Esophagectomy in Octogenarians: Does it come at a cost?

Sujata Ojha

Mentor: Rohan Jeyarajah, MD

Abstract

Research Question

Do octogenarians, or patients above the age of 80, who undergo esophagectomy have a higher mortality and morbidity in comparison to patients younger than the age of 80 years? Is surgical intervention in patients with esophageal cancer over the age of 80 a favorable course of treatment?

Background

Esophageal cancer is highly aggressive cancer and typically presents at a later stage at diagnosis. The increasing incidence of esophageal cancer in combination with early metastasis and a relatively poor survival rate makes this one of the most aggressive cancers worldwide. Esophageal cancer is asymptomatic in initial stages, therefore more than 30% of patients have metastatic cancer at the time of diagnosis. Due to the late stage of diagnosis combined with accelerated metastasis, esophageal cancer has an increased fatality rate. The incidence of esophageal cancer increases with age. With the ageing population and the increasing number of people over the age of 65, it is anticipated that there will be a rise in the demand for more surgical intervention in this demographic. Due to the aggressive nature of the disease, and its anatomical and physiological properties, surgical approach is an appropriate choice of treatment. Esophagectomy is the main-stay surgical procedure for the treatment of esophageal cancer. Surgical intervention in the geriatric population has a higher risk of perioperative morbidity and mortality due to higher prevalence of comorbidities such as heart disease, diabetes, chronic obstructive pulmonary disorder, increased frailty, and lack of compensatory physiologic reserve.

The literature on esophagectomy in octogenarians, patients over the age of 80, is limited. There are apparent concerns of patients in the older demographics being denied surgical interventions. In order to determine the safety of esophagectomy in this cohort, this study aims to analyze the outcomes of esophagectomies performed on octogenarians who have esophageal cancer.

Materials and Methods

In this IRB-approved study, 143 esophagectomies performed for esophageal cancer between 2012 and 2020 were retrospectively examined. Oncologic outcomes, surgical results, and patient demographics were examined. The octogenarian group was compared to patients younger than 80 years of age.

Results

Out of a total of 143 esophagectomies, 136 patients were <80 years old while 7 were ≥80 years old. Octogenarians received significantly less neoadjuvant therapy compared to younger patients (42.9% vs 80.2%, p=0.02). No statistically significant difference was noted in complication rate, length of stay (LOS), estimated blood loss (EBL), or mortality. However, octogenarians were found to have an increase in severity of complications compared to younger patients.

Conclusion

Esophagectomy can be performed in octogenarians who are carefully selected. This study shows that esophagectomy in octogenarians does not increase complication rates or mortality however does have an increased severity of complication. With explicit expectations and preparation for the significant risk of more serious postoperative sequelae, our evidence suggests that esophagectomy can be administered selectively to older patients.

Research Question

Do octogenarians, or patients above the age of 80, who undergo esophagectomy have a higher mortality and morbidity in comparison to patients younger than the age of 80 years? Is surgical intervention in patients with esophageal cancer over the age of 80 a favorable course of treatment while compared to patients younger than 80 years old?

We hypothesize that patients over the age of 80 who undergo esophagectomy for esophageal cancer intervention have a higher likelihood of morbidity and mortality due to the presence of increased comorbidities, decreased immunity, and increased physical fragility. We expect this to be supported objectively by the post- operative evaluation including the length of stay at the hospital, complications post- esophagectomy, and illness severity.

