Am. J. Trop. Med. Hyg., 97(3), 2017, pp. 888–895
doi:10.4269/ajtmh.17-0084

Identifying Helminth Infections via Routine Fecal Parasitological Examinations in Korea

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Abstract. We conducted this study to explore the extent of occult helminth infection identified by fecal parasitological examinations or organ-specific examinations such as colonoscopy and abdominal ultrasonography (US) during health checkups. We analyzed 197,422 fecal samples from 99,451 subjects who received health checkups at a single center over 10 years. We found that 3,472 (1.8%) samples from 3,342 (3.4%) subjects tested positive for parasitic ova, including clonorchiasis, metagonimiasis, trichuriasis, ascariasis, trichostrongylosis, taeniasis, and enterobiasis. The detection rate for clonorchiasis was higher in those who were taking their first examination than in those who had been examined previously. The detection rate for clonorchiasis decreased gradually over the 10 years. Only 2.5% of the patients with clonorchiasis showed US or computed tomography (CT) images that were compatible with the disease. Clonorchiasis patients who had abdominal US or CT images that suggested clonorchiasis were older and had lower body mass indices and higher eosinophil counts than did those whose US or CT images did not suggest the disease. We observed worms in 9% of the patients with trichuriasis who had received a colonoscopy. Colonoscopy also uncovered adult worms in 0.03% of subjects who were not identified as having *Trichuris trichiura* ova in their fecal helminth examinations. In summary, our study shows that occult helminth infection is fairly frequently identified by a variety of methods during health checkups, which suggests that doctors need to make greater effort to identify and treat occult helminth infections in Korea.

INTRODUCTION

Parasitic infection is an important public health issue with different clinical significance according to each country's public health status.[1] These infections are also an important clinical problem in Korea; clonorchiasis has been the most common helminth infection, although the overall helminth infection prevalence is low.[2] Clonorchiasis detection is important because the parasite usually has no symptoms but it is a biocarcinogen for cholangiocarcinoma, which suggests that detecting it may contribute not only to enhancing general public health but also to preventing cholangiocarcinoma.[3–5] However, data regarding specific parasitic screening recommendations, even for the carcinogenic clonorchiasis, are limited.

Health checkups provide a good opportunity to detect silent enteral parasitic infections because fecal examinations are routinely included and performed as an official screening method to detect colon cancer in Korea and other countries.[6,7] Fecal examinations are simple, noninvasive, and effective for detecting enteral parasites and fecal occult blood during health checkups,[5,8] and the screening is unlikely to bother patients because one fecal sample can be used to detect parasitic ova and occult blood simultaneously.

Abdominal ultrasonography (US) and colonoscopy are widely performed during liver and colon cancer screening, and these organ-specific examinations may also contribute to detecting enteral parasitic infection.[9,10] Clonorchiasis is reported to cause specific abdominal US or computed tomography (CT) findings of diffuse dilatation of the peripheral intrahepatic bile ducts without dilation of the larger bile ducts in the liver.[11–13] However, data about the performance of these images in detecting clonorchiasis are limited.[14] Adult worms may be detected during colonoscopy in trichuriasis patients.[9] However, we could find no data about actual detection rates for adult worms by colonoscopy among patients with trichuriasis.

We performed this study to explore two questions[1]: What is the magnitude of occult helminth infection identified by fecal parasitological examinations during health checkups? and[2] By which organ-specific examinations (abdominal US, CT, colonoscopy) are enteral parasites detected?

MATERIALS AND METHODS

Study subjects. Between October 2003 and October 2013, 99,451 patients (53,284 males and 46,167 females) received a fecal examination during their health checkups at the Seoul National University Hospital Healthcare System Gangnam Center in Seoul, Korea. Our subjects had high socioeconomic status such as high ranking post in companies or organizations in Korea and many of them lived in urban areas. We collected a total of 197,422 fecal samples from these patients and analyzed them for the presence of parasitic ova.

Methods. Each patient answered a questionnaire, underwent anthropometric assessment, and had laboratory tests and a radiologic study (abdominal US or CT) on the same day as the checkup. From the questionnaires, we collected data about age, gender, and residing area. Abdominal US was performed on everyone to evaluate liver, gall bladder, bile duct, pancreas, kidney, and spleen. Abdominal CT was performed in those whose abdominal US revealed any abnormal findings, which needed further evaluation by CT or whose sonic window was poor for evaluating intraabdominal organs adequately. Colonoscopy was performed on everyone above age 50, and on those who were fecal occult blood positive or had family history of colon cancer in their first-degree relatives even though their age was below 50. We calculated body mass index (BMI) by dividing the weight in kilograms by the square of the height in meters; the laboratory tests included white blood cell count and percentage of eosinophils. We collected blood samples from each patient before 10 AM after an overnight fast. We performed all biochemical analyses of

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the blood samples in the same quality-controlled laboratory according to standard laboratory methods. We calculated eosinophil count by multiplying the white blood cell count by the percentage of eosinophils, and we defined eosinophilia as > 500 eosinophils/uL.[15] Radiologists assessed all US and CT scans and considered images with uniformly and diffusely dilated peripheral intrahepatic bile ducts without dilatation of the large bile ducts and focal obstructing lesion to be compatible with clonorchiasis.[12] Colonoscopy was performed by board-certified gastroenterologists from the Seoul National University Hospital Healthcare System Gangnam Center.

