

Estimation and Projection of Prevalence of Colorectal Cancer in Iran, 2015–2020

Abstract

Background: Population aging and more prevalent westernized lifestyle would be expected to result in a markedly rising burden of colorectal cancer (CRC) in the future years. The aim of this study is to estimate the limited-time prevalence of CRC in Iran between 2015 and 2020. **Materials and Methods:** Aggregated CRC incidence data were extracted from the Iranian national cancer registry (IR.NCR) reports for 2003–2009 and from GLOBOCAN-2012 database for 2012. Incidence trends were analyzed by age groups, genders, histopathologic, and topographic subtypes to estimate annual percentage changes. Incidence was projected for 2020. The prevalence was estimated applying an adopted version of a previously introduced equation to estimate limited-time prevalence based on the incidence and survival data. Monte Carlo sensitivity analyses were applied to estimate 95% uncertainty levels (ULs). In each scenario, incidence, survival, annual percentage changes, and completeness of case ascertainment at IR.NCR were replaced under pre-assumed distributions. **Results:** Number of estimated within 1, 2-3 and 4-5-year CRC patients in 2015 were 13676 (95% UL: 10051–18807), 20964 (15835–28268), and 14485 (11188–19293), respectively. Estimated 5-year prevalence for 2020 (99463; 75150–134744) was 2.03 times of that for 2015. Highest 5-year prevalence was estimated in ages 55–59 for females and 75 + for males. Adenocarcinoma (41376; 31227–55898) was the most prevalent histologic subtype. The most prevalent tumor location was colon (30822, 23262–41638). **Conclusion:** A substantial growth in the prevalence of CRC survivors is highly expected for future years in Iran. Establishment of specialized institutes is highly recommended to provide medical and especially social supports for Iranian CRC survivors.

Keywords: Cancer, colorectal, Iran, modeling, prevalence, projection

Introduction

Iran, as an in-transition country, is experiencing population aging and rising prevalence of the western lifestyle.^[1-3] Therefore, continuing rising burden of colorectal cancer (CRC) is reasonably expected in future years, while its incidence and mortality rates are still relatively high in Iran.^[4-8] Accordingly, population of Iranian CRC survivors would be considerably increased. However, as we know, data on the CRC prevalence in Iran are very scarce.^[9-11] This scarcity is mainly due to the lack of a long-lasting national population-based cancer registry in Iran.

Despite the statement of the Parliament of Islamic Republic of Iran on the mandatory reporting of cancer diagnosis at 1984, and the establishment of the Iranian National Cancer Registry (IR.NCR) and then efforts to improve it, up to now, the IR.NCR remains as a pathology based cancer

registry. Seven national cancer reports have been released by the IR.NCR for annual cancer incidence in Iran during 2003–2009. Data on date of diagnosis, topography, histopathology, age at diagnosis, and gender are gathered from pathological laboratories throughout Iran. Data are abstracted by university cancer registrars at university cancer registries. Ninth version of the International classification of diseases for oncology (ICD-O) is used for coding by all of university cancer registries. Periodical reports are sent to the IR.NCR by university cancer registries. Received reports to the IR.NCR are emerged and cleaned and prepared for report. However, no updated data are available on the cancer incidence in Iran for years after 2009, except for estimated statistics by GLOBOCAN 2012 project.

There is only one out-of-date national report on the prevalence of CRC in Iran for 2007.^[10] In which, authors have ignored

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that IR.NCR suffers from serious incompleteness of case ascertainment^[12-14] and consequently estimated CRC prevalence by then are highly underestimated.

Herein, number of Iranian CRC survivors who are within initial treatment, clinical follow-up, and cured phases was estimated for the years 2015 and 2020. We applied an adoption of the method used by Bray *et al.*^[15]

Materials and Methods

Statistical and modeling procedures

We adopted formula used by Bray *et al.*^[15] to estimate the global prevalence of cancer. Our adopted equation was including incidence counts, estimates of survival rates, percentage of incompleteness of case ascertainment at IR.NCR and estimated annual percentage change (APC) of incidence trends in Iran. In a Monte Carlo sensitivity analysis, this equation was repeated 5000 times, and in each repetition (hereafter: scenario) the values for incompleteness, survival rate and also APC were randomly replaced. Random replacements were done with different normal distributions with different assumptions according to different strata.

