Assessment of the Clinicopathologic Characteristics and Survival Rates of Colorectal Cancer Among Syrian Refugees and Turkish Population in Gaziantep Province

Canan Karan, MD[1]; İlker Nihat Okten, MD[2]; Oğuzhan Kesen, MD[3]; Atalay Çelikyürek, MD[4]; Fatih Teker, MD[1]; and Şuayib Yalçın, MD[5]

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ABSTRACT

PURPOSE Syrian refugees (SRs) have had difficulties in the diagnosis, treatment, and follow-up of chronic diseases, such as cancer, because of the conflict in the region. The cancer diagnosis and treatment process of SR are also a matter of curiosity. We aimed to compare the demographic characteristics and survival outcome data of SRs and Turkish citizens (TCs), and colorectal cancer (CRC) is one of the most common cancer types seen with similar frequency globally.

MATERIALS AND METHODS A total of 421 patients with CRC were included. Overall survival (OS) was estimated using the Kaplan-Meier method, and the log-rank test was used for comparison. Patient demographic data were compared using the Pearson Chi-square test and independent *t* test.

RESULTS In total, 421 patients (282 TCs and 139 SRs) were included in this study. The mean age was 52.9 ± 14.3 years for the entire population: 55.3 ± 14.1 years for TCs and 47.9 ± 13.4 years for SRs. Forty (29%) SRs and 60 (21.4%) TCs had de novo metastatic disease ($P = .08$). The median OS in the general population was 57.9 months (95% CI, 40.1 to 75.7), whereas it was 80.9 months (95% CI, 56.5 to 97.2) in TCs and 42.2 months in SRs (95% CI, 27.0 to 57.4; $P = .006$). In the nonmetastatic group, the median OS did not reach (NR) in TCs, and it was 52.6 months (95% CI, 43.7 to 61.5) in SRs ($P = .02$). In the metastatic group, the median OS was 21 months (95% CI, 8.5 to 29.2) in TCs, and it was 18.9 months in SRs (95% CI, 16.3 to 25.7; $P = .93$).

CONCLUSION The survival rate was lower in the SR group. Since CRC is also common among refugees, developing and implementing methods to improve the welfare of vulnerable populations is necessary.

ACCOMPANYING CONTENT

Data Supplement

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INTRODUCTION

Turkey received a huge influx of Syrian refugees (SRs) since the onset of the Syrian conflict in 2011. Approximately 6.6 million people have migrated to around 130 neighboring countries.[1] Turkey, which has hosted the most significant number of people in need of international protection, has more than 3.6 million refugees under temporary and international protection.[1] Turkey started to provide health care to refugees, mainly in camps, in the aftermath of the crisis and then expanded the provision of health care with the Temporary Protection Regulation in 2014, which integrated refugee health management into the national health system by 2015, so SR has access to health services at all levels, from primary to tertiary care and migrant health centers.[2]

As a vulnerable population, refugees require substantial support from the global community and host governments, with accessible health care being a critical component. They face heightened risks of acute conditions such as injury and communicable diseases, as well as chronic diseases linked to unhealthy lifestyles.[3,4] Cancer, a leading cause of death, necessitates a robust health care system capable of delivering comprehensive, interdisciplinary care, including accurate diagnosis, treatment options (surgery, chemotherapy, immunotherapy, radiotherapy), and palliative care.[5]

The conflict poses significant challenges to cancer management, often leading to delays in diagnosis and limited access to treatment, which negatively affect survival outcomes for refugees.[5] Colorectal cancer (CRC) is the third most common malignancy globally and in Turkey, with a 9% occurrence rate, according to the Global Cancer Observatory database.[6-9] Advancements in CRC diagnosis and treatment have significantly improved survival rates, particularly in metastatic cases.[10,11] However, SRs with CRC often experience

CONTEXT

Key Objective

Refugees' health problems and access to treatment options are essential to world health. Cancer is a significant health problem for refugees and host countries. Considering that Turkey hosts a high number of Syrian refugees (SRs) and provides free health services to them, this study examined the clinicopathologic features and survival outcomes of SRs and Turkish patients with colorectal cancer (CRC), which is common worldwide.

Knowledge Generated

SRs were diagnosed with CRC at a younger mean age, typically younger than 50 years, compared with Turkish patients. In addition, they experienced poorer survival outcomes.

Relevance

The younger age and poorer prognosis of SRs highlight their vulnerability to CRC-related mortality. Considering low socioeconomic status that may cause factors such as limited knowledge about early diagnosis, difficulties in maintaining treatment adherence, and follow-up care put this population at higher risk. Addressing these barriers is essential for improving cancer outcomes among refugees.

delayed diagnoses and limited access to these advancements because of ongoing conflict. This study aimed to analyze the clinical and pathologic features of SRs with CRC treated at the center and compare their survival rates with Turkish citizens (TCs) to assess the impact of conflict on cancer outcomes.

