applied sciences

MDPI

Article

Survival of Korean Patients with Malignant Pleural Mesothelioma Compensated for the Asbestos Injury Relief

Min-Sung Kang [1,†], Sung-Soo Lee [2,†], Soon-Chan Kwon [3], Da-An Huh [4] and Yong-Jin Lee [1,3,*]

1 Asbestos Environmental Health Center, Soonchunhyang University Cheonan Hospital, 31 Suncheonhyang 6-gil, Dongnam-gu, Cheonan-si 31151, Korea; kms83korea03@hanmail.net
2 Department of Preventive Medicine, Soonchunhyang University College of Medicine, 31 Suncheonhyang 6-gil, Dongnam-gu, Cheonan-si 31151, Korea; sungsool@sch.ac.kr
3 Department of Occupational and Environmental Medicine, Soonchunhyang University Cheonan Hospital, 31 Suncheonhyang 6-gil, Dongnam-gu, Cheonan-si 31151, Korea; sckwon@sch.ac.kr
4 Institute of Health Sciences, Korea University, Anam-ro 145, Seongbuk-gu, Seoul 02841, Korea; black1388@korea.ac.kr
* Correspondence: schcard34274@naver.com; Tel.: +82-41-570-3811
† These authors contributed equally to the publication.

Abstract: Background: The purpose of this study was to identify the epidemiologic characteristics and prognostic factors for malignant pleural mesothelioma in Korea, which are currently insufficient. The data were derived from malignant mesothelioma patients who registered under the Asbestos Injury Relief Act; Methods: A total of 728 patients received compensation from the Asbestos Injury Relief Act due to malignant mesothelioma between 2011 and 2015. Of these, 313 patients (43.0%) with malignant pleural mesothelioma were included in the study. The study variables were sex (male, female), age at diagnosis (<59, 60–69, ≥70), smoking history (yes, no), surgery (yes, no), chemotherapy (yes, no), occupational exposure to asbestos (yes, no), and histological subtype (epithelioid, nonepithelioid); Results: Median survival of mesothelioma was 8.0 months (95% confidence interval: 6.2 to 9.8). The 1-year, 2-year, and 5-year survival rates (%) were 43.5%, 23.6%, and 12.5%, respectively. In multivariate analysis of Cox's proportional hazards model; sex, age, smoking history, occupational asbestos exposure, and histological subtype were not significant prognostic factors, but surgery and chemotherapy combined was a significant predictor; Conclusions: Although the representativeness of these data is limited, our study estimates the epidemiologic characteristics of malignant pleural mesothelioma. Non-occupational exposure had a similar prognosis to occupational asbestos exposure, and there was no sex difference. In addition, it was found that receiving a combination of surgery and chemotherapy affects the survival rate, but there is a limitation in that factors such as performance status, comorbidities, and stage that contribute to survival are not considered.

Keywords: asbestos; malignant pleural mesothelioma; surgery; chemotherapy; survival

Citation: Kang, M.-S.; Lee, S.-S.; Kwon, S.-C.; Huh, D.-A.; Lee, Y.-J. Survival of Korean Patients with Malignant Pleural Mesothelioma Compensated for the Asbestos Injury Relief. *Appl. Sci.* **2021**, *11*, 9713. https://doi.org/10.3390/app11209713

Academic Editor: Francesco Cappello

Received: 30 August 2021
Accepted: 15 October 2021
Published: 18 October 2021

1. Introduction

Malignant mesothelioma is a rare and aggressive tumor of the pleura or peritoneum caused mainly by asbestos. It is known that about 80% of malignant mesothelioma cases are due to asbestos [1]. Malignant mesothelioma has a very poor prognosis with an average survival period of about 12 months [2]. Although asbestos is not currently used in Korea, the disease has been increasing significantly in recent years as a result of its long incubation period, and it is expected that the incidence of mesothelioma in Korea will continue to increase over the next 20 years [1]. In the future, continuous efforts will be needed to reduce exposure to asbestos and slow this trend. Malignant mesothelioma is strongly associated with asbestos exposure worldwide. Unlike lung cancer, malignant mesothelioma is known to develop after an incubation period of 20 to 40 years or more after exposure to small amounts of asbestos. Asbestos exposure in Korea increased dramatically in the 1930s when

asbestos mines were developed and then decreased briefly after liberation. However, as asbestos imports surged during the course of economic development in the 1970s, it was widely used in a variety of materials, including building materials such as slate, various mechanical parts, and insulation. In particular, even today, when the use of asbestos is prohibited or minimized, not only workers but also the general public are exposed to asbestos through the demolition or reconstruction of buildings containing asbestos [3]. As in other countries, Kwak et al. (2021) mentioned that malignant mesothelioma in Korea will continue to increase until around 2040 due to the large amount of asbestos used in the past [4]. Korea has an industrial accident compensation insurance system for patients with malignant mesothelioma due to occupational exposure to asbestos, and since 2011, according to the Asbestos Injury Relief Act, malignant mesothelioma patients suspected of being exposed to environmental asbestos irrespective of occupational exposure, can be managed. In Korea, compensation for occupational accidents due to occupational exposure among malignant mesothelioma outbreaks was only 39 in 2006–2015 [5], but 728 patients received relief from asbestos damage during the same period. Therefore, it can be said that the number of people receiving asbestos injury relief is much higher than the number of recognized occupational accidents caused by occupational asbestos exposure. However, in Korea, studies to investigate the scale of malignant mesothelioma caused by asbestos are still insufficient [6]. If asbestos injury relief data continue to be gathered, it is expected that greater clarity with respect to the specific epidemiologic characteristics of patients with malignant mesothelioma will be obtained. Recently, therapeutic approaches have been attempted to prolong the survival of patients with malignant mesothelioma, including surgery and chemotherapy [7]. Several studies have continued to debate about the optimal treatment strategy for the long-term survival of patients with mesothelioma [8].

