch et al. [21] | Cohort | 71 Hemi-pancreatectomy (PD) | Early post-op: Length of time with NG tube | Post-op ≥ 4 months | Early post-op: NG intubation for > 7 days | 6 patients had biliary fistula | No | No | No | 7 |
|      |        |              | 13 Total pancreatectomy | Late post-op: 113mIn labelled liquid or 99mTc labelled solid meal. Radioactivity was recorded by scintigraphy | | Late post-op: Not defined. Statistical significance compared to controls | 7 patients had pancreatic fistulas or collections | | | | |
|      |        |              | 3 Completion total pancreatectomy | | | | | | | | |
|      |        |              | 5 Controls | | | | | | | | |
| 1987 | Patti et al. [22] | Case–control | 10 PPPD | 99mTc labelled meal. Radioactivity was recorded by scintigraphy at regular intervals | 1–45 months | Abnormal if 2 or more points were more than 2 standard deviations from the mean of the control subjects OR more than 20% of activity remains in the stomach after 3 h | Objective gastric emptying results | No, but endoscopic assessment performed on a single patient | No | No | 16 |
|      |        |              | 5 Controls | | | | | | | | |
| 1988 | Fink et al. [13] | Case–control | 6 PD | 99mTc labelled meal (solid and liquid phase). Radioactivity was recorded by scintigraphy at regular intervals | 1–7 years | Statistical significance compared to the different groups | Liquid phase-emptying took longer in PD than PPPD. PPPD similar to controls | Yes | No | No | 18 |
| Year  | Author                  | Study design | Patient number | Method of assessing DGE                                                                 | Time   | DGE definition (s)                                                                 | Results                                                                 | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|-------|-------------------------|--------------|----------------|----------------------------------------------------------------------------------------|--------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------|---------------------------------------------------------------------|------------------|
| 1989  | Hunt and McLean [23]    | Case series  | 11 Head of pancreas resection 5 Total pancreatectomy | • Early post-op: Length of time with NG tube                                           | • Post-op: 3 months | • Early post-op: Not defined<br>• Late post-op: Abnormal if outside the criteria of 50% liquid emptying between 15–20 min OR 0.8–1.0% per minute clearance of solid emptying | No, but implied<br>No, but intra-abdominal complications recorded | No, but implied<br>No, but intra-abdominal complications recorded | No<br>No, but intra-abdominal complications recorded | No, but intra-abdominal complications recorded | 13 |
| 1991  | Lerut et al. [24]        | Case series  | 18 Partial pancreatectomy 2 Total pancreatectomy | • Early post-op: Length of time with NG tube<br>• Late post-op: $^{99m}$Tc labelled meal (solid and liquid phase). Radioactivity was recorded by scintigraphy at regular intervals | • Post-op: 3–6 months | • Early post-op: NG tube requirement for > 7 days<br>• Late post-op: not defined | No | No, but intra-abdominal complications recorded | No, but intra-abdominal complications recorded | No, but intra-abdominal complications recorded | 11 |
| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition (s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|-------------|----------------|-------------------------|------|-------------------|---------|---------------------------------------------------------------|-----------------------------------------------|------------------------------------------------------------------|------------------|
| 1993 | De Bernardinis et al. [25] | Case series | 11 PPPD with modifications | • Early post-op: Length of time with NG tube<br>• Late post-op: $^{99m}$Tc labelled meal (solid phase). Radioactivity was recorded by scintigraphy at regular intervals | •6 months | • Early post-op: NG tube intubation for > 10 days<br>• Late post-op: $T_{1/2}$ was longer than 80 min | • Early post-op: 4 patients had ‘gastric stasis’<br>• Late post-op: 2 patients had delayed gastric emptying | No. Endoscopy performed, but not for assessment for mechanical obstruction | No | 13 |
| 1993 | Kingsnorth et al. [26] | Case series | 30 PPPD | • Early post-op: Length of time with NG tube, passage of flatus, oral tolerance<br>• Late post-op: $^{99m}$Tc labelled solid meal. Radioactivity was recorded by scintigraphy | •Post-op 3–18 months | • Early post-op: NG intubation for > 7 days and commencement of oral fluids after 7 days<br>• Late post-op: Normal defined as > 50% emptying after 60 min in controls | • Early post-op: 1 patient (of 30) had delayed emptying<br>• Late post-op: All normal | No. Endoscopy performed, but not clearly defined to assess for mechanical obstruction | No | 13 |
| 1993 | Williamson et al. [27] | Cohort | 12 PD 24 PPPD | • Early post-op: Length of time with NG tube/oral tolerance<br>• Late post-op: $^{113m}$In labelled liquid and $^{99m}$Tc labelled solid meal. Radioactivity was recorded by scintigraphy | •Post-op 2 months–5 years | • Early post-op: NG intubation for > 8 days<br>• Late post-op: <br>(a) Upper limit of normal $T_{1/2}$ for liquid emptying- 70 min<br>(b) Upper limit of normal $T_{1/2}$ for solid emptying- 110 min | • Early post-op: delayed in 2/24 of the PPPD patients, 1/12 in PD (had anastomotic dehiscence)<br>• Late post-op:<br>(a) 57% in PPPD and 45% in PD normal. (13/23, 5/11)<br>(b) 42% in PPPD and 17% in PD normal. (10/24, 2/12) | No. Endoscopic and barium studies were mentioned in the results to assess for mechanical obstruction in some patients | No | 7 |
| Year | Author          | Study design | Patient number | Method of assessing DGE | Time   | DGE definition (s)                                                                                                                                   | Results                                                                                       | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|----------------|--------------|----------------|-------------------------|--------|------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------|--------------------------------------------------------------------------------|-----------------|
| 1993 | Yeo et al. [28] | RCT          | 18 PD 100 PPPD | • Length of time with NG tube, oral tolerance <br> • 113mIn labelled liquid and 99mTc labelled solid meal. Radioactivity was recorded by scintigraphy | Post-op 10 days | • NG intubation for > 10 days and (1) one of the following: <br> (a) emesis after nasogastric tube removed <br> (b) postoperative use of prokinetic agents after postoperative day 10 <br> (c) reinsertion of nasogastric tube <br> (d) failure to progress with diet Or (2) nasogastric tube in place fewer than 10 days plus two of (a)–(d) above | • Erythromycin group (11/58), Control group (18/60) had DGE OR Erythromycin group (7/49), Control group (14/47) had DGE excluding complications <br> • Erythromycin associated with improved gastric emptying | No | No | No | Low |
| 1993 | Yung et al. [29] | Case series  | 50 PPPD 4 PD  | • 113mIn labelled liquid and 99mTc labelled solid meal. Radioactivity was recorded by scintigraphy | 7–15 days | • Statistical significance compared to the different groups | • No statistical difference between the 3 different views | No | No | No | 19 |
| 1995 | Pastorino et al. [30] | Case series | 15 PPPD | • 99mTc labelled solid meal. Radioactivity was recorded by scintigraphy | 3–30 months | • Normal range of T1/2 was defined as between 40 and 70 min | • Earlier follow-up was associated with higher half-life than later follow-up | No | Endoscopy performed, but not for assessment for mechanical obstruction | No | No | 13 |
| 1997 | Bruno et al. [31] | Case–control | 7 PD 5 PPPD | • 99mTc labelled solid meal and 131I labelled ECPM. Radioactivity was recorded by scintigraphy | 30 ± 12 months | • Statistical significance compared to the different groups | • Transit time between ECPM vs pancake meal were not statistically different | No | No | No | 18 |
| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition (s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|--------------|----------------|-------------------------|------|-------------------|---------|-----------------------------------------------------------|-----------------------------------------------|-----------------------------------------------|------------------|
| 1998 | Lupo et al. [32] | Case series | 17 PPPD | • Early post-op: NG tube output<br>• Late post-op: $^{99m}$Tc labelled solid meal. Radioactivity was recorded by scintigraphy | • Post-op<br>$5-7$ months | • Early post-op: NG output for $>1$ day for $>7$ days<br>• Late post-op: DGE was defined as $T_{1/2} > 85$ min | • Early post-op: 1/17 had DGE<br>• Late post-op: Rapid gastric emptying $3/11$, normal $5/11$, delayed gastric emptying $3/11$ | No | No | No | 18 |
| 1999 | Hishinuma et al. [33] | Case–control | 24 PPPD<br>2 Controls | • $^{113m}$In labelled meal with $^{99m}$Tc intravenous injection. Radioactivity was recorded by scintigraphy | • 28 days to 67 months | • Not defined but the 2 normal controls had 43% and 66% gastric retention at 1 h after imaging | • Rate of gastric emptying improved compared to pre- and post- 2 months post-op | No | No | No | 16 |
| 1999 | Sumida et al. [34] | Cohort | 14 PPPD with preserved superior pyloric branch<br>13 PPPD without nerve preservation | • $^{99m}$Tc labelled meal. Radioactivity was recorded by scintigraphy | • 1 month | • Statistical significance compared to the different groups | • $3/11$ showed delayed gastric emptying | No | No | No | 7 |
| 1999 | Thor et al. [35] | Cohort | 18 PD<br>10 PPPD | • Liquid gastric emptying: Ultrasound used (not specified)<br>• Solid gastric emptying: $^{99m}$Tc labelled solid meal. Radioactivity was recorded by scintigraphy<br>• Electrogastrography performed | • Pre-op and 2 months | • Normal range of $T_{1/2}$ was $45 \pm 9$ min and delayed if $T_{1/2}$ was increased more than 1 standard deviation above normal<br>• EGG- not defined | • Pre-op:<br>• (a) Liquid DGE in 5/18 and 2/10<br>• (b) Solid DGE in 8/18 and 2/10<br>• Post-op:<br>• (a) Liquid rapid GE in 16/18 and 0/10<br>• (b) Liquid DGE in 1/18 and 6/10<br>• (c) Solid rapid GE in 12/18 and 0/10<br>• (d) Solid DGE in 4/18 and 5/10 | No | No | No | 7 |
| 2000 | Sato et al. [36] | Case series | 8 PD<br>8 PPPD | • $^{99m}$Tc labelled meal. Radioactivity was recorded by scintigraphy | • $>2$ years | • Not defined | • Gastric emptying half-life ranged between 9 and 147 min | No | No | No | 12 |
### Table 1 continued

| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition(s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|--------------|----------------|-------------------------|------|------------------|---------|-------------------------------------------------------------|-------------------------------------------------|-------------------------------------------------------------|-------------------|
| 2000 | Sato et al. [37] | Cohort | 9 PD- Imanaga, 9 PPPD- Imanaga | \(^{99m}\)Tc labelled meal. Radioactivity was recorded by scintigraphy | > 2 years | •Statistical significance compared to the different groups | •Gastric emptying half-life was significantly shorter in the PDI vs the PpPDI group in a sitting position but no difference in the supine position | No | No | No | 8 |
| 2003 | Caronna et al. [38] | Case series | 25 PD | •Scintigraphy (not specified) was completed | 3 months | •Not defined | •Good rhythmic and regular gastric emptying | No | No | No | 10 |
| 2005 | Kim et al. [39] | Case series | 47 PPPD | •Clinical: Inability to tolerate oral diet •Objective: \(^{99m}\)Tc labelled meal. Radioactivity was recorded by scintigraphy | Post-op •Pre-op and post-op | •Clinical: Inability to tolerate oral diet by 8 days post-op •Objective: DGE defined as gastric retention of the test meal > 55% at 2 h | •Preoperative GET: abnormal in 20/39 •Postoperative GET: abnormal in 13/35 | No | No | No | 20 |
| 2005 | Shan et al. [40] | RCT | 23 PPPD | •Clinical: Length of time with NG tube •Objective: \(^{99m}\)Tc labelled meal (solid and liquid phase). Radioactivity was recorded by scintigraphy | Post-op •14 days | •Clinical: Not defined •Objective: sDGE defined as gastric emptying T\(_{1/2}\) increased more than the mean ± 2SD (58.2) mins | •Subjective: sDGE was higher in the somatostatin group (9/11, 82%) vs the non-somatostatin group (3/12, 25%) •Objective: sDGE was higher in the somatostatin group (10/11, 91%) vs the non-somatostatin group (3/12, 25%) | No | No | No | Low |
| Year | Author          | Study design | Patient number | Method of assessing DGE                                                                 | Time          | DGE definition(s)                                                                 | Results                                                                 | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|----------------|--------------|----------------|----------------------------------------------------------------------------------------|---------------|----------------------------------------------------------------------------------|------------------------------------------------------------------------|-------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------|------------------|
| 2005 | Shan et al. [41] | Cohort       | 33 PD          | • Clinical: Length of time with NG tube<br>Objective: 99mTc labelled meal (solid and liquid phase). Radioactivity was recorded by scintigraphy <br>• Pre-op, 14 days and 6 months | Post-op       | • Clinical: NG intubation for ≥ 10 days<br>• Objective: (a) Delayed liquid emptying diagnosed if $T_{1/2} > 23$ min<br>   (b) Delayed solid emptying diagnosed if $T_{1/2}$ increased by more than 2 standard deviations above the mean | No<br>Subjective: sDGE higher in PPPD than PD (9/21 vs 5/33) at 14 days and 0 for both groups at 6 months<br>Objective: (a) Pre-op: PPPD group (5/21 had delayed LGE, 6/21 had delayed SGE), PD group (3/33 had delayed LGE, 7/33 had delayed SGE)<br>  (b) Post-op day 14: PPPD group (76% LGE, 42% SGE), PD group (91% LGE, 88% SGE)<br>  (c) 6 months: PPPD group (4.7% LGE, 4.7% SGE), PD group (37% LGE, 30% SGE) | No                                              | No                                              | No                                              | 7                              |
| 2007 | Shan et al. [42] | Cohort       | 21 PPPD        | • Clinical: Length of time with NG tube<br>Objective: 99mTc labelled meal (solid and liquid phase). Radioactivity was recorded by scintigraphy <br>• Post-op, 12 days (liquid) and 14 days (solid) and 6 months | Post-op       | • Clinical: NG intubation for ≥ 10 days OR if patient experiences emesis after removal of NG tube, reinserter of NG tube or failure to progress with diet<br>Objectives:<br>  (a) Delayed liquid emptying diagnosed if $T_{1/2} > 23$ min<br>  (b) Delayed solid emptying diagnosed if $T_{1/2}$ increased by more than 2 standard deviations above the mean<br>  (c) Proximal to distal stomach radiation count (P/D) ratio was used | No<br>Subjective: 9/21 had sDGE<br>Objective: P/D for the patients were lower than the controls for both liquid and solid phase at both 14 days and at 6 months in general | No                                              | No                                              | No                                              | 5                              |
| Year   | Author                  | Study design | Patient number | Method of assessing DGE                                                                 | Time | DGE definition (s)                                                                 | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|--------|-------------------------|--------------|----------------|----------------------------------------------------------------------------------------|------|---------------------------------------------------------------------------------|---------|---------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------------|------------------|
| 2008   | Kollmar et al. [14]     | RCT          | 62 PPPD 5 PD   | • Length of time with NG tube • $^{99m}$Tc labelled meal. Radioactivity was recorded by scintigraphy | Post-op 7 days | • NG intubation for > 10 days and/or intolerance of normal diet beyond 14 days • Not defined | No      | No, but pancreatic fistula was analysed for DGE vs non-DGE    | No, but pancreatic fistula was analysed for DGE vs non-DGE       | Low                 |                  |
| 2013   | van Samkar et al. [43]  | Case–control | 28 PPPD 16     | Double-bypass procedure • Clinical: ISGPS consensus • Objective: $^{99m}$Tc labelled meal (solid phase). Radioactivity was recorded by scintigraphy | Post-op Pre-op and 7 days | • Clinical: ISGPS criteria for DGE (B or C) • Objective: Upper normal limit of normal is retention of 60% at 2 h | No      | No                                                            | No                                                            | 19                  |                  |
| 2015   | Eshuis et al. [44]      | RCT          | 38 retrocolic 35 antecolic 63 PPPD 10 PD | • Clinical: ISGPS consensus • Objective: $^{99m}$Tc labelled meal (solid phase). Radioactivity was recorded by scintigraphy | Post-op Pre-op and 7 days | • Clinical: ISGPS criteria for DGE (B or C) • Objective: Upper normal limit of normal is retention of 60% at 2 h | No      | No                                                            | No                                                            | Low                 |                  |
| 2017   | Samaddar et al. [15]    | Case–control | 21 PD          | • Clinical: ISGPS consensus • Objective: $^{99m}$Tc labelled meal (solid phase). Radioactivity was recorded by using a SPECT machine | Post-op Pre-op and 10 and 21 days | • Clinical: ISGPS criteria for DGE (A or above) • Objective: Normal taken as > 50% clearance at 1 h and $t_{1/2}$ of < 80 min | No      | No                                                            | No                                                            | 19                  |                  |
rather, they compared the results to different groups within their respective studies or to preoperative results. Additionally, one study used the acetaminophen/paracetamol absorption test for the liquid phase and sulphamethizole capsule for the solid phase [48].

