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Quantitative Assessment of Asbestos Fibers in Abdominal Organs: A Scoping Review

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Abstract

Background: *Quantification of asbestos fibers has been mainly performed in the lung but rarely in other organs. However, this may be relevant to understanding better translocation pathways and the oncogenic effects of asbestos on the human body. Electron microscopy is the best technology available to assess the type of fiber, dimensions, and distribution of asbestos fibers in different tissues and as a biomarker of cumulative dose.* **Objectives:** *This scoping review aims to summarize the findings of the studies in which asbestos fibers have been quantified by electron microscopy, occasionally associated with X-ray microanalysis, in normal and pathological tissue of ten abdominal organs.* **Methods:** *A scoping review has been performed by searching articles that quantified asbestos fibers in abdominal organs by electron microscopy (Scanning- SEM or Transmission-TEM).* **Results:** *The colon and rectum, kidney, bladder, and abdominal lymph nodes were the organs with at least ten samples available with quantification of asbestos fibers. Asbestos fibers were detected in all the abdominal organs considered: the highest value (152,32 million fibers per gram of dry tissue) was found in the colon and was identified using STEM with EDS.* **Conclusion:** *The studies included were heterogeneous in terms of exposure and cases, type of samples, as well as analytical techniques, therefore we cannot confirm a specific pattern of distribution in any organ, based on the low homogeneity of the exposure status. The colon is the organ in which the number of fibers is the highest, probably because of exposure arising from both internal distribution of inhaled fibers and ingestion. Additional studies of the number of asbestos fibers in abdominal organs should be made to achieve better representativity.*

1. Introduction

Diseases caused by asbestos fibers still represent a relevant issue not only for medical reasons, but also for the social, legal, financial, and political consequences they entail [1].

Mineral fibers have been studied for decades using techniques including optical microscopy,

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scanning electron microscopy and energy dispersive spectrometry [2], but, surely, the advantages of electron microscopy (higher resolving power and the possibility to gain information on the chemical composition and crystalline structure of the fibers) make this technique the most accurate to quantify asbestos fibers in human tissues [3]. Despite the correlation found between exposure to asbestos and pulmonary and non-pulmonary diseases [4-5], the quantification of the fibers has not been widely explored, not even in organs for which asbestos is considered a risk factor for cancer (with the notable exception of the lung).

In two previous review articles, we reported the concentration of asbestos fibers in peritoneal and pleural tissue. In peritoneal tissue [6], asbestos fibers were found in 58% of the 100 samples collected. In pleural tissue [7], asbestos fibers were detected in 111 samples (78%) and were below the detectable limit in 31 samples (22%). The concentration of asbestos fibers detected in the positive samples was distributed from as low as 0.01 million fibers per gram of dry tissue (mfgdt) up to 240 mfgdt. However, the minimum concentration of fibers overlaps in the three types of tissues (normal pleura, pleural plaque, mesothelioma) in terms of range of magnitude.

We explored the current literature on asbestos fibers detected with electron microscopy in pathological and normal abdominal tissue of ten organs: the stomach, colorectum, small intestine, spleen, bladder, kidney, gallbladder, liver, pancreas, and intra-abdominal lymph nodes.

2. Materials and Methods

As this was conceived as an exploratory endeavor, PRISMA extension for scoping reviews was followed to summarize the literature [8] and evaluate if a systematic review could eventually be performed. The literature search was performed on the following databases: PubMed, Embase, Scopus, Web of Science, Ovid, and Cochrane. The search strategy was conceived to detect papers in which the asbestos fibers in tissues were determined by electron microscopy, so the string used was: "(asbestos) AND (electron*) AND ((stomach) OR (colo*) OR (intestin*) OR (spleen) OR (renal OR kidney) OR (bladder) OR (liver OR hepatic) OR (gallbladder OR colangio*) OR (pancreas) OR (abdom* AND lymph*))" on 26 April 2023.

The inclusion criteria for this review were: i) articles written in any language, regardless of the publication date; ii) articles reporting a quantification of asbestos through electronic microscopy in subjects with defined or undefined asbestos exposure; iii) articles reporting a quantification of asbestos present in the following organs: stomach, colorectum, small intestine, spleen, bladder, kidney, gallbladder, liver, pancreas, and intra-abdominal lymph nodes. The exclusion criteria were: i) articles not reporting a quantitative measure of the number of asbestos fibers found or reporting a measure by techniques other than electron microscopy; ii) studies in animals.

We also decided that case reports would be included in this review and that the exposure pathway to asbestos would not represent an exclusion or inclusion criterion. The results have been presented, where appropriate, taking in consideration the subjects with an occupational exposure to asbestos and the ones with an environmental or unclear exposure.

Figure 1 illustrates the results of the literature search; 1,937 articles were identified: after removing duplicates, and not pertinent articles, 23 articles were checked in the full text. 12 studies that fit our inclusion criteria were identified (all were published between 1981 and 2021). The references of each relevant article were manually searched, yielding no more papers.

The studies included in this scoping review reported the number of asbestos fibers mainly for grams of wet tissue, so we transformed the value for wet tissue into dry tissue, multiplying by 10.

