Oesophagectomy for Carcinoma Esophagus - Peshawar Experience of 270 cases in 4 years

A BILAL A BASEER T NISHTAR* MMUSLIM MSALIM MSNABI VASLAM F MAJEED Department of Cardiothoracic Surgery & Radiotherapy*, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar Correspondence to Dr. Amer Bilal, Associate Professor

Objective: To audit the results of 270 Oesophagectomies done for Carcinoma Oesophagus over a 4 year period. Material & methods: This observational descriptive study was conducted at Department of Cardiothoracic Surgery, Lady Reading Hospital and Khyber Medical Centre Peshawar from Sep 2002 to Sep 2006. Computerized clinical data of 270 cases of Oesophagectomy for Carcinoma Oesophagus was retrospectively analyzed. All patients had apart from routine investigations, Barium studies, Endoscopy and biopsy, CT Thorax/Upper abdomen with Oral and I/V Contrast and Abdominal ultrasound. Detailed examination of clinical record was made to determine the surgical outcome. Results: Out of 270 cases 189 were Males 81 were Females with a mean age of 51.6 years. The age range was 17-80 years. In out of two hundred and seventy cases one hundred and sixty two (162/270) (60%) cases had lower one third tumors, one hundred and five (105/270) (38.88%) cases had middle one third tumors while three (3/270) (1.11%) tumors were just below the thoracic inlet. Of the one hundred and sixty two lower one third tumors stomach involvement was present in eighty one (81/162) (30%) cases. Adenocarcinoma was present in one hundred and seventeen (117/270) (43.33%) cases, Squamous cell carcinomas was present in one hundred and forty four (144/270) (53.33%), Adenosquamous was six (6/270) (2.22%), Carcinoma in situ was two (2/270) (0.74%) and Leiomyoma was one (1/270) (0.370%). Morbidity was 28/270 (10.370%) and comprised anastomotic leaks 09, aspiration pneumonia 06, wound infection 03, hoarseness 03, and strictures 03,. Thirty day mortality was 14/270(5.185%) and included aspiration pneumonia-respiratory failure 02, myocardial infarction 03, anastomotic leak 03, tracheal injury 02 and presumed pulmonary embolism 04. Conclusion: Two hundred and seventy cases in four years is a very high volume of Oesophageal work load for malignancy. Our morbidity of 10.370% and mortality of 5.18% shows that such major operations can be done safely in thoracic centers.

Key words: CA oesophagus, oesophagecotmy,. Peshawar experience

Carcinoma of the esophagus comprises the vast majority of malignant tumors and represents the seventh most common malignancy world wide, with its incidence reaching endemic proportions in specific geographic locations in Asia and Africa¹.

One of the major developments in the surgical therapy of the oesophageal cancer has been the marked reduction in surgical morbidity and mortality as a result of staging technique, patient selection and support system^{2, 3,4}.

The modern staging of carcinoma of the Oesophagus is based on the tumor/node/metastasis (TNM) classification developed by the American Joint Committee on cancer⁵. Imaging modalities used in Oesophageal cancer staging include Computed Tomography (CT), Endoscopic Ultrasonography (US), Fluorine 18 Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) and techniques that involve minimally invasive Surgery, such as Laparoscopy and Thoracoscopy^{6,7,8}.

PET/CT is now the favored modality along with preoperative Laparoscopy during which Feeding Jejunostomy is also placed. However, we do not have access to these modalities and the main stay of our preoperative staging remains CT Thorax/Upper Abdomen. Czerny performed the first resection for carcinoma of the Oesophagus in 1877.

Attempts at resection of the intrathoracic Oesophagus were stymied by the inevitable catastrophic Pneumothorax and Mediastinal tamponade before the introduction of Positive Pressure Ventilation. Nonetheless the first successful Transthoracic Oesophagectomy was performed in New York by Franz Torek (1913) before the advent of Intratracheal Ventilation. Subsequent attempts by other Surgeons met with catastrophic consequences for a variety of reasons including severe Intrathoracic anastomotic dehiscence. In the ensuing decades, advances in the evaluation of esophageal resection and reconstruction were made by pioneering thoracic surgeon such as Sweet and Belsy. ¹⁰ In 1978 Orringer and Sloan reported their experience with Transhiatal Oesophagectomy. ¹¹

Resection of the Thoracic Oesophagus can be accomplished with a variety of surgical approaches. The commonly used approach for Tumor of lower two thirds of Thoracic Oesophagus is a right Thoracotomy and Laparotomy as initially proposed by Lewis. A modification was proposed by McKeown whereby an additional cervical incision allows the anastomosis to be performed in the neck. Historically Tumors of the distal Oesophagus and Cardia have been approached through a variety of left chest incisions 12.

