Systematic review

Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery

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Background: Anastomotic leak after gastrointestinal surgery is an important postoperative event that leads to significant morbidity and mortality. Postoperative leak rates are frequently used as an indicator of the quality of surgical care provided. Comparison of rates between and within institutions depends on the use of standard definitions and methods of measurement of anastomotic leak. The aim of this study was to review the definition and measurement of anastomotic leak after oesophagogastric, hepatopancreaticobiliary and lower gastrointestinal surgery.

Methods: A systematic review was undertaken of the published literature. Searches were carried out on five bibliographical databases (Medline, Embase, The Cochrane Library, Cumulative Index for Nursing and Allied Health Literature and HealthSTAR) for English language articles published between 1993 and 1999. Articles were critically appraised by two independent reviewers and data on definition and measurement of anastomotic leak were extracted.

Results: Ninety-seven studies were reviewed and a total of 56 separate definitions of anastomotic leak were identified at three sites: upper gastrointestinal (13 definitions), hepatopancreaticobiliary (14) and lower gastrointestinal (29). The majority of studies used a combination of clinical features and radiological investigations to define and detect anastomotic leak.

Conclusion: There is no universally accepted definition of anastomotic leak at any site. The definitions and values used to measure anastomotic failure vary extensively and preclude accurate comparison of rates between studies and institutions.

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Introduction

Leakage from an anastomosis in the gastrointestinal tract is a major complication that is often associated with increased morbidity, mortality and prolonged hospital stay. The frequency and consequences of anastomotic failure vary according to the site within the gastrointestinal tract. Anastomotic breakdown is the most important early complication after oesophageal anastomosis; incidences of up to 53 per cent have been reported[1]. It is also a serious complication after pancreatic surgery because dehiscence of anastomoses with autodigestion and destruction of surrounding tissue from leaking pancreatic juice is associated with a high mortality rate[2]. Dehiscence after colorectal anastomosis increases the perioperative mortality rate due to peritonitis and septicaemia, and adversely affects the late outcome in survivors because of increased local recurrence of carcinoma[3]. Anastomotic leak may be used as an indicator of the quality of surgical care, and comparisons of leak rates may be made between and within surgical centres[4]. However, the accuracy of such comparisons depends on the use of standard definitions and methods of measurement.

The aim of this study was to assess, systematically, the quality of definition, measurement, reporting and monitoring of anastomotic leak in the contemporary surgical literature. The study was undertaken within a wider systematic review of surgical adverse events.

Methods

Search strategy

A systematic search for English language literature published between 1993 and 1999 was undertaken on five biomedical bibliographical databases: Medline, Embase, Cumulative Index for Nursing and Allied Health Literature, The Cochrane Library and HealthSTAR. Initial searches focused on the validity and reliability of

the definition and measurement of anastomotic leak. Owing to the lack of relevant literature, the search was subsequently expanded to include all prospective studies where anastomotic leak was included in the abstract, title or medical subject heading (MeSH). The final strategy consisted of textwords and MeSH terms on anastomosis (anastomosis, surgical; anastomotic leak, leakage, dehiscence, breakdown) combined with study design terms (prospective, longitudinal, follow-up, cohort studies).

Studies eligible for inclusion were those that contained a definition of anastomotic leak and/or details of clinical and radiological assessment. Articles were excluded for the following reasons: (1) retrospective study design; (2) failure to include a definition of anastomotic leak, a description of clinical features or methods used to detect leak; (3) non-gastrointestinal anastomoses; and (4) meta-analyses or review articles without inclusion of definitions, clinical features or investigations from primary studies. Reference lists from each study, review article and meta-analysis were searched for further relevant literature.

Critical appraisal and data extraction

The remit of the study was a systematic and comprehensive review of the definition, measurement and monitoring of anastomotic leak. Explicit criteria for evaluation and critical appraisal were determined at an early stage in the review and articles were appraised by two independent reviewers. The following data were extracted: study details; surgical procedure or intervention; definition of anastomotic leak; clinical factors considered in assessment; details of investigations undertaken; details on validity, accuracy, sensitivity, specificity, inter- and intra-rater reliability, practicality and acceptability of the definition, measure or diagnostic test.

Validity is an assessment of the extent to which something measures what it purports to measure. Definitions were assessed for face validity, or clinical sense, by noting what properties of leak were included. Reliability is an assessment of the extent to which the definition and measurement of anastomotic leak are repeatable and reproducible. If a definition has poor repeatability, this will lead to poor agreement between observers or different methods of measurement. Information was extracted on whether a definition or measurement was repeated on more than one occasion and/or by more than one observer, and estimates of repeatability (intra-rater reliability) and reproducibility (inter-rater reliability) were sought (e.g. κ values). Finally, definitions and methods of measurement must be acceptable, comprehensible and suitable for use in the clinical setting, and so comments on the practicality of definitions or methods were recorded.

