

# Supplementary Materials: Three-Dimensional Conformal Radiotherapy-Based or Intensity-Modulated Radiotherapy-Based Concurrent Chemoradiotherapy in Patients with Thoracic Esophageal Squamous Cell Carcinoma

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**Table S1.** Characteristics of patients with TESCC receiving CCRT with intensity-modulated radiation therapy or three-dimensional conformal radiation therapy (AJCC clinical stages presented with TN system).

Variables	All		IMRT		3D-CRT		P value
	n = 2062	(%)	n = 1524	(%)	n = 538	(%)	
<b>Age</b>							
Mean ± SD	57.92	± 11.00	57.85	± 10.86	58.44	± 11.37	0.1342
20-29	6	(0.29)	4	(0.26)	2	(0.37)	0.5096
30-39	55	(2.67)	40	(2.62)	15	(2.79)	
40-49	472	(23.09)	345	(22.64)	127	(23.61)	
50-59	714	(34.82)	545	(35.76)	169	(31.41)	
60-69	500	(23.97)	367	(24.08)	133	(24.72)	
70-79	240	(11.45)	168	(11.02)	72	(13.38)	
80-89	72	(3.52)	52	(3.41)	20	(3.72)	
90-100	3	(0.14)	3	(0.20)	0	(0.00)	
<b>Sex</b>							
Male	1960	(95.05)	1447	(94.95)	513	(95.35)	0.4189
Female	102	(4.95)	77	(5.05)	25	(4.65)	
<b>Follow-up time(year)</b>							
Median, IQR	2.02	1.15	2.02	1.15	2.00	1.14	0.1848
(q1, q3)	(0.92,	2.77)	(0.93,	2.78)	(0.99,	2.74)	
(min, max)	(0.09,	7.29)	(0.09,	7.29)	(0.12,	6.96)	
<b>CCI score</b>							
mean ± SD	1.25	± 1.39	1.25	± 1.40	1.29	± 1.34	0.4568
0	697	(34.03)	533	(34.97)	164	(30.48)	0.2443
1	721	(35.10)	525	(34.45)	196	(36.43)	
2	353	(16.78)	253	(16.60)	100	(18.59)	
>3	291	(14.09)	213	(13.98)	78	(14.50)	
<b>Radiation dose (Gy)</b>							
Median, IQR	50.40	± 0.30	50.40	± 0.31	50.40	± 0.22	0.9617
<b>Cumulative cisplatin dose (mg/m<sup>2</sup>)</b>							
Mean (SD)	255.57	± 57.65	255.57	± 58.61	253.56	± 59.16	0.1152
<b>Clinical T stages</b>							
T1	5	(0.42)	5	(0.33)	0	(0.00)	<0.0001
T2	131	(6.35)	66	(4.33)	65	(7.43)	
T3	816	(39.57)	549	(36.02)	267	(38.48)	
T4	1110	(53.83)	904	(59.31)	206	(38.28)	
<b>Clinical N stages</b>							
N0	316	(15.32)	218	(14.30)	98	(18.22)	<0.0001
N1	401	(19.44)	274	(17.98)	127	(23.61)	
N2	721	(34.97)	543	(35.63)	178	(33.09)	
N3	624	(30.26)	489	(32.09)	135	(25.09)	
<b>Year of diagnosis</b>							
2006-2010	798	(39.08)	450	(29.53)	348	(64.68)	<0.0001
2011-2014	1264	(60.92)	1074	(70.47)	190	(35.32)	
<b>Toxicity profile</b>							
Major heart events	58	(2.81)	41	(2.69)	17	(3.16)	0.5687

Radiation pneumonitis grade 2	465	(22.55)	334	(21.92)	122	(22.67)
<b>Death</b>						<0.0001
No	454	(21.84)	372	(24.41)	82	(15.24)
Yes	1608	(78.16)	1152	(75.59)	456	(84.76)

CCRT, concurrent chemoradiotherapy; CCI, Charlson comorbidity index; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; AJCC, American Joint Committee on Cancer; ref, reference; IMRT, intensity-modulated radiation therapy; IQR, interquartile range; SD, standard deviation; Gy, Gray; 3D-CRT, three-dimensional conformal radiation therapy.