The commonly used is a left Thoracotomy and Trans diaphragmatic approach to the abdomen while others advocate left Thoracolaprotomy, thus mobilization of the stomach is greatly facilitated. Resection of the intrathoracic esophagus may be accomplished through a transhiatal approach with an upper abdominal and cervical incision. Transhiatal Oesophagectomy is best suited for the

Tumors of the Cardia but is also used for resection of the Intrathoracic Oesophagus¹³. We audited on 270 cases in 4 years at Lady Reading Hospitals and Khyber Medical Centre Peshawar using left thoracolaparotomy and left neck anastomosis to evaluate and assess ourselves.

Materials and methods

From Sep 2002 to Sep 2006 a retrospective descriptive analysis was done of 270Oesophagectomies done at Lady Reading Hospital and Khyber Medical Centre (189 were males and 81 were females with a mean age of 51.6 years. The age range was 17-80 years). Of these 219 were done at Lady Reading Hospital and 51 at Khyber Medical Center.

The data base included data regarding all age, sex and preoperatively staging .All those with inoperable tumors on preoperative assessment (clinical examination, general fitness, Barium, Endoscopy & histology, CT Thorax/Upper Abdomen, Abdominal ultrasound) and unfit for surgery were excluded from the study. Similarly those found irresectable on operative table were excluded as well. All patients had apart from routine investigations, Barium studies, Endoscopy and biopsy, CT Thorax/ Upper abdomen with oral and I/V contrast and abdominal ultrasound. Protocols for CT thorax/upper abdomen for preoperative staging of carcinoma Oesophagus were discussed with Radiologists and consensus was built on giving oral and I/V contrast, with fine cuts at the level of tumor, and again at the level of pancreas but in the prone position to better visualize the pancreas.

All those considered resectable were than referred for anesthetic opinion and those who were finally declared fit were booked for surgery. Those found irresectable operatively were excluded. All patients had left Thoracolaprotomy with left neck anastomosis except for two cases. Of these two, one had a Mc Keown three stage procedure because of a suspicious nodule in right middle lobe which turned out to be a hydatid cyst and another one who also underwent Mc Keown along with right Decortication because of right Empyema subsequent to iatrogenic perforation by Endoscopist.

Post operatively all patients were kept in thoracic intensive care unit for 24 hours, then shifted to high dependency unit for 72 hours and finally discharged on seven post operative day. They were all seen as a out door patient after two weeks with the histology result of resected specimen and then followed up at gradually increasing intervals. The hospital records and operation reports of these patients were carefully analyzed for demographic features.

Results

Out of 270 cases 189 were Males 81 were Females with a mean age of 51.6 years. The age range was 17-80 years. In out of two hundred and seventy cases one hundred and sixty two (162/270) (60%) cases had lower one third tumors, one hundred and five (105/270) (38.88%) cases

had middle one third tumors while three (3/270)(1.11%) tumors were just below the thoracic inlet. Of the one hundred and sixty two lower one third tumors stomach involvement was present in eighty one (81/162) (30%) cases. Adenocarcinoma was present in one hundred and seventeen (117/270) (43.33%) cases, Squamous cell carcinomas was present in one hundred and forty four (144/270) (53.33%), Adenosquamous was six (6/270) (2.22%), Carcinoma in situ was two (2/270) (0.74%) and Leiomyoma was one (1/270) (0.370%) (Table 1). Morbidity was 28/270 (10.370%) and comprised anastomotic leaks 09, aspiration pneumonia 06, wound infection 03, hoarseness 03, and strictures 03(Table II). Thirty day mortality was 14/270(5.185%) and included aspiration pneumonia-respiratory failure 02, myocardial infarction 03, anastomotic leak 03, tracheal injury 02 and presumed pulmonary embolism 04 (Table III).