3. Results

The 12 studies included in this review comprised 204 cases with at least 325 samples analyzed. For

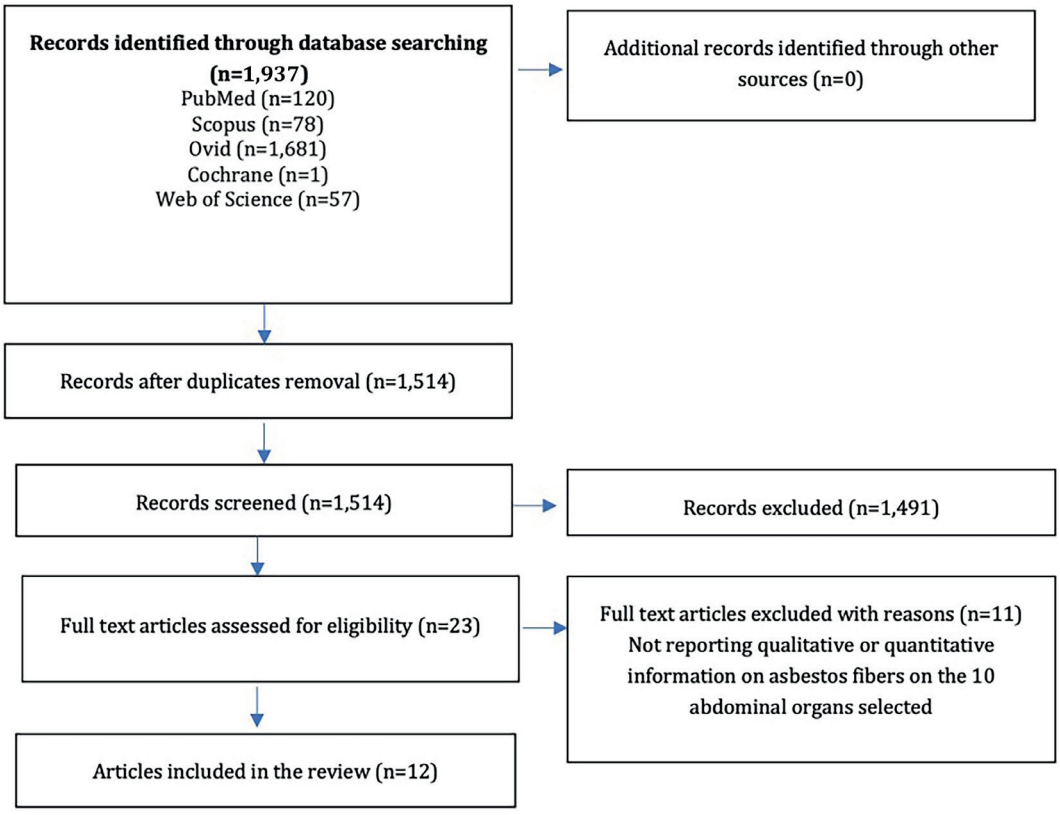

Figure 1. Flowchart showing the selection process of the articles included in the scoping review.

simplicity and better readability, we present the results divided by organs as follow:

- Table 1 reports a description of the patients and conditions included in the studies either normal or pathological tissue;
- Table 2 reports the detection limit (DL) of asbestos fibers in the intra-abdominal tissue (expressed as millions of fibers per gram of dry tissue: mfgdt) and the analytical technology used; when the detection limits was not specified in the study, we listed the lowest concentration of asbestos fibers reported.

The studies were performed on autopsy samples or biopsies. One study assessed stomach, small intestine, pancreas, spleen [9], five studies assessed large intestine [9, 10, 11, 12, 13], two assessed liver [9, 14], one assessed gallbladder [15], four studies assessed kidney (both cancerous and normal tissue) [9, 14, 16, 17], three studies assessed bladder [14, 18, 19], and one assessed abdominal lymph-nodes [20]. Seven of the studies found chrysotile [10, 13, 15, 16, 18, 20], seven found amphiboles [9, 10, 13, 14, 17, 19, 20], and two studies did not report which type of asbestos fibers were identified [11, 12]. The study with the highest number of samples was published by Ehrlich et al. [10], with 101 samples.

Out of the 204 cases, 72 (34.8%) were diagnosed with colon cancer, 25 (12.2%) with bladder cancer, 20 (9.8%) were controls with non-pathological colon, 5 (2.4%) with kidney cancer, 5 (2.4%) were controls with normal kidneys, 76 (37.2%) were either considered as other conditions or had pleural/lung cancer. In contrast, one (0.5%) was a "special-normal" kidney. This latter case was

Table 1. Number of cases and conditions found in the studies, grouped by the authors of the article.

Organ condition	N° of Cases or Samples	Reference Cronological Order
5 Normal Kidneys 5 Primary Adenocarcinomas of the Kidney 1 "Special-Normal Kidney"	9 Autopsies 2 Biopsies	Patel-Mandlik, 1981 [16]
1 Lung Cancer 2 Other Causes	3 Autopsies	Huang et al., 1988 [9]
40 Colon Cancers 20 Colon Controls	60 Biopsies	Ehrlich et al., 1991 [10]
12 Bladder Cancers	12 Biopsies	Molinini et al., 1992 [18]
1 Lung Cancer	1 Autopsy	Tossavainen et al., 1994 [17]
13 Bladder Cancers 12 Benign Prostatic Hypertrophies	25 Biopsies	Pollice et al., 1995 [19]
2 Asbestosis 1 Other Cause	3 Autopsies	Pollice et al., 1997 [14]
31 Colon Cancers 30 Other Causes	61 Cases	Muller et al., 2001 [12]
10 Lung Cancers 2 Asbestosis 2 Lung Fibrosis 8 Other Causes	22 Autopsies	Uibu et al., 2009 [20]
1 Malignant Pleural Mesothelioma	1 Autopsy	Croce et al., 2018 [15]
1 Colon Cancer	1 Biopsy	Rinaudo et al., 2021 [13]

categorized as "special-normal" because the subject had had kidney cancer on the contralateral kidney, which had been surgically removed.

