

Esophageal cancer: results of treatment (10 years of experience)

Arnoldas Krasauskas¹,

Saulius Cicėnas¹,

Eugenijus Stratilovas²,

Dainius Amerigas Pišėikas¹,

Romas Mickevičius³,

Juozas Kurtinaitis⁴

¹ *Department of Thoracic Surgery and Oncology, Institute of Oncology, Vilnius University, Vilnius, Lithuania*

² *Department of Abdominal Surgery and Oncology Institute of Oncology, Vilnius University, Vilnius, Lithuanian*

³ *Department of Radiotherapy, Institute of Oncology, Vilnius University, Vilnius, Lithuania*

⁴ *Institute of Oncology, Vilnius University, Vilnius, Lithuania*

Objectives. 1. To evaluate the efficacy of surgical, radiation and palliation treatments for esophageal cancer (EC) patients (pts). 2. To compare median survival (MS) by stages (II, III, IV), method of treatment and gender.

Materials and methods. From 1994 to 2003, 159 pts underwent subtotal esophageal resections in Departments of Thoracic and Abdominal Surgery, Institute of Oncology, Vilnius University. For analysis, we included 116 operated on pts (group 1), 169 pts (group 2) who underwent radical radiation therapy in Department of Radiotherapy, and 98 pts – best supportive care patients because of advanced disease, age or concomitant diseases (group 3).

Results. Median survival after radical esophageal resections were by stages: stage II – 728 days, stage III – 317 days and stage IV – 160 days. MS of group 1 patients after subtotal esophageal resections were 384 days. MS after radical radiation therapy by stages were: stage II – 260 days, stage III – 251 days and stage IV – 183 days. MS in group 2 was 253 days. In group 3 the median survival was only 96 days.

Conclusions. 1. Median survival in group 1 of patients (surgery) was 384 days, in group 2 (radiotherapy) – 253 days and in group 3 (best supportive care) – 96 days. Difference in survival rates after subtotal esophageal resection, radiotherapy and best supportive care was statistically significant between methods of treatment (gr. 1 > gr. 2 > gr. 3). 2. Statistically significant difference in the mode of treatment was for group 1 patients in stage II of EC (728 / 260 days, groups 1 and 2 respectively) and stage III (317 / 251 days groups 1 and 2 respectively). There was no difference in the mode of treatment between groups 1 and 2 in stage IV of the disease (160 and 183 days). 3. By gender, in group 1 the results of MS were very different (366 / 1089 male / female). In group 2 we observed difference of MS by days (249/305 days m / f) with benefit for the female group, but with no statistically significant difference ($p = 0.3972$). No difference by gender between patients in group 3 (95/96 m / f; $p = 0.6719$) was found.

Key words: esophageal cancer, subtotal esophageal resection, median survival, radiotherapy, best supportive care

INTRODUCTION

Esophageal cancer (EC) plays an important role between all malignances in males. The incidence of EC in Lithuania was 4.9 / 100,000 (9.1 / 100,000 in males and 1.2 / 100,000 in females) in 2003 and remains relatively unchanged in the last 10 years (8.1

/ 100,000 in males group and 0.7 / 100,000 in females in 1994) (1). The incidence of EC in the world varies depending on region and race. Highly prevalent regions of EC are Northern China, Iran, Iraq, Southeastern Africa and Northwestern France (> 51 / 100,000) (3). In the other parts of France the incidence of EC varies within 10–19 / 100,000 and is the same as among blacks in the USA. In the UK and Southern Europe the incidence rates remain within 5–9 / 100,000. In Scandinavia, Central, Eastern Europe and among whites in the USA the incidence rates don't reach 5 cases per 100,000 inhabitants.

