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What is the most cost-effective strategy to screen for second primary colorectal cancers in male cancer survivors in Korea?

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Abstract

AIM: To identify a cost-effective strategy of second primary colorectal cancer (CRC) screening for cancer survivors in Korea using a decision-analytic model.

METHODS: A Markov model estimated the clinical and economic consequences of a simulated 50-year-old male cancer survivors' cohort, and we compared the results of eight screening strategies: no screening, fecal occult blood test (FOBT) annually, FOBT every 2 years, sigmoidoscopy every 5 years, double contrast barium enema every 5 years, and colonoscopy every 10 years (COL10), every 5 years (COL5), and every 3 years (COL3). We included only direct medical costs, and our main outcome measures were discounted lifetime costs, life expectancy, and incremental cost-effectiveness ratio (ICER).

RESULTS: In the base-case analysis, the non-dominated strategies in cancer survivors were COL5, and COL3. The ICER for COL3 in cancer survivors was $5593/life-year saved (LYS), and did not exceed $10 000/LYS in one-way sensitivity analyses. If the risk of CRC in cancer survivors is at least two times higher than that in the general population, COL5 had an ICER of less than $10 500/LYS among both good and poor prognosis of index cancer. If the age of cancer survivors starting CRC screening was decreased to 40 years, the ICER of COL5 was less than $7400/LYS regardless of screening compliance.

CONCLUSION: Our study suggests that more strict and frequent recommendations for colonoscopy such as COL5 and COL3 could be considered as economically reasonable second primary CRC screening strategies for Korean male cancer survivors.

Key words: Cost-effectiveness; Second primary colorectal cancer; Screening; Cancer survivor

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INTRODUCTION

A recent improvement in cancer survival owing to early diagnosis and advances in treatment has raised the issue of second primary cancers (SPCs) in cancer survivors after their primary treatment[1,2]. Due to carcinogenic effects of cancer-related treatment, genetic susceptibil-

ity or unhealthy behavior such as smoking, alcohol and obesity, cancer survivors are at increased risk for SPCs, not only at the original site but at other sites as well[3,4]. Recent studies have shown that the age-standardized incidence rate was 2.3 times higher for an SPC than for a first cancer in the Korean general male population[5]. Specifically, the age-standardized incidence rate was about four times higher for second than for first primary colorectal cancers (CRCs)[5]. It is well-known that screening for CRC reduces mortality through detection of malignancy at an earlier, more treatable stage as well as by identification and removal of the precursor lesion, the adenomatous polyp[6]. These findings suggest that more thorough surveillance and screening for second primary CRC is needed for the cancer survivors.

Many previous studies have focused on the cost-effectiveness (CE) of CRC screening in the general population[6-9], and several panels have recommended CRC screening for the general population[10-12]. As the risk of CRC and life expectancy are quite different between cancer survivors and the general population, screening guidelines for the general population could not be applied to the cancer survivors. However, until now, there have been few recommendations for CRC screening for cancer survivors. To suggest a feasible economic strategy of second primary CRC screening for cancer survivors in Korea, we constructed a decision-analytic model, and compared the CE results of cancer screening in cancer survivors and in the average-risk general population.

MATERIALS AND METHODS

The natural history of a simulated male cancer survivors' cohort was modeled with and without second primary CRC screening until age of 75 years (Figure 1). For simplicity and comparison with results from the general population, we assumed that all male cancer survivors enter at age 50 years, which most guidelines for the general population recommended for starting CRC screening[10-12]. We developed a Markov model using TreeAge-Pro 2007 software (TreeAge Software Inc., Williamstown, Massachusetts). The Markov model estimated the clinical and economic consequences of eight different screening strategies as follows: (1) no screening, (2) fecal occult blood test (FOBT) annually (FOBT1), (3) FOBT every 2 years (FOBT2), (4) sigmoidoscopy every 5 years (SIG5), (5) double contrast barium enema every 5 years (DCBE5), (6) colonoscopy every 10 years (COL10), (7) colonoscopy every 5 years (COL5), and (8) colonoscopy every 3 years (COL3).

Individuals were placed into health states defined by the presence or absence of a colorectal polyp or second primary CRC (early or advanced) 1 year after the index cancer diagnosis. Cases of positive screening test results were worked up with a colonoscopy, and individuals diagnosed with polyps underwent polypectomy. The probability of perforation was assigned to colonoscopy, sigmoidoscopy, DCBE and polypectomy[8,13,14]. Mortality caused by the risk of perforation was assumed to be

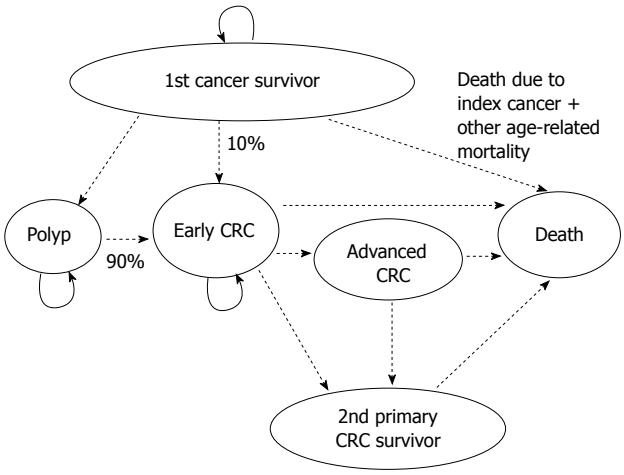

Figure 1 Markov model of second colorectal cancer (CRC) screening in Korean male cancer survivors.

