

Esophageal diverticula and cancer

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SUMMARY. Esophageal diverticula are rare. The association of cancer and diverticula has been described. Some authors adopt a conservative non-surgical approach in selected patients with diverticula whereas others treat the symptoms by diverticulopexy or myotomy only, leaving the diverticulum *in situ*. However, the risk of malignant degeneration should be taken in account if the diverticulum is not resected. The correct evaluation of the possible risk factors for malignancy may help in the decision making process. We performed a literature review of esophageal diverticula and cancer. The incidence of cancer in a diverticulum is 0.3–7, 1.8, and 0.6% for pharyngo-esophageal, midesophageal, and epiphrenic diverticula, respectively. Symptoms may mimic those of the diverticulum or underlying motor disorder. Progressive dysphagia, unintentional weight loss, the presence of blood in the regurgitated material, regurgitation of pieces of the tumor, odynophagia, melena, hematemesis, and hemoptysis are key symptoms. Risk factors for malignancy are old age, male gender, long-standing history, and larger diverticula. A carcinoma may develop in treated diverticula, even after resection. Outcomes are usually quoted as dismal because of a delayed diagnosis but several cases of superficial carcinoma have been described. The treatment follows the same principals as the therapy for esophageal cancer; however, diverticulectomy is enough in cases of superficial carcinomas. Patients must be carefully evaluated before therapy and a long-term follow-up is advisable.

KEY WORDS: epiphrenic diverticulum, esophageal cancer, esophageal diverticulum, esophagus, zenker diverticulum.

INTRODUCTION

Esophageal diverticula are rare with a prevalence of 0.06 to 3.6% based on radiologic and endoscopic series.^{1,2} Classically described as pulsion or traction diverticula, they may occur in the pharyngo-esophageal transition area, in the mid-esophagus or distally (epiphrenic).³

A large proportion of patients with esophageal diverticula may be asymptomatic. However, serious complications, such as tracheal fistula, hemorrhage, vocal cord paralysis, and retained foreign body may

occur.⁴ In addition, the risk of malignancy has also been described; even though the true risk is still elusive. The carcinogenesis may be caused by chronic irritation by food, inflammation and repeated injury,^{5–7} a pathogenesis similar to that of achalasia.⁸

Preoperative diagnosis of a carcinoma in an esophageal diverticulum may be difficult. Symptoms may mimic those of the diverticulum or underlying motor disorder. Progressive dysphagia and unintentional weight loss are key symptoms.^{9–11} Barium esophagram may be misleading as some lesions are not apparent, presentation of the tumor is variable and food residues may be a confounding factor.¹⁰ Burton and Lund found a sensitivity of only 30% for the detection of these tumors in a literature review.¹¹ Upper endoscopy must be part of the preoperative workup.¹² The possibility of carcinoma arising from a Zenkers diverticula should also be considered when evaluating patients with cervical metastatic squamous cell carcinoma with an unknown primary cancer.

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Some authors adopt a conservative non-surgical approach in selected patients with diverticula^{13,14} whereas others^{15,16} treat the symptoms by diverticulopexy or myotomy only, leaving the diverticulum *in situ*. In both cases, the risk of malignant degeneration may be taken in account for the therapeutic decision as the diverticulum is not resected. The correct evaluation of the risk factors may help the management of these diverticula.

METHODS

A literature search was performed using Medline/Pubmed database. The following search headings were used: [diverticulum] or [diverticula] or [pouch] AND [esophageal] or [esophagus] or [pharyngeal] or [pharynx] or [Zenker] or [Killian] or [epiphrenic] AND [cancer] or [neoplasm] or [carcinoma]. Only related articles in English were reviewed. Additional articles were found searching the references of the selected articles.

