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Research Article

Outcomes from a single institution cohort of 248 patients with stage I–III esophageal cancer treated with radiotherapy: Comparison of younger and older populations

Carrie Lavergne [a,*], Andrew Youssef [b], Mark Niglas [a,c], Deanna Ng Humphreys [a], Youssef Youssef [a]

[a] R.S. McLaughlin Durham Regional Cancer Centre, Lakeridge Health Oshawa, Oshawa, Ontario L1G 2B9, Canada
[b] Institute of Medical Science, University of Toronto, Toronto, Ontario M5S 1A8, Canada
[c] Queen's University, Department of Oncology, Kingston, Ontario, Canada

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ABSTRACT

Outcomes for patients receiving radiotherapy (RT) for non-metastatic esophageal cancer at a single institution were assessed, as well as the impact of factors including age and intensity modulated RT (IMRT) planning on patient outcomes. A retrospective cohort of patients treated with RT for stage I-III esophageal cancer between 2010 and 2018 was identified. Among 248 identified patients, 28 % identified as older (≥75 years of age). Other than histology, there were no other statistically significant differences in patient and tumour characteristics between the younger and older populations. Treatments varied between the two age groups, with significantly less older patients completing trimodality treatments (17 % vs 58 %). Median overall survival (M−OS) and progression-free survival (M−PFS) were 20 months and 12 months for all patients and 40 months and 26 months for trimodality patients, respectively. In the older patients, the M−OS improved from 13 months for all to 34 months for trimodality patients; and M−PFS from 10 months to 16 months. On multivariate analysis, the use of trimodality therapy showed improved OS (HR 0.26, $p < 0.001$). In the non-surgical older patient group, significantly better survival was seen in patients who had a heart V30Gy under 46 %. There was no significant difference in M−OS in patients planned with IMRT compared with 3D-conformal RT. Clinical outcomes in the treatment of esophageal cancer vary significantly by treatment approach, with the most favourable results in those receiving trimodality therapy. Among older patients deemed fit after assessment by the multidisciplinary team for trimodality treatments, the M−OS is comparable to the younger patient group.

Introduction

Esophageal carcinoma (EC) is an aggressive malignancy with a well-known poor prognosis. In 2023, it was estimated there were 2700 new cases, with 2400 deaths in Canada. EC is ranked in the top ten of cancer-related mortalities, with an estimated five-year survival of 16 % [1,2].

In the absence of metastases, individual management of EC is variable and can be based on both tumour and patient factors. Age is one patient factor that can often be a large determinant on the management of EC. Older patients, defined in this paper as those ≥75 years of age at diagnosis, may not be considered for the same treatment options as those younger than 75. Trials such as CROSS [3] excluded patients over the age of 75; therefore, there is no consensus on the optimal treatments for this patient population. Furthermore, the number of older patients having surgery for esophageal cancers is increasing [4]. Although limited literature exists on the management of these patients, studies of this population are suggesting that advanced age is not a contraindication for curative intent treatment for EC [4–18].

EC treatment options include combinations of radiation therapy (RT), chemotherapy and surgery. RT plays a key role in the treatment of both inoperable and operable EC [19]. RT technologies continue to evolve with time; from two-dimensional (2D) treatment planning on plain film x-rays, to three-dimensional (3D) treatment planning on computerized tomography (CT), resulting in the ability to perform 3D-conformal radiation therapy (3D-CRT). With the evolution of these technologies, improvements have been seen in target dose conformity

* Corresponding author.
E-mail address: clavergne@lh.ca (C. Lavergne).

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and normal tissue sparing. The introduction of Intensity-Modulated RT (IMRT) has further shown advancements, as seen in several studies of patients with EC, demonstrating additional improved target conformity [20], and reduced normal tissue doses to the lungs [21,22] and heart [23], resulting in fewer acute and late toxicities [24] compared with 3D-CRT planning. Further studies have suggested that the dosimetric advantages of IMRT including decreased dose to the cardiopulmonary organs could translate into a clinical benefit, with improved overall survival (OS) and local–regional control seen in patients with EC treated with IMRT compared with those treated with 3D-CRT [20,25,26]. With the addition of more modern techniques, the need to include older populations in studies is emphasized due to the potential benefits for this group of patients.

The primary goal of this retrospective study was to assess the impact of age on outcomes of patients with non-metastatic EC receiving RT, plus or minus chemotherapy and surgery, at a single institution. A secondary goal was to assess the impact of the introduction of IMRT planning on patient outcomes.

Materials and methods

Study cohort

This study was a single institutional retrospective cohort analysis, approved by the local research board prior to initiation. The review consisted of consecutive patients diagnosed with non-metastatic EC between January 1, 2010 and December 31, 2018. All patients who were prescribed RT with total doses equal to or greater than 40 Gy were included. All patients were discussed prior to treatment initiation at a multidisciplinary case conference (MCC), attended by a team including at least one pathologist, radiologist, surgeon, medical and radiation oncologist. The decision to have chemotherapy and/or pursue surgery was based on patient preference, medical/surgical evaluation and multidisciplinary discussion. This includes consideration of both patient and tumour characteristics, and performance status.

