The Effects of Transhiatal and Transthoracic Approaches on Mortality, Morbidity, Hospital Stay and Survey in the Surgical Treatment of Esophageal Cancer

Özofagus Kanseri Cerrahi Tedavisinde Transhiatal ve Transtorasik Yaklaşımların Mortalite, Morbidite, Hastanede Kalış ve Yaşam Süresi Üzerine Etkileri

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ABSTRACT Objective: In this retrospective clinical series we evaluated early postoperative morbidity, mortality, hospital stay and long-term prognosis of the patients with adenocarcinoma of the esophagus that were treated with either the transhiatal (TH) or the transthoracic (TT) operative approaches. **Material and Methods:** 60 cases, which underwent resection via transhiatal (TH) or transthoracic (TT) approach for esophagus cancer between January 2002 and December 2007 in the Gastroenterological Surgery Clinic of Turkiye Yuksek Ihtisas Hospital has been recruited retrospectively in the study. Age, sex, preoperative ASA scoring values, hemoglobin, albumin and CEA values, localization of the tumor, tumor diameter, tumor histopathology, tumor stage, presence of lymph node metastasis, preoperative respiratory functions, preoperative nutrition situations, and anastomosis types are taken into consideration in patients, who have undergone an operation by transhiatal (Group 1) or transthoracic (Group 2) approach. Their early terms of postoperative mortality rates, major morbidity rates, hospital stay and lifetime durations were compared. **Results:** Thirtysix (60%) of the patients were male while 24 (40%) of them female with the average age of 55 (38-78). Twentyeight (%46) of the cases were operated via transhiatal approach and 32 (%54) via transthoracic approach. There were no statistically significant difference in age, preoperative ASA scoring values, tumor localization, tumor diameter and histopathology, tumor stages, and follow-up durations between the groups as well as in terms of early term mortality, major morbidity, hospital stay and lifetime durations ($p>0.05$). **Conclusion:** We conclude that the type of surgical approach does not make any difference on the early term postoperative mortality and major morbidity rates, hospital stay and lifetime durations in esophagus cancers.

Key Words: Esophagus neoplasms; general surgery; esophagectomy

ÖZET Amaç: Bu retrospektif çalışmamızda amacımız, özofagus kanserlerinde transhiatal ve transtorasik yaklaşımların erken dönem postoperatif mortalite, morbidite, postoperatif hastanede kalış ve yaşam süreleri üzerine etkilerini incelemektir. **Gereç ve Yöntemler:** Türkiye Yüksek İhtisas Hastanesi Gastroenteroloji Cerrahisi Kliniğinde Ocak-2002-Aralık 2007 yılları arasında özofagus kanseri nedeniyle transhiatal (TH) ve transtorasik (TT) yaklaşım ile rezeksiyon uygulanan toplam 60 olgu retrospektif olarak çalışma kapsamına alındı. Transhiatal (Grup 1) ve transtorasik (Grup 2) yaklaşımla opere edilen hastalar yaş, cinsiyet, preoperatif ASA skoru, hemoglobin, albümin değerleri, tümör çapı, tümör yerleşimi, tümör histopatolojisi, evre, lenf nodu metastazı varlığı, preoperatif solunum fonksiyonları, preoperatif beslenme durumları, anastomoz tipi açısından incelendi. Postoperatif erken dönem mortalite, majör morbidite oranları, hastanede kalış ve yaşam süreleri karşılaştırıldı. **Bulgular:** Hastaların 36'sı (%60) erkek, 24'ü (%40) kadın olup; yaş ortalaması 55,0 (38-78) idi. 28 olgu (%46) transhiatal yaklaşım ile, 32 olgu (%54) transtorasik yaklaşım ile opere edildi. Gruplar yaş, cinsiyet, preoperatif ASA skoru, preoperatif solunum fonksiyonları, preoperatif hemoglobin ve albümin değerleri, tümör yerleşimi, tümör çapı ve histopatolojik tipi, evre, lenf nodu metastazı varlığı açısından benzerdi ($p>0,05$). Her iki grup arasında erken dönem mortalite, majör morbidite, hastanede kalış süreleri ve yaşam süreleri açısından istatistiksel anlamlı fark saptanmadı ($p>0,05$). **Sonuç:** Özofagus kanserlerinde transhiatal yada transtorasik yaklaşım postoperatif erken dönem mortalite ve majör morbidite oranları ile, hastanede kalış ve yaşam sürelerini değiştirmemektedir.

