Original Article

Temporal Trends of Incidence of Colorectal Cancer in Isfahan, Iran, 2000–2011

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Abstract

Background: Case finding was improved to the population-based method at the Isfahan Cancer Registry (ICR) during 2005–2008. However, its effects on the number of registered colorectal cancer (CRC) cases and patients' age are not investigated. Therefore, present study designed to investigate the effect of that improvement on the trend of incidence of CRC, and age of CRC cases in ICR's catchment area. **Methods:** Data from the ICR were retrieved by years for 2000–2011. Annual age-standardized incidence rates (ASRs), truncated ASRs and 95% confidence intervals (95% CIs) were estimated for both genders. Rates were standardized based on the 2000 world standard population. Trends were analyzed, and significant change-points were identified using Joinpoint Regression software. Age of CRC cases compared between periods before and after the improvement. **Results:** A total of 2902 CRC cases had been registered by ICR. Estimated ASRs (95% CI) for 2000 and 2011 were 3.47 (3.45, 3.50) and 10.22 (10.19, 1025) per 100,000 persons, respectively. Two significant change-points were identified (i.e., at 2003 and 2006). However, estimated average annual percent change was as 11. There was no significant difference between mean of patients' age before and after the time of improvement (P = 0.88). **Conclusions:** Trends of incidence of CRC had been rising in central Iran for males and females, during 2000–2011. It seems that the estimated slope for this trend had been partially artificial and significantly affected by the improvement of case-finding method. However, the improvement had no effect on the patients' age.

Keywords: *Colorectal cancer, incidence, Iran, neoplasm, trend*

Introduction

Colorectal cancer (CRC) is the fourth most common malignancy in Iran.[1] Around 6200 new CRC cases were registered by Iranian national cancer registry during 2009, which is equal with a low annual age-standardized incidence rate (ASR) of 11 per 100,000 population.[2] However, terrible rising trends of its incidence and mortality rates are reported from national and subnational studies for a period of 2000–2010.[3-5]

The Iranian lifestyle has slowly changed to western lifestyle during last three decades.[6] Accordingly, a gentle increase of incidence of CRC is unavoidable, even for low-risk regions.[7-10]

On the other hand, Iranian regional pathology-based cancer registries have improved to population-based registries at 2005–2008, according to the Iranian National Cancer Office (INCO).[2] Therefore, they start to collect data from death registries, hospitals, and clinics at that time. As it is clear, more data sources in cancer registries improve completeness of case ascertainment.[11] Consequently, an artificial increase in incidence trends would be unavoidable.

We think that previously reported terrible rising trends of CRC incidence in Iran could be affected by improvement in the completeness of case ascertainment at regional registries and may be partially artificial.

Joinpoint Regression (SEER, NCI, Maryland, USA) is a powerful statistical methods to the analysis of trends of cancer incidence and mortality and simultaneously detect probable significant change-points in trends.[12,13] We think that if improvement of the completeness had been an effective intervention, a significant change point would be detectable in the temporal trend of cancer incidence.

On the other hand, case finding from different data sources could lead to different epidemiological patterns.[14] Therefore,

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case finding from death registers, hospitals, and clinics in addition of pathological laboratories, what that has been applied in Iranian cancer registries since 2007–2008, could change the epidemiology and especially age distribution of cancer incidence.

The aim of this work was to identify the effect of above-mentioned improvement of case finding method on the trend of incidence of CRC in the most populous province in central Iran, Isfahan, using Joinpoint Regression modeling, and also at the age of CRC cases at the time of registration in this area.