0.02%[9,14]. Colonoscopy was repeated every 3 years for surveillance after polypectomy[15]. We assumed that 80% of male cancer survivors underwent the initial screening test, independent of whether they were compliant with past tests. The compliance of follow-up or surveillance colonoscopy was assumed to be 100%. We also assumed that 90% of CRCs develop from polyps[15,16], and the latent period between early stage and advanced stage was assumed to be 2 years[9]. The relative risk of CRC in Korean male cancer survivors was assumed to be four times higher than that in the general population[5]. Age-specific transition probabilities and prevalence were calculated between normal, polyp, and CRC to yield an incidence rate of polyp and CRC derived from previous literature and the Korea Central Cancer Registry[7,17-19]. The stage-specific CRC mortality were applied uniformly to all malignancies regardless of the means of detection (by symptoms or screening) or the state of detection (diagnosed *vs* undiagnosed cancer). Age-specific mortality from index cancer and other causes was estimated based on the above sources combined with statistics published by the National Center for Health Statistics[20] and Korea Central Cancer Registry[21]. As there have been few studies on mortality from second primary CRC, we calculated the additional yearly probability of dying from a second primary CRC based on cancer stage from previous studies of CRC as the first index cancer[21-23].

We obtained the data on the costs of CRC treatment by stage and time period from the National Health Insurance Corporation (social insurer of the national health insurance (NHI) with a universal coverage of population)[24]. Costs of screening tests were obtained from the fee schedule of the National Health Insurance Corporation (the NHI of Korea has a fee schedule applied to all insured services)[25]. Costs were expressed in US dollars and the exchange rate was 955 Korean Won for one US dollar in 2006[26]. As the indirect costs of cancer screening are not established in Korea, we included only direct medical costs.

Our main outcome measures were discounted lifetime costs, life expectancy, incremental cost-effectiveness

Table 1 Summary of assumptions

	Parameter	Base case value (range)	Ref.
Sensitivity & specificity of colorectal screening tests	Sensitivity of FOBT for colorectal polyps/cancer	0.1/0.5	[27-30]
	Sensitivity of colonoscopy for colorectal polyps/cancer	0.9/0.95	[6,31,32]
	Sensitivity of double contrast barium enema for colorectal polyps/cancer	0.5/0.8	[6,33,34]
	Sensitivity of sigmoidoscopy for colorectal polyps/cancer	0.46/0.52	[31,32,35]
	Specificity of FOBT	0.9	[28-30]
	Specificity of colonoscopy	1	[6,31,32]
	Specificity of double contrast barium enema	0.9	[6,33,34]
	Specificity of sigmoidoscopy	0.95	[6,31,32]
Natural history of colorectal polyp/cancer sequence	Prevalence of polyps at age 50 yr	0.20 (0.1-0.4)	[14,35]
	Annual polyp incidence rate in cancer survivors	Age specific	[14,35,36]2
	Percent of cancers originating as polyps	90%	[37,38]
	Relative risk of colorectal cancer in cancer survivor compared with the general population	4 (1-5)	[5]
	Age specific incidence rate of colorectal cancer without polypoid precursors in cancer survivors	Age specific	[5,39,40]2
	Age specific incidence rate of colorectal cancer with polypoid precursors in cancer survivors	Age specific	[5,39,40]2
	Dwelling time of colorectal cancer in early stages	2 yr	[29,41]
	Percent of colorectal cancers detected in early stages with no screening	5% (2%-10%)	[23]
	Five-year all cause survival for early 2nd primary colorectal cancer	90% (80%-95%)	[18,22,23]
	Five-year all cause survival for advanced 2nd primary colorectal cancer	60% (40%-70%)	[18,22,23]
Natural history of cancer survivors	Five-year survival for index cancer	40% (20%-80%)	[18]
	Age specific mortality except the index cancer	Age specific	[21]
	Age of cancer survivors for starting colorectal cancer screening, year	50 (40-60)	[10-12]
	Compliance of 2nd colorectal cancer screening	80% (60%-100%)	
Complications and unintended consequences	Rate of perforation of colon in colonoscopy	0.20% (0.1%-0.3%)	[13,14,42]
	Rate of perforation of colon in polypectomy	0.40% (0.2%-0.5%)	[13,14,42]
	Rate of perforation from sigmoidoscopy	0.01% (0.005%-0.05%)	[13,14,42]
	Rate of perforation from double contrast barium enema	0.005% (0.001%-0.01%)	[42]
	Death rate due to perforated colon	0.2% (0.1%-5%)	[19,39,42]
Cost (dollar[1]) & discount rate	Sigmoidoscopy	31.3	[25]
	Colonoscopy	61.7	[25]
	Double contrast barium enema	68.5	[25]
	FOBT	2.7	[25]
	Polypectomy, biopsy and pathologic exam	189	[25]
	Treatment of early cancer for first year	7330 (5860-8800)	[7,25]
	Treatment of advanced cancer for first year	14660 (10050-15080)	[7,25]
	Treatment of cancer after first year	2094 (1670-2510)	[7,25]
	Cost to repair the endoscopic perforation	3141 (2510-3770)	[7]
	Discount rate	0.03 (0-0.05)	