**Table S2.** Cox proportional hazard regression analysis of mortality risk among patients with TESCC receiving CCRT (AJCC clinical stages presented with TN system).

Variable	HR	Univariate analysis			Multivariate analysis		
		95% CI	P	aHR*	95% CI	P	
<b>RT Modalities</b>							
3D-CRT (ref)	1			1			
IMRT	0.89	(0.80, 0.99)	0.0372	0.86	(0.75, 0.91)	0.0116	
<b>Sex</b>							
Female (ref)	1			1			
Male	1.12	(0.89, 1.40)	0.3378	1.04	(0.91, 1.36)	0.5729	
<b>Age</b>							
20-29 (ref)	1			1			
30-39	2.07	(0.29, 14.86)	0.4680	2.24	(0.41, 16.59)	0.3987	
40-49	2.25	(0.32, 15.88)	0.4149	2.33	(0.37, 16.75)	0.4613	
50-59	1.79	(0.25, 12.59)	0.5600	1.74	(0.34, 13.91)	0.4847	
60-69	1.65	(0.23, 11.65)	0.6141	1.75	(0.28, 11.61)	0.6538	
70-79	1.62	(0.23, 11.42)	0.6311	1.87	(0.25, 13.87)	0.6140	
80-89	1.92	(0.27, 13.76)	0.5144	2.15	(0.35, 13.40)	0.5215	
90-	2.14	(0.23, 20.44)	0.5075	3.01	(0.52, 27.61)	0.4184	
<b>CCI score</b>							
0 (ref)	1			1			
1	0.98	(0.87, 1.11)	0.7628	1.03	(0.92, 1.11)	0.8313	
2	0.94	(0.81, 1.08)	0.3725	1.01	(0.89, 1.08)	0.8927	
>3	0.96	(0.83, 1.12)	0.6291	1.09	(0.96, 1.32)	0.1267	
<b>Year of diagnosis</b>							
2006-2010 (ref)	1			1			
2011-2014	0.96	(0.87, 1.07)	0.4678	0.97	(0.89, 1.09)	0.5830	
<b>Clinical T stages</b>							
T1 (ref)	1			1			
T2	1.03	(0.77, 1.13)	0.8537	1.02	(0.94, 1.12)	0.8735	
T3	1.23	(1.08, 1.15)	0.0231	1.19	(1.04, 1.25)	0.0345	
T4	1.96	(1.35, 2.43)	<0.0001	1.94	(1.34, 2.23)	<0.0001	
<b>Clinical N stages</b>							
N0 (ref)	1			1			
N1	1.08	(1.04, 1.23)	0.0342	1.12	(1.09, 1.21)	0.0342	
N2	1.41	(1.27, 1.97)	<0.0001	1.39	(1.29, 2.08)	<0.0001	
N3	2.16	(1.71, 2.26)	<0.0001	1.99	(1.87, 2.43)	<0.0001	

\*All variables were used in multivariate analysis. HR, hazard ratio; CI, confidence interval; aHR, adjusted hazard ratio. CCRT, concurrent chemoradiotherapy; CCI, Charlson comorbidity index; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; AJCC, American Joint Committee on Cancer; ref, reference group; IMRT, intensity-modulated radiation therapy; 3D-CRT, three-dimensional conformal radiation therapy.

**Table S3.** T and N-stage-stratified Cox proportional hazards model for mortality risk associated with treatment modalities in patients with TESCC receiving CCRT.