MATERIALS AND METHODS

Study Design and Sample

In this cross-sectional retrospective study, we included data from patients with CRC treated at the Gaziantep Dr Ersin Arslan Training and Research Hospital between 2011 and 2021. The Gaziantep University Institutional Board and Gaziantep Provincial Health Directorate approved this study (Gaziantep University Ethical Committee: December 21, 2022; Number 473). Patient file/health records were reviewed retrospectively using a hospital-based electronic health information system.

The study sample comprised all adult SRs and TCs who were diagnosed with CRC and received treatment at a single medical oncology clinic in Gaziantep Dr Ersin Arslan Training and Research Hospital, located in the southern province of Turkey, between January 1, 2011, and December 31, 2021. This center is located near the Turkey-Syrian border, and SRs account for 17.2% of the population in Gaziantep.[12]

Data Extraction and Variables

The data collection focused on patients with invasive colon and rectal cancer. Key variables included smoking and alcohol consumption, comorbidities, cancer symptom onset, diagnosis details (date, location, stage, tumor characteristics), treatment methods (surgery, chemotherapy, radiotherapy), disease progression, and outcomes (relapse, patient status, death). Eligible patients were age 18 years or older and had invasive colon and rectal cancer, including those diagnosed in Syria (appropriate pathology reports added). Exclusions were for in situ tumors or those with fewer than three clinic visits.

Treatment protocols involved surgery, chemotherapy, and radiotherapy. Surgical and radiotherapeutic approaches varied on the basis of the stage of the disease and patient eligibility in the treatment of CRC. For nonmetastatic, early-stage cancer, curative surgeries such as right hemicolectomy, left colectomy, total colectomy, and abdominoperineal resection were performed according to tumor localization. In metastatic cases, palliative surgeries were conducted during emergencies, such as ileus or bowel perforation. If appropriate, curative surgery was considered and performed for patients whose metastatic organs and primary tumors became resectable after systemic therapy. Radiotherapy was applied for both curative and palliative treatments. In early and locally advanced rectal cancer, it was used as a neoadjuvant or adjuvant treatment. For metastatic CRC, radiotherapy was applied palliatively to manage symptoms, particularly in cases of bone and brain metastases. Patients were administered chemotherapy in neoadjuvant/adjuvant or metastatic settings. Chemotherapy was administered per the local standard (treatment regimens are shown in the Data Supplement). If treatment was linked to leukopenia, leukopenic infections, or delayed thrombocytopenia (>7 days), treatment was delayed until clinical recovery. The subsequent chemotherapy doses were reduced by 20%. Treatment was discontinued in cases of disease progression, unacceptable toxicity, or on patient request.

Disease relapse was defined as new evidence of disease after remission or curative surgery. Genomic analysis for *KRAS*-

NRAS and *BRAF* mutations, as well as *microsatellite instability status*, was performed for patients with metastatic disease. Outcomes were tracked by follow-up until death or the last hospital visit.

Outcomes

Patients were evaluated according to the response criteria to detect treatment efficacy. These were complete remission (complete response), no evidence of cancer; partial response, substantial (usually >50%) reduction in size of the tumor; stable disease, neither improvement nor worsening in size of the cancer; and progressive disease, increasing the size of the tumor. The objective response rate (ORR) was defined as the proportion of patients whose tumors were destroyed or significantly reduced by treatment using the above response criteria.

Overall survival (OS) time was defined as the period from treatment initiation to the last follow-up and/or death. The primary end point was the comparison of OS between SRs and TCs diagnosed with CRC. The additional secondary end point was to compare the OS rates of these subgroups among the nonmetastatic and distant metastatic stages.

Statistical Analysis

The data were analyzed using IBM SPSS statistics version 25.0. Descriptive statistics were presented as numbers and percentages for categorical variables and as mean ± standard deviation for continuous variables. Chi-square or Fisher exact test was used to compare categorical variables. Mann-Whitney *U* and Student tests were used to compare two groups of numerical data on the basis of their distribution. The Kaplan-Meier method was used to compare survival times between the various clinical parameter groups. OS was defined as the duration between the date of diagnosis and the date of death or most recent visit. A $P < .005$ was considered statistically significant.