Therefore, this study aimed to investigate the characteristics of and prognostic factors for malignant pleural mesothelioma patients in Korea, based on the data of patients registered under the Asbestos Injury Relief Act.

2. Materials and Methods

A total of 728 patients received compensation from the Asbestos Injury Relief Act due to malignant mesothelioma between 2011 and 2015. Of these, 321 patients (43.5%) were unable to complete the survey. The reasons for this were that 180 (24.7%) patients had a change of contact information, and 141 patients (19.4%) refused to participate. Of the 407 patients (56.5%) who were eligible for the survey, 94 patients (12.9%) were excluded because they had malignant mesothelioma of other sites, and 313 patients (43.0%) with malignant pleural mesothelioma were included in the study (Figure 1).

Data on malignant mesothelioma patients recognized through the asbestos injury relief system were obtained and analyzed. Demographic characteristics and asbestos exposure information were provided by the bereaved family in the case of death of the study subject, or by the subject himself/herself in the case of survivors, through a 1:1 interview method by a pre-trained researcher using a standardized asbestos health effect questionnaire. Asbestos exposure information such as occupational direct exposure and occupational indirect exposure, domestic exposure of other cohabiting families due to occupational exposure, outdoor environmental exposure, and indoor environmental exposure were identified. With the consent of the individual or his/her family members, the patient's medical records were analyzed, and the date of diagnosis, date of death, nature of the diagnosis, and treatment methods were investigated. The diagnosis of malignant mesothelioma was based on pathological biopsy (immunohistochemical test) data shown in the medical record, except in one case (by CT), and the diagnosis time was based on the date of the biopsy result. The survival period was from the time of diagnosis to the time of death, or in the case of survival, from the time of diagnosis to the time of investigation, March 2019.

The study variables were sex (male versus female), age at diagnosis (classification: <59, 60–69, ≥ 70), smoking history (yes, no), surgery (yes, no), chemotherapy (yes, no), occupational exposure to asbestos (yes, no), and histological subtype (epithelioid, nonep-

ithelioid). The effects of prognostic factors on the survival of patients with malignant mesothelioma were analyzed using the Kaplan–Meier method with univariate analysis and the Cox proportional hazards model with multivariate analysis of prognostic factors. Statistical significance was set at $p < 0.05$, and SPSS 26.0 (IBM, New York, NY, USA) was used for all analyses.

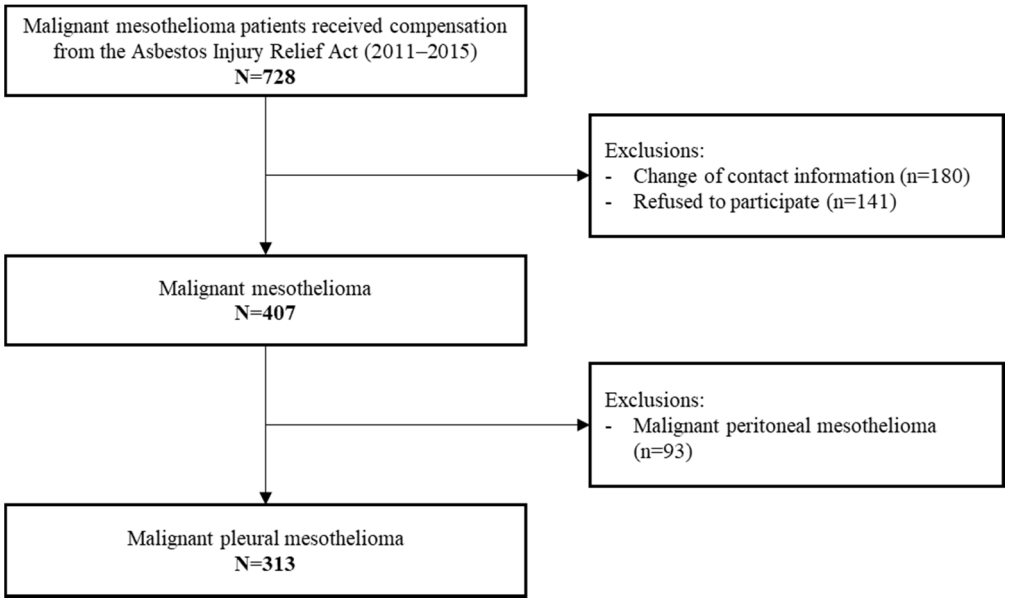

Figure 1. Flowchart showing the selection of study patients.

3. Results

Of 313 patients with malignant pleural mesothelioma, 216 were male (69.0%) and 97 were female (31.0%) (Table 1). The mean age at diagnosis of all subjects was 63.1 ± 12.0 years. In terms of age distribution, 94 people (30.0%) were in their 70s, followed by 92 people in their 60s (29.4%), 71 people in their 50s (22.7%), and 42 people in their 40s (13.4%). The mean survival period after diagnosis was 21.7 ± 33.0 months, and the median survival period was 8.0 months (95% confidence interval: 6.2–9.8). The 1-year, 2-year, and 5-year survival rates were 43.5%, 23.6%, and 12.5%, respectively. There were 159 cases of smoking history (50.8%) and 180 cases (57.5%) where asbestos exposure sources were occupational factors. However, 42.5% were non-occupational exposure. Among the subjects, 34.4% had surgery, and 71.6% had chemotherapy. The year of diagnosis was highest from 2011 to 2013 in 80 patients (25.6%), which coincided with when the Asbestos Injury Relief Act was enforced, and the lowest was from 2014 to 2016 with 32 patients (10.2%). Information on histological subtypes was available in 45.0% of patients. The most frequently observed subtype was epithelioid in 58.9%, sarcomatoid in 10.3%, biphasic in 13.7%, and NOS in 17.1% (Table 1).