Correspondence to: A. Krasauskas, Department of Thoracic surgery and Oncology, Institute of Oncology, Vilnius University, Santariøkiø 1, LT-08660 Vilnius, Lithuania, E-mail: arno.k@one.lt

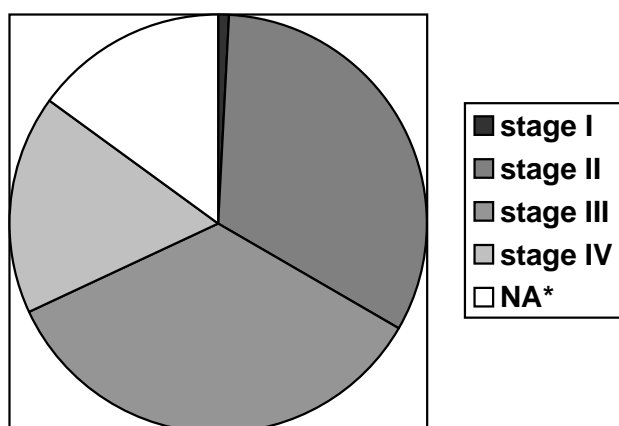


Fig. 1. Esophageal cancer distribution by stages in Lithuania in 2003 (NA – not acceptable for staging)

EC prevails in males (6–7:1): 137–147 new cases in males and 15–22 in females were diagnosed per year in Lithuania (1). Tobacco smoking, concentrate alcohol abuse, nutrition and fat food are the major etiological reasons for development of EC. The highest mortality rate is observed in the 50–65-year age group. Mortality rates per year in Lithuania were 7.3–8.0 / 0.8–1.2 for 100.000 males and females, respectively.

Median 5-year survival data in the world for white patients with EC remain to be 8–15.1% and for black patients only 6–9% (2, 4, 7). Five-year survival in Lithuania varies within 6–8% among males and 9–13% for females. The main cause of these low results is the late manifestation of symptoms: 60–75% of patients are admitted with an advanced stage of the disease (stages III, IV) Figure 1 shows the distribution of EC by stages in 2003 in Lithuania (1).

Radical surgery can be used only for 10–20% of pts and remains to be the principal method of EC treatment; 40–45% of all EC pts are treated by radiation therapy and the other with best supportive care. Both radical treatments cause some complications (25–35%), which often become lethal. These problems raise the question: do radical surgery or radiotherapy benefit for EC pts in terms of survival? Our objective was to evaluate the efficacy of surgical, radiation and palliation treatments for EC pts, to compare the median survival (MS) by stages (II, III, IV), method of treatment and gender.

MATERIALS AND METHODS

From 1994 to 2003, of 482 pts treated for EC at the Institute of Oncology, Vilnius University, 383 (79.5%) were included for analysis: 116 operated on pts (group 1), 169 pts, who underwent radical irradiation at Department Radiotherapy (group 2) and 98 pts received best supportive care (group 3).

159 pts underwent subtotal esophageal resections with immediate reconstruction of the food pipe. We

included to group 1 116 pts (73%) – 111 (95.7%) males and 5 (4.3%) females. We performed 91 (78.4%) transthoracal esophageal resections for middle EC localization and for 25 (21.6%) transhiatal esophageal resections the lower part. group 1 of pts by stage: stage I – 4 pts (3.6%), stage II – 29 pts (26.1%), stage III – 62 pts (55.9%) and stage IV – 16 pts (14.4%). 99 pts (85.3%) had squamous cell carcinoma and 17 pts (14.7%) adenocarcinoma.

169 patients were irradiated in group 2: 147 (87%) males and 22 (13%) females. Group 2 of males by stages: stage II – 26 pts (18.4%), stage III – 99 (70.2%) and stage IV – 15 pts (10.6%). Radiotherapy (external beam or in combination with brachytherapy) was a standard non-surgical treatment for localized carcinoma of the esophagus. In treatment planning, three-point setup, 3-D CT and isocentric technique with the patient supine were the basic techniques. The patients were treated with daily fractions of 2.0 Gy, five times per week to a total dose of 66–70 Gy / 33–35 fx / 7 weeks. The irradiation volume was reduced after 40 Gy if the external beam technique was used only and after 54 Gy when the total dose to GTV (Gross Tumor Volume) was escalated by brachytherapy.

98 pts were included groups: 87 males (88.8%) and 11 females (11.2%). These patients were treated symptomatically because of advanced disease, age, performance status or concomitant disease – best supportive care, dilating stricture and insertion of stent or by gastrostomy.

