Survival Rate of Colorectal Cancer in Eastern Mediterranean Region Countries: A Systematic Review and Meta-Analysis

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Abstract

Colorectal cancer (CRC) is the second most common cause of cancer-related deaths worldwide. Survival rates are among the most important factors in quality control and assessment of treatment protocols. This study was aimed to assess the survival rate of colorectal cancer in Eastern Mediterranean Region Countries. In the present study we comprehensively searched 6 international databases including PubMed/Medline, ProQuest, Scopus, Embase, Web of Knowledge and Google Scholar for published articles until November 2018. The Newcastle-Ottawa Quality Assessment Form for Cohort Studies was applied to evaluate the quality of included studies. The heterogeneity of papers was assessed with the Cochran Test and I-Square statistics. Meta-regression test was performed based on publication year, sample size and Human Development Index (HDI) of each study. Among the total of 1023 titles found in the systematic search, 43 studies were eligible to be included in the present meta-analysis. According to the results, the I-year, 3-year and 5-year survival rate of patients with Colorectal Cancer was 88.07% (95% CI, 83.22-92.92), 70.67% (95% CI, 66.40-74.93) and, 57.26% (95% CI, 50.43-64.10); respectively. Furthermore, Meta-regressions did not show significant correlations between survival rate and year, sample size or Human Development Index. Survival rates, especially the 5-year survival rate in the EMRO were less than European countries and the USA. Documented and comprehensive evidence-based findings of the present meta-analysis can be used to enhance policies and outcomes of different medical areas including prophylaxis, treatment and health related objectives in colorectal cancer.

Keywords

colorectal cancer, EMRO, survival, systematic review, meta-analysis.

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Background

Nowadays, Non-communicable diseases are the most important cause of death worldwide. It is anticipated that cancer is going to be one of the most critical causes of death and by itself the most extensive cause of decreasing the quality of life in 21 century.¹ Worldwide, Colorectal Cancer is the fourth most common cancer in men and the third among women.^{2,3} This cancer is the most common type of gastrointestinal cancers and is the second leading cause of mortality by malignancies.⁴⁻⁶ Based on the latest article published by the International Agency for Research on Cancer (2018Globocan IARC), in 2018, Colorectal Cancer consists 10.2% of all cancer cases and 9.2% of cases of cancer mortality.⁷ Over 1.8 million new colorectal cancer and 881000 deaths were estimated in 2018. The lowest incidence of Colorectal Cancer is in Africa and southern Asia and the highest rate is in male population of the Republic of Korea and in female population of Macedonia.⁴ Colorectal cancer was also responsible for 19.0 million (18.5-19.5) DALYs globally in 2017, with an age-standardized rate of 235.7 (229.7-242.0) DALYs per 100000 person-years, which decreased between 1990 and 2017 (-14.5%) [-20.4 to -10.31).⁸

Incidence and mortality of cancer is increasing globally. These factors are multiplex, but the aging of communities and population growth, as well as changes in the prevalence and distribution of the main risk factors of cancers participate in this matter. All these are a few factors that are associated with the development of socio-economic status (SES).⁹ So, it is fair to say that this increase in trend of Colorectal cancer is alarming and the importance of consideration to the recent guidelines of National Comprehensive Cancer Network (NCCN) is crucial for colon and rectal cancers.¹⁰

The increased incidence rate, especially overall changes in the age-period-cohort analysis implies the effects of nutritional patterns, obesity, and lifestyle. Meanwhile decreased mortality rate in developed countries, depicts improvement in survival, which is related to effective treatment methods, appropriate and enhanced management in these countries.^{11,12} High consumption of red meat or processed food was associated with increased risk of colon cancer, but it was not associated with rectal cancer.¹³ Consumption of processed meat, alcohol, and high body mass index increments the likelihood of colon cancer while physical activity was a protective factor.¹⁴

Diverse factors are involved in the survival of colorectal cancer as potential factors such as stage, grade, tumor location,^{15,16} coexisting cancers,¹⁷ provider profile, socioeconomic status(SES),¹⁸ and prompt treatment¹⁹ due to earlier diagnosis and advances in chemotherapy, surgery and radiotherapy. These factors improved survival of Colorectal Cancer considerably over the past decade.²⁰ Although the promotion of therapeutic and diagnostic methods has led to increased survival of these patients, there is clearly a geographical discrepancy in the survival of this cancer globally.²¹

The first step to control a disease and its complications in each population, is recognizing its state as well as gathering data about its incidence, survival rates, types and locations. Studies on the survival rates of Colorectal cancer in the Eastern Mediterranean Region have achieved divergent results and the population of the researches is also different in these studies. Familiarity with the multi-year survival rate of Colorectal cancer in this region can provide precious information regarding control, prevention and treatment of patients. A unitary and thorough study regarding survival rate of Colorectal cancer in the eastern Mediterranean region has not yet been done.