Table 1 Anastomotic terminology

General anastomotic terms	Grading terms
Leak	Partial leak
Breakdown	Occult leak
Leakage	Complete leak
Insufficiency	Overt leak
Dehiscence	Minor, moderate, major leak
Competence	Covert leak
Suture insufficiency	Trivial clinical leak
Integrity	Gross leakage
Suture line disruption	Serious clinical leak
Security	Clinically silent leak
Frank clinical leak	Free leak
Patency	Subclinical leak
Controlled leak	Contained leak
Early leak	Asymptomatic leak
Radiological leak	Generalized leakage
Delayed or late leak	Symptomatic leak
Confirmed leak	Localized leakage
	Biochemical leak
	Clinical leak

Results

A total of 1908 abstracts were read and 240 articles were obtained for full critical appraisal. A large proportion of abstracts related to non-gastrointestinal anastomoses as a result of the sensitive rather than specific search strategy. Ninety-seven studies were included and the results are presented below according to broad location of surgery: upper gastrointestinal, hepatopancreaticobiliary (HPB) and lower gastrointestinal. *Table 1* illustrates the variation in terminology.

One 'standard' definition of anastomotic leak was proposed by the UK Surgical Infection Study Group (SISG) for use in clinical audit and to form the basis for meaningful comparisons[5]. Leak was defined as 'the leak of luminal contents from a surgical join between two hollow viscera. The luminal contents may emerge either through the wound or at the drain site, or they may collect near the anastomosis, causing fever, abscess, septicaemia, metabolic disturbance and/or multiple-organ failure. The escape of luminal contents from the site of the anastomosis into an adjacent localized area, detected by imaging, in the absence of clinical symptoms and signs should be recorded as a subclinical leak'. Although this definition was proposed in 1991, it has not been widely adopted; neither has it been used or referred to in any individual appraised study.

Upper gastrointestinal surgery

Thirty-three studies of oesophagogastric surgery were identified, only 13 of which included a definition of anastomotic leak or described the clinical features used to

Table 2 Overview of definition and assessment of upper gastrointestinal anastomotic leaks

Reference	Operation	Study design	Sample size	No. of leaks	Definition	Test	Timing of test*
Anikin *et al.*[6]	OG	Cohort	113	6 (5)	No	WS contrast	6
Choi *et al.*[7]	OG	RCT	40	0 (0)	Yes	WS contrast and endoscopy	7
Craig *et al.*[8]	OG	RCT	100	7 (7)	No	Barium contrast	5
Curry *et al.*[9]	RGB	Cohort	38	0 (0)	No	None routinely	—
Deshmane and Shinde[10]	OG	Cohort	75	5 (7)	Yes	Barium contrast	10
Fernandez-Fernandez *et al.*[11]	TG	Cohort	101	5 (5)	Yes	Unspecified contrast	7
Fernandez-Fernandez *et al.*[12]	TG	RCT	86	4 (5)	Yes	Unspecified contrast	7
Goel *et al.*[13]	OG	RCT	25	3 (12)	Yes	WS contrast	5
Gupta[14]	OG	Cohort	250	38 (15)	No	Unspecified contrast	5
Gupta *et al.*[15]	OG	Cohort	29	7 (24)	No	Unspecified contrast	NS
Hansson *et al.*[16]	OG	Cohort	53	14 (26)	No	WS contrast	7
Honkoop *et al.*[17]	OG	Cohort	269	60 (22)	No	WS contrast	7–10
Isozaki and Okajima[18]	G	Cohort	1114	52 (5)	Yes	WS contrast	7–14
Jacobi *et al.*[19]	OG	Cohort	33	6 (18)	No	WS contrast	7
Kuwano *et al.*[20]	OG	Cohort	69	5 (7)	Yes	WS contrast and Urografin infusion	14
Law *et al.*[21]	OG	RCT	122	4 (3)	No	WS contrast and endoscopy	7
Machens *et al.*[22]	OG	Cohort	12	6 (50)	Yes	WS contrast, drain amylase	7
Nambirajan *et al.*[23]	OA	Cohort	37	4 (11)	Yes	WS contrast	5–7
Obertop *et al.*[24]	OG	Cohort	10	7 (70)	Yes	Unspecified contrast and CT when suspected	—
O'Rourke *et al.*[25]	OG	Cohort	116	2 (2)	No	WS contrast	7–10
Pol *et al.*[26]	TG	Cohort	176	5 (3)	No	WS contrast	Week 2
Schardey *et al.*[27]	TG	RCT	205	14 (7)	Yes	WS contrast or indigo carmine blue test	7
Schilling *et al.*[28]	OG	Cohort	35	2 (6)	No	WS contrast	NS
Svanes *et al.*[29]	OG	Cohort	83	5 (6)	No	WS contrast	8–10
Swails *et al.*[30]	OG	RCT	25	3 (12)	No	WS contrast	4–5
Thiede *et al.*[31]†	OG	RCT	1042	6 (1)	Yes	WS contrast	8
Thomas *et al.*[32]	CI	Cohort	60	10 (17)	No	WS contrast	8–12
Trentino *et al.*[33]	OG	Cohort	39	4 (10)	No	WS contrast	8–9
van Lanschot *et al.*[34]	OG	RCT	60	14 (23)	No	WS contrast	7
Vigneswaran *et al.*[35]	OG	Cohort	131	32 (24)	No	WS contrast	7
Wu *et al.*[36]	G	Cohort	474	24 (5)	No	WS contrast	NS
Zieren *et al.*[37]	OG	RCT	107	20 (19)	Yes	WS contrast	7
Zilling *et al.*[38]	TG	Cohort	174	20 (11)	No	WS contrast	4–7