Chemotherapy treatments

Chemotherapy was administered based on a standard institutional protocol under the supervision of the treating medical oncologist. The two most common regiments utilized during our study period were weekly intravenous carboplatin (AUC 2) and paclitaxel (50 mg/m^2) given concurrently with radiation therapy; or two cycles of intravenous cisplatin (75 mg/m^2) combined with continuous infusion of 5-fluorouracil (1000 mg/m^2) for four days, given concurrently with weeks 1 and 5 of radiation therapy. Dose adjustments or deferrals were made based on performance status, hematological, and non-hematological toxicities at the discretion of the treating medical oncologist.

Radiation treatments

For radiation treatment, patients were typically simulated using a four-dimensional (4D) CT, immobilized with a Vac Lok bag or Wingstep device with both arms abducted and externally rotated for thoracic esophageal tumours. The gross tumour volume (GTV) was delineated based on the CT, previous diagnostic imaging including previous positron emission tomography (PET)/CT, as well as endoscopic findings. The clinical tumour volume (CTV) included the GTV plus a margin of approximately 3–4 cm craniocaudally, and 0.5 cm circumferentially (respecting normal boundaries of spread). The internal target volume (ITV) incorporated the CTV with any internal motion seen on the 4D-CT. The planning target volume (PTV) included the ITV with 0.6 cm margin craniocaudally and 0.5 cm margin elsewhere. Aligned with the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) dose constraints, organs-at-risk dosimetric constraints included a maximum spinal canal dose of 45 Gy, heart V30Gy of <46 % and combined lung V20Gy of < 30 % [27]. Patients were planned using Monaco treatment planning software. All patients were planned with either 3D-CRT or IMRT. A radiation oncologist and/or radiation oncology nurse assessed patients weekly while on treatment.

Outcomes

In alignment with the Cancer Care Ontario guidelines, follow-up visits were done with the radiation oncologist, medical oncologist and/or surgeon, and usually began four weeks after treatment completion, and subsequently occurring at three to six month intervals. [28]. Overall survival (OS) was defined as the time from diagnosis to death, from any cause. Progression free survival (PFS) was defined as the time from diagnosis to any recurrence or death from any causes, whichever came first. Freedom from local progression (FFLP) was defined as the time from diagnosis to local progression. Early-death was defined as death within six months of diagnosis.

Statistical analysis

Statistical analysis was performed using Stata14.2 [29]. Descriptive statistics were compared using the *t*-test and chi-squared test when appropriate. Survival analyses were performed using the Kaplan-Meier method. OS, PFS and FFLP were defined as above. The cox proportional hazards model was used for both univariate analysis and multivariate analysis. A univariate screen was performed with variables having a $p \leq 0.1$ to be included in the multivariate model. The log-rank test was used to test survival outcomes between subgroups. A p-value < 0.05 was considered significant for all statistical tests.

Results

Patient characteristics

The patient and tumour characteristics of the 248 patients eligible for this study are summarized in Table 1. The median age at diagnosis was 68.1 years, with a range of 41.4–90.6 years of age. Eighty-one percent of patients were male. The most common tumour histology

Table 1
Patient and Tumour Characteristics.

Characteristic	All Patients (N = 248)	Age < 75 years (N = 179)	Age ≥ 75 years (N = 69)	*p* Value
Age, median (range)	68.1 (41.4–90.6)	64.4 (41.4–74.9)	79.9 (75–90.6)	**$p <$ 0.001**
Male sex, N (%)	201 (81.0)	145 (81.0)	56 (81.1)	$p =$ 0.98
Histology, N (%)				
Adenocarcinoma	174 (70.1)	133 (74.3)	41 (59.4)	**$p =$ 0.04**
Squamous cell	45 (18.2)	26 (14.5)	19 (27.6)	
Other	29 (11.7)	20 (11.2)	9 (13)	
Tumour Length, median (cm)	6.3	6.4	6.1	$p = 0.6$
Location of primary, N (%)				
Proximal third	6 (2.4)	5 (2.8)	1 (1.5)	$p = 0.3$
Middle third	46 (18.6)	29 (16.2)	17 (24.6)	
Distal third	196 (79)	145 (81)	51 (73.9)	
Clinical Nodal Status, N (%)				
Node Negative	101 (40.7)	73 (40.8)	28 (40.6)	$p =$ 0.98
Node Positive	147 (59.3)	106 (59.2)	41 (59.4)	

was esophageal adenocarcinoma (EAC) (70.1 %) compared with 18.2 % esophageal squamous cell carcinoma (ESCC). The median tumour length was 6.3 cm, with 79 % of tumours occurring in the distal third of the esophagus. Ninety-four percent of patients had a PET scan during initial work-up. Fifty-nine percent of patients had clinically node positive disease on PET or CT.

There were 69 patients (28 %) identified as older patients in this study. When comparing the two age groups of those who were younger than 75, and the older patients who were 75 and older, the older population had a higher percentage of squamous cell carcinoma histology (27.6 % compared with 14.5 %, $p = 0.04$). There were no other statistically significant differences with respect to the patient and tumour characteristics of these two groups.

Treatment regimens

The treatment regimens are summarized in Table 2. Eighty-eight percent of all patients received between 41.4 and 50.4 Gy. Ninety-three percent of patients were prescribed concurrent chemotherapy, with the most common regimen of Carboplatin-Paclitaxel (75.4 %). Ninety-two percent of all patients completed their radiation, whereas eighty-one percent of patients completed their chemotherapy planned courses with or without a dose reduction. Forty-seven percent of patients went on to have surgery.