Table 2 compares the median survival period according to factors affecting 5-year survival. The median survival period according to age group was 12.0 months (95% confidence interval: 8.3 to 15.7) in the age group under 59 years old; 11.0 months (95% confidence interval: 6.3 to 15.7) in the age group 60–69 years, and 6.0 months (95% confidence interval: 4.7 to 7.2) in the age group 70 years and older. There was a statistically significant difference according to age group ($p < 0.001$). The median survival time according to the surgery and chemotherapy groups ($n = 67$) was more than higher than those in the surgical group ($n = 28$), in the chemotherapy group ($n = 157$), and non-surgical and non-chemotherapy group ($n = 61$), respectively. However, there was no significant difference in the median survival time according to sex, smoking history, occupational exposure to asbestos, and histological subtype.

Table 1. General characteristics of the study subjects.

Variable	Malignant Pleural Mesothelioma N (%)
Sex	
Male	216 (69.0)
Female	97 (31.0)
Age(years)	
Mean ± SD [1]	63.1 ± 12.0
Median (95% CI [2])	64.0 (61.7, 64.4)
<50	42 (13.4)
50–59	71 (22.7)
60–69	92 (29.4)
70–79	94 (30.0)
≥80	14 (4.5)
Survival duration(months)	
Mean ± SD [1]	21.7 ± 33.0
Median (95% CI [2])	8.0 (6.2, 9.8)
Overall survival (% (95% CI [2]))	
1 year	43.5 (37.9, 49.0)
2 year	23.6 (18.9, 28.4)
5 year	12.5 (8.9, 16.1)
Smoking history	
No	154 (49.2)
Yes	159 (50.8)
Surgery	
No	218 (69.6)
Yes	95 (30.4)
Chemotherapy	
No	89 (28.4)
Yes	224 (71.6)
Year of diagnosis	
1997–2004	61 (19.5)
2005–2007	67 (21.4)
2008–2010	73 (23.3)
2011–2013	80 (25.6)
2014–2015	32 (10.2)
Occupational exposure	
No	133 (42.5)
Yes	180 (57.5)
Histological subtype	
Epiththelioid	86 (58.9)
Sarcomatoid	15 (10.3)
Biphasic	20 (13.7)
NOS	25 (17.1)

[1] standard deviation. [2] confidence intervals.

Table 2. The 5-year survival duration of malignant pleural mesothelioma according to potential prognostic factors.

Variable	Malignant Pleural Mesothelioma (n = 313)		
	n	5-Year Survival (Months) Median (95% CI [1])	*p*-Value [2]
Total subjects	313	8.0 (6.2, 9.8)	
Sex			
Male	216	8.0 (6.2, 9.8)	0.225
Female	97	9.0 (4.9, 13.1)	
Age(years)			

Table 2. *Cont.*

Variable	Malignant Pleural Mesothelioma (n = 313)		
	n	5-Year Survival (Months) Median (95% CI [1])	*p*-Value [2]
<60	113	12.0 (8.3, 15.7)	<0.001
60–69	92	11.0 (7.3, 15.7)	
≥70	108	6.0 (4.7, 7.2)	
Smoking history			
No	154	9.0 (6.0, 12.0)	0.790
Yes	159	8.0 (5.7, 10.3)	
Treatment			
Surgery and chemotherapy	67	23.0 (16.1, 29.9)	<0.001
Surgery only	28	8.0 (1.1, 14.9)	
Chemotherapy only	157	7.0 (5.7, 8.3)	
No surgery, no chemotherapy	61	3.0 (1.7, 4.3)	
Occupational exposure			
No	133	10.0 (6.5, 13.5)	0.163
Yes	180	8.0 (5.8, 10.2)	
Histological subtype			
Epithelioid	86	10.0 (6.8, 13.3)	0.342
Nonepithelioid	60	5.0 (2.8, 7.2)	

[1] confidence interval. [2] log-rank test.

Figure 2 compares the Kaplan–Meier curves of 5-year survival rates according to treatment methods. The survival rate of the combined surgical and chemotherapy group was significantly higher than that of the surgery group, chemotherapy group, and no treatment group ($p < 0.001$).