RESULTS

Patients' Characteristics

Of the 421 patients with CRC included in this study, 282 (66.9%) were TCs and 139 (33.0%) were SRs. Twenty-seven patients (six TCs and 21 SRs) did not join the follow-up and were excluded from survival analysis. The mean age was 52.9 ± 14.3 years for the entire population, 55.3 ± 14.1 years for TCs, and 47.9 ± 13.4 years for SRs ($P < .001$). The baseline demographic and clinical characteristics, treatment modalities, and response rates of the patients are presented in Table 1. The histological type of all the patients was adenocarcinoma. Overall, there were more male than female patients in both groups. The incidence of smoking and alcohol consumption was comparable in both groups ($P = .82$). Among the enrolled patients, a family history of CRC was more common in the SR group than in the TC group (20.7% and 14.3%, respectively). Presentation with ileus was common in both groups, with 82.2% of TCs and 85.1% of SRs. Weight loss was significantly more frequent in the TC group ($P = .01$). Rectal cancer was the most common type in all groups. Right-sided colon cancer incidence was higher in SRs (29.9% *v* 25.4%; $P = .23$). Primary tumor resection was done in 108/139 (91.5%) SRs and 219/282 (91.6%) TCs. Relapse after resection was detected in 66 TCs (27%) and 28 (23.3%) SRs. Forty SRs (29%) and 60 TCs (21.4%) had de-novo metastatic disease ($P = .08$). Not all patients with metastatic disease could undergo molecular tests for *RAS/RAF* and *microsatellite instability* analysis. The evaluation of the results of these tests in our study was the ratio of patients with positive results to all patients who underwent the test. *RAS/RAF* mutations and immunohistochemistry (IHC) tests that define DNA mismatch repair deficiency (dMMR) genes were available for 136 and 59 patients, respectively. dMMR was more common in SRs (9/20, 45%) compared with TCs (5/39, 17.2%; $P = .03$). *RAS/RAF* wild-type patients were higher in TCs (57/95, 60%) than in SRs (15/41, 36.6%; $P = .003$). The adjuvant treatment modalities were similar in both groups, with 6 months of leucovorin calcium + fluorouracil + oxaliplatin combination (FOLFOX regimen) treatment being the most common. In the first-line metastatic setting, the treatment modalities were identical in both groups, with the most common being chemotherapy and bevacizumab. The ORRs of patients who received first-line palliative chemotherapy were 77.9% for TCs and 86.4% for SRs. As seen in Table 1, weight loss as a primary symptom ($P = .01$), *RAS* mutation status ($P = .003$), dMMR ($P = .03$), and age ($P < .001$) showed a statistically significant difference between the groups.

Survival Outcomes

At the end of the study period, 42.3% (n = 180) of the patients died within a median follow-up period of approximately 43 months. The rates of survival were 56.9% for TCs and 48.3% for SRs. The median OS of the entire group was 57.9 months; it was 80.9 months (95% Cl, 56.5 to 97.2) in the TC group and 42.2 months (95% Cl, 27.0 to 57.4) in the SR group ($P = .006$; Table 2; Figs 1-3). The 2-year OS rates were 67.1% in the TC group and 53.6% in the SR group, whereas the 5-year OS rates were 51.6% and 32.2%, respectively. In patients in the early stage, the median OS was not reached (NR) in TCs, and it was 52.6 months in SRs ($P = .02$). Among patients with metastatic disease, the median OS was 21.0 months in TCs and 18.8 months in SRs ($P = .93$). Additionally, the median OS of men was shorter. The 2-year OS rate was 77.2% in women and 67.0% in men, whereas the 5-year OS rate was 53.8% in women and 46.9% in men. OS rate of patients with left-sided primary disease was lower than that of patients with right-sided disease ($P = .44$; Table 2).

DISCUSSION

Remarkably, our study revealed that SRs were diagnosed at an earlier age than TCs, and the mean age of SRs was younger

TABLE 1. Baseline Clinicopathologic Characteristics and Treatment Modalities of TCs and SRs With Colorectal Cancer