Examining the treatment regimens by age group, significantly more older patients (56.5 %) were prescribed greater than 41.4 Gy and equal to or less than 50.4 Gy, compared with the younger population (44.1 %) ($p = 0.04$). Almost one quarter (23.2 %) of older patients compared with only one percent of the younger patients were not prescribed chemotherapy ($p < 0.001$). Almost seventy percent of the younger patients completed the planned chemotherapy courses, whereas only fifty-one percent of the older patients did. Significantly less older patients (17.4 % compared with 58.1 %) completed trimodality treatment ($p < 0.001$).

Table 2
Treatment Regimens.

Treatment	All Patients (N = 248)	Age < 75 years (N = 179)	Age ≥ 75 years (N = 69)	*p* Value
Intended Treatment, N (%)				
Surgery, Radiation and Chemotherapy	142 (57.3)	123 (68.7)	19 (27.5)	**p < 0.001**
Radiation Therapy and Chemotherapy	91 (36.7)	54 (30.2)	37 (53.6)	
Radiation Therapy only	15 (6.0)	2 (1.1)	13 (18.8)	
RT Completed, N (%)	228 (91.9)	174 (97.2)	64 (92.7)	*0* = 0.1
RT Prescribed (cGy), N (%)				
4140	100 (40.3)	81 (45.3)	19 (27.5)	***p* = 0.04**
>4140 ≤ 5040	118 (47.6)	79 (44.1)	39 (56.5)	
>5040	30 (12.1)	19 (10.6)	11 (15.9)	
IMRT, N (%)	120 (48.4)	81 (45.3)	39 (56.5)	*p* = 0.1
Chemotherapy, N (%)				
None	18 (7.3)	2 (1.1)	16 (23.2)	***p* < 0.001**
Carboplatin/Paclitaxel	187 (75.4)	137 (76.5)	50 (72.5)	
5-Fluorouracil/Cisplatin	37 (14.9)	35 (19.6)	2 (2.9)	
Other	6 (2.4)	5 (2.8)	1 (1.5)	
Chemotherapy Completed, N (%)				
Completed planned courses	150 (65.2)	123 (69.5)	27 (50.9)	***p* < 0.001**
Completed planned courses with dose reduction	37 (16.1)	28 (15.7)	9 (17)	
Did not complete planned courses	43 (18.7)	26 (14.7)	17 (32.1)	
Surgery				
Surgery Completed, N (%)	116 (46.8)	104 (58.1)	12 (17.4)	***p* < 0.001**

After discussion at MCC, the intended treatments (trimodality, bimodality or radiation therapy alone) was determined for each patient, as summarized in Table 2. Sixty-nine percent of patients in the younger group were planned for trimodality treatment, however only 58 % received it. In the older population, 28 % of patients were planned for trimodality treatment, however 17 % completed it. Starting in 2016, most patients were planned and treated with IMRT (91.2 %). Prior to this year, the majority of patients were planned and treated with a 3D-CRT approach (Table 3). When comparing the 3D-CRT and IMRT groups, no significant differences were seen in the field lengths or lung V20Gy doses. Eight percent of patients exceeded the lung V20 dose constraint of <30 %. The patients planned with IMRT had significantly lower heart V30Gy doses, with a mean of 29.5 % compared with the 3D-CRT planned group mean of 42.8 % ($p < 0.01$). Most patients, in both age groups were given Carboplatin and Paclitaxel chemotherapy agents. After 2013, no patients were offered 5-Flurouracil and Cisplatin agents.

When examining the treatment planning regimens in the younger and older populations, the only significant difference was seen in the heart dose, with statistically significantly lower heart doses (V30Gy) seen in the IMRT-planned patients, both in the younger ($p < 0.001$) and older patients ($p = 0.003$).

Survival outcomes – Overall survival

For the entire cohort of patients, the median follow-up was 17.4 months, and for those patients alive at last follow-up was 34.4 months. The median OS was 20.3 months and 37.2 months and median PFS was 12.1 and 23.4 months for all patients and trimodality patients, respectively (Table 4). Fig. 1ABC demonstrates the Kaplan-Meier curves of OS, PFS and FFLP for these two respective groups.

In the older population specifically, for all patients and those patients who completed trimodality treatments, the median OS was 12.9 months and 33.7 months, and median PFS was 10.2 months and 16.4 months, respectively.

Fig. 1D demonstrates the Kaplan-Meier OS curves in the whole cohort. Patients undergoing trimodality treatment had superior survival outcomes regardless of age. Nineteen patients (7.7 %) experienced an early death, defined as those who died within six months of diagnosis. Of this group, twelve (63.2 %) patients were in the older population. Only one of these 19 patients completed trimodality treatments, and this patient was in the younger population.

Survival outcomes – Multivariate analysis

Univariate screen using the cox proportional hazard model included patient sex, tumour histology, tumour length, location of the primary (upper, mid or lower esophagus), nodal status, delivered radiation dose, the use of IMRT, the use of chemotherapy, specific chemotherapy regimens used, completion of intended chemotherapy, number of chemotherapy cycles, the use of surgery, year of treatment (2010–2015 versus 2015–2019), lung V20Gy over 30 %, heart V30 over 46 % and the use of IMRT. The final multivariate models are reported in Tables 5 and 6.

