ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 4, Issue – 1, January - 2019, Page No. : 87 - 93

A comparison of survival in elderly as compare to young patients in locally advanced esophageal carcinoma treated by definitive chemoradiation

Shweta Mohata [1], H.S. Kumar[1], Neeti Sharma[1], S.L. Jhakhar[1],Surendra beniwal[2] , Kamlesh kumar harsh[1]

[1]Department of radiotherapy, Acharya Tulsi Regional Cancer Treatment and Research Institute (ATRCTRI), Bikaner, Rajasthan

[2]Department of medical oncology,(ATRCTRI),Bikaner, Rajasthan

Corresponding Author: H.S. Kumar**,** Department of radiotherapy, Acharya Tulsi Regional Cancer Treatment and Research Institute (ATRCTRI), Bikaner, Rajasthan

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Introduction: The benefit of definitive chemoradiotherapy (CRT) in elderly patients with locally advanced esophageal cancer is not well established .We perform a single institutional retrospective study of CRT in terms of median survival in elderly patients (age more than 60 years)as compare with young cohort(age less than 60 years) in locally advanced non metastatic esophageal cancer .

Material And Methods: Total 70 patients, 38 in young age(group A) and 32 patients of elder age(group B)of carcinoma esophagus with ECOG 0-1 selected with stage II and III squamous cell carcinoma, who had undergone definitive CRT at our institute from January 2015 – June 2016. Chemotherapy was cisplatin (40 mg/m^2) given concurrently on weekly basis with radiotherapy(RT). Median dose of RT was 50-50.4 Gy @ 1.8-2 Gy/#. Median age was 40 years(25-58 years) and 65 years(60-75 years) in young and elderly group respectively. Follow up is done at 3-42 months after treatment.

Result: Median overall survival (OS) is 18 months (4-40 months) & 17 months (1-39 months) seen in young and elderly patients respectively. No stastically significant difference is seen in median survival in young and elderly group .

Conclusion: Our conclusion is that patients with adequate functional status should not be excluded from curative CRT based on age alone.

Keywords: Elderly Patients, Oesophageal Cancer, Chemoradiotherapy, Overall Survival, DFS.

Introduction

Esophageal cancer is the eighth most common cancer worldwide with an estimated 456,000 new cases diagnosed in 2012 with highest incidence and mortality in Asian and African countries[1] .Fewer than 1 million cases occur per year in india. Esophageal cancer is the fourth common cause of cancer-related deaths in India. It is prevalent among both men and women. Squamous cell carcinoma (SCC) accounts for up to 80% of these cancers [2].Radiation oncologists increasingly face elderly patients of esophageal cancer one of the cause of this could be the prolongation of life expectancy . Approximately 2/3rd of cancer related death occur in elderly patients of age >60 years. Management of elderly patients with cancer is a

therapeutic challenge because of associated comorbities and poor functional reserve as compare to young patients, because of that they prefer less intensive treatment including surgery . Definitive CRT could be the treatment of choice in this group of patients. RTOG 85-01 has established the superiority of chemoradiation to radiotherapy alone in terms of 5 year OS(26%vs 0%)and median survival(12.5 vs 9 months.However only 23% of >70 years were taken in the study. As less data is available for this particular group of patients ,the aim of our study is to assess the survival of squamous oesophageal cancer in patients of age >60 years as compare to young population of age <60 years, undergoing definitive Chemoradiotherapy .

Patients and methods

A total of 70 patients of non metastatic squamous cell esophageal cancer were selected who were treated with definitive CRT at ATRCTRI ,Bikaner Rajasthan between January 2015 to June 2016. Due to retrospective analysis ,we have to depend upon the collected information at our center. Patients inclusion criteria was 1)ECOG 0-1; 2) Clinical stage II and III based on AJCC-TNM classification 8th edition ,2018 ;3) Histologically confirmed squamous cell esophageal carcinoma; 4) No prior therapy; 5)No history of concurrent or previous malignancy; 6)Complete and retrievable records ;7)Patients received prescribed curative radiotherapy dose. All Patients were treated with weekly cisplatin chemotherapy concurrent with radiotherapy and were strictly monitored and managed for any treatment related toxicity during the treatment. All patients were followed on July 2018 that is after 42 months of start of study.