RESULTS

Median survival after radical surgical esophageal resections by stages was: stage II – 728 days, stage III – 317 days and stage IV – 160 days. MS of all group 1 patients after subtotal esophageal resections was 384 days. Male survival rates by stages are shown in Fig. 2. Five-year survival in group 1 was 10.1%.

Survival rates by gender in group 1 are shown in Fig. 3.

Median survival after radical irradiation of males according to stages was: stage II – 260 days, stage III – 251 days and stage IV – 183 days (Fig. 4). Median survival in group 2 was 253 days, five year survival being only 2.9%. To compare, in group 3 median survival was only 96 days.

Survival rates by gender in group 2 are shown in Fig. 5.

Median survival of males in group 1 was 366 days, in group 2 249 days and in group 3 95 days ($p = 0.0001$). Male survival by method of treatment is shown in Fig. 6.

Median survival of females in group 1 was 1089 days group 2 305 days and group 3 96 days ($p = 0.1176$). Survival curves of females by the method of treatment are shown in Fig. 7.

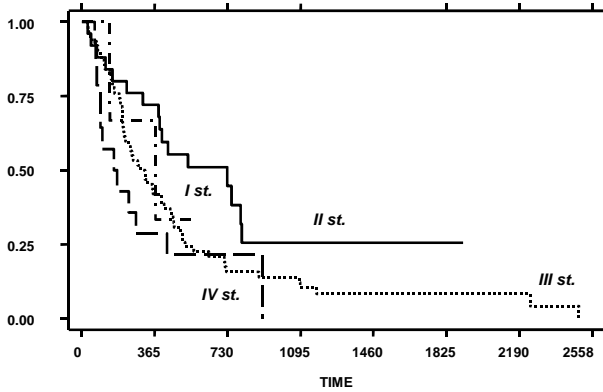


Fig. 2. Survival curves of males by stages in group 1.