3.1. Gastrointestinal Organs

3.1.1 Stomach

Only one study [9] reported asbestos fibers in the stomach. Overall, three patients were evaluated: two had been respectively surely or possibly occupationally exposed to asbestos, while the third one was not exposed. The samples were obtained during autopsies, and the analysis was conducted with TEM and EDXA technology.

The median of asbestos fibers detected was 2.62 mfgdt. Amphibole has been identified only in one sample, while the type of asbestos fibers found for the two other samples was not reported. Considering the three values, we can see a difference in asbestos fiber concentration between the exposed subjects (2.62 and 3.82 mfgdt) and those not exposed to asbestos during his working life (0.04 mfgdt).

3.1.2 Small Intestine

A quantification of fibers in small intestine tissue was done in one study [9]. Huang et al. [9] analyzed three small intestine samples (three cases) using TEM with EDXA. One case was not exposed to asbestos before, and no fibers were detected. Another case was occupationally exposed; the sample had a burden of 0.54 mfdgt (only amphiboles were found). The last case was occupationally exposed, and the sample had a burden of 1.24 mfdgt (mostly amphiboles).

3.1.3 Colon and Rectum

Studies which assessed colon and rectum content of asbestos are reported in Table 3. Five studies [9, 10, 11, 12, 13] analyzed the number of asbestos

Table 2. Detection limit of asbestos fiber's type and technology used.

Technology used	Chrysotile LOD*	Amphibole LOD*	Reference Cronological Order
TEM with SAED	**	**	Patel-Mandlik, 1981 [16]
TEM with EDX	0.04	0.04	Huang et al., 1988 [9]
STEM with EDS	0.076 (control group) 0.95 (exposed group)	0.076 (control group) 0.95 (exposed group)	Ehrlich et al., 1991 [10]
TEM with EDS	0.02	0.02	Molinini et al., 1992 [18]
SEM	0.1	0.1	Tossavainen et al., 1994 [17]
TEM with EDS	0.006	0.006	Pollice et al., 1995 [19]
TEM with EDS	0	0	Pollice et al., 1997 [14]
SEM with EDX	0.063	0.063	Muller et al., 2001 [12]
TEM with EDX	0.05	0.02	Uibu et al., 2009 [20]
SEM and EDS	3	3	Croce et al., 2018 [15]
SEM with EDS	0.03 (Healthy tissue) 0.08 (Neoplastic tissue)	0.03 (Healty tissue) 0.08 (Neoplastic tissue)	Rinaudo et al., 2021 [13]

* **Limit of Detection (mfgdt):** *When the DL was not specified the lowest value observed was reported.*
***The article reports, "If no fibers were observed in ten grid openings of two grids prepared from 100 mg dry weight of tissue, the value of F/mg dry weight would be Below Detection (BD) level."*
TEM= Transmission electron microscope, SAED= Selected area electron diffraction, EDX=Energy Dispersive X-ray Analysis. EDS=Energy dispersive X-ray spectroscopy, SEM=Scanning electron microscope, ATEM=Analytical Transmission electron microscope. STEM: Scanning Trasmission Electron Microscopy

fibers in the colorectal area. Overall, 210 samples were collected from 134 patients. The authors did not find asbestos fibers on 93 samples out of the total 210, representing 44.2% of the sample. Both normal tissues and cancerous tissues were analyzed. Most of the samples were collected from biopsies except for seven autopsies. The group includes subjects with known or probable occupational exposure (n=107) and subjects with unknown or impossible occupational exposure (n=27). The patients (n=61) included in the study from Muller et al., 2001 [12], were mixed (both occupational and unknown exposure). Amphiboles have been detected only in seven, and chrysotiles in eleven samples. The only amphiboles reported were amosite [10] and tremolite [13]. In the other cases, the type of asbestos fiber was not reported.

The range of asbestos fibers detected in the exposed subjects was 0.03-152.32 mfgdt; the range of fibers detected in unexposed or with unknown exposure subjects was 0.10-16 mfgdt. Only one study [10] did not find asbestos fibers in unexposed subjects.

In one study [9], the assessment was carried on using TEM and EDXA; in another study [10] STEM and EDS were used. In the 3 remaining articles, the sample evaluation was made using SEM and EDXA. [11-13]

In the study by Rinaudo et al. [13], three samples were digested and assessed to count the quantity of fibers, while three other samples were sliced, embedded in paraffin, and assessed for length and thickness. The range for length goes from 4.81 to 12.21 μm, while for thickness ranged from 0.98 to 2.1 μm.

3.1.4 Pancreas

An analysis of pancreatic tissue appears only in the study by Huang et al., 1988 [9]. The authors took a single sample from each of the three male subjects they had available and analyzed them using TEM and EDXA. Two of three pancreatic samples (66%) presented asbestos fibers, while one did not. As described in the article, case 1 had lung cancer with occupational exposure to asbestos and several

Table 3. Studies which assessed colon and rectum content of asbestos.