Pre Treatment evaluation

All patients had undergone for initial workup which include complete history ,physical examination, routine blood investigations like complete blood count, liver function test, renal function test, Barium swallow, Upper GI endoscopy with biopsy, CECT scan thorax and abdomen and ultrasound abdomen and pelvis as per need. All patients had checked for HIV, HBsAg, and HCV routinely. Tumor baseline characteristics were collected as much as possible (Location, length, diameter, histology, nodal involvement, involvement of surrounding structures, any metastasic lesion).TNM staging was done according to AJCC 2018, 8th edition. All biopsy proven squamous cell esophageal cancer patients were enrolled at our center.

Treatment regimen

All patients received cisplatin chemotherapy concurrently with radiotherapy. Cisplatin given in the dose of 40 mg /m^2 on weekly basis with standard premedication and adequate hydration. Application of CRT was performed after careful evaluation of organ function , performance status, sensitivity of chemotherapy, severity of comorbidities. Dose evaluation of chemotherapy was considered if any grade 3 hematological or gastrointestinal toxicity occur. Treatment was stopped at grade 4 toxicities. Radiation therapy was delivered by telecobalt machine(Bhabhatron II(panacea medical technologist,india) ,Theratron ,780C & 780 E ,team best ,Canada) and 6 MV linear accelerator (LA)(Varian,Clinac 2300 CD,Pal alto,USA). Radiation was given @ 2 gray (Gy) or 1.8 Gy per fraction five days in a week. Target volume of cobalt machine was 3-5 cm superior and inferior and 2.5-3 cm radially to tumor bulk as seen on endoscopy or imaging. Radiation planning on LA was done by 3D CRT. GTV was defined as any visible tumor on endoscopy or CT imaging and included any visible lymph nodes.CTV was the GTV plus 3 cm superiorly and inferiorly and 2 cm lateral margins and all regional lymph nodes.PTV was created by adding 1 cm in superior – inferior dimension and 0.8 cm radially to CTV .Median

prescription dose was 50/50.4 Gy to target volume in 25/28 # administered in phased manner over 5-6 weeks.

Evaluation of response

During the whole treatment all patients were under strict vigilance for any treatment related local or systemic toxicities. The clinical tumor response was evaluated 6-8 weeks after completion of radiotherapy with general physical examination, UGIE, or Ba swallow and if necessary CECT chest and abdomen .After completion of treatment ,response was evaluated by response evaluation criteria in solid tumors (RECIST guidelines version 1.1). Complete Clinical Response (CCR) was defined as no remnant of disease on endoscopy or CT scan .Local recurrence as seen on endoscopy was confirmed with biopsy .

Follow up

Follow- up was done in all patients undergoing treatment every 3 months for the first 2 years and then every 6 months until death or last follow up i.e. July 2018.

Statistical analysis

Overall survival (OS) was calculated from the date of treatment until the time of death or date for last follow up. Survival curve was made by using Kaplan-Meier method. We performed an analysis of median OS difference between old age population >60 years and young population<60years. All statistical analyses were performed with a two side significance value of 0.05.

Results

Patient and tumor characteristics

Patient age ranged from 60 years to 75 years (median 65 years)in old age group, while in young population youngest patient was of age 25 years with a median age of 40 years. There were 32 female and 38 male patients. All patients had a ECOG 0-1.All patients were having Squamous cell carcinoma ,out of SCC 42(A=20,B=22) were of MDSCC while 6 (A=3/B=3)were having WDSCC and 9 (A=5/B=4) were of PDSCC while 13 (A=10/B=3)patients were having unknown differentiation. All patients were of clinically stage II/III by Ba swallow ,UGIE or CECTscan . Baseline characteristics are listed in Table 1.

Treatment outcome and survival

Approximately 67% (n=47;A=26/B=21) of patients had no evidence of disease, while 23 (A=12/B=11) patients revealed residual disease post treatment either on endoscopy or CT scan. Patients with residual disease had received adjuvant cisplatin based chemotherapy. A total of 12 (A=5/B=7) patients had relieved from dysphagia with regular endoscopic dilations while 3 (A=1/B=2) patients has to undergo stent placement(Table 2).