Characteristic	Total Population (N = 421)	TCs (n = 282)	SRs (n = 139)	*P*
Age, years, mean ± standard deviation	52.9 ± 14.3	55.3 ± 14.1	47.9 ± 13.4	<.001
Sex, No. (%)				
Female	173 (41.1)	118 (41.8)	55 (39.6)	.65
Male	248 (58.9)	164 (58.2)	84 (60.4)	
Stage at diagnosis, No. (%)				
Nonmetastatic	318 (76.1)	220 (78.6)	98 (71.0)	.08
Metastatic	100 (23.9)	60 (21.4)	40 (29.0)	
Smoking history, No. (%)				
No	197 (46.7)	117 (41.4)	60 (43.1)	.82
Yes	224 (53.2)	165 (58.5)	79 (56.8)	
Alcohol consumption, No. (%)				
No	302 (71.7)	196 (69.5)	106 (76.2)	.93
Yes	119 (28.2)	86 (30.4)	33 (23.7)	
Family history of CRC, No. (%)				
No	203 (83.5)	138 (85.7)	65 (79.3)	.20
Yes	40 (16.5)	23 (14.3)	17 (20.7)	
ECOG, No. (%)				
0	4 (1.0)	2 (0.7)	2 (1.5)	.51
1	402 (96.6)	269 (96.4)	133 (97.1)	
2	10 (2.4)	8 (2.9)	2 (1.5)	
Ileus presentation, No. (%)				
No	70 (16.9)	50 (17.8)	20 (14.9)	.46
Yes	345 (83.1)	231 (82.2)	114 (85.1)	
Weight loss, No. (%)				
Yes	350 (84.5)	246 (87.5)	104 (78.2)	.01
No	64 (15.5)	35 (12.5)	29 (21.8)	
Location of primary tumor, No. (%)				
Rectum	185 (45.1)	131 (47.5)	54 (40.2)	.38
Left colon	115 (28.1)	75 (27.2)	40 (29.9)	
Right colon	110 (26.8)	70 (25.4)	40 (29.9)	
Primary tumor removed, No. (%)				
Completely removed	327 (78.4)	219 (91.6)	108 (91.5)	.97
Partially resected	30 (7.2)	20 (8.4)	10 (8.5)	
Unresected	60 (14.4)	ND	ND	
Relapse disease after resection, No. (%)				
No	270 (71.6)	178 (73)	92 (76.7)	.44
Yes	94 (24.9)	66 (27)	28 (23.3)	
Unknown	13 (3.5)			
Unknown		13 (3.5)		
Site of metastasis, No. (%)				
Liver	38 (20)	21 (17.2)	17 (25)	.35
Bone	4 (2.1)	3 (2.5)	1 (1.5)	
Lung	12 (6.3)	10 (8.2)	2 (2.9)	
Peritoneum	17 (8.9)	9 (7.4)	8 (11.8)	
Lymph node	23 (12.1)	17 (13.9)	6 (8.8)	
Brain	1 (0.5)	0 (0)	1 (1.5)	
Multiple metastasis	72 (37.9)	47 (38.5)	25 (36.8)	
Local relapse of disease	15 (7.9)	11 (9)	4 (5.9)	
Adnexal masses	8 (4.2)	4 (3.3)	4 (5.9)	

(continued on following page)

TABLE 1. Baseline Clinicopathologic Characteristics and Treatment Modalities of TCs and SRs With Colorectal Cancer (continued)

Characteristic	Total Population (N = 421)	TCs (n = 282)	SRs (n = 139)	*P*
Musinous component (primary resection), No. (%)				
No	233 (77.2)	158 (76)	75 (79.8)	.46
Yes	69 (22.8)	50 (24)	19 (20.2)	
LVI (primary resection), No. (%)				
No	204 (68.9)	140 (67.3)	64 (72.7)	.35
Yes	92 (31.1)	68 (32.7)	24 (27.3)	
PNI (primary resection), No. (%)				
No	225 (76)	158 (76)	67 (76.1)	.97
Yes	71 (24)	50 (24)	21 (23.9)	
Adjuvant chemotherapy, No. (%)				
Capecitabine 6 months	29 (12.8)	21 (12.8)	8 (12.7)	.26
Fluorourasil 6 months	14 (6.2)	11 (6.7)	3 (4.8)	
Capeox 3 months	41 (18.1)	32 (19.5)	9 (14.3)	
Capeox 6 months	52 (22.9)	34 (20.7)	18 (28.6)	
Folfox 3 months	10 (4.4)	5 (3)	5 (7.9)	
Folfox 6 months	81 (35.6)	61 (37.3)	20 (31.7)	
Radiotherapy (definitive treatment of rectum), No. (%)				
Neoadjuvant	75 (60)	58 (61.1)	17 (56.7)	.66
Adjuvant	50 (40)	37 (38.9)	13 (43.3)	
Mutation frequency, No. (%)				
Wild-type	72 (17.9)	57 (60)	15 (36.6)	.003
K RAS mutant	59 (14.7)	36 (37.9)	23 (56.1)	
N RAS mutant	3 (0.7)	0 (0)	3 (7.3)	
BRAF V600E mutant	2 (0.5)	2 (2.1)	0 (0)	
Unknown	285 (66.2)			
dMMR status, No. (%)				
Deficient	14 (9.3)	5 (17.2)	9 (45)	.03
Proficient	35 (23.3)	24 (82.8)	11 (55)	
Unknown	101 (67.4)			
First-line palliative chemotherapy, No. (%)				
Chemotherapy + anti-VEGF	98 (78)	57 (53.3)	41 (66.2)	
Chemotherapy + anti-EGFR	15 (12)	32 (29.9)	10 (16.1)	.12
Chemotherapy only	12 (10)	18 (16.8)	11 (17.7)	
Response of first line palliative chemotherapy, No. (%)				
CR	30 (18.4)	17 (16.3)	13 (22)	.41
PR	79 (48.5)	48 (46.2)	31 (52.5)	
SD	23 (14.1)	16 (15.4)	7 (11.9)	
PD	31 (19)	23 (22.1)	8 (13.6)	
Mortality, No. (%)				
Alive	214 (50.8)	157 (56.9)	57 (48.3)	.11
Exitus	180 (42.8)	119 (43.1)	61 (51.7)	