Pharyngoesophageal diverticula (Zenker and Killian)

Friedrich A. von Zenker did not first describe the 'Zenker's diverticulum.' Actually, it was defined as a 'preternatural dilatation of (and bag formed in), the pharynx' by Ludlow more than one century earlier.¹⁷ In 1908, Killian described the presence of a lateral slit close to the outer lateral border of the cricoid cartilage at the insertion of the cricopharyngeal muscle, corresponding to the passage of the inferior laryngeal nerve.¹⁷

The first description of the association of a carcinoma in a Zenker's diverticulum is often quoted as Vinson in 1933;¹⁸ however, Pitt in 1896.¹⁹ Turner¹⁰ collected 45 cases of carcinoma in a pharyngoesophageal diverticulum in the 1960s. The prevalence of cancer in this diverticulum ranges from 0.3 to 7% in different series,^{20–30} with no time-trend change (Fig. 1). The most representative reports come from Huang *et al.*²⁵ who retrospectively reviewed over 1000 patients from the Mayo Clinic and found 6 patients with carcinoma, for a prevalence of 0.4%. Siddiq and Sood³¹ surveyed United Kingdom surgeons that operate Zenker's diverticulum. Forty-eight surgeons among 227 stated that they had encountered a carcinoma. Indeed, nine surgeons had encountered more than one such case, accounting for a total of 63 cases.

Odd symptoms have been described and must alert to the possibility of malignancy, such as the presence of blood in the regurgitated material, regurgitation of peaces of the tumor, odynophagia, and hematemesis.^{10,11,21,32–35}

The main risk factors for the development of malignancy are frequently quoted as old age of the patient, the duration over which the pouch has been

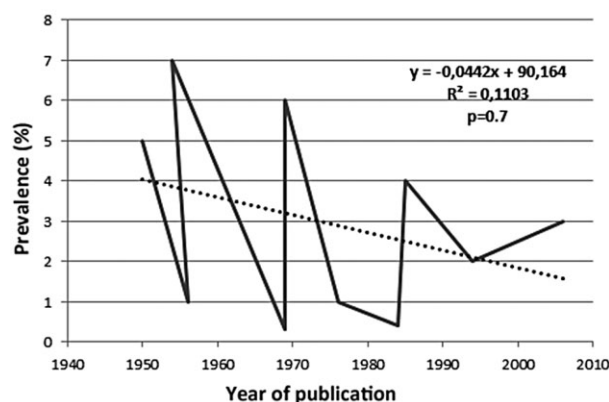


Fig. 1 Time-trend prevalence for the association of pharyngoesophageal diverticulum and cancer.

present, and its size.³⁴ In the 49 squamous cell carcinoma cases we collected (Table 1) the mean age of the patients was 69 years. Although the youngest patient was 43 years old, 80% of them were over 60. Of note, 80% of the patients were men. The mean time from the start of symptoms was 10 years. The mean size of the diverticula was 5 cm.

The diagnosis of the malignancy may be done before, during or after the operation.^{42,47} Siddiq and Sood³¹ reported 63 cases where the diagnosis had been suspected at the initial endoscopic examination of the pouch in 48 (76%) of cases, in the remaining 15 cases (24%), the carcinoma was only diagnosed post-operatively on histological examination.

Outcomes are usually quoted as dismal because of a delayed diagnosis. In fact, most cases are advanced tumors at the time of the operation.^{7,10,18,40} However, several cases of superficial carcinoma have been described.^{26,28,37,40,45,47}

The treatment follows the same principals as the therapy for esophageal cancer.

Several cases of carcinoma in previously treated diverticula have been reported, especially after endoscopic treatment.^{7,20,27,34,47} Very interestingly, however, a carcinoma may develop in treated diverticula, even after resection.^{7,20,23,27,34,47,48}

Benign tumors are rarely reported in a pharyngoesophageal diverticulum. Razin and Adler published the concomitance of a 5 × 8-cm lipoma in a Zenker diverticulum in a 62-year-old female patient.⁵⁴

Midesophageal diverticula

Midesophageal diverticula are traditionally considered traction diverticula secondary to mediastinal inflammatory reaction,⁵⁵ although 90% of these patients may present with abnormal esophageal motility.^{1,56} They are rare. Hoghooghi *et al.*¹ found a prevalence of less than 4% in esophagrams in adult patients with no prior history of gastroesophageal