Fecal collection and examination. Plastic containers were distributed with printed instructions for the procedure for fecal sample collection 7 days before the health examination date; the patients collected the samples early on the mornings of their examinations and submitted them on the same day. We examined the samples for parasite ova by the cellophane thick smear technique (the Kato-Katz method).[8]

Statistical analysis. The data are expressed as mean ± SD. We explored intergroup differences in the continuous variables using Student's *t* test, the Kruskal–Wallis test, or analysis of variance. We checked for intergroup differences in the frequency variables using the χ^2 test and checked the significance of trend changes over time using the Cochran–Armitage trend test. We used SAS 9.2 version (SAS Institute, Cary, NC) for the statistical analyses and considered a two-tailed *P* value less than 0.05 to be statistically significant.

Ethics statement. The study protocol was approved by the institutional review board of Seoul National University Hospital (IRB No. H-1508-113-696). The board waived informed consent because this was a retrospective study that did not harm any study subjects.

RESULTS

Baseline characteristics. Among the 197,422 fecal specimens, 3,472 (1.8%) were positive for parasitic ova. Trichuriasis was additionally diagnosed by colonoscopy in 11 subjects whose fecal helminth examination results were negative for *Trichuris trichiura* ova. Fifty patients had dual infections: 38 had both clonorchiasis and metagonimiasis, five had both metagonimiasis and trichuriasis, three had both clonorchiasis and trichuriasis, two had both ascariasis and clonorchiasis, one had both ascariasis and metagonimiasis, and one had both trichuriasis and trichostrongylosis. Ninety-one patients tested positive for the same ova more than two times in their fecal helminth examinations: 54 had clonorchiasis, 11 had metagonimiasis, 24 had trichuriasis, and two had ascariasis. That is, only 3,342 (3.4%) of the 99,451 subjects had parasitic infections. The baseline characteristics of the subjects with enteral parasitic infections are summarized in Table 1. Clonorchiasis was the most common infection, followed by metagonimiasis, trichuriasis, ascariasis, trichostrongylosis, taeniasis, and enterobiasis; ascariasis, trichostrongylosis, and enterobiasis were more common in females. Patients with trichuriasis who were residing in foreign countries were more likely to reside in Malaysia or Indonesia than were patients with clonorchiasis, metagonimiasis, or ascariasis.

TABLE 1
Baseline characteristics of the subjects with enteral parasitic infections detected by fecal examination or colonoscopy

	Clonorchiasis	Metagonimiasis	Trichuriasis	Ascariasis	Trichostrongylosis	Taeniasis	Enterobiasis
Number*	1454	948	842†	140	5	2	1
Repeated ova positive‡	54	11	24	2	0	0	0
Age, mean, (SD)	50.6 (9.7)	49.7 (10.1)	46.7 (10.7)	50.1 (10.7)	50.2 (10.0)	45.5 (2.1)	35
< 40	183	143	213	26	1	0	1
40–49	462	328	303	32	1	2	0
50–59	550	334	229	56	3	0	0
≤ 60	259	143	97	26	0	0	0
Male, *n* (%)	1081 (74.4)	647 (68.3)	479 (56.9)	67 (47.9)	3 (60.0)	1 (50.0)	0
BMI, mean, (SD)	24.3 (2.8)	24.0 (2.9)	23.6 (3.2)	23.1 (2.9)	24.5 (4.5)	25.6 (2.3)	17.7
Residential area							
Domestic	1444	938	824	133	5	2	1
Seoul and Gyeonggi-do	905	701	710	114	5	2	1
Gyeongsangnam-do	191	88	39	4	0	0	0
Gyeongsangbuk-do	180	52	25	6	0	0	0
Jeollanam-do	66	55	12	1	0	0	0
Jeollabuk-do	17	6	5	1	0	0	0
Chungcheongnam-do	43	17	26	5	0	0	0
Chungcheongbuk-do	27	5	5	0	0	0	0
Gangwon-do	7	11	2	2	0	0	0
Jeju-do	8	3	0	0	0	0	0
Foreign	10	10	18	7	0	0	0
United States	2	2	6	0	0	0	0
Malaysia and Indonesia	0	1	12	2	0	0	0
China	4	4	0	4	0	0	0
Russia	2	1	0	0	0	0	0
Greece	1	0	0	0	0	0	0
Egypt	1	0	0	1	0	0	0
Vietnam	0	1	0	0	0	0	0
United Kingdom	0	1	0	0	0	0	0

BMI = body mass index.
* 50 subjects had dual parasitic infections: 38 had both clonorchiasis and metagonimiasis; five had both metagonimiasis and trichuriasis; three had both clonorchiasis and trichuriasis; two had both ascariasis and clonorchiasis; one had both ascariasis and metagonimiasis; and one had both trichuriasis and trichostrongylosis.
† Trichuriasis was detected by fecal examination in 831 subjects and by colonoscopy in 11 subjects.
‡ 91 patients were positive for the same ova more than two times in their fecal helminth examinations: 54 had clonorchiasis, 11 had metagonimiasis, 24 had trichuriasis, and two had ascariasis.

