Long-term risk of colorectal cancer by gender after positive colonoscopy: population-based cohort study

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ABSTRACT
Background: Evidence for surveillance intervals of colonoscopy are primarily based on adenoma recurrence rate rather than on colorectal cancer (C.R.C.) incidence. Little is known about long-term risk of C.R.C. after positive colonoscopy. In view of men have significantly higher C.R.C. risk than women, we aimed to estimate the gender-specific C.R.C. incidence after positive colonoscopy (adenoma or malignant lesion) at follow-up colonoscopy.

Methods: A retrospective cohort study was conducted using data from a database of colonoscopy screening and surveillance. Patients having had a colonoscopy (January 2010–March 2014) were selected as study subjects and the history of prior colonoscopies was reviewed. Multivariable Weibull regression models were used to estimate the incidence of C.R.C. at follow-up colonoscopy for subjects who were assigned a stratified risk level. The benchmark risk was defined according to a national survey.

Results: The interval incidence of C.R.C. at a 10 year follow-up was 164 (95% C.I. 63–343) and 79 (95% C.I. 26–188) per 100,000 person-years for low-risk men and women respectively, which tallied with our benchmark risk. Men exceeded the benchmark risk in 3–5 years if they had an incomplete polyp removal, ≥3 adenomas during their last colonoscopy or a personal C.R.C. history, and in 7–8 years if they only had familial C.R.C. history. Women had a lower risk of C.R.C., and reached a same risk level 3–5 years later than men. Coexisting above risk factors resulted in a sharp increase in the incidence of C.R.C. at follow-up exceeding the benchmark much earlier.

Conclusion: Surveillance intervals for men based on incidence of C.R.C. are in line with that recommended by the current guidelines for colonoscopy. However, an extension of 3–5 years may be appropriate for women. To target personalized medicine, a risk predictive model could be used to identify an appropriate surveillance interval for each individual in the future.

Introduction

In the United States, over 14 million colonoscopies per year are performed for colorectal cancer (C.R.C.) screening. This is, in part, due to the colonoscopy, with removal of adenomas, being a powerful tool in the reduction of C.R.C. incidence and mortality. The time interval to surveillance colonoscopy after adenoma removal is one of the crucial determinants for the feasibility and cost-effectiveness of colonoscopy-based C.R.C. In the guidelines for colonoscopy surveillance after screening and polypectomy, recommended surveillance intervals in the United States are 5–10 years for the majority of people with adenomas (i.e. those with one or two small tubular adenomas with no high-grade dysplasia), while surveillance intervals of 3 years (even less than 3 years) are recommended for those with high-risk adenomas. However, evidence for surveillance intervals continues to be based primarily on adenoma recurrence rather than on C.R.C. incidence. A few studies have emerged in the literature indicating that surveillance colonoscopy after detection and removal of adenomas has been overused among low-risk patients and underused among high-risk patients. Furthermore, little is known about long-term risk of C.R.C. after positive colonoscopy (adenoma or malignant lesion) through examining C.R.C. incidence. Thus, it is important to measure C.R.C. incidence as a means of optimizing surveillance intervals.

Previous case–control studies have indicated that extension of surveillance intervals to 5 years should be considered even after detection and removal of high-risk polyps, and screening intervals for C.R.C. by colonoscopy could be longer than the commonly recommended 10 years even among people with a family history of C.R.C.. Because case–control studies cannot calculate C.R.C. incidence, cohort studies are needed to provide stronger evidence for further tailoring of surveillance intervals. The lack of evidence from cohort studies might be the reason why the latest guideline for colonoscopy surveillance after screening and polypectomy by
the U.S. Multi-Society Task Force on C.R.C. in 2012 continues to use the 2006 recommendations for next examination except for serrated polyps. In this study, our objectives were to estimate the incidence of C.R.C. in patients who underwent a colonoscopy and had had a prior colonoscopy that was identified through a database, and to compare the difference in C.R.C. incidence between males and females.

**Methods**

**Study design**

This was a population-based, retrospective cohort study in central Illinois representing a population of about 1.4 million persons. This study utilized a well administrated database of colonoscopy screening and surveillance from seven hospitals and medical centers, in which 28,782 colonoscopies were enrolled during the period from January 2010 to March 2014. Results from prior colonoscopy were available in the database during that period or there was a record of a patient report of results from the prior colonoscopy.