Methods

Data sources and study population

This study was a trend analysis of incidence data from Isfahan Cancer Registry (ICR). ICR is one of the most qualified regional cancer registries throughout Iran and affiliated by Isfahan University of Medical Science (MUI). This registry has worked since 1998, as a pathology-based registry. Its catchment area had been extended to all most all of Isfahan province resident population at 2004.[2] Isfahan province is the most populous province in central Iran. Its population reported to be about 5 million with a sex-ratio of 1.03, based on the recent national census, 2011.[15]

According to INCO, ICR improved to a population-based registry from 2005. At that time, passive case finding extended to the Isfahan death registry, hospitals, and clinics in addition of pathological laboratories.[2] However, as we know, case finding from sources other than pathological laboratories failed in recent years, and consequently, the most of the Iranian cancer epidemiologists believe that almost all of the university cancer registries are pathology-based cancer registries in Iran.[16]

Data are abstracted, and ICD-O coded (ICD-O-2 up to 2002 and ICD-O-3 since 2002 up to now) by experienced registrars at the ICR. Then data are transferred to the INCO, periodically. At the INCO, received data from the ICR and other regional registries are IARC checked and then reallocated to regional registries based on the cases' field address. Cleaned data transferred to regional registries annually. In this study, we used this reallocated data.

Data manipulation and statistical analysis

Data for CRC cases (ICD-O-3 Codes: C18.0-C20.9) were extracted by age, gender, and year of diagnosis. Extracted data were cleansed, duplicated and multiple primaries were identified and removed.

Cases were counted and age categorized (18 groups) for both genders and by calendar years. Annual age-specific incidence rates were calculated for males and females. Applying 2000 world population age group weights, direct ASRs, and also direct age-standardized truncated rates (TASRs) at 25 years, and Poisson 95% confidence intervals (95% CIs) were estimated, according to Boyle and Parkin.[14] Population data for Isfahan province retrieved from official website of Iranian national bureau of population and statistics.[15] As age for 29 cases was missing, standardized rates were corrected for missing data.[14]

Change-points and trends were analyzed using Joinpoint Regression software (version 4.0.1). Annual percent changes (APC) and average annual percent changes (AAPC) were also estimated. Incidence trends were graphed and smoothed using Excel software (version 2013).

Mean, median, and range of age of CRC cases were estimated according to calendar years. Mean age of cases was estimated for periods before and after the improvement. Two independent sample *t*-test was used to comparing the mean of patients' age. Rate standardization and statistical analysis were done by Stata software version 11.2 (StataCorp, Texas, USA).

Results

A total of 2902, CRC cases had been registered by the ICR during 2000 to 2011. Among these, 1654 (57%) cases were male and 1248 (43%) were female. Mean (standard deviation [SD]), median and range of age at diagnosis were 58.9 (14.6), 59 and 3–93 years for females and 61.1 (14.3), 63 and 4–94 years for males [Table 1]. Age was missing for 13 and 16 cases for females and males, respectively.

Females were slightly younger than males (58.90, SD: 14.58 vs. 61.05, SD: 14.31, $P = 0.0001$), steadily for study years. There was no statistically significant difference between the mean of age of patients who had been registered before and who registered after the improvement (60.21, SD: 13.63 vs. 60.10, SD: 14.67, $P = 0.88$). Mean of age at diagnosis was smaller than its median for almost all of the study years in both genders [not statistically tested; Table 1].

Trend of incidence of CRC increased dramatically during 2000–2011 [Table 2 and Figure 1a]. The ASRs for 2005 increased dramatically up to 3 and 5 times of its previous year (2004) for males and females, respectively.

Two change-points were detected in the trend of incidence of CRC, one at the year 2003 (uncertainty level: 2002–2005) and another one in the year 2006 (uncertainty level: 2005–2009). Considering these two change-points, three APCs were estimated, as −21.5 (95% CI: −54.3–34.7), 116.0 (−26.7–536.5), and 2.8 (−19.2–30.2) percentage for 2000 to 2003, 2003 to 2006, and 2006 to 2011, respectively. Estimated APCs for the trend of incidence of CRC was exceed 27.2 (17.4–37.8) for males and females assuming no change point. Trends in females and males were parallel with each other [$P = 0.055$, Figure 1a].

Estimated TASRs were meaningfully higher than estimated ASRs. Average growth in TASRs compared with ASRs

was 3.6 for females and 5.00 (per 100,000 persons) for males. Estimated AAPC for the trend of the TASRs was 17 (–14.7–63.0) percentage which was not statistically significant from zero. Trends of TASRs in females and males were parallel [P = 0.06, Figure 1b].