Fluoroscopy

6 studies used fluoroscopy to define DGE following PD. Following the ingestion of barium or Gastrografin® (sodium amidotrizoate/amidotrizoate meglumine) contrast, serial radiographs were taken to determine the location and amount of contrast to assess gastric retention, emptying and therefore function. The 3 case series identified did not provide a fluoroscopic definition for DGE [17, 54, 55] while 2 studies defined DGE if contrast was present in the stomach after a defined time interval (1 and 4 h, respectively) [12, 18]. Furthermore, Nojiri et al. [19] described a classification system dividing gastric emptying into three grades depending on gastric distension and stasis appearances on fluoroscopic imaging.

13C-acetate breath test

3 studies used the 13C-acetate breath test to define DGE following PD. Following ingestion of a 13C-labelled triglyceride meal, serial breath samples were obtained to determine the concentration of exhaled 13CO2 or other metabolites using spectrometry, and the time to peak 13CO2 was determined. No quantitative definition for DGE was used, rather, results were compared between different groups within the studies or to preoperative results. All studies were performed preoperatively and at least 1 month after surgery, but not immediately after surgery [61, 62].

Correlation between clinical and objective DGE

All objective measures of DGE identified in this review had implied or explicit correlations between clinical and objective measures of DGE. These results are summarized in Table 3. Results were too heterogeneous to allow meta-analysis.