Table 1:	Preoperative	date of patients	(n-270)

Variables	=n	
Sex	189	
Male	181	
Female		
Age		
Male <40	80	
Male >40	109	
Female <40	27	
Female >40	54	
Clinical presentation		
Progressive dysphagia	250	
Weight loss	230	
Level		
Upper third	03	
Middle third	105	
Lower third	162	
Histology		
Squamous cell carcinoma	144	
Adenocarcinoma	117	
Adenosquamous	06	
Carcinoma in situ	02	
Leiomyoma	01	

Table II: Morbidity 28/270 (10.370%)

Complication	=n	%age	
Anastomotic leak	09	3.33	
Hoarseness	03	1.11	
Aspiration	06	2.22	
Stricture	07	2.59	
Wound infection	03	1.11	

Table 3: Mortality 14/270 (5.185%)

Complication	=n	%age	
Respiratory failure	02	0.74	
Pulmonary embolism	04	1.48	
Aspiration pneumonia	03	1.11	
Myocardial infarction	03	1.11	
Tracheal injury	02	0.74	

Discussion

In North America squamous cell carcinoma of the esophagus represents 1.5 to 2% of all cancers and approximately 5 to 7 % of all gastrointestinal neoplasms. Geographic variation in incidence is striking. Even at the level of world areas, a 15 fold increase exists between high risk Southern African men and low risk Western African men¹⁴. According to Parkin and associates (1999) other areas of relatively high risk are eastern Africa, South America and South Asia. In certain small geographic areas throughout the world the incidence has almost reached epidemic proportion¹⁵. In China near the Southern mountain range, cancer of the Oesophagus is the most common cause of death, an incidence of more than 130/100000 person¹⁶. In our study we noticed high incidence of esophageal cancer among patients either belonging to Afghanistan or Afghan living in Pakistan. A high incidence belt exists starting from Caspian Sea, extending towards Iran, Afghanistan, North West Frontier of Pakistan and further in the mountains of China 17,18. Hot fluids (Qahwa), contaminated spring water and snuff have been postulated to be the cause in Afghans. However this needs to be studied scientifically and is the subject of an ongoing study.

No unanimity of opinion exists as to what is the best operation for the removal of a cancer of the esophagus. Each surgeon or surgical group has a procedure or procedure of choice for removing tumors at various locations of the thoracic esophagus^{1, 2}. The controversy as to which is the best operation probably will not be resolved and may as well be of little importance3, 4. Standard Trans thoracic Oesophagectomy is performed through either a right or left Thoracotomy depending on the location of the tumour¹⁹. Lesions of the distal Oesophagus and Gastric Cardia have been approached through a variety of left chest incisions which vary in the degree to which they extend into the abdomen. Upper two third of Oesopahgus are most directly approached through a right thoracotomy usually in the fifth interspace. After a standard Transthoracic Oesophageal resection the mobilized stomach is positional in the original esophageal bed. The posterior Mediastinum is the preferred position, because it is shortest and most direct route between neck and Abdominal cavity and if subsequent anastomotic dilation is required it is usually easy to carryout Endoscopy and dilatation. Transhiatal Oesophagectomy is best reserved for patients in whom palliation is clearly the objective of treatment because of the advanced stage of the disease or the presence of serious co morbidity²⁰. Proponents of Transhiatal Oesophagectomy maintain that overall survival rates are not significantly different than standard Transthoracic resection, in patient without nodal metastasis. Critics of Transhiatal Oesophagectomy however argue that a complete Lymphadenectomy is a necessary component of resection for curative purposes.

through Advantages of our approach Thoracolaprotomy were that there was adequate exposure of Oesophagus and Stomach. Feeding jejunostomy tube was placed with ease. It is a natural source of nutrition, cheaper than TPN and not associated with metabolic and septic complications which occur with TPN. There was no need for gastric drainage procedure, as due to vertical position of the stomach chances of gastric stasis are markedly reduced. Due to neck anastomosis there is no fear of mediastinitis. The other advantages of a neck anastomosis are (i) it is technically easier to do then an intrathoracic anastomosis and (ii) you get very generous tumor free margin, resulting in adequate clearance and less chances of recurrence. Finally our results in terms of morbidity and mortality are comparable with other studies²¹.

Squamous cell carcinoma is the most common malignant tumor of the body of the Esophagus and represents more than 95% of esophagus malignancies some series^{22,12}. Primary Adenocarcinoma is rare, less than 1% to 7% of esophageal malignancies. The common glandular Tumor is an Adenocarcinoma that arises in the columnar Epithelium of Barrett's esophagus which represents 86% of all Adenocarcinoma in one series⁴. In our study 144/270 (53.33%) patients had squamous cell carcinoma whereas Adenocarcinoma was reported in 117/270 (43.33%) patients. Adenosquamous cell carcinoma was reported in 6/270(2.22%) patients. Lower third Oesophagus was involved in 162/270 (60%) patients, while middle third tumor was reported in 105/270 (38.88%) patients. In three cases (03/270)(1.11%) the tumor was just below the thoracic inlet.

