Original article

Management and outcomes of anastomotic leaks after oesophagectomy

B. Dent, S. M. Griffin, R. Jones, S. Wahed, A. Immanuel and N. Hayes

Northern Oesophago-Gastric Cancer Unit, Royal Victoria Infirmary, Newcastle upon Tyne, UK

Correspondence to: Professor S. M. Griffin, Northern Oesophago-Gastric Cancer Unit, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP, UK (e-mail: michael.griffin@nuth.nhs.uk)

Background: **Leaks following oesophagectomy include true anastomotic leaks, leaks from the gastrotomy and gastric conduit necrosis. Historically, these complications were associated with high mortality rates. Recent improvements in outcome have been attributed to the wider use of oesophageal stents in patient management. This study examined outcomes of patients who developed a leak in a single high-volume institution that did not use stenting as a primary treatment modality.**

Methods: **All patients undergoing an oesophagectomy between January 2009 and December 2013 were included. Patients were identified from a prospectively maintained database.**

Results: **A total of 390 oesophagectomies were performed (median age 65 (range 32–81) years). In 96·7 per cent of patients this was a two-stage subtotal oesophagectomy. Overall in-hospital and 90-day mortality rates were both 2·1 per cent (8 patients). Some 31 patients (7·9 per cent) developed a leak (median age 64·5 (range 52–80) years), of whom 27 (87 per cent) were initially managed without surgery, whereas four (13 per cent) required immediate thoracotomy. The median length of stay for patients with a leak was 41·5 (range 15–159) days; none of these patients died.**

Conclusion: **Leaks can be managed with excellent outcomes without using oesophageal stents. The results do not support the widespread adoption of endoscopic stenting.**

Presented to the 18th Annual Scientific Meeting of the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland, Brighton, UK, September 2014; published in abstract form as *Br J Surg* 2014; **101**(Suppl 6): 6

Paper accepted 22 February 2016

Published online 5 May 2016 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.10175

Introduction

Outcomes following oesophagectomy continue to improve, with low mortality rates at specialist centres. Postoperative morbidity is, however, still common. Anastomotic leak is a feared complication that has historically been associated with high mortality rates[1]. The Esophagectomy Complications Consensus Group (ECCG) has recently defined anastomotic leaks as full-thickness defects involving the oesophagus, anastomosis, staple line or conduit, irrespective of the presentation or method of identification[2]. In this classification, leaks are divided into three types based on management strategy. Type 1 leaks require no change in therapy, medical management or dietary modification. Type 2 leaks require interventional but not surgical therapy, and type 3 leaks require surgical intervention. True anastomotic leaks, those due to focal conduit necrosis and gastrotomy-line leaks can be distinguished accurately with modern imaging and endoscopic techniques. In recent series[3–7], rates of anastomotic leak have been reported as between 3·8 and 11·7 per cent. The latest results from the UK National Oesophago-gastric Cancer Audit in 2013 reported an overall anastomotic leak rate of 7·4 per cent[8].

The management of anastomotic leaks is evolving. Surgical management has increasingly been replaced with non-operative strategies. Reports of the routine use of endoscopic stenting in these patients are growing[9]. Stenting itself is associated with significant complications and mortality[10]. This study aimed to assess the outcomes in patients who developed an anastomotic leak following oesophagectomy in a single high-volume institution over a 5-year period without the use of stenting as a primary component of management.

Methods

All patients who underwent an oesophagectomy at the Northern Oesophago-Gastric Unit, Newcastle upon Tyne, between January 2009 and December 2013 were identified

from a prospectively created database. The unit acts as both a regional and national referral centre. Patients found to have inoperable disease at the time of surgery were excluded.

Patients with middle or lower-third tumours underwent an open two-stage subtotal oesophagectomy with radical two-field lymphadenectomy. A gastric tube at least 5 cm in width was fashioned in all patients along with routine pyloroplasty. An intrathoracic anastomosis was constructed close to the apex of the thorax in all patients at the high point of the stomach using a circular stapler. The gastrotomy line was closed with a linear stapler and inverted with a continuous suture. Omental wrapping of the anastomosis and gastrotomy line was performed in all patients. Those with more proximal tumours underwent an open three-stage subtotal oesophagectomy with radical two-field lymphadenectomy. The gastric tube was fashioned in an identical method with a cervical two-layer hand-sewn anastomosis, again with omental wrapping[11].