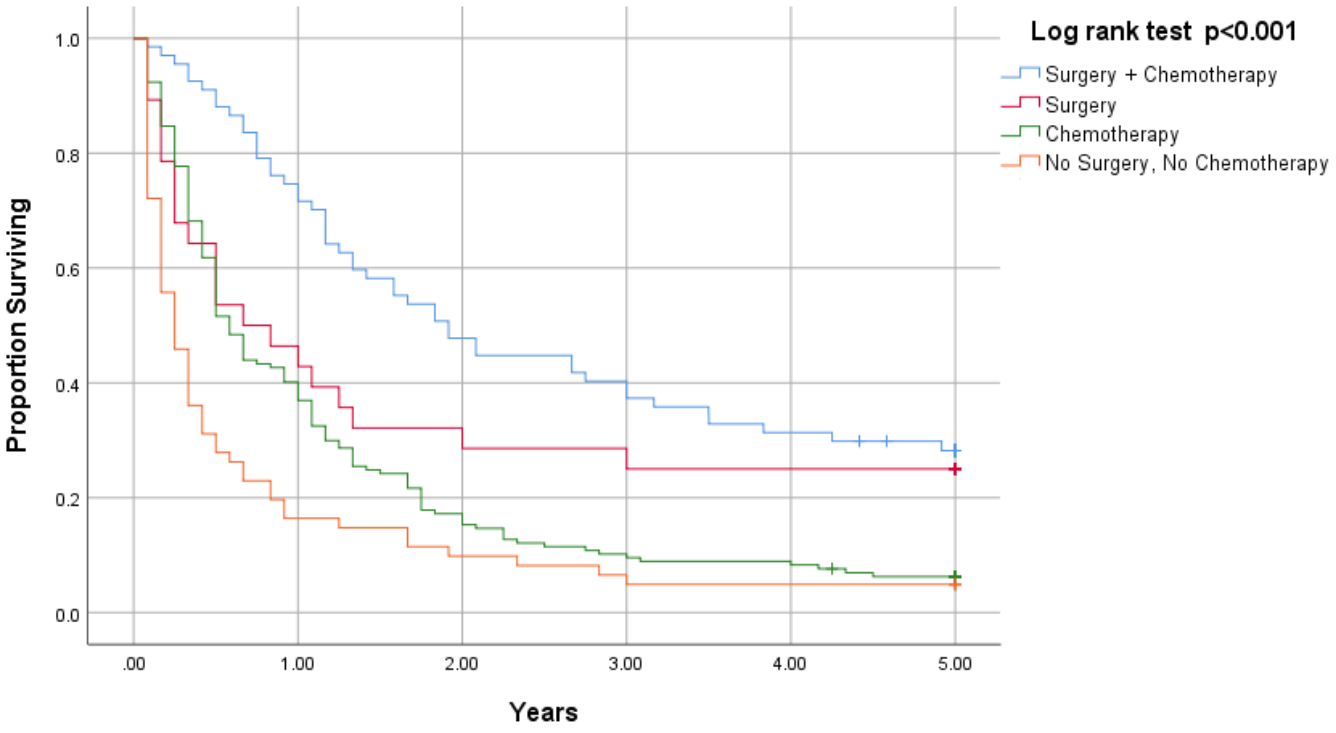

Figure 2. Kaplan–Meier curves among patients with malignant pleural mesothelioma by treatment methods.

Table 3 shows that based on multivariate analysis of Cox's proportional hazards model for 5-year survival, sex, age, smoking history, and histological subtype, and occupational asbestos exposure were not significant prognostic factors, but surgery and chemotherapy combined was a significant suitable predictor.

Table 3. Cox's proportional hazards analysis according to potential prognostic factors for 5-year survival of malignant pleural mesothelioma.

Variables	Adjusted HR (95% CI [1])	*p*-Value
Sex (0 = female, 1 = male)	1.48 (0.86, 2.54)	0.156
Age		
<60	Reference	
60–69	0.99 (0.61, 1.61)	0.969
≥70	1.35 (0.85, 2.12)	0.216
Smoking history (0 = no, 1 = yes)	0.77 (0.49, 1.20)	0.244
Occupational exposure (0 = no, 1 = yes)	1.17 (0.79, 1.76)	0.456
Treatment		
No surgery, no chemotherapy	Reference	
Surgery only	0.59 (0.29, 1.18)	0.132
Chemotherapy only	0.72 (0.44, 1.18)	0.186
Surgery and chemotherapy	0.28 (0.15, 0.53)	<0.001
Histological subtype (0 = Nonepithelioid, 1 = Epihelioid)	0.73 (0.50, 1.06)	0.102

[1] confidence interval.

4. Discussion

Korea's Asbestos Injury Relief System is intended to compensate people who have experienced environmental or occupational exposure to asbestos but have not received compensation for occupational accidents. Therefore, if there has been occupational exposure, but the victim cannot prove it, it may be included in the case of injury relief. Malignant mesothelioma resulting from asbestos exposure may be covered by the national occupational disease compensation system or civil action if occupational or environmental exposure can be clearly demonstrated. The Asbestos Injury Relief System was introduced to solve the problem that victims of asbestos-related diseases cannot receive compensation through the existing national occupational disease compensation system. The countries implementing asbestos victim relief schemes worldwide are France (2002), Japan (JPN) (2006), Belgium (2007), Netherland (2007), England (2008), and South Korea (2011) [9].

The results of previous studies on malignant mesothelioma in Korea are as follows. A total of 39 cases of malignant mesothelioma were approved as occupational diseases for 10 years from 2006 to 2015. Among them, 35 cases (89.7%) were male, and 4 cases (10.3%) were female. The primary sites of malignant mesothelioma were pleura 23 (59.0%), peritoneum 11 (28.2%), and the rest were other sites. The number of annual occurrences was less than 5. According to the malignant mesothelioma cancer registration, 361 males and 195 females were registered from 2009 to 2013, and if calculated per year, 72 males and 39 females [5]. According to the Korean Malignant Mesothelioma Surveillance System conducted from 2001 to 2012, 171 cases (65%) in men and 91 cases (35%) in women were reported from 2006 to 2010, with 34 cases per year for men and 18 cases for women [10]. Currently, the malignant mesothelioma monitoring system has been discontinued, and there is a limit to understanding the overall scale. Malignant mesothelioma, which received injury relief according to the Asbestos Injury Relief Act, was determined by the Asbestos Injury Judgment Committee, which consists of 10 people including respiratory internal medicine specialists, after collecting medical data of all cancer patients in the chest among domestic cancer registration data. Therefore, the number of malignant mesotheliomas reported to the government in our country is the sum of the number of patients recognized

by the Asbestos Injury Relief Act and the number of malignant mesothelioma patients recognized by occupational accidents. Therefore, in Korea, there are very few malignant mesotheliomas recognized as industrial accidents, and most of them are malignant mesotheliomas recognized by the Asbestos Injury Relief Act.