Patients undergoing surgery had improved survival in both the entire cohort and the older subgroup (HR 0.53$p < 0.001$ and HR 0.67$p = 0.05$ respectively). Comparing EAC to ESCC, there were no differences in survival in the multivariate model. The “other” histology (non-EAC or ESCC) had an increased risk of death in the entire cohort (HR 1.57$p = 0.05$), however this was not significant in the older subgroup. In the

Table 3
3D-CRT vs IMRT.

	All Patients (N = 248)			Age < 75 years (N = 179)			Age ≥ 75 years (N = 69)		
	3D-CRT	IMRT	*p* Value	3D-CRT	IMRT	*p* Value	3D-CRT	IMRT	*p* Value
Treatment Utilization by Year, N (%)									
2010–11	26 (78.8)	7 (21.2)	***p* < 0.001**	20 (87.0)	6 (13.0)	***p* < 0.001**	6 (60)	4(40)	***p* < 0.001**
2012–13	45 (78.9)	12 (21.1)		37(82.2)	8 (17.8)		8(66.7)	4(33.3)	
2014–15	50 (92.6)	4 (7.4)		35(92.1)	3(7.9)		15(93.8)	1(6.3)	
2016–17	6 (8.8)	62 (91.2)		5 (10.2)	44(89.8)		1(5.3)	18(94.7)	
2018–19	1 (3.0)	35 (97.0)		1(4.2)	23(95.8)		0(0)	12(100)	
Field Length (cm)*	19.3	19.9	$p = 0.3$	19.6	20.6	$p = 0.1$	18.4	18.3	$p = 0.9$
Lung V20Gy (%)*	19.2	18.2	$p = 0.3$	18.9	18.2	$p = 0.5$	20.1	18.2	$p = 0.3$
Heart V30Gy (%)*	42.8	29.5	***p* < 0.01**	41.5	28.6	***p* < 0.001**	47.0	31.2	***p* = 0.003**

*Values are presented as means.

Table 4
Survival, measured in months (mos) by treatments completed and by age.

	All Patients			Trimodality Patients		
	All (N = 248)	<75 years (N = 179)	≥75 years (N = 69)	All (N = 116)	<75 years (N = 104)	≥75 years (N = 12)
Median Follow-up, mos.	17.4	20.1	12.3	31.6	31.0	34.7
Median Follow-up for patients alive at last follow-up, mos.	34.4	35.3	28.8	42.5	41.1	53.2
Median Overall Survival, mos.	20.3	24.3	12.9	37.2	40.2	33.7
Median Progression Free Survival, mos.	12.1	13.6	10.2	23.4	26.4	16.4

older population, heart V30Gy over 46 % was associated with increased risk of death in the multivariate model (HR 2.57p = 0.003), although this was not seen in the cohort as a whole.

FFLP was significantly impacted by both the use of surgery (Fig. 1C) and the use of IMRT (Fig. 2A). When accounting for other variables, the use of IMRT had an improvement in local control as compared to using 3D-CRT planning in the entire cohort as well as the older subgroup (HR 0.55p = 0.039 and HR 0.19p = 0.022 respectively). This finding remained significant on sensitivity analysis, wherein our analysis was limited to patients treated between 2014 and 2017 (N = 124), indicating the results were not dependent on the treatment period.

Discussion

The goal of this retrospective, single-institution study was to assess the impact of age on outcomes of patients at our institution with non-metastatic EC who received RT. Following along with many trials and studies [3,10,12,14,30–32], we found that patients who had trimodality treatments of concurrent chemoradiation therapy (CRT) followed by surgery had the best OS, PFS and FFLP outcomes. Management of EC is improved with multidisciplinary tumour board discussions [33,34], as is done at our centre. It allows for comprehensive presentation and discussion surrounding the patient's case, emphasizing the importance of individual decision-making. It also takes into account the patient's physiological status, and tumour and disease characteristics [34].

EC has a very poor prognosis. A study by Otterstatter et al. [1] examined EC trends within Canada, using the Canadian Cancer Registry, the National Cancer Incidence Reporting System and the Canadian Vital Statistics Death databases. They found the five-year relative survival ratio to be 13 %. They noted that survival generally decreased with age, with the best five-year survival of 18 % seen in the 15 to 44 age group, and the worst five-year survival of 10 % seen in the 75 to 99 age group [1].

It is projected that rates of EAC will increase by an additional 40 % and 50 % in men and women, respectively, from 2006 to 2026 [1]. An epidemiological study of EC in Canada between 1992 and 2010 reported an increase in EAC, but a decrease in SCC [35]. It is hypothesized that the increase in EAC may be explained by a concurrent worsening obesity pandemic in Canada, and the knowledge of higher rates of obesity is linked with increased rates of EAC. Furthermore, a decrease in tobacco smoking in Canadians, may explain part of the decline in ESCC [1,35]. We conducted a subgroup analysis among the different histological subtypes. There was no significant differences comparing overall survival in EAC and ESCC, in both the entire cohort and the older group of patients. This finding was similar in other studies, specifically in the older population [7,36–38].