Several complex surgical procedures have reduced mortality when they are performed at high volume centers. Hospitals that perform a high volume of Oesophagectomies have better results with early clinical outcomes and marked reductions in mortality compared with low volume hospitals⁸. We have the highest number of patients being operated during two years period when compared with other national studies ^{8, 10}. Our 30 day mortality was 5.185%.

As the Vagi are divided, most surgeons perform some form of a gastric drainage procedure. However most of them are doing an Ivor Lewis procedure with anastomosis in right chest, or a transhiatal ^{10, 11, 12}. In our series, with our technique of left Thoracolaprotomy and left neck anastomosis, we did not do any drainage procedure. The rational behind it was that when an adequately mobilized stomach is brought up, under vision to be comfortably anastomized in the neck, it is converted into a vertical tube, which empties by gravity. In our follow-up one month to 27 months no adverse effects regarding gastric stasis were observed ^{23, 24,25}. In other series stasis after vagotomy ranges from 0–37% ^{7,9}, but was relieved after 3 months ^{7,9}

We routinely placed a jejunostomy feeding tube in all our patients, using a 14F rubber tube secured in place with a Wetzel maneuver. The relatively few potential complications are far out weighed by its advantages i.e. facilitation of early ambulation, supplemental nutritional support and the best means of providing nutrition in the event of an anastomotic disruption 11,12. esophageal replacement with stomach is essentially an upper abdominal operation that requires minimal manipulations of the intestines, postoperative ileus for more than 48-72 hours is unusual. It is therefore possible to begin jejunostomy tube feeding with juices with in 2-3days of the operation and advance to full strength tube feedings soon thereafter, allowing discontinuation of I/V fluids and greater ease of ambulation for the patient as oral intake is being increased. Location and technique of esopahgogastric anastomosis is a subject of much discussion. The site of anastomosis is selected upon the location of primary Tumor and preference of the surgeon. The site of anastomosis becomes an issue when the primary Tumor is in the middle or the lower thoracic esophagus. Should it be in the chest or in the neck? Ribet et al²⁶ reports that a cervical anastomosis provides an average additional Tumor clearance of 3.18cm. Cervical anastomosis avoids the potential hazard of mediastinitis of an intrathoracic anastomosis²⁷. Moreover the inverse between the height of esopahgogastric anastomosis and the degree of subsequent gastro esophageal reflux is well established^{28,29} i.e. low intrathoracic esopahgogastric anastomosis is almost invariably associated with marked gastro esophageal reflux whereas with cervical esopahgogastric anastomosis, considerable gastro esophageal reflux is uncommon. In several studies an anastomosis in the neck has a higher incidence of postoperative leak than does chest placement but the incidence of postoperative mortality is lower if a leak occurs in the neck than in the chest³⁰. The occurrence of an anastomotic leak after oesophagectomy is multifactorial. Blood supply and good surgical technique are the two most important factors in avoiding a leak³¹.

The overall anastomotic leak rate following cervical esopahgogastric anastomosis with the stomach positional in the posterior mediastinum in the original esophageal bed is 7.9%³²¹. The incidence of anastomotic leak in our study was 3.3%. Mathisen et al33 emphasized the techniques of anastomosis 1) Atraumatic handling of tissue, 2) Peservation of blood supply of both esophagus and stomach, 3) Avoidance of tension at the anastomosis, 4) Avoidance of the use of crushing clamps, 5) Cutting the tissues with a sharp knife^{34,35}. In our series cervical anastomosis yielded a proximal and distal tumor free margin in 269/270 cases, circumferential margin was involved in 18 cases while in one case the distal margin (stomach) was involved. Leaks were observed in only 09/270 (3.3%) of which seven responded to conservative treatment, while two died. We routinely used postoperative

adjuvant therapy in all our patients. Preoperative down staging of tumors is an important modality, which is the subject of another ongoing study, but such patients were not included in this study.

Conclusion

Our series of 270 Oesophagectomies in four years in one centre is one of the largest in national as well as international literature. Thoracolaprotomy with left neck anastomosis in the hands of a trained thoracic surgeon with appropriate anesthesia and intensive care unit, we find it the best treatment option and feeding jejunostomy is a safe, cheap and effective mode of nutrition for these patients.