Definition or description of clinical assessment given in text. Values in parentheses are percentages. *Day or week after operation. †Upper and lower gastrointestinal procedures performed, but results for upper only presented here. WS, water-soluble; NS, not specified; OG, oesophagectomy or oesophagogastrectomy; G, gastrectomy; TG, total gastrectomy; OVA, oesophagovisceral anastomosis; RGB, resectional gastric bypass; OA, repair of oesophageal atresia; CI, colon interposition; RCT, randomized clinical trial; CT, computed tomography

judge anastomotic failure (*Table 2*). The clinical features used to assess upper gastrointestinal leak included: evidence of haematoma or seroma formation at the neck wound[7]; septicaemia[24]; peritonitis[18]; perianastomotic collection[10]; leak at the neck site[13]; local inflammation at anastomotic site or if air or saliva was found in the cervical drain bag[22]; and saliva in the chest drain, mediastinitis or abscess, pneumothorax, empyema[23].

Six studies relied on radiological extravasation of contrast medium[11,12,18,23,27,37]. The majority of studies reported routine postoperative use of radiographic water-soluble contrast swallows. Two groups of authors reported routine use of barium solution[8,10] and one group reported routine postoperative endoscopy with contrast studies[7]. The timing of administration of routine radiological tests ranged from 3 to 14 days after operation. Three studies conducted radiological investigation only when a leak was suspected clinically[9,24,39].

Five sets of authors proposed systems for classifying upper gastrointestinal leaks (*Table 2*). In general, an attempt was made to separate minor (detected radiologically) leaks from more major (clinically apparent) leaks[10,18,23]. Similarly, Csendes *et al.*[40] classified the radiological appearance of leakage as type I (localized) or type II (a great dissemination or diffusion to the pleural or abdominal cavities). These two types roughly correspond with the clinical and subclinical groups proposed by other authors. A meta-analysis by Bardini *et al.*[1] adds additional refinements to the above systems by defining four types of leak (*Table 3*). While the addition of a group including 'total disruption of the anastomosis resulting from an inadequate blood supply' is useful from the point of subsequent management, it

Table 3 Upper gastrointestinal classification systems

Reference	Grading	Description
Bardini *et al.*[1]	Radiological or minor	Asymptomatic and diagnosed only at radiographic check
	Clinical or moderate	Presence of fever, leucocytosis and local signs of inflammation
	Serious	Usually an early leak with severe disruption of the anastomosis
	Necrosis	Total disruption of the anastomosis resulting from an inadequate blood supply to the viscus sutured to the oesophagus and ischaemia of the area bordering the anastomosis
Csendes *et al.*[40]	Type 1 subclinical	A local fistula involving the anastomosis, with no spillage or dissemination through a fistulous tract to the pleural or abdominal cavity, or the appearance of contrast material in any abdominal drain
	Type II clinical	A leakage with great dissemination or diffusion to the pleural or abdominal cavity with the appearance of contrast medium in any of the abdominal drains
Deshmane and Shinde[10]	Small leak, asymptomatic	Detected only at radiological study
	Large leak, clinical	Perianastomotic collection manifested clinically
Isozaki and Okajima[18]	Minor	Leakage of contrast medium recognized radiologically as a fringe-like image from the anastomotic site or limited to a small area around the anastomotic site, but no leakage recognized from drain
	Major	Visualization of extensive intra-abdominal contrast medium radiologically and leakage of contrast medium from the drain, or cases where symptoms of peritonitis required the insertion of a new drain
Nambirajan *et al.*[23]	Incidental	Small radiological leak, no clinical symptoms
	Minor	Saliva in chest drain, but clinically well
	Major	Mediastinitis or abscess, pneumothorax, empyema, radiologically confirmed major oesophageal disruption