[1]Exchange rate: 955 Korean Won for one US dollar in 2006; [2]Estimated by calibration to national data on colorectal polyp and cancer incidence.

ratio (ICER), which were compared for different CRC screening strategies. Because there are uncertainties with respect to quality of life associated with CRC screening, colorectal polyp, and second CRC, we conducted the base case analysis using increase in life expectancy as the primary outcome. Incremental CE analysis was performed by ranking the 16 strategies in order of increasing effectiveness. After eliminating strategies that were more or equally costly and less effective than a competing strategy [i.e. ruled out by simple dominance), we calculated the ICER for each strategy (additional cost divided by life-year saved (LYS)] compared with the next least expensive strategy. Strategies exhibiting extended dominance were eliminated from the rank-ordered list, and ICERs of the remaining strategies were recalculated[27]. Future costs and life-years were discounted at an annual rate of 3%. We compared the results from male cancer survivors with that from general male population.

Sensitivity analyses were performed to assess the stability of the results of a plausible range of several parameters, such as prevalence of colorectal polyps at age 50 years, 5-year survival rates of second primary CRC, complications of screening test or polypectomy *etc* (Table 1). We performed detailed analyses by changing key variables of the index cancer such as 5-year survival rate of first cancer, relative risk of CRC in cancer survivors compared with that in general population. In addition, we evaluated the effects of changing age of subjects for starting second primary CRC screening and compliance rate on the CE of our results.

RESULTS

Base case

In the base-case analysis at 80% screening compliance, all screening strategies extended life expectancy both in male cancer survivors and the general population (Table 2). The strategies which were not ruled out by simple

Table 2 Cost-effectiveness of colorectal screening strategies among male cancer survivors and the general population in Korea (80% compliance)

Male general population				Male cancer survivors			
Strategy (abbreviation)	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E[2], dollar[1] per life-year gained	Strategy (abbreviation)	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E[2], dollar[1] per life-year gained
COL every 10 yr	437.3	17.260	…	COL every 5 yr	463.5	7.572	
No screening	448.0	17.243	…	COL every 10 yr	480.1	7.568	…
COL every 5 yr	478.3	17.263	14456.8	COL every 3 yr	480.2	7.575	5592.9
DCBE every 5 yr	542.3	17.256	…	DCBE every 5 yr	563.4	7.562	…
SIG every 5 yr	542.4	17.255	…	SIG every 5 yr	571.8	7.560	…
COL every 3 yr	554.4	17.265	38876.8	No screening	632.2	7.544	…
FOBT every 2 yr	810.0	17.252	…	FOBT every 2 yr	735.2	7.557	…
FOBT every 1 yr	1130.9	17.257	…	FOBT every 1 yr	842.3	7.564	…

COL: Colonoscopy; SIG: Sigmoidoscopy; DCBE: Double contrast barium enema; FOBT: Fecal occult blood test. Ellipse indicates no data (incremental CR ratios not calculated for these strategies because they were dominated). [1]Exchange rate, 955 Korean Won for one US dollar in 2006; [2]Incremental CE ratio (dollar/year) = Incremental cost per person/incremental years of life gained.