The database contained records for this cohort of patients who had had colonoscopies performed over 50 years. They were identified if they had a colonoscopy between January 2010 and March 2014 and included if a record or a patient report of findings from a prior colonoscopy were available. Their risk category for C.R.C. was determined based on the prior colonoscopy. The incidence of C.R.C. over the time period between the two most recent colonoscopies was determined for patients in whom a diagnosis of C.R.C. was available.

Aside from patients with C.R.C. history, patients were assigned into three risk categories: high, medium and low according to the guidelines. Patients at high risk had at least one of the following: 1) three or more adenomas, 2) a large (1 cm+) adenoma or 3) any advanced adenoma (villous, severe dysplasia, serrated or/and incomplete polyp removal) on the prior colonoscopy. Patients that did not have a polyp on their prior colonoscopy were considered low risk. Patients categorized as at medium risk of C.R.C. represented those between high and low risk.

**Data collection**

Shared reporting of colonoscopies (screening and surveillance) in central Illinois was established by the development of a quality of health index database in 2010. The database was initially created by Quality Quest for Health of Illinois and included seven participating sites: the Central Illinois Endoscopy Center, Decatur Digestive Disease Center, Decatur Memorial Hospital, Methodist Medical Center of Illinois, OSF Saint Francis Medical Center, Pekin Hospital and Proctor Hospital in the central Illinois. Each site was responsible for abstracting their own screening and surveillance colonoscopies (ICD-9 code: V76.51) and then entering data into the Central Illinois Colonoscopy Access database and electronically transferring data to Quality Quest for Health of Illinois. The database is currently managed by the Department of Medicine in the University of Illinois College of Medicine at Peoria.

The information in the database which was used in this study includes age in years (exam year), gender, previous and current procedure date, personal history of C.R.C. (yes/no), family history of C.R.C. including first and second degree relatives (yes/no), pathology of previous and current colonoscopies (number and size of adenomas removed, villous adenoma, severe dysplasia, incomplete polyp removal, serrated adenoma, and C.R.C.), bowel prep type and assessment (adequate or inadequate preparation), examination completion (yes/no), and American Society of Anesthesiology (A.S.A.) classification score with a range of 1–5.

**Ethical issues**

All the data in the database was de-identified. This was a retrospective study where results would not change the course of patient care or current patient outcomes. No risk was involved in collecting patient data as information was the minimum necessary information for research purposes. This study was approved by the Institutional Review Board (I.R.B.) at University of Illinois College of Medicine at Peoria.

**Exclusion criteria**

Colonoscopy records were excluded from the analysis as follows: incomplete examinations \((n = 258)\), poor bowel preparations \((n = 850)\), and incomplete history of a previous colonoscopy \((n = 349)\). From the 28,782 available colonoscopies, a total of 1457 were excluded resulting in a final dataset that included 27,325 colonoscopies (Figure 1).

**Statistical analysis**

The primary outcome was the incidence of C.R.C. at follow-up colonoscopy. The C.R.C. prevalence was determined from patients who had never had a prior colonoscopy (real baseline) or there was no data from a prior colonoscopy in the database. In the univariable (unadjusted) analysis, an incidence and 95% confidence interval were calculated for each subgroup population including people with history of C.R.C., high risk, medium risk and low risk of C.R.C.

In the multivariable (adjusted) analyses, two Weibull regression models were used to estimate the incidence of C.R.C. (margin risk probability) at a follow-up colonoscopy given the patient’s follow-up time and the patient’s risk level/
We chose the Weibull model rather than the Cox model because we wanted to predict the time-to-event outcome (incidence of C.R.C.) instead of the relative risk. Model 1 used a stratified risk level (personal history of C.R.C., high risk, medium risk and low risk) whereas Model 2 used specific risk factors (number and size of adenomas removed, villous adenoma, severe dysplasia, incomplete polyp removal, serrated adenoma on last colonoscopy, familial history of C.R.C. and personal history of C.R.C.) to predict the probability of C.R.C. over time while controlling for age, gender, family history of C.R.C. and A.S.A. score.

For Models 1 and 2, a benchmark risk was defined as 65–165 C.R.C. cases per 100,000 population aged 50–69 years in the U.S. according to the recently published national survey. This was considered a rational and feasible definition due to the lack of an existing standard benchmark of risk.