Our study demonstrated an increased risk of death in patients with the "other" histology (non-EAC and non-ESCC), however this was not significant in the older population. This differed in the Surveillance, Epidemiology and End Results (SEER) analysis of patients aged ≥75 years, in which the "other" histological subtype actually had a decreased risk of death in the univariate analysis; however this trend did not hold on multivariate analysis. However, another SEER database analysis looked specifically at one of the "other" histologies: esophageal neuroendocrine carcinoma (ENEC), and compared it with ESCC. The ENEC histology comprised 2.4 % of the patients. Similar to our study, the ENEC histology was associated with worse prognosis compared to those patients with ESCC [39].

Older population

The peak incidence of EC has shifted in recent years, from 65–70 years to 70–79 years of age [40]. In a Canadian national population-based EC study, over 90 % of people with EC were older than 60 years, with an average age at diagnosis of 67.5 [35]. With this increasing incidence of EC in Canada, along with the country's aging population, it is important to understand the outcomes for EC, specifically in the older population. Defining "older patients" is arbitrary, and varies across the studies [11,15]. Prospective data for older patients is limited due to the lack of inclusion in randomized control trials [41], such as CROSS which excluded patients over the age of 75 [30]. It was decided we would define older patients as those aged 75 years and older. This older population constituted almost one third (28 %) of our entire cohort similar with other studies [42]. Our institution's outcomes remained similar when comparing the older and younger populations, with the best OS, PFS and FFLP outcomes seen in those patients who had trimodality treatments, regardless of age.

Controversies exist in the literature regarding the effect of increasing age and the outcome of surgery in patients with EC. Some studies have demonstrated that the older have been found to have increased mortality risks after esophagectomy [4,11,31,42,43], and that survival after esophagectomy worsens with increasing age, specifically after age 70

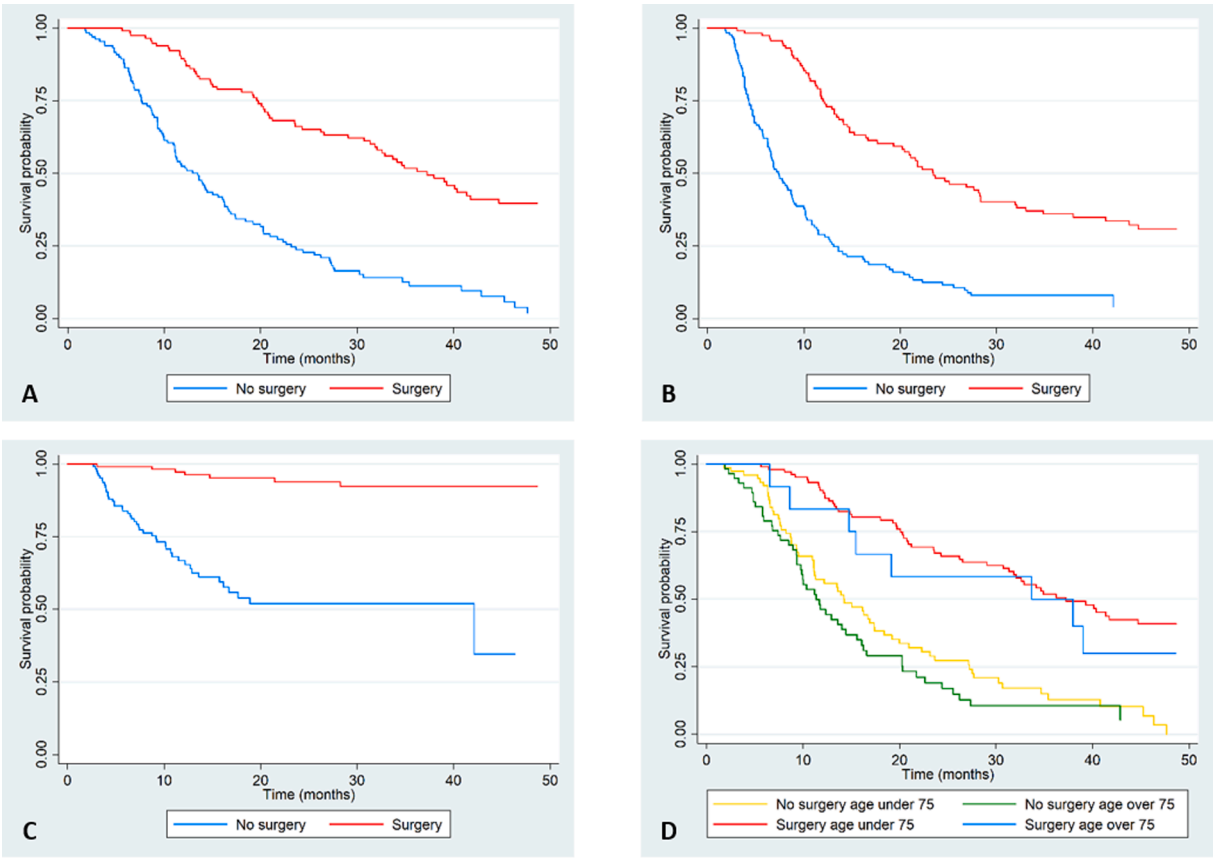

Fig. 1. Overall survival (A), Progression free survival (B) and Freedom from Local Progression (C) for the entire cohort of patients. Overall survival comparing surgery and no surgery, and age <75 and ≥75 years of age (D).