In each scenario, CRC incidence counts for 2012 were corrected for strata-specific incompleteness rates. Then, this corrected incidence values were projected by linear regression models up to 2015 and 2020, assuming strata-specific APCs (R2 for these prediction models were ranged from 0.67 to 0.81). Finally, projected incidence counts were multiplied with respective proportions of 1–5-year survival (range: 0–1).

Now, we have 5000 estimations for each of 1, 2-3 and 4-5-year prevalence of CRC in Iran for 2015 and 5000 for 2020. Mean of these single-scenario-estimated prevalence statistics was considered as the point estimate of CRC prevalence in Iran. To estimate 95% uncertainty levels (UL) of point prevalence, single-scenario-estimated prevalence statistics were sorted, and percentiles of 2.5 and 97.5 were considered as lower and upper levels of point estimates.

Trend analyses and estimation of APCs were done using joinpoint regression software (Version 4.1.1; National Cancer Institute, Bethesda, MD, USA). Data preparation, calculation, and sensitivity analyses were done using MS Excel software.

Providing input data

Age standardized and age-specific incidence rates of CRC in Iran in 2003–2012 were extracted from IR.NCR reports according to gender, histologic subtype, and tumor location. Trends of these rates were analyzed using logarithmic Poisson Joinpoint regression. After removing the effect of an unstable improvement in IR.NCR (case finding from hospitals and clinics had been done for 2008–2009 but had been failed for the next years), APCs and respective 95%

confidence intervals (CI) were estimated for different strata including age groups (10 age groups), genders (male and female), the five most common histologic subtypes and also tumor locations (Colon, ICD-O-3 code: C18; recto-sigmoid, C19; rectum, C20; anus and anal canal, C21).

Strata-specific CRC incidence counts were also extracted from the GLOBOCAN 2012 database.^[16]

As there is no reliable population-based estimate of cancer survival rate in Iran, 1–5-year survival rates for CRC patients in Iran were generated according to three sources. Maximum values of survival rate were extracted from the UK cancer research web site^[17] and minimum values were assumed as those have been reported by Gelband *et al.* (2016) for low- and middle-income countries.^[18] Two-, three-, and four-year survival rates were interpolated considering the pattern of survival rates reported by three recently published Iranian papers.^[19-21] Survival rates were estimated for different strata.

According to our previous research,^[13] minimum and maximum percentage for completeness of case ascertainment at IR.NCR were assumed as 30 and 70, respectively. As its average is estimated to be around 50%, we assume a normal distribution for a percentage of incompleteness in our sensitivity analysis.

Results

Trend of overall incidence rates were increasing (APC = 11.5, 95% CI = 6.6–16.4). There was no statistically significant difference between estimated APCs for rising trends of incidence of different histologic subtypes and tumor locations. APCs were not significantly but meaningfully different (95% CIs overlapped each other; data not shown) for age groups and genders.

According to the GLOBOCAN database, estimated numbers of new CRC cases were 3811 for men and 3352 for women in Iran in 2012. Modeling inputs including survival rates are presented in Appendix 1.

Number of alive within 1, 2-3 and 4-5-year CRC patients in 2015 were estimated to be 13676 (95% UL: 10051–18807), 20964 (95% UL: 15835–28268), and 14485 (95% UL: 11188–19293), respectively. Total number of alive male and female within 5 years from diagnosis of CRC were 28079 (95% UL: 21041–38095) and 21046 (95% UL: 16033–28273), respectively in 2015 [Table 1].

Total number of alive within 5-year CRC patients was estimated to be 43110 (95% UL: 32832–58065) for females and 56353 (42318–76676) for males at the end of 2020. Percentage of within 1, 2-3 and 4-5-year patients was estimated to be 27.8, 42.7, and 29.5, respectively.

The first three age groups with the highest 5-year prevalence of CRC survivors were 55–59 (within 5-year prevalence: 3194, 95% UL: 2450–4269), then 50–54 (2916,

2239–3912) and then 75+ (2832, 2155–3809) in females and 75+, (6190, 4644–8363) then 55–59 (3385, 2515–4611) and then 50–54 (3146, 2336–4318) in males [Figure 1].

The most prevalent histologic subtypes were adenocarcinoma (5-year prevalence, 41376; 95% UL, 31227–55898), mucinous adenocarcinoma (2232; 95% UL, 1684–3015), and mucin-producing adenocarcinoma (1384; 95% UL, 1044–1869), respectively [Table 2].