All analyses were conducted with S.A.S. 9.4 (by S.A.S. Institute Inc., Cary, NC, U.S.A.). Variables were reported as mean ± standard deviation, median and range for continuous variables, and percentage for categorical variables. The chi-square test was used to compare the histopathology between patients with and without follow-up. A two-tailed p-value was calculated for all tests, p < 0.05 was considered as being of statistical significance, and p < 0.1 as a threshold to identify potential risk factors.

### Results

#### Demographics

A total of 27,325 colonoscopies conducted in 26,301 patients (50% male) with an average age of 61 ± 9 years were included in this study. Less than half (44%) had a follow-up colonoscopy. Approximately 15% of the patients had family histories of C.R.C. in their first degree relatives.

The time to a follow-up colonoscopy is shown in Table 1. Among the 11,942 follow-up colonoscopies, the shortest follow-up (within 3 years) was for patients that had personal histories of C.R.C. (45%) or for patients considered to have a high risk of C.R.C. (37%). Patients with low risk of C.R.C. had the longest period of time (42% between 6 and 10 years, 24% ≥10 years) for a follow-up colonoscopy.

#### Histopathological findings

The histopathological results at the prior colonoscopy differed in number and prevalence between those with and without follow-up. As shown in Table 2, the histopathological prevalence of C.R.C. or villous adenoma at the prior colonoscopy was only 0.5% and 4.5% for those with a prior-only colonoscopy compared to 8.2% and 12% for those with a follow-up colonoscopy.

### Table 1. Demographics.

| Characteristics at prior or current colonoscopy | No prior colonoscopy (n = 15,383, %) | Patients with prior colonoscopy (column percentage)* | Total (n = 11,942) | History of C.R.C. (n = 976) | High risk (n = 2478) | Medium risk (n = 2715) | Low risk (n = 5773) |
|-----------------------------------------------|--------------------------------------|------------------------------------------------------|--------------------|---------------------------|----------------------|----------------------|----------------------|
| Age in years (mean ± S.D.)                    | 58 ± 7                               | 59 ± 10                                              | 66 ± 11            | 63 ± 10                   | 61 ± 9               | 56 ± 10               |
| <50                                           | 2.6                                  | 14.7                                                 | 7.4                | 7.3                       | 9.6                  | 21.5                 |
| 50–59                                         | 60.9                                 | 26.3                                                 | 21.8               | 30.7                      | 36.2                 | 41.1                 |
| 60–69                                         | 28.4                                 | 32.4                                                 | 32.5               | 37.2                      | 36.8                 | 28.3                 |
| ≥70                                           | 8.1                                  | 16.6                                                 | 38.3               | 24.8                      | 17.4                 | 9.1                  |
| Gender                                        |                                      |                                                      |                    |                           |                      |                      |
| Male                                          | 47.9                                 | 51.9                                                 | 53.0               | 54.6                      | 57.1                 | 48.0                 |
| Female                                        | 52.1                                 | 48.1                                                 | 47.0               | 45.4                      | 42.9                 | 52.0                 |
| Family history of C.R.C. in first degree relatives |                                      |                                                      |                    |                           |                      |                      |
| No                                            | 90.4                                 | 78.5                                                 | 86.3               | 84.1                      | 79.0                 | 74.5                 |
| Yes                                           | 9.6                                  | 21.5                                                 | 13.7               | 15.9                      | 21.0                 | 25.5                 |
| Family history of C.R.C. in second degree relatives |                                      |                                                      |                    |                           |                      |                      |
| No                                            | 93.9                                 | 92.1                                                 | 91.4               | 92.5                      | 91.1                 | 92.6                 |
| Yes                                           | 6.1                                  | 7.9                                                  | 8.6                | 7.5                       | 8.9                  | 7.4                  |
| A.S.A. score†                                 |                                      |                                                      |                    |                           |                      |                      |
| Not recorded                                  | 0.8                                  | 0.6                                                  | 0.9                | 0.7                       | 0.6                  | 0.5                  |
| 1                                             | 21.5                                 | 10.2                                                 | 3.5                | 8.7                       | 12.5                 | 11.0                 |
| 2                                             | 71.9                                 | 79.4                                                 | 77.9               | 80.7                      | 77.9                 | 79.7                 |
| 3                                             | 5.6                                  | 9.6                                                  | 17.3               | 9.7                       | 8.8                  | 8.6                  |
| 4                                             | 0.1                                  | 0.2                                                  | 0.4                | 0.2                       | 0.1                  | 0.2                  |
| 5                                             | 0.0                                  | 0.0                                                  | 0.0                | 0.0                       | 0.0                  | 0.0                  |
| Time interval to follow-up colonoscopy         |                                      |                                                      |                    |                           |                      |                      |
| <3 years                                      | N.A.                                 | 13.3                                                 | 45.0               | 37.2                      | 2.7                  | 2.6                  |
| 3–5 years                                     | N.A.                                 | 44.2                                                 | 41.7               | 51.3                      | 65.7                 | 31.4                 |
| 6–10 years                                    | N.A.                                 | 30.2                                                 | 12.2               | 10.7                      | 29.8                 | 41.7                 |
| 10+ years                                     | N.A.                                 | 12.4                                                 | 1.1                | 0.8                       | 1.8                  | 24.3                 |