Treatment	n	death	death rate (%)	Univariate analysis			Multivariate analysis		
				HR	95% CI	P value	aHR*	95% CI	P value
<b>All stage</b>	<u>2062</u>	<u>1608</u>							
3D-CRT	538	456	84.76	1			1		
IMRT	1524	1152	75.59	0.89	(0.80, 0.99)	0.0372	0.86	(0.75, 0.91)	0.0116
<b>Early T stage (T1-T2)</b>	<u>136</u>	<u>81</u>							
3D-CRT	65	39	60.00	1			1		
IMRT	71	42	59.15	0.99	(0.71, 2.32)	0.8677	0.98	(0.77, 2.25)	0.9854
<b>Advanced T stage (T3-T4)</b>	<u>1926</u>	<u>1527</u>							

3D-CRT	473	402	84.99	1			1		
IMRT	1453	1125	77.43	0.84	(0.74, 0.91)	0.0037	0.86	(0.74, 0.96)	0.0277
<b>Early N stage (N0)</b>	<b>316</b>	<b>218</b>							
3D-CRT	98	68	69.39	1			1		
IMRT	218	150	68.81	0.89	(0.68, 1.98)	0.4344	0.91	(0.67, 1.95)	0.5746
<b>Advanced N stage (N1-N3)</b>	<b>1746</b>	<b>1390</b>							
3D-CRT	440	391	88.86	1			1		
IMRT	1306	999	76.49	0.81	(0.71, 0.92)	0.0015	0.83	(0.74, 0.94)	0.0140

\*All variables in Supplemental Table 2 were used in multivariate analysis. HR, hazard ratio; CI, confidence interval; aHR, adjusted hazard ratio. CCRT, concurrent chemoradiotherapy; CCI, Charlson comorbidity index; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; AJCC, American Joint Committee on Cancer; ref, reference group; IMRT, intensity-modulated radiation therapy; 3D-CRT, three-dimensional conformal radiation therapy.

**Table S4. Characteristics of patients with TESSC receiving CCRT with IMRT or 3D-CRT and their propensity score-matched cohort.**

Variables	All		IMRT		3D-CRT		P value
	n = 1076	(%)	n = 538	(%)	n = 538	(%)	
<b>Age</b>							
Mean±SD	58.51	±10.62	58.58	±9.86	58.44	±11.37	0.8289
							1.0000
20-29	4	(0.37)	2	(0.37)	2	(0.37)	
30-39	30	(2.79)	15	(2.79)	15	(2.79)	
40-49	254	(23.61)	127	(23.61)	127	(23.61)	
50-59	338	(31.41)	169	(31.41)	169	(31.41)	
60-69	266	(24.72)	133	(24.72)	133	(24.72)	
70-79	240	(13.38)	72	(13.38)	72	(13.38)	
80-89	144	(3.72)	20	(3.72)	20	(3.72)	
90-100	0	(0.00)	0	(0.00)	0	(0.00)	
<b>Sex</b>							1.0000
Male	1026	(95.35)	513	(95.35)	513	(95.35)	
Female	50	(4.65)	25	(4.65)	25	(4.65)	
<b>Follow-up time (year)</b>							0.4418
Median, IQR	2.02	1.14	2.04	1.14	2.00	1.14	
(q1, q3)	(0.99,	2.73)	(0.98,	2.77)	(0.99,	2.74)	
(min, max)	(0.09,	6.69)	(0.09,	6.29)	(0.12,	6.96)	
<b>CCI score</b>							
mean±SD	1.29	±1.34	1.29	±1.34	1.29	±1.34	1.0000
0	328	(30.48)	164	(30.48)	164	(30.48)	1.0000
1	392	(36.43)	196	(36.43)	196	(36.43)	
2	200	(18.59)	100	(18.59)	100	(18.59)	
>3	156	(14.50)	78	(14.50)	78	(14.50)	
<b>Radiation dose (Gy)</b>							1.000
Median, IQR	50.40	±0.21	50.40	±0.21	50.40	±0.22	
<b>Cumulative cisplatin dose (mg/m<sup>2</sup>)</b>							0.6970
Mean (SD)	253.77	±59.39	254.97	±59.61	253.56	±59.16	
<b>AJCC clinical stages</b>							1.0000
Early stage (IA-IIIB)	208	(19.33)	104	(19.33)	104	(19.33)	
Advanced stage (IIIA-IIIC)	868	(80.67)	434	(80.67)	434	(80.67)	
<b>AJCC clinical stages</b>							1.0000
IA	0	(0.00)	0	(0.00)	0	(0.00)	
IB	14	(1.30)	7	(1.30)	7	(1.30)	
IIA	94	(8.74)	47	(8.74)	47	(8.74)	
IIB	100	(9.29)	50	(9.29)	50	(9.29)	
IIIA	156	(14.50)	78	(14.50)	78	(14.50)	
IIIB	438	(40.71)	219	(40.71)	219	(40.71)	
IIIC	274	(25.46)	137	(25.46)	137	(25.46)	
<b>Year of diagnosis</b>							1.0000
2006-2010	696	(64.68)	348	(64.68)	348	(64.68)	
2011-2014	380	(35.32)	190	(35.32)	190	(35.32)	
<b>Death</b>							<0.0001
No	214	(19.89)	132	(24.54)	82	(15.24)	
Yes	862	(80.11)	406	(75.46)	456	(84.76)	