Anahtar Kelimeler: Özofagus tümörleri; genel cerrahi; özofajektomi

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Esophageal cancer surgery may be the most controversial issue of gastrointestinal oncologic surgery. The patients at advanced or metastatic stage are generally referred to specialized centers. However, only a small number of the patients were appropriate for curative resection in early stage. The discussions are focused and concentrated on these groups of patients. Various surgical procedures are performed for esophageal lesions. The optimal operative approach for esophageal carcinoma remains controversial. The technique for resection is determined depending on tumor localization, the natural course of cancer and the individual preference of the surgeon. For that purpose, transhiatal or transthoracic intervention have been described and used worldwide. Choices are esophageal resection through a right or left thoracotomy or transhiatal blunt esophagectomy without thoracotomy. Transhiatal resection has the advantage of less postoperative morbidity and shorter operation time. Transhiatal esophagectomy is often advocated as the preferred surgical approach in patients with benign or early tumors or localization of lower third of the esophagus. This approach has been criticized because of there were no resection of thoracal lymph nodes with the risk of major vascular or airway injury. In addition some studies indicate that transhiatal approach must be applied meticulously on selected cases with middle esophagus cancers. Transthoracic intervention is more appropriate for esophagus cancers. A very good exposure is provided, tumor may be dissected better from the peripheral tissues and a curative surgical resection can be performed by a complete lymph node dissection.[1,2] In this study, our aim is to compare these two surgical approaches with regard to postoperative mortality, major morbidity, hospital stays and survivals of the patients.

MATERIAL AND METHODS

Total of 60 cases who had been operated for esophagus cancer and undergone resection between years of 2002-2007 were analiyzed retrospectively in the study. All data for the included cases were recorded on prepared esophagus cancer forms and saved on computers for analysis. The detailed physical examination of all patients was performed and their clinical findings, types and durations of the symptoms, risk factors and ASA values were recorded. Preoperative blood samples for hemogram, hemostasis, biochemistry, liver function tests, and tumor markers, and ECG, lung graphics, and respiratory function tests were required routinely. Upper gastrointestinal system endoscopy and biopsy, thoracic and abdominal CT, abdominal USG were done for all patients, and barium graphics of esophagus-stomach-duodenum were performed additionally for some patients. Following the preoperative examinations, tumors without distant organ metastasis and adjacent organ invasion were considered resectable and appropriate for surgery. The cases were examined in two groups, those operated via transhiatal approach (Group 1) and the other operated via transthoracic approach (Group 2). We had 28 (46%) patients in group one and 32 (54%) patients in group two.

The patients in both transhiatal (Group 1) and transthoracic (Group 2) approach groups were evaluated with respect to their age, sex, preoperative ASA scores, preoperative hemoglobin level, albumin and CEA levels, localization of the tumor, tumor histopathology, presence of lymph node metastasis, preoperative respiratory function tests (FVC1), preoperative nutrition status, anastomosis type during operation (using stapler or hand-stitched), early term postoperative mortality rates, major morbidity, hospitalization and lifetime durations. The preference of transhiatal or transthoracic approach was made considering patient condition, tumor localization and individual preference of surgeon. For tumors with upper or middle thoracic localization, transthoracic approach was preferred for safer meditational dissection, whereas transhiatal approach was preferred in cases with tumors localized in the 1/3 distal region and distinctive co morbidity. The tumor clearance was provided macroscopically. Extended lymph node dissection wasn't applied to all cases. For esophageal reconstruction, stomach was used in 57 cases, right colon was used in two cases, and jejunum was used in one case following the surgi-

cal resection. Performing manual or stapler anastomosis was the surgeon's choice. In the 6th or 7th day following the operation barium passage x-ray controls was done and drains and chest tubes were removed. All major reasons for operative and postoperative morbidities (bleeding, anastomotic leakage, respiratory deficiency, difficulty in gastric discharge, and chilothorax) were documented. Mortalities during hospitalization and in the first 30 days following the operation were considered as perioperative mortality. We checked the patients to record whether they are alive by calling them on regular basis for survival analysis. We have contacted patients whom could not be reached by phone through their social security numbers. Three patients from TT group and one patient from TH group were not reached and thus their data were censored during survival analysis. Remaining 50 patients were followed-up to see if they are alive or not and their date of death was recorded for survival analysis. The statistical analysis between groups were done by using SPSS (SPSS Inc., Chicago IL, USA) statistical software and chi-square, t-student, Fischer exact, One-Way Anova, Mann-Whitney U and Kaplan-Meier Survey tests were utilized to determine statistical significance. The value $p<0.05$ was accepted for statistical significance.