Table 4 Definition and assessment of hepatopancreaticobiliary anastomotic leaks

Reference	Operation	Study design	Sample size	No. of leaks	Definition*	Test
Bottger *et al.*[41]	P	Cohort	221	28 (13)	Yes	Amylase and drain fluid levels; relaparotomy
Chou *et al.*[42]	P	RCT	93	9 (10)	Yes	Amylase and drain fluid levels
Davidson *et al.*[43]	OLT	RCT	100	17 (17)	Yes	Routine retrograde cholangiography on day 10–14 after operation
Evans *et al.*[44]	P	Cohort	63	7 (11)	Yes	Amylase and drain fluid levels
Gupta *et al.*[45]	BDI	Cohort	13	3 (23)	Yes	Biliary nucleotide scintigraphy and transhepatic cholangiography (timing not stated)
Hamanaka and Suzuki[46]	P	Cohort	48	2 (4)	Yes	Routine Gastrografin swallow (day 7); amylase and drain fluid levels
Hardy *et al.*[47]	OLT	Cohort	129	7 (5)	Yes	Cholangiography or percutaneous transhepatic cholangiography (day 7)
Howard[48]	P	Cohort	56	0 (0)	Yes	Amylase and drain fluid levels
Kapoor *et al.*[49]	CJ	Cohort	41	6 (15)	No	Isotope hepatobiliary scanning (timing not stated)
Kayahara *et al.*[2]	P	Cohort	150	43 (29)	Yes	Drain fluid amylase content and radiological confirmation of pancreatic ductography (timing not stated)
Lowy *et al.*[50]	P	RCT	110	27 (25)	Yes	Amylase and drain fluid levels
Matsusue *et al.*[51]	P	Cohort	100	9 (9)	Yes	Amylase and drain fluid levels
Nagakawa *et al.*[52]	P	Cohort	64	10 (16)	Yes	Urinary and serum amylase levels
Reissman *et al.*[53]	P	Cohort	35	5 (14)	Yes	Amylase and drain fluid levels
Roder *et al.*[54]	P	Cohort	85	15 (18)	Yes	Radiologically documented leaks; amylase and drain fluid levels

Values in parentheses are percentages. *Definition or a description of investigation performed to detect leak. BDI, bile duct injury; CJ, cholangiojejunostomy; OLT, orthotopic liver transplantation; P, pancreatic surgery; RCT, randomized clinical trial

requires the use of endoscopy to verify an area of necrosis. Clearly, the more severe leaks have the least favourable outcome.

Hepatopancreaticobiliary surgery

Fifteen studies related to HPB surgery were eligible for inclusion: pancreatic surgery (11 studies), orthotopic liver transplant (two), cholangiojejunostomy (one) and bile duct injury (one). Fourteen of the 15 studies included a clear definition of HPB leak or described the investigations undertaken to detect leak (*Table 4*). The clinical signs extracted from individual studies included: peritonitis, pyrexia, sepsis[46]; bile drainage from drains placed at anastomosis area[45]; fever, raised leucocyte count, sepsis[54]. Kayahara *et al.*[2] accepted 'drainage of bile or enteric fluid

Table 5 Pancreatic surgery leak values

Reference	Description	Drain fluid volume	Amylase value	Timing
Bottger *et al.*[41]	Pancreatic fistula	—	Drain fluid amylase level > 2000 units/l	Daily
Chou *et al.*[42]	Pancreatic leak or fistula	Persistent drainage > 50 ml/day	Amylase-rich drain fluid	Daily for > 2 weeks
Evans *et al.*[44]	Pancreatic fistula	> 50 ml/day	Abdominal fluid level > 1000 units/l	Daily
Hamanaka and Suzuki[46]		Volume measured daily	—	Daily
Howard[48]	Pancreatic fistula	Peritoneal drain and pancreatic tube fluid assessed	Serum amylase level > 3 times normal; amylase levels in drain and tube fluid	2-day intervals for 8–12 days
Kayahara *et al.*[2]	Dehiscence	Drain removed when < 50 ml/day	Amylase in drain fluid > 3 times serum amylase level	Daily
Lowy *et al.*[50]	Clinical leak	Drain removed day 3 if < 200 ml/day and amylase level normal	> 2·5 times upper limit of normal in serum	Daily
	Biochemical leak	Drain fluid on or after day 3 that was asymptomatic and resolved spontaneously	> 2·5 times upper limit of normal for serum	Daily
Matsusue *et al.*[51]	Peripancreatic sepsis	Prolonged suppurative discharge < 50 ml/day	Low amylase drain fluid level < 1000 units for > 1 week	Daily
	Pancreatic fistula	Prolonged suppurative discharge > 50 ml/day	High amylase drain fluid level of > 1000 units for > 1 week	Daily
Nagakawa *et al.*[52]	Pancreatic leak	—	High urinary or serum amylase level for 3 days or more	Daily
Reissman *et al.*[53]	Pancreatic leak	Peripancreatic drain fluid for > 7 days	Amylase-rich fluid ⩾ 40 ml/day (> 10 times normal plasma level)	Daily
Roder *et al.*[54]	Pancreatic fistula	Fluid collection of > 50 ml during entire postoperative course	Drain fluid amylase content > 3 times serum amylase level	