CCRT, concurrent chemoradiotherapy; CCI, Charlson comorbidity index; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; AJCC, American Joint Committee on Cancer; ref, reference; IMRT, intensity-modulated radiation therapy; IQR, interquartile range; SD, standard deviation; Gy, Gray; 3D-CRT, three-dimensional conformal radiation therapy.

**Table S5. Cox proportional hazard regression model for mortality risk among patients with TESCC receiving CCRT in their propensity score-matched cohort.**

Variable	Univariate analysis			Multivariate analysis				
	HR	95% CI		P	aHR*	95% CI		P
<b>RT Modalities</b>								
3D-CRT (ref)	1				1			
IMRT	0.86	(0.78,	0.93)	0.0172	0.85	(0.76,	0.91)	0.00231
<b>Sex</b>								
Female (ref)	1				1			
Male	1.03	(0.90,	1.09)	0.9989	1.02	(0.94,	1.08)	0.9990
<b>Age</b>								
20-29 (ref)	1				1			
30-39	0.96	(0.61,	10.20)	0.3804	1.02	(0.41,	9.82)	0.5017
40-49	1.05	(0.76,	11.42)	0.3351	1.03	(0.77,	10.50)	0.4846
50-59	1.08	(0.49,	8.15)	0.4599	1.06	(0.51,	8.12)	0.4865
60-69	1.12	(0.67,	7.21)	0.5252	1.11	(0.68,	7.01)	0.6736
70-79	1.13	(0.77,	7.06)	0.5222	1.12	(0.78,	7.04)	0.6362
80-89	1.14	(0.63,	9.92)	0.4955	1.12	(0.67,	9.91)	0.5532
<b>CCI score</b>								
0 (ref)	1				1			
1	1.07	(0.84,	1.21)	0.5517	1.04	(0.88,	1.19)	0.6524
2	1.08	(0.85,	1.25)	0.4836	1.14	(0.89,	1.24)	0.6850
>3	1.13	(0.87,	1.42)	0.4289	1.16	(0.91,	1.33)	0.4752
<b>Year of diagnosis</b>								
2006-2010 (ref)	1				1			
2011-2014	0.93	(0.87,	1.04)	0.8978	0.91	(0.87,	1.05)	0.8241
<b>AJCC clinical stages</b>								
Early stage (ref)	1				1			
Advanced stage	1.28	(0.48,	1.57)	0.5047	1.89	(.51,	1.63)	0.4955

\*All variables were used in multivariate analysis. HR, hazard ratio; CI, confidence interval; aHR, adjusted hazard ratio. CCRT, concurrent chemoradiotherapy; CCI, Charlson comorbidity index; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; AJCC, American Joint Committee on Cancer; ref, reference group; IMRT, intensity-modulated radiation therapy; 3D-CRT, three-dimensional conformal radiation therapy.



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