Table 5
Multivariate analysis of OS, PFS, and FFLP using the cox proportional hazards model in the entire cohort. Hazard ratio (HR), confidence interval (CI). (N = 248).

	Overall Survival (OS)			Progression Free Survival (PFS)			Freedom from Local Progression(FFLP)		
	HR	*p* Value	95 % CI	HR	*p* Value	95 % CI	HR	*p* Value	95 % CI
Age ≥ 75 years	1.34	0.09	0.96–1.88	0.91	0.59	0.66–1.27	0.91	0.77	0.50–1.68
Histology (in relation to adenocarcinoma)									
Squamous Cell	1.04	0.84	0.71–1.53	0.89	0.54	0.62–1.29	0.91	0.79	0.46–1.81
Other	1.57	**0.05**	1.00–2.45	1.42	0.13	0.90–2.21	0.78	0.63	0.27–2.19
Surgery	0.53	**<0.001**	0.45–0.63	0.51	**<0.001**	0.43–0.60	0.08	**<0.001**	0.05–0.19
Heart V30Gy > 46 %	1.26	0.13	0.93–1.75	1.24	0.17	0.91–1.70	*NA**		
IMRT Use	*NA**			*NA**			0.55	**0.039**	0.31–0.97

Table 6
Multivariate analysis of OS, PFS, and FFLP using the cox proportional hazards model in patients 75 years and older. Hazard ratio (HR), confidence interval (CI). (N = 69).

	Overall Survival (OS)			Progression Free Survival (PFS)			Freedom from Local Progression (FFLP)		
	HR	*p* Value	95 % CI	HR	*p* Value	95 % CI	HR	*p* Value	95 % CI
Histology (in relation to adenocarcinoma)									
Squamous Cell	1.51	0.22	0.78–2.92	1.71	0.11	0.89–3.30	1.17	0.80	0.34–4.01
Other	2.13	0.81	1.01–4.52	4.28	**0.001**	1.89–9.73	0.97	0.97	0.21–4.01
Surgery	0.67	**0.05**	1.00–4.52	0.72	0.10	0.49–1.07	0.07	**0.02**	0.007–0.68
Heart V30Gy > 46 %	2.57	**0.003**	1.39–4.73	2.99	**0.001**	1.54–5.814	*NA**		
IMRT Use	*NA**			*NA**			0.19	**0.022**	0.06–0.57

[11,12]. In contrast, other studies have demonstrated that age has minimal effects on outcome and survival [13,17,18,34,44]. Regardless, these studies have emphasized that curative surgery can be safe and viable for older populations with a survival benefit and better quality-of-life, requiring the need for careful clinical selection criteria [4,10,11,31,45]. A large American review of the National Cancer Database of older patients (defined as ≥70 years of age) with locally advanced EC demonstrated that 10 % of patients had trimodality

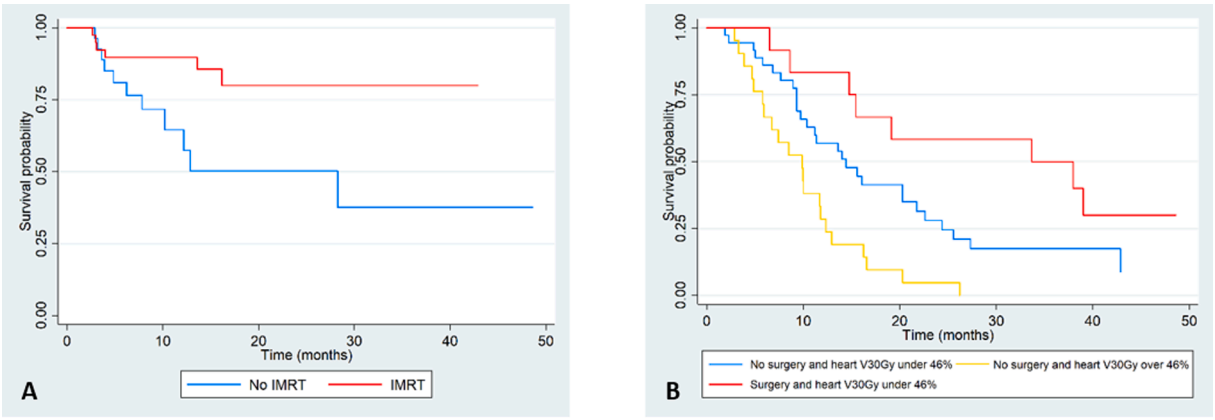

Fig. 2. Freedom from local progression in patients ≥75 years of age, comparing IMRT and non-IMRT planning (A). Overall survival in the older ≥75 years of age, comparing no surgery and surgery, with heart V30Gy (B).

treatment. Although this number is less than our study's finding of 17 % of older patients completing trimodality treatment, it must be acknowledged that this was in relation to all older patients with EC, including those who had no treatments. Our study did not include all patients diagnosed with EC, but only patients who underwent, at minimum, RT with doses greater than 40 Gy. Our findings are similar to the retrospective study at another Canadian cancer centre, with 14 % of their older patients (≥75 years of age) completing trimodality therapy [37].