Therefore, in this study we aimed to do a systematic review and meta-analysis to calculate the survival rate of Colorectal Cancer in the Eastern Mediterranean region.

Methods

The present study is a systematic review and meta-analysis on the survival rate of Colorectal Cancer in the Eastern Mediterranean region (EMRO) countries. This study was designed and implemented and report based on PRISMA checklist (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) in 2018.²²

Search Strategies

We searched 6 international databases; Medline, PubMed, Pro-Quest, Scopus, Embase and Web of knowledge to November 2018. We also searched Google Scholar to find gray literature.

Selected keywords for international databases included: ("Neoplasm," "Cancer," "Carcinoma," "Malignancy," "Colorectal Cancer," "Colorectal Neoplasms," "Colorectal carcinoma," "Colorectal Tumor," "Cancer of Colorectal," "Neoplasms of Colorectal," "Colonic Neoplasm," "Rectal Neoplasms," "Survival, "Survival Analysis," "Survival Rate," "Afghanistan," "Bahrain," "Iran," "Iraq," "Jordan," "Kuwait," "Lebanon," "Oman," "Pakistan," "Qatar," "Saudi Arabia," "Syria," "United Arab Emirates," "Djibouti," "Egypt," "Morocco," Palestine," "Somalia," "Sudan," "Tunisia,"

Retrieved records were entered in EndNote, X7 software and duplicated records were automatically deleted. Two independent researchers examined all the papers.

Inclusion and Exclusion Criteria

All observational studies (cross-sectional, case-control and cohort) that investigated the survival rate of Colorectal Cancer in the EMRO regions, were included in our project. Studies that involved other cancers and studies that involved metastasis and relative survival rates were excluded as it's a procedure with systematic reviews and meta-analysis. Studies that did not disclose the sample size or confidence interval of survival rates were not included in the meta-analysis.

Quality Assessment

To assess the quality of articles included in our investigation, the Newcastle-Ottawa Quality Assessment Form for Cohort Studies was applied. This tool consists of 3 separate sections: selection (4 items), comparison (1 item) and, result (3 items Studies scored based on the overall scores and divided into 3 categories: Good (3 or 4 stars in selection domain, 1 or 2 stars in comparability domain, and 2 or 3 stars in outcome/exposure domain), Fair (2 stars in selection domain, 1 or 2 stars in comparability domain, and 2 or 3 stars in outcome/exposure domain) and Poor (0 or 1 star in selection domain or 0 stars in comparability domain or 0 or 1 stars in outcome/exposure domain).²³

Screening of Studies

Two independent reviewers screen the records (based on title, abstract and full-text), appraise the quality of included studies and extract the data. A third reviewer resolved potential disagreement.

Data Extraction Form

We used a pre-prepared checklist for data extraction. This checklist included the author's name, the year of publication, the period of study, the sample size, the country of study, gender and, survival rate in colon, rectum and colorectal cancer.

Statistical Analysis

The heterogeneity of the studies was evaluated by Cochran Test (with a significant level less than 0.1) and evaluated using I2 statistics. Regarding heterogeneity, random effect-model was utilized with the inverse-variance method, and if there was no heterogeneity, fixed effects model was used. In case of heterogeneity among the studies, methods such as metaregression and sub-groups analysis were performed.

In the first stage, studies were analyzed based on 1, 3 and 5-year survival rates and based on the location of cancer: colon, rectum and colorectal categories. Obtaining the 2-year and 4-year survival rates was only possible for Colorectal cancer. All analyses were fulfilled by STATA statistical software version 13.

Additional Analysis

Because of the high heterogeneity of the studies, the metaregression analysis was operated. One of the indexes that has been used for this purpose is the Human Development Index. HDI is a relative standard for measuring life expectancy, literacy, learning level, and overall level of life standards in human societies. Human development index is anticipated by measuring the level of well-being, especially well-being among children and individuals with low age. We can use this index to assess the development of countries, the impact of economic policies on life standards.²⁴ This index is utilized in our study to exhibit the survival rates of colorectal cancer in each of these countries. Other factors that were used in meta-analysis were the year of study and sample size. Additionally, the survival rate of Colorectal cancer in each country was also declaredso It should be highlighted that for subgroups analysis calculate the survival rates in each gender, within the 43 of the studies that were included in this meta-analysis, only 5 studies were able to demonstrate the results with segregation of gender. Specific year survival rate analysis between subgroups based on gender was not possible with the data we gathered.

Risk of Bias

The random-effects model was used to reduce the risk of bias in the studies.^{25,26} The Egger bias test was also used to evaluate the risk of publication bias.²⁷

Results

Study Selection

In total, 1678 articles were identified for potential inclusion. After reviewing the titles and abstracts, a total of 108 articles were entered to the next phase. Finally, 43 articles fulfilled all criteria and were included in our study (Figure 1).