Value or range Range of Asbestos Fibers (mfgdt)	Type of Asbestos (N Samples With/ Without Fibers)	Asbestos Exposure	Type of Tissue Analyzed	N Subjects/ N Samples	Reference
*(0.10)	Total (1/0)	Unexposed	Colon	1/1	Huang, 1988 [9]
*(0.15)	Total (1/0)	Unexposed	Rectum	1/1	
*(0.47)	Total (1/0)	Occupational	Colon	1/1	
*(0.29)	Amphiboles (1/0)	Possible (occupational)	Colon	1/1	
*(0.88)	Total (1/0)	Occupational	Rectum	1/1	
*(0.20)	Amphiboles (1/0)	Possible (occupational)	Rectum	1/1	
ND	Total (0/40)	Unexposed	Colon (cancerous & normal mixed)	20/40	Ehrlich, 1991 [10]
*(11.29)	Amphiboles (1/39)	Occupational	Colon (cancerous)	40/40	
1.21-152.32	Chrysotile (9/31)				
1.85-5.86	Amphiboles (2/19)	Occupational	Colon (normal)	21/21	
ND	Total (0/1)	Unknown	Colon (normal)	1/1	Saitoh, 1993 [11] *
MD-0.000001	Total (2/1)	Unknown	Colon (normal)	3/3	
ND	Total (0/1)	Occupational	Colon (cancerous)	1/1	
0.06-0.35	Total (31/0)	Occupational/ unknown	Colon (cancerous tumor area)	31/31	Muller, 2001 [12]
0.06-0.21	Total (31/0)	Occupational/ unknown	Colon (cancerous non tumor area)	31/31	
0.06-0.21	Total (30/0)	Occupational/ unknown	Colon (normal)	30/30	
*(0.03)	Total (2/0)	Unknown	Colon (normal)	1/2	Rinaudo, 2021 [13]
*(0.08)	Total (1/0)	Unknown	Colon (cancerous)	1/n.a.	

** Only one value. Range not available*

asbestos fibers of 1.3 mfgdt, case 2 died from a cardiovascular accident with possibly occupational exposure, and the sample showed an asbestos amount of 0.45 mfgdt, case 3 died for other cause without asbestos exposure, and no fibers were found in the pancreatic tissue. Both amphiboles and chrysotiles were found with a higher concentration of the first type than the second type. Data about the length of fibers was available and described for case 1 and case 2. The case 3 had no information. Fiber size from case 1 had a mean length of 5.1 μm and a range from 2.1 to 16.0 μm. Case 2 had a mean length of 3.0 μm and a range from 1.6 to 7.8 μm. The ranges in fiber lengths varied widely in both lungs and other organs.

3.1.5 Liver

By analyzing three autopsies, Huang et al. [9] studied the association between asbestos fibers in human lung tissues and those in other extrapulmonary organs. Case 1 was occupationally exposed to asbestos for a prolonged period and suffered from asbestosis; occupational asbestos exposure in case 2

was possible but not certain, and no evidence of occupational asbestos exposure was found in case 3. The amount, type, and dimensions of asbestos fibers in the tissues of the liver and other organs were identified and measured by transmission electron microscopy (TEM). The detection limit for the liver tissue was 0.11 mfgdt. A concentration of 0.92 mfgdt was found in case 1, a concentration of 0.40 mfgdt was found in case 2, while in case 3, the fibers were not detectable.

Liver fiber type and length data were reported aggregated with pancreas and spleen data, so it is impossible to be more specific. The percentages of different types of asbestos fibers found by EDXA indicated that for case 1, 84.7% of fibers in the liver, spleen, and pancreas tissues were amosite; in case 2, 85.7% was anthophyllite. The mean fiber length in the liver, spleen, and pancreas was 5.1 μm in case 1 (range 2.1 μm -16.0 μm) and 3.0 μm in case 2 (range 1.6 μm -7.8 μm).

Pollice et al. [14] reported the concentration of asbestos fibers in 24 samples from 3 cases. The samples were extracted from different body organs, and only 1 was liver tissue sample analyzed with TEM and EDXA. The authors report that two subjects were affected by asbestosis with an occupational history of asbestos exposure. The case number 3 was a control with no occupational asbestos exposure reported. The analytical procedure described in the study does not specify the detection limit, but the minimum concentration detected was 0.1 mfgdt. Amphiboles were found in the liver tissue of one case (concentration: 0.15 mfgdt; mean length: 12μm, mean width 0.4μm), in the other case, and the control case, the authors found no fibers in liver tissue.

3.1.6 Gallbladder

The gallbladder tissue has been investigated only in one study [15], where the authors analyzed a section of the gallbladder from an 80-year-old woman who died of malignant pleural mesothelioma and was also affected by severe bile-tract problems (not specified). The exposure of this patient to asbestos was both environmental and occupational. Only chrysotile fibers were found in the sample analyzed with a concentration of 3 mfgdt. The techniques used for the detection of asbestos were SEM and EDS.

3.2. Urinary Tract

3.2.1 Kidney

Studies which assessed the content of asbestos fibers in the kidney are reported in Table 4. A quantitative assessment of asbestos fibers in kidney tissue was done in four studies [9, 14, 16, 17].

