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Review Article

Colorectal cancer and asbestos exposure—an overview

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Abstract: The relationship between colorectal cancer and asbestos exposure has not been fully clarified. This study aimed to determine the associations between asbestos exposure and colorectal cancer. We performed a meta-analysis to quantitatively evaluate this association. A fixed effects model was used to summarize the relative risks across studies. Sources of heterogeneity were explored through subgroup analyses and meta-regression. We analyzed the dose-effect relationship using lung cancer standardized mortality ratio (SMR) and the risk of mesothelioma as a percent (%) as exposure surrogates. A total of 47 cohort studies were included. We identified 28 incidence cohort studies from 17 separate papers and extracted colorectal cancer standardized incidence ratio (SIR). Cancer mortality data were extracted from 19 separate cohorts among 13 papers. The overall colorectal cancer SMR for synthesis cohort was 1.07 (95% CI 1.02–1.12). Statistically significant excesses were observed in exposure to mixed asbestos (SMR/SIR=1.07), exposure to production (SMR/SIR=1.11), among asbestos cement workers (SMR/SIR=1.18) and asbestos textile workers (SMR/SIR=1.11). Additionally, we determined that the SMR for lung cancer increased with increased exposure to asbestos, as did the risk for colorectal cancer. This study confirms that colorectal cancer has a positive weak associations with asbestos exposure.

Key words: Asbestos, Colorectal cancer, Standardized mortality ratio, Standardized incidence ratio, Meta-analysis

Introduction

"Asbestos" is a term used to characterise a number of natural mineral fibres of silica that can be categorised according to their structure in the serpentine-type fiber, namely chrysotile, and the amphibole-type fibres, which include crocidolite, amosite, anthophyllite, actinolite and tremolite[1)]. Asbestos is one of the most serious occupational carcinogens and causes approximately half of all occupational cancer deaths[2, 3)].

The IARC Monographs on asbestos concluded that all forms of asbestos are carcinogenic to humans (sufficient evidence in humans). These monographs concluded that asbestos causes mesothelioma and cancer of the lung, larynx and ovary (sufficient evidence in humans), and they note that there are positive associations that have been observed between asbestos and cancer of the pharynx, stomach and colorectum (limited evidence in humans)[4)]. In 1964, Selikoff found a three-fold increase in the risk of cancer of the stomach, colon, and rectum among insulation workers exposed to asbestos for 20 or more years[5)].

At present, some studies suggest that asbestos exposure can lead to an increased risk of gastric cancer[6–8)]. However, the relationship between asbestos exposure and colorectal cancer has not been fully clarified. According to the World Health Organization, cancer caused 8.8 million deaths worldwide in 2015, of which 774,000 people died from colorectal cancer[9)]. In addition to lung and liver cancer, colorectal cancer is the third most common type of cancer in the world.

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The studies about asbestos exposure and colorectal cancer are mainly cohort studies. Several studies suggest that asbestos exposure increases the risk of colorectal cancer or death[5, 10, 11]. At present, there is a lack of in-depth and systematic reporting that could contribute to correlation analyses of intensity, correlation quantitative analyses, studies of exposure-response and other aspects. In 1994, Homa *et al.* conducted the only meta-analysis on colorectal cancer and asbestos exposure[12]. Homa *et al.* noted that the exposure to amphibole asbestos may be associated with colorectal cancer. The results also suggest that serpentine asbestos is not associated with colorectal cancer. In 2008, Gamble weighed the evidence to assess the validity of the hypothesis that asbestos exposure causes stomach, colon or rectal cancer[13]. This hypothesis was based on three criteria, the strength of association, the biological gradient, and the consistency. This researcher observed no consistent exposure-response (E-R) trends, and the strength of the associations were consistently weak for the four types of gastrointestinal cancers. Gamble used the lung cancer SMR as exposure surrogates to show that the colorectal cancer SMR was 0.97 (95% CI 0.89–1.05)[13].

The relationship between colorectal cancer and asbestos exposure was not yet confirmed, and there was a need for a larger cohort study. Considering the limitations of any single study, we therefore aimed to review the epidemiology studies that have reported the association of asbestos exposure with colorectal cancer incidence or mortality and perform a meta-analysis of those studies to quantitatively evaluate whether exposure to asbestos could cause colorectal cancer risk.

Although Homa *et al*'s study has reported a meta-analysis on the association between asbestos exposure and colorectal cancer, there were still some deficiencies in his research[12]. In Homa *et al*'s study, the research literatures were published before 1990 and the literatures were limited (only 16). Only mortality was used as the outcome and subgroups were limited. In view of the above deficiencies, this paper therefore conducted a meta-analysis on the risk between asbestos exposure and colorectal cancer. In this paper, data on mortality/incidence as outcome were extracted for 47 cohorts from 30 separate papers. Additionally, this paper added subgroups including cohort size, follow-up period, exposure way, occupation and gender.