Discussion

We showed that trend of incidence of CRC in Isfahan province had been strongly affected by case finding from sources other than pathological laboratories. However, the age of registered CRC cases was relatively stable and had not affected by the improvement of case finding applied by the ICR.

By results, the incidence of CRC had been raised for both of males and females, by 27.2%/years during past decade in central Iran. Although this rising trend is partially justifiable by demographic and epidemiologic transition in Iran,[17,18] but it is reasonable if one think that some parts of this increase is a result of improvements in the cancer registration during the study period. As it is showed in graphs, estimated ASRs had been increased suddenly at 2005. This increase is mainly an effect of the case finding from death registries, hospitals, and clinics. Several relatively similar trends are reported for elsewhere in Iran.[3,4,19] Therefore, estimated APCs for trends of CRC incidence in Iran are artificially higher than reality.

Despite meaningful effect of shifting from pathology-based to population-based cancer registry, almost all of Iranian cancer epidemiologists believe that none of the Iranian university cancer registries are population-based and more efforts are needed in this field.[16] In addition, as we know, case finding from death registries, hospitals, and clinics

Table 1: Incidence counts and age distribution of colorectal cancer by genders, central Iran, Isfahan, 2000-2011

Year	Count (%)		Age			
	Males	Females	Mean (SD)		Median (range)	
			Male	Female	Male	Female
2000	75 (52)	69 (48)	61.12 (13.74)	58.21 (12.05)	64 (19-84)	60 (31-83)
2001	9.0 (45)	11 (55)	61.77 (12.00)	60.27 (13.94)	63 (44-75)	66 (32-80)
2002	33 (55)	27 (45)	58.19 (15.90)	56.74 (14.41)	65 (16-80)	57 (34-93)
2003	27 (60)	18 (40)	57.08 (11.05)	56.94 (13.98)	61 (34-73)	57 (28-90)
2004	44 (67)	22 (33)	60.34 (15.26)	58.95 (10.60)	60 (11-85)	60 (37-78)
2005	143 (56)	112 (44)	62.06 (13.61)	61.14 (14.00)	63 (28-85)	62 (30-94)
2006	190 (62)	117 (38)	62.45 (14.45)	58.52 (16.45)*	64 (10-94)	60 (7.0-87)
2007	204 (55)	165 (45)	61.10 (14.82)	58.10 (15.90)*	64 (6.0-85)	58 (15-86)
2008	236 (57)	176 (43)	58.72 (15.26)	59.16 (13.72)	60 (11-89)	60 (28-93)
2009	238 (57)	178 (43)	61.17 (13.42)	58.06 (14.38)*	62 (20-86)	58 (22-89)
2010	217 (56)	169 (44)	62.75 (14.60)	58.28 (14.26)*	63 (4.0-89)	58 (22-89)
2011	238 (56)	184 (44)	60.81 (13.80)	60.21 (15.18)	63 (20-88)	62 (3-90)
Overall	1654 (57)	1248 (43)	61.05 (14.3)	58.90 (14.60)*	63 (4.0-94)	59 (3-93)

*Comparing with males, significant at P<0.05. SD=Standard deviation

Table 2: Age standardized incidence rates and truncated age standardized incidence rate s of colorectal cancer by genders, central Iran, Isfahan, 2000-2011