from the drain, the detection of enteric bacteria in the drainage fluid, radiographic confirmation of dehiscence of pancreatic ductography, or an amylase level in the drainage fluid of > 3 times the serum amylase level'. Each of the studies involving pancreatic surgery defined a leak by the volume of drain output and/or drain fluid enzyme concentrations (*Table 5*). There was considerable variation in fluid volume, values and the timing of test administration between individual studies.

Two HPB classification systems were identified[50,51]. Matsusue *et al.*[51] distinguished between peripancreatic sepsis and a pancreatic fistula, based on amylase content and level of drainage fluid in patients undergoing pancreaticojejunostomy. In a randomized controlled trial of octreotide after pancreaticoduodenectomy, Lowy *et al.*[50] gave clear criteria for clinical and biochemical pancreatic leaks. A clinical pancreatic anastomotic leak was defined as the drainage of amylase-rich fluid (more than 2·5 times the upper limit of normal for serum amylase) in association with fever (above 38°C), leucocytosis (white blood cell count greater than 10 000 per litre), sepsis (haemodynamic instability requiring transfer to the intensive care unit) or the need for percutaneous drainage of an amylase-rich fluid collection. A biochemical pancreatic leak was defined as a raised level of amylase (more than 2·5 times the upper limit of normal for serum amylase) in the drain fluid on or after postoperative day 3 that was asymptomatic and resolved spontaneously. This was the only study with distinct parameters for sepsis, leucocytosis and fever.

One review was identified that examined the efficacy of octreotide, a potent inhibitor of exocrine pancreatic secretion, in reducing postoperative complications[55]. The authors distinguished between pancreatic leakage and pancreatic fistula, where leakage was defined as 'leakage from pancreatic, biliary, or intestinal anastomosis as determined by radiographic or intraoperative findings/relaparotomy'. A pancreatic fistula was diagnosed 'if (1) the concentrations of amylase and lipase in the drainage fluid were > 3 times higher than in the serum of *n* [not specified by authors] consecutive postoperative days and (2) a drainage volume of > 10 ml/24 h was present. The serum and drainage fluid amylase and/or lipase concentration were determined on postoperative days 1, 3, 4, 5 and 7 and twice weekly thereafter'. However, only two of the original seven controlled trials had used these standard definitions.

Lower gastrointestinal surgery

A total of 49 lower gastrointestinal studies were eligible for inclusion, 29 of which included a definition (*Table 6*). The clinical signs and symptoms most frequently described included: signs of localized or generalized peritonitis (12 studies); faecal discharge from the wound and/or drain (11);