RESULTS

The demographic characteristics and preoperative findings of the cases in this study were summarized (Table 1). There were 36 (60%) male and 24 (40%) female total 60 cases with the average age of 55 (38-78). Of 28 cases operated via TH approach, 16 were female and 12 were male, and of 32 cases operated via TT approach, 24 were male and 8 were female. No statistically significant difference was found between groups in terms of age and sex ($p>0.05$). The preoperative ASA grading of cases operated via TH were: 5 cases ASA 1, 16 cases ASA 2, and 7 cases ASA 3. Cases operated via TT were: ASA 1 for 6 cases, ASA 2 for 24 cases, ASA 3 for 1 case and ASA 4 for 1 case. No statistically significant difference was found between groups with respect to preoperative ASA scores ($p>0.05$). The preoperative mean hemoglobin value of 60 patients was 13.297±1.242 g/dL. The hemoglobin mean value of the patients operated by TT was 13.494±1.188 g/dL (16.4-11.1), whereas hemoglobin mean value of the patients operated by TH was 13.071±1.285 g/dL (10.8-15.5). The mean preoperative albumin value of 60 patients was 3.810±0.072 g/dL. The albumin mean value of the patients operated by TT was 3.797±0.580 g/dL (2.5-4.7) whereas albumin mean value of the patients operated by TH was

TABLE 1: Demographic characteristics and preoperative findings of the patients in transhiatal esophagectomy (TH) and transthoracic esophagectomy(TT) groups.

Characteristics	TH	TT	P value	Total
Average age			P>0.05	
Sex: Male	12	24	P>0.05	36 (60%)
Female	16	8		24 (40%)
ASA score				
ASA 1	5	6	P>0.05	11 (18%)
ASA 2	16	24		40 (67%)
ASA 3	7	1		8 (14%)
ASA 4	–	1		1 (1%)
Preoperative respiratory function (FVC1)	80.25	81.09	P>0.05	
Preoperative total parenteral nutrition (day)	5	12	P>0.05	17
Average Hb value (g/dl)	13.07	13.49	P>0.05	
Albumin value (g/dl)	3.82	3.79	P>0.05	
CEA value (g/dl)	3.23	3.41	P>0.05	

3.825±0.546 g/dlL (2.7-4.8). The preoperative CEA mean value of 60 patients was 3.327±1.623 ng/dl. The CEA mean value of the patients operated by TT was 3.411±1.447 g/dL (1.10-7.80), whereas CEA mean value of one's operated by TH was 3.231±1.826 g/dL (1.10-7.67). No statistically significant difference was detected between Group 1 and Group 2 with respect to preoperative hemoglobin, albumin, and CEA mean levels (p>0.05).

In patients operated via transhiatal approach, tumor diameter involving esophagus was ≥ 5 cm in 2 cases (7%) and in 26 cases it was < 5 cm (93%). Seven patients (22%) who were operated via transthoracic approach had tumor diameter involving esophagus ≥ 5 cm and 25 patients (78%) had tumor diameter involving esophagus < 5 cm. Of the cases operated via transhiatal approach, one patient was (5%) Stage 1, nine patients were Stage 2 (32%) and 18 patients were Stage 3 (63%). Of the cases operated via transthoracic approach, 7 were (22%) stage 2, 25 were (78%) stage 3. No statistically significant difference was detected between groups in respect to tumor diameter and stage (p>0.05). The analysis of the postoperative findings comparing the groups was summarized (Table 2). The TH cases were consisted of, 2 (7%) cervical, 4 (14%) middle thoracic, and 22 (79%) distal esophagus localization. The TT group were comprised of 1 (3%) cervical, 3 (9%) middle, and 28 (88%) distal esophagus localization. No statistically signifi-

TABLE 2: Postoperative results of the patients.