Huang et al. [9] analyzed three kidney samples (three cases) with TEM and EDXA. One of the cases had not been exposed to asbestos previously; the sample was free of asbestos fibers. Another case was possibly occupationally exposed; the sample had a burden of 0.47mfdgt (only amphiboles were found). The last case was occupationally exposed; the sample had a burden of 12.5mfdgt (mostly amphiboles). In the two cases in which asbestos was found, fibers were also assessed by length; in the possibly occupationally exposed case, the mean value for fibers' length was 3.1 μm, with a range of 2.2 to 4.3 μm. In the occupationally exposed case, the mean value for fibers' length was 5.1, with a range of 1 to 16 μm. No assessment was made concerning the width of the fibers.

Pollice et al. [14] analyzed three kidney samples (three cases) via TEM and EDS (Energy dispersive Spectrometry). One of the cases had not been exposed to asbestos previously; the sample was free of asbestos fibers. The other two cases were occupationally exposed; asbestos fibers were found in one of them (50%), which had a burden of 0.2 mfgdt. Only amphiboles were found, with a mean length of 18 μm and a mean diameter of 0.2 μm.

Patel-Mandlik et al. [16] analyzed two groups of people: one with kidney cancer and one without. Tissue samples were taken from medulla and/or cortex of both cancerous and normal kidney, or from a pool of medulla and cortex when it was not possible to define which part of the kidney had been sampled or when it had both portions. From the kidney cancer group, four samples of cortex and four of medulla were analyzed from three cases; another

Table 4. Studies which assessed the content of asbestos fibers in the kidney .

*Asbestos Fibers (mfgdt)**	*Type of Asbestos (N Samples With/ Without Fibers)*	*Asbestos Exposure*	*Type of Tissue Analyzed*	*N° of Subjects/ n° of Samples*	*Reference*
ND – 18.23	Chrysotile (1/3)	Unexposed	Cortex (normal kidney)	4/4	Patel-Mandlik, [16]
ND – 3.14	Chrysotile (2/2)	Unexposed	Medulla (normal kidney)	4/4	
Only one value (1.60)	Chrysotile (1/0)	Unexposed	Cortex and medulla pool (normal kidney)	1/1	
Only one value (24.55)	Chrysotile (1/0)	Unexposed	Cortex (cancerous kidney-tumor area)	1/1	
1.10–20.41	Chrysotile (3/0)	Unexposed	Cortex (cancerous kidney-non tumor area)	3/3	
0.74–86.91	Chrysotile (2/0)	Unexposed	Medulla (cancerous kidney-tumor area)	2/2	
1.27–47.92	Chrysotile (2/0)	Unexposed	Medulla (cancerous kidney-non tumor area)	2/2	
3.90–16.16	Chrysotile (2/0)	Unexposed	Cortex and medulla pool (cancerous kidney-tumor area)	2/2	
ND	Total (0/1)	Unexposed	Cortex and medulla pool (cancerous kidney-non tumor area)	1/1	
ND	Total (0/1)	Unexposed	Cortex (special-normal kidney)	1/1	
Only one value (17.63)	Chrysotile (1/0)	Unexposed	Medulla (special-normal kidney)	1/1	
ND	Total (0/1)	Occupational	Medulla (cancerous kidney-tumor area)	1/1	
ND	Total (0/1)	Occupational	Cortex and medulla pool (cancerous kidney-non tumor area)	1/1	
ND	Total (0/1)	Unexposed	Kidney	1/1	Huang [9]
Only one value (12.5)	Total (1/0)	Occupational	Kidney	1/1	
Only one value (0.47)	Amphiboles (1/0)	Possible (occupational)	Kidney	1/1	
Only one value (30)	Crocidolite (1/0)	Occupational	Kidney cortex	1/1	Tossavainen et al., [17]
ND-0.2	Amphiboles (1/1)	Occupational	Kidney	2/2	Pollice et al., [14]
ND	Total (0/1)	Unexposed	Kidney	1/1	

ND: Not detectable

sample of medulla tissue was taken from another case. Four other samples of pool of medulla and cortex were studied. From the normal kidney group, four samples of cortex and four of medulla were analyzed from four cases. Another sample of pool of medulla and cortex from another case was studied.

One last sample taken from a "normal-special" kidney was analyzed; it was categorized as "normal-special" because the case had a kidney cancer on the contralateral kidney, which had been surgically removed.

All samples were then analyzed with TEM and SAED (Selected area electron diffraction). In non-cancerous cortex, three samples were found free of asbestos fibers (75%); in the remaining sample 18.23 mfgdt were found. None of the cases were occupationally exposed. In non-cancerous medulla, two samples were found free of asbestos fibers (50%). The other two samples ranged from 2 to 3.1 mfgdt. The cases and samples were considered the same for non-cancerous cortex. For the non-cancerous medulla and cortex pool one sample was studied and it had asbestos fibers (1.6 mfgdt). The case was not occupationally exposed. In the cancerous cortex, 100% of the samples had asbestos fibers. The fibers ranged from 1.1 to 24.5 mfgdt. In cancerous medulla, one sample was found free of asbestos (20%), the other four samples ranged from 0.74 to 47.9 mfgdt. The only sample free of asbestos fibers was the only occupationally exposed case. In the group composed of cancerous pooled medulla and cortex two samples were free of asbestos (50%). The other two samples were from the same case, and they ranged from 3.9 to 16.1 mfgdt. Only one of the cases was occupationally exposed and it was free of asbestos fibers. Only chrysotile fibers were found in this study; there was not a significant difference in length and width of fibers between normal and cancerous kidneys. As stated in the article, the length of most fibers was between 0.4 to 0.6 μm, while the total range varied between 0.15 to 2.15 μm. The range of width was similarly very wide, with a minimum of 0.02 μm and a maximum of 0.15 μm in diameter.