Subjects and Methods

Literature search

Studies were identified by searching PubMed, Ovid, Cochrane library and other foreign language databases. Additionally, the China National Knowledge Internet database, VIP database and Wan Fang database were searched. All literature was retrieved prior to July 2017. The retrieval type is defined as colorectal cancer or colon cancer or rectal cancer or gastrointestinal cancers or intestinal cancer or digestive cancers and asbestos and cohort studies. The search terms for the Chinese databases were tumor, asbestos, and cohort.

Selection of studies and inclusion criteria

The inclusion criteria for the literature that was selected for analysis are as follows: asbestos as a clear exposure factor; standardized mortality ratio (SMR), standardized incidence ratio (SIR) and hazard ratio (HR) record is included; research method is a cohort study. If the outcome under study is rare in all populations and subgroups under review, one can generally ignore the distinctions among the various measures of relative risk[14]. Because colorectal cancer is a rare disease in all population, the distinctions between the colorectal cancer SMR and the colorectal cancer SIR can be ignored.

The exclusion criteria of the literature are as follows: repeated articles or data; animal experiment data; review of records that were not original; incomplete data information; as some papers on the same cohort study were published several times, only the newest or most informative single article was included.

The selection of the literature was performed independently by two evaluators. After the repeated literature was excluded, the summaries and the full texts were read, and the references were included. This step was followed by applying the exclusion criteria. Only the literature that met the criteria were selected. If there were different opinions, the dispute was resolved through consultation or by a third evaluator.

Literature quality evaluation and data extraction

Two evaluators independently evaluated the quality of the literature through the Newcastle-Ottawa Scale (NOS), a literature quality evaluation scale. The two evaluators independently extracted the relevant data. Disagreements were resolved by consultation. For each study, we extracted the following data (when the information was available): first author, publication year, country, geographical area, occupation, asbestos exposure way, asbestos type, gender, period of employment, follow-up period, beginning follow-up year, cohort-size, person-years, colorectal cancer SMR/SIR, lung cancer SMR and the risk of mesothelioma.

Statistical analysis

The fixed effects model was used to assess the heterogeneity of each cohorts SMR or SIR and its 95% confidence interval. For papers that did not list the SMR/SIR confidence interval value, the confidence interval was calculated using the simple calculation method of the SMR confidence interval[15]. We conducted a subgroup analysis on gender, occupation, asbestos exposure way, follow-up period, cohort-size, lung cancer SMR, asbestos type and effects index. We also used meta-regression to identify other influential factors in asbestos carcinogenesis to generate a sensitivity analysis. We used Begg's funnel plot and the Egger's test to make a deviation evaluation. Moreover, the p value of each inspection level is set to 0.05. We analyzed the dose-effect relationship using lung cancer SMR and the risk of mesothelioma as a percent (%) as exposure surrogates. The dose-effect assessment of the risk of asbestos and colorectal cancer was performed by subgroups as the asbestos type and the follow-up period.

Results

Characteristics of eligible studies

The results of the literature search are as follows. We used software for data consolidation and removal of duplicate literature to retrieve 1,036 references. We finally identified 30 references and 47 cohorts for inclusion (Tables 1, 2).

Mortality and incidence were the outcome in the cohort studies reviewed. Data on mortality were extracted for 19 cohorts from 13 separate papers, and data on incidence were extracted for 28 separate cohorts from 17 papers. The earliest beginning follow-up year of cohorts was in 1910 and the latest one was in 1993. Cohorts ranged in follow-

Table 1. Characteristics of studies included in the meta-analysis

Study characteristics	Incidence cohorts		Mortality cohorts	
	No. of studies	%	No. of studies	%
Area				
Oceania	1	4	0	0
America	0	0	11	58
Europe	27	96	8	42
Occupation				
Workers involved in welding and insulation	8	28	6	32
Asbestos cement worker	5	18	3	16
Asbestos textile worker	10	36	7	37
Miners and millers	4	14	1	5
Others	1	4	2	10
Asbestos type				
Amphibole	4	14	2	10
Mixed	21	75	15	79
Serpentine	3	11	2	11
Gender				
Female + male	6	21	4	21
Female	5	18	3	16
Male	17	61	12	63
Beginning follow-up year				
Before 1949	2	7	11	58
From 1950 to 1969	12	43	7	37
After 1970	14	50	1	5
Follow-up period				
<35	17	61	4	21
≥35	11	39	15	79
Cohort size				
<1,000	10	36	4	21
1,000–1,500	2	7	3	16
>1,500	16	57	12	63