Table 1 Association of pharyngoesophageal diverticulum and cancer

Author	Gender (M = male × F = female)	Age (years)	Size (cm)	Time of symptoms	Note
Acharya <i>et al.</i> ³⁴	M	71	4	6 years	Previous stapling
Brücher <i>et al.</i> ³⁶	M	65	NR	NR	
Turner ¹⁰	M	63	3.5	30 years	3 years
	F	82	NR	NR	
Sparks ¹¹	M	59	5	30 years	
Bullock <i>et al.</i> ³⁷	M	66	3.5	3 years	
Riberi <i>et al.</i> ³³	F	82	6	20 years	
Pierce <i>et al.</i> ³⁸	M	55	5	10 years	
Garlock <i>et al.</i> ³⁹	M	70	6	8 years	
Kerner <i>et al.</i> ²⁶	M	66	4	1 year	
Jubi ²⁷	M	43	NR	14 years	Previous endoscopic diathermy
Baraka <i>et al.</i> ²⁸	M	76	NR	NR	
	M	75		2 years	
Stevens ⁷	F	85			31 years
	M	73	NR	2 years	
	M	91		4 years	Previous Dohlman's procedure
	F	79		15 years	
Burton ⁴⁰	F	71	NR	3 years	15 years
	M	83		NR	
Liberson <i>et al.</i> ⁴¹	M	62	NR	20 years	
Fischer <i>et al.</i> ⁴²	M	67	NR	6 years	
Som <i>et al.</i> ⁴³	M	76	5	NR	Retroesophageal abscess
Johnson <i>et al.</i> ⁴⁴	M	62	NR	NR	
Vinson ¹⁸	M	63	NR	10 years	
Zonnevylee <i>et al.</i> ⁴⁵	M	73	2.5	2 months	
Rojas <i>et al.</i> ⁴⁶	M	67	NR	NR	Previous Dohlman's procedure
Bradley <i>et al.</i> ⁴⁷	F	68	NR	11 years	
	M	70	NR	NR	
	M	76	NR	6 months	5 years
	F	63	NR	NR	
Huang <i>et al.</i> ²⁵	F	80	6	NR	70
	M	70	6.5	NR	
Zitsch <i>et al.</i> ³²	M	57	NR	5 years	
Dionigi <i>et al.</i> ²⁴	M	75	5	2 months	
Wychulis <i>et al.</i> ²⁹	M	64	NR	5 years	6
	M	56	6	13 years	
	M	89	2	16 years	20 years
	M	80	5	NR	
Nanson ⁴⁸	M				Previous resection with recurrence after 15 years
	M				
Bowdler <i>et al.</i> ⁴⁹	M	70	NR	NR	10 years
	M	50	NR	NR	
Lindskog <i>et al.</i> ²³	M	82	NR	NR	Previous diverticulopexy
Jensen <i>et al.</i> ³⁵	F	65	4.5 cm	10 years	
Kay <i>et al.</i> ²¹	NR	62	NR	3 years	
Mackay ²⁰	M	56	NR	NR	Previous Dohlman's procedure 11 years
Capps <i>et al.</i> ⁵⁰	M	59	12	30 years	
Kune ⁵¹	M	57	4	20 years	
Anonymous ⁵²	M	64	NR	10 years	
Chaurasia <i>et al.</i> ⁵³	F	61	NR	NR	10 years
	M	82	NR	NR	

surgery. Midesophageal diverticula are frequently asymptomatic and therefore they are not treated.⁵⁵

Song *et al.*⁵⁷ reported a prevalence of cancer in midesophageal diverticula of 1.8%. We were able to collect five squamous cell carcinoma cases from the literature (Table 2). Interestingly, one case was an adenocarcinoma and one patient was asymptomatic. Cases of superficial⁶ and advanced⁵⁸ carcinoma were described.

Benign tumors have rarely been reported. Nese⁵⁹ described the association of leiomyoma and diverticula in two patients: two females with 40 and 48

years. Dillow *et al.* reported an incidence of one leiomyoma in a midesophageal diverticulum in a series of 11 esophageal leiomyomas in all locations (9%).⁶⁰

Epiphrenic diverticula

Epiphrenic diverticulum is a pulsion diverticulum, usually located in the distal 10 cm of the esophagus. It is caused by the herniation of mucosa and submucosa through the muscle layers of the esophageal wall.¹²