Tossavainen et al. [17] analyzed via SEM (scanning electron microscopy) a single sample of kidney cortex from an occupationally exposed case with a diagnosis of lung carcinoma; the sample had a burden of 30 mfgdt. Only crocidolite fibers were found, with a length median value of 2.6 μm and a range that varies from 1 to 10 μm and a width median value of 0.12 μm and a range that varies from 0.05 μm to 0.21 μm.

3.2.2 Bladder

Studies that assessed the bladder content of asbestos are reported in Table 5. A quantitative assessment of asbestos fibers in bladder tissue was done in three studies [14, 18, 19].

Pollice et al. [14] analyzed three bladder samples using TEM and EDS (2 cases, occupationally exposed, and one control case, not exposed). The non-exposed worker was free of asbestos fibers in the bladder. Amongst the exposed workers, one of them (50%) was free of asbestos fibers in the bladder; the other one (50%) had a burden of 0.3 mfgdt. Only crocidolite was found, with a mean length of 3μm and a mean diameter of 0.05 μm.

Molinini et al. [18] analyzed 12 samples (12 cases of bladder cancer) via TEM and EDS. Eight of the cases had not been occupationally exposed to asbestos. Three out of 8 (37.5%) did not have any asbestos fibers; the other five cases (62.5%) had a burden of asbestos fibers that ranged from 0.075 to 0.58 mfgdt; in all cases only chrysotile fibers were found. The four remaining cases had been occupationally exposed to asbestos. In all of them (100%) asbestos fibers were found, ranging from 0.09 to 0.28 mfgdt; in all cases chrysotile fibers were found; in one of them, it was found along with tremolite. The dimension of asbestos fibers was assessed, with an overall mean length of 8 μm and a mean overall diameter of 0.16 μm. If only positive cases are taken into consideration, the mean length grows to 11 μm and mean diameter to 0.13 μm. Only in one case fibers longer than 40 μm were found.

Pollice et al. [19] analyzed 25 samples (13 cases of bladder cancer and 12 controls) using TEM and EDS. They divided exposure in five classes: class 1 (likely not exposed), class 2 (possible occupational exposure), class 2a (possible environmental exposure), class 3 (likely exposed), class 4 (occupationally exposed). Amongst the 13 cases of bladder cancer four belonged to class 1, six belonged to class 2, two belonged to class 3, and only one belonged to class 4. Eleven (84.6%) of them were free of asbestos fibers, the remaining two (15.4%) had a burden of 0.006 mfgdt (class 2, only chrysotile fibers were found), and 0.03 mfgdt (class 4, only crocidolite

Table 5. Studies that assessed the bladder content of asbestos.

Range of Asbestos Fibers (mfgdt)	Type of Asbestos Found (N Samples With / Without Fibers)	Asbestos Exposure	Type of Tissue Analyzed	N Subjects / N Samples	Reference
ND – 0.58	Chrysotile (5/3)	Unexposed	Bladder (cancerous)	8/8	Molinini et al., 1992 [18]
0.09– 0.28	Chrysotile (4/0)	Occupational	Bladder (cancerous)	4/4	
Only one value (0.26)	Total (1/3)				
ND	Total (0/4)	Unlikely	Bladder (cancerous)	4/4	Pollice et al., 1995 [19]
Only one value (0.006)	Chrysotile (1/5)	Possible	Bladder (cancerous)	6/6	
ND	Total (0/2)	Likely/ Occupational	Bladder (cancerous)	2/2	
Only one value (0.03)	Amphiboles (1/0)	Occupational	Bladder (cancerous)	1/1	
ND	Total (0/1)	Unexposed	Bladder	1/1	Pollice et al., 1997 [14]
ND-0.3	Amphiboles (1/1)	Occupational	Bladder	2/2	

fibers were found). Among the 12 controls, ten belonged to class 1, and two belonged to class 2. All of them were free of asbestos fibers. No dimensions of fibers were described in the article.

3.3. Lymphatic System

3.3.1 Spleen

Only one study reported the quantitative assessment of asbestos fibers in the spleen [9]. Overall, three patients were evaluated: two had been surely or possibly occupationally exposed to asbestos, while the third was not. The samples were taken during autopsies. The sample obtained by the unexposed patient did not show asbestos fibers, while the authors reported for the other two samples, respectively, 1.65 and 1.25 mfgdt. Amphibole has been identified in 1 sample, while the type of asbestos fibers analyzed for the other samples was not reported. The sample evaluation has been conducted with TEM and EDXA.

3.3.2 Intra-Abdominal Lymph Nodes

Studies assessing the asbestos content of intra-abdominal lymph nodes are reported in Table 6. Uibu et al. [20] analyzed by TEM with EDXA para-aortic and mesenteric lymph nodes and lung tissue from 17 subjects who underwent medico-legal autopsies for suspicion of asbestos-related disease and from 5 controls. It was shown that asbestos fibers could also translocate to the retroperitoneal and mesenteric lymph nodes besides their accumulation in lung tissue. Even low-level occupational exposure resulted in chrysotile or amphiboles in these abdominal lymph nodes. The mean concentration for the 10 subjects with a lung asbestos content of at least 1 mfgdt was 0.85 mfgdt in the para-aortic lymph nodes and 0.55 mfgdt in the mesenteric lymph nodes. The respective mean values for the 12 persons with a lung asbestos concentration of less than 1 mfgdt were 0.7 mfgdt for the para-aortic lymph nodes and 0.03 mfgdt for the mesenteric lymph nodes.