Introduction, Significance, and Rationale

Esophageal cancer is a cancer that occurs in the esophagus and is a highly aggressive malignancy associated with a high mortality rate. It ranks as the sixth leading cause of cancer-related deaths worldwide. [1] Esophageal cancer predominantly affects the elderly population and is a male-dominated malignancy and peaks in incidence after 65 years of age. [2] In 2022 the estimated number of new esophageal cancer cases is 20,640 followed by an estimated death of 16,410 individuals with a median age at diagnosis of 68 years.[3] Since 2006, there has been a steady increase of 20.6% cases of esophageal adenocarcinoma per year.[3] The median age at death for patients with esophageal cancer is 70 years. Despite advancements in surgical techniques and perioperative therapy, esophageal cancer continues to have a poor prognosis with a 5-year relative survival rate of 20.6%.[3] The lymphatic drainage of the esophagus is densely interconnected leading to early and aggressive spread of the carcinoma. Esophageal cancer can be classified into smoking-related squamous- cell carcinoma that arises in the upper third of the squamous epithelium and adenocarcinoma arising from the Barrett's columnar glandular epithelium in the lower third of the esophagus.[4] Esophageal cancer is initially asymptomatic but progresses to dysphagia, odynophagia, and weight loss. During initial stages when the cancer has invaded mucosa and submucosa, a viable option is esophagectomy, endoscopic tumor resection, and mucosal ablation using radiofrequency. In advanced stages, chemoradiotherapy is used prior to surgery. However, due to the late presentation of symptoms, esophageal cancer is diagnosed in advanced stages and is classified as a cancer with poor prognosis.

Esophagectomy is a complex surgical procedure that has a high risk of morbidity and mortality.[5] It is crucial to comprehend how esophagectomy affects the elderly population as the population matures. It is controversial what the best course of action should be for elderly

patients with esophageal cancer. The literature supports that esophagectomy in octogenarians can be performed successfully, but there is still worry that older individuals will be turned away from surgery due to a bias over results.[6] Other factors that lead to the relative controversy is the question of long-term survival benefit in this population. Data suggests that these patients should be offered a chance at surgery.[7–10] Several studies suggest that octogenarians undergoing esophagectomy for the treatment of esophageal cancer have similar early morbidity, mortality, and overall survival while compared with younger population. Age should not be the only limiting factor while choosing the course of treatment for esophageal cancer. Indeed, physiology, and not chronology, should be the deciding factor.[11]

In order to more accurately determine the true risk that elderly patients assume by undergoing surgery, this study will examine the surgical outcomes of esophagectomy in octogenarians. The results of these study can be significant in providing older patients with a wider course of treatment options including surgical treatment approach. The distinctive feature of our study, in contrast to other ones that have been published, is that these operations were primarily carried out utilizing minimally invasive procedures, and we questioned whether this may affect the result in this vulnerable group of patients. Additionally, the patients that were analyzed in this study did not undergo a thoracic approach and went through a transhiatal approach instead.[12,13]

Research Materials and Methods

This study was approved by the IRB (037.HPB.2018.R) at Methodist Richardson Medical Center. A retrospective electronic chart review was performed. Concern of patient privacy is

addressed because the data was de-identified and did not contain identifying patient information. A total of 143 consecutive transhiatal esophagectomies were performed at a single institution for esophageal cancer from 2012 to 2020. CPT codes 43107-8, 43280, and 43286-9 were used to collect this data. Patient information including patient demographics (age, gender, ethnicity), surgical outcomes, and oncologic outcomes were collected and analyzed. The patient group divided into two groups for comparison, those 80 years of age and older and those younger than 80 years of age. The surgical outcomes including the complication rates, Clavien-Dindo (CD) score, 30-day mortality rates, average length of stay (LOS), and average estimated blood loss (EBL) was reviewed and analyzed. The complications were classified based on the Clavien-Dindo classification system for surgical complications. The oncologic outcomes included tumor node metastasis (TNM) staging, and resection margin status based on the American Joint Committee on Cancer (AJCC) 8th edition guidelines. The two separate groups were compared using nonparametric, univariate statistical analysis including Chi-square test, Fisher's exact test, and Mann-Whitney t-test. A p-value less than 0.05 was considered statistically significant. Statistical analysis was conducted using JASP (JASP Team (2020). JASP (Version 0.16.2) [Computer software]).