Annual changes in the detection rate for each parasite. We explored the changes in the annual detection rates for each parasite according to whether the patient was receiving a first or a repeat examination. The clonorchiasis detection rate was significantly higher among initial examination takers, and this difference was maintained over the 10 years (Figure 1); the detection rate decreased significantly over the 10 years in both groups. However, we observed no steady decreases in the detection rates for metagonimiasis, trichuriasis, and ascariasis.

Highest mean eosinophil counts in subjects dually infected with clonorchiasis and metagonimiasis. Parasitic infection is one of the main causes of eosinophilia. We first examined whether the mean eosinophil counts in the patients with parasitic infection were higher than those in the patients without it, and the mean counts were significantly higher in patients with an infection (Figure 2). We decided to compare the mean eosinophil counts within subjects with enteral parasitic infection in detail as a next step; we compared the mean counts in the dually infected patients with those in patients with each corresponding single infection. The mean eosinophil counts in the patients with both clonorchiasis and metagonimiasis were higher than those in the patients with either one or the other, but we found no significant differences in the mean counts in other dually infected patients compared with the counts in patients with corresponding single infections. Then, we compared the mean eosinophil counts in patients without enteral parasitic infection with the counts in patients with clonorchiasis, metagonimiasis, trichuriasis, ascariasis, or dual clonorchiasis and metagonimiasis infection. The mean count in the patients who were dually infected with clonorchiasis and metagonimiasis was significantly higher than the counts for other parasitic infections (Figure 2).

Low detection rate for clonorchiasis by abdominal US or CT. Of the 1,454 total patients with clonorchiasis, 1,451 (99.8%) received abdominal US and/or CT, and only 2.5% of these had images that were compatible with clonorchiasis (Table 2); specifically, 1.5% of patients who received US and 3.4% of those who received CT had clonorchiasis-compatible images. BMI was lower in patients with images that suggested clonorchiasis than in those without them (Figure 3). Mean age was significantly higher in patients with US images that suggested clonorchiasis than in those without them, but age was not significantly different between the two groups (Figure 4). Eosinophil counts were higher in patients with images that suggested clonorchiasis than in those without them (Figure 5), and gender was not different between the two groups of patients (data not shown).

Only 0.3% of subjects had clonorchiasis-compatible images among 93,755 subjects who received US but who tested