Study Characteristics

More specifically, the present review included studies published between 2000 and 2018. Based on geographical location, 29 studies were from Iran,²⁸⁻⁵⁶ 4 study from Saudi Arabia,⁵⁷⁻⁶⁰ 3 from Oman,⁶¹⁻⁶³ 2 from Jordan,^{64,65} 1 from Libya,⁶⁶ 1 from Kuwait,⁶⁷ 1 from Lebanon,⁶⁸ 1 from Pakistan⁶⁹ and 1 was from United Arab Emirates.⁷⁰ The characteristics of the studies are illustrated in Table 1.

Quality Assessment

The quality evaluation results are provided in Online Appendix 1. Based on our review using the relevant checklist, 25 studies had good quality and 18 articles had moderate quality.

Results of Meta-Analysis

First, the articles were arranged based on the publication year. Then the survival rates obtained were stratified by the following: The survival rate of 1, 2, 3, 4 and 5 years and the survival rates of Colon, Rectum and Colorectal cancer individually. Furthermore, Meta-regression was executed based on the year of the study, HDI index and sample size. As specified before subgroup analysis based on gender was not possible due to the lack of reports of the articles.

One-Year Survival Rate

Of the final articles, 10 studies illustrated 1-year survival rate of Colorectal cancer. Based on the random-effect model, the study demonstrated that 1-year survival rates in the Eastern Mediterranean region was 88.07% (95% CI, 83.22-92.92)



Figure 1. Flowchart of the included eligible studies in systematic review.

(Figure 2). Furthermore, studies that disclosed colon and rectal cancer 1-year survival rate stated the rates as following 91.17% (95% CI, 86.73-95.61) and 95.14% (95% CI, 92.84-97.45) respectively (Online Appendix 2 and 3).

Two-Year Survival Rate

Of the final articles, 8 studies reported the 2-year survival rate of colorectal cancer. All the reports were based on colorectal cancer exclusively. Based on random-effect model, the results showed that 2-year survival in the Eastern Mediterranean region was 83.19% (95% CI, 80.54-85.84) (Online Appendix 4).

Three-Year Survival Rate

Of the final articles, 11 studies announced the 3-year survival rate of colorectal cancer. Based on the random-effect model, the results of the study portrayed that 3-year survival rate in the Eastern Mediterranean region was 70.67% (95% CI, 66.40-74.93) (Figure 3). In addition, studies that reported colon and

rectal cancer illuminated a 3-year survival rate of 65.29% (95% CI, 56.96-73.62) and 71.02% (95% CI, 57.94-84.10) respectively (Online Appendix 5 and 6).

Four-Year Survival Rate

Of the final articles, 5 studies reported the 4-year survival rate of Colorectal Cancer. All the reports were based on only Colorectal cancer and there was no data about colon or rectal cancer individually. Based on the random-effect model, the results of the study demonstrated that 4-year survival in the Eastern Mediterranean region was 68.87% (95% CI, 61.46-76.28) (Online Appendix 7).

Five-Year Survival Rate

Of the final articles, 29 studies reported the 5-year survival rates of Colorectal Cancer. Based on random-effect model, 5-year survival rate in the Eastern Mediterranean region was 57.26% (95% CI, 50.43-64.10) (Figure 4). Also, studies that