Results *[14]*

Among the 143 patients who underwent esophagectomies, 136 were under 80 years old (range 39-79) and 86.0% were men, whereas 7 were over the age of 80 years (range 80-87) and 71.4% were men. Neoadjuvant treatment (NAT) was given to most patients in the less than 80 years cohort (80.2%), whereas in the ≥80 group, 42.9% of patients received NAT. Due to their

state, four patients in the ≥80 cohort did not get NAT. Additionally one patient declined any preoperative care. In the <80 cohort, open surgery accounted for a total of thirty-three (24.3%) patients while in in the ≥80 group, 2 patients (28.6%) underwent open surgery. Minimally invasive transhiatal esophagectomy accounted for the surgical approach for all other patients remaining. Compared to the younger patients (M = 291.8 mL; SD = 324.1 mL), there was no statistically significant difference in the estimated blood loss (EBL) between the octogenarian's group (M = 1050 mL; SD = 1947.8 mL) (Mann-Whitney U, p = 0.83). Additionally, compared to younger patients (11.6 days, SD = 7.1 days), the average length of stay (LOS) for the octogenarians (22.1 days, SD = 15.1 days), was also shown to not be statistically significant (Mann-Whitney U, p = 0.06).

Additionally, the overall morbidity was also not statistically significant, (X^2 (1, N = 143) = 0.807, p = 0.369), despite the morbidity rate in the younger patients being 69.9% and 86.7% in the octogenarian cohort. However, octogenarian group had more severe complications with most complications in the Clavien-Dindo (CD) 4 category accounting 57.1%, while <80 group had more complications in the CD 2 category (23.5%) (X^2 (7, N = 143) = 21.2, p = < .01) [Figure 1 and Figure 2]. The mortality rate demonstrated an upward trend in octogenarians (1/7) compared to younger patients (2/136), 14.3% and 1.5%, respectively, but did not reach statistical significance (p = 0.141) [Table 1].

There were two mortalities in the <80 group. Among the two mortalities, one patient's family elected to withdraw care. This patient had a history of hepatitis C with hepato-pulmonary syndrome and died on post-operative day 27 with complications secondary to the syndrome. The second mortality occurred in a patient with vascular disease leading to bowel ischemia on post-operative day 11. There was one mortality in the ≥80 cohort. On postoperative day 4, the patient

developed respiratory and cardiovascular complications and the family elected to withdraw care.

Resections margins were negative for 115 (84.6%) patients in the <80 group and 6 (85.7%) patients in the ≥80 age group [Table 2]. It is worth noting that minimally invasive esophagectomy (MIE) resulted in significantly higher rates of negative resection margins (89.8%) compared to open esophagectomy (OE) (68.6%, p = < .01).

Figure 1: Clavien-Dindo (CD) Grading for Surgical Complications [15]

Grade	
1	*Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions* *Allowed therapeutic regimens are drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.*
2	*Requiring pharmacological treatment with drugs other than such allowed for grade I complications.* *Blood transfusions and total parenteral nutrition are also included.*
3	*Required surgical, endoscopic, or radiological intervention*
3a	*Intervention not under general anesthesia*
3b	*Intervention under general anesthesia*
4	*Life threatening complication (includes CNS complication) requiring IC/ICU management*
4a	*Single organ dysfunction (including dialysis)*
4b	*Multiorgan dysfunction*
5	*Death of a patient*

Figure 2: Clavien-Dindo Score in >80 age group and <80 age group[14]