Malignant mesothelioma is a malignant tumor that occurs in the mesothelium due to asbestos fibers penetrating the pleura or peritoneum, with asbestos exposure representing a major risk factor [7]. However, malignant mesothelioma is difficult to diagnose, and there is often a delay in diagnosis. As a result, most malignant mesotheliomas are diagnosed at an advanced stage, and even with extensive treatment, the survival rate is low [8]. In this study, the median survival period of patients with pleural mesothelioma was 8.0 months (95% confidence interval: 6.2 to 9.8), which is less than one year. This is similar to other findings in that the prognosis is very poor at about one year [11–16]. However, some studies have reported median survival times greater than 1 year [17,18].

These differences in survival periods are thought to be influenced by the characteristics, including the stage, comorbidities, and the degree of treatment of the mesothelioma subjects.

In our study, the 1-year, 2-year, and 5-year survival rates of subjects were 43.5%, 23.6%, and 12.5%, respectively. Faig et al. [19] found that the 1-year, 2-year, and 5-year survival rates of 303 patients with malignant pleural mesothelioma were 73.1%, 22.9%, and 12.0%, respectively, which was higher at one year than in this study, but the 2-year survival rate was marginally lower than was seen in this study. In addition, in Carioli et al.'s study [20] of patients with malignant pleural mesothelioma, the 1-year, 2-year, and 5-year survival rates were 45.4%, 24.8%, and 9.6%, respectively, indicating that the 1-year and 2-year survival rates were slightly higher than in our study. However, the 5-year survival rate tended to be slightly lower. In the study of Montanaro et al. [12], the 5-year survival rate was 12.1% for pleural mesothelioma, which was similar to the 5-year survival rate of 12.5% in our study. In the study of Milano and Zhang [2], the 5-year survival rate of pleural mesothelioma was 5%, and in the study of Kanazawa et al. [16], the 5-year survival rate of pleural mesothelioma was 5.4% for men and 6.0% for women, both of which were lower than in this study. In addition, in the study of patients with malignant pleural mesothelioma by Iyoda et al. [21], the 1-year and 2-year survival rates were 48.8% and 23.3%, respectively, which were slightly higher than in our study, and the 2-year survival rates were similar. In the study of Beckett et al. [13], the 1-year survival rate was 41.4%, which was slightly lower than in this study. In the study of Edwards et al. [15], the 1-year and 2-year survival rates of patients with malignant pleural mesothelioma were 21.3% and 3.5%, respectively, which were lower than in this study.

The sex distribution of the subjects of this study was 69.0% male and 31.0% female. In general, diseases caused by occupational hazards tend to occur more frequently in men than in women [19]. However, among the prognostic factors affecting the survival of patients with malignant pleural mesothelioma in this study, sex was not a significant factor in Cox multivariate analysis. However, several studies have reported that sex is often associated with prognosis [2,22–27]. Most of these studies reported that women had higher survival rates, but in women, there is the possibility of early detection [28] and also the possibility of histologically suitable tumors [2]. In addition, women were more likely to have lower asbestos exposure or a slower progression [29]. It has also been suggested that women may enjoy a protective effect due to estrogen [27] and possibly a protective effect from the interaction between estrogen and the estrogen receptor in the tumor [30]. In a study by Amin et al. [31], women with malignant mesothelioma had a longer survival period than men, and they suggested that this may be due to a lower level of smoking in women or a different level of exposure to the environment. In a study by Kwak et al. [32], the sex ratio of malignant mesothelioma in Korea was about 1.9:1, and predominantly male. Studies in other countries have reported a sex ratio of 4 to 3:1 [12,18]. Jung et al. [10] found that the high percentage of women with malignant mesothelioma in Korea is because the percentage of cases exposed to environmental asbestos is relatively higher in women than in men, and women are less likely to be exposed to asbestos occupationally.

Age has also been found to be a very important determinant of survival in several studies. Montanaro et al. [12] stated that age is a very important factor in determining the survival of malignant mesothelioma and that the risk of death increases in the elderly. Most of the subjects of this study were between the ages of 50 and 79, and considering the incubation period of malignant mesothelioma, it is thought that this may be related to the high degree of asbestos use in Korea in the 1980s and 1990s. In the univariate analysis of this study, the risk of death increased in the group over 70 years old. The elderly had relatively poorer health conditions than the young, and in addition, have difficulty with invasive diagnostic procedures and are not able to be tested quickly upon suffering symptoms. Consequently, the survival of older people will be lower [12].

In this study, the exposure type was divided into occupational exposure or non-occupational exposure and compared. In the case of occupational exposure, it is known that asbestos concentration tends to be higher than that of non-occupational exposure [19,33,34]. In our study, non-occupational exposure has a similar prognosis to occupational asbestos exposure. Assessing asbestos exposure in home or environment is difficult. In addition, several areas exposed to naturally occurring asbestos substances have been shown to increase the incidence of mesothelioma. These different pathways of environmental asbestos exposure are poorly understood [35]. In the future, there should be studies to evaluate the importance of mesothelioma risk due to environmental exposure.

In our study, the median 5-year survival period for the surgery and chemotherapy group was 23 months, which was higher than the surgery alone group for 8 months, the chemotherapy group for 7 months, and the non-surgical and non-chemotherapy group for 3 months. In other studies, it is reported that the combination of surgery and chemotherapy increases the survival period of patients with malignant mesothelioma, as in our study [14,36]. Berzenji and Van Schil [37] also reported that the median survival time for untreated pleural mesothelioma was 6–9 months.