intinued)	(ככ											
Я	9.43	ЛĶ	NK	NK	NK	Colorectal	Total	1127	2006-2011	Iran	Ahmadi (2014)	16
ЯZ	68.30	R	NR	R	R	Colorectal	Total	580	2005-2006	Iran	Heidarnia (2013)	15
R	43.40	R	NR	NR	NR	Colorectal	Total	227	2004-2008	Iran	Aryaie (2013)	4
	50.60						Female					
	41.00						Male		2000-2004			
	44.30								1994-1999			
	44.70							:)				2
ЯZ	44.60	R	R	R	R	Colorectal	Total	549	1994-2004	Saudi Arabia	Al-Ahwal (2013)	<u></u>
R	27.20	NR	50.30	R	93.90	Colorectal	Total	243	2003-2008	Iran	Mehrabani (2012)	12
	I		80		100			8(poor- advanced)				
	56		56		71			29(poor- advanced)				
	33		67		001			4 (poor-early)				
	4		42		87			l 6(poor-early)				
	36		48		86			55(Moderate-advanced)				
	45		59		16	Rectal		90(Moderate-advanced)				
	54		80		16			37(moderate-early)				
	61		23		66			90(moderate-early)				
	95		67		ä			53/Wall -advanced)				
	47		59		83			o (vell -early) 184(Well -advanced)				
	- :		22 F		2 2			184(Well -early)				
R	63.30	R	75.90	RR	91.70	Colorectal	Total	530(total)	2002-2007	Iran	Ghabeljoo(2011)	=
5.00	5.00	R	R	ЯZ	R	Colorectal	Total	484	1990-2006	Iran	Fathollahi (2011)	0
ЯZ	45.00	R	NR	RR	88.00	Colorectal	Female	957				
R	39.00	R	ЛR	R	86.00	Colorectal	Male	1235				
R	41.00	43.00	54.00	68.00	84.00	Colorectal	Total	2192	2000-2005	Iran	Moradi (2009)	6
R	61.00	RR	73.10	R	91.10	Colorectal	Total	1138	2001-2006	Iran	Moghimi-Dehkordi (2009)	œ
R	56.40	R	RR	R	RR	Colorectal	Total	61 (Sporadic)	2003-2008)	
ЯZ	82.50	NR	NR	R	NR	Colorectal	Total	60(HNPCC)	2003-2008	Iran	Haghighi (2009)	7
ЯЯ	63.30	69.00	75.90	83.70	91.70	Colorectal	Total	1219	2002-2007	Iran	Asghari-Jafarabadi (2009)	6
ЯЯ	49.01	NR	NR	NR	NR	Colorectal	Female					
ЯЯ	46.10	NR	NR	R	R	Colorectal	Male					
ЯЯ	47.36	R	NR	R	RR	Colorectal	Total	2342	2001-2005	Iran	Esna-Ashari (2008)	5
R	41.00	RR	ЛR	R	RR	Colorectal	Female	846				
R	44.00	RR	RR	R	RR	Colorectal	Male	713			~	
R	41.50	RR	NR	R	RR	Colorectal	Total	1559	1999-2001	Oman	Faris (2003)	4
ЯЯ	63.70	NR	NR	R	RR	Colorectal	Total	114	1985-1998	United Arab Emirates	Al-Shamsi (2003)	e
ЯZ	R	NR	NR	R	NR	Colorectal	Total	62(Stage3)	1998-2000			
ЯХ	R	NR	NR	NR	R	Colorectal	Total	62 (Stage2)	1998-2000	Kuwait	Behbehani (2000)	7
R	39.00	RR	NR	RR	R	Colorectal	Total	106	1990-1998	Saudi Arabia	lsbister (2000)	_
0	S	4	m	2	_	Type	Sex	Sample size	Time period	Location	Author (year)	Order
		al rate	Surviv									

Table 1. Basic Information of Included Studies.

									Surviva	rate		
Order	Author (year)	Location	Time period	Sample size	Sex	Туре	_	2	3	4	5	01
17	Akbar (2014)	Pakistan	2005-2010	38	Total	Colorectal	NR	NR	NR	NR	38.00	R
0				 	-++ C -		00 20		00 00		57.00	
<u>0</u> 6	Aknavan (2014) Al Nsour (2014)	Iran Iordan	2003-2007	117	Total	Colorectal	00.7% NR	NR	88.00 NR	R	57.70	X X X
				• • •		Colon					52.40	
						Kectal					42.80	
50	Nosrati (2014)	Iran	2002-2012	50	Total	Colorectal	ÅZ :	R Z Z Z	R R	ЯŻ	33.83	R R
21	Alsanea (2015)	Saudi Arabia	1994-2004	549	Total	Colorectal	R	RR	NR	R	44.60	RR
					Male		ÅZ :	RR Z	RR R	R Z	41.00	
					Female		RR	R	R	RR	50.60	
			1994-1999 2000-2004		Total		R	R	R	NR	44.70	R
			2002-2008		Total		R	NR	NR	NR	65.90	NR
					Male		R	NR	NR	RR	65.10	RR
					Female		RR	NR	NR	R	64.90	RR
			1990-1998		Total	Colorectal	RR	RR	NR	RR	39.00	RR
			1994-2010			Colon					55.00	R
						Rectal					44.30	R
22	Baghestani(2015)	Iran	2002-2007	900	Total	Colorectal		ЯХ	~		R	R
23	El Mistiri (2015)	Libya	2003-2005	139	Total	Colorectal	R	RR	NR	R	29.50	R
24	Fatemi (2015)	lran	2004-2013	107	Total	Colorectal	R	NR	NR	RR	73.80	NR
						Colon					75.90	
						Rectal					70.00	
25	Kumar (2015)	Oman	2000-2014	162(Stage 1)	Total	Colorectal	R	RR	NR	R	100.00	RR
				162(Stage 2)							60.00	
				162(Stage 3)							60.00	
26	Saravi (2015)	Iran	2006-2012	130	Total	Colorectal	R	R	NR	R	48.00	R
27	Semnani (2015)	Iran	2006-2008	227	Total	Colorectal	71.00	R	52.00	R	44.0	R
28	Dianatinasab (2016)	Iran	2009-2014	220	Total	Colorectal	95.00	RR	87.00	R	51.00	RR
29	Ghahremani (2016)	Iran	2005-2009	24807(Stage 2)	Total	Colorectal	100.00	98.00	96.00	93.00	93.00	R
				24807(Stage3)			99.00	97.00	94.00	90.00	84.00	
30	Semnani (2016)	Iran	2006-2007	227	Total	Colorectal	71.00	R	52.00	R	44.00	R
					Male		73.00		52.00		48.00	
					Female		69.00		50.00		38.00	
31	Zahir (2016)	Iran	2010-2015	60	Total	Colorectal	R	R	NR	R	53.00	NR
					Male						51.00	
					Female						53.00	
32	Zare-Bandamiri (2016)	Iran	2005-2010	570		Colorectal	R	R	NR	R	58.50	R
33	Aldiab (2016)	Saudi Arabia	2010-2015	175	Male	Colorectal	R	RR	67.34	R	38.77	R
					Female				57.14		22.07	
											(coi	itinued)