Table 2. Detailed information list of 47 included cohorts

First author	Publication year	Country	Occupation	Asbestos type	Gender	Period of employment	Follow-up period	Cohort size	SMR/SIR
McDonald JC	1980	Canada	Miners and millers	Serpentine	Male	1891–1920	1910–1975	10,939	SMR
Ohlson CG	1984	Sweden	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1939–1980	1951–1980	3,297	SMR
Hodgson JT	1986	UK	Asbestos textile worker	Mixed	Male	Before 1969	1969–1981	31,150	SMR
Kjuus H	1986	Norway	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1953–1970	1953–1983	790	SIR
Seidman H	1986	USA	Repair welding and insulation materials for shipbuilding, railway and workshop	Amphibole	Male	1941–1945	1945–1982	820	SMR
Enterline PE	1987	USA	Asbestos textile worker	Mixed	Male	1941–1967	1941–1980	1,074	SMR
Hughes JM	1987	USA	Asbestos cement worker	Mixed	Male	1937–1970	1937–1982	6,931	SMR
Hughes JM	1987	USA	Asbestos cement worker	Serpentine	Male	1937–1970	1937–1982	2,565	SMR
Hughes JM	1987	USA	Asbestos cement worker	Mixed	Male	1937–1970	1937–1982	4,366	SMR
Tola S	1988	Finland	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1945–1960	1953–1981	7,775	SIR
Tola S	1988	Finland	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1945–1960	1953–1981	4,918	SIR
Raffn E	1989	Denmark	Asbestos cement worker	Mixed	Male	1928–1984	1943–1984	7,996	SIR
Danielsen TE	1993	Norway	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1940–1979	1940–1990	4,571	SIR
Magnani C	1993	Italy	Others	Mixed	Female	1950–1986	1965–1988	1,964	SMR
Koivisto PN	1994	Finland	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	Since the beginning of 1967	1953–1991	8,391	SIR
Meurman LO	1994	Finland	Miners and millers	Amphibole	Male	1953–1967	1953–1991	736	SIR
Meurman LO	1994	Finland	Miners and millers	Amphibole	Female	1953–1967	1953–1991	167	SIR
Meurman LO	1994	Finland	Miners and millers	Amphibole	Female + male	1953–1967	1953–1991	903	SIR
Jeffrey LL	1998	USA	Asbestos textile worker	Amphibole	Female + male	1954–1972	1954–1993	1,130	SMR
Berry G	2000	UK	Asbestos textile worker	Mixed	Female + male	1933–1964	1933–1980	5,100	SMR
Ulvestad B	2002	Norway	Asbestos cement worker	Mixed	Male	1942–1976	1953–1999	541	SIR
Koskinen K	2003	Finland	Asbestos textile worker	Mixed	Female + male	1950s–1992	1991–1998	24,215	SIR
Koskinen K	2003	Finland	Asbestos textile worker	Mixed	Male	1950s–1992	1991–1998	23,285	SIR
Koskinen K	2003	Finland	Asbestos textile worker	Mixed	Female	1950s–1992	1991–1998	930	SIR
Finkelstein MM	2004	Canada	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	From 1949	1949–1999	25,285	SMR
Reid A	2004	Australia	Miners and millers	Amphibole	Male	1943–1966	1979–2000	5,685	SIR
Smailyte G	2004	Lithuania	Asbestos cement worker	Serpentine	Female + male	1956–1978	1978–2000	1,887	SIR
Smailyte G	2004	Lithuania	Asbestos cement worker	Serpentine	Male	1956–1978	1978–2000	1,285	SIR
Smailyte G	2004	Lithuania	Asbestos cement worker	Serpentine	Female	1956–1978	1978–2000	602	SIR

Table 2. Continued

First author	Publication year	Country	Occupation	Asbestos type	Gender	Period of employment	Follow-up period	Cohort size	SMR/SIR
Ulvestad B	2004	Norway	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1930–1975	1953–1999	1,116	SIR
Kjærheim K	2005	Norway	others	Mixed	Male	1917–1967	1960–2002	726	SIR
Krstev S	2006	USA	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Female + male	1950–1964	1950–2001	4,702	SMR
Krstev S	2006	USA	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1950–1964	1950–2001	4,413	SMR
Krstev S	2006	USA	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Female	1950–1964	1950–2001	289	SMR
Clin B	2009	France	Asbestos textile worker	Mixed	Male	before 1978	1978–2004	1,604	SIR
Clin B	2009	France	Asbestos textile worker	Mixed	Female	before 1978	1978–2004	420	SIR
Clin B	2009	France	Asbestos textile worker	Mixed	Female + male	before 1978	1978–2004	2,024	SIR
Pesch B	2010	Germany	Others	Mixed	Male	1993–1997	1993–2007	576	SMR
Strand LA	2010	Norway	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1950–1987	1953–2007	28,345	SIR
Benedicte C	2011	France	Asbestos textile worker	Mixed	Female + male	1928–1978	1978–2004	2,024	SIR
Hogstedt C	2013	Sweden	Repair welding and insulation materials for shipbuilding, railway and workshop	Mixed	Male	1918–2006	1958–2006	6,320	SIR
Boulanger M	2015	France	Asbestos textile worker	Mixed	Female + male	1960–2009	1978–2009	2,024	SIR
Boulanger M	2015	France	Asbestos textile worker	Mixed	Male	1960–2009	1978–2009	1,605	SIR
Boulanger M	2015	France	Asbestos textile worker	Mixed	Female	1960–2009	1978–2009	419	SIR
Pira E	2016	Italy	Asbestos textile worker	Mixed	Female + male	1946–1984	1946–2013	1,977	SMR
Pira E	2016	Italy	Asbestos textile worker	Mixed	Female	1946–1984	1946–2013	1,083	SMR
Pira E	2016	Italy	Asbestos textile worker	Mixed	Male	1946–1984	1946–2013	894	SMR