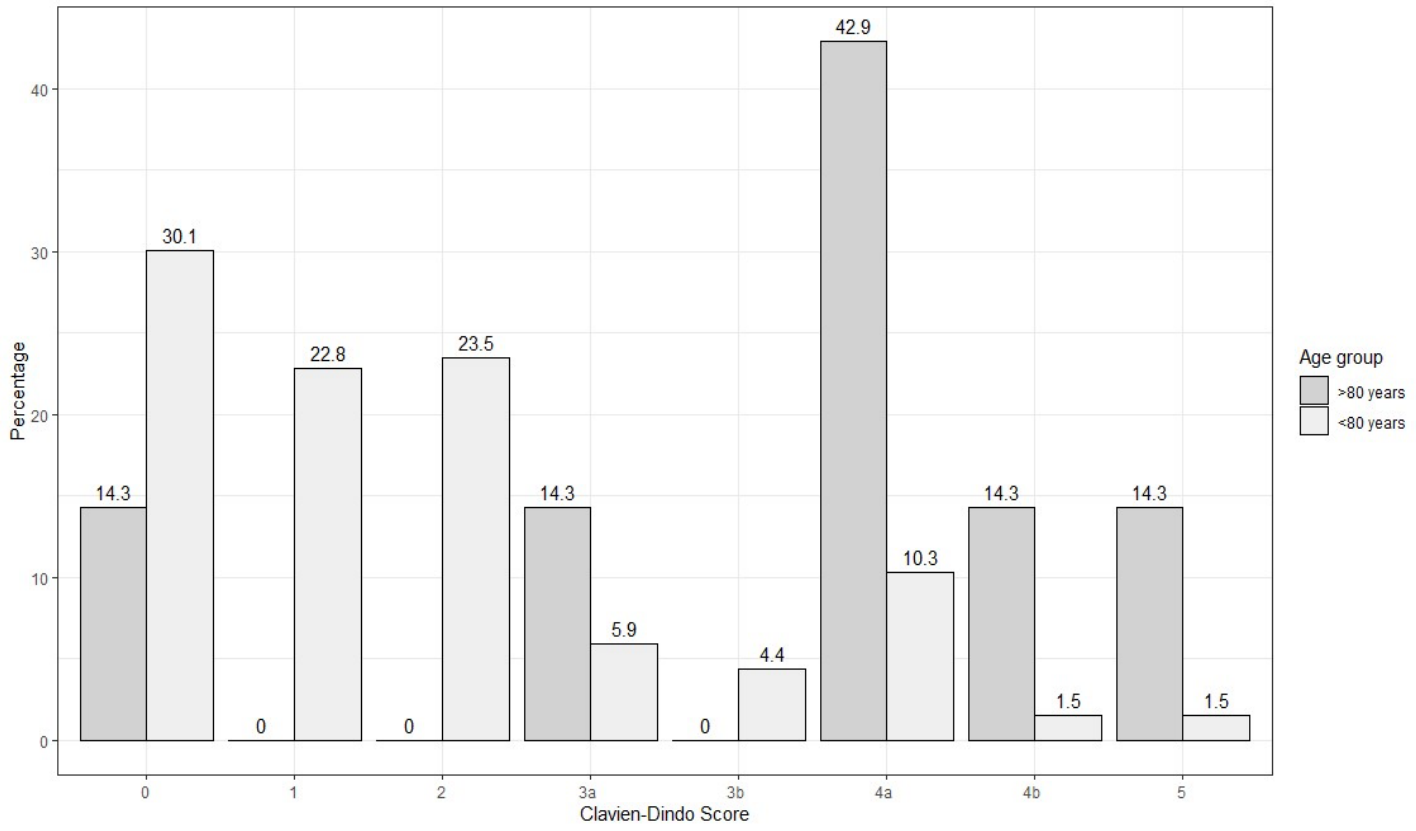

Table 1: Surgery Profiles [14]

	<80 years of age (n=136)	≥80 years of age (n=7)	p-value
Type of Surgery			X^2 (1, N = 143) =
Open	33 (24.3%)	2 (28.6%)	0.01, p = 0.79
MIE	103 (75.7%)	5 (71.4%)	
Average EBL (mL)	291.8	1050.00	Mann-Whitney U, p = 0.82
LOS (days)	11.6	22.1	Mann-Whitney U, p = 0.06

Average #LN	14.46	11.57	Mann-Whitney U, p = 0.29
Complication			X^2 (1, N = 143) =
Yes	95 (69.9%)	6 (85.7%)	0.81, p = 0.46
No	41 (30.1%)	1 (14.3%)	0.37
Mortality	2 (1.5)	1 (14.3%)	Fisher's exact test p = 0.141

Table 2: Pathologic Profiles [14]