8 studies correlated clinical DGE with gastric scintigraphy. Of these, 2 studies by Patti et al. and Hunt and Maclean, found no correlation between clinical DGE and scintigraphy [22, 23]. One study by Shan et al. [41] compared rates of clinical (subjective) DGE (‘sDGE’) and objective DGE (‘oDGE’). In the pylorus-preserving PD group, 42% had sDGE and 42% had oDGE, while in the pylorus-resecting PD group, 15% had sDGE and 88% had oDGE. However, no conclusion was drawn on the correlation between the clinical and objective DGE. Eshuis et al. [44] found a strong association between scintigraphy
| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition(s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|--------------|----------------|-------------------------|------|------------------|---------|------------------------------------------------------------|-------------------------------------------------|------------------------------------------------------------|-----------------|
| 1992 | Watanabe et al. [12] | Cohort 10 PD with either Billroth I or Billroth II reconstruction | 8 Controls | Early post-op, subjective: Length of time with NG tube, oral tolerance Early post-op, objective: Barium fluoroscopy Late post-op: Acetaminophen added to a meal. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration | Post-op ≥ 3 months | Early post-op, subjective: Not defined. Time elapsed before removal of intragastric tube and resumption of oral intake Early post-op, objective: Gastric emptying considered to be adequate according to radiography if the barium ingested (150 mL) was almost entirely eliminated within 1 h Late post-op: Statistical significance compared to the different groups | No difference between subjective gastric emptying between 2 reconstruction techniques Barium fluoroscopy-1/10 had delayed gastric emptying. No difference between the reconstruction techniques Patients had delayed gastric emptying than controls using the acetaminophen technique | No | Barium radiography was used to assess for gastric emptying, rather than for mechanical obstruction | No No No 6 |
| 1995 | Ueno et al. [46] | Cohort 8 PD | 18 PPPD 8 Cholecystectomy 4 Transabdominal esophageal transection 10 Distal partial gastrectomy 32 Controls | Acetaminophen added to a meal. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration | < 2 months or > 3 months | Statistical significance compared to the different groups | Early postoperative period (a) Lower acetaminophen concentration in PPPD and PD compared to controls (b) No difference in acetaminophen concentration in PPPD and PD compared to controls | No | No | No 5 |
| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition(s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|--------------|----------------|------------------------|------|------------------|---------|-------------------------------------------------------------|-----------------------------|----------------------------------------------------------------|-------------------|
| 1997 | Müller et al. [47] | Cohort | 10 Duodenum-preserving pancreatic head resections | 10 PPPD | 6 Controls | Acetaminophen added to a meal. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration | Pre-op | 10 days | 6 months | Statistical significance compared to the different groups | No | No | No | 7 |
| 1998 | Kobayashi et al. [48] | Case series | 14 PPPD | Liquid gastric emptying: Acetaminophen added to water. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration | 27–53 days | Statistical significance compared to the preoperative levels | No | No | No | 19 |
| 1999 | Takeda et al. [49] | RCT | 16 PPPD | Acetaminophen added to a meal. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration | Pre-op and 1, 3, 6, 9, 12 months | 2–4 weeks and 6–12 months | Statistical significance compared to the different time points | No | No | No | Low |
| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition (s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|--------------|----------------|------------------------|------|-------------------|---------|---------------------------------------------------------------|-------------------------------------------------|--------------------------------------------------|-----------------|
| 2002 | Ohtsuka et al. [50] | Cohort 57 PPPD 25 Controls | • Acetaminophen added to a meal. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration | • 1 month | • From 7–14 days and repeated weekly until gastric Phase 3 identified | • Statistical significance compared to the different groups | • Time to first gastric phase 3 activity | No | No | No | 6 |
| 2005 | Strommer et al. [51] | Cohort 18 PD 13 PPPD | • Clinical: Length of time with NG tube | • Post-op | | • Clinical: NG intubation for ≥ 10 days or recurrent vomiting on day 9–10 post-op | • Objective: A delayed gastric emptying rate was defined as $T_{\text{max}} > 240$ min and/or $C_{\text{max}} < 25 \mu M$ | No | No | No | 7 |
| 2007 | Ohuchida et al. [52] | Cohort 31 PPPD | • Acetaminophen added to a meal. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration | • 1–2 months | • 6–12 months | • Statistical significance compared to the preoperative levels | • Short-term gastric emptying was slowed | No | No | No | 7 |
| 2014 | Harmuth et al. [53] | Cohort 13 PD 13 PPPD | • Paracetamol added to a meal. Blood tests for paracetamol levels obtained pre-administrations and serially post-administration | • Between 5–199 months | • Statistical significance compared to the different groups | • PD had better gastric emptying than PPPD | No | No | No | 8 |
| Year | Author                         | Study design | Patient number | Method of assessing DGE                                                                 | Time   | DGE definition(s)                                                                 | Results | Primary and secondary DGE clearly differentiated | Routine exclusion of mechanical obstruction clearly defined | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|-------------------------------|--------------|----------------|----------------------------------------------------------------------------------------|--------|----------------------------------------------------------------------------------|---------|-----------------------------------------------|-------------------------------------------------|-------------------------------------------------|------------------|
| 2014 | Tamandl et al. [16]           | RCT          | 64 PPPD        | • Clinical: Length of time with NG tube, oral tolerance                                  | Post-op| Clinical: NG intubation for ≥ 10 days and one of the following:                    | No      | No                                            | No                                              | No, but pancreatic fistula and intra-abdominal infection were analysed for DGE vs non-DGE | Low               |
|      |                               |              |                | • Objective: Paracetamol added to a meal. Blood tests for paracetamol levels obtained pre-administrations and serially post-administration | 10 days| (a) Emetesis after nasogastric tube removed                                          |         |                                               |                                                  |                                                 |                   |
|      |                               |              |                |                                                                                       |        | (b) Reinsertion of nasogastric tube                                                 |         |                                               |                                                  |                                                 |                   |
|      |                               |              |                |                                                                                       |        | (c) Failure to progress with diet                                                   |         |                                               |                                                  |                                                 |                   |
|      |                               |              |                |                                                                                       |        | (d) Use of prokinetics after day 10 post-op                                         |         |                                               |                                                  |                                                 |                   |
|      |                               |              |                |                                                                                       |        | • Objective: Statistical significance compared to the different groups              |         |                                               |                                                  |                                                 |                   |
|      |                               |              |                |                                                                                       |        |                                                                                   |         |                                               |                                                  |                                                 |                   |
| 1980 | Traverso and Longmire [54]    | Case series  | 8 PPPD         | • Barium upper gastrointestinal series                                                  | 2–6 months | Not defined                                                                       | No      | No                                            | No                                              | No, but barium radiography was used to assess for gastric emptying, rather than for mechanical obstruction | 10               |
|      |                               |              |                | • Standard Hunt test- not specified                                                    |        |                                                                                   |         |                                               |                                                  |                                                 |                   |
| 1992 | Watanabe et al. [12]          | Cohort       | 10 PD with either Billroth I or Billroth II reconstruction | Early post-op, subjective: Length of time with NG tube, oral tolerance                | Post-op| ≥ 3 months                                                                         | No      | No                                            | No                                              | No, but barium radiography was used to assess for gastric emptying, rather than for mechanical obstruction | 6                |
|      |                               |              | 8 Controls     | Early post-op, objective: Barium fluoroscopy                                             |        |                                                                                   |         |                                               |                                                  |                                                 |                   |
|      |                               |              |                | Late post-op: Acetaminophen added to a meal. Blood tests for acetaminophen levels obtained pre-administrations and serially post-administration |        |                                                                                   |         |                                               |                                                  |                                                 |                   |
|      |                               |              |                |                                                                                       |        |                                                                                   |         |                                               |                                                  |                                                 |                   |

**Fluoroscopy**
| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition (s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|-------------|----------------|-------------------------|------|-------------------|---------|----------------------------------------------------------|-----------------------------------------------|-------------------------------------------------|----------------|
| 2001 | Abdel- Wahab et al. [17] | Case series | 81 PD | •Barium upper gastrointestinal series | •1,3,6,12 months | Not defined | •7/81 patients (8.9%) had delayed gastric emptying | No | Endoscopy performed, but not clearly defined to assess for mechanical obstruction | No, but pancreatic fistula and intra-abdominal infection were analysed for DGE vs non-DGE | No | 11 |
| 2015 | Krishna et al. [18] | Case series | 52 PD | •Clinical: Length of time with NG tube, nutritional requirement OR •Objective: Gastrografin® study | •5 days | •DGE defined as (a) Reinsertion of NG after removal (b) Requirement of prolonged TPN or FJ (> 7 days) (c) Hold-up of oral contrast in stomach for more than 4 h after oral Gastrografin® study (Objective) | •DGE present in 3/52 patients | No | No, but postoperative complications were analysed for DGE vs non-DGE | No | 14 |
| 2018 | Nojiri et al. [19] | Case–control | 160 subtotal stomach-preserving PD | •Clinical: ISGPS consensus •Objective: Barium meal followed by serial abdominal x-rays | •Post-op 7 days | •Clinical: ISGPS criteria for DGE •Objective: Gastric emptying divided into 3 grades depending on gastric dilation and gastric stasis appearances on imaging •Subjective: DGE identified in 30 patients. Non-DGE in 130 patients •Objective: 14/64 Grade 2 and 4/64 Grade 3 gastric emptying | No | No | No, but postoperative complications were analysed for DGE vs non-DGE | No | 16 |
| 2020 | Krishna et al. [55] | Case series | 467 PD | •Gastrografin® study | •5 days | •Not defined | •DGE present in 96/467 patients | No | Endoscopy performed, but not for assessment for mechanical obstruction | No | 12 |
Table 2 continued