SMR: standardized mortality ratio; SIR: standard incidence ratio.

up period between 7 and 67 yr. The number of subjects involved in these studies ranged from 167 to 31,150 persons.

Incidence cohorts studies ranged in size between 167 and 28,345 workers. In this paper, there were 12 incidence cohorts studies in which lung cancer SMR was less than or equal to 2, 7 incidence cohorts studies in which lung cancer SMR was greater than 2, and 9 studies in which lung cancer SMR was not mentioned. The largest overall cohort SIR was among asbestos miners with an SIR of 2.61 (95% CI 0.71–6.68)[16].

Mortality cohort studies ranged from 289 to 31,150 workers. In this paper, there were 12 mortality cohort studies with a lung cancer SMR less than or equal to 2 and 7 mortality cohort studies with a lung cancer SMR greater than 2. The largest overall cohort SMR for colorectal cancer was among asbestos workers involved in repair welding and insulation materials for shipbuilding, railway and workshop with an SMR of 1.85 (95% CI 1.16–2.80)[10].

Quantitative data synthesis and subgroup analysis

As shown in Fig. 1, summarizing the evidence from these 47 studies, the combined SMR/SIR was 1.07 (95% CI 1.02–1.12).

Based on the basic characteristics of the study cohorts, the associations between asbestos exposure and colorectal cancer in different subgroups were evaluated. SMR/SIR in most subgroups ranged from 1 to 1.5, which meant a low-level association between asbestos exposure and colorectal cancer, as shown in Fig. 2. When used lung cancer SMR as an exposure intensity surrogate, we found SMR of colorectal cancer was statistically significant (SMR=1.32, $p<0.05$) in the subgroup of high lung cancer SMR; For the occupations, the SMR was statistically significant in the subgroup of asbestos textile workers (SMR=1.11, $p<0.05$) and asbestos cement workers (SMR=1.18, $p<0.05$); For the exposure way, the SMR was statistically significant (SMR=1.11, $p<0.05$) in the subgroup of asbestos production workers; For the asbestos types, the SMR of exposure to amphibole asbestos and mixed asbestos were beyond 1, but the SMR of amphibole asbestos was not statistically significant (SMR=1.18, $p>0.05$), while serpentine asbestos exposure was slightly lower than 1, but not statistically significant.

Meta-regression analysis

The results of meta-regression analysis suggested that lung cancer SMR and cohort size were the significant source of heterogeneity (Table 3).

Sensitivity analysis

Single heterogeneity was not directly found in sensitivity analysis.

Evaluation of publication bias

The center point of the Begg' funnel plot is distributed in the funnel and when subjected to the Egger's test $p>0.05$. Therefore, it can be considered that the publication bias is small in the literature (Fig. 3).

Dose-effect assessment

According to asbestos type and the follow-up period of the subgroup, this paper determined the dose-effect assessment of the risk of asbestos and colorectal cancer.

Lung cancer SMR was used as an exposure surrogate. When lung cancer SMR is less than 2.88, the trend of the colorectal cancer SMR is 1. When lung cancer SMR is greater than 2.88, indicating a strong association, the colorectal cancer SMR showed a gentle increasing trend (trend for 2). The results show that the risk of colorectal cancer increased gently with higher accumulation. When the risk of mesothelioma, represented as a percent (%), was used as an exposure surrogate, no dose-effect trend was observed (Fig. 4).

Lung cancer SMR was used as a surrogate for exposure with the subgroup of asbestos type. When the asbestos type was amphibole asbestos, the colorectal cancer SMR of two of the five cohorts was less than 1. The colorectal cancer SMR of three of the five cohorts were greater than 1.5. This finding indicated a weak correlation between amphibole asbestos and the incidence of colorectal cancer; however, the trend towards a correlation was not observable. When the asbestos type was mixed asbestos, when the lung cancer SMR is less than 2.71, the trend of the colorectal cancer SMR is 1. When the lung cancer SMR is greater than 2.71 (close to a strong correlation), the colorectal cancer SMR showed a gentle increase (trend for 2). The results show that the risk of colorectal cancer increased gently with higher accumulation.