NOTE. No. (%): Pearson Chi-s quare test, mean ± standard deviation: independent *t* test, $P < .05$ statistically significant.
Abbreviations: anti-EGFR, anti-epidermal growth factor receptor monoclonal antibodies; anti-VEGR, anti-vascular endothelial growth factor antibodies; CR, complete response; CRC, colorectal cancer; dMMR, DNA mismatch repair deficiency; ECOG, Eastern Cooperative Oncology Group; LVI, lymphovascular invasion; PD, progressive disease; PNI, perinoral invasion; PR, partial response; SD, stable disease; SRs, Syrian refugees; TCs, Turkish citizens.

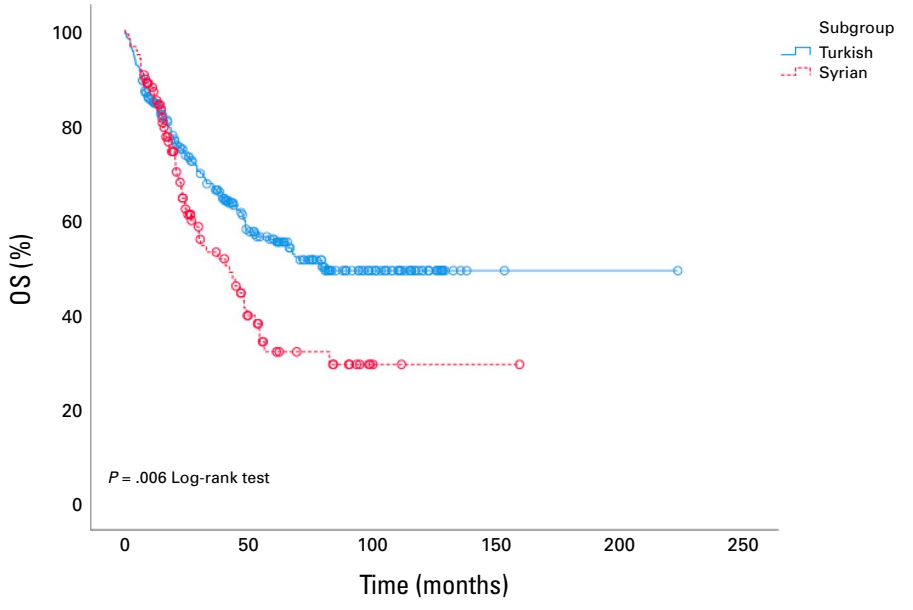
TABLE 2. The OS in Turkish and Syrian Patients

Characteristic	OS, Months, Median (95% CI)	*P*
Total population	57.9 (40.1 to 75.6)	
Sex		
Female	70.2 (43.7 to 96.6)	.38
Male	52.6 (38.0 to 67.1)	
Total population		
TC	80.9 (56.5 to 97.2)	.006
SR	42.2 (27.0 to 57.4)	
Nonmetastatic patients		
TC	NR	.02
SR	52.6 (43.7 to 61.4)	
Distant metastatic patients		
TC	21.0 (16.3 to 25.7)	.93
SR	18.8 (8.5 to 29.2)	
Location of primary tumor		
Rectum	56.3 (31.9 to 80.7)	.66
Left colon	54.3 (30.2 to 78.3)	
Right colon	79.5 (51.7 to 97.2)	

NOTE. Kaplan-Meier curve, log-rank test, $P < .05$ statistically significant. Abbreviations: NR, not reached; OS, overall survival; SR, Syrian refugee; TC, Turkish citizen.