	<80 years of age (n=136)	≥80 years of age (n=7)
pT (X^2 (1, N = 143) = 3.61, p = 0.82)		
	19 (14.0%)	1 (14.3%)
0	3 (2.2%)	0
1	16 (11.8%)	2 (28.6%)
1A	24 (17.6%)	2 (28.6%)
1B	14 (10.3%)	1 (14.3%)
2	55 (40.4%)	1 (14.3%)
3	1 (0.74%)	0
4A	4 (2.9%)	0
Tis		

pN (X^2 (1, N = 143) = 3.54,		
p = 0.47)	82 (60.3%)	4 (57.1%)
0	25 (18.4%)	3 (42.9%)
1	18 (13.2%)	0
2	10 (7.4%)	0
3	1 (0.74%)	0
X		
Grade (X^2 (1, N = 143) =		
3.24, p = 0.66)	1 (0.74%)	0
0	10 (7.4%)	1 (14.3%)
1	59 (43.4%)	1 (14.3%)
2	43 (31.6%)	4 (57.1%)
3	2 (1.5%)	0
4	21 (15.4%)	1 (14.3%)
X		
Resection Margins		
- Open		
o Negative	23 (69.7%)	1 (50.0%)
o Positive	10 (30.3%)	1 (50.0%)
- MIE		
o Negative	92 (89.3%)	5 (100.0%)
o Positive	11 (10.7%)	0 (0.0%)

- Total (X^2 (1, N =143)

  = 9.16, p = < .01)

  - Negative
  - Positive 115 (84.6%) 6 (85.7%)

    21 (15.4%) 1 (14.3%)

Discussion and Innovation

Esophagectomy in octogenarians comes at a cost with an increased severity of post-operative complications without a significant difference in complications or mortality rates. This study emphasizes the significance of careful patient selection with an understanding for increased post-operative sequelae, especially in the octogenarian population. The authors of this paper conclude that esophagectomy should be offered to octogenarians for esophageal cancer, compared to the alternative.

For the first time in American history, older people will surpass children due to the aging of the baby boomer generation and the aging of the general population.[16] By 2040, 14.4 million individuals are projected to be over the age of 85, more than doubling the population who were over that age in 2020.[17] The incidence of cancer will rise as individuals live longer, which will increase the number of elderly people who require surgical intervention.

Numerous research has reported an increase in complications in the elderly population for octogenarians undergoing esophagectomy for esophageal cancer[8,18,19] while other studies have shown no significant difference when compared to a younger cohort. [9,20,21] In a study conducted by, Markar et al., 500 patients who underwent esophagectomy were analyzed, of which 32 were

≥80 years, and reported that octogenarians' incidence of postoperative morbidity was higher.[8] This, according to the authors, was brought on by underlying comorbidities and a low prevalence of NAT.[8]

Additionally, a ten-year prospective cohort study analysis of 1,777 esophagectomy patients resulted that the postoperative morbidity rate was 50% and thirty-day mortality rate was 10%.[19] The study concludes that preoperative conditions such as diabetes mellitus and chronic obstructive lung disease, as well as age, were risk factors for higher total morbidity.[19] Additionally, intraoperative factors including the requirement for intraoperative blood transfusion, increased time in the operating room, and the patient's emergent status indicated a rise in morbidity.[19] In fact, our results would suggest that the differences between the ≥80 and <80 groups in this study may be explained by the very low mortality in the younger group. In fact, the mortality in the octogenarian group is comparable to studies of all esophagectomies, making the argument for surgery even stronger in the group. [19,22,23]

A significant increase in postoperative major complications was observed in octogenarians (62.5%) compared to patients aged 70 to 79 years (47.6%), and patients under the age of 70 years (37.2%), in a study by Tapias et al. that analyzed the short and long-term outcomes after esophagectomy for elderly patients.[24] A rise in mortality for octogenarians undergoing an esophagectomy has also been reported in other research studies.[8,18] As demonstrated by the Clavien-Dindo score, in our study the octogenarians cohort also showed an increase in complication severity. However, even though mortality in the group of octogenarians showed an increasing trend, we could not detect a statistically significant difference.