When compared two subgroups by cohorts follow-up period, we found that the colorectal cancer SMR was around 1 and didn't change as the increase of lung cancer SMR in cohorts with period less than 35 yr. While in cohorts with 35 yr or more follow-up period, when the lung cancer SMR was greater than 2.88 (close to a strong correlation), the colorectal cancer SMR showed a gentle increase. The results supported that the risk of colorectal cancer increased gently with higher asbestos accumulation.

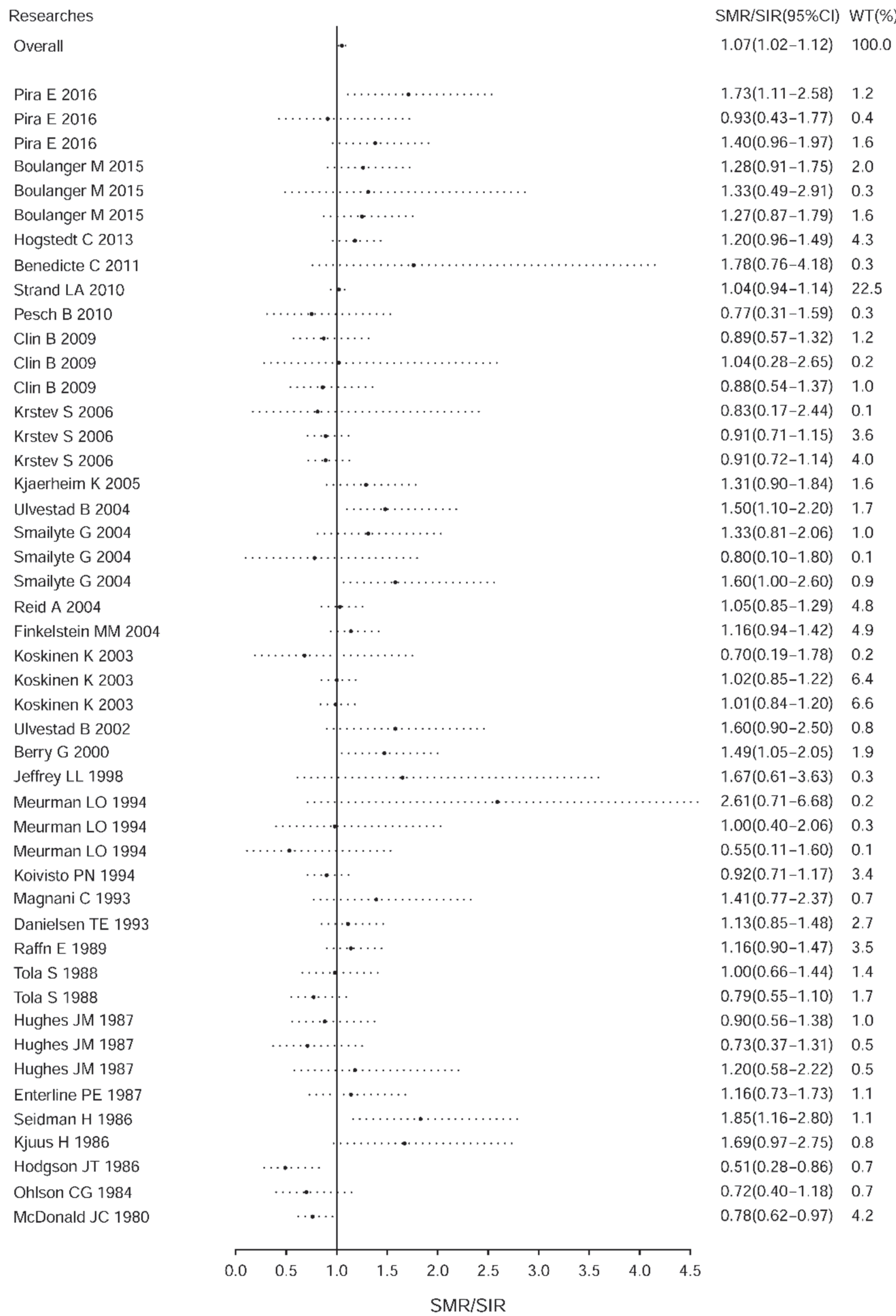

Fig. 1. Forest plot of colorectal cancer risk associated with asbestos exposure.

Comparison of the relationship between asbestos exposure and colorectal cancer and gastric cancer

Based on this cohort study, we compared the relationship between asbestos exposure and colorectal cancer and gastric cancer. The results showed that the correlation between asbestos exposure and colorectal cancer was statistically significant (SMR/SIR 1.07; 95% CI, 1.02, 1.12). The results also showed the correlation between asbestos