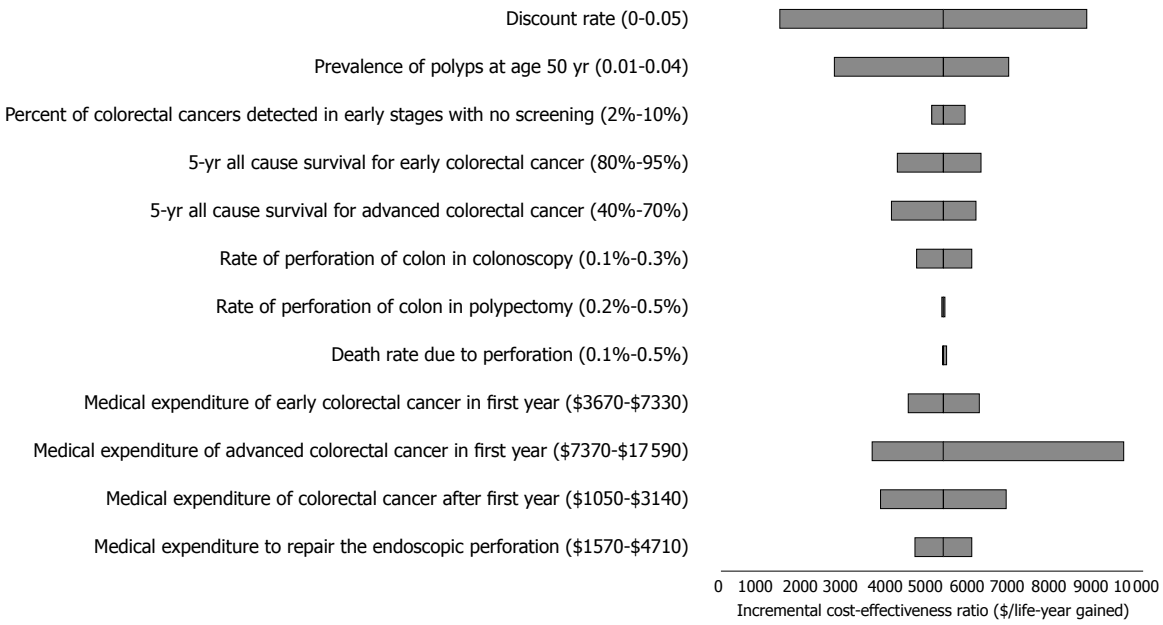

Figure 2 Sensitivity analyses on cost-effectiveness from the perspective of colonoscopy every 3 years *vs* colonoscopy every 5 years in male cancer survivors.

dominance nor extended dominance (non-dominated strategies) in the general population were COL10, COL5, and COL3, while those in cancer survivors were COL5 and COL3. The ICER for COL3 in cancer survivors was $5593 per LYS. In cancer survivors, the lifetime total cost per person associated with "FOBT annually" was larger than that associated with no screening, while COL5 and COL3 were less costly than no screening.

Sensitivity analyses

Figure 2 shows the results of one-way sensitivity analyses on CE from the perspective of COL3 *vs* COL5 in male cancer survivors. In most cases, COL5 and COL3 were non-dominated strategies, and the ICER of COL3 ranged between $1480 and $9192.

Table 3 shows the results of two-way sensitivity analyses by changing risk of second CRC and 5-year survival rate of index cancer in Korean male cancer survivors. If the risk of CRC in cancer survivors was at least three times higher than that in the general population, screening with COL5 in cancer survivors had an ICER of less than $4000 per LYS in the entire range of 5-year survival of index cancer between 20% and 80%. If the risk of CRC in cancer survivors was two times higher than that in the general population, COL5 in cancer survivors had an ICER of less than $10500 per LYS in both types of index cancer with poor and good prognosis. If the risk of CRC in cancer survivors was the same as that in the general population, non-dominated strategies were no screening, COL10, COL5, and COL3, and the ICER of COL5 was more than $25000 per LYS, while the ICER of COL10 ranged between $2315 in index cancer with good prognosis and $19650 in index cancer with poor prognosis.

Table 4 shows the results of sensitivity analysis by changing compliance of CRC screening and age of cancer

Table 3 Two-way sensitivity analysis by changing variables of index cancer such as 5-yr survival rate of first cancer and relative risk of colorectal cancer in Korean male cancer survivors

Relative risk of colorectal cancer in cancer survivor compared with that in general population	5-yr survival of index cancer = 20%				5-yr survival of index cancer = 40%				5-yr survival of index cancer = 80%			
	Non-dominated strategy	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E^2 (dollar)[1] per life-year gained	Non-dominated strategy	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E^2 (dollar)[1] per life-year gained	Non-dominated strategy	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E^2 (dollar)[1] per life-year gained
5	COL5	329.0	4.512		COL5	532.5	7.567		COL5	957.9	13.829	
	COL3	339.2	4.514	4921.7	COL3	542.2	7.571	2634.4	COL3	962.6	13.836	658.2
4	COL5	306.7	4.516		COL5	463.5	7.572		COL10	826.0	13.837	
	COL3	329.0	4.517	18078.3	COL3	480.2	7.575	5592.9	COL5	831.1	13.843	835.2
									COL3	879.7	13.847	11508.2
3	COL10	266.6	4.517		COL10	401.4	7.576		COL10	682.9	13.847	
	COL5	270.3	4.518	2685.2	COL5	409.6	7.579	3365.6	COL5	701.9	13.851	4104.9
	COL3	295.5	4.519	27126	COL3	447.3	7.580	22760.2	COL3	761.9	13.854	18922.1
2	No screening	185.4	4.512		COL10	324.4	7.582		COL10	533.5	13.857	
	COL10	224.5	4.52	4912	COL5	340.1	7.583	9506.4	COL5	566.7	13.860	10725.2
	COL5	232.3	4.521	8378.3	COL3	383.7	7.584	39469.5	COL3	638.6	13.862	34075.6
	COL3	260.4	4.522	45556.4								
1	No screening	96.1	4.519		No screening	175.9	7.580		No screening	342.6	13.853	
	COL10	180.5	4.523	20568.2	COL10	244.0	7.587	9196.3	COL10	377.2	13.867	2424.5
	COL5	192.4	4.524	25817.6	COL5	267.2	7.588	28343.9	COL5	425.1	13.869	31064.6
	COL3	223.5	4.524	103111.0	COL3	316.8	7.589	91808.0	COL3	509.3	13.870	81681.8

COL10: Colonoscopy every 10 years; COL5: Colonoscopy every 5 years; COL3: Colonoscopy every 3 years; Dominated strategy is a strategy that is more or equally costly and less effective than a competing strategy. [1]Exchange rate, 955 Korean won for one US dollar in 2006; [2]Incremental CE ratio (dollar/year) = Incremental cost per person/Incremental years of life gained.