A similar retrospective institutional review was done by, specifically examining the outcomes of older patients with EC. The patient characteristics in this study were very similar to our study. In this study of 89 patients ≥75 years of age, 23.5 % (21 patients) underwent surgery. For the entire cohort, the median OS and PFS was 28 and 15 months, respectively. The older patients who underwent trimodality treatment demonstrated significantly better OS (86 months vs 19 months) and PFS (44 months vs 9.8 months). This data is significantly better than other retrospective studies such as in these three studies of patients ≥70 years of age with OS of 12.1–18.6 months [7,17,46]. Furthermore, the OS in this study exceeds trials such as CROSS, which reported an OS in trimodality treatment arm in the younger age group (<75 years of age) of 48.6 months, suggesting the results of the study Rahimy et al. [10] are outliers related to the small sample and actuarial survival data.

Our older patients who completed trimodality therapy had an OS of 33.7 months. The most similar comparison found in the literature is the study by Natori et al. [37], where patients with similar characteristics including age ≥75 had an OS of 33.1 months. This study differed from ours by considering curative treatment intent to include trimodality treatment, surgery alone or definitive CRT. Similarly, many studies differed from ours where curative intent treatment was considered to include options of trimodality treatment, definitive CRT, surgery alone or RT alone. It appears the OS in most of these studies with differing "curative" definitions are decreased compared to ours, such as 18.6 months [6,7] and 17.8 months [36]. Tougeron et al. [36] examined baseline parameters that influenced the therapeutic decisions and outcomes in older EC patients. The authors identified factors including weight loss >10 %, WHO performance status >1, Charlson score >1 as well as age >75 years to be contraindications for aggressive treatment. This contradicts our findings, in which patients ≥75 years of age had a significant improvement in OS when completing curative trimodality treatment; compared with those who did not. This highlights the importance of understanding the patient's physiological age and not basing decision making strictly on chronological age [44].

Several studies have emphasized the importance of considering an onco-geriatric assessment prior to decision-making, to aid oncologists/surgeons in the final decision [36,37,47,48]. Van Holstein et al. [48] utilized a geriatric assessment to identify patients at high risk of treatment toxicities. In their study, the majority of the EC patients studied (>70 years) were frail and malnourished during the assessment. Interestingly, with the assessment, a high percentage (40.6 %) of patients completed trimodality treatment. Unfortunately, they also found high one-year mortality rates of 37 %, irrespective of treatment. The authors noted that further research is required to determine the geriatric assessment's predictive value.

As people age, older people may begin to become more frail; indicating loss of their functional and/or physiological reserve. This can often lead to more negative outcomes including hospitalization with longer admissions, increased emergency visits and even death [49,50]. Additionally, older adults frequently have chronic health conditions, with 80 % of Canadians living with at least one, and 50 % living with at least two chronic conditions [51]. Given the complexity of varying degrees of frailty, combined with comorbid health conditions when managing older cancer patients, it is critical to identify which patients are fit or resilient and may benefit from standard cancer care or a more tailored or modified approach. Unfortunately, the literature is inconsistent in providing concrete evidence for how this approach is best done; whether this is through frailty screening, geriatric assessment, or utilization of a patient's performance status scale.

We did not regularly capture a patient's performance status in our electronic health record, or refer for a geriatric or frailty assessment. Our approach includes discussion of each EC patient at MCC, with all oncological disciplines. This discussion incorporates a patient's performance status and age into their clinical factors. All patients that were potentially a surgical candidate, were further assessed by a thoracic surgeon. If there were any concerns about a patient's fitness for surgery, they were further referred and assessed by respirology and/or cardiology prior to final decision-making.

Given this approach, the percent of older patients (27.5 %) offered trimodality treatment was less than the younger population (68.7 %); however similar outcomes were seen regardless of age group in those who completed the intended trimodality treatments. This finding reflects our ability to incorporate physiological factors into treatment decision-making, rather than only considering age. Fortunately, this contradicts the finding by the National Cancer Equality Initiative in the UK where it has been found clinicians over-rely on chronological age to indicate a patient's frailty [52].

IMRT vs. 3D-CRT planning and treatment

Unlike in the studies by Lin et al. [18,25,26], Bai et al. [20] and Kowalchuk et al. [53] which found significant improvements in OS in the IMRT-planned and treated patients compared with the 3D-CRT patients, our study found no difference in OS between the two groups. These results were similar to another similar-sized study by Freilich et al.

[54] who retrospectively reviewed 232 patients with EC, comparing IMRT and 3D-CRT, and observed no significant difference based on radiation technique with respect to median OS. This was again seen in the analysis of four prospective clinical trials, which found no clinical significance on OS in the IMRT- and 3D-CRT-planned EC patients [24]. Our study did demonstrate a trend towards improvement in local control in the IMRT patients compared with the 3D-CRT patients, similar to the studies by Lin et al. [25,26], however this finding needs to be interpreted cautiously since there was no difference in OS seen. The association seen here with radiation technique and improved FFLP may be a reflection of the risk of distant versus local recurrence in determining overall survival.