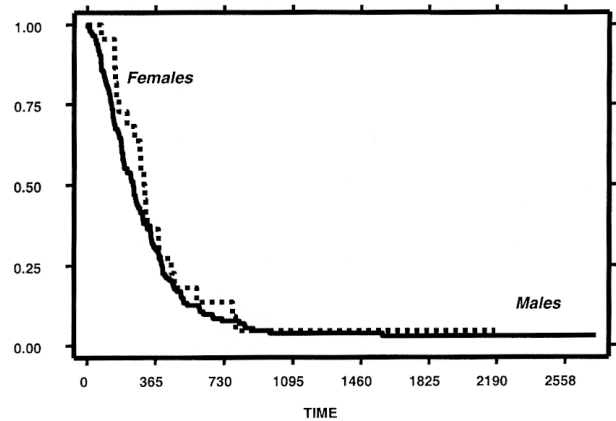


Fig. 5. Survival curves by gender in group 2

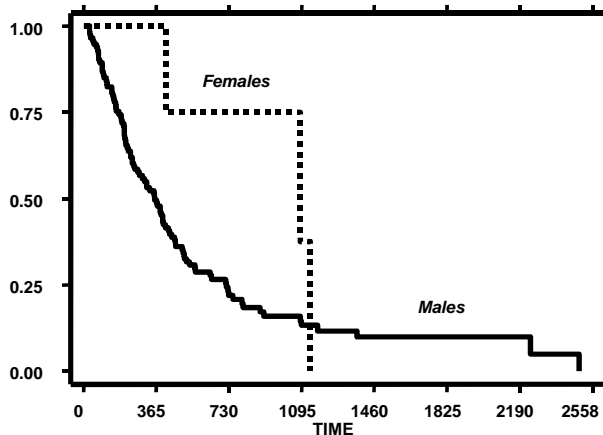


Fig. 3. Survival curves by gender in group 2

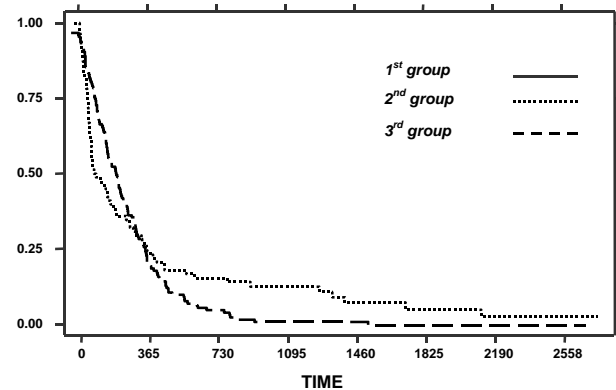


Fig. 6. Survival of males by method of treatment

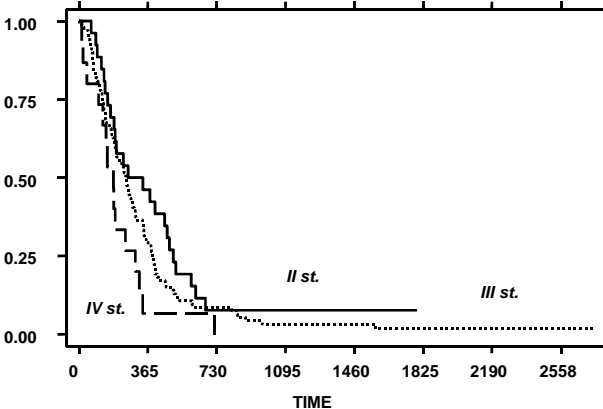


Fig. 4. Survival curves of males by stages in group 2

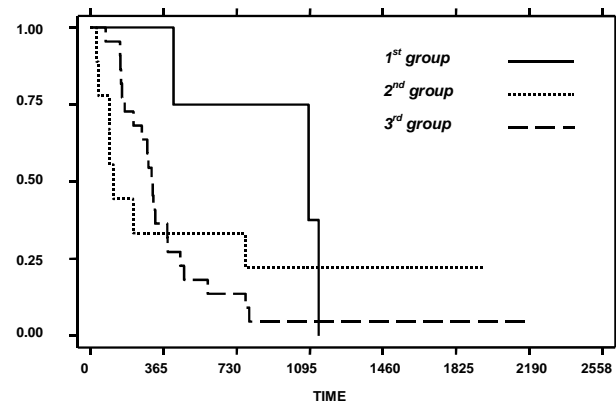


Fig. 7. Survival curves of females by method of treatment

DISCUSSION

This is the first study in Lithuania to establish results of treatment of EC patients who underwent radical and palliation treatment. We evaluated the efficacy of surgical, radiation and palliation treatments for esophageal cancer patients in search of the answer to our main question: Do radical surgery or radiotherapy benefit for EC pts in terms of survival? We compared median survival by stages (II, III and IV), method of treatment and gender. In group 1 median survival was 384 (~13 months) days and 5-year survival 10.1%. These data are lower than tho-

se reported by Collard (2001), Hulscher et al. (2002), Law and Wong (2004), Wayne et al. (2002) (26–39%) (4, 6, 8, 9, 10), possibly because we didn't separate our patients into subgroups by histology and localization. Treatment of the abdominal part of EC (adenocarcinoma) is more successful and with better survival results. In our study, the patients were not divided by surgical approach (transthoracic or transhiatal esophageal resections; with 2- or 3-field lymphadenectomy), because survival benefit was observed for patients with the extended approach and 3-field lymphadenectomy. In group 2 median survival was 253 days and 5-year survival 2.9%. The comprehen-

sive and critical review by Earlam and Cunha-Melo (1980), Hayter et al. (2000), Tak and Naunheim (2004), Ilson (2003) with esophageal cancer treated with radiotherapy alone revealed a 5-year survival rate more than 6% (11–14). Without any doubt, the patients' performance status, local spread of cancer made a major impact on median survival in the group. In our experience, radiotherapy alone can be effective only for palliation of dysphagia for inoperable patients. An objective response was obtained in 91% of patients and palliation of symptoms was observed in 73% of patients in whom radiation therapy improved the quality of life and prolonged the survival period. In patients for whom definitive treatment with curative intent is not possible, palliation can be achieved by radiation therapy in approximately 75%.