Characteristics	TH n=28	TT n=32	P value	Total n=60
Tumor localization				
Cervical esophagus	2	1	P>0.05	3 (5%)
Thoracal esophagus	4	3		7 (12%)
Distal esophagus	22	28		50 (83%)
Tumor histopathology				
Squamous Ca	27	30	P>0.05	57 (95%)
Adeno Ca	1	2		3 (5%)
Tumor diameter >5 cm	2	7	P>0.05	9 (15%)
<5 cm	26	25		51 (85%)
Tumor stage				
Stage 1	1	–	P>0.05	1 (1%)
Stage 2	9	7		16 (27%)
Stage 3	18	25		43 (72%)
Lymph node metastasis (LNM) (+)	18	26	P>0.05	44 (73%)
(LNM) (-)	10	6		16 (27%)
Anastomosis type				
Hand-sewn anastomosis	28	15	P=0.00	43 (72%)
Stapler anastomosis	–	17		17 (28%)
Mortality	3	3	P>0.05	6 (10%)
Major complications				
Anastomosis leak	4	6	P>0.05	10 (16%)
Hemorrhage	2	–		2 (3.3%)
Respiratory insufficiency	7	3		10 (16%)
Hoarseness	–	1		1 (1.6%)
Chilothorax	–	1		1 (1.6%)
Postoperative hospital stay (days)	18.0±10.1	16.6±7.6	P>0.05	
Neoadjuvan chemo-radiotherapy	1	1	P>0.05	2 (3.3%)
Median survive (months)	26 (2-72)	26 (9-45)	P=0.769	
Survival (%)				
1 year	74.8%	92.3%	P>0.05	
2 year	52.0%	59.9%		
3 year	36.4%	29.1%		

cant difference was detected between groups with respect to tumor localization (p>0.05). Twenty-seven cases (96%) were reported as squamous carcinoma, and 1 case (4%) was reported as adenocarcinoma in the TH group, wheras 30 cases (94%) squamous carcinoma, and 2 cases (6%) adenocarcinoma in the TT group. No statistically significant difference was detected between groups with respect to tumor histopathology (p>0.05). There were no lymph node metastasis in 16 cases (27%), whereas lymph node metastasis were present in 44 cases (73%). No statistically significant difference was detected between groups with respect to lymph node metastasis (p>0.05). Fourty-three cases (%72) were used hand sewn anastomosis technique and 17 cases (%28) were used stapled anastomosis. A statistically significant difference was detected between the groups with respect to anastomosis type (p=0.0001). The number of anastomotic leakage were 4 (23%) who applied anastomosis using a stapler, whereas that were 6 (14%) in hand-stitched anastomosis. Mortality was seen in 5 cases (11%) who applied hand-stitched anastomosis, but it was only seen in one case of stapler used. No statistically significant difference was found with respect to anastomosis type and anastomotic leakage- mortality (p>0.05). We have seen 24 (40%) major morbidity in patients and 6 (10%) mortality. Morbidity was occured in 11 cases (35%) operated via TT, and 13 (46%) cases operated via TH. In the TH group, anastomotic leakage was seen in 4 (14%) patients, postoperative bleeding in 2 (7%) patients and respiratory failure in 7 (25%) patients. In cases operated via TT, 6 patients (18%) had anastomotic leakage, 3 patients (9%) had respiratory failure, 1 patient (4%) had dysphonia and gastric motility disorder and 1 patient had chilothorax. No statistically significant difference was found between groups with respect to major morbidity (p>0.05). Mortality was seen 3 (9%) of the cases operated via TT, whereas 3 of the cases (10%) operated via TH. The reasons for mortality were determined as anastomotic leakage, MRSA sepsis and severe respiratory deficiency for both groups. No statistically significant difference was found between groups with respect to mortality (p>0.05). Mean postoperative hospitalization duration were 18.0±10.1 days in ones operated via transhiatal approach, and that were 16.6±7.6 days in ones operated via transthoracic approach. No statistically significant difference was found between groups with respect to mean postoperative hospitalization duration (p>0.05). Neoadjuvan chemotherapy was administered to 1 case (4%) from TH group and 1 case (3%) from TT group. Median follow-up durations were 22,6 (2-72) months in both groups. One of the 25 patients in TH group couldn't be reached. The median survival duration was calculated as 26 (2-72) for 24 patients of TH group by their follow-up. Three of 25 patients in TT group couldn't be reached. The median survival duration was found as 26 (9-45) for 26 patients of TT group by their follow-up. No statistically significant difference was found between groups with respect to mean lifetime durations (p=0.769). The survival durations of 1 year, 2 years, and 3 years in TH group were found as 74.8%, 52.0%, 36.4%, respectively. The lifetime durations of 1 year, 2 years, and 3 years in TT group were found as 92.3%, 59.9%, 29.9%, respectively. The analysis of cumulative lifetime duration was shown as a figure (Figure 1).