Table I. (continued)

6

Table I	l. (continued)											
									Surviva	al rate		
Order	Author (year)	Location	Time period	Sample size	Sex	Туре	_	2	3	4	5	0
34	Baghestani (2017)	Iran	2004-2015	1462	Total Male Female	Colorectal Colon Rectal colorectal	R	R	NR R	R	56.96 60.50 53.50 55.60 58.80	Я
35	El Rassy (2017)	Lebanon	2000-2015	70	Total	Colorectal	NR	98.00	NR	NR	95.00	ЯХ
36	Madadizadeh (2017)	Iran	2005-2015	561	Total	Colorectal	NR	R	RR	RR	59.60	R
37	Mafiana (2017)	Oman	2006-2016	170	Total	Colorectal	R	R	RR	RR	83.56	R
38	Mehrdad (2017)	Iran	2002-2014	183	Total	Colorectal	R	R	R	N R	84.61	R
39	Moamer (2017)	Iran	2004-2015	372	Total	Colorectal	NR	RR	R	R	62.05	RR
					Male						63.34	
					Female						60.35	
				372(Stage I)	Total						81.00	
				372(Stage2)							85.00	
				372(Stage3)							69.00	
				372(Stage4)							37.00	
40	Rasouli (2017)	Iran	2009-2015	335	Total	Colorectal	87.00	69.00	57.00	42.00	33.00	R
4	Sharkas (2017)	Jordan	2005-2010	3005	Total	Colorectal	NR	R	NR	RR	58.20	51.80
42	Jalaeikhoo (2018)	Iran	2000-2017	689	Total	Colorectal	NR		NR	R	53.20	43.70
					Male Female			76.20 76.90				
43	Yoosefi (2018)	Iran	1985-2012	446	Total	Colorectal	93.00	85.00	79.00	74.00	70.00	R
*NR: No	t Reported.											

Author,			%
year	Ν	ES (95% CI)	Weight
Iran			
Asghari-Jafarabadi (2009)	1219	 91.70 (90.15, 93.25) 	10.37
Dianatinasab (2016)	220	95.00 (92.12, 97.88)	10.10
Ghahremani (2016)	24807	99.00 (98.88, 99.12)	10.48
Mehrabani (2012)	243	93.90 (90.89, 96.91)	10.07
Moghimi-Dehkordi (2009)	1138	91.10 (89.45, 92.75)	10.35
Moradi (2009)	2192	84.00 (82.47, 85.53)	10.37
Rasouli (2017)	335	87.00 (83.40, 90.60)	9.90
Semnani (2015)	227	✤ 71.00 (65.10, 76.90)	9.07
Semnani (2016)	227	✤ 71.00 (65.10, 76.90)	9.07
Yoosefi (2018)	446	• 93.00 (90.63, 95.37)	10.22
Subtotal (I-squared = 98.9%, p	= 0.000)	88.07 (83.22, 92.92)	100.00
Overall (I-squared = 98.9%, p =	0.000)	88.07 (83.22, 92.92)	100.00
NOTE: Weights are from randor	n effects analysis		
	-99.1	0 99.1	

Figure 2. Forest plot of 1-year survival rate of Colorectal cancer in EMRO countries.

Author, vear	N	ES (95% CI)	% Weight
,			g
Iran			
Asghari-Jafarabadi (2009)	1219	75.90 (73.50, 78.30)	8.90
Dianatinasab (2016)	220	87.00 (82.56, 91.44)	8.33
Ghahremani (2016)	24807	■ 96.00 (95.76, 96.24)	9.15
Ghahremani (2016)	24807	• 94.00 (93.70, 94.30)	9.15
Mehrabani (2012)	243	✤ 50.30 (44.01, 56.59)	7.63
Moghimi-Dehkordi (2009)	1138	* 73.10 (70.52, 75.68)	8.86
Moradi (2009)	2192	• 54.00 (51.91, 56.09)	8.96
Rasouli (2017)	335	 57.00 (51.70, 62.30) 	8.02
Semnani (2016)	227	✤ 52.00 (45.50, 58.50)	7.55
Semnani (2015)	227	 52.00 (45.50, 58.50) 	7.55
Yoosefi (2018)	446	 79.00 (75.22, 82.78) 	8.54
Subtotal (I-squared = 99.7%,	p = 0.000)	◊ 70.94 (66.55, 75.34)	92.64
Saudi Arabia			
Aldiab (2017)	175	+ 67.34 (60.39, 74.29)	7.36
Subtotal (I-squared = .%, p =	.)	67.34 (60.39, 74.29)	7.36
	,		
Overall (I-squared = 99.6%, p	= 0.000)	\$ 70.67 (66.40, 74.93)	100.00
NOTE: Weights are from rando	om effects analysis		