A total of 32(A=18/B=14) patients are without evidence of disease. Non cancer cause of death was severe hypotension(group A) ,sudden cardiac arrest, and renal failure (group B). Local recurrence was seen in 12(A=7/B=5) patients, while 3(A=1/B=2) patients developed distant metastases during the follow up period(table 2).Out of 12 recurrences only two patients(A=1/B=1), while one patient with metastases (B=1) were alive at the time of follow up.

Discussion

Esophagus presenting at mean age group is Approximately 67.3 years (Dale etal,2003)and they present with late stage of III or IV.Based on several clinical trials chemoradiotherapy has been the standard treatment for LAEC and it is superior to RT alone[4-6].Despite the late age group presentation, very few studies have been done on this particular subject. The main problem with geriatric group of patients is tolerance of aggressive CRT therapy,as most of this age group patients have associated comorbid conditions .

National cancer data based review ,2017 shows that elderly patients should not be deprived of treatment that

may improve their survival ,but they are less likely to receive aggressive therapy[2].

Anderson et al [7](2007) shows the significant result from a single institution experience of CRT in 25 elderly patients older than 65 years with esophageal cancer.On the basis of median follow up of 32 months ,the CCR rate was 68% and 2 year survival rate was 64%.

D Tougeron et al[8] (2008) evaluated tolerance and outcome of 109 elderly patients older than 70 years treated with cisplatin based CRT for non metastatic esophageal cancer.CCR was seen in 57.8% and 2 year survival was 35.5%.Toxicity of grade >3 were seen in 23.8%.They also suggest that CRT can be given in elderly patient without major toxicity.

Our study was based on retrospective data that suggest that in LAEC cisplatin based CRT regimen is as efficacious and tolerable in old age group patients as in young population of less than 60 years of age.The study also show no stastically significant OS difference between the two groups .Our median survival is 18 mths and 17 months in young and elderly group respectively. The mean age is 25-75 years . We found that this regimen could be an alternative for esophageal cancer patients who cannot tolerate standard CRT regimen of cisplatin ,5 –FU especially, elderly patients who can not tolerate surgical burden and have associated comorbid conditions. This regimen is having low and manageable hematologic, GI toxicity with good survival.

Geriatric group should have proper treatment and have not to defer treatment just because of their perception of increased toxicity. We are showing the comparable result outcome in elderly patients as to younger population . Limitation of our study is non affordability of our patient ,poor nutritional status as well as retrospective nature .

Conclusion

Our conclusion is that patients with adequate functional status should not be excluded from curative CRT based on age alone.

Table1.Patient and tumor characteristics

Age				p-value
<60 years	38			
>60 years	32			
Gender	Total(n=70)	Young(n=38) Group A	Elderly(n=32) Group B	
Male	38	17	21	0.132
Female	32	21	11	
Tumor Site	Total(n=70)	Young(n=38) Group A	Elderly(n=32) Group B	
U/3	11	6	5	0.44
M/3	42	25	17	
L/3	17	7	10	
Histological	Total(n=70)	Young(n=38) Group A	Elderly(n=32) Group B	
WD	6	3	3	0.436
MD	42	20	22	
PD	9	5	4	
Unknown	13	10	3	
Investigation	Total(n=70)	Young(n=38) Group A	Elderly(n=32) Group B	
Ba swallow	35	18	17	
CECT	62	34	28	
UGIE	46	26	20	
Comorbid	Total(n=70)	Young(n=38) Group A	Elderly(n=32) Group B	
Diabetes	8	1	7	
CAD	2	0	2	
PVD	1	0	1	
Pulmonary disease	3	1	2	

Table 2: Treatment response

	Total (n=70)	AGE<60(n=38)	AGE>60(n=32)	p-value
CCR	32	18	14	0.97
RECURRENCE	12	7	5	0.95
RESIDUAL	23	12	11	0.948

METS	3	1	2	0.903
DEATH	39	21	18	0.876
ALIVE	31	17	14	0.869

Table 3: Survival analysis

Year	AGE<60(n=38) Death	AGE>60(n=32) Death	p-value
1	4	5	0.840
2	6	7	0.813
3	8	9	0.791