References

- Korst RJ, Altorki NK. Esophageal cancer. In: Winchester DP, Daly JM, Jones RS, Murphy GP, editors. Cancer surgery for the general surgeon. Philadelphia: Lippoincott-Raven; 1999.p. 155-72.
- Birkmeyer JD, Siewers AE, Finlayson EVA, et al. Hospital volume and surgical mortality in the united states. N Engl J Med 2002;346:1128-1137.
- 3. Donington JS. Preoperative preparation for esophageal surgery. Thorac surg clin.2005 May; 15 (2):277-85.
- Siewert JR, Holscher AH, Dittler HJ. Preoperative staging and risk analysis in oesophageal carcinoma.
- 5. Hepatogastroentrology. 1990 Aug 37 (4):382-7.
- Greene FL,Page DL, Fleming ID, et al, eds. AJCC Cancer Staging Manual, 6th ed .NewYork:Springer-Veriag,2002
- 7. Whyte RI. Advances in the staging of intrathoracic malignancies. World J Surg 2001; 25:167-173.
- Korst RJ, Altorki NK. Imaging for esophageal tumours. Thorac Surg Clin 2004; 14:61-69.
- Van Westreenen HL, Westerterp M, Bossuyt PM et al. Systematic review of the staging performance of 18 Ffluorodeoxyglucose positron emission tomography in oesophageal cancer. J Clin Oncol 2004;22:3805-3812.
- Nabeya Y, Ochiai T, Matsubara H, Okazumi S, Shiratori T, Shuto K et al. Neoadjuvant chemoradiotherapy followed by esophagectomy for initially resectable squamous cell carcinoma of the esophagus with multiple lymph node metastasis. Dis Esophagus 2005; 15(6): 388 – 97.
- Sujendran V, Sica G, Warren B, Maynard N. Oesophagectomy remains the gold standard for treatment of high-grade dysplsia in Barrett's oesophagus. Eur J Cardiothorac Surg 2005 Nov; 28(5): 763–6.
- 12. Nozoe T, Kakeji Y, Baba H, Maehara Y. Two-field lymph node dissection may be enough to treat patients with submucosal squamous cell carcinoma of the thoracic esophagus. Dis Esophagus 2005; 18(4): 226 9.
- 13. Di Martino N, Izzo G, Cosenza A, Cerullo G, Torelli F, Monaco L et al. Surgical therapy of adenocarcinoma of the esophagogastric junction: analysis of prognostic fctors. Hepatogastroenterology 2005 Jul-Aug; 52(64): 1110 –5.
- 14. Gockel I, Heckhoff S, Messow CM, Kneist W, Junginger T. Transhiatal and transthoracic resection in adenocarcinoma of the esophagus: does the operative approach have an influence on the lung-term prognosis? World J Surg Oncol 2005 Jun 24; 3: 40.