Table 6. Quantification of asbestos in the lymph nodes, grouped by fiber type and range and nature of exposure.

Asbestos Fibers (Mfgdt)*	Type of Asbestos Found (N Samples With/ Without Fibers)	Asbestos Exposure	Type of Tissue Analyzed	N Subjects / N Samples	Reference
ND - 4.36	Amphiboles (11/6)	Likely occupational	Para-aortic lymph node	17/17	Uibu et al., 2009 [20]
ND - 2.86	Amphiboles (10/7)	Likely occupational	Mesenteric lymph node	17/17	
ND	Amphiboles (0/4)	Unknown	Para-aortic lymph node	5/5	
ND	Chrysotile (0/1)				
ND	Total (0/1)				
ND	Amphiboles (0/3)	Unknown	Mesenteric lymph node	5/5	
ND	Chrysotile (0/1)				
Only one value (0.13)	Total (1/0)				

ND: Non Detectable

Table 7. Quantification of asbestos fibers in abdominal organs on studies with at least 10 samples available.

Range of Asbestos Fibers (Mfgdt) in Subjects With Unknown Exposure	Range of Asbestos Fibers (Mfgdt) in Unexposed Subjects	Range of Asbestos Fibers (Mfgdt) in Exposed (Or Possibly Exposed) Subjects	Organ
0.03–16	0.10–0.2	0.20–152.3	Colon and rectum
ND	0 – 86.9	0.2 – 30	Kidney
ND	0–0.6	0–0.3	Bladder
<0.05–0.13	Not detected	2.9–4.4	Abdominal lymph nodes

ND: Non Detectable

3.4. Number of Fibers in the Different Organs

Table 7 summarizes the results of the number of asbestos fibers in organs where at least 10 samples had been evaluated (colorectum, bladder, kidney, and intra-abdominal lymph nodes): the results are reported for 3 groups of subjects, categorized as exposed or possibly exposed, unexposed, or with unknown exposure.

The number of asbestos fibers in colorectal tissue is the highest among exposed (or possibly exposed) workers, with up to 152.32 mfgdt; additionally, it has the highest value for subjects with unknown exposure.

The kidney was the second organ with the highest number of fibers; however, it is remarkable to see that this organ's highest number of fibers (86.9 mfgdt) was detected in the unexposed group. The presence of any asbestos fibers was described in a study where the pooled relative risk of kidney cancer for asbestos exposure was 0.94 (95% confidence interval, 0.84-1.04), with no differences according to the type of asbestos fiber, geographic region, period of exposure, or estimated quality of the study [21]. No obvious differences can be observed for bladder tissue in the range of asbestos fibers in the three groups of subjects. Likewise, abdominal lymph nodes did not have any fibers detected in the unexposed group, which is

remarkable and contrasts with the two other groups of subjects and organs analyzed.

3.5. Asbestos Fibers Dimensions

Seven articles [9, 13, 14, 16, 17, 18, 20] out of 12 studies reported data for the length and/or diameter of the asbestos fibers. Some articles reported the median, mean, or only the mode. For instance, Huang et al. [9] reported the overall dimension of the fibers as a whole and not divided by organ, hampering the possibility of predicting the distribution and/or any possible pattern of the fibers on diverse organs. Fibers' length was also assessed for the gastrointestinal tract in 2 cases; in the possibly occupationally exposed case, the mean value for fibers' length was 2.1 μm, with a range of 0.5-13 μm. In the occupationally exposed case, the mean value of fibers' length was 4 μm, with a range of 0.6 - 19 μm [9]. Another study reported the mode value of fibers' length (40 μm, with a range of 10-100 μm) and diameter (1.8 μm, with a range of 0,6-2.8 μm) in the colon samples analyzed [12].

3.6. Type of Fibers

Despite the large variability of studies described above, some conclusions can be drawn.

1. For the organs for which at least ten samples were available, the different range of asbestos fiber concentrations between exposed (or possibly exposed) subjects, non-exposed subjects, and subjects whose exposure was not clearly defined.
2. No significant differences have been observed in the detection limits in studies performed in different years, despite the technological advances in electron microscopy. Illustrative of that are Molinini's [18] and Uibu's [20] studies (published in 1992 and 2009 respectively): in both the detection limit using TEM microscopy was 0.02 mfgdt. An explanation for that is the improved sensitivity in today's technology: in past years differentiating between asbestos fibers and other types of fibers might have been difficult, therefore allowing for misclassification of the fibers themselves. Additionally, a critical factor in the detection of asbestos fibers in the sample is represented by the amount of tissue available.
3. For every organ, at least one article reported the presence of asbestos fibers, demonstrating a tropism for asbestos for all intra-abdominal organs. The translocation pathway of asbestos fibers and their tropism for some intra-abdominal organs might have a presumed role in carcinogenesis of some neoplasms [22]. In this study, both intraperitoneal and extra-peritoneal organs have been included.
4. The highest value for asbestos fiber concentration (152.32 mfgdt) was found in the colon by Ehrlich et al. [10] and it was identified using STEM with EDS. This also represents the highest value for chrysotile fiber concentration. The highest value for amphibole fiber concentration was also found in the colon by Ehrlich et al. and it was 11.92 mfgdt.
5. After analyzing all the articles found, we cannot highlight a distribution pattern in any organs. This cannot be generalized due to the low homogeneity of the exposure, and one must be prudent with the discussion of these results because the studies retrieved were performed on "convenience samples" This does not necessarily mean that those studies do not have a value: anyway, the information provided is not enough to draw firm conclusions about any possible pattern of distribution, but it is a good starting point.