Within 5-year prevalence of colon, rectosigmoid, rectum, and anal cancers were 30822 (23262–41638), 3953 (2984–5341), 13157 (9929–17775), and 1193 (899–1614), respectively [Table 2]

Discussion

Prevalence statistics are needed for more effective cancer control planning in addition of incidence and mortality.^[22] The success of advances in timely cancer detection and treatment and also increasing number of new cancer

cases in the world and especially in developing countries resulted in a growing number of cancer survivors, who have various social and medical needs during different phases of disease.^[23–25] They may be fearful of cancer recurrence, depressed or anxious, affected by cancer stigmatization, and loosed their job and also social and intellectual capacity.^[23,26–29] Accordingly, any national cancer control programs need to cover this growing population and their needs. In this study, we estimated the number of Iranian within 5 years CRC survivors in the years 2015 and 2020.

According to our results, 5-year prevalence of CRC was estimated to be around 49125 patients at the end of 2015. Our estimate is around 3.5 times of the previous report (for 2007) and 3.0 times of estimates which have been provided by GLOBOCAN 2012.^[10,16] Although this inconsistency may be partially justified by increasing trend of incidence of CRC in Iran (Overall

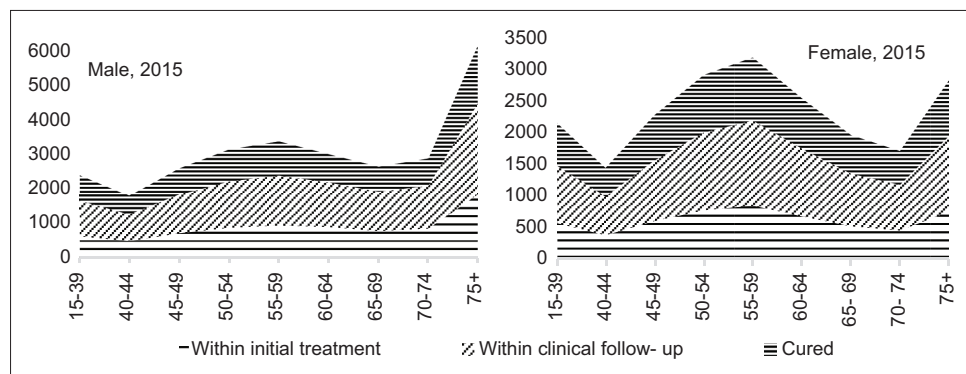


Figure 1: Age distribution of limited time-prevalence (counts) of colorectal cancer in Iran at the end of 2015 by gender

Table 1: Prevalence of colorectal cancer in Iran according to gender in 2015 and 2020

Gender	Year	1 year	2-3 year	4-5 year
Male	2015	8136 (5909-11249)	12,018 (9011-16,287)	7925 (6121-10,559)
	2020	16,395 (11,941-22,721)	24,149 (18,174-32,812)	15,809 (12,203-21,146)
Female	2015	5540 (4142-7558)	8946 (6824-11,981)	6560 (5067-8734)
	2020	11,994 (8996-16,340)	18,452 (14,055-24,795)	12,664 (9781-16,932)

Table 2: 5-year prevalence of colorectal cancer according to histologic and topographic subtypes in Iran, 2015

Histologic subtype	Male	Female
Adenocarcinoma, NOS	23,567 (17,660-31,973)	17,809 (13,567-23,925)
Mucinous adenocarcinoma	1279 (958-1735)	953 (726-1280)
Mucin-producing adenocarcinoma	776 (581-1052)	608 (463-817)
Signet ring cell carcinoma	462 (346-627)	263 (200-353)
Squamous cell carcinoma, NOS	157 (117-213)	99 (75-132)
Other	1840 (1379-2496)	1315 (1002-1766)
Location*		
Colon	17,460 (1,3083-23,688)	13,362 (10,179-17,950)
Rectosigmoid	2280 (1709-3093)	1673 (1275-2248)
Rectum	7558 (5664-10,254)	5599 (4265-7521)
Anal	781 (585-1060)	412 (314-554)

*ICD-O codes: Colon, C18; Rectosigmoid, C19; Rectum, C20; Anal, C21. NOS: Not otherwise specified

APC = 11.5%)^[30] mainly is due to serious incompleteness of cases ascertainment at IR.NCR. As reported by previous reports a 26%–68% of CRC new patients are registered by IR.NCR.^[12-14] Accordingly, average incompleteness could be assumed around 50%. As incidence estimates reported by GLOBOCAN 2012 are not corrected for incompleteness,^[31] so a rough estimate for number of new CRC cases is estimated to be 14,300 in 2012. Now, assuming an 11.5% of annual growth, it is estimated to be around 19800 new CRC cases in 2015 in Iran. Considering this rough estimate for the number of new cases, our prevalence estimates could be reasonable.