- Zhang X, Watson DI, Jamieson GG, Lally C, Bessell JR, Devitt PG. Outcome of oesophagectomy for adenocarcinoma of the oesophagus and oesophagogastric junction. ANZ J Surg 2005 Jul; 75(7): 513 – 9.
- Deschamps C, Nichols FC 3rd, Cassivi SD, Allen MS, Pairolero PC. Long-term function and quality of life after esophageal resection for cancer and Barrett's. Surg Clin North Am 2005 Jun; 85(3): 649 – 56.
- Lee SJ, Lee KS, Yim YJ, Kim TS, Shim YM, Kim K. Recurrence of squamous cell carcinoma of the oesophagus after curative surgery: rates and patterns on imaging studies correlated with tumour location and pathological stage. Clin Radiol 2005 May; 60(5): 547 – 54.
- Tachibana M, Kinugasa S, Yoshimura H, Shibakita M, Tonomoto Y, Dhar DK, Nagasue N. Clinical outcomes of extended esophagectomy with three-field lymph node dissection for esophageal squamous cell carcinoma. Am J Surg 2005 Jan; 189(1): 98 – 109.
- Marriete C, Finzi L, Piessen G, Van Seuningen I, Triboulet JP. Esophageal carcinoma: prognostic differences between squamous cell carcinoma and adenocarcinoma. World J Surg 2005 Jan; 29(1): 39-45.
- D'Journo XB, Doddoli C, Michelet P, Loundon A, Trousse D, Giudicelli R, Fuentes PA, Thomas PA. Transthoracic esophagectomy for adenocarcinoma of the oesophagus: standard versus extended two-field mediastinal lymphadenopathy? Eur J Cardiothorac Surg 2005 Apr; 27(4): 697 704.
- 21. Fujita H, Sueyoshi S, Tanaka T, Tanaka Y, Matono S, Mori N et al. Esophagectomy: is it necessary after chemoradiotherapy for a locally advanced T4 esophageal cancer? Prospective nonrandomized trial comparing chemoradiotherapy with surgery versus without surgery. World J Surg 2005 Jan; 29(1): 25 30.
- Maliasrie SC, Untch B, Aranha GV, Mohideen N, Hantel A, Pickleman J. Neoadjuvant chemoradiotherapy for locally advanced esophageal cancer: experience at a single institution. Arch Surg 2004 May; 139(5): 532 – 8.
- 23. Donington JS, Miller DL, Allen MS, Deschamps C, Nichols FC 3rd, Pairolero PC. Preoperative chemoradiation therapy does not improve early survival after esophagectomy for patients with clinical stage III adenocarcinoma of the esophagus. Ann Thorac Surg. 2004 Apr; 77(4): 1193 8.
- Role of Feeding Jejunostomy in Oesophageal Surgery: Journal of Post Graduate Medical Institute, JPMI, Peshawar Vol. 15, No. 1, 2001.
- One Year Experience of Treating Ca Oesophagus Journal of Post Graduate Medical Institute, JPMI, Peshawar, Vol. 18, No. 3, 2004.

- 26. An experience of 108 cases of Esophagectomy using left Thoracolaparotomy and Cervical Anastomosis with Feeding Jejunostomy, without Gastric Drainage Procedure Annals Journal King Edwards Vol. 10, No. 4, Nov – Dec 2004.
- 27. Koh P, Turnbull G, Attia E, LeBurn P, Casson AG. Functional assessment of the cervical esophagus after gastric transition and cervical esophagusatrotomy. Eur J Cardiothoracic Surg 2004 Apr: 25(4): 480 5.
- Clements DM, Bowrey DJ, Havard TJ. The role of staging investigations for oesophago-gastric carcinoma. Eur J Surg Oncol. 2004 Apr; 30(3): 309 -12.
- Igaki H, Tachimori Y, Kato H. Improved survival for patients with upper and / or middle mediastinal lymph node metastasis of squamous cell carcinoma of the lower thoracic esophagus treated with 3-field dissection. Ann Surg 2004 Apr; 239(4): 483–90.
- Lerut T, Coosemans W, Decker G, De Leyn P, Moons J, Nafteux P, Van Raemdonck. Extended surgery for cancer of the esophagus and gastroesophageal junction. J Surg Res. 2004 Mar; 117(1): 58 – 63.
- Nakagawa S, Kanda T, Kosugi S, Ohashi M, Suzuki T, Hatakkeyama K. Recurrence pattern of squamous cell carcinoma of the thoracic esophagus after extended radical esophagectomy with three-field lymphadenectomy. J Am Coll Surg. 2004 Feb; 198(2): 205–11.
- Rizk NP, Bach PB, Schrag D, Bains MS, Turnbull AD, Karpeh M, Brennan MF, Rusch VW. The impact of complications on outcomes after resection for esophageal and gastroesophageal junction carcinoma. J Am Coll Surg. 2004 Jan; 198(1): 42–50.
- J.B. Dimick, J.A Cowan Jr, G. Ailawadi, R.M. Waines, G. R. Upchurch Jr. National Variation in operative Mortality Rates for Esophageal Resection and Need for Quality Imrpovement. Arch Surg December, 2003; 138(12): 1305 1309.
- D. M. Shahian, S. L. T. Normand. The Volume-outcome relationship: from Luft to Leapfrog Ann Thoracic Surg March, 2003; 75(3): 1048-1058.
- J. B. Dimick, P. J. Pronovost, J. A. Cowan, and P. A. Lipsett. Surgical volume and quality of care for esophageal resection: do high-volume hospitals had fewer complications? Ann Thoracic Surg February, 2003; 75(2): 337-341.
- Elebert Y. Kino, Yu Chiao Chang, Cameron D. Wright. Impact of hospital volume on clinical and economic outcomes for esophagectomy. Ann Thoracic Surg 2001; 72: 1118-1124.