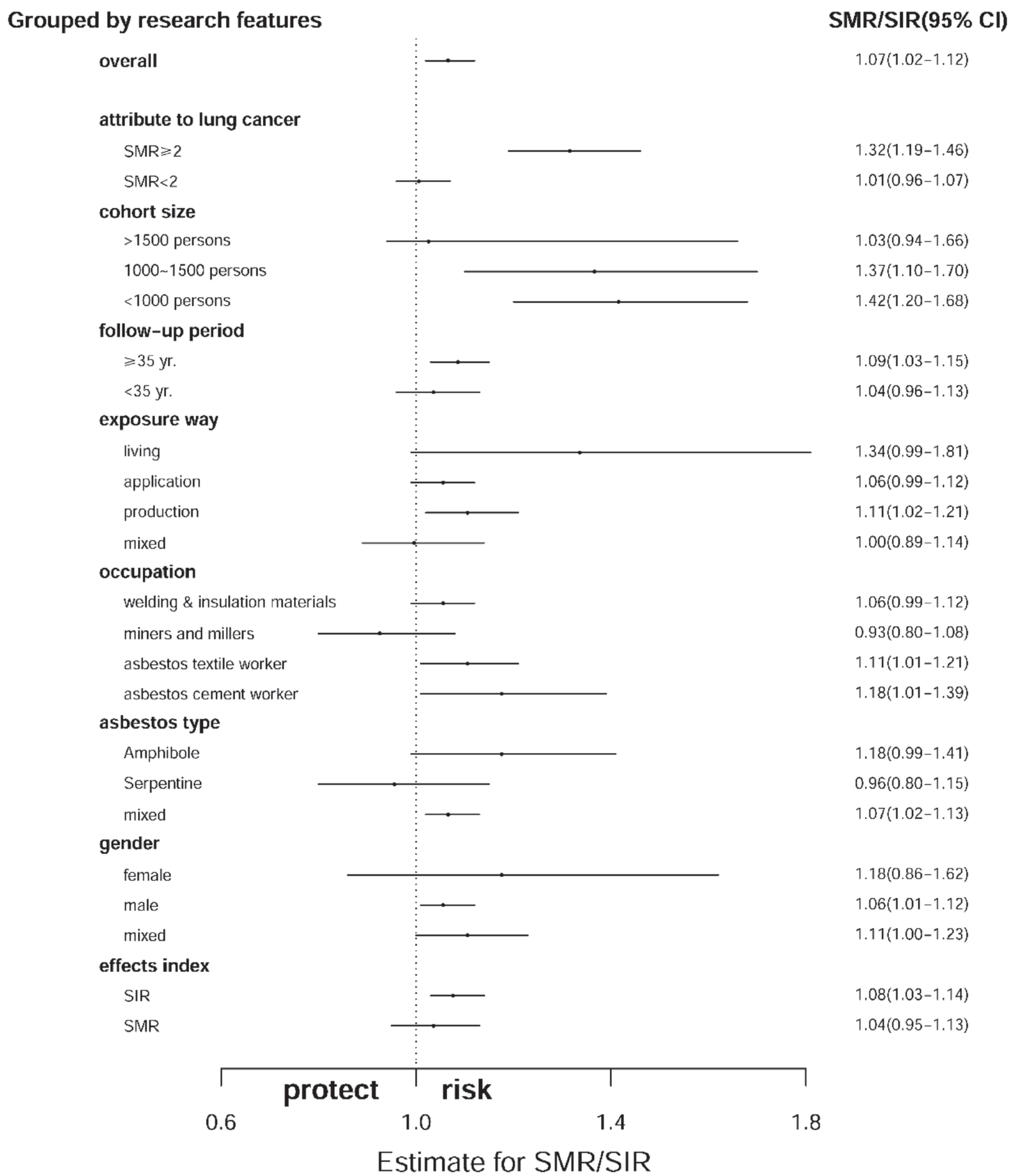

Fig. 2. Pooled results of colorectal cancer with asbestos exposure by study characteristics.

exposure and gastric cancer was not statistically significant (SMR/SIR 1.04; 95% CI, 0.98, 1.10). According to the subgroup analysis, excess mortality of colorectal cancer and gastric cancer have been observed in some subgroups. The correlation between asbestos exposure and colorectal cancer is relatively clear. The attribute to lung cancer (SMR≥2) subgroup, the follow-up period (≥35) subgroup, and the exposure to production subgroup all showed statistically significant difference (Table 4).

Discussion

In this paper, a meta-analysis was performed to quantitatively measure the relationship between asbestos exposure and colorectal cancer risk in 30 publications. The results showed that the risk of colorectal cancer in people exposed to asbestos is 1.07 times greater than that of the general population.

According to the subgroups of gender, this paper determined the relative risks among genders: male (SMR/

Table 3. Meta-regression analysis to explore potential sources of heterogeneity

Variable	Coefficient	p	t	I^2_{res}	Adj R^2 (%)
Lung cancer SMR	0.27	0	4.14	15.2	93.5
Cohort size	−0.17	0	−3.59	19.8	81.6
SMR/SIR	−0.06	0.46	−0.74	37.3	−7.59
Gender	0.04	0.42	0.82	37.4	10.7
Geographical area	0.09	0.25	1.16	35.8	4.1
Occupation	−0.02	0.52	−0.66	37.1	−3.43
Exposure	−0.03	0.4	−0.85	36.9	−6.67
Asbestos type	−0.01	0.88	−0.15	37.6	−12.6
Follow-up period	0.07	0.34	0.97	37.4	−9.73
Publication year	0.12	0.13	1.56	35.2	8.18
Beginning follow-up year	−0.03	0.53	−0.63	37.3	6.76

SMR: standardized mortality ratio; SIR: standard incidence ratio.