All complications were recorded in the database. Routine postoperative contrast swallows were not used. All patients suspected to have an anastomotic leak based on clinical or biochemical grounds were assessed by contrast-enhanced CT and flexible video upper gastrointestinal endoscopy with minimal insufflation. Contrast swallows were used in selected patients where diagnostic uncertainty remained. Leaks were classified according to the definitions proposed by the ECCG[2]. Patients with conduit necrosis in the absence of anastomotic or conduit leak were not included. All patients were managed according to an established algorithm (*Fig. 1*). Management decisions were based on the size and aetiology of the leak, the degree of local contamination, and severity of the associated systemic response.

All patients were admitted to a critical care unit. Aggressive non-operative management consisted of: nasogastric decompression (endoscopically placed), nil by mouth, intravenous antimicrobials (including antifungals), intravenous proton pump inhibition and low molecular weight heparin. Radiological drainage of pleural or anastomotic collections was performed as required. Regular clinical, biochemical and radiological reassessment was undertaken. Enteral nutrition was provided via a feeding jejunostomy.

In patients who required operative management of the leak, surgery was performed immediately after initial resuscitation. Criteria for immediate operation were significant pleural or mediastinal contamination, or severe sepsis. The preferred operation involved closure of the leak over a T tube to create a controlled fistula, but with large defects or severe anastomotic contamination the policy was to take the anastomosis down with formation of a defunctioning oesophagostomy. Delayed surgery was considered in patients managed without surgery in the presence of worsening sepsis or contamination, or failure to improve clinically.

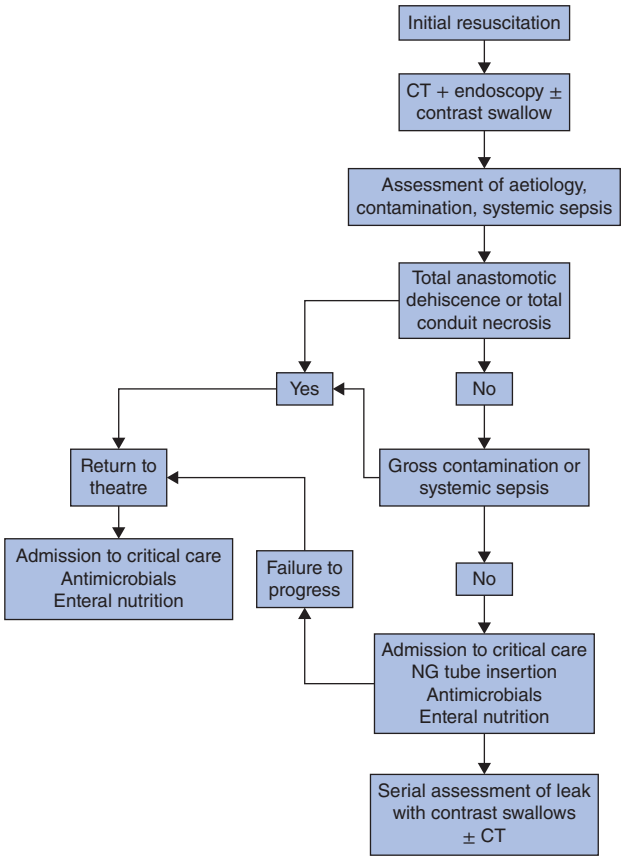

Fig. 1 Algorithm for the management of leaks. NG, nasogastric

Statistical analysis

All data are presented as median (range). Statistical analysis was carried out using SPSS® for Windows® version 19·0 (IBM, Armonk, New York, USA).