Table 4 Two-way sensitivity analysis on cost-effectiveness of 2nd primary colorectal cancer screening by compliance of screening and age of Korean male cancer survivors for starting screening

Age for starting screening	Compliance of 2nd colorectal cancer screening = 60%				Compliance of 2nd colorectal cancer screening = 80%				Compliance of 2nd colorectal cancer screening = 100%			
	Non-dominated strategy	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E^2 (dollar)[1] per life-year gained	Non-dominated strategy	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E^2 (dollar)[1] per life-year gained	Non-dominated strategy	Lifetime cost per person (dollar)[1]	Life expectancy (yr)	Incremental C/E^2 (dollar)[1] per life-year gained
40	COL5	370.0	8.633		COL10	341.0	8.326		COL10	352.2	8.328	
	COL3	388.9	8.636	7584.1	COL5	343.7	8.329	872.5	COL5	369.2	8.330	7375.9
					COL3	383.7	8.330	26483.2	COL3	424.1	8.331	50842.3
50	COL3	479.2	7.665		COL5	463.5	7.572		COL10	475.0	7.571	
					COL3	480.2	7.575	5592.9	COL5	476.0	7.574	330.8
									COL3	508.1	7.577	14571.1
60	COL3	528.3	7.668		COL3	522.1	6.057		COL5	519.5	6.057	
									COL3	529.5	6.059	4186.7

COL10: Colonoscopy every 10 years; COL5: Colonoscopy every 5 years; COL3: Colonoscopy every 3 years. Dominated strategy is a strategy that is more or equally costly and less effective than a competing strategy. [1]Exchange rate: 955 Korean Won for one US dollar in 2006. [2]Incremental CE ratio (dollar/year) = Incremental cost per person/Incremental years of life gained.

survivors for starting CRC screening. If the age of cancer survivors for starting CRC screening was 50 years or older, COL3 had an ICER of less than $14600 per LYS, regardless of the screening compliance. If age for starting CRC screening in cancer survivors was 40 years, the ICER of COL5 was less than $7400 per LYS saved in all cases of CRC screening compliance.

DISCUSSION

We constructed a computer simulation to suggest economic strategies of second primary CRC screening for cancer survivors in Korea, and compared the CE results of CRC cancer screening in cancer survivors and in the average-risk general population. As all non-dominated strategy were those using colonoscopy in both cancer survivors and the general population, more strict and frequent recommendation of colonoscopy such as COL5 and COL3 could be considered economic strategies for male cancer survivors.

Until now, there has been no explicit threshold of CE below which policy makers will consider accepting the strategy. In the US, a figure of $50000 per Quality Adjusted Life-Year (QALY) has frequently been quoted

for many years as being cost-effective[43]. The World Health Report 2002 suggested that interventions costing less than three times Gross Domestic Product (GDP) per capita for each Disability Adjusted Life-Year (DALY) averted represented good value for money[44], which is usually well in excess of $50 000 per QALY in many high-income countries[43]. In our study, the ICER for COL3 was less than $6000 per LYS in a base line analysis, and did not exceed $10 000 per LYS in one-way sensitivity analyses. Our findings also suggest that if the risk of CRC in cancer survivors is at least two times higher than that in the general population, COL5 could be a cost-effective strategy for second primary CRC screening for cancer survivors of both good and poor prognosis of index cancer, with an ICER of less than $10 500 per LYS. As our primary outcomes are not QALY or DALY, direct comparisons might be difficult. The GDP per capita of Korea was more than $20 000 in 2006. When we approximately applied these CE thresholds, in most cases, COL5 and COL3 could be considered a cost-effective method for second primary CRC screening for Korean male cancer survivors, regardless of the index cancer. Even if the index cancer were CRC, our finding could be applied and be consistent with the CRC surveillance guidelines of the American Society of Clinical Oncology (ASCO)[45]. In ASCO guidelines, routine annual colonoscopies are not recommended for all CRC patients, and colonoscopy every 3-5 years could be sufficient to detect new CRCs and polyps[45].

It is also important to consider the changes in CE of these strategies according to age of starting second primary CRC screening in cancer survivors. Little is known about the CE if cancer survivors start second primary CRC screening above or below age 50, at which most guidelines recommend starting CRC screening in the general population. Our findings suggest that for male cancer survivors in older age, COL3 had more favorable CE results, regardless of screening compliance. For younger cancer survivors aged 40 years old, COL5 could be considered a CE strategy with ICER of less than $7600 per LYS.