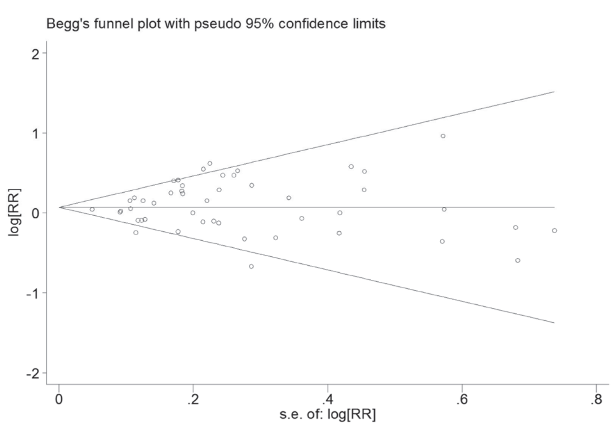

Fig. 3. Begg's funnel plot of colorectal cancer risk associated with asbestos exposure.

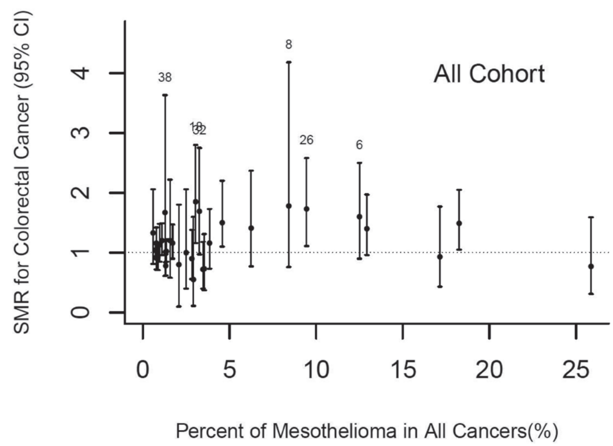

Fig. 4. Risk of colorectal cancer stratified by risk of mesothelioma in asbestos-exposed cohorts.

Table 4. Comparison of SMR/SIR between gastric cancer and colorectal cancer

Pooled groups	Gastric cancer		Colorectal cancer	
	SMR/SIR	95%CI	SMR/SIR	95%CI
Overall	1.04	0.98–1.10	1.07	1.02–1.12
Exposure way				
Production	1.22*	1.11–1.34	1.11*	1.02–1.21
Application	0.88*	0.80–0.96	1.06	0.99–1.12
Living	1.41	0.95–2.10	1.34	0.99–1.81
Mixed	1.14	0.93–1.41	1	0.89–1.14
Asbestos type				
Serpentine	1.20*	1.03–1.40	0.96	0.80–1.15
Amphibole	0.99	0.92–1.06	1.18	0.99–1.41
Mixed	1.37*	1.05–1.78	1.07*	1.02–1.13
Follow-up period				
<35	1.11*	1.03–1.20	1.04	0.96–1.13
≥35	0.92	0.83–1.02	1.09*	1.03–1.15
Attribute to lung cancer				
SMR <2	0.98	0.92–1.06	1.01	0.96–1.07
SMR ≥2	1.32*	1.13–1.54	1.32*	1.19–1.46

SMR: standardized mortality ratio; SIR: standard incidence ratio. *p<0.05.

SIR=1.06) and female (SMR/SIR=1.18). This indicated that there was a weak correlation between asbestos exposure and the risk of colorectal cancer in males. Wan noted that there were more males with colorectal cancer than females. However, the trend is that the risk increased faster in females, especially for colon cancer, compared to males. In developed countries, there are equal or more females with colon cancer than males, whereas males tend to be more frequently diagnosed with rectal cancer[17)].

According to subgroups of asbestos type, this paper indicated the relative risks for serpentine asbestos (SMR/SIR=0.96), amphibole asbestos (SMR/SIR=1.18), and mixed asbestos (SMR/SIR=1.07). This paper indicates that there is no correlation between serpentine asbestos and colorectal cancer risk. Mixed asbestos were weakly correlated with colorectal cancer risk. Wang conducted a 37 yr prospective cohort study on the workers of the chrysotile textile factory and did not find any correlation between the chrysotile and digestive tract cancer risk[18)]. Wang's study conducted a 26 yr follow-up of the chrysotile miners and found that the chrysotile may lead to digestive tract cancer of chrysotile miners with smoking habits[19)]. Loomis *et al.* and Berry also found that chrysotile exposure was not associated with colorectal cancer risk[20, 21)]. Du *et al.* found that chrysotile miners had a high incidence of liver cancer and lung cancer, as well as other cancers, such as stomach cancer and colon cancer; however, compared with control groups, there were no statistically significant differences[22)]. Li *et al.* performed a meta-analysis of cancer mortality among workers exposed to asbestos chrysotile[23)]. His study suggested that there was a correlation between pure chrysotile exposure and gastric cancer risk. Other meta-SMR of digestive system tumors did not significantly increase. That point of view is consistent with the research in this paper.