S.D., standard deviation; C.R.C., colorectal cancer; A.S.A., American Society of Anesthesiology classification; N.A., not available.

*History of C.R.C. represented the patients who had follow-up colonoscopies and personal histories of C.R.C.; those patients who had follow-up colonoscopies but without personal history of C.R.C. were assigned into three risk levels of C.R.C. (high, medium and low) according to prior colonoscopy.

†A.S.A. score was defined as five levels (1 = healthy, no comorbidities; 2 = mild-to-moderate medical conditions – controlled; 3 = disease severely limits activities; 4 = severe life-threatening disorders; 5 = moribund).
Unadjusted interval incidence of colorectal cancer

As shown in Table 3, the unadjusted interval incidence of C.R.C. at a follow-up colonoscopy in this study was 191 (95% C.I. 86–425) and 166 (95% C.I. 96–286) per 100,000 person-years among the patients who had a personal history of C.R.C. and those who were at a high risk level, respectively. This represents a risk over four times greater than those at a low risk level. However, it was not possible to demonstrate the trend of C.R.C. interval incidence over time in the unadjusted analysis.

Adjusted interval incidence of colorectal cancer

After controlling for age, gender, family history of C.R.C. and A.S.A. score, the Weibull regression models (Supplementary Appendix 1) predicted the interval incidence of C.R.C. at follow-up colonoscopy over time under diverse circumstances (Figures 2–4).

In Model 1, using risk level factor, the incidence of C.R.C. for male patients was beyond the upper limit of benchmark

| Table 2. | Histopathology at prior or current colonoscopy. |
|----------|--------------------------------------------------|
| Histopathology at prior or current colonoscopy | Patients without prior colonoscopy (n = 15,383, %) | Patients with prior colonoscopy (n = 11,942, %) |
| Colorectal cancer* | | |
| No | 99.5 | 91.8 |
| Yes | 0.5 | 8.2 |
| Number of adenoma removed* | | |
| 0 | 61.0 | 43.9 |
| 1 | 22.2 | 41.5 |
| 2 | 8.8 | 12.4 |
| 3 or more | 8.0 | 2.2 |
| Size of largest adenoma removed* | | |
| 0 mm | 44.3 | 59.4 |
| 1–5 mm | 30.8 | 17.0 |
| 6–10 mm | 18.3 | 13.0 |
| >11 mm | 6.6 | 10.6 |
| Villous adenoma* | | |
| No | 95.5 | 88.0 |
| Yes | 4.5 | 12.0 |
| Severe dysplasia* | | |
| No | 99.3 | 96.0 |
| Yes | 0.7 | 4.0 |
| Incomplete polyp removal | | |
| No | N.A. | 94.6 |
| Yes | N.A. | 5.4 |
| Serrated adenoma* | | |
| No | 93.3 | 94.8 |
| Yes | 6.7 | 5.2 |

N.A., not available.