A statistically significant difference was found in both groups 1 and 2 for patients with stage I–III of the disease. There was no significant difference between radical therapy and best supportive care (160–183/95–96 days respectively) in stage IV of EC. In the comprehensive reviews by Sihvo et al. and Xinopoulos et al. (2004), the median survival data of palliation-treated patients with esophageal cancer varied within 116–211 days (4, 5). We had in the control group nearly the same results (96 days). Thus, surgical resection remains the main way of treatment of EC (in stage I–III of the disease) against which other modalities should be compared. Radiation therapy alone could be applied only for patients with a lower performance status and in cases of non-advanced esophageal cancer. Stenting or gastrostomy must be applied for palliation purposes only for patients with advanced dysphagia caused by esophageal cancer.

CONCLUSIONS

1. Median survival in group 1 of EC patients (surgery) was 384 days, in group 2 (radiotherapy) – 253 days and in group 3 (best supportive care) 96 days. The differences in survival rates after subtotal esophageal resection, radiotherapy and best supportive care are statistically significant (group 1 > group 2 > group 3).

2. A statistically significant difference in the mode of treatment was found for group 1 patients in stage II of EC (728 / 260 days, groups 1 / 2) and stage III (317 / 251 days, groups 1 / 2). No difference in the mode of treatment between groups 1 and 2 in stage IV of the disease (160 / 183 days) was stated.

3. By gender, in group 1 the results of medium survival (MS) differed greatly (366 / 1089, male / female). In group 2 we observed a difference in MS by days (249 / 305 days, male / female) with benefit for females, but no statistically significant (p

= 0.3972). No difference by gender in third group (95 / 96 male/female; p = 0.6719) was stated.

Received 29 August 2005
Accepted 2 November 2005

References

- Kurtinaitis J, Aleknavičienė B, Tamašauskienė J. Pa grindiniai onkologinės pagalbos rezultatai Lietuvoje. 2003 metai (apskaitos duomenys). Vilnius, 2004.
- Roth JA, Ruckdeschel JC, Weisenburger TH. Thoracic oncology 2nd edition. Philadelphia 1995: 277–439.
- Siewert JR, Stein HJ, Feussener H. Esophageal Cancer. Heidelberg, 2004.
- Sihvo EIT, Luostarinen ME, Jarmo AS. Fate of patients with adenocarcinoma of the esophagus and the esophagogastric junction: a population-based analysis. *Am J Gastroenterol* 2004; 99(3): 419–24.
- Xinopoulos D, Dimitroulopoulos D, Moschandrea I, Skordilis P, Bazinis A, Kontis M, Paraskevas I, Kouroumalis E, Paraskevas E. Natural course of inoperable esophageal cancer treated with metallic expandable stents: quality of life and cost-effectiveness Analysis. *J Gastroenterol Hepatol* 2004; 19(12): 1397–402.
- Collard JM. Exclusive radical surgery for esophageal adenocarcinoma. *Cancer* 2001; 91: 1098–104.
- Silverstein MD, Nietert PJ, Ye Xiaobu, Lackland DT. Access to care and stage at diagnosis for patients with lung cancer and esophageal cancer. Analysis of the Savannah River Region Information System Cancer Registry Data. *South Med J* 2002; 95(8): 900–8.
- Hulscher JBF, van Sandick JW, de Boer AGEM et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med* 2002; 347: 1662–9.
- Law S, Wong J. Therapeutic options for esophageal cancer. *J Gastroenterol Hepatol* 2004; 19(1): 4–12.
- Wayne H, Swisher SG, Correa AM, Hess K, Putnam JB Jr., Ajani JA, Dolormente M, Rhodette F, Komaki RR, Lara A, Martin F, Rice DC, Sarabia AJ, Smythe WR, Vaporciyan AA, Walsh GL, Roth JA. Treatment outcomes of resected esophageal cancer. *Ann Surg* 2002; 236(3): 376–85.
- Hayter CRR, Huff-Winters C, Paszat L, Youssef M, Youssef A, Shelley WE, Schulz K. A prospective trial of short-course radiotherapy plus chemotherapy for patients of dysphagia from advanced esophageal cancer. *Radiotherapy and Oncology* 2000; 56(3): 329–33.
- Tak VM, Naunheim KS. Current status of multimodality therapy for esophageal carcinoma. *J Surg Res* 2004; 117: 22–29.
- Ilson DH. Anti-tumour treatment of oesophageal cancer: new developments in systemic therapy. *Canc Treat Rev* 2003; 29: 525–32.
- Earlam R, Cunha-Melo JR. Oesophageal squamous cell carcinoma: I. A critical review of surgery. *Br J Surg* 1980; 67: 381–90.