According to the subgroups of occupation, this paper indicates the following relative risks: asbestos cement workers (SMR/SIR=1.18), asbestos textile workers (SMR/SIR=1.11), asbestos miners and millers (SMR/SIR=0.93), repair welding and insulation materials for shipbuilding, railway and workshop (SMR/SIR=1.06). This finding suggested that occupations including asbestos cement workers and asbestos textile workers have a weak correlation with colorectal cancer risk.

According to the subgroups of exposure way, this paper indicates the following relative risks: exposure to production (SMR/SIR=1.11), exposure to application (SMR/SIR=1.06), exposure to living (SMR/SIR=1.34), and mixing exposed sources (SMR/SIR=1.00). This paper indicated that exposure to production has weak correlation with colorectal cancer risk. It should be noted that the third group has only 2 cases of life pollution and the data should be used cautiously. This suggests that asbestos exposure to production have a weak correlation with colorectal cancer risk.

According to the subgroups of the follow-up period, this paper indicates the following relative risks: the follow-up period less than 35 yr (SMR/SIR=1.04) and the follow-up period greater than or equal to 35 yr (SMR/SIR=1.09). This paper indicated asbestos exposure has a weak correlation with risk of cancer in cohorts greater than or equal to 35 yr. This finding showed that there was an association with risk of cancer with exposure to a higher cumulative dose.

Lung cancer SMR was used as a substitute for the exposure measurements because of the clear relationship between asbestos exposure and lung cancer[24)]. According to the subgroups of lung cancer SMR, this paper indicated the following relative risks: for lung cancer SMR less than 2 (colorectal cancer SMR/SIR=1.01) and for lung cancer SMR greater than or equal to 2 (colorectal cancer SMR/SIR=1.32). The lung cancer SMR difference was statistically significant within the two groups. This finding suggested that when the lung cancer SMR increases, that is, the increase in exposure to asbestos, the colorectal cancer risk increased.

Meta-regression analysis in this study indicated that the cohort size and lung cancer SMR were an important source of heterogeneity. Sensitivity analysis in this study indicated that the results of meta-analysis are reliable and stable.

This paper showed colorectal cancer risk increased gently with lung cancer SMR when used as a substitute for the exposure measurements. According to the subgroups of asbestos type, we concluded that when the mixed asbestos exposure was highly intense, there was a gradual increase in colorectal cancer risk (correlation strength was from 1 to 2). We did not observe a trend of colorectal cancer risk with amphibole asbestos exposure. According to the subgroups of the follow-up period, we observed a continued weak correlation (trend for 1) between exposure and colorectal cancer risk in a short follow-up period. In a long follow-up period, we observed increased colorectal cancer risk (trend for 2). That finding indicated that a longer follow-up with a greater cumulative dose would cause the colorectal cancer risk to increase.

Kang *et al.* conducted a study to assess the relationship between high asbestos exposure occupations and the occurrence of gastrointestinal (GI) cancer. He pointed that the proportionate mortality ratios (PMRs) could be biased because the PMRs for GI cancer might be affected by increases in other diseases caused by asbestos exposure[25]. Colorectal cancer is severely affected by life style like as other GI cancers. For this reason, this paper compared the relationship between asbestos exposure and colorectal cancer and gastric cancer, with colorectal cancer SMR/SIR and gastric cancer SMR/SIR extracted from the same 47 separate cohorts among 30 papers. Although the overall gastric cancer SMR/SIR for synthesis cohort was insignificant, excess mortality of gastric cancer have been observed in some subgroups yet. Therefore this paper supports the idea that asbestos exposure is associated with digestive tract cancer.

One of the advantage of this paper was the use of subgroup analysis. Also, lung cancer SMR was used as a surrogate for exposure with the subgroup of asbestos type and subgroup of follow-up period. No other literature has been reported with these methods. There are two limitations to this study that should be acknowledged. First, due to the imperfect cohort data, there is no way to further complete the dose-effect relationship. Second, there are inherent defects in meta-analysis, such as publication bias and simplification. Therefore, certain results need to be more thoroughly scrutinized.

Key points

Our review supported that colorectal cancer has a positive weak associations with asbestos exposure. Exposure to mixed asbestos has a weak correlation with colorectal cancer risk. Asbestos exposure to production such as asbestos cement workers and asbestos textile workers may has a low risk of colorectal cancer.

Conflict of Interest

None declared.

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None.

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