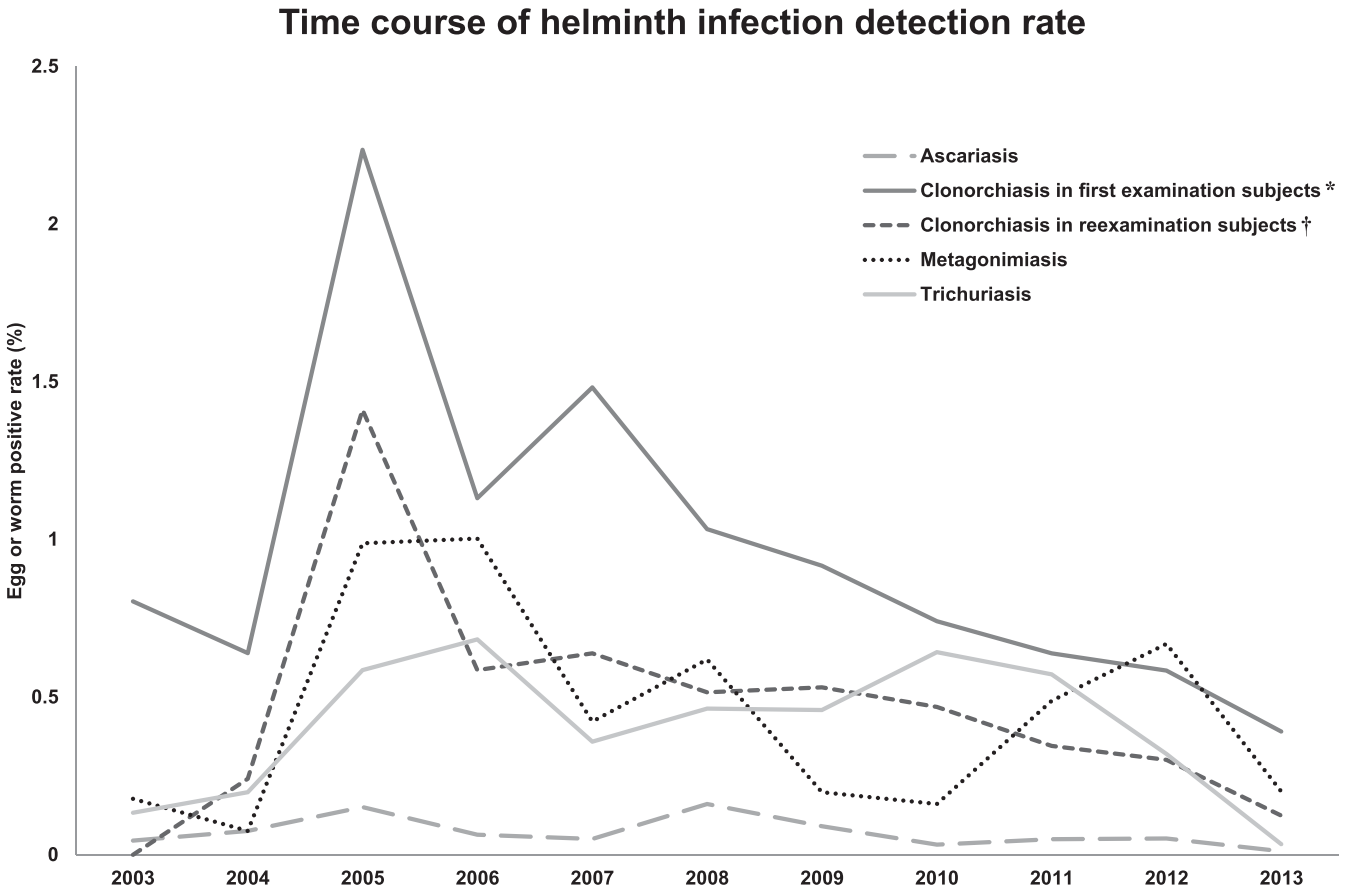

FIGURE 1. Time course of each helminth detection rate for 10 years. $P < 0.001$ analyzed by χ^2 test comparing the difference in the clonorchiasis detection rate between first-examination subjects and reexamination subjects. *Cochran–Armitage trend test Z statistic = 8.9, $P < 0.001$; Somers' D(R|C) value = –0.15 (95% confidence interval: –0.18 to –0.12), which means that the detection rate in the first-examination subjects decreased significantly over time. †Cochran–Armitage trend test Z statistic = 9.3, $P < 0.001$; Somers' D(R|C) value = –0.25 (95% confidence interval: –0.3 to –0.2), which means that the clonorchiasis detection rate in the and reexamination subjects.

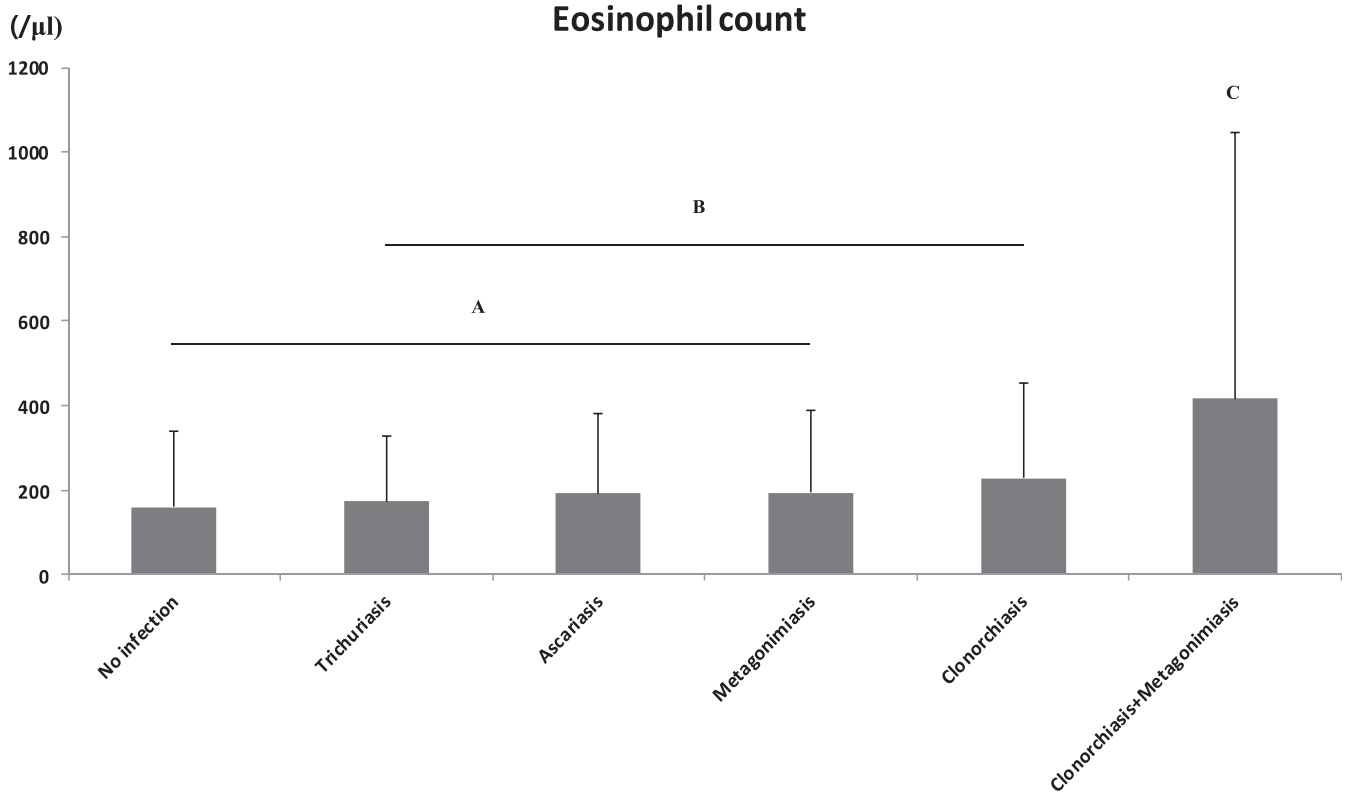

FIGURE 2. Comparison of the mean eosinophil counts in subjects with each enteral parasitic infection. Data are expressed as mean ± SD. Letters A, B, and C are groups with significantly different mean eosinophil counts analyzed by analysis of variance with Tukey's Studentized range test ($P < 0.001$).

negative for clonorchiasis in their fecal helminth examinations (Table 3).