4. Discussion

Currently, it is estimated that 125 million people are still environmentally exposed to asbestos worldwide, even in countries that banned its use [23]; however, no original articles have been published in the last five years regarding quantification of asbestos fibers in abdominal organs, being the latest study published on 2021 [13], except for a scoping review about quantification of fibers in the peritoneum published on 2022 [6].

It is well known that asbestos fibers enter the body through the respiratory system, from which they may be distributed to the whole body by the bloodstream or the lymphatic system. Asbestos fibers, mainly of the short type, have been found in all the abdominal organs included in this review: the stomach, colorectum, small intestine, spleen, bladder, kidney, gallbladder, liver, pancreas, and intra-abdominal lymph nodes.

The main contribution of this scoping review was to categorize ten abdominal organs to understand the presence of asbestos fibers and make an analytical assessment of the presence technology used and the dimension of the fibers found. The previous two scoping reviews [6,7] did not address the size of the fibers, so this is the first study that pays particular attention to the diameter and length of asbestos fibers.

It is known that the fibrogenicity and carcinogenicity of asbestos fibers depend on several fiber parameters including fiber dimensions [24].

It is important to emphasize that the quality of the findings does not exclusively depend on the microscope technology used but also on other factors such as the preparation of the samples (e.g., digestion procedure - strong acids/bases, plasma ashing, enzymatic digestion, etc.), the expertise of the laboratory personnel and the of the fiber's dimensions. In this regard, the amount of tissue analyzed is important: samples from autopsies generally have enough material, whereas this could not be the case for biopsies; thus, caution is required when comparing data from the two procedures.

Six studies included in this review used TEM and six used SEM. A comparison between SEM and TEM is a complex issue beyond this review's scope. The TEM vs SEM strengths are mainly the higher resolution, high magnification, and the possibility to get crystallographic information by SAED. At the same time, the main limitations are (i) the sample size (very small), (ii) complex sample preparation (quite critical), and (iii) limited surface detail and field depth. Field-emission SEM may allow us to obtain TEM-like magnification and resolution without the complexities of TEM.

A critical point in making sense of the data about the number of asbestos fibers present in each organ is not only the correct technique used for their determination but also that the sample should give a valid representation of the whole organ content. An additional issue is the clearance of asbestos fibers from the organ; this has been described, for example, for chrysotile fibers from the lung, but there are no studies regarding other human organs (most importantly, the pleura), although such studies exist in animals [25] and suggest that short fibers are more efficiently removed by mesothelium than long fibers. This adds to the critical importance of the issue of fibers' length.

One of the limitations of the current study is the significant variability among the articles. Since most of the samples analyzed have been convenient samples, it is possible to make the proper analysis to compare the studies, having only a non-probability sampling method.

The number of asbestos fibers in colorectal tissue is highest among exposed (or possibly exposed) workers, with up to 152.32 mfgdt. Additionally, it has the highest value for subjects with unknown exposure. We do not know the reason for this. Still, we speculate that all the population (including exposed and unexposed subjects) may introduce asbestos fibers through drinkable water, as during the last century, it has been a widespread practice in several countries to use cement-asbestos pipes to distribute potable water [26], and food. Thus, the colon (as the whole gut) would be subject to a double load of asbestos fibers: the fibers absorbed by the lungs and distributed through the bloodstream or the lymphatic circulation, and the fibers ingested with water and food. Drinkable water may contain asbestos fibers over millions per liter [27], and some foods may contain asbestos fibers over millions per gram [28]. In another study [29] that assessed asbestos fibers in extra-abdominal tissue it was found that the lymph nodes of occupationally exposed subjects has the highest value (7400 mfgdt).

In general, there is a prevalence of small fibers in the different organs included in this scoping review rather than longer fibers, which might be expected because longer fibers may have greater difficulty penetrating and traveling in the blood or lymphatic system.

To summarize, the studies included in this scoping review appear to be highly heterogeneous in terms of the study designs, the type of electron microscopy used for asbestos fibers assessment, and the exposure to asbestos in the selected cases as well, so one has to be cautious about the discussion of the type of fibers found, because the type of fibers in the samples would depend essentially on the kind of exposure. For example, if a subject has been exposed to chrysotile, the fibers found on the tissue would be chrysotile and not amphiboles.

Moreover, the fiber content of the different organs overlaps between exposed, possibly exposed, and unexposed subjects.

To reduce the inhomogeneity of the studies, we recommend that the quantification of asbestos fibers in human tissue should be made systematically on autopsies and biopsies when the technology and expertise are available, together with high-quality information about exposure to asbestos of the subject.

Further association of the quantification of the fibers in different organs shall be made with epidemiological studies with healthy or pathological tissues of abdominal organs so that the representativeness of the results about the general population may be more accurate.

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