Figure 3. Forest plot of 3-year survival rate of Colorectal cancer in EMRO countries.

reported colon and rectal cancer had a 5-year survival rate of 51.95% (95% CI, 43.81-60.02) and 47.44% (95% CI, 42.39-52.48) respectively (Online Appendix 8 and 9).

Survival Rate of Colorectal Cancer in Each Country

In general, the survival rate outcomes of colorectal cancer in all 6 countries are illustrated in Table 2. The highest 5-year

Author. year	N	ES (95% CI)	% Weight
Iran Ahmadi (2014) Ayghari-Jafarabadi (2009) Dianatinasab (2016) Esna-Ashari (2008) Fatemi (2015) Ghahremani (2016) Heidarnia (2013) Jalaeikhoo (2018) Maadetadeh (2017) Maamer (2017) Moamer (2017) Moatazer Haghighi (2009) Montazer Haghighi (2009) Montazer Haghighi (2009) Mortazer Haghighi (2009) Mortazer Haghighi (2019) Moradi (2017) Semnani (2018) Xare-Bandamiri (2016) Subtotal (I-squared = 99.8%, p = 0.000)	1127 227 1219 220 2342 107 24807 24807 560 6681 243 243 117 110 116 29 1138 60 81 2192 1132 50 81 2192 183 3357 246 570	9 43 (7 72, 11, 14) 43,40 (36, 65, 49, 85) 63,30 (60, 59, 66, 01) 51,00 (44, 39, 57, 61) 47,36 (45, 34, 49, 38) 73,80 (65, 47, 82, 13) 93,00 (92, 68, 93, 32) 84,00 (83, 64, 54, 49, 38) 53,60 (45, 77, 20, 93) 53,60 (45, 77, 20, 93) 53,60 (45, 77, 20, 93) 54,00 (58, 77, 72, 10) 57,20 (58, 77, 84), 83, 11) 85,00 (60, 58, 77, 42) 56,40 (43, 96, 68, 84) 56,40 (43, 96, 68, 84) 44,100 (38, 94, 43, 06) 84,51 (79, 33, 89, 84) 44,100 (38, 94, 43, 06) 84,51 (79, 33, 89, 84) 44,100 (38, 94, 43, 06) 84,51 (79, 33, 89, 84) 44,100 (27, 96, 38, 43, 06) 84,51 (79, 33, 89, 84) 56,50 (54, 45, 62, 55) 58, 51 (54, 45, 62, 55) 59, 13 (50, 66, 67, 60)	2 55 2 49 2 54 2 49 2 54 2 55 2 55 2 55 2 55 2 55 2 55 2 55
Jordan Mohannad (2014) Sharkas (2017) Subtotal (I-squared = 0.0%, p = 0.729)	1896 3005	57.70 (55.48, 59.92) 58.20 (56.44, 59.96) 58.01 (56.63, 59.39)	2.54 2.55 5.09
Lebanon El Rassy (2017) Subtotal (I-squared = .%, p = .)	70	95.00 (89.89, 100.11) 95.00 (89.89, 100.11)	2.51 2.51
Libya El Mistiri (2015) Subtotal (I-squared = .%, p = .)	139	29.50 (21.92, 37.08) 29.50 (21.92, 37.08)	2.47 2.47
Oman Kumar (2015) Kumar (2015) Subtotal (I-squared = 99.0%, p = 0.000)	162 162	100.00 (97.11, 100.00) 60.00 (52.46, 67.54) 80.18 (40.98, 119.38)	2 55 2 47 5 02
Saudi Arabia Al-Ahwal (2013) Al-Ahwal (2013) Al-Ahwal (2013) Adiab (2015) Adiab (2015) Alsanea (2015) Alsanea (2015) Alsanea (2015) Isbister (2000) Subtolal (I-squared = 92.2%, p = 0.000)	549 549 175 549 549 549 549 549 549 549 106	44, 60 (40, 44, 48, 76) 44, 70 (40, 54, 48, 86) 34, 77 (31, 54, 48, 86) 34, 77 (31, 54, 54, 59) 44, 70 (40, 54, 48, 76) 44, 70 (40, 54, 48, 76) 44, 70 (40, 54, 48, 76) 56, 50 (61, 53, 69, 77) 30, 50 (29, 77), 48, 29) 44, 52 (40, 40, 51, 43)	2 53 2 53 2 53 2 53 2 53 2 53 2 53 2 53
Overall (I-squared = 99.8%, p = 0.000)		\$ 57.26 (50.43, 64.10)	100.00

Figure 4. Forest plot of 5-year survival rate of Colorectal cancer in EMRO countries.