*p < 0.05.

| Table 3. | Interval incidence of colorectal cancer (C.R.C.) on follow-up colonoscopy. |
|----------|--------------------------------------------------|
| Stratified group | Number of cancers | Person-years | Unadjusted Incidence and 95% CI (per 100,000 person-years) | Predicted 10 year incidence and 95% C.I. in Model 1† (per 100,000 person-years) |
| Personal history of C.R.C. | | | | |
| Risk level of C.R.C.* | | | | |
| High risk | 6 | 3144 | 191 (86–425) | 791 (438–1232) |
| Medium risk | 13 | 7824 | 166 (96–286) | 1023 (601–1518) |
| Low risk | 8 | 14,068 | 57 (28–114) | 298 (132–557) |
| High risk | 19 | 47,943 | 86 (425) | 164 (63–343) |

*The patients without C.R.C. history were categorized as high, medium or low risk on C.R.C. according to the baseline colonoscopy. High risk indicated three or more adenomas, or a large (1 cm+) adenoma or any advanced adenomas (villous, severe dysplasia, serrated and/or incomplete polyp removal) on the baseline colonoscopy. Low risk meant no polyp was found on the baseline colonoscopy. Medium risk represented those between high risk and low risk.

†Multivariable Weibull regression model adjusted by age, gender, familial history of C.R.C. and A.S.A. score (American Society of Anesthesiology classification).

Discussion

This study estimates the long-term risk of C.R.C. after positive colonoscopy in a large population-based cohort of colonoscopies that were conducted in clinical practice. The findings for men support the current colonoscopy surveillance intervals of every 3–5 years for people at medium to high risk, and every 10 years for people at low risk, that is recommended by the guidelines of the U.S. Multi-Society Task Force on Colorectal Cancer7,9. Further, the findings suggest that the guideline recommendations differentiate between men and women because men had more than double the risk of C.R.C. than women across all stratified risk levels. In addition, the recommendations should be modified to reflect the increased risk for those people who have two or more of the following risk factors: three or more adenomas removed, incomplete polyp removal on last colonoscopy, familial history of C.R.C., and personal history of C.R.C.

Compared to previous studies, our study clearly demonstrates the trend of C.R.C. incidence at follow-up colonoscopy over time, and provides strong supporting evidence for the current guideline recommendations. Modifications that conflict with the recommended guidelines have been proposed. These recommendations suggest extending screening and surveillance intervals to people that are considered at risk range in 3–5 years if they had a high risk or personal history of C.R.C. based on previous colonoscopy, and in 7–8 years or 10 years if they had a medium or low risk of C.R.C. based on previous colonoscopy, as shown in Figure 2. Compared to men, women had a delay of 3–5 years to get the same level risk of C.R.C.

In Model 2, risk factors (number and size of adenomas removed, villous adenoma, severe dysplasia, incomplete polyp removal, serrated adenoma on last colonoscopy, familial history of C.R.C. and personal history of C.R.C.) were used to determine the effect of the specific risk factors on the incidence of C.R.C. Figure 3 depicts the top four risk factors which significantly impacted Model 2. Although these results are similar to those in Model 1, the use of risk factors in Model 2 improves upon the C.R.C. incidence predictability when there are coexisting risk factors (two or more risk factors together) as shown in Figure 4. In this figure, a patient that had two of these four risk factors exceeded the benchmark risk in less than 2–3 years indicating a sharp increase in the incidence of C.R.C. at follow-up colonoscopy.
increased risk of C.R.C. (i.e. detection and removal of high-risk polyps, and family history of C.R.C.)\textsuperscript{13,14}. Our study findings suggest that this may be appropriate for men but not for women. Further evaluation of the differences in C.R.C. interval surveillance by gender is required to substantiate these inferences.

Previous studies suggest that men have significantly higher age-adjusted C.R.C. incidence rates across all categories of age, race, tumor subsite, stage and region\textsuperscript{19–23}. Our study also reports a significant difference in C.R.C. risk between men and women. When to initiate C.R.C. screening in men and women has been discussed without consensus since 2007\textsuperscript{24}; our finding supports the idea that due to the delayed risk for women future guidelines could consider adapting different recommendations for men and women. Therefore, an additional extension of 3–5 years’ surveillance interval may be appropriate for women.

Our study found that a sharp increase in the incidence of C.R.C. occurs when there are coexisting risk factors, and indicates that the surveillance interval could be reduced to 1–3 years. Although there are very few individuals that present with two or more coexisting risk factors, they represent an important group due to their relative higher risk and modification of this recommendation is warranted.