DISCUSSION

Most of esophagus cancers are advanced stage at the time of diagnosis. The 40-60% of cases is ac-

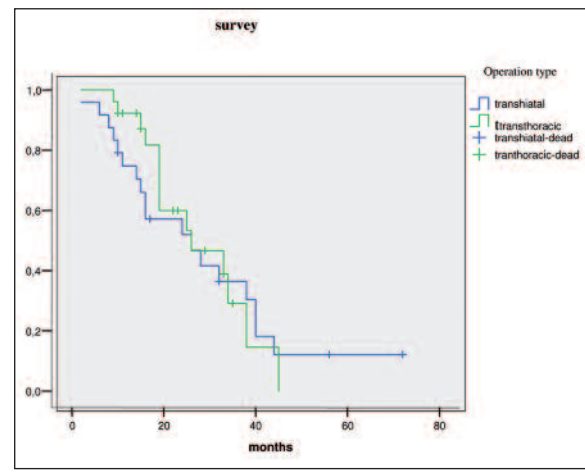

FIGURE 1: Cumulative survey analysis between groups.

cepted as an inoperable due to high operative risk, presence of distant metastasis and inability to resect the incurable nodes. Long-term survival duration is unfortunately low in patients who underwent esophagectomy. However, surgical resection continues to be a primary modality therapy that provides highest chance for long-term palliation of dysphasia and cures in esophagus cancers.[3] Esophagus cancer patients are usually at local advanced or metastases stage. Problems are sourced from difficulties and deficiencies in clinical staging. Actually, the rate of patients being appropriate for curative resection in early stage is very low. Most of the patients we examined in clinics were uncaught at an early stage but with without distant organ metastasis (M1). The major determinants on survival duration are biological behavior of tumor and the stage of the tumor at the moment of resection rather than operative approach.[4] Transhiatal and transthoracic approaches have been compared with respect to factors such as mortality, morbidity, hospitalization duration, and survival duration in the literature for surgery of esophagus cancers. Chou et al. have compared both approaches with respect to mortality, morbidity, survival duration and postoperative pain in esophagus cancers.[5] They have stated that there was no difference between groups with respect to mortality, morbidity, and survival duration; however, TH approach was a better preference with respect to postoperative pain. Pac et al have compared transhiatal and transthoracic approaches with respect to postoperative complications, intraoperative blood loss, mortality, late complications and survival duration in their serial of 238 cases.[6] Although there was no difference with respect to survival duration, transhiatal approach showed statistically significant superiority on transthoracic approach with respect to factors such as morbidity, hospitalization duration. Boyle et al have compared both approaches similarly with respect to mortality, morbidity and survival duration of 5 years in their serial of 65 cases and they haven't found a statistically significant difference between groups.[7] Johansson et al. have compared transthoracic en block esophagectomy and transhiatal esophagectomy.[8] They have shown that transthoracic en block esophagectomy provides higher survival duration in ones with T3N1 disease and metastases in lymph nodes less than 9. The other comprehensive study was conducted by Hulscher et al.[9] It reveals an operative mortality rate of 5.7% and 5-year survival rate of 23% in TH group including 3301 cases. The TT group including 3942 cases has presented an operative mortality rate of 9.2% and 5-year survival rate of 23%. We have presented a mortality rate of 10% in TH group and that of 9% in TT group in our study correlatively with these studies. It has been reported that transhiatal approaches provide less postoperative morbidity and shorter operation duration. Additionally, making anastomosis in neck provides lower risk of mediastenitis and more gradual course of morbidity. Schrump et al. have stated that an open thoracic intervention provides a very good exposure, thus tumor may be dissected more from the neighbor tissues and a curative surgical resection may be conducted via a complete lymph node dissection.[2] As though, the major morbidity rates in cases operated via transhiatal intervention was a little bit more comparatively with transthoracic intervention in our study, no statistically significant difference was found ($p>0.05$). There has been a remarkable decrease in mortality rates following esophageal resections in the last three decades.[10] Hofstetter et al. have reported that operative mortality has decreased from 12% to 6%.[11] Also in our study, there is a mortality rate of 10% in TH group and that of 9% in TT group concordantly with literature. No statistically significant difference was found between the groups with respect to mortality rate ($p>0.05$).