Table 2. Result of Meta-Analysis and Heterogeneity of Survival Rate of Colorectal Cancer in EMRO Base on Each Country and Year of Survival.

						Year of survi	val					
		I				3				5		
Country	# of study	Effect estimate	l ²	P-value	# of study	Effect estimate	l ²	P-value	# of study	Effect estimate	l ²	P-value
Iran	10	88.07 (83.22-92.92)	98.9	<0.001	11	70.94 (66.55-75.34)	97.7	<0.001	25	59.13 (50.66-67.60)	99.8	<0.001
Saudi Arabia	-	NR	NR	NR	1	67.34 (60.39-74.29)	-	-	9	45.92 (40.40-51.43)	92.2	<0.001
Oman	-	NR	NR	NR	-	NR	NR	NR	2	80.18 (40.98-119.38)	99.0	<0.001
Jordan	-	NR	NR	NR	-	NR	NR	NR	2	58.01 (56.63-59.39)	-	-
Libya	-	NR	NR	NR	-	NR	NR	NR	I	29.50 (21.92-37.08)	-	-
Lebanon	-	NR	NR	NR	-	NR	NR	NR	1	95.00 (89.89-100)	-	-
Overall	10	89.80 (88.67-90.93)	99.2	<0.001	12	70.67 (66.40-74.93)	99.6	<0.001	40	57.26 (50.43-64.10)	99.8	<0.001

*NR; Not reported.

survival rate of colorectal cancer was in Lebanon (68) and Oman (62) and the lowest survival rate was established in Libya (66) and Saudi.^{58,59}

Meta-Regression

Meta-regression results did not show a significant relationship based on the variables studied. In survival rate studies based on the year of study, no significant relationship was obtained. (Reg coefficient = 0.004, p = 0.752). Therefore, survival rates do not change based on the year of the study. Also, the results of meta-regression between the HDI index and the 5-year survival rate of Colorectal cancer did not manifest a significant relationship (Reg coefficient =-1.1, p = 0.591). There was no relationship between the sample size and survival rates (Reg coefficient = 0.0002, p =0.110). The meta-regression results are illustrated in Figure 5.



Figure 5. Result of meta-regression for 5 years survival rate of Colorectal cancer based on HDI, sample size and year of study.



Figure 6. The map-chart of 5 year survival rate of colorectal cancer in EMRO countries.

Map-Chart

The map-chart of 5-year survival rate of colorectal cancer in EMRO countries are shown in Figure 6.

Publication Bias

At last, we draw funnel plots for assessing the publication bias for survival rates of Colorectal cancer. Egger test confirmed our assessment (P < 0.001). (Online Appendix 10). This finding suggested that studies that reported lower survival rate appear to have been more widely published.

Discussion

Colorectal cancer is among the most common types of cancer that leads to more than 500,000 deaths in the world each year.⁷¹ In our investigation, the survival rates of 1, 3 and 5-year of

patients with CRC in the Eastern Mediterranean region was analyzed by meta-analysis. The 1-year survival in these countries was 88.07% (with CI 95%: 83.22-92.99). Studies show that 1-year survival rate of CRC patients in European countries including Sweden, Denmark, England, Australia and Norway are less than this comparison and are, 83.8%, 77.7%, 74.7%, 84.9% and 82.4% respectively.⁷² This rate is also less in Canada than the estimated rates for countries in the East Mediterranean region and it is 83.5%.72 The present research showed that 3-year survival rates in the EMRO region was 70.67% (CI 95%: 66.40-74.93). In 2013, Yuan et al corresponded that the 3-year survival rate of CRC patients in China, the most populous country in East Asia is 74%, which is more than the estimated survival rate in our study.⁷³ The studies demonstrated that in India, 1 and 3-year survival rates of patients with CRC was63.04% and 42.20%, respectively.⁷⁴

On the other hand, 5-year survival rate in the Eastern Mediterranean region was 57.26% (CI 95%: 50.43-64.10). However, it is not acceptable to estimate the survival rate level in countries, as this number is related to diversified factors. However, to look at this matter, observationally only the highest 5-year survival rate was in Lebanon (95%) and the lowest was in Iran (9.43%) (Table 2). However, several studies have broadcasted the survival rate of colorectal cancer in Iran and the results of the meta-analysis in subgroups showed a 5-year survival rate in Iran estimated to be59.13% (Table 2). A study executed by Yeole et al⁷⁴ in 2001 exhibited that this rate was 33.6% in India, while in some Eastern Asian countries such as China and Japan the rate was more than the estimated rate in the present study and was 68% and 61.4% respectively.73,75 In another study conducted in Malaysia, the 5-year survival rate of patients with Colorectal Cancer was 34.3%.76 On the other hand, the 5-year survival rate of these patients in the US was 65%.77 However, in some European countries, such as France, Germany and Italy this rate was more than the Eastern Mediterranean region; 60.33%, 65% and 59.33% respectively, and in The United Kingdom the rate was casted down and was in the range of 50 to 55%.⁷⁸ The 5-year CRC survival rate in the African continent countries including Uganda and Gambia was less than 8%.79 The survival rate in the Eastern Mediterranean region is less than European countries and the US and more than some Asian and African countries, but it is expected that now with increasing economic growth, higher living standards and the average age of death of gastrointestinal cancers will also increase.