Table 2 Association of midesophageal diverticulum and cancer

Author	Gender (M = male × F = female)	Age (years)	Size (cm)	Time of symptoms	Note
Kimura <i>et al.</i> ⁶	M	65	NR	Asymptomatic	Adenocarcinoma
Avisar <i>et al.</i> ⁵⁸	M	60	NR	3 months	
Song <i>et al.</i> ⁵⁷	M	51	2.5 cm	4 years	
	M	59	4 cm	4 years	
	F	45	3 cm	10 years	

Allen *et al.*⁶¹ reported a prevalence of cancer in this diverticulum of 0.6%.⁶¹ Plous *et al.*⁶² collected three cases in the literature in 1964 and Saldana *et al.*⁶³ reviewed 10 cases in 1982. We were able to collect 17 squamous cell carcinoma cases from the literature (Table 3). The mean age of the patients is 68 years, although patients as young as 34 years old have been reported. Similar to pharyngoesophageal diverticula, 83% of the patients were men. The mean time from the start of symptoms was 7 years. The mean size of the diverticula was 5 cm.

Uncommon symptoms have been described, and must alert to the possibility of malignancy, such as melena, hematemesis, and hemoptysis.^{64–66}

Diagnosis may be done before, during or after the operation.^{9,62,67} Cases were diagnosed both as superficial^{5,9,62,65,67–69} or advanced carcinoma.^{64,69}

Once more, treatment follows the same principals as the therapy for esophageal cancer. Different approaches have been described, making difficult to choose a uniform approach.

Several cases of benign tumors have been reported in epiphrenic diverticula, most of them leiomyomas. Dillow *et al.* reported an incidence of one leiomyoma in a series of 11 esophageal leiomyomas in all locations (9%)⁶⁰ whereas Bonavina *et al.*⁷³ found a prevalence of 6%. There is a clear female preponderance of

5:2 with age younger than the cases of cancer, ranging from 24 to 59 years.^{74–79} One case of neurinoma has also been published in a 42-year-old male.⁵⁹

Pseudodiverticulosis

Intramural pseudodiverticulosis of the esophagus is a rare benign disease of the esophageal wall, with dilation of the submucosal glands.⁸⁰ It is not a real diverticulum of the esophagus but an increased risk of esophageal carcinoma has been demonstrated in patients with pseudodiverticulosis.⁸¹

CONCLUSIONS

Esophageal diverticula are rare and the association of cancer in a diverticulum is even rarer. Because of this very low incidence, all articles reviewed comprise case reports or small case series with no more than six patients. However, even with this limitation, we believe our review showed that the concomitance of esophageal diverticulum and cancer is uncommon but not negligible.

Carcinogenesis in an esophageal diverticulum is probably linked to stasis, similarly to achalasia that has a comparable index of malignant degeneration,

Table 3 Association of epiphrenic diverticulum and cancer

Author	Gender (M = male × F = female)	Age (years)	Size (cm)	Time of symptoms	Note
Honda <i>et al.</i> ⁵	M	80	4.5	6 years	Autopsy study
Lai <i>et al.</i> ⁹	M	70	5	3 months	
	F	34	4	2 years	
Jordan <i>et al.</i> ¹³	NR	NR	NR	9 years	
Allen <i>et al.</i> ⁶¹	NR	NR	NR	NR	
Plous <i>et al.</i> ⁶²	M	79	6.5	2 years	
Saldana <i>et al.</i> ⁶³	M	65	8.5	25 years	
Zinner ⁶⁴	M	64	NR	2 years	
Thomas ⁶⁵	M	77	NR	5 years	
Schultz <i>et al.</i> ⁶⁶	F	78	NR	4 months	
	M	84	NR	3 months	
Conklin <i>et al.</i> ⁶⁷	M	80	NR	6 years	
Shin ⁶⁸	M	73	NR	16 years	
Gawand <i>et al.</i> ⁶⁹	M	55	NR	3 years	
Goodman <i>et al.</i> ⁷⁰	M	63	1.5	3 months	
Guerra <i>et al.</i> ⁷¹	M	66	7	NR	Esophagopleural fistula
Philippakis <i>et al.</i> ⁷²	F	59	NR	3 years	

NR, not reported.

between 1 and 3%.^{8,82,83} Interestingly, patients with achalasia keep a higher risk for malignancy even after treatment.^{82,83} A parallel thinking leads to the assumption that resection is necessary for the management of esophageal diverticula. Moreover, microscopic carcinoma will be missed by techniques where the pouch is not excised. On the other side, small diverticula (<2 cm) may be left *in situ* because of the low risk associated to this diverticula. Moreover, after esophageal myotomy, small diverticula, either Zenker's or epiphrenic diverticula, will vanish preventing stasis and decreasing the risk for cancer.