A retrospective analysis of data from the National Cancer Database (NCDB) for patients with esophageal cancer between 2004 and 2015 included 21,710 octogenarians and showed that surgical approach provides an improved survival in surgically fit octogenarians with locally advanced esophageal cancer.[25] Preoperative rehabilitation, dietary optimization, and NAT are essential in preparing patients for surgery and lowering the risk of postoperative morbidity.[26–28] The treatment of esophageal cancer presents a challenge when considering NAT for elderly patients. The choice to administer therapy is made after carefully assessing the risk of toxicity, the advantages and disadvantages of additional surgery, and life expectancy.[29] The octogenarians cohort typically tend to receive less NAT while compared to the younger patients due to their advanced age.[30] Surgery alone continues to be the most crucial element in improving survival in esophageal cancer, despite the fact that NAT has been demonstrated to improve the rates of complete resection when paired with surgery.[31]

In numerous systematic literature studies, Open Esophagectomy (OE) and Minimally Invasive Esophagectomy (MIE) have been compared and the outcomes of these two surgical approaches have been analyzed.[32,33] In some studies, the authors report a significant improvement in perioperative morbidity with patients who underwent MIE compared to those who underwent an OE.[34,35] Octogenarians who have a MIE have lower post-operative morbidity and better oncologic results, including better resection margin status.[36]

There are a few weaknesses and limitations to this study. Firstly, this is a retrospective study analyzing data from a single practice of three surgeons. Additionally, the study had a small sample and disproportionate sample size leading difficulties while making a generalizable statement. The sample size also decreased the power of our study in terms of statistical analysis.

Lastly, the study only examined individuals who underwent esophagectomy surgery for esophageal cancer; it did not include individuals whose surgeries were not performed due to advanced oncologic parameters or medical reasons. Data on octogenarians with esophageal cancer that elected not to undergo surgery was not available which presents a selection bias. Therefore, further evaluation warrants a larger sample size.

Future Directions

The future direction of this project should include a larger sample size to fully access the term survival of octogenarians versus patients who are younger than 80 years of age. Other related areas of exploration can assess the types of comorbidities that can lead to higher rates of complications while performing esophagectomy in patients younger than 80 while compared to the patient over the age of 80.

Conclusions

In conclusion, this study demonstrated that esophagectomy can in fact be performed carefully in octogenarians and partially disproved our hypothesis. It shows that age shouldn't be the only limiting factor. According to the findings of this study, in carefully selected octogenarians, esophagectomy can be performed for esophageal cancer without an increased risk of mortality. The study however showed that octogenarians who undergo esophagectomy have an increased severity of complication but not an increase in complication rates. With explicit expectations and preparation for the elevated risk of more serious post-operative complications, our evidence suggests that esophagectomy can be administered selectively to older patients.

Compliance

This study was approved by the IRB (037.HPB.2018.R) at Methodist Richardson Medical Center.

References

1. Domper Arnal MJ, Ferrández Arenas Á, Lanas Arbeloa Á. Esophageal cancer: Risk factors, screening and endoscopic treatment in Western and Eastern countries. World J Gastroenterol. 2015;21(26):7933-7943. doi:10.3748/wjg.v21.i26.7933

2. Cancer of the Esophagus - Cancer Stat Facts. SEER. Accessed May 19, 2021. https://seer.cancer.gov/statfacts/html/esoph.html

3. Wang Y, Zhu L, Xia W, Wang F. Anatomy of lymphatic drainage of the esophagus and lymph node metastasis of thoracic esophageal cancer. Cancer Manag Res. 2018;10:6295-6303. doi:10.2147/CMAR.S182436

4. American Cancer Society | Cancer Facts & Statistics. American Cancer Society | Cancer Facts & Statistics. Accessed April 6, 2021. http://cancerstatisticscenter.cancer.org/

5. Xu QL, Li H, Zhu YJ, Xu G. The treatments and postoperative complications of esophageal cancer: a review. J Cardiothorac Surg. 2020;15(1):163. doi:10.1186/s13019-020-01202-2