| Year | Author | Study design | Patient number | Method of assessing DGE | Time | DGE definition (s) | Results | Routine exclusion of mechanical obstruction clearly defined | Primary and secondary DGE clearly differentiated | Was results of the objective assessment of DGE used to alter treatment? | Risk of bias score |
|------|--------|-------------|----------------|-------------------------|------|-------------------|---------|-------------------------------------------------|---------------------------------|------------------------------------------------|------------------|
| 2009 | Chijiwa et al. [56] | RCT | 17 Antecolic PPPD 18 Vertical retrocolic PPPD | Clinical: Length of time with NG tube, oral tolerance  
Objective: ¹³C-acetate labelled liquid meal was administered and serial breath samples were taken | Post-op  
Pre-op and 30 days | Clinical: DGE defined by either  
(a) NG intubation for > 10 days OR  
(b) reinsertion of nasogastric tube OR  
(c) failure to progress with diet by 14 days  
Objective: Statistical significance compared to the preoperative levels | No  
No  
No | Low |
| 2012 | Hiyoshi et al. [57] | Cohort | 8 Subtotal stomach-preserving PD 33 PPPD | ¹³C-acetate labelled liquid meal was administered and serial breath samples were taken | Pre-op and 1.3,6,9,12 months | Statistical significance compared to the preoperative levels | No. Assessment for mechanical obstruction mentioned, but not clearly explained | No  
No  
No | 8 |
| 2014 | Kawai et al. [20] | Cohort | 66 PD 64 PPPD | ¹³C-acetate labelled liquid meal was administered and serial breath samples were taken | Pre-op and 6,12,24 months | Statistical significance compared to the different groups | No | No  
No, but pancreatic fistula and intra-abdominal infection were analysed for DGE vs non-DGE | 9 |

DGE delayed gastric emptying, ISGPS International Study Group in Pancreatic Surgery, NG nasogastric, PD pancreaticoduodenectomy, PPPD pylorus-preserving pancreaticoduodenectomy, RCT randomized control trial
results and clinically relevant DGE (grade B or C) and concluded that gastric scintigraphy performed on day 7 following surgery predicted the severity of clinical DGE. Similarly, van Samkar et al. [43] found that scintigraphy performed at day 10 and day 21 had 100% positive predictive value and 100% specificity for clinical DGE.

For the acetaminophen/paracetamol group, 2 studies implied a correlation between the clinical and objective measure of DGE. Although no statistical analysis was performed, both studies found that patients with low serum acetaminophen/paracetamol also had concurrent clinical DGE, suggesting correlation [16, 51].

Krishna et al. [18] was the only study using fluoroscopy which implied an association with clinical DGE, with all 3 patients requiring reinsertion of NG tube demonstrating prolonged gastric Gastrografin® retention.

Only 1 study by Chijiwa et al. [56] implied a correlation between clinical DGE and the $^{13}$C-acetate breath test. No

| Year | Author | Correlation between clinical and objective DGE |
|------|--------|------------------------------------------------|
| 1987 | Patti et al. [22] | No correlation found between immediate postoperative clinical DGE and late objective DGE |
| 1989 | Hunt and McLean [23] | No correlation between clinical DGE post-op with objective gastric emptying 3 months later |
| 2005 | Shan et al. [40] | Somatostatin group: 9/11 had clinical DGE and 10/11 had objective DGE |
| 2005 | Shan et al. [41] | Post-op day 14, clinical: 42% PPPD and 15% PD had DGE |
| 2005 | Shan et al. [41] | Post-op day 14, objective: 52% for solid gastric emptying and 76% for liquid gastric emptying in PPPD and 88% for solid gastric emptying and 91% for liquid gastric emptying in PD were delayed |
| 2005 | Shan et al. [41] | Post-op 6 months, objective: 4.7% for solid gastric emptying and 4.7% for liquid gastric emptying in PPPD and 30% for solid gastric emptying and 37% for liquid gastric emptying in PD were delayed |
| 2007 | Shan et al. [42] | The proximal to distal stomach radiation count ratio was statistically smaller for those with clinical DGE than those without clinical DGE ($p = 0.025$) |
| 2013 | van Samkar et al. [43] | Patients with ISGPS grade B or C had higher median residual activity in the stomach at 120 min than patients with no DGE or ISGPS grade A (94% vs 39%, $p = 0.004$) |
| 2015 | Eshuis et al. [44] | Objective DGE on post-op day 7 is predictive of severity of clinical DGE |
| 2017 | Samaddar et al. [15] | Objective DGE at post-op day 10 |
| 2014 | Tamanidl et al. [16] | At any time point after ingestion of the test meal, the serum acetaminophen/paracetamol levels were lower in patients with DGE |

**Acetaminophen/paracetamol absorption Test**

| Year | Author | Correlation between clinical and objective DGE |
|------|--------|------------------------------------------------|
| 2005 | Strommer et al. [51] | 6/9 with clinical DGE also had objective DGE (1/9 later excluded) |
| 2005 | Strommer et al. [51] | 12/22 without clinical DGE did not have objective DGE (2/22 later excluded) |
| 2014 | Tamanidl et al. [16] | At any time point after ingestion of the test meal, the serum acetaminophen/paracetamol levels were lower in patients with DGE |

**Fluoroscopy**

| Year | Author | Correlation between clinical and objective DGE |
|------|--------|------------------------------------------------|
| 2015 | Krishna et al. [18] | 3/3 patients with clinical DGE also had prolonged retention of Gastrografin® |

**$^{13}$-acetate breath test**

| Year | Author | Correlation between clinical and objective DGE |
|------|--------|------------------------------------------------|
| 2009 | Chijiwa et al. [56] | No significant difference in the incidence of clinical DGE ($p = 0.34$) and no significant difference in $^{13}$C-acetate breath test results between the antecolic and retrocolic groups |

*DGE* delayed gastric emptying, *ISGPS* International Study Group in Pancreatic Surgery, *NPV* negative predictive value, *PD* pancreaticoduodenectomy, *PPPD* pylorus-preserving pancreaticoduodenectomy, *PPV* positive predictive value.
statistical difference in both the incidence of clinical and objective DGE were found in the subgroups.

### Correlations between symptoms and objective DGE

3 objective measures of DGE had implied or explicit correlations between symptoms (including abdominal pain, early satiety, nausea and vomiting and/or loss of appetite) and objective DGE, with 1 study each (Table 4). No studies were identified for fluoroscopy.

For gastric scintigraphy, Pastorino et al. [30] demonstrated a reduced gastric emptying time (49.3 min compared to 82.3 min) with patients who had better clinical outcomes (score 1 and 2 according to the questionnaire used) compared to those with a poorer clinical outcome.

For the acetaminophen/paracetamol absorption test, Takeda et al. [49] found that the improvement of test results coincided with the recovery of symptoms. Specifically, the area under the curve at 90 min following administration was 48.1% at 1 month postoperatively which returned to preoperative baseline values at 6 months, coinciding with the improvement in symptoms.

For $^{13}$C-acetate breath test, only 1 study by Kawai et al. [20] demonstrated symptoms in the immediate postoperative period was associated with DGE on the $^{13}$C-acetate breath test months after the surgery, suggesting association.

### Discussion

Delayed gastric emptying is a common complication following PD and is associated with increased morbidity, prolonged hospitalization and increased costs to healthcare [3, 4]. While the ISGPS definition for DGE is the most widely used, it relies on subjective clinical judgement and only diagnoses DGE at the end of the clinical course. This literature review identified 4 objective modalities to assess the presence of DGE following PD. These include gastric scintigraphy, acetaminophen/paracetamol absorption test, fluoroscopy and $^{13}$C-acetate breath test. All modalities had at least 1 study that explicitly or implied a correlation with clinical DGE definition.