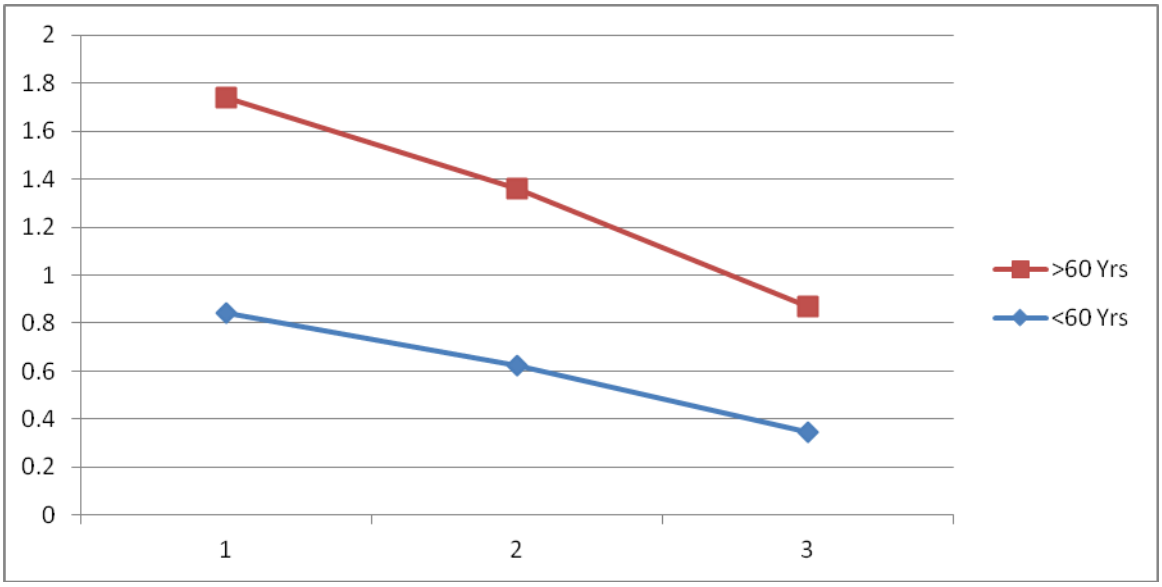

Figure 1. Survival curve

References

1. Globocan 2012 ,estimated cancer incidence,mortality and prevalence worldwide in 2012.International agency for research on cancer (WHO).
2. National Cancer Institute SEER cancer statistics review. http://seer.cancer.gov/csr/1975_2013/Date: 1975–2013(Last accessed 3Jan, 2019)
3. Herskovic A, Martz K, al-Sarraf M, Leichman L, Brindle J, Vaitkevicius V, Cooper J, Byhardt R, Davis L, Emami B (1992) Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Engl J Med 326: 1593 – 1598
4. Coia LR, Minsky BD, Berkey BA, John MJ, Haller D, Landry J, Pisansky TM, Willett CG, Hoffman JP, Owen JB, Hanks GE (2000) Outcome of patients receiving radiation for cancer of the esophagus: results of the 1992 – 1994 patterns of care study. J Clin Oncol 18: 455 – 462
5. Di Fiore F, Lecleire S, Galais MP, Rigal O, Vie´ B, David I, Hamidou H, Paillot B, Jacob JH, Michel P (2006b) Impact of radiation schedule and chemotherapy duration in definitive chemoradiotherapy regimen for esophageal cancer. Gastroenterol Clin Biol 30: 845 – 851
6. Di Fiore F, Lecleire S, Rigal O, Galais MP, Ben Soussan E, David I, Paillot B, Jacob JH, Michel P

(2006a) Predictive factors of survival in patients treated with definitive chemoradiotherapy for squamous cell esophageal carcinoma. World J Gastroenterol 12: 4185 – 4190.

7. Anderson SE, Minsky BD, Bains M, Hummer A, Kelsen D, et al. (2007) Combined modality chemoradiation in elderly oesophageal cancer patients. Br J Cancer 96: 1823–1827.
8. Tougeron D, Hamidou H, Scotte´ M, Di Fiore F, Antonietti M, et al. (2010) Esophageal cancer in the elderly: an analysis of the factors associated with treatment decisions and outcomes. BMC Cancer 10: 510.