Interestingly, in our study of Korea, COL10, COL5 and COL3 had lower total medical costs than no screening of male cancer survivors. In other countries, screening for CRC usually leads to more costs than no screening. Cost estimates for the medical care of CRC treatment in the US range from $25 000 to $70 000 and the cost of COL is about $1000[9,16]. However, in Korea, the cost estimate of CRC treatment in the first year ranges from $7000 to $14 000 while the cost of COL was about $60[24,25]. The ratio of treatment cost to COL cost ranges from 25:1 to 70:1 in the US and 120:1 to 230:1 in Korea. Due to the difference in cost structures, screening with colonoscopy might be more cost-effective in Korea than in other countries. However, CRC screenings are not covered by the Korean NHI scheme in either the general population or cancer survivors. Instead, the Korean government started the national cancer screening program (NCSP) in 1999, which was extended to include CRC screening in 2004[11]. The government covers 50% of the screening cost for the insured and 100% for low-income people. However, the primary method for CRC screening in the Korean NCSP is FOBT annually. Our study shows that the strategy of "FOBT annually" is always the dominant strategy in male cancer survivors, and costs more than the strategy of no screening.

The major barrier to promotion of colonoscopy as a primary CRC screening tool is the lack of manpower to deliver colonoscopy to the public in Korea. In these human-resource limited setting, it is important to identify the more vulnerable population who has a greater potential to receive benefits. Our study suggests that cancer survivors who are at increased risk of second primary CRC have a favorable result of CE of CRC screening compared with the general population. Even in younger cancer survivors aged 40 years old, COL5 might be economically feasible, while COL10 is usually recommended for the Korean general population aged 50 years old. Therefore, at least for cancer survivors, CRC screening should be covered by the Korean NHI scheme and screening methods using colonoscopy are needed to be recommended as a primary screening strategy for CRC in this population.

Limitations

Our analysis has several limitations. In the design of the model, we tried to reduce the complex natural history of CRC to a few essential states and to avoid assumptions on treatments for which little or no published data existed. For instance, we assumed that 90% of second primary CRC arose from polyps. We used several sets of data from the general population, such as prevalence of colorectal polyp by age, polyp recurrence rate, and treatment costs of second primary CRC, if there were no published data available in cancer survivors. There were possible differences between these two populations. However, when we performed sensitivity analyses, the CE results were usually insensitive to the plausible range of these uncertain parameters. Second, we calculated only the direct costs and did not take into account the impact of CRC and screening on indirect costs. Third, in our study, recently developed CRC screening strategies such as CT colonoscopy were not included. However, the cost of CT colonoscopy is about four times higher than that of colonoscopy in Korea, while the sensitivity and specificity of CT colonoscopy is not superior to that of colonoscopy[46], and this new method does not seem to be an economically-efficient strategy.

In conclusion, with an increased population of long-term cancer survivors, effective systems for their health promotion are needed. Implementation of the economic SPC screening program might be one of the important interventions to improve their health. Our study showed that COL3 or COL5 might be suggested as a primary strategy for second primary CRC screening in cancer survivors who have a higher risk of CRC than the general population. This study supports the evidence

and rationale for second primary CRC screening in male cancer survivors.

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COMMENTS

Background

Recent improvement in cancer survival due to early diagnosis and advances in treatment has raised the issue of second primary cancers (SPCs) in cancer survivors after their primary treatment. The age-standardized incidence rate is about four times higher for second primary colorectal cancer (CRC) than for first primary CRC in Korea. However, until now, there have been few recommendations and economic evaluations of CRC screening for cancer survivors.

Research frontiers

To suggest a feasible economic strategy of second CRC screening for cancer survivors in Korea, the authors constructed a decision-analytic model, and compared the cost-effectiveness results of cancer screening between in male cancer survivors.

Innovations and breakthroughs

Non-dominated strategies were those using colonoscopy in both cancer survivors and the general population, and more strict and frequent recommendations for colonoscopy (COL) such as COL5 (screening every 5 years) and COL3 (screening every 3 years) could be considered as economic strategies for male cancer survivors.

Applications

The major barrier to promoting colonoscopy as a primary CRC screening tool is the lack of manpower to deliver colonoscopy to the public in Korea. In these human-resource limited settings, it is important to identify the most vulnerable population who has more potential to receive the benefits. In younger cancer survivors aged 40 years old, COL5 might be economically feasible, while COL10 is usually recommended for the Korean general population aged 50 years old. Therefore, at least for cancer survivors, CRC screening should be covered by the Korean national health insurance scheme and screening methods using colonoscopy should be recommended as a primary screening strategy for CRC in this population.

Terminology

SPC: A SPC is a new primary cancer developing in a person with a history of cancer.

Peer review

The authors investigated the cost-effective strategy of CRC screening for cancer survivors in Korea. The article is well written and the contents are reliable.