Risk factors for malignancy are old age, male gender, long-standing history, and larger diverticula. The reports are not always clear on the presence of general risk factors for esophageal cancer in the patients, such as smoking and drinking. However, it is interesting that the association of esophageal diverticula and esophageal carcinoma in different locations is extremely rare.⁸⁴ Malignancy was found within the diverticula in all the cases reviewed.

Treatment of cancer in a diverticulum follows the same principles of the treatment for esophageal carcinoma. This review included series from a long time span. Different approaches have been described, from radiotherapy alone to resection plus chemoradiotherapy, following the tendency at the time of the publication. Diagnosis during the operation may also change the surgical approach. As a practical guideline, if a carcinoma is discovered before operation or even during operation and it is suspected to be a superficial cancer, the diverticulum must be resected and frozen sections obtained for confirmation. A diverticulectomy is the sole treatment in these cases since several authors pointed that excellent results can be obtained with diverticulectomy only in superficial cancers.^{24,25,28,62} If an advanced carcinoma is suspected, an esophagectomy should be performed.

We recommend long-term follow in treated and non-treated patients. Siddiq and Sood reported that 75% of the UK otolaryngologists follow patient for less than 6 months and only 5% follow patients for over 1 year.

References

- Hoghooghi D, Coakley F V, Breiman R S, Qayyum A, Yeh B M. Frequency and etiology of midesophageal diverticula at barium esophagography. *Clin Imaging* 2006; 30: 245–7.
- Watanabe S, Matsuda K, Arima K *et al.* Detection of subclinical disorders of the hypopharynx and larynx by gastrointestinal endoscopy. *Endoscopy* 1996; 28: 295–8.
- Thomas M L, Anthony A A, Fosh B G, Finch J G, Maddern G J. Oesophageal diverticula. *Br J Surg* 2001; 88: 629–42.
- Sen P, Kumar G, Bhattacharyya A K. Pharyngeal pouch: associations and complications. *Eur Arch Otorhinolaryngol* 2006; 263: 463–8.
- Honda H, Kume K, Tashiro M *et al.* Early stage esophageal carcinoma in an epiphrenic diverticulum. *Gastrointest Endosc* 2003; 57: 980–2.
- Kimura H, Konishi K, Tsukioka Y *et al.* Superficial esophageal carcinoma arising from the diverticulum of the esophagus. *Endoscopy* 1997; 29: S53–4.
- Stevens D J. Carcinoma of the pharyngeal pouch. *J Laryngol Otol* 1989; 103: 695–7.
- Herbella F A, Oliveira D R, Del Grande J C. Are idiopathic and Chagasic achalasia two different diseases? *Dig Dis Sci* 2004; 49: 353–60.
- Lai S T, Hsu C P. Carcinoma arising from an epiphrenic diverticulum: a frequently misdiagnosed disease. *Ann Thorac Cardiovasc Surg* 2007; 13: 110–3.
- Turner M J. Carcinoma as a complication of pharyngeal pouch. *Br J Radiol* 1963; 36: 206–10.
- Sparks J V. Report of a case of pharyngeal diverticulum containing a neoplasm in its walls. *Br J Radiol* 1933; 6: 233–6.