Planning studies have shown that IMRT is superior to 3D-CRT in reducing the volume of lung and heart irradiated [55]. Our findings demonstrated that the heart V30Gy was significantly lower in the IMRT patients compared with the 3D-CRT patients. Understanding how and if this dosimetric advantage translates into clinical benefit is not as well known. There have been many studies investigating radiation-induced heart disease (RIHD), including in patients with EC; with the strong belief that RIHD is related to heart dose and irradiated heart volume. More recent studies have been investigating the relationship between cardiac substructures and dosimetric parameters along with patient outcomes [56]. Garant et al. [57] conducted a multi-institutional review of EC patients undergoing trimodality therapy, to explore the association of radiation dose-volume histogram (DVH) parameters and cardiopulmonary toxicities. They found an increased heart dose was associated with increased risk of cardiac toxicity. Interestingly in our study, in the non-surgical older patient group, we found that the cardiac dose was a factor in OS, with patients who had a heart V30Gy less than 46 % having significantly better survival.

Morota et al. (2009) examined late toxicities after definitive CRT, and interestingly found the 2-year cumulative incidence of late cardiopulmonary toxicities (Grade 3 and greater) was 29 % for patients aged 75 years or older; compared with only 3 % of the younger patients ($p = 0.005$). These patients had extensive fields, which included the primary tumour along with the local metastatic lymph nodes in the supraclavicular, mediastinal and celiac axis nodes; resulting in the authors suggesting the extensive field protocol is not appropriate for older patients. They also found that age was the only significant predictor for incidence of late cardiopulmonary toxicities. The authors did not comment on any link between the cardiopulmonary toxicities and overall survival, but did mention that two (of the 74) patients died without cancer recurrence, but related to cardiopulmonary toxicity [58]. In the study by Beukema et al. (2022) who examined late cardiac toxicity in EC survivors, patients who completed neoadjuvent CRT prior to surgery had an increased rate of myocardial fibrosis and atrial fibrillation (AF) compared to those treated with surgery alone. Furthermore, those patients who had AF had markedly higher heart doses than the irradiated group that did not develop AF [59]. The development of AF, which also develops more commonly in ages 75–85, puts patients at higher risk of developing a stroke, heart failure and results in worse overall survival [60].

The esophageal cancer guidelines by the National Comprehensive Cancer Network (NCCN) recommend ensuring the V30Gy is less than 30 % of the heart [61]. Data suggests that for every 10 % reduction in heart V30Gy, the risk of cardiac event was reduced by 19 % [57]. A large study by Lin et al. [62] identified over 3400 patients older than 65 years of age with non-metastatic EC. The authors found the use of IMRT was associated with lower cardiac-specific mortality. The authors concluded that IMRT may be a factor in overall health, specifically related to the cardiac health of patients with curable EC.

One can argue that the increased heart dose is a direct surrogate of an increased field length and subsequent tumour length and/or nodal volume, indicating potentially worsening disease. However, when analyzing outcomes including OS, field length did not pass the univariate screen, and only the heart V30Gy volume was including in the multivariate analysis. This was similar in the study by Jin et al. (2024) who found tumour/field length was not prognostic in patient outcomes [56]. Field length was a factor in cardiac toxicity in the older population in the study by Morota et al. (2009), however these authors had extensive field lengths of 31 cm despite a median tumour length of 6 cm, and only utilized anterior-posterior beam arrangements [58]. Our median tumour length was also 6 cm, but median field length was only 19.6 cm. Furthermore, we utilized either a 3D-CRT or IMRT planning technique.

We did not find any statistical differences in the lung V20Gy in patients treated with IMRT or 3D-CRT, nor the lung V20Gy effect on OS. This is similar to the study by Garant et al. [57], where the correlation between the lung V5Gy and V10Gy and OS was unclear.

Study limitations

Study limitations are mostly attributed to the retrospective nature of data collection. This includes the limitation due to some factors that were not able to be collected because of the lack of availability in the electronic health record. Specifically, this includes the lack of T staging due to limited utilization of endoscopic ultrasound and no recorded performance status. Furthermore, generalizability of the results is limited as the data presented is from a single institution. When interpreting the results of the link with patient outcomes and dosimetric planning, as well as patient outcomes and age, there are many confounding factors that need to be considered including the heterogeneity of the prescription doses and chemotherapy agents used. Therefore, cautious interpretation is necessary. Lastly, we want to recognize that the inherent nature of a potential selection bias in this non-randomized, retrospective study, as patients were carefully selected for each treatment modality in the interprofessional MCC based on their clinical and physiological factors, as discussed above.

Future directions

Although randomized control trials provide the best evidence for cancer treatments and management, older patients are historically excluded to the complexities surrounding their age, comorbidities and disabilities, and additionally barriers surrounding recruitment and retention in the older population [63]. A prospective data collection with a large data registry focusing on the older population is required. Fortunately, there is a large population registry in Ontario currently in progress – "The Population Registry of Esophageal and Stomach Tumours in Ontario (PRESTO)" that can be utilized to specifically analyze EC in the older population [64]. This large prospective database will allow the optimization of care for this disease; specifically in our interest in the older population.

Conclusion

In our patient cohort, compared to younger patients, older patients with EC are less likely to receive trimodality treatments or chemotherapy as part of their treatments. Their probability of completing a prescribed radiation course is comparable to that of younger patients. Among older patients who are deemed fit after assessment by the multidisciplinary team, and accept trimodality treatments, the overall survival is comparable with the overall survival in younger patients. Further, early death rate is not increased in this group compared to the younger group of patients. Among older patients, radiation dose constraints on the heart correlates with overall survival. The dose constraints are achieved more frequently when IMRT techniques are used.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

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