In a study by Taioli et al. [26] on malignant mesothelioma, young age, female, early stage, and surgery were suitable prognostic factors. Montanaro et al. [12] also revealed young age, epithelial histological type, and female sex as suitable prognostic factors in a multivariate analysis of patients with malignant pleural mesothelioma. In Cox's proportional hazards multivariate model, sex, age, and smoking history were not all significant prognostic factors for 1-, 2-, and 5-year survival, but the group that underwent surgery had a 5-year survival rate that was 2.28 (95% CI: 1.78–2.94) times higher than the group that did not. Meyerhoff et al. [38] reported that histological subtype (epithelial shape) and stage (early stage) were associated with improved survival after surgery in malignant pleural mesothelioma. Based on all of this, in order to compare the survival of patients with malignant mesothelioma, it is necessary to analyze the differences in characteristics between subjects, that is, age, sex, histology, stage, treatment regimen, etc. carefully. However, patients with pleural malignant mesothelioma are often diagnosed at an advanced stage, and although treatment methods are still being developed, there are many cases where the detection is late, and the treatment effect may be low. Enewold et al. [14] reported that the elderly among pleural mesothelioma patients were less likely to receive treatment. These results suggest that malignant mesothelioma was detected at an early stage, and there were many single tumors that did not spread. In addition, it is judged that surgery will be selected according to the patient's overall set of clinical conditions such as lung and heart function and comorbidities.

The main treatments for malignant pleural mesothelioma are surgery, chemotherapy, and radiation therapy [7]. Surgical methods include extrapleural pneumonectomy and pleurectomy/decortication, and chemotherapy is usually a combination of platinum-based chemotherapy and folic acid antimetabolites. Recently, immunotherapy is emerging as a possible treatment option. Single-modality therapy is not an effective treatment strategy for malignant mesothelioma. Combinations of surgery, chemotherapy, immunotherapy, and RT are being explored by researchers as a variety of complex therapies [37]. There is still no definitive answer as to which combination treatment combination is most effec-

tive [8]. In this study, we tried to see the effect of two combination therapies: surgery and chemotherapy. As a result, it was found that the combination of surgery and chemotherapy had a better effect on survival rate than surgery or chemotherapy alone. Future studies will need to add a combination of radiation therapy and immunotherapy.

However, treatment options such as surgery are selected based on a combination of factors such as the patient's performance status, lung and heart function, comorbidities, and stages contributing to survival, unfortunately not in our study data. Therefore, although the analysis was conducted in consideration of age, sex, and histological type, there is a limitation in that the influence of the above factors was not considered.

It has been 10 years since the asbestos injury relief scheme was launched. Although the use of asbestos products has been banned in Korea, the number of malignant mesothelioma patients is expected to continue to increase. Asbestos injury relief data will be accumulated as a large amount of data that provides important clues about the epidemiologic characteristics of malignant mesothelioma caused by asbestos exposure in Korea. However, there are limitations in revealing the exact epidemiological characteristics and prognostic factors due to limitations in the representativeness of the data, but it can be used as basic data for policy decisions on the management of malignant mesothelioma in the future.

Our study had several limitations. This study is based on data from 5 years after the enforcement of the Asbestos Injury Relief Act. In addition to patients with malignant mesothelioma, bereaved family members were able to participate in the interview, and recall bias could occur during the exposure history investigation process. In addition, there are cases where contact cannot be made due to death or other reasons, which may reduce the representativeness of asbestos injury relief data. In addition, our data do not show the incidence of malignant mesothelioma in the entire Korean population, and industrial accident compensation data are excluded. Therefore, there is a limit to the generalization of the interpretation of the results. Since these data on asbestos injury were not obtained for research from the beginning, there is also a problem with the integrity of the data. Histological subtype data were available in only 46.6% of 313 patients. These points should be supplemented in future studies

5. Conclusions

Although the representativeness of these data is limited, our study estimates the epidemiologic characteristics of malignant pleural mesothelioma. Non-occupational exposure had a similar prognosis to occupational asbestos exposure, and there was no sex difference. In addition, it was found that receiving a combination of surgery and chemotherapy affects the survival rate, but there is a limitation in that factors such as performance status, comorbidities, and stage that contribute to survival are not considered.

Author Contributions: Conceptualization, M.-S.K. and S.-S.L.; methodology, M.-S.K. and S.-S.L.; validation, S.-C.K.; formal analysis, S.-S.L.; investigation, M.-S.K., D.-A.H. and Y.-J.L.; writing—original draft preparation, S.-S.L. and S.-C.K.; writing—review and editing, M.-S.K. and D.-A.H.; project administration, Y.-J.L.; funding acquisition, M.-S.K. and Y.-J.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The institutional review board of Soonchunhyang University Cheonan Hospital approved the collection and use of data for this study (2009-04-001).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The entire data of this study cannot be shared publicly because it contains sensitive patient information and location data. Researchers must inform the Research Ethics Committee of their research's purpose and obtain approval for access to the data. For data inquiries about this research, you can contact or send an e-mail to the administrator from the ethics committee of Soonchunhyang University Cheonan Hospital. E-mail: schcarib@schmc.ac.kr.