Historically, DGE assessments and definitions have been heterogeneous, making meaningful comparisons between different studies difficult. However, in 2007, the ISGPS developed a consensus definition for DGE following pancreatic surgery [4]. This definition classified the severity of DGE (A, B or C) based on the duration of NG intubation or reinsertion, with the condition of no underlying mechanical obstruction to cause symptoms. Only 1 study in this review clearly included this condition in their methodology [13]. Moreover, DGE can be further subclassed into primary or secondary, dependent on the presumed cause being attributed to the surgical procedure or postoperative complications, respectively [7]. While secondary DGE is expected to resolve following the treatment of postoperative complications, this is not necessarily true for primary DGE, and is therefore the focus of this review.

Several studies have now validated the ISGPS definition. These studies have found statistically significant differences in postoperative clinical outcomes, including further diagnostic evaluations (such as endoscopy or imaging), treatment, parenteral nutrition, ICU admission duration and overall hospitalization duration between the different DGE severities (including those with no DGE) [1, 5, 6]. Since the consensus statement, almost all studies examined in this literature review, including those exclusively using the clinical definition, used the ISGPS definition.

There are several advantages to the clinical ISGPS definition of DGE. In particular, it is non-invasive and requires minimal cost to the patient or health system. It allows a standardized definition for audit and research purposes and the development of risk stratification tools for DGE following PD [63]. However, there are some disadvantages. Firstly, this definition relies on clinician
judgement on whether to maintain or re-insert the NG tube. This decision is based on symptoms (e.g., food intolerance, nausea, vomiting), which, albeit pragmatic, is an experience-based assessment of the patient’s underlying gastric physiological status. Secondly, medications, such as antiemetics or prokinetics, may also influence patient symptoms and therefore clinician judgement [46]. Finally, the ISGPS definition is a retrospective assessment and while it is useful for audits and research, it does not allow a real-time diagnosis of DGE and thereby does not aid in guiding immediate inpatient management or predicting recovery. As such, several authors have proposed that a real-time and objective measure of DGE may provide a more accurate way of assessing the patient’s true gastric physiology, to potentially allow future research into this area to become more standardized and therefore guide postoperative management, such as decision for early parenteral nutrition support if stomach recovery is expected to be prolonged or other novel therapies [15, 39, 41, 43, 64]. Indeed, no studies identified in this review used the results of the objective assessment of DGE to guide inpatient management, thus would be a focus for future research. An ideal test would not only exclude mechanical obstruction but also assesses gastric motility, and there is currently a lack of such testing modality.

This literature review has identified several non-clinical or objective measures to assess and define DGE with the most common technique being gastric scintigraphy. First described by Griffith et al. [65] in 1966, this technique is still considered the standard for objectively assessing gastric emptying [58, 66], with a 2008 consensus statement developed by Abell et al. [58] to standardize protocols. Limitation to this measure include its relative cost, access to equipment, impracticality to apply in the immediate postoperative setting and concerns on the use of radioactive isotopes [46, 50]. Moreover, it may also not be feasible to administer the test meal in patients experiencing severe nausea or vomiting. Eight studies assessed the presence of associations between clinical DGE and gastric scintigraphy. Three studies, all published prior to 2006, either found no correlation between clinical DGE and gastric scintigraphy or did not conclude a correlation between the two measures. In contrast, the more recent studies have all found or implied a correlation between clinical DGE definitions and gastric scintigraphy [15, 40–44], which may be due to the standardization of DGE assessment protocols and definitions.

The other non-clinical or objective measures of DGE identified in the literature review all have advantages and disadvantages. In the acetaminophen/paracetamol absorption test, the advantages include its relative accessibility, the benefits of a bedside test, that it does not involve the nuclear medicine department and avoids radiation. However, it does require serial blood tests posing risks and requiring intensive input by both clinicians and laboratory. It is also not a direct measure of gastric emptying, albeit being correlated with clinical DGE following PD [58]. In the $^{13}$C-acetate breath test, the main advantage is its non-invasive nature. However, there are concerns of unreliable results following pancreatic surgery due to the possibility of altered physiology and intestinal absorption, thereby affecting test accuracy and reliability [67]. For fluoroscopy, the main advantages are that this technique is well-established in other fields of medicine, is readily available and allows a real-time assessment of gastric function. Limitations include its subjective nature, difficulty in quantifying results and radiation exposure.

While the aforementioned objective measures of gastric emptying are valuable measures of gastric function, they all represent indirect functional measures of gastric transit in contributing to the patient’s symptoms. Rather, it may be more useful to assess the direct physiological status of gastric motility after pancreateoduodenectomy, particularly in patients with primary DGE to inform targeted treatments. By understanding the underlying pathophysiology of these patients, rather than functional status, clinicians may potentially be able to predict, assess and even aim to treat DGE with novel strategies, such as gastric pacing or ablation, which are currently under research [68]. Numerous studies have investigated gastric physiology or function by assessing either the peristaltic or electrophysiological activity of the stomach, termed gastric slow waves [69, 70]. Non-surgical and post-surgical gastric dysfunctions have been associated with gastric slow wave abnormalities [71–73]. Recent bioengineering developments now allow for more accurate quantification of these gastric slow waves to be possible, particularly with the recent development of non-invasive high-resolution electrogastrography devices to assess gastric electrical activity [68]. This validated technique has been correlated with patient symptom severity in other conditions, albeit never in PD patients [74]. Further research is now required to determine whether these novel techniques may better assess the pathophysiology of DGE post-PD [35, 75].

The strength of this review was the broad search strategy, which allowed a large number of studies to be included in this literature search. The main limitation of this review was the relatively few studies for each objective technique with heterogeneous protocols (including different interventions and time points after surgery), meaning that statistical comparisons between various techniques (e.g. network meta-analysis) could not be performed. A further limitation was the lack of high-quality studies and studies directly comparing objective assessment of DGE with clinical DGE or symptoms. This review now provides the foundations for future research into this area of clinical
assessment and the development of an objective clinical tool to more accurately assess DGE following PD.

Conclusion

This literature review identified several techniques which objectively assess gastric function following surgery, with the most common being gastric scintigraphy. There is currently no consensus on the preferred objective measure of delayed gastric emptying following pancreatic surgery. Therefore, a consensus may be useful in defining or developing a more objective and standardized measure of delayed gastric emptying following pancreaticoduodenectomy.

Funding T H.-H. Wang was supported by the Auckland Medical Research Foundation Douglas Goodfellow Medical Research Fellowship.

Declarations

Conflict of interest GOG is the director and shareholder of Alimetry. All authors agree that GOG’s conflict of interest has not impacted on the results of this study (GOG was not involved in the data collection nor data analyses). There are no other conflicts of interest.