- Soares R, Herbella F A, Prachand V N, Ferguson M K, Patti M G. Epiphrenic diverticulum of the esophagus. From pathophysiology to treatment. *J Gastrointest Surg* 2010; 14: 2009–15.
- Jordan P H Jr, Kinner B M. New look at epiphrenic diverticula. *World J Surg* 1999; 23: 147–52.
- Castrucci G, Porziella V, Granone P L, Picciocchi A. Tailored surgery for esophageal body diverticula. *Eur J Cardiothorac Surg* 1998; 14: 380–7.
- Nehra D, Lord R V, DeMeester T R *et al.* Physiologic basis for the treatment of epiphrenic diverticulum. *Ann Surg* 2002; 235: 346–54.
- Rizzetto C, Zaninotto G, Costantini M *et al.* Zenker's diverticula: feasibility of a tailored approach based on diverticulum size. *J Gastrointest Surg* 2008; 12: 2057–64.
- Herbella F A, Matone J, Del Grande J C. Eponyms in esophageal surgery, part 2. *Dis Esophagus* 2005; 18: 4–16.
- Vinson P P. Simultaneous occurrence of multiple lesions in the esophagus. report of three cases. *Arch Otolaryngol* 1927; 5: 502–6.
- Pitt G N. Epithelioma in an esophageal pouch. *Trans Pathol Soc Lond* 1896; 47: 44.
- Mackay I S. The treatment of pharyngeal pouch. *J Laryngol Otol* 1976; 90: 183–90.
- Kay E B, Cross F S. Chronic esophagitis. A possible factor in the production of carcinoma of the esophagus. *AMA Arch Intern Med* 1956; 98: 475–81.
- Dunhill T. Pharyngeal diverticulum. *Br J Surg* 1950; 37: 404–15.
- Lindskog G E, Stern H. Diverticulum of the esophagus. *Yale J Biol Med* 1954; 26: 285–94.
- Dionigi G, Sessa F, Rovera F, Boni L, Carrafiello G, Dionigi R. Ten year survival after excision of squamous cell cancer in Zenker's diverticulum: report of a case. *World J Surg Oncol* 2006; 28: 17.
- Huang B S, Unni K K, Payne W S. Long-term survival following diverticulectomy for cancer in pharyngoesophageal (Zenker's) diverticulum. *Ann Thorac Surg* 1984; 38: 207–10.
- Kerner M M, Bates E S, Hernandez F, Mickel R A. Carcinoma-in-situ occurring in a Zenker's diverticulum. *Am J Otolaryngol* 1994; 15: 223–6.
- Juby H B. The treatment of pharyngeal pouch. *J Laryngol Otol* 1969; 83: 1067–71.
- Baraka M E, Sadek S A. Carcinomatous changes in pharyngeal diverticula. *J Laryngol Otol* 1985; 99: 297–9.
- Wychulis A R, Gunnlaugsson G H, Clagett O T. Carcinoma occurring in pharyngoesophageal diverticulum: report of three cases. *Surgery* 1969; 66: 976–9.
- Hoover W B. Carcinoma associated with esophageal diverticulum. *Surg Clin North Am* 1945; 25: 707–12.
- Siddiq M A, Sood S. Current management in pharyngeal pouch surgery by UK otorhinolaryngologists. *Ann R Coll Surg Engl* 2004; 86: 247–52.
- Zitsch R P, O'Brien C J, Maddox W A. Pharyngoesophageal diverticulum complicated by squamous cell carcinoma. *Head Neck Surg* 1987; 9: 290–4.
- Riberi A, Battersby J S, Vellios F. Epidermoid carcinoma occurring in a pharyngoesophageal diverticulum. *Cancer* 1955; 8: 727–30.
- Acharya A, Jennings S, Douglas S, Mirza S, Beasley N. Carcinoma arising in a pharyngeal pouch previously treated by endoscopic stapling. *Laryngoscope* 2006; 116: 1043–5.
- Jensen B M, Kruse-Andersen S, Andersen K. Carcinoma in a pharyngeal diverticulum. *J Clin Gastroenterol* 1989; 11: 119.