Polyp detection and removal is presumed to enhance the detection of precancerous adenomas which will, in turn, serve to potentially reduce the risk of C.R.C. Corley \textit{et al}. found that the adenoma detection rate was inversely associated with the risks of interval C.R.C.\textsuperscript{25}. Three additional studies also indicated the inverse association between the rate of colonoscopic polypectomy and the risk of interval cancer\textsuperscript{26–28}. Clearly, frequent colonoscopy could increase the chance of detecting precancerous adenomas but it could result in an increased number of unnecessary colonoscopies which would unnecessarily use healthcare resources, burden patients and enhance the risk of side effects. Hence, it is very important to balance the frequency of colonoscopy and to find the most appropriate surveillance interval. The benefit of this examination of interval

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Prediction of colorectal cancer (C.R.C.) interval incidence over time based on stratified risk level. *Patients without C.R.C. history were categorized as being at high, medium or low risk of C.R.C. according to the baseline colonoscopy (Lieberman, 2012\textsuperscript{7}). High risk indicated three or more adenomas, or a large (1 cm+) adenoma or any advanced adenomas (villous, severe dysplasia, serrated and/or incomplete polyp removal) on the baseline colonoscopy. Low risk meant no polyp was found on the baseline colonoscopy. Medium risk represented those between high risk and low risk. The benchmark risk was defined as 65–165 C.R.C. cases per 100,000 population aged 50–69 years old in the U.S. (Abotchie, 2012\textsuperscript{19}).}
\end{figure}
incidence of C.R.C. at follow-up colonoscopy is that it personalizes the surveillance interval for those high-risk patients.

A few limitations to this study might need to be considered. First, it did not take account of multiple visits due to using colonoscopy-level data instead of patient-level data. In view of ethical concerns and patient privacy, patient identifiers were restricted in the database. However, the impact of patient clustering on our results is negligible because the majority (96.3%) of colonoscopies were from unique patients. Also, the long-term risk of C.R.C. at follow-up colonoscopy is predictable based on the previous colonoscopy even if a patient has multiple examinations. Second, only a few high-risk patients had ten or more than ten years’ follow-up in our database which, to a certain extent, might add uncertainty when the results are estimating a very long-term incidence of C.R.C. at follow-up colonoscopy, such as 20–30 years. Third, the study was not able to analyze other demographics except for age and sex, but A.S.A. score was used to adjust patient characteristics. Moderate or severe medical conditions might limit patients’ activities and decrease exercise time, leading to an increase of C.R.C. risk. Fourth, recall bias should be a concern for any retrospective study. We assume that the majority of patients could clearly remember the findings of a prior colonoscopy because it’s a very important event in their lives. Fifth, it was challenging to control the quality of data collection from multisite hospitals. This study used a standard electronic database for all seven hospitals, and persons entering data were well trained (Supplementary Appendix 2). Sixth, only one national survey was selected for the benchmark risk because we failed to find other relevant studies. Finally, although the number of cases (46 cancers) was acceptable for the C.R.C. incidence estimates, we may expect other studies with bigger sample sizes to validate our findings.

Conclusions

Surveillance intervals for men based on incidence of C.R.C. are in line with that recommended by the current national guidelines for colonoscopy surveillance after screening and polypectomy. However, an extension of 3–5 years of surveillance intervals may be appropriate for women. The effect of coexisting risk factors should be further examined and validated in other studies in order to avoid a delay in C.R.C. detection by the recommended surveillance intervals. To meet the goal of personalized medicine, a risk predictive
model could be used to identify an appropriate surveillance interval for each individual in the future.

**Transparency**

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**Authors’ contributions:** Study concept and design: J.R., C.S.K., and C.V.A.; manuscript drafting and revision: J.R., C.S.K., C.V.A., S.P., and M.K.; statistical analysis: J.R., and C.S.K.; data acquisition: J.R., C.S.K., C.V.A., and S.P.

**Declaration of financial/other relationships**

J.R., C.S.K., M.K., C.V.A., and S.P. have disclosed that they have no significant relationships with or financial interests in any commercial companies related to this study or article.

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**Figure 4.** Prediction of colorectal cancer (C.R.C.) interval incidence over time based on coexisting risk factors. *The specific risk factors of C.R.C. were identified based up the prior colonoscopy (Lieberman, 2012). Risk factor A, incomplete polyp removal; risk factor B, three or more adenomas removed during last colonoscopy; risk factor C, personal history of C.R.C. In the patients with follow-up, 52 patients had a combination of A&B, 75 patients had a combination of A&C, and 13 patients had a combination of B&C. The benchmark risk was defined as 65–165 C.R.C. cases per 100,000 population aged 50–69 years old in the U.S. (Abotchie, 2012).*
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