Trichuriasis detection by colonoscopy. Colonoscopy was performed in 256 (30.4%) of the 842 patients with trichuriasis, and it detected adult worms in 9% of them (Table 4). Colonoscopy was also performed in 41,477 subjects who tested negative for trichuriasis in their fecal examinations, and adult trichuriasis worm was detected in 0.03% of them (Table 4).

DISCUSSION

Among the total health checkup subjects in our data, 3.4% had helminth infections, which suggests that helminth infection is not uncommon and that it might be necessary to identify occult helminth infection in Korean health-care recipients. Because people who receive health checkups are mostly healthy without any discomfort and the most common helminth infection was clonorchiasis in our data, fecal parasitological examinations during health checkups may provide valuable opportunities to identify and treat silent helminth infections in Korea. Technical developments enabled detailed examination of the liver by abdominal US or CT and of the colon by colonoscopy, and these examinations might also contribute to identifying occult helminth infections.[9,13,16] However, comparative data on the ability to detect enteral parasitic infection between fecal examinations and organ-specific examinations such as abdominal US, CT, and colonoscopy have been limited. We could try to compare the ability to detect enteral parasitic infection between fecal examinations and organ-specific examinations such as abdominal US, CT, and colonoscopy because we had data about abdominal US, CT, and colonoscopy, which were performed as a part of age-appropriate cancer screening. Our data showed that only 2.5% of patients with clonorchiasis who had received abdominal US and/or CT had images that suggested clonorchiasis, which suggests that CT and US may not replace fecal examinations for detecting clonorchiasis.[11,14] However, US and CT may contribute to detecting occult past clonorchiasis infection, and educating at-risk subjects not to eat raw

TABLE 2
Proportion of positive abdominal US or CT images that suggested clonorchiasis among clonorchiasis subjects

	US		CT		Total
Subjects (*n*)	1431		475		1451
	US only	US and CT		CT only	
	976	455		20	
Clonorchiasis compatible images (*n*)	16	5 (positive at US)	16 (positive at CT)	0	37
Detection rate, *n* (%)	21 (1.5)		16 (3.4)		37 (2.5)

US = ultrasonography; CT = computed tomography.