REFERENCES

1 **National Cancer Institute**. Surveillance, epidemiology, and end results (SEER). Accessed online September 29, 2004. Available from: URL: http://www.seer.cancer.gov

2 **Living beyond cancer: finding a new balance: President's Cancer Panel 2003-2004 annual report.** Bethesda, Md.: President's Cancer Panel, National Cancer Institute, National Institutes of Health, U.S. Dept. of Health and Human Services, 2004

3 **Dong C**, Hemminki K. Second primary neoplasms in 633,964 cancer patients in Sweden, 1958-1996. *Int J Cancer* 2001; **93**: 155-161

4 **Dikshit RP**, Boffetta P, Bouchardy C, Merletti F, Crosignani P, Cuchi T, Ardanaz E, Brennan P. Risk factors for the development of second primary tumors among men after laryngeal and hypopharyngeal carcinoma. *Cancer* 2005; **103**: 2326-2333

5 **Park SM**, Lim MK, Jung KW, Shin SA, Yoo KY, Yun YH, Huh BY. Prediagnosis smoking, obesity, insulin resistance, and second primary cancer risk in male cancer survivors: National Health Insurance Corporation Study. *J Clin Oncol* 2007; **25**: 4835-4843

6 **Frazier AL**, Colditz GA, Fuchs CS, Kuntz KM. Cost-effectiveness of screening for colorectal cancer in the general population. *JAMA* 2000; **284**: 1954-1961

7 **Park SM**, Yun YH, Kwon S. Feasible economic strategies to improve screening compliance for colorectal cancer in Korea. *World J Gastroenterol* 2005; **11**: 1587-1593

8 **Shimbo T**, Glick HA, Eisenberg JM. Cost-effectiveness analysis of strategies for colorectal cancer screening in Japan. *Int J Technol Assess Health Care* 1994; **10**: 359-375

9 **Wagner JL**, Herdman RC, Wadhwa S. Cost effectiveness of colorectal cancer screening in the elderly. *Ann Intern Med* 1991; **115**: 807-817

10 **Smith RA**, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer, 2006. *CA Cancer J Clin* 2006; **56**: 11-25; quiz 49-50

11 **Ministry of Health and Welfare, Korea**. National cancer screening programmes guidelines, 2006. Seoul: Ministry of Health and Welfare; 2006

12 **U.S. Preventive Services Task Force, Colorectal cancer screening summary of recommendations (2002)**. Accessed November 29, 2004. Available from: URL: www.ahrq.gov/clinic/uspstf/uspscolo.htm

13 **Kavic SM**, Basson MD. Complications of endoscopy. *Am J Surg* 2001; **181**: 319-332

14 **Anderson ML**, Pasha TM, Leighton JA. Endoscopic perforation of the colon: lessons from a 10-year study. *Am J Gastroenterol* 2000; **95**: 3418-3422

15 **Winawer SJ**. Appropriate intervals for surveillance. *Gastrointest Endosc* 1999; **49**: S63-S66

16 **Ladabaum U**, Song K. Projected national impact of colorectal cancer screening on clinical and economic outcomes and health services demand. *Gastroenterology* 2005; **129**: 1151-1162

17 **Shin HR**, Won YJ, Jung KW, Kong HJ, Yim SH, Lee JK, Noh HI, Lee JK, Pisani P, Park JG, Ahn YO, Lee SY, Lee CW, Woo ZH, Lee TY, Choi JS, Yoo CI, Bae JM. Nationwide cancer incidence in Korea, 1999-2001; First result using the National Cancer Incidence Database. *Cancer Res Treat* 2005; **37**: 325-331

18 **Kim TS**, Kang YS, Jung SY, Cho HJ, Kim DS, Lee DH. Prospective evaluation of colorectal polyps in 1,683 consecutive colonoscopies. *Korean J Gastrointest Endosc* 1999; **19**: 887-896

19 **Choe JW**, Chang HS, Yang SK, Myung SJ, Byeon JS, Lee D, Song HK, Lee HJ, Chung EJ, Kim SY, Jung HY, Lee GH, Hong WS, Kim JH, Min YI. Screening colonoscopy in asymptomatic average-risk Koreans: analysis in relation to age and sex. *J Gastroenterol Hepatol* 2007; **22**: 1003-1008

20 **Annual Report on the Cause of Death Statistics (based on vital registration)**. National Statistical Office, Republic of Korea. Seoul, 2001

21 **Jung KW**, Yim SH, Kong HJ, Hwang SY, Won YJ, Lee JK, Shin HR. Cancer survival in Korea 1993-2002: a population-based study. *J Korean Med Sci* 2007; **22** Suppl: S5-S10

22 **Bae JM**, Won YJ, Jung KW, Suh KA, Yun YH, Shin MH, Ahn YO, Lee DH, Shin HR, Ahn DH, Oh DK, Park JG, 134 KCCR-affiliated Hospitals. Survival of Korean Cancer Patients Diagnosed in 1995. *Cancer Res Treat* 2002; **34**: 319-325