Ethical approval All authors comply with WJS’s ethical policies.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

References

1. Welsch T, Borm M, Degrate L et al (2010) Evaluation of the International Study Group of Pancreatic Surgery definition of delayed gastric emptying after pancreaticoduodenectomy in a high-volume centre. BJS 97:1043–1050
2. Varghese C, Bhat S, Wang TH et al (2021) Impact of gastric resection and enteric anastomotic configuration on delayed gastric emptying after pancreaticoduodenectomy: a network meta-analysis of randomized trials. BJS Open 5(3):zrab035
3. Francken MFG, van Roessel S, Swijnenburg RJ et al (2021) Hospital costs of delayed gastric emptying following pancreaticoduodenectomy and the financial headroom for novel prophylactic treatment strategies. HPB 23:1865–1872
4. Wente MN, Bassi C, Dervenis C et al (2007) Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGOPS). Surgery 142:761–768
5. Malleo G, Crippa S, Butturini G et al (2010) Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy: validation of International Study Group of Pancreatic Surgery classification and analysis of risk factors. HPB 12:610–618
6. Park JS, Hwang HK, Kim JK et al (2009) Clinical validation and risk factors for delayed gastric emptying based on the International Study Group of Pancreatic Surgery (ISGOPS) Classification. Surgery 146:882–887
7. Courvoisier T, Donatini G, Faure JP et al (2015) Primary versus secondary delayed gastric emptying (DGE) grades B and C of the International Study Group of Pancreatic Surgery after pancreaticoduodenectomy: a retrospective analysis on a group of 132 patients. Updates Surg 67:305–309
8. Page MJ, McKenzie JE, Bossuyt PM et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372:n71
9. Sterne JAC, Savovic J, Page MJ et al (2019) RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 366:14898
10. Wells GA, Shea B, O’Connell D et al (2014) T Newcastle-Ottawa quality assessment scale cohort studies. University of Ottawa
11. Slim K, Nini E, Forestier D et al (2003) Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. ANZ J Surg 73:712–716
12. Watanabe Y, Tsumura H, Sakurai H et al (1992) Gastric emptying after pancreateoduodenectomy with total stomach preservation and selective proximal vagotomy. Surg Today 22:426–431
13. Fink AS, DeSouza LR, Mayer EA et al (1988) Long-term evaluation of pylorus preservation during pancreatectoduodenectomy. World J Surg 12:663–670. https://doi.org/10.1007/BF01655880
14. Kollmar O, Moussavarian MR, Richter S et al (2008) Prophylactic octreotide and delayed gastric emptying after pancreatectoduodenectomy: results of a prospective randomized double-blind placebo-controlled trial. Eur J Surg Oncol 34:868–875
15. Samadder A, Kaman L, Dahiya D et al (2017) Objective assessment of delayed gastric emptying using gastric scintigraphy in post pancreatectoduodenectomy patients. ANZ J Surg 87:E80–E84
16. Tamandl D, Sahora K, Prucker J et al (2014) Impact of the reconstruction method on delayed gastric emptying after pylorus-preserving pancreatectoduodenectomy: a prospective randomized study. World J Surg 38:465–475. https://doi.org/10.1007/s00268-013-2274-4
17. Abdel-Wahab M, Sultan A, ElGwaly N et al (2001) Modified pyloric stapling after pylorus-preserving pancreaticoduodenectomy: experience with 81 cases, Wahab modification. Hepatogastroenterology 48:1572–1576
18. Krishna A, Bansal VK, Kumar S et al (2015) Preventing delayed gastric emptying after Whipple’s procedure—isolated Roux loop reconstruction with pancreaticogastrostomy. Indian J Surg 77:703–707
19. Noriiri M, Yokoyama Y, Maeda T et al (2018) Impact of the gastrojejunal anatomic position as the mechanism of delayed gastric emptying after pancreaticoduodenectomy. Surgery 163:1063–1070
20. Kawai M, Tani M, Hirono S et al (2014) Pylorus-preserving pancreatectoduodenectomy offers long-term outcomes similar to those of pylorus-preserving pancreatectoduodenectomy: results of a prospective study. World J Surg 38:1476–1483. https://doi.org/10.1007/s00268-013-2420-z
21. Braasch JW, Deziel DJ, Rossi RL (1986) Pyloric and gastric preserving pancreatic resection. Experience with 87 patients. Ann Surg 204:411–418
22. Patti MG, Pellegrini CA, Way LW (1987) Gastric emptying and small bowel transit of solid food after pylorus-preserving pancreatectoduodenectomy. Arch Surg 122:528–532
23. Hunt DR, McLean R (1989) Pylorus-preserving pancreatectomy: functional results. BJG 76:173–176
24. Lerut J, Luder PJ, Krahenbuhl L et al (1991) Pylorus-preserving pancreatoduodenectomy. Experience in 20 patients. HPB Surg 4:109–119
25. De Bernardinis G, Agnìlità A, Gola P et al (1993) An original reconstructive method after pylorus-preserving pancreatoduodenectomy. Surg Today 23:481–485
26. Kingsnorth AN, Gray MR, Berg JD (1993) A novel reconstructive technique for pylorus-preserving pancreatoduodenectomy: avoidance of early postoperative gastric stasis. Ann R Coll Surg Engl 75:38–42
27. Williamson RCN, Blouin R, Cooper MJ et al (1993) Gastric emptying and entero gastric reflex after conservative and conventional pancreatoduodenectomy. Surgery 114:82–86
28. Yeo CJ, Barry MK, Senter PK et al (1993) Erthyromycin accelerates gastric emptying after pancreatoduodenectomy. A prospective, randomized, placebo-controlled trial. Ann Surg 218:229–237
29. Yung BC, Sostre S, Yeo CJ et al (1993) Comparison of left anterior oblique, anterior, and geometric mean methods in gastric emptying assessment of postpancreactoduodenectomy patients. Clin Nucl Med 18:776–781
30. Pasturino G, Ermilli F, Zappatore F et al (1995) Multiparametric evaluation of functional outcome after pylorus-preserving duodenopancreatectomy. Hepatogastroenterology 42:62–67
31. Bruno MJ, Borm JJJ, Hoek FJ et al (1997) Comparative effects of enteric-coated pancreatic microsphere therapy after conventional and pylorus-preserving pancreatoduodenectomy. BJSG 84:952–956
32. Lupo LG, Pannarale OC, Alomar DF et al (1998) Is pyloric function preserved in pylorus-preserving pancreatoduodenectomy? Eur J Surg 164:127–132
33. Hishinuma S, Ogata Y, Matsui J et al (1999) Evaluation of pylorus-preserving pancreatoduodenectomy with the Imanaga reconstruction by hepatobiliary and gastrointestinal dual scintigraphy. BJSG 86:1306–1311
34. Sumida K, Nimura Y, Yasui A et al (1999) Influence of vagal pyloric branches on gastric acid secretion and gastrointestinal motility in patients following a pylorus-preserving pancreato duodenectomy. Hepatogastroenterology 46:336–342
35. Thor P, Matyja A, Popiela T et al (1999) Early effects of standard and pylorus-preserving pancreatoduodenectomy on myoelectric activity and gastric emptying. Hepatogastroenterology 46:1963–1967
36. Sato T, Konishi K, Yabushita K et al (2000) A new examination for both biliary and gastrointestinal function after pancreateobiliary surgery—single-isotope two-day method. Hepatogastroenterology 47:140–142
37. Sato T, Konishi K, Yabushita K et al (2000) Long-term postoperative functional evaluation of pylorus preservation in Imagnas pancreateoduodenectomy. Dig Dis Sci 45:1907–1912