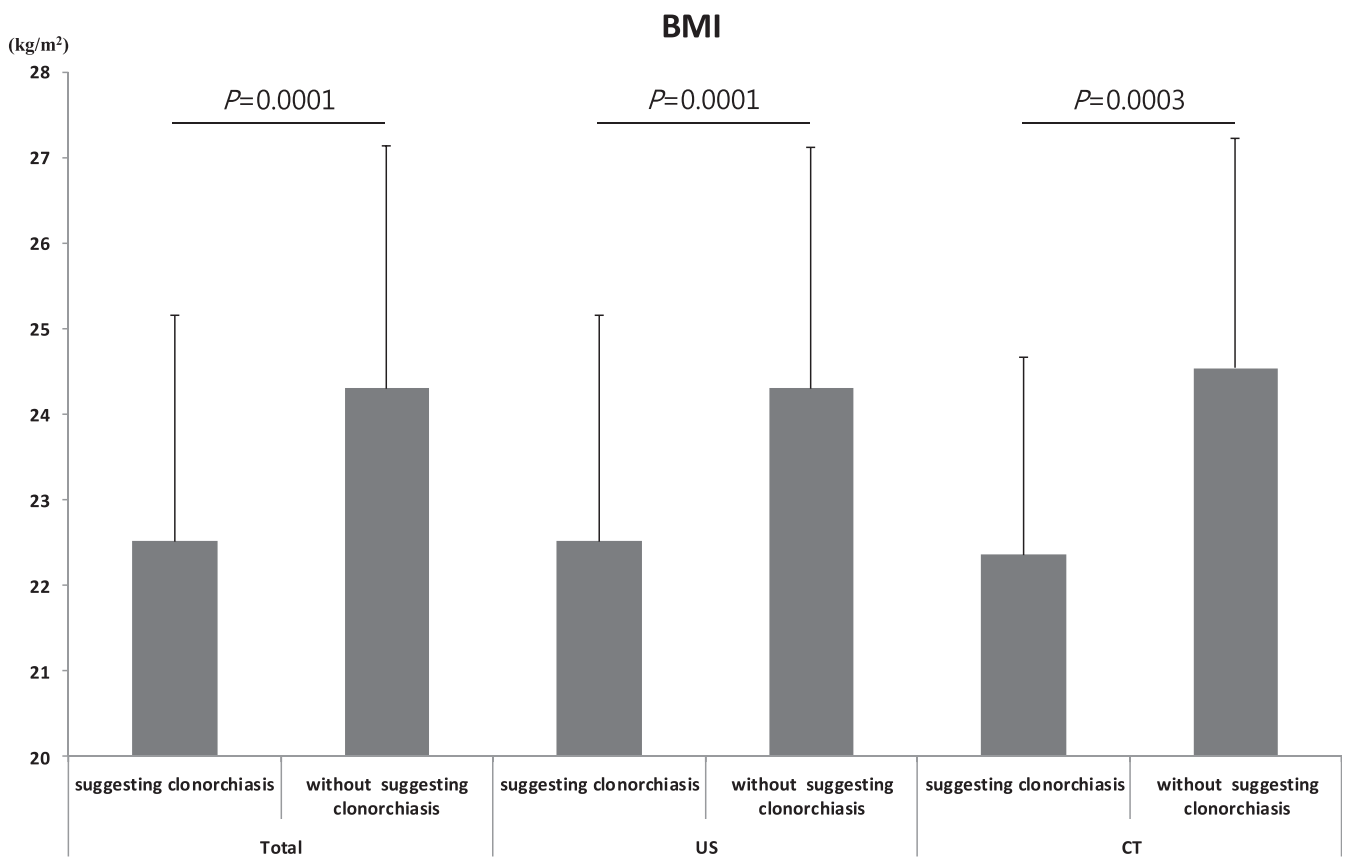

FIGURE 3. Mean body mass index (BMI) differences between subjects with and without images that suggested clonorchiasis analyzed by Student's *t* test. Data are expressed as mean ± SD.

freshwater fish; these examinations can also help prevent clonorchiasis reinfection considering that 0.3% subjects also had abdominal US images that suggested clonorchiasis. Our data showed that clonorchiasis patients who had abdominal US or CT images that suggested clonorchiasis were older and had lower BMIs and higher eosinophil counts than did those whose US or CT images did not suggest the disease. This suggests that longer infection time, clear liver background without fatty liver, and more severe immune reaction may be necessary for abdominal US or CT images to suggest clonorchiasis.[12] Colonoscopy uncovered adult worms in 9% of patients with trichuriasis, which suggests that colonoscopy can also identify occult trichuriasis even though fecal helminth examination is the main trichuriasis screening method. Our study may be the first analytic report of more than 200 trichuriasis patients to include both fecal examination and colonoscopy results from a single center.[9,17] Vigorous bowel preparation in patients with light infection may have washed out worms and caused the low trichuriasis detection rate by colonoscopy. Interestingly, colonoscopy also uncovered adult worms in 0.03% of subjects who were not identified as having *T. trichiura* ova in their fecal helminth examinations. This may be because the trichuriasis had no ova because the worms were male or did not produce ova, and colonoscopy may have strength for diagnosing trichuriasis in these situations.[17,18]

Our data showed that the rate of clonorchiasis detection in patients who were receiving their first examinations was significantly higher than that in other patients, and the annual detection rate for clonorchiasis decreased gradually over 10 years of health checkups. This decrease in the annual clonorchiasis detection rates might have been achieved by eradicating clonorchiasis with praziquantel and educating infected patients not to eat raw freshwater fish to prevent reinfection.[19] Education regarding avoiding eating raw freshwater fish and the increased risk of cholangiocarcinoma among patients with clonorchiasis also could have led to this lower detection rate among patients who were receiving repeat examinations, which also suggests the importance of fecal parasitological examinations for identifying occult helminth infection during health checkups. We observed no similar decreases in detection rates over time for other enteral parasitic infections.

The mean eosinophil count was highest in patients who were dually infected with clonorchiasis and metagonimiasis compared with patients with other parasitic infections or without an infection, as shown in Figure 2. We could find no previous data about synergistic effects on high eosinophil counts or eosinophilia by clonorchiasis or metagonimiasis; future studies might be needed to confirm a synergistic effect on eosinophilia by clonorchiasis or metagonimiasis or their mechanisms. We also confirmed that eosinophil counts were significantly higher in patients with a parasitic infection than in those without one.[20]

Knowledge about the infection source is important for eradicating helminth infection, especially under circumstances such as those in Korea where occult helminth infections are frequently detected; we found 91 patients who had