**Arnoldas Krasauskas, Saulius Cicėnas,
Eugenijus Stratilatovas, Dainius Amerigas Piðėikas,
Romas Mickeviėius, Juozas Kurtinaitis**

**STEMPLĖS VĖPYS: GYDYMO REZULTATAI (10
METŲ PATIRTIS)**

Santrauka

Tikslai. 1. Ąvertinti stemplės vėþiu (SV) serganėiø ligoniø chirurginio, spindulinio ir simptominio gydymø efektyvumà. 2. Palyginti ligoniø vidutinę gyvenimo trukmę (VGT) pagal SV stadijas, gydymo metodà ir lytà

Tyrimø objektas ir metodai. Vilniaus universiteto Onkologijos instituto Krūtinių ir Pilvo chirurgijos skyriuose nuo 1994 iki 2003 metų 159 ligoniams buvo atliktos subtotalinės stemplės rezekcijos. Analizei buvo atrinkta 116 (73%) operuotø ligoniø (1-oji grupė), 169 ligoniai (2-oji grupė), kuriems buvo taikoma radikali spindulinė terapija, ir 98 ligoniai, gydyti tik simptomiškai dėl SV išplitimo, amþiaus ar sunkios lydinėios terapinės patologijos (3-ioji grupė).

Rezultatai. Vidutinė gyvenimo trukmė (VGT) 1-oje grupėje pagal stadijas buvo: II st. – 728 d., III st. – 317 d. ir IV st. – 160 d. Operuotø ligoniø VGT buvo 384 d., o penkeriø metų gyvenimo trukmė sudarė 10,1%. Po spindulinio ligoniø gydymo VGT atitinkamai pagal stadijas buvo: II st.

– 260 d., III st. – 251 d. ir IV st. – 183 d. VGT 2-oje grupėje buvo 253 d., o penkeriø metų išgyvenamumas sudarė 2,9%. Treėioje grupėje VGT buvo tik 96 dienos, o penkerius metus išgyvenusiø ligoniø nebuvo.

Išvados. 1. Pirmoje operuotø ligoniø grupėje VGT buvo 384 dienos, 2-oje ðvitintø ligoniø grupėje – 253 dienos ir 3-ioje simptominiø ligoniø grupėje – 96 dienos. Pagal taikytà gydymo metodà apskaiėiuotas statistiškai patikimas skirtumas tarp operuotø ir ðvitintø ligoniø grupiø bei simptomiškai gydytø ligoniø grupės (1 gr. > 2 gr. > 3 gr.). 2. Statistiškai patikimas skirtumas apskaiėiuotas tarp II st. (728/260 d. 1/2 gr.) ir III st. (317/251 d. 1/2 gr.) stemplės vėþiu serganėiø ligoniø. VGT nesiskyrė tarp 1-os ir 2-os tiriamøjø grupiø IV st. SV serganėiø ligoniø (160/183 dienos atitinkamai). 3. Pirmoje grupėje pagal lytà apskaiėiuoti labai skirtingi VGT rezultatai (366/1089 vyr./mot.), taėiau statistiškai nevertinti dėl maþo moterø skaiėiaus (111 vyr./ 5 mot.). Antroje grupėje SV serganėiø ligoniø VGT rezultatui pagal dienas išsiskyrė (249/305 dienos v/m), taėiau statistiškai patikimo skirtumo nebuvo ($p = 0,3972$). Nebuvo jokio VGT skirtumo ir tarp simptomiškai gydytø vyrø bei moterø kontrolinėje grupėje (95/96 v/m; $p = 0,6719$).

Raktaþodþiai: stemplės vėþys, subtotalinė stemplės rezekcija, spindulinė terapija, simptominis gydymas, vidutinė gyvenimo trukmė