Table 6 Definition and assessment of lower gastrointestinal anastomotic leaks

Reference	Operation	Study design	Sample size	No. of leaks	Definition	Test	Timing
Ambrosetti *et al.*[56]	CR	Cohort	199	5 (3)	No	WS contrast	Routine on day 9–11
Biondo *et al.*[57]	CR	Cohort	63	3 (5)	No	Unspecified contrast	When suspected
Bokey *et al.*[58]	C/CR	Cohort	1846	79 (4)	Yes	WS contrast, abdominal reoperation	When suspected
Bouillot *et al.*[59]	C	Cohort	50	1 (2)	No	Unspecified radiography	Unclear
Burke *et al.*[60]	CR	RCT	186	7 (4)	Yes	WS contrast	Routinely on day 7 in first half of study, then changed to when leak suspected
Cornwell *et al.*[61]	C	Cohort	56	3 (5)	Yes	Surgical re-exploration, CT or WS contrast	Variable
De Wever *et al.*[62]	CR	Cohort	16	5 (31)	No	Endoscopy and unspecified radiological test	3–4 months
Debus *et al.*[63]	CR	Cohort	77	6 (8)	No	Barium contrast	When suspected
Deen and Smart[64]	C	Cohort	53	2 (4)	Yes	Unspecified radiography	When suspected
Dehni *et al.*[65]	CR	Cohort	258	31 (12)	Yes	WS contrast, imaging or reoperation	Routine contrast study 8–10 weeks before stoma
Docherty *et al.*[66]	CR	RCT	652	38 (6)	Yes	WS contrast, reoperation	Routine on day 4–14
Fingerhut *et al.*[67]	CR	RCT	159	10 (6)	Yes	WS contrast, sinography	Routine contrast study on day 7
Fingerhut *et al.*[68]	CR	RCT	113	17 (15)	Yes	WS contrast, sinography, reoperation	Routine contrast study on day 7
Hallbook *et al.*[69]	CR	RCT	97	9 (9)	Yes	Digital and endoscopic examination, contrast, reoperation, CT	Routine contrast study before stoma closure
Hansen *et al.*[70]	CR	Cohort	615	9 (1)	Yes	Unspecified radiography	When suspected
Hida *et al.*[71]	CR	RCT	43	2 (5)	No	WS contrast	Routinely at 2 months
Iversen *et al.*[72]	CR	Cohort	161	17 (11)	No	WS contrast	When suspected
Junger *et al.*[73]					Yes	LPS concentration	LPS level assessed daily
Karanjia *et al.*[74]	CR	Cohort	219	38 (17)	Yes	WS contrast	When suspected
Kessler *et al.*[75]	CR	MRCT	621	88 (14)	Yes	Unspecified radiological tests, methylene blue test	When suspected
Kockerling *et al.*[76]	CR	MRCT	949	46 (5)	No	Unspecified	Unspecified
Kracht *et al.*[77]	C	MRCT	440	31 (7)	Yes	WS contrast, reoperation	Routine contrast on day 8–10
Mann *et al.*[78]	CR	Cohort	370	11 (3)	Yes	WS contrast	When suspected
Merad *et al.*[79]	CR	RCT	705	53 (8)	Yes	WS contrast, reoperation	Routine contrast on day 8
Merad *et al.*[80]	CR	RCT	494	32 (6)	Yes	WS contrast, reoperation	Routine contrast on day 7
Miller *et al.*[81,82]	CR	Cohort	103	6 (6)	Yes	WS contrast	Routine contrast on day 10
Moore *et al.*[83]	CR	Cohort	300	34 (11)	No	Unspecified radiological examination, reoperation (clinically significant)	Routine before stoma closure
Norris *et al.*[84]	L	Cohort	156	6 (4)	No	Unspecified imaging or reoperation	When suspected
Pakkastie *et al.*[85]	CR	RCT	38	15 (39)	Yes	WS contrast	Routine contrast on day 7–10
Petersen *et al.*[3]	CR	Cohort	467	41 (9)	Yes	WS contrast	When suspected
Redmond *et al.*[86]	CR	Cohort	111	13 (12)	Yes	WS contrast	Routine contrast on day 10–12
Sagar *et al.*[87]	CR	RCT	100	12 (12)	Yes	WS contrast	Routine contrast on day 5–7
Santos *et al.*[88]	CR	RCT	149	11 (7)	Yes	Unspecified radiological examination	When suspected
Slim *et al.*[89]	Lap CR	Cohort	65	6 (9)	Yes	WS contrast, reoperation for peritonitis	When suspected
Stewart *et al.* [90]	CR	RCT	88	1 (1)	Yes	Unspecified	Unspecified
Tagart[91]	CR	Cohort	220	79 (36)	No	Limited barium contrast	Routine contrast on day 14
Thompson *et al.*[4]	CR	Cohort	535	18 (3)	No	None	Unspecified (not done routinely)
Watson *et al.*[92]	C/CR	Cohort	477	9 (2)	No	WS contrast	When suspected
Wheeler and Gilbert[93]	CR	Cohort	102	7 (7)	No	WS contrast	Routine contrast on day 8

Values in parentheses are percentages. C, colonic resection; CR, colorectal surgery; CT, computed tomography; L, laparotomy (for Crohn's disease); Lap, laparoscopic; LPS, lipopolysaccharide; MRCT, multi-randomized clinical trial; RCT, randomized clinical trial; WS, water-soluble

abscess (ten); purulent discharge from drain, wound or anus (seven); and fever (six). Some studies defined a clinical anastomotic leak as that requiring reoperation[83,86], whereas others accepted signs of leakage without further surgery. None of the studies defined peritonitis.

The majority of lower gastrointestinal series used contrast (water-soluble) radiography, either routinely or when a leak was suspected. Assessment of timing of administration was often difficult to interpret as some authors combined leak results from routine investigation with those conducted when leak was suspected. The timing of administration of routine contrast ranged from day 4 to day 14 after operation, although timing was later in patients with an ileoanal pouch (*Table* 7).