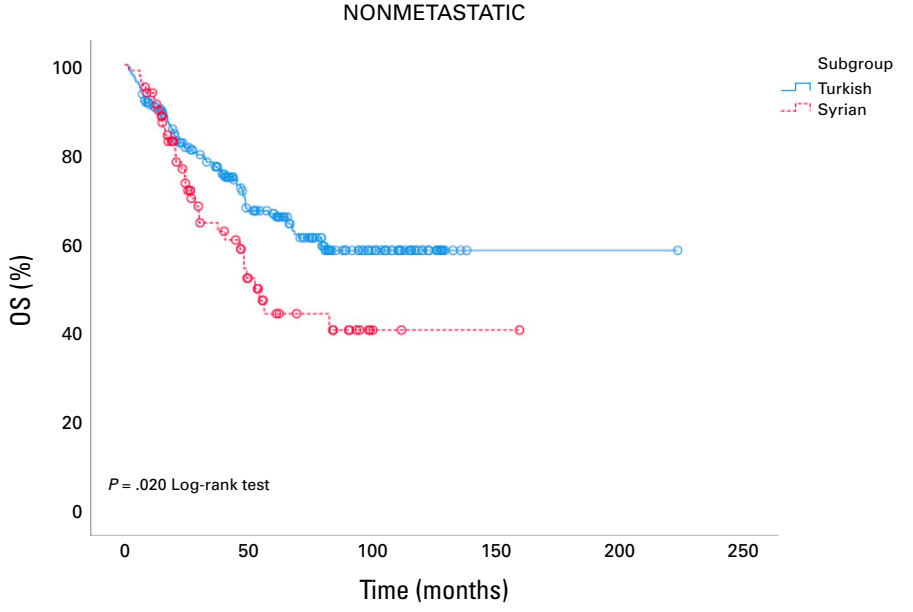
than 50 years. The median OS in the general group was 57 months; however, in the SR group, it dramatically reduced to 42 months. Notably, in the nonmetastatic group, OS was NR in the TC group, but it was much shorter in the SR group, with 52 months.

According to available statistics, the overall 5-year survival rate of patients with CRC in the United States is 65%.[7] However, the 5-year survival rate drops to 14% in patients with distant metastases.[7] A retrospective hospital-based cross-sectional study was conducted in Turkey, following 1,114 adult SRs diagnosed with cancer, and CRC was discovered in 5.5% (61/1,114) of individuals.[13] The survival rate of adult patients diagnosed with various cancers was found to be 31.1%, 17.4%, and 15.4% for those with the early, locally advanced, and metastatic stages of the disease, respectively. On examining CRC, it was discovered that the survival rates for CRC at all stages at 5 years were 11.4%. By contrast, our study found that the median 5-year OS rate for all stages in the general group was 46.7%, 51.6% for TCs, and 32.2% for SRs. In the distant metastatic group, the median 5-year OS rates were 9.1%, 12.6%, and 0% in the general, TC, and SR groups, respectively. The survival rates in both groups in our study, with poorer survival in SRs compared with TCs, were lower than the global data for patients with CRC. The low survival rates observed in refugees may be attributed to low



Group of Patients	Patients, No.	OS, Months, Median (95% CI)	2-Year OS Rate, % (95% CI)	5-Year OS Rate, % (95% CI)
TC	276	80.9 (56.5 to 97.2)	67.1 (48.5 to 86.3)	51.6 (33.6 to 72.4)
SR	118	42.2 (27.0 to 57.4)	53.6 (39.6 to 71.2)	32.2 (18.4 to 51.1)

FIG 1. Demonstration of the Kaplan-Meier curves for OS of total population with colorectal cancer stratified according to TCs and SRs. NR, not reached; OS, overall survival; SRs, Syrian refugees; TCs, Turkish citizens.