Results

Between January 2009 and December 2013, 390 patients underwent oesophagectomy, of whom 281 (72·1 per cent) were men. The median age of patients was 65 (range 32–81) years. The aetiology of the disease for which surgery was undertaken is detailed in *Table 1*. Most patients (96·7 per cent) underwent a two-stage subtotal oesophagectomy with two-field lymphadenectomy for cancer. Eleven patients had a three-stage oesophagectomy with three-field lymphadenectomy, and two had a left

Table 1 Demographics, surgical details and outcomes of patients included in the study

	All patients ($n = 390$)	Mediastinal leaks				
		All ($n = 31$)	True anastomotic leak ($n = 15$)	Conduit necrosis ($n = 12$)	Gastrotomy staple-line leak ($n = 3$)	Peptic ulcer ($n = 1$)
Age (years)*	65 (32–81)	64·5 (52–80)	63 (52–80)	67·5 (61–76)	73 (61–73)	55
Sex ratio (M : F)	281 : 109	18 : 13	10 : 5	6 : 6	2 : 1	1 : 0
Histology						
Adenocarcinoma	277 (71·0)	19	11	4	3	1
SCC	86 (22·1)	11	4	7	0	0
High-grade dysplasia	9 (2·3)	1	0	1	0	0
Other	18 (4·6)	0	0	0	0	0
Neoadjuvant chemotherapy	236 (60·5)	20	9	8	2	1
Operation						
Two-stage	377 (96·7)	27	13	10	3	1
Three-stage	11 (2·8)	4	2	2	0	0
Thoracoabdominal	2 (0·5)	0	0	0	0	0
Management of leak						
Operative	–	4	2	2	0	0
Non-operative	–	27†	13†	10	3	1
ECCG classification[2]						
Type 1	–	15	8	5	2	0
Type 2	–	11	4	5	1	1
Type 3	–	5	3	2	0	0
Time to diagnosis of leak (days)*	–	10 (6–21)	10 (6–15)	9 (6–14)	10 (8–12)	21
Length of hospital stay (days)*	17 (7–202)	41·5 (15–159)	41 (26–159)	47 (20–138)	36 (35–54)	91
In-hospital mortality	8 (2·1)	0	0	0	0	0
90-day mortality	8 (2·1)	0	0	0	0	0

Values in parentheses are percentages. †One patient required surgery after initial non-operative management. SCC, squamous cell carcinoma; ECCG, Esophagectomy Complications Consensus Group.

thoracoabdominal oesophagectomy owing to previous pleurodesis.

In total, 31 patients (7·9 per cent) were identified with an anastomotic leak in the postoperative period (18 men and 13 women). These patients were aged 64·5 (52–80) years. The time to diagnosis of a postoperative leak was 10 (6–21) days. Twenty-seven patients had undergone a two-stage subtotal oesophagectomy with two-field lymphadenectomy, and four a three-stage oesophagectomy with three-field lymphadenectomy and cervical anastomosis. All patients had undergone reconstruction with a gastric conduit. Of these 31 patients, 15 had a true anastomotic leak, 12 focal conduit necrosis, and three a leak from the gastrotomy staple line. One patient developed a leak from a perforated peptic ulcer in the gastric conduit. There was no total conduit necrosis.

Among these 31 patients, 30 had invasive cancer and 1 had high-grade dysplasia alone. Twenty patients had received neoadjuvant chemotherapy, and two had undergone salvage oesophagectomy after radical chemoradiotherapy.

Initial management was non-operative in 27 patients, of whom nine required radiologically guided drainage of pleural or mediastinal collections. Three drains were placed within 12 h of diagnosis of the leak, a further three within 48 h and the remainder at 6, 9 and 16 days. Four patients had immediate operative management on the day of diagnosis of the leak, with closure of the leak over a T tube in two and defunctioning oesophagostomy after taking down the anastomosis in the other two patients. In both patients treated with T tubes, there was a fistula between the anastomosis and bronchus, repaired with an intercostal muscle flap. Three patients had a feeding jejunostomy formed via a minilaparotomy, the remaining 24 already having had a feeding jejunostomy placed at the time of oesophagectomy. A single patient who was initially managed without surgery required conversion to operative management 4 days after diagnosis owing to worsening of systemic sepsis and progression of the leak. This patient underwent T tube closure of the leak.

Two patients managed without surgery had a covered stent inserted to allow earlier resumption of oral diet despite the presence of a feeding jejunostomy. These stents were inserted 20 and 23 days after the diagnosis of the leak and did not form part of the initial management. In both patients there was a contained cavity with no ongoing local contamination or systemic sepsis before stenting. The stents were removed 1 and 3 months after insertion.