Year	ASR* (95% Poison CI), per 100,000 person		TASR* (95% poison CI), per 100,000 person	
	Male	Female	Male	Female
2000	3.51 (3.48–3.53)	3.17 (3.15–3.20)	6.05 (6.01–6.09)	5.55 (5.51–5.59)
2001	0.42 (0.41–0.43)	0.56 (0.55–0.57)	0.73 (0.71–0.75)	0.98 (0.96–1.00)
2002	1.52 (1.51–1.54)	1.27 (1.26–1.29)	2.59 (2.56–2.61)	2.22 (2.20–2.24)
2003	1.30 (1.29–1.32)	0.85 (0.84–0.86)	2.27 (2.24–2.30)	1.49 (1.46–1.51)
2004	2.16 (2.14–2.18)	1.04 (1.03–1.06)	3.70 (3.67–3.73)	1.83 (1.80–1.86)
2005	6.91 (6.88–6.94)	5.42 (5.40–5.45)	12.08 (12.03–12.13)	9.50 (9.43–9.57)
2006	8.96 (8.93–8.99)	5.54 (5.51–5.56)	15.58 (15.53–15.63)	9.40 (9.34–9.46)
2007	9.78 (9.75–9.81)	7.58 (7.55–7.61)	16.83 (16.78–16.88)	12.96 (12.91–13.01)
2008	10.97 (10.94–11.01)	8.36 (8.32–8.39)	18.74 (18.68–18.80)	14.61 (14.56–14.67)
2009	11.43 (11.40–11.46)	8.39 (8.36–8.42)	19.90 (19.85–19.95)	14.62 (14.57–14.67)
2010	10.42 (10.40–10.44)	7.97 (7.94–8.00)	18.13 (18.08–18.18)	13.88 (13.82–13.93)
2011	11.56 (11.53–11.60)	8.92 (8.89–8.95)	20.01 (19.96–20.06)	15.34 (15.30–15.40)

*Age adjusted to 2000 world population. ASR=Age standardized incidence rate, CI=Confidence interval, TASR=Truncated age standardized incidence rate at 25 years

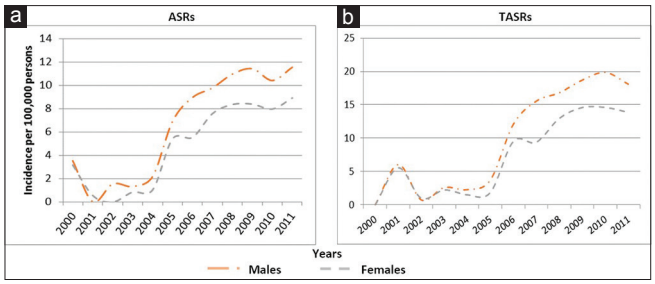

Figure 1: (a and b) Smotted trends of incidence of colorectal cancer in males and females, central Iran, Isfahan, 2000–2011

continued up to 2010 and unfortunately failed after that year. Accordingly, it is most likely that estimated APCs for trend of CRC incidence during 2006 to 2011 be the closest one to the reality. In this study, estimated annual growth (2.83%/year) for 2006 to 2010 was considerably lower than what estimated for 2000–2011 (27.2%/year assuming no change point).

According to our results, age at diagnosis was stable for 2000–2011. It means that case finding from sources other than pathological laboratories had no effect on the age distribution of registered CRC cases. Therefore, one could conclude that it is more probable that cases who are diagnosed clinically are similar with who are diagnosed by pathological tests. However, it is presumable that these tumors be at a different stage. Further studies would be enlightening.

Annual means of the age of registered cases were relatively similar with respective medians. This finding depicts that around half of registered cases had been younger than means. This finding is not consistent with previous studies which shown that Iranian CRC cases are younger than cases from western populations.[20,21]

Our findings showed that estimated ASRs of CRC were lower for females than males, steadily during the study period. This finding is in concordance with other local[22-24] and international reports.[25,26] However, risk differences for recent years (2006–2011) are higher than what for earliest years (2000–2005). Although it may be interpreted as an evidence of more rising trend of incidence of CRC in males according to study findings trend in males had been parallel with trend line in females.

Females CRC cases were younger than males, slightly [Table 1]. This finding is consistent with Seydao *et al*.[27] and may be due to more and timely care-seeking behavior of women which lead to detection of cancer at earlier stages and subsequently younger ages than men.

Conclusions

Cases finding from sources other than pathological laboratories have been an effective intervention to improve the completeness of case ascertainment at ICR. Consequently, estimated incidence rates of CRC had an artificially strong growth at 2005, which results in a terrible rising trend. The estimated slopes for the trend of incidence of CRC in Iran would be carefully interpreted.

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Conflicts of interest

There are no conflicts of interest.

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