In this study, the survival rate of patients based on the localization of the tumor was also investigated. The results of this research showed that the highest survival rate was dedicated for rectal cancer, which was 95.14% for 1-year and 71.02% for 3-year. While the 5-year survival rate of patients with colon cancer was more than others; 51.91% in comparison with 41.63%. In a meta-analysis study, which was recently done by Maajani et al in Iran, it was suggested that the paramount 1-year survival rate in Iran was colon cancer which was estimated to be near 90%.⁷⁷

In meta-regression analysis, which was conducted in this study, there was no significant correlation between the survival rate of CRC with sample size, the year which the studies were conducted in and the Human Development Index of the countries. Several factors can affect the survival rate of colorectal cancer in these measures. One of the most important items that can affect the incidence of patients with Colorectal cancer is gender. A study in the UK depicted that the incidence of Colorectal cancer in women is about 47% less than men.⁸⁰ In addition, it has been seen that the 5-year survival rate of women in CRC is superior than men.^{81,82} Among other effective factors that can influence the survival rate in patients is smoking and consuming alcohol.⁸³ Phips and Newcomb in 2011 stated that smoking significantly reduced the survival rate of patients with CRC.⁸⁴ To add, the cohort study done by Kangwha cohort study in South Korea stated that the chances of death in CRC patients were about 5 times more than non-alcoholic patients.85 Among other factors that may affect the survival rate in CRC patients, race, tumor stage, grade should be distinguished as well.⁷⁷ In general, it seems that the discrepancies in survival rates can be in relation to various risk factors, the increase in inherent incidence of cancer, or the better report of mortality rates.

Among the limitations of the present study, was that the reported information was not complete in the papers that were included in our survey, and therefore, many risk factors such as ethnicity, sex, smoking and alcohol consumption, stage and grade of the tumor were not entered into sub-group analyses. These elements can also justify the significant heterogeneity that was found between the studies, which even existed in the subgroups. In addition, in this survey, we evaluated the survival rate based on the location of the tumors. Studies that broadcasted the survival rate of metastatic patients were excluded, since the survival rate of these patients are utterly different from patients with non-metastatic tumors. In addition, more than half of the Eastern Mediterranean region had not published any studies on the survival rate of patients with CRC and in 5 counties we found a solo publication. Therefore, in order to make a more accurate estimate, augmented studies are essential to be done in the countries of this region especially in countries who had no data at all. We in this present study, attempted to contact the authors of the publications to gather more data and information, but only few reached out. In order to adjust the heterogeneity of studies, we used a random-effect model which was discussed earlier.

Our meta-analysis had invigorated aspects too, including usage of observational studies with a cohort approach for the study and utilizing meta-analysis to identify heterogeneity of the categorized groups. The results of the present study can be considered as an acceptable estimate of the survival rate of patients in the Eastern Mediterranean region, and it is applicable for planning prevention and treatment programs. Finally, the survival rate was not estimated for some years (such as Survival rate of 2, 4, 7 and 10 year) because a few of the studies had reports on them and this aspect should be carried out in the future in this matter. Also, we suggested that investigation for the survival rate in patients with metastatic cancer should also be considered as it can be critical in clinical decision making and treatment options.

Conclusion

Colorectal cancer is one of the most preventable malignancies and if it is diagnosed in the early stages, it can significantly increase survival rates of patients. The results of this study illustrated the survival rates in the Eastern Mediterranean region and indicated that this rate of survival, especially the 5-year survival rate in this region is less than Europe and the US. The results of this study, based on the results of the published studies, can furnish this documentary and comprehensive evidence, the fundamental basis of many policies and decision makings in many different aspects of medical development, including evaluation of screening programs, treatment and health interventions in the field of colorectal cancer.

Authors' Note

Our study was approved by The Research Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (approval no. 98-01-106-20383). The written informed consent not applicable for this study design (systematic review). Saber Ghaffari-fam is now affiliated with School of Nursing of Miyandoab, Urmia University of Medical Sciences, Urmia, Iran and Morteza Arab-Zozani is now not affiliated with Iranian Center of Excellence in Health Management, School of Management and Medical Informatics, Tabriz University of Medical Sciences, Iran.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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