According to the proposed ECCG classification for anastomotic leaks, the series included 15 patients with a type 1 leak, 11 with a type 2 leak, and five with a type 3 leak (*Table 1*).

The median length of stay for all patients undergoing oesophagectomy was 17 days, in contrast to that among those who developed a leak, which was 41·5 (range 15–159) days. Overall in-hospital and 90-day mortality rates for all patients undergoing oesophagectomy were both 2·1 per cent (8 of 390 patients). There was no in-hospital or 90-day mortality amongst the 31 patients who developed an anastomotic leak.

Ten patients required subsequent dilatations for anastomotic stricturing. The median number of dilatations required per patient was 6 (range 1–15). At follow-up of 21 (4–62) months, seven (23 per cent) of the 31 patients who developed an anastomotic leak had developed disease recurrence.

Discussion

Anastomotic leak remains a common and serious complication of oesophagectomy. The present data demonstrate that within a high-volume unit anastomotic leaks can be managed without associated mortality. The need for surgery to manage anastomotic leaks is now the exception. Routine stenting is not required in these patients.

This approach to the management of anastomotic leaks depends on early detection and prompt initiation of treatment. Attempts have been made to identify factors associated with anastomotic leaks after oesophagectomy[6,12–15], but in practice a high index of suspicion is required in all patients irrespective of perceived risk. Prompt CT and endoscopy should be used in the investigation of all suspected anastomotic leaks[5,16]. Early diagnosis reduces the severity of contamination and sepsis, which are important determinants of the need for surgical intervention[17]. Non-operative management should not be considered as conservative treatment. Aggressive treatment with antimicrobials including antifungals[18] and radiological insertion of drains, with or without critical care admission, are important components of patient care. Nutrition is essential for patient recovery and should be delivered via the enteral route if possible[19]. Placement of a feeding jejunostomy at the time of oesophagectomy allows routine postoperative feeding, but, more importantly, also allows extended feeding in the event of an anastomotic leak. Serial assessment of patients treated without surgery is essential. In the present series, conversion from non-operative to operative management was rare when these principles were applied.

A lack of standardized definitions for postoperative complications has led to wide variations in the reporting of incidence and outcomes from anastomotic leaks[20]. The recent UK National Audit[8] and many other series have reported anastomotic leak rates without defining whether this includes conduit necroses and gastrotomy-line leaks. The ECCG recently proposed definitions for all postoesophagectomy complications[2]. Anastomotic leaks incorporate all full-thickness gastrointestinal defects and are subgrouped into three grades based on the management required. Strict adherence to these definitions should ensure that future series and audits are more comparable.

In modern case series, leaks are still associated with significant mortality[6,21]. The UK National Audit[8] reported that patients who suffered an anastomotic leak had higher rates of other postoperative complications and increased 30- and 90-day mortality rates. Routine stenting in the management of anastomotic leaks has been reported[22] to achieve good radiological and clinical outcomes, with overall mortality rates of 13 per cent. Many of these series combine spontaneous and iatrogenic oesophageal perforations[10,23,24]. The mortality rate associated with oesophageal perforation is high[25,26], which impacts substantially on the interpretation of these series. The commonest cause of death in patients treated with stents is sepsis, related to infected fluid or an abscess outside the oesophageal wall[22]. There are, therefore, high rates of associated thoracic drainage procedures, including thoracotomy, performed in conjunction with stent placement[24,27]. It is impossible to determine the relative contributions of the stent and drainage procedure in the outcomes of these patients. Stents do cause complications. Migration, tracheobronchial fistulation, erosion, haemorrhage and perforation at the time of stent removal have all been described[28–30], along with stent-related mortality[10,24]. In one series of 17 patients, three died from stent erosion into the thoracic aorta[4].

The major strength of the present study is that it includes a large number of patients treated within a short time interval. This ensured that patients were managed in a consistent manner throughout the study. Outcomes reflect contemporary management of patients with anastomotic leaks. A potential weakness is that subclinical anastomotic leaks would not have been detected. The importance of these leaks is questionable in the absence of clinical signs or symptoms. Neither routine postoperative contrast swallows nor endoscopy have been shown to improve patient outcomes[5,31]. The present study has demonstrated that routine stenting is not essential in this patient group, although this is not to say that selective stenting may have a beneficial role. Stenting can lead to a prompt resumption

of oral diet[32], and was used to this effect in two patients. The median length of stay in the present series for patients with a leak was relatively long. This may be something that can be shortened through the selective use of removable stents. These potential benefits must be balanced carefully against the risks of stenting.