Acknowledgments: This research was supported by the Ministry of Environment (Environmental Health Center for Asbestos) and the Soonchunhyang University Research Fund.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Kim, H.R.; Ahn, Y.-S.; Jung, S.-H. Epidemiologic Characteristics of Malignant Mesothelioma in Korea. *J. Korean Med. Assoc.* **2009**, *52*, 449. [CrossRef]
2. Milano, M.T.; Zhang, H. Malignant pleural mesothelioma: A population-based study of survival. *J. Thorac. Oncol.* **2010**, *5*, 1841–1848. [CrossRef] [PubMed]
3. Koo, J.-W.; Kim, H.R. Occupational and Environmental Asbestos Exposure in Korea. *J. Korean Med. Assoc.* **2009**, *52*, 442–448. [CrossRef]
4. Kwak, K.; Cho, S.-I.; Paek, D. Future Incidence of Malignant Mesothelioma in South Korea: Updated Projection to 2038. *Int. J. Environ. Res. Public Health* **2021**, *18*, 6614. [CrossRef] [PubMed]
5. An, Y.S.; Kim, H.D.; Kim, H.C.; Jeong, K.S.; Ahn, Y.S. The characteristics of asbestos-related disease claims made to the Korea Workers' Compensation and Welfare Service (KCOMWEL) from 2011 to 2015. *Ann. Occup. Environ. Med.* **2018**, *30*, 45. [CrossRef]
6. Ahn, Y.-S.; Kang, S.-K. Asbestos-related Occupational Cancers Compensated under the Industrial Accident Compensation Insurance in Korea. *Ind. Health* **2009**, *47*, 113–122. [CrossRef] [PubMed]
7. Taioli, E.; Wolf, A.S.; Flores, R.M. Meta-analysis of survival after pleurectomy decortication versus extra-pleural pneumonectomy in mesothelioma. *Ann. Thorac. Surg.* **2015**, *99*, 472–480. [CrossRef] [PubMed]
8. Treasure, T.; Lang-Lazdunski, L.; Waller, D.; Bliss, J.M.; Tan, C.; Entwisle, J.; Snee, M.; O'Brien, M.; Thomas, G.; Senan, S.; et al. Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: Clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomized feasibility study. *Lancet Oncol.* **2011**, *12*, 763–772. [CrossRef]
9. Lee, K.; Godderis, L.; Furuya, S.; Kim, Y.; Kang, D. Comparison of Asbestos Victim Relief Available Outside of Conventional Occupational Compensation Schemes. *Int. J. Environ. Res. Public Health* **2021**, *18*, 5236. [CrossRef]
10. Jung, S.-H.; Kim, H.-R.; Koh, S.-B.; Yong, S.-J.; Chung, M.J.; Lee, C.-H.; Han, J.; Eom, M.-S.; Oh, S.-S. A decade of malignant mesothelioma surveillance in Korea. *Am. J. Ind. Med.* **2012**, *55*, 869–875. [CrossRef]
11. Moore, A.J.; Parker, R.J.; Wiggins, J. Malignant mesothelioma. *Orphanet J. Rare Dis.* **2008**, *3*, 1–11. [CrossRef]
12. Montanaro, F.; Rosato, R.; Gangemi, M.; Roberti, S.; Ricceri, F.; Merler, E.; Gennaro, V.; Romanelli, A.; Chellini, E.; Pascucci, C.; et al. Survival of pleural malignant mesothelioma in Italy: A population-based study. *Int. J. Cancer* **2009**, *124*, 201–207. [CrossRef]
13. Beckett PEdwards, J.; Fennell, D.; Hubbarde, R.; Woolhouse, I. Demographics, management and survival of patients with malignant pleural mesothelioma in the National Lung Cancer Audit in England and Wales. *Lung Cancer* **2015**, *88*, 344–348. [CrossRef]
14. Enewold, L.; Sharon, E.; Thomas, A. Patterns of care and survival among patients with malignant mesothelioma in the United States. *Lung Cancer* **2017**, *112*, 102–108. [CrossRef]
15. Edwards, J.G.; Abrams, K.; Leverment, J.N.; Spyt, T.J.; Waller, D.A.; O'Byrne, K.J. Prognostic factors for malignant mesothelioma in 142 patients: Validation of CALGB and EORTC prognostic scoring systems. *Thorax* **2000**, *55*, 731–735. [CrossRef]
16. Kanazawa, N.; Ioka, A.; Tsukuma, H.; Ajiki, W.; Oshima, A. Incidence and Survival of Mesothelioma in Osaka, Japan. *Jpn. J. Clin. Oncol.* **2006**, *36*, 254–257. [CrossRef] [PubMed]
17. Chouaid, C.; Assié, J.B.; Andujar, P.; Blein, C.; Tournier, C.; Vainchtock, A.; Scherpereel, A.; Monnet, I.; Pairon, J.C. Determinants of malignant pleural mesothelioma survival and burden of disease in France: A national cohort analysis. *Cancer Med.* **2018**, *7*, 1102–1109. [CrossRef] [PubMed]
18. Wu, T.-H.; Lee, L.J.-H.; Yuan, C.-T.; Chen, T.W.-W.; Yang, J.C.-H. Prognostic factors and treatment outcomes of malignant pleural mesothelioma in Eastern Asian patients—A Taiwanese study. *J. Formos. Med. Assoc.* **2018**, *118 Pt 2*, 230–236. [CrossRef]
19. Faig, J.; Howard, S.; Levine, E.A.; Casselman, G.; Hesdorffer, M.; Ohar, J.A. Changing Pattern in Malignant Mesothelioma Survival. *Transl. Oncol.* **2015**, *8*, 35–39. [CrossRef] [PubMed]
20. Carioli, G.; Bonifazi, M.; Rossi, M.; Zambelli, A.; Franchi, M.; Zocchetti, C.; Gasparini, S.; Corrao, G.; La Vecchia, C.; Negri, E. Management and Survival of Pleural Mesothelioma: A Record Linkage Study. *Respiration* **2018**, *95*, 405–413. [CrossRef]
21. Iyoda, A.; Yusa, T.; Kadoyama, C.; Sasaki, K.; Kimura, H.; Yamakawa, H.; Shiba, M.; Fujisawa, T.; Yoshino, I. Diffuse malignant pleural mesothelioma: A multi-institutional clinicopathological study. *Surg. Today* **2008**, *38*, 993–998. [CrossRef]
22. Alpert, N.; van Gerwen, M.; Flores, R.; Taioli, E. Gender differences in outcomes of patients with mesothelioma. *Am. J. Clin. Oncol.* **2020**, *43*, 792–797. [CrossRef]
23. Van Gerwen, M.; Alpert, N.; Wolf, A.; Ohri, N.; Lewis, E.; Rosenzweig, K.E.; Flores, R.; Taioli, E. Prognostic factors of survival in patients with malignant pleural mesothelioma: An analysis of the National Cancer Database. *Carcinogenesis* **2019**, *40*, 529–536. [CrossRef]
24. Flores, R.M.; Zakowski, M.; Venkatraman, E.; Krug, L.; Rosenzweig, K.; Dycoco, J.; Lee, C.; Yeoh, C.; Bains, M.; Rusch, V. Prognostic Factors in the Treatment of Malignant Pleural Mesothelioma at a Large Tertiary Referral Center. *J. Thorac. Oncol.* **2007**, *2*, 957–965. [CrossRef] [PubMed]