6. Bakhos CT, Salami AC, Kaiser LR, Petrov RV, Abbas AE. Outcomes of octogenarians with esophageal cancer: an analysis of the National Cancer Database. Dis Esophagus Off J Int Soc Dis Esophagus. 2019;32(10):1-8. doi:10.1093/dote/doy128

7. Paulus E, Ripat C, Koshenkov V, et al. Esophagectomy for cancer in octogenarians: should we do it. Langenbecks Arch Surg. 2017;402(3):539-545. doi:10.1007/s00423-017-1573-x

8. Markar SR, Low DE. Physiology, not chronology, dictates outcomes after esophagectomy for esophageal cancer: outcomes in patients 80 years and older. Ann Surg Oncol. 2013;20(3):1020-1026. doi:10.1245/s10434-012-2703-x

9. Ruol A, Portale G, Zaninotto G, et al. Results of esophagectomy for esophageal cancer in elderly patients: age has little influence on outcome and survival. J Thorac Cardiovasc Surg. 2007;133(5):1186-1192. doi:10.1016/j.jtcvs.2006.12.040

10. Baranov NS, van Workum F, van der Maas J, et al. The Influence of Age on Complications and Overall Survival After Ivor Lewis Totally Minimally Invasive Esophagectomy. J Gastrointest Surg Off J Soc Surg Aliment Tract. 2019;23(7):1293-1300. doi:10.1007/s11605-018-4062-9

11. Monson K, Litvak DA, Bold RJ. Surgery in the aged population: surgical oncology. Arch Surg Chic Ill 1960. 2003;138(10):1061-1067. doi:10.1001/archsurg.138.10.1061

12. Bp W, S L, Sc M, A A, J W. Analysis of reduced death and complication rates after esophageal resection. Ann Surg. 2001;233(3):338-344. doi:10.1097/00000658-200103000-00006

13. Miyata H, Yamasaki M, Makino T, et al. Clinical Outcome of Esophagectomy in Elderly Patients With and Without Neoadjuvant Therapy for Thoracic Esophageal Cancer. Ann Surg Oncol. 2015;22 Suppl 3:S794-801. doi:10.1245/s10434-015-4769-8

14. Ojha S, Darwish MB, Benzie AL, et al. Esophagectomy in octogenarians: is it at a cost? Heliyon. 2022;8(12). doi:10.1016/j.heliyon.2022.e11945

15. Morand GB, Anderegg N, Kleinjung T, et al. Assessment of Surgical Complications With Respect to the Surgical Indication: Proposal for a Novel Index. Front Surg. 2021;8. Accessed February 20, 2023. https://www.frontiersin.org/articles/10.3389/fsurg.2021.638057

16. Bureau UC. Older People Projected to Outnumber Children. The United States Census Bureau. Accessed April 6, 2021. https://www.census.gov/newsroom/press-releases/2018/cb18-41-population-projections.html

17. Vespa J, Armstrong DM, Medina L. Demographic Turning Points for the United States: Population Projections for 2020 to 2060. Washington, DC: US Department of Commerce, Economics and Statistics Administration, US Census Bureau; 2018.

18. Moskovitz AH, Rizk NP, Venkatraman E, et al. Mortality Increases for Octogenarians Undergoing Esophagogastrectomy for Esophageal Cancer. Ann Thorac Surg. 2006;82(6):2031-2036. doi:10.1016/j.athoracsur.2006.06.053

19. Bailey SH, Bull DA, Harpole DH, et al. Outcomes after esophagectomy: A ten-year prospective cohort. Ann Thorac Surg. 2003;75(1):217-222. doi:10.1016/S0003-4975(02)04368-0

20. Alibakhshi A, Aminian A, Mirsharifi R, Jahangiri Y, Dashti H, Karimian F. The effect of age on the outcome of esophageal cancer surgery. Ann Thorac Med. 2009;4(2):71. doi:10.4103/1817-1737.49415

21. Zehetner J, Lipham JC, Ayazi S, et al. Esophagectomy for cancer in octogenarians. Dis Esophagus. 2010;23(8):666-669. doi:10.1111/j.1442-2050.2010.01081.x