Acknowledgements

The authors thank H. Jaretzke for her assistance with data recording and collection.
Disclosure: The authors declare no conflict of interest

References

1 Junemann-Ramirez M, Awan MY, Khan ZM, Rahamim JS. Anastomotic leakage post-esophagogastrectomy for esophageal carcinoma: retrospective analysis of predictive factors, management and influence on longterm survival in a high volume centre. *Eur J Cardiothorac Surg* 2005; **27**: 3–7.
2 Low DE, Alderson D, Cecconello I, Chang AC, Darling GE, D'Journo XB *et al*. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). *Ann Surg* 2015; **262**: 286–294.
3 van der Schaaf M, Lagergren J, Lagergren P. Persisting symptoms after intrathoracic anastomotic leak following oesophagectomy for cancer. *Br J Surg* 2012; **99**: 95–99.
4 Schweigert M, Dubecz A, Stadlhuber RJ, Muschweck H, Stein HJ. Risk of stent-related aortic erosion after endoscopic stent insertion for intrathoracic anastomotic leaks after esophagectomy. *Ann Thorac Surg* 2011; **92**: 513–519.
5 Griffin SM, Lamb PJ, Dresner SM, Richardson DL, Hayes N. Diagnosis and management of a mediastinal leak following radical oesophagectomy. *Br J Surg* 2001; **88**: 1346–1351.
6 Kassis ES, Kosinski AS, Ross P Jr, Koppes KE, Donahue JM, Daniel VC. Predictors of anastomotic leak after esophagectomy: an analysis of the society of thoracic surgeons general thoracic database. *Ann Thorac Surg* 2013; **96**: 1919–1926.
7 Low DE, Kunz S, Schembre D, Otero H, Malpass T, Hsi A *et al*. Esophagectomy – it's not just about mortality anymore: standardized perioperative clinical pathways improve outcomes in patients with esophageal cancer. *J Gastrointest Surg* 2007; **11**: 1395–1402.
8 Health and Social Care Information Centre. *National Oesophago-gastric Cancer Audit – 2013, Annual Report*. http://www.hscic.gov.uk/catalogue/PUB11093 [accessed 24 August 2015].
9 Dasari BV, Neely D, Kennedy A, Spence G, Rice P, Mackle E *et al*. Role of esophageal stents in the management of esophageal anastomotic leaks and benign esophageal perforations. *Ann Surg* 2014; **259**: 852–860.
10 van Boeckel PG, Dua KS, Weusten BL, Schmits RJ, Surapaneni N, Timmer R *et al*. Fully covered self-expandable metal stents (SEMS), partially covered SEMS and self-expandable plastic stents for the treatment of benign esophageal ruptures and anastomotic leaks. *BMC Gastroenterol* 2012; **12**: 19.
11 Griffin SM, Raimes SA, Shenfine J. *Oesophagogastric Surgery: a Companion to Specialist Surgical Practice* (5th edn). Saunders: Edinburgh, 2013.
12 Juloori A, Tucker SL, Komaki R, Liao Z, Correa AM, Swisher SG *et al*. Influence of preoperative radiation field on postoperative leak rates in esophageal cancer patients after trimodality therapy. *J Thorac Oncol* 2014; **9**: 534–540.
13 Markar SR, Arya S, Karthikesalingam A, Hanna GB. Technical factors that affect anastomotic integrity following esophagectomy: systematic review and meta-analysis. *Ann Surg Oncol* 2013; **20**: 4274–4281.
14 Noble F, Curtis N, Harris S, Kelly JJ, Bailey IS, Byrne JP *et al*; South Coast Cancer Collaboration – Oesophago-Gastric (SC-OG). Risk assessment using a novel score to predict anastomotic leak and major complications after oesophageal resection. *J Gastrointest Surg* 2012; **16**: 1083–1095.
15 Stawicki SP, Prosciak MP, Gerlach AT, Bloomston M, Davido HT, Lindsey DE *et al*. Atrial fibrillation after esophagectomy: an indicator of postoperative morbidity. *Gen Thorac Cardiovasc Surg* 2011; **59**: 399–405.
16 Lantos JE, Levine MS, Rubesin SE, Lau CT, Torigian DA. Comparison between esophagography and chest computed tomography for evaluation of leaks after esophagectomy and gastric pull-through. *J Thorac Imaging* 2013; **28**: 121–128.
17 Griffin SM, Lamb PJ, Shenfine J, Richardson DL, Karat D, Hayes N. Spontaneous rupture of the oesophagus. *Br J Surg* 2008; **95**: 1115–1120.
18 Elsayed H, Shaker H, Whittle I, Hussein S. The impact of systemic fungal infection in patients with perforated oesophagus. *Ann R Coll Surg Engl* 2012; **94**: 579–584.
19 Mazaki T, Ebisawa K. Enteral *versus* parenteral nutrition after gastrointestinal surgery: a systematic review and meta-analysis of randomized controlled trials in the English literature. *J Gastrointest Surg* 2008; **12**: 739–755.
20 Bruce J, Krukowski ZH, Al-Khairy G, Russell EM, Park KG. Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. *Br J Surg* 2001; **88**: 1157–1168.
21 Escofet X, Manjunath A, Twine C, Havard TJ, Clark GW, Lewis WG. Prevalence and outcome of esophagogastric anastomotic leak after esophagectomy in a UK regional cancer network. *Dis Esophagus* 2010; **23**: 112–116.
22 van Boeckel PG, Sijbring A, Vleggaar FP, Siersema PD. Systematic review: temporary stent placement for benign rupture or anastomotic leak of the oesophagus. *Aliment Pharmacol Ther* 2011; **33**: 1292–1301.