The anastomotic leakages are the most common complications following surgical resections and their mortality rates change depending on whether they are intrathoracic or cervical region.[12] Baulieux et al. have reported that the mortality rates in intrathoracic anastomotic leakages are higher than cervical anastomotic leakages.[13] As though, the numbers of anastomotic leakages and mortality were similar in our study, the fact that anastomotic leakage caused one-third of mortali-

ties in TH group whereas it was responsible for all mortalities in TT group, supports this conclusion. It has been stated in the literature that anastomosis type as hand-sewn or using a stapler doesn't result a difference in the incidence of anastomotic leakage.[14] The incidence of anastomotic leakages following esophageal resections has been reported as higher than 30% in some studies.[15] In a randomized study conducted in Faculty of Medicine, University of Hong Kong, no significant difference was found in anastomotic leakage rates via both techniques, but however, a significant difference (40% to 9%) was found in narrowness rates.[16] In our study, number of anastomotic leakages was 4 (23%) in anastomosis by using a stapler, whereas that was 6 (14%) in hand-sewn anastomosis. The number of mortalities was 1 (6%) in anastomosis by using a stapler, whereas that was 5 (11%) in hand-sewn anastomosis. No statistically significant difference was found with respect to anastomotic leakage and mortality rate depending on anastomosis type ($p>0.05$). Of the total 60 cases operated, 3 (5%) were adenocarcinoma and its rarity in the literature has been interpreted as exclusion of gastroesophageal junction tumors from this study. Homesh et al have reported the cases in Stage 3 in a rate of 94%.[17] Also in our study, as revealing a majority between our cases, 63% of ones operated via TH and 75% of ones operated TT were patients in Stage 3. These rates confirm the conclusion that mostly esophageal cancers are in the advanced level at the time of diagnosis. In our study, mean postoperative hospitalization duration was 18.0±10.1 days in TH group and was 16.6±7.6 days in TT group concordantly with the literature. The positive effect of neoadjuvan chemoradiotheraphy on prognosis in esophageal cancers has been shown in one study, but however, couldn't been confirmed by other studies.[18,19] The surgeons in the western countries have an opinion that the esophagus cancers are the disseminated diseases and thus they prefer neoadjuvan chemoradiotheraphy.[20] In our study, 1 case (4%) in TH group and 1 case (3%) in TT group were administered neoadjuvan chemoradiotheraphy. It has been detected that in both cases during the operation that tumor dimension was reduced and reresection was applied. Both patients are still alive and one of them has been followed-up since 68 months and the other has been followed-up since 12 months. In esophagus cancers, different survival durations have been reported for TH and TT approaches. Orringer et al have reported a rate of 27% with respect to 5-year mean survival duration in patients operated via TH including a serial of 417 cases.[21] The 5-year survival duration rates are remarkably higher in the patients without lymph node metastases. Altorki et al have reported the 5-year survival rate as 34% in stage 3 patients who undergone 2-field lympho node dissection (LND) and as 54% in stage 3 patients who undergone 3-field LND.[22] Yalcinkaya et al. have reported that survival time changes were between 2 months and 6 years, mean time was 33.4 months and 5 years survival rate was 12% in stage IIa esophageal cancer.[23] Chou et al. reported that transhiatal esophagectomy is a safe and fast procedure and i ts leakage rate was lower and quality of life was better. The survival was similar to that of transthoracic approach.[24] Boshier et al. reported a meta-analysis about transthoracic versus transhiatal esophagectomy for the treatment of esophagogastric cancer. Fifty-two studies, comprising 5905 patients (3389 transthoracic and 2516 transhiatal) were included in the analysis. This meta-analysis of studies comparing transthoracic with transhiatal esophagectomy for cancer demonstrates no difference in 5-year survival.[25] Although we couldn't give 5-year survival rate due to the short follow-up period of our study, mean survival durations of 1 year, 2-year and 3-year have been calculated as 92.3%, 59.9% and 36.4% for TH group, respectively. Those have been observed as 74.8%, 52.0% and 36.4% for TH group, respectively. No statistically significant difference was found between groups with respect to median and mean survival durations ($p=0,769$). In our study group, 2-field lymph node dissection was applied to all patients except only one patient who was applied a 3-field LND. The high survival duration rates in literature may probably not be reached in TT group due to this reason.

CONCLUSION

As a conclusion of our study; it has been found that the type of surgical approach for esophagus cancers doesn't change the early term postoperative mortality, major morbidity rates, hospitalization duration and survival duration. We conclude that the most important determinants on survival duration are the biological behavior of tumor and its stage at the time of resection rather than the type of surgical approach.

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