- 36 Brücher B L D M, Sarbia M, Oestreicher E *et al.* Squamous cell carcinoma and Zenker diverticulum. *Dis Esophagus* 2007; 20: 75–8.
- 37 Bullock W K, Snyder E N Jr. Carcinoma in situ occurring in a pharyngeal diverticulum. *Cancer* 1952; 5: 737–9.
- 38 Pierce W S, Johnson J. Squamous cell carcinoma arising in a pharyngoesophageal diverticulum. *Cancer* 1969; 24: 1068–70.
- 39 Garlock J H, Richter R. Carcinoma in a pharyngoesophageal diverticulum. *Ann Surg* 1961; 154: 259–62.
- 40 Burton M J, Lund W S. Pharyngeal pouch carcinoma: two unusual cases. *J Laryngol Otol* 1990; 104: 821–3.
- 41 Lieberson M, Riese K T. Carcinoma in a large pharyngo-esophageal diverticulum. *Gastroenterology* 1960; 38: 817–20.
- 42 Fischer M J, Bond J F. Carcinoma in a pharyngoesophageal diverticulum. *J Thorac Cardiovasc Surg* 1967; 53: 500–3.
- 43 Som M L, Deitel M. Carcinoma in a large pharyngo-esophageal diverticulum. *Arch Surg* 1967; 94: 35–8.
- 44 Johnson J T, Curtin H D. Carcinoma associated with Zenker's diverticulum. *Ann Otol Rhinol Laryngol* 1985; 94: 324–5.
- 45 Zonneville J A, Waldeck K J, Hamming J J. Carcinoma in situ in a pharyngo-oesophageal diverticulum. *Neth J Surg* 1981; 33: 94–7.
- 46 Rojas F A, Szymanowski R T, Fujita S. Zenker's diverticulum – carcinoma of the esophagus? *J Otolaryngol* 1979; 8: 266–70.
- 47 Bradley P J, Kochar A, Quraishi M S. Pharyngeal pouch carcinoma: real or imaginary risks? *Ann Otol Rhinol Laryngol* 1999; 108: 1027–32.
- 48 Nanson E M. Carcinoma in a long-standing pharyngeal diverticulum. *Br J Surg* 1976; 63: 417–9.
- 49 Bowdler D A, Stell P M. Carcinoma arising in posterior pharyngeal pulsion diverticulum (Zenker's diverticulum). *Br J Surg* 1987; 74: 561–3.
- 50 Capps F C W, Dunhill T P. Squamous cell carcinoma occurring in pouch. *Br J Surg* 1933; 20: 689.
- 51 Kune G A. Carcinoma in a pharyngeal pouch five year survival after resection. *Aust NZ J Surg* 1972; 41: 249–50.
- 52 Case records of the Massachusetts General Hospital, case 26032. *N Engl J Med* 1940; 222: 113–6.
- 53 Chaurasia M K, Grier A M, Brodie S W. Development of carcinoma in retro-pharyngeal diverticulae. *J R Coll Surg Edinb* 1987; 32: 380–2.
- 54 Razin E, Adler R H. Association of benign esophageal tumors and diverticula. *NY State J Med* 1962; 62: 2554–9.
- 55 Cassivi S D, Deschamps C, Nichols F C 3rd, Allen M S, Pairolero P C. Diverticula of the esophagus. *Surg Clin North Am* 2005; 85: 495–503.
- 56 do Nascimento F A, Lemme E M, Costa M M. Esophageal diverticula: pathogenesis, clinical aspects, and natural history. *Dysphagia* 2006; 21: 198–205.
- 57 Song Y C, Zhang Y D, Wang Q Z *et al.* Carcinoma in the esophageal diverticulum. *Chin Med J (Engl)* 1985; 98: 895–8.
- 58 Avisar E, Luketich J D. Adenocarcinoma in a mid-esophageal diverticulum. *Ann Thorac Surg* 2000; 69: 288–9.
- 59 Nese G. Benign tumours and cysts of the esophagus. *Acta Chir Scand* 1958; 114: 165–71.
- 60 Dillow B M, Neis D D, Sellers R D. Leiomyoma of the esophagus. *Am J Surg* 1970; 120: 615–9.
- 61 Allen T H, Clagett O T. Changing concepts in the surgical treatment of pulsion diverticula of the lower esophagus. *J Thorac Cardiovasc Surg* 1965; 50: 455–62.
- 62 Plous E, Freedman J, Wolf P L. carcinoma within a lower esophageal (epiphrenic) diverticulum. *J Thorac Cardiovasc Surg* 1964; 47: 129–32.