Table 7 Definition and assessment of ileoanal pouch leaks

Reference	Operation	Study design	Sample size	No. of leaks	Definition	Test	Timing
Breen *et al.*[94]	IPAA	Cohort	628	28 (4)	Yes	WS contrast	Routinely before stoma closure
Dayton and Larsen[95]	IPAA	Cohort	510	21 (4)	Yes	—	Unclear
Flohr *et al.*[96]	Ileal neobladder	Cohort	306	1 (0)	No	Multiple investigations performed (ileal neobladder); IVP and voiding cystography at 1 year	Routine IVP and cystography at 1 year
Hrung *et al.*[97]	IPAA	Cohort	37	3 (8)	Yes	WS and/or barium contrast	Routine imaging at 8–12 weeks
Hulten[98]	IPAA	Cohort	307	31 (10)	Yes	Endoscopy and radiological examination	Routine contrast 6–8 weeks before closure of ileostomy or when suspected
Kartheuser *et al.*[99]	IPAA	Cohort	171	2 (1)	No	Unspecified radiological investigation under general anaesthesia	2 months
Kelly *et al.*[100]	IPAA	Cohort	85	10 (12)	Yes	Unspecified contrast	5–6 weeks before stoma closure
Richard *et al.*[101]	Pelvic pouch	Cohort	753	91 (12)	No	WS contrast or CT with contrast	Unspecified
Wexner *et al.*[102]	IAA	Cohort	83	0 (0)	No	Unspecified contrast	Routine contrast before stoma closure, time not specified

Values in parentheses are percentages. CT, computed tomography; IAA, ileoanal anastomosis; IPAA, ileal pouch–anal anastomosis; IVP, intravenous pyelography; WS, water-soluble

Discussion

This review identified a total of 56 definitions of anastomotic leak from 97 studies but failed to identify any formal validity evaluation of the identified definitions and classifications. Although a standard definition for anastomotic leak was proposed by a UK multidisciplinary group (SISG)[5], this definition was not used or referred to by any of the appraised studies, perhaps because it is too general for use in different clinical situations. Other studies have developed definitions and grading systems specific to parts of the gastrointestinal tract and so studies were subdivided in the review by the location of surgery.

In the 33 papers reviewed that involved oesophagogastric surgery, the grading systems for leakage contained components similar to those in the SISG definition: fever, abscess and organ failure. Most authors reported using routine water-soluble contrast investigation in the first postoperative week. Rates of postoperative leaks may be influenced according to timing of administration and standard procedures and/or protocols. The postoperative leak rates for 31 upper gastrointestinal studies (excluding two containing fewer than 12 patients[22,24]) ranged from 0 to 26 per cent. Although Curry *et al.*[9] reported no postoperative leaks, routine postoperative radiography was not performed and asymptomatic leaks could not have been detected.

Following biliary and pancreatic anastomoses, leakage of bile and pancreatic fluid is common but not clinically relevant if there are no untoward clinical symptoms. Such leakage in the first few days after operation ceases spontaneously. Excess and/or prolonged drainage of fluid has been used in HPB studies. However, the values for drainage volume and enzyme concentration required to diagnose clinically significant leakage varied considerably between centres. For example, drain fluid amylase levels ranged from 2·5 to 10 times normal plasma levels. In studies of pancreatic surgery, leak rates ranged from 0 to 29 per cent. Furthermore, the arbitrary levels of drainage volume and amylase content used by some authors will be greatly influenced by the use of octreotide, which effectively eliminates pancreatic exocrine function, and the concentration of enzymes in drain fluid.

There were more clinical trials and larger sample sizes in the studies of lower gastrointestinal surgery. The German Colorectal Carcinoma Study Group reported leak rates in a large cohort based on clinical assessment of leak without radiological confirmation[75]. Results were presented according to individual criteria for faecal fistula, local abscess and peritonitis, with overall anastomotic leak rates. The presentation of individual features of clinical leakage permits intra- and inter-institutional comparison. While the rate of leakage increases with lower anastomoses, and this may make direct examination easier, the level of a colorectal anastomosis does not influence the definition or diagnosis of a leak. Overall, clinical features were used more commonly for diagnosis in the lower gastrointestinal studies than in studies of upper gastrointestinal and HPB surgery. The definitions of leak after bowel surgery usually included peritonitis (localized or generalized), faecal or purulent drainage from the wound and/or drain, presence of an abscess, and fever. Fifteen lower gastrointestinal reports in this review described routine contrast examination during the first or second postoperative week to determine