38. Caronna R, Cardi M, Sammartino P et al (2003) Functional results of a personal technique of reconstruction after pancreati coduodenectomy. J Exp Clin Cancer Res 22:187–189
39. Kim DK, Hindenburg AA, Sharma SK et al (2005) Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreatoduodenectomy? Ann Surg Oncol 12:222–227
40. Shah N, Sy ED, Tsai ML et al (2005) Effects of somatostatin prophylaxis after pylorus-preserving pancreatoduodenectomy: increased delayed gastric emptying and reduced plasma motilin. World J Surg 29:1319–1324. https://doi.org/10.1007/s00268-005-7943-5
41. Shah N, Tsai ML, Chiu NT et al (2005) Reconsideration of delayed gastric emptying in pancreatoduodenectomy. World J Surg 29:873–879. https://doi.org/10.1007/s00268-005-7473-1
42. Ohmura J, Chijiwa K, Ohuchida J et al (2007) Pylorus-preserving pancreatoduodenectomy: preoperative pancreatic function and outcome. Hepatogastroenterology 54:913–916
43. Harmuth S, Wewalka M, Holst JJ et al (2014) Distal gastrectomy in pancreaticoduodenectomy is associated with accelerated gastric emptying, enhanced postprandial release of GLP-1, and improved insulin sensitivity. J Gastrointest Surg 18;52–59
44. Traverso LW, Longmire WP Jr (1980) Preservation of the pylorus in pancreaticoduodenectomy a follow-up evaluation. Ann Surg 292:306–310
45. Sharma SK, Ohuchida J et al (2009) Prospective randomized controlled study of gastric emptying assessed by (13)C-acetate breath test after pylorus-preserving pancreateoduodenectomy: comparison between antecolic and vertical retrocolic duodenopenjunosutomy. J Hepatobiliary Pancreat Surg 16:49–55
46. Hiyoshi M, Chijiwa K, Ohuchida J et al (2012) Comparative study of gastric emptying and nutritional status after pylorus-preserving vs. subtotal stomach-preserving pancreaticoduodenectomy. Hepatogastroenterology 59:1018–1022
47. Ueno T, Tanaka A, Hamamuka Y et al (1995) A proposal for early delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. Hepatogastroenterology 42:269–274
48. Muller MW, Friess H, Beger HG et al (1997) Gastric emptying following pylorus-preserving Whipple and duodenopancreaticoduodenectomy after pylorus-preserving pancreatoduodenectomy. BJG 85:927–930
49. Takeda T, Yoshida J, Tanaka M et al (1999) Delayed gastric emptying after Billroth I pylorus-preserving pancreatoduodenectomy: effect of postoperative time and cisapride. Ann Surg 229:223–229
50. Ohtsuka T, Takahata S, Ohuchida J et al (2002) Gastric phase 3 motility after pylorus-preserving pancreateoduodenectomy. Ann Surg 235:417–423
51. Strommer L, Raty S, Hennig R et al (2005) Delayed gastric emptying and intestinal hormones following pancreateoduodenectomy. Pancreatology 5:537–544
52. Ohuchida J, Chijiwa K, Ohtsuka T et al (2007) Pylorus-preserving pancreatoduodenectomy: preoperative pancreatic function and outcome. Hepatogastroenterology 54:913–916
53. Kobayashi I, Miyachi M, Kanai M et al (1998) Different gastric emptying of solid and liquid meals after pylorus-preserving pancreatoduodenectomy. BJG 85:927–930
54. Shabbazov R, Naziruddin B, Yadav K et al (2018) Risk factors for early readmission after total pancreatectomy and islet auto transplantation. HPB 20:166–174
55. Ueno T, Tanaka A, Hamanaka Y et al (1995) A proposal for early delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. BJS 84:952–956
56. Ueno T, Tanaka A, Hamanaka Y et al (1995) A proposal for early delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. BJS 84:952–956
57. Hiyoshi M, Chijiwa K, Ohuchida J et al (2012) Comparative study of gastric emptying and nutritional status after pylorus-preserving vs. subtotal stomach-preserving pancreaticoduodenectomy. Hepatogastroenterology 59:1018–1022
58. Abell TL, Camilleri M, Donohoe K et al (2008) Consensus recommendations for gastric emptying scintigraphy: a joint report of the American neurogastroenterology and motility society and the society of nuclear medicine. J Nucl Med Technol 36:44–54
59. Heading R, Nimmo J, Prescott L et al (1973) The dependence of paracetamol absorption on the rate of gastric emptying. Br J Pharmacol 47:415
60. Willems M, Quartero AO, Numans ME (2001) How useful is paracetamol absorption as a marker of gastric emptying? A systematic literature study. Dig Dis Sci 46:2256–2262
61. Braden B, Adams S, Duan L-P et al (1995) The [13C] acetate breath test accurately reflects gastric emptying of liquids in both liquid and semisolid test meals. Gastroenterology 108:1048–1055
62. Nakamura H, Morifuji M, Murakami Y et al (2009) Usefulness of a 13C-labeled mixed triglyceride breath test for assessing pancreatic exocrine function after pancreatic surgery. Surgery 145:168–175
63. Werba G, Sparks AD, Lin PP et al (2022) The PREDICT-DGE score as a simple preoperative screening tool identifies patients at increased risk for delayed gastric emptying after pancreaticoduodenectomy. HPB 24:30–39
64. Reber HA (2007) Delayed gastric emptying—what should be required for diagnosis? Surgery 142:769–770
65. Griffith G, Owen G, Kirkman S et al (1966) Measurement of rate of gastric emptying using chromium-51. Lancet 1:1244–1245
66. Fried M (1994) Methods to study gastric emptying. Dig Dis Sci 39:114S–115S
67. Nguyen NQ, Bryant LK, Burgstad CM et al (2013) Gastric emptying measurement of liquid nutrients using the (13)C-octanoate breath test in critically ill patients: a comparison with scintigraphy. Intensive Care Med 39:1238–1246
68. Carson DA, O’Grady G, Du P et al (2021) Body surface mapping of the stomach: new directions for clinically evaluating gastric electrical activity. Neurogastroenterol Motil 33:e14048
69. Farrugia G (2008) Interstitial cells of Cajal in health and disease. Neurogastroenterol Motil 20:54–63
70. Cheng LK (2015) Slow wave conduction patterns in the stomach: from Waller’s foundations to current challenges. Acta Physiol 213:384–393
71. Angeli TR, Cheng LK, Du P et al (2015) Loss of interstitial cells of Cajal and patterns of gastric dysrhythmia in patients with chronic unexplained nausea and vomiting. Gastroenterology 149(56–66):e55
72. Wang TH, Angeli TR, Beban G et al (2019) Slow-wave coupling across a gastroduodenal anastomosis as a mechanism for postsurgical gastric dysfunction: evidence for a “gastrointestinal aberrant pathway.” Am J Physiol Gastrointest Liver Physiol 317:G141–G146
73. O’Grady G, Wang TH, Du P et al (2014) Recent progress in gastric arrhythmia: pathophysiology, clinical significance and future horizons. Clin Exp Pharmacol Physiol 41:854–862
74. Gharibans AA, Calder S, Varghese C et al (2022) Gastric dysfunction in patients with chronic nausea and vomiting syndromes defined by a novel non-invasive gastric mapping device. medRxiv
75. Dua MM, Navalgund A, Axelrod S et al (2018) Monitoring gastric myoelectric activity after pancreaticoduodenectomy for diet “readiness.” Am J Physiol Gastrointest Liver Physiol 315:G743–G751

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.