22. Finlayson E, Fan Z, Birkmeyer JD. Outcomes in octogenarians undergoing high-risk cancer operation: a national study. J Am Coll Surg. 2007;205(6):729-734. doi:10.1016/j.jamcollsurg.2007.06.307

23. Adam DJ, Craig SR, Sang CTM, Cameron EWJ, Walker WS. Esophagectomy for carcinoma in the octogenarian. Ann Thorac Surg. 1996;61(1):190-194. doi:10.1016/0003-4975(95)00932-9

24. Tapias LF, Muniappan A, Wright CD, et al. Short and long-term outcomes after esophagectomy for cancer in elderly patients. Ann Thorac Surg. 2013;95(5):1741-1748. doi:10.1016/j.athoracsur.2013.01.084

25. Calvo HD, Nguyen DT, Chan EY, Chihara R, Graviss EA, Kim MP. Surgery provides improved overall survival in surgically fit octogenarians with esophageal cancer after chemoradiation therapy. J Thorac Dis. 2021;13(10). doi:10.21037/jtd-21-928

26. Steenhagen E. Preoperative nutritional optimization of esophageal cancer patients. J Thorac Dis. 2019;11(Suppl 5). doi:10.21037/jtd.2018.11.33

27. Low DE, Allum W, De Manzoni G, et al. Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations. World J Surg. 2019;43(2):299-330. doi:10.1007/s00268-018-4786-4

28. Otero J, Arnold MR, Kao AM, et al. Short-term Outcomes of Esophagectomies in Octogenarians-An Analysis of ACS-NSQIP. J Surg Res. 2019;235:432-439. doi:10.1016/j.jss.2018.07.044

29. Vlacich G, Samson PP, Perkins SM, et al. Treatment utilization and outcomes in elderly patients with locally advanced esophageal carcinoma: a review of the National Cancer Database. Cancer Med. 2017;6(12):2886-2896. doi:10.1002/cam4.1250

30. Tougeron D, Di Fiore F, Thureau S, et al. Safety and outcome of definitive chemoradiotherapy in elderly patients with oesophageal cancer. Br J Cancer. 2008;99(10):1586-1592. doi:10.1038/sj.bjc.6604749

31. Urschel JD, Vasan H, Blewett CJ. A meta-analysis of randomized controlled trials that compared neoadjuvant chemotherapy and surgery to surgery alone for resectable esophageal cancer. Am J Surg. 2002;183(3):274-279. doi:10.1016/s0002-9610(02)00795-x

32. Mitzman B, Lutfi W, Wang CH, Krantz S, Howington JA, Kim KW. Minimally Invasive Esophagectomy Provides Equivalent Survival to Open Esophagectomy: An Analysis of the National Cancer Database. Semin Thorac Cardiovasc Surg. 2017;29(2):244-253. doi:10.1053/j.semtcvs.2017.03.007

33. Sgourakis G, Gockel I, Radtke A, et al. Minimally invasive versus open esophagectomy: meta-analysis of outcomes. Dig Dis Sci. 2010;55(11):3031-3040. doi:10.1007/s10620-010-1153-1

34. Nagpal K, Ahmed K, Vats A, et al. Is minimally invasive surgery beneficial in the management of esophageal cancer? A meta-analysis. Surg Endosc. 2010;24(7):1621-1629. doi:10.1007/s00464-009-0822-7

35. Noble F, Kelly JJ, Bailey IS, Byrne JP, Underwood TJ, South Coast Cancer Collaboration - Oesophago-Gastric (SC3-OG). A prospective comparison of totally minimally invasive versus open Ivor Lewis esophagectomy. Dis Esophagus Off J Int Soc Dis Esophagus. 2013;26(3):263-271. doi:10.1111/j.1442-2050.2012.01356.x

36. Darwish MB, Nagatomo K, Jackson T, Cho E, Osman H, Jeyarajah DR. Minimally Invasive Esophagectomy for Achieving R0. JSLS. 2020;24(4):e2020.00060. doi:10.4293/JSLS.2020.00060