- 63 Saldana J A, Cone R O, Hopens T A, Bannayan G A. Carcinoma arising in an epiphrenic esophageal diverticulum. *Gastrointest Radiol* 1982; 7: 15–8.
- 64 Zinner E. Carcinoma within an epiphrenic diverticulum. *Bull Gastrointest Endosc* 1963; 10: 14–6.
- 65 Thomas R C. Carcinoma in epiphrenic diverticula. *Ann Thorac Surg* 1968; 6: 85–7.
- 66 Schultz S C, Byrne D M, De Cunzio P, Byrne W B. Carcinoma arising within epiphrenic diverticula. A report of two cases and review of the literature. *J Cardiovasc Surg (Torino)* 1996; 37: 649–51.
- 67 Conklin J H, Singh D, Katlic M R. Epiphrenic esophageal diverticula: spectrum of symptoms and consequences. *J Am Osteopath Assoc* 2009; 109: 541–3.
- 68 Shin M S. Primary carcinoma arising in the epiphrenic esophageal diverticulum. *South Med J* 1971; 64: 1022–4.
- 69 Gawande A S, Batiuchok W, Barman A A, Mule J E. Carcinoma within lower esophageal (epiphrenic) diverticulum. *NY State J Med* 1972; 72: 1749–51.
- 70 Goodman H I, Parnes I H. Epiphrenic diverticula of the esophagus. *J Thorac Surg* 1952; 23: 145–59.
- 71 Guerra J M, Zuñil M, Garcia I, Moreno E. Epiphrenic diverticula, esophageal carcinoma and esophagopleural fistula. *Hepatogastroenterology* 2001; 48: 718–9.
- 72 Philippakis M, Karkanas G G, Sakorafas G H. Carcinoma within an epiphrenic esophageal diverticulum. Case report. *Eur J Surg* 1991; 157: 617–8.
- 73 Bonavina L, Segalin A, Rosati R, Pavanello M, Peracchia A. Surgical therapy of esophageal leiomyoma. *J Am Coll Surg* 1995; 181: 257–62.
- 74 Ben-Menachem Y, Akhtar M, Duke J H Jr, Harberg B L. Angiographic characteristics of esophageal leiomyoma. *AJR Am J Roentgenol* 1977; 128: 479–82.
- 75 Hamilton S. Esophageal leiomyoma arising in an epiphrenic diverticulum. *Eur J Radiol* 1988; 8: 118–9.
- 76 Göthlin J, Bloch R, Sundgren R. Intraepiphrenic esophageal leiomyoma associated with diverticula preoperatively diagnosed by angiography. *Acta Radiol Diagn (Stockh)* 1975; 16: 673–8.
- 77 Hoyne R M, Rogers J C T. Esophageal fibromyoma associated with diverticulum. *Am J Surg* 1951; 81: 592–4.
- 78 Stewart J D Jr. Myoma of the esophagus with associated diverticula. *Arch Pathol* 1931; 12: 77–84.
- 79 Hodge G B. Esophageal leiomyoma associated with an epiphrenic diverticulum and hiatus hernia. *Am Surg* 1970; 36: 538–43.
- 80 Herter B, Dittler H J, Wuttge-Hannig A, Siewert J R. Intramural pseudodiverticulosis of the esophagus: a case series. *Endoscopy* 1997; 29: 109–13.
- 81 Plavsic B M, Chen M Y, Gelfand D W *et al.* Intramural pseudodiverticulosis of the esophagus detected on barium esophagograms: increased prevalence in patients with esophageal carcinoma. *AJR Am J Roentgenol* 1995; 165: 1381–5.
- 82 Leeuwenburgh I, Scholten P, Alderliesten J *et al.* Long-term esophageal cancer risk in patients with primary achalasia: a prospective study. *Am J Gastroenterol* 2010; 105: 2144–9.
- 83 Zaninotto G, Rizzetto C, Zambon P, Guzzinati S, Finotti E, Costantini M. Long-term outcome and risk of oesophageal cancer after surgery for achalasia. *Br J Surg* 2008; 95: 1488–94.
- 84 Cheng H, Ren H, Yu H, Zhang Z, Li Z. Esophageal diverticulum associated with carcinoma of the esophagus—a report of four cases. *Chin Med Sci J* 1991; 6: 244–6.