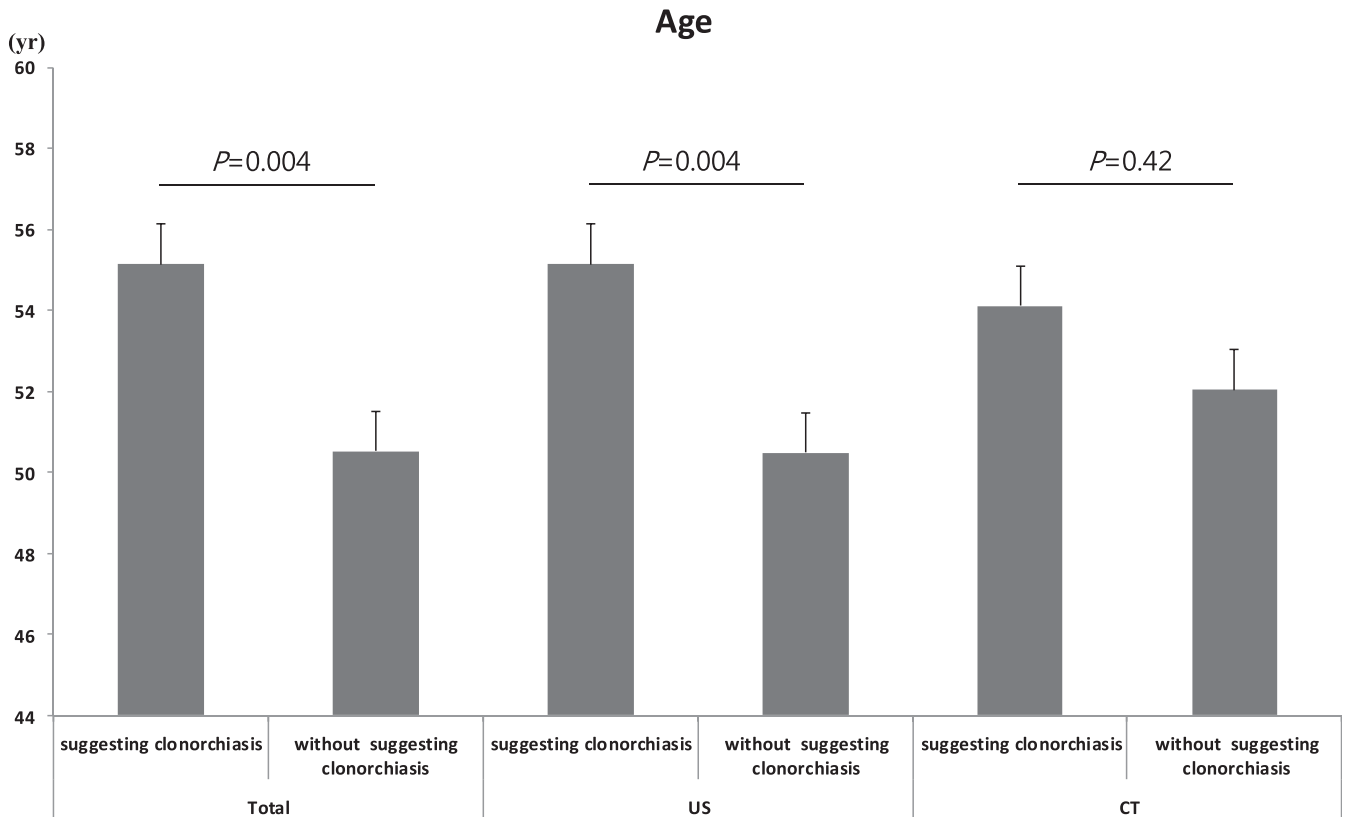

FIGURE 4. Mean age differences between subjects with and without images that suggested clonorchiasis analyzed by Student's *t* test. Data are expressed as mean ± SD.