Our results showed the 5-year prevalence of CRC in 2020 would be around 99400 new cases if current situations be continued. Around one of three of them (28%) would be within initial treatment phase and they need infrastructures for surgical treatment, adjuvant and neoadjuvant chemo, and radiation therapies. According to a previous report, the most of Iranian new CRC patients are diagnosed in Stage II and III.^[32] Proportion of survivors who will be within clinical follow-up phase patients was estimated to be 42.8% of CRC survivors in 2020. These patients need to be medically assessed for possible recurrences or second primary tumors. In addition, their physical or psychosocial consequence of CRC treatment needs to be managed.^[29]

Study results showed that age distributions of different types of the prevalence of CRC are highly different between male and female. According to this finding, cancer policy makers could decide about the share of each of age groups in overall CRC prevalence in Iran by gender and the phase of the patients' disease. However, estimated gender and age distribution of within 5 years CRC patients in our study is mainly due to the age distribution of reported incidence numbers by IR.NCR which may be underestimated in older ages and affected by the nature of pathology-based registration in IR.NCR.^[12,33,34] Therefore, our estimated age and gender distribution should be used warily.

However, as we know, there are only few charities in Iran (Such as Mahak charity in Tehran) which mainly support cancer survivors medically. We could not find any report regarding needs assessment in Iranian CRC cancer survivors. In briefs, in the shadows of previous highly underestimated statistics of cancer prevalence, this growing population and their needs are forgotten, even by Iranian cancer researchers.

As any other effort to estimate cancer prevalence in regions without durable population-based cancer registry, our study had some limitations. Lack of population-based survival estimates in Iran was a major limitation in our study. Although there are several studies which have reported CRC survival rates no one was a population-based study.^[20,35,36] As in almost all of them, participants had been recruited hospital or pathology based. However, we

considered this limitation in our sensitivity analysis and estimation of 95% ULs.

Incompleteness of case ascertainment at IR.NCR was another influential limitation. It widened our estimated 95% ULs. We believe that our assumption regarding incompleteness rate at IR.NCR was the best available estimates and hope it is true.

In addition, we inevitably used incidence data based on reports by IR.NCR which is not a population-based registry.^[12] Therefore, the resulted distribution for age groups, gender, histologic subtypes, and tumor locations may be underestimated for elderlies or cases who are diagnosed in hospitals or private clinics.^[37]

Conclusion

Five-year prevalence of CRC in Iran is much more than previous reports. Rapid growth in the prevalence of CRC survivors is highly expected for future years in Iran. Establishment of specialized institutes, as a part of national comprehensive cancer control program, is highly recommended to provide medical and especially social supports for Iranian CRC cancer survivors.

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Conflicts of interest

There are no conflicts of interest.

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Appendix

Appendix 1: Modeling assumptions and inputs (minimum value - maximum value)						
Age	Gender					
	Male			Female		
	0-39	40-59	60+	0-39	40-59	60+
S, 1 year	0.714-0.774	0.714-0.774	0.684-0.744	0.679-0.739	0.679-0.739	0.649-0.709
S, 2 year	0.658-0.718	0.658-0.718	0.628-0.688	0.630-0.690	0.630-0.690	0.600-0.660
S, 3 year	0.613-0.673	0.613-0.673	0.583-0.643	0.591-0.651	0.591-0.651	0.561-0.621
S, 4 year	0.579-0.639	0.579-0.639	0.549-0.609	0.562-0.622	0.562-0.622	0.532-0.592
S, 5 year	0.534-0.594	0.534-0.594	0.504-0.564	0.523-0.583	0.523-0.583	0.493-0.553
APC	0.034-0.158	0.057-0.20	0.115-0.229	0.033-0.157	0.096-0.164	0.091-0.189
2012 incidence counts	330	1488	1993	311	1530	1511

S: Relative survival rate, APC: Annual percentage change