Table 8 Components of definition of anastomotic leak by anatomical site

Grade	Symptoms and signs	Management
Upper GI leak		
Radiological	Detected only on routine imaging; no clinical signs	No change in management
Clinical minor	Presence of luminal contents through the drain or wound site causing local inflammation, e.g. fever (temperature > 38°C) or leucocytosis (white cell count > 10 000/litre). Leak may also be detected on imaging studies	No change in management or intervention but may have prolonged hospital stay and/or delay in resuming oral intake
Clinical major	As clinical minor. Severe disruption to anastomosis. Leak may also be detected on imaging studies	Change in management and intervention required
HPB leak		
Radiological	Detected only on routine imaging study. No clinical signs	No change in immediate management
Clinical minor	Leakage defined if persistent drainage of > 50 ml per day via drain or serum amylase level > 2 times normal or signs of fever (temperature > 38°C) or leucocytosis (white cell count > 10 000/litre). Leak may also be detected on imaging studies	No change in management or intervention. May have prolonged hospital stay
Clinical major	As clinical minor. Severe disruption to anastomosis. Leak may also be detected on imaging studies	Change in management and intervention required
Lower GI leak		
Radiological	Detected only on routine study. No clinical signs	No change in management
Clinical minor	Presence of luminal contents through the drain or wound site causing local inflammation, e.g. fever (temperature > 38°C), leucocytosis (white cell count > 10 000/litre), faecal discharge from wound or drain or abscess. Leak may also be detected on imaging studies	No change in management or intervention but may have prolonged hospital stay
Clinical major	As clinical minor. Severe disruption to anastomosis. Leak may also be detected on imaging studies	Change in management and intervention required

GI, gastrointestinal; HPB, hepatopancreaticobiliary

anastomotic integrity. Such tests are no longer routine in most practices because of the clinical irrelevance of occult leaks and the small risk of radiological investigation[60].

The Australian Council of Healthcare Standards accepted anastomotic leak as a clinical outcome indicator for colorectal carcinoma resection on the basis that clinical leaks are 'easily identifiable'[103]. However, clear, well defined criteria must be agreed on to ensure that postoperative leak prevalence rates are directly comparable. At present, there is considerable variation in the definition and interpretation of clinical leakage and, until single definitions are adopted, it is unlikely that inter-institutional comparisons are valid. Validity assessment is hampered by the lack of a standard definition that has been accepted by surgeons. The majority of the definitions require subjective assessment, particularly the definitions in lower bowel surgery, which tend to depend on clinical judgement. These definitions will be subject to variation in interpretation, as clinical assessment is likely to be made by more than one member of a surgical team over a period of hospital stay. Assessment and diagnosis of anastomotic leak may differ between surgeons according to grade and experience. No formal assessment of inter-rater reliability was found in this review. The application of a single definition of anastomotic leak by two independent assessors to the same group of patients would allow assessment of reproducibility (inter-rater reliability). Statistical estimates of agreement between assessors using definitions of other postoperative surgical events (e.g. wound infection, deep vein thrombosis) have been conducted, but this systematic review failed to find evidence of similar work for anastomotic leak.

There was no chronological element in the definitions of anastomotic leakage, as is routine for postoperative mortality (30-day cut-off) or late wound infection detected after discharge from hospital (30 days). This criterion should be considered for inclusion in the definition of anastomotic leakage because such leakage may become apparent only after discharge from hospital. Readmission may be required because of sepsis or fistula formation but occasionally leakage that was clinically occult may be demonstrated on routine contrast radiology performed, for example, before closure of a stoma. It seems logical to categorize leaks according to timing of presentation. A number of patients will die after an operation that included an intestinal anastomosis, but not all will have had anastomotic integrity confirmed before death by contrast radiology. In some of these patients an autopsy will reveal occult leakage or confirm suspected leakage. The post-

mortem examination rate for patients who die after anastomotic surgery should be stated in all reports.

The SISG definition of anastomotic leak is useful as a generic definition. *Table 8* shows a proposal for three definitions specific to anatomical site, based on components from the SISG definition and those identified in the systematic review. These definitions include signs and symptoms, level of severity, and components of clinical management. In essence, any leak that requires a change in management, including prescription of antibiotics, with subsequent delay in the reintroduction of oral intake or discharge from hospital, would be considered a major clinical leak. The definitions proposed in this review may stimulate debate. Acceptance of a standard definition among surgeons is an important step for clinical audit and epidemiological research.

Conclusion

No validated definition of anastomotic leak by site was found in the contemporary literature. One definition of anastomotic leak was proposed at a UK consensus workshop, but no evidence was found for its use other than in the original publication. There is a need for surgeons to agree a standard definition by anatomical site, that is valid and reliable. It should distinguish between clinically minor (radiological) and major anastomotic leaks after gastrointestinal surgery.

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