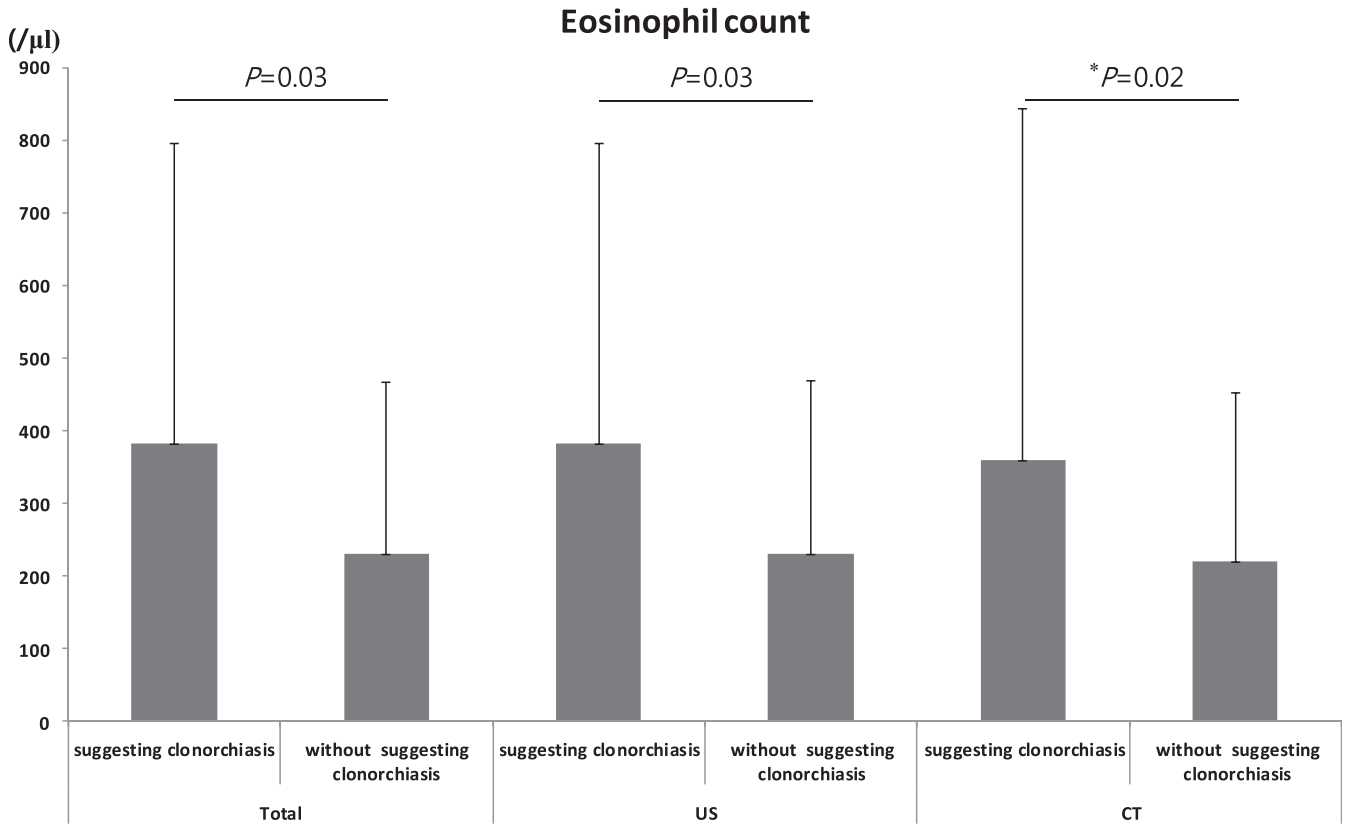

FIGURE 5. Mean eosinophil count differences between subjects with and without images that suggested clonorchiasis analyzed by Student's *t* test or *Kruskal–Wallis test. Data are expressed as mean ± SD.

TABLE 3

Proportion of positive abdominal US images that suggested clonorchiasis between subjects with and without *Clonorchis sinensis* ova on fecal helminth examination

	Clonorchiasis detected by fecal examination	No clonorchiasis detected by fecal examination
Subjects with abdominal US images suggesting clonorchiasis	21	264
Subjects without abdominal US images suggesting clonorchiasis	1,410	93,491
Proportion of subjects with abdominal US images suggesting clonorchiasis (%)	1.5	0.3

US = ultrasonography. $P < 0.001$ analyzed by χ^2 test.

tested positive more than twice for the same ova during their fecal helminth examinations. The two most common helminth infections in our data were clonorchiasis and metagonimiasis, and the most common coinfection was also by clonorchiasis and metagonimiasis. These results are because both clonorchiasis and metagonimiasis are trematodes, which are transmitted through freshwater fish.[21] Thus, educating patients with clonorchiasis not to eat raw freshwater fish is very important for preventing reinfection by both clonorchiasis and metagonimiasis. A recent study from Korea reported that the prevalence of clonorchiasis along five major rivers in Korea was as high as 8.4%, higher than the rates we found in this study or the findings from other studies, which suggests that educating people not to eat raw fish may be particularly necessary and more effective in areas where clonorchiasis is endemic.[22] Trichuriasis and ascariasis were the next-most common helminth infections in our data. Both of these are soil-transmitted helminth infections that are transmitted by ingesting eggs in contaminated vegetables or from unwashed hands after handling contaminated soils, and therefore food, personal hygiene, and sanitation are important for preventing these infections.[23,24] It is considered that soil-transmitted helminth infections have nearly disappeared in Korea.[25] However, in our data, the egg-positive rates of trichuriasis and ascariasis were 0.8% and 0.1%, respectively. These rates are slightly higher than those from the seventh national survey of the prevalence of intestinal parasitic infections performed in 2004 (0.3% and 0.05%, respectively).[2] These data were embarrassing because our study populations had relatively high socioeconomic status and good sanitation. We assumed three possible reasons for our results: first, more frequent business or leisure travel to areas where soil-transmitted helminth infections are endemic; second, ingesting helminth eggs by eating foods grown in egg-contaminated soil or grown using human feces as a fertilizer; and third, ingesting helminth eggs because hands were not washed after a person handled egg-contaminated soil. One clue to these assumptions was that patients with trichuriasis who lived in a foreign country were concentrated in Malaysia and Indonesia, which coincides with the fact that trichuriasis has been the most common enteral parasitic infection in these countries.[1] Education about hand washing and eating cleanly prepared foods may be necessary for subjects who travel frequently to or live in areas where soil-transmitted helminth infections are endemic.

We found one interesting case of enterobiasis identified by fecal examination. It is known that enterobiasis is difficult to find by fecal examination because female *Enterobius vermicularis* worms shed their eggs in the anal skin folds rather than excreting them in the colon; therefore, an adhesive tape test is recommended for detecting enterobiasis.[26]

Our study has the potential limitations related to retrograde studies, although the complete medical records might have helped to overcome them. There are also limits to generalizing our study results to the Korean population because our patients had high socioeconomic status and many of them lived in urban areas. However, large numbers of subjects may help to overcome this limitation.

In conclusion, our data showed that occult parasite infection is fairly frequently detected by a wide variety of methods during health checkups, which suggests that doctors need to make more efforts to identify and treat occult helminth infections in Korea.

TABLE 4

Comparison of the detection rate for adult worms by colonoscopy between subjects with and without *Trichuris trichiura* ova on fecal helminth examination

	Trichuriasis detected by fecal examination	No trichuriasis detected by fecal examination
Trichuriasis detected by colonoscopy	23	11
No trichuriasis detected by colonoscopy	233	41,466
Detection rate of adult trichuriasis worm (%)	9.0	0.03

$P < 0.001$ analyzed by χ^2 test.

Received February 6, 2017. Accepted for publication May 30, 2017.

Published online July 24, 2017.

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