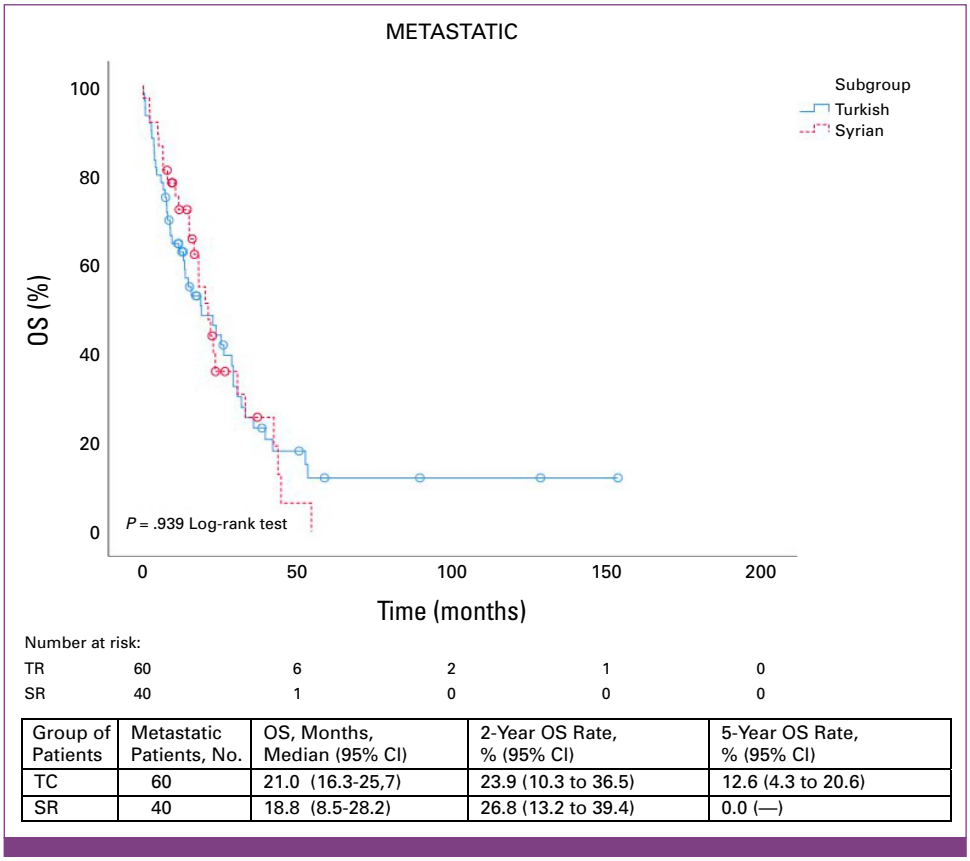


Group of Patients	Patients, No.	OS, Months, Median (95% CI)	2-Year OS Rate, % (95% CI)	5-Year OS Rate, % (95% CI)
TC	220	NR	78.2 (56.5 to 90.1)	61.5 (48.5 to 73.4)
SR	98	52.6 (31.6 to 68.4)	64.7 (46.6 to 80.3)	43.9 (28.4 to 62.1)

FIG 2. Demonstration of the Kaplan-Meier curves for OS of nonmetastatic patients with colorectal cancer stratified according to TCs and SRs. OS, overall survival; SRs, Syrian refugees; TCs, Turkish citizens.

socioeconomic status (SES) backgrounds. SES encompasses not only income but also educational attainment, occupational prestige, and subjective perceptions of social status and social class. SES reflects quality-of-life attributes and opportunities afforded to people within society.[14] The SR in our study are registered under Temporary Protection ID (TPID), a legal status given to Syrian nationals in Turkey that enables them to access all health care services, including cancer screening, free of charge. This ID status also indicates that the patients are not officially employed, if employed at all, and registered in the Turkish Social Security system, as this ID is replaced by a work permit ID card in case of registered employment.[15] Lower SES is prevalent in SR as they have been either not officially employed or unemployed. Both groups have the same rights in access to health care services, including all aspects of cancer treatment. Lower SES was found to be a contributing factor to increased incidence and mortality rates associated with CRC, highlighting the substantial negative impacts of lower SES on cancer susceptibility and health outcomes.[16] A positive correlation is expected between low SES and CRC incidents as the prevalence of several known modifiable risk factors of CRC, including smoking, alcohol usage, poor diet, obesity, and lack of physical activity, is higher in low socioeconomic populations.[17] Hence, one of the contributing factors to the slight difference in incident and mortality rates among TCs and SRs can be explained through socioeconomic factors.[17] However, we found no difference in smoking or alcohol consumption and could not reach other lifestyle characteristics across groups in our patient file review.

Considering the clinicopathologic findings of the patients in our study, similarities and notable distinctions were observed between SRs and TCs. The mean age of SRs was lower than TCs. Notably, CRC incidence in patients younger than 50 years (early-onset CRC) has been increasing worldwide for reasons not yet fully understood.[18] Early-onset CRC survival data are inconsistent, although some trials suggest a dismal prognosis based on molecular etiology and hereditary and familial syndromes.[19-22] Considering that the mean age of refugees is younger than 50 years, the higher incidence of early-onset CRC among Syrians can be attributed to the increased susceptibility to precancerous factors associated with the conflict, such as exposure to chemical carcinogens and chronically high levels of unmanageable stress.[23] The other factor causing this lower age at onset may be the high incidence of hereditary conditions. In our study, the incidence of dMMR was significantly higher in SRs. We did not anticipate that nutritional factors such as being red meat consumers or lacking fiber in the diet may play a role in this



Group of Patients	Metastatic Patients, No.	OS, Months, Median (95% CI)	2-Year OS Rate, % (95% CI)	5-Year OS Rate, % (95% CI)
TC	60	21.0 (16.3-25,7)	23.9 (10.3 to 36.5)	12.6 (4.3 to 20.6)
SR	40	18.8 (8.5-28.2)	26.8 (13.2 to 39.4)	0.0 (—)

FIG 3. Demonstration of the Kaplan-Meier curves for OS of distant-metastatic patients with colorectal cancer stratified according to TCs and SRs. OS, overall survival; SRs, Syrian refugees; TCs, Turkish citizens.

result since the food and gastronomy cultures are similar. Limitations in hospital access for elderly patients with CRC in the SR population may also cause this situation.