23 **Kim KH**, Lee YS, Lee BC. A Clinical Study on the Carcinoma of the Colon and Rectum. *J Korean Surg Soc* 1991; **41**: 215-222

24 **National Health Insurance Corporation**. 2002. 2001 Research on Clinical Practice Pattern of Cancer patient in National Health Insurance. Seoul: National Health Insurance Corporation (in Korea)

25 **National Health Insurance Corporation**. 2004. Contracting Medical Price in National Health Insurance Corporation. Seoul: National Health Insurance Corporation (in Korea)

26 **World Bank's Global Development Finance**. World Development Indicators 2007. Washington: World Bank, 2007

27 **Hunink M**, Glasziou P, Siegel J, Weeks J, Pliskin J, Elstein

A, Weinstein M. Decision-Making in Health and Medicine: Integrating Evidence and Values. New York: Cambridge University Press, 2001: 277-289
28 **Lieberman DA**, Weiss DG. One-time screening for colorectal cancer with combined fecal occult-blood testing and examination of the distal colon. *N Engl J Med* 2001; **345**: 555-560
29 **Khandker RK**, Dulski JD, Kilpatrick JB, Ellis RP, Mitchell JB, Baine WB. A decision model and cost-effectiveness analysis of colorectal cancer screening and surveillance guidelines for average-risk adults. *Int J Technol Assess Health Care* 2000; **16**: 799-810
30 **Ahlquist DA**. Occult blood screening. Obstacles to effectiveness. *Cancer* 1992; **70**: 1259-1265
31 **Rex DK**, Cutler CS, Lemmel GT, Rahmani EY, Clark DW, Helper DJ, Lehman GA, Mark DG. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology* 1997; **112**: 24-28
32 **Hixson LJ**, Fennerty MB, Sampliner RE, Garewal HS. Prospective blinded trial of the colonoscopic miss-rate of large colorectal polyps. *Gastrointest Endosc* 1991; **37**: 125-127
33 **Winawer SJ**, Stewart ET, Zauber AG, Bond JH, Ansel H, Waye JD, Hall D, Hamlin JA, Schapiro M, O'Brien MJ, Sternberg SS, Gottlieb LS. A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. National Polyp Study Work Group. *N Engl J Med* 2000; **342**: 1766-1772
34 **Glick S**, Wagner JL, Johnson CD. Cost-effectiveness of double-contrast barium enema in screening for colorectal cancer. *AJR Am J Roentgenol* 1998; **170**: 629-636
35 **Kim DH**, Shin MH, Ahn YO. Incidence pattern of colorectal cancer in Korea by subsite of origin. *J Korean Med Sci* 2000; **15**: 675-681
36 **Eide TJ**, Stalsberg H. Polyps of the large intestine in Northern Norway. *Cancer* 1978; **42**: 2839-2848
37 **Jackman RJ**, Mayo CW. The adenoma-carcinoma sequence in cancer of the colon. *Surg Gynecol Obstet* 1951; **93**: 327-330
38 **Spratt JS Jr**, Ackerman LV. Small primary adenocarcinomas of the colon and rectum. *JAMA* 1962; **179**: 337-346
39 **Stryker SJ**, Wolff BG, Culp CE, Libbe SD, Ilstrup DM, MacCarty RL. Natural history of untreated colonic polyps. *Gastroenterology* 1987; **93**: 1009-1013
40 **Muto T**, Bussey HJ, Morson BC. The evolution of cancer of the colon and rectum. *Cancer* 1975; **36**: 2251-2270
41 **Eddy DM**. Screening for colorectal cancer. *Ann Intern Med* 1990; **113**: 373-384
42 **Misra T**, Lalor E, Fedorak RN. Endoscopic perforation rates at a Canadian university teaching hospital. *Can J Gastroenterol* 2004; **18**: 221-226
43 **Eichler HG**, Kong SX, Gerth WC, Mavros P, Jonsson B. Use of cost-effectiveness analysis in health-care resource allocation decision-making: how are cost-effectiveness thresholds expected to emerge? *Value Health* 2004; **7**: 518-528
44 **WHO Commission on Macroeconomics and Health: Macroeconomics and health: investing in health for economic developmen**t. Report of the Commission on Macroeconomics and Health. Geneva: World Health Organization, 2001
45 **Desch CE**, Benson AB 3rd, Smith TJ, Flynn PJ, Krause C, Loprinzi CL, Minsky BD, Petrelli NJ, Pfister DG, Somerfield MR. Recommended colorectal cancer surveillance guidelines by the American Society of Clinical Oncology. *J Clin Oncol* 1999; **17**: 1312
46 **Cotton PB**, Durkalski VL, Pineau BC, Palesch YY, Mauldin PD, Hoffman B, Vining DJ, Small WC, Affronti J, Rex D, Kopecky KK, Ackerman S, Burdick JS, Brewington C, Turner MA, Zfass A, Wright AR, Iyer RB, Lynch P, Sivak MV, Butler H. Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. *JAMA* 2004; **291**: 1713-1719

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