23 Freeman RK, Ascioti AJ, Giannini T, Mahidhara RJ. Analysis of unsuccessful esophageal stent placements for esophageal perforation, fistula, or anastomotic leak. *Ann Thorac Surg* 2012; **94**: 959–965.
24 D'Cunha J, Rueth NM, Groth SS, Maddaus MA, Andrade RS. Esophageal stents for anastomotic leaks and perforations. *J Thorac Cardiovasc Surg* 2011; **142**: 39–46.e1.
25 Wahed S, Dent B, Jones R, Griffin SM. Spectrum of oesophageal perforations and their influence on management. *Br J Surg* 2014; **101**: E156–E162.
26 Salo JA, Isolauri JO, Heikkilä LJ, Markkula HT, Heikkinen LO, Kivilaakso EO *et al*. Management of delayed esophageal perforation with mediastinal sepsis. Esophagectomy or primary repair? *J Thorac Cardiovasc Surg* 1993; **106**: 1088–1091.
27 David EA, Kim MP, Blackmon SH. Esophageal salvage with removable covered self-expanding metal stents in the setting of intrathoracic esophageal leakage. *Am J Surg* 2011; **202**: 796–801.
28 Hirdes MM, Vleggaar FP, Van der Linde K, Willems M, Totte ER, Siersema PD. Esophageal perforation due to removal of partially covered self-expanding metal stents placed for a benign perforation or leak. *Endoscopy* 2011; **43**: 156–159.
29 El Hajj II, Imperiale TF, Rex DK, Ballard D, Kesler KA, Birdas TJ *et al*. Treatment of esophageal leaks, fistulae, and perforations with temporary stents: evaluation of efficacy, adverse events, and factors associated with successful outcomes. *Gastrointest Endosc* 2014; **79**: 589–598.
30 Swinnen J, Eisendrath P, Rigaux J, Kahegeshe L, Lemmers A, Le Moine O *et al*. Self-expandable metal stents for the treatment of benign upper GI leaks and perforations. *Gastrointest Endosc* 2011; **73**: 890–899.
31 Page RD, Asmat A, McShane J, Russell GN, Pennefather SH. Routine endoscopy to detect anastomotic leakage after esophagectomy. *Ann Thorac Surg* 2013; **95**: 292–298.
32 Freeman RK, Vyverberg A, Ascioti AJ. Esophageal stent placement for the treatment of acute intrathoracic anastomotic leak after esophagectomy. *Ann Thorac Surg* 2011; **92**: 204–208.