Even if the recurrence rate of operated disease was higher in TCs (27% *v* 23.3%; $P = .44$), based on decreased OS of SRs with early stage, it might be caused by not applying to the hospital regularly. The decreased OS observed in early-stage cancer in SR may be attributed to several factors, including some patients with suboptimal surgical procedures in Syria, poor use of adjuvant medicines (eg, wrong usage of oral capecitabine because of misunderstanding the communication language), the presence of more aggressive tumor biology associated with early-onset age, and lack of adherence to surveillance protocols that lead to not evaluate the recurrence of disease in the high-risk patient group.

All patients with metastatic disease had tumor samples that could not be studied for *RAS-RAF* mutations or dMMR genetic markers. Therefore, we presented the ratio of these molecular tests in patients with positive results to the patients to whom the test could be applied. Thus, ratios were higher than real-world statistics. The *RAS/RAF* mutations associated with poor prognosis were statistically more frequent in SRs. Although the overall incidence of *KRAS* mutations in CRC is approximately 50% worldwide,[24,25] this rate was 56.1% in SRs and 37.9% in TCs. Even if the first-line chemotherapy in the metastatic stage showed a decreased response rate among TCs, this difference was not statistically significant (ORR, 77.9% and 86.4%, respectively; $P = .41$). *RAS* wild-type patients with metastatic disease who could receive anti-EGFR agents were more common in TCs (60%), and this might have led to improved OS compared with the SRs (36.6%; $P = .003$). Again, among the patients who had been examined for dMMR by IHC testing of tumor tissue, the dMMR ratio was 45% (9/20) in SR and 17.2% (5/29) in TC. CRC tumors with deficient mismatch repair (dMMR)/high microsatellite instability (MSI-H) account for approximately 12%-17% of all cases worldwide, varying depending on the detection methods employed, and most CRC with dMMR/MSI-H are sporadic and not hereditary.[26-29] Even if we could not analyze it accurately, the incidence of dMMR was higher in the SR group. Additionally, the SR group had a higher family history of CRC. Therefore, hereditary diseases such as Lynch syndrome may be more common in SRs because of various environmental and hereditary factors, and genetic counseling is necessary in the management of this patient group.

As mentioned above, to summarize the reasons for decreased survival rates of SRs compared with TCs:

1. All Syrian patients admitted to our hospital were under TPID. We evaluated those who were supposed to have low SES and considered this situation as a sign of a poor prognosis for CRC.
2. The mean age at diagnosis of SRs was younger than 50 years. Early-onset CRC is associated with worse prognosis. Although advanced-stage rates and pathologic findings such as lymphovascular invasion, perinoral invasion, mucinous pattern, and metastatic status were similar in both groups, the early-onset nature of CRC may lead to lower survival rates in SRs.
3. The higher incidence of *RAS* mutations and dMMR status in metastatic disease in SR may be associated with a poor prognosis.

This study had several limitations, including its retrospective nature, the small sample size of Syrians, and the inability to undertake genetic consultations for all metastatic patients. The significance of our study lies in the fact that Gaziantep, a border city, shares a structure comparable with Syria and consists of two homogeneous groups with similar features. This allowed us to highlight the effects of conflict on patients by comparing TC and SR treatment conditions.

AFFILIATIONS

[1]Department of Oncology, Gaziantep Liv Hospital, Gaziantep, Turkey
[2]Department of Oncology, Istanbul Oncology Hospital, Istanbul, Turkey
[3]Department of Oncology, Faculty of Medicine Rize, Recep Tayyip Erdogan University, Rize, Turkey
[4]Department of Public Health, Faculty of Medicine, Pamukkale University, Denizli, Turkey
[5]Department of Oncology, Faculty of Medicine, Hacettepe University, Ankara, Turkey

CORRESPONDING AUTHOR

Canan Karan, MD; e-mail: karancanan16@gmail.com.

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AUTHOR CONTRIBUTIONS

Conception and design: Canan Karan, İlker Nihat Okten, Fatih Teker, Şuayib Yalçın
Financial support: Canan Karan, İlker Nihat Okten
Administrative support: Canan Karan, İlker Nihat Okten, Oğuzhan Kesen
Provision of study materials or patients: Canan Karan, İlker Nihat Okten, Fatih Teker
Collection and assembly of data: Canan Karan, İlker Nihat Okten, Atalay Çelikyürek
Data analysis and interpretation: Canan Karan, İlker Nihat Okten, Oğuzhan Kesen, Atalay Çelikyürek, Şuayib Yalçın
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Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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