25. Flores, R.M.; Riedel, E.; Donington, J.S.; Alago, W.; Ihekweazu, U.; Krug, L.; Rosenzweig, K.; Adusumilli, P.S.; Carbone, M.; Pass, H.I. Frequency of Use and Predictors of Cancer-Directed Surgery in the Management of Malignant Pleural Mesothelioma in a Community-Based (Surveillance, Epidemiology, and End Results [SEER]) Population. *J. Thorac. Oncol.* **2010**, *5*, 1649–1654. [CrossRef] [PubMed]
26. Taioli, E.; Wolf, A.S.; Camacho-Rivera, M.; Flores, R.M. Women With Malignant Pleural Mesothelioma Have a Threefold Better Survival Rate Than Men. *Ann. Thorac. Surg.* **2014**, *98*, 1020–1024. [CrossRef] [PubMed]
27. Wolf, A.S.; Richards, W.G.; Tilleman, T.R.; Chirieac, L.; Hurwitz, S.; Bueno, R.; Sugarbaker, D.J. Characteristics of Malignant Pleural Mesothelioma in Women. *Ann. Thorac. Surg.* **2010**, *90*, 949–956. [CrossRef] [PubMed]
28. Yan, T.; Popa, E.; Brun, E.A.; Cerruto, C.A.; Sugarbaker, P.H. Sex difference in diffuse malignant peritoneal mesothelioma. *BJS* **2006**, *93*, 1536–1542. [CrossRef]
29. Hillerdal, G. Mesothelioma: Cases associated with non-occupational and low dose exposures. *Occup. Environ. Med.* **1999**, *56*, 505–513. [CrossRef]
30. Pinton, G.; Brunelli, E.; Murer, B.; Puntoni, R.; Puntoni, M.; Fennell, D.A.; Gaudino, G.; Mutti, L.; Moro, L. Estrogen receptor-beta affects the prognosis of human malignant mesothelioma. *Cancer Res.* **2009**, *69*, 4598–4604. [CrossRef]
31. Amin, W.; Linkov, F.; Landsittel, D.P.; Silverstein, J.C.; Bashara, W.; Gaudioso, C.; Feldman, M.D.; Pass, H.I.; Melamed, J.; Friedberg, J.S.; et al. Factors influencing malignant mesothelioma survival: A retrospective review of the National Mesothelioma Virtual Bank cohort. *F1000Research* **2018**, *7*, 1184. [CrossRef]
32. Kwak, K.M.; Paek, D.; Hwang, S.-S.; Ju, Y.-S. Estimated future incidence of malignant mesothelioma in South Korea: Projection from 2014 to 2033. *PLoS ONE* **2017**, *12*, e0183404. [CrossRef]
33. Metintas, S.; Metintas, M.; Ucgun, I.; Oner, U. Malignant mesothelioma due to environmental exposure to asbestos: Follow-up of a Turkish cohort living in a rural area. *Chest* **2002**, *122*, 2224–2229. [CrossRef]
34. Lacourt, A.; Gramond, C.; Rolland, P.; Ducamp, S.; Audignon, S.; Astoul, P.; Chamming'S, S.; Ilg, A.G.S.; Rinaldo, M.; Raherison, C.; et al. Occupational and non-occupational attributable risk of asbestos exposure for malignant pleural mesothelioma. *Thorax* **2014**, *69*, 532–539. [CrossRef] [PubMed]
35. Noonan, C.W. Environmental asbestos exposure and risk of mesothelioma. *Ann. Transl. Med.* **2017**, *5*, 234. [CrossRef] [PubMed]
36. Nelson, D.B.; Rice, D.C.; Niu, J.; Atay, S.; Vaporciyan, A.A.; Antonoff, M.; Hofstetter, W.L.; Walsh, G.L.; Swisher, S.G.; Roth, J.A.; et al. Long-Term Survival Outcomes of Cancer-Directed Surgery for Malignant Pleural Mesothelioma: Propensity Score Matching Analysis. *J. Clin. Oncol.* **2017**, *35*, 3354–3362. [CrossRef]
37. Berzenji, L.; Van Schil, P. Multimodality treatment of malignant pleural mesothelioma. *F1000Research* **2018**, *7*, 1681. [CrossRef] [PubMed]
38. Meyerhoff, R.R.; Yang, C.-F.J.; Speicher, P.J.; Gulack, B.C.; Hartwig, M.G.; D'Amico, T.A.; Harpole, D.H.; Berry, M.F. Impact of mesothelioma histologic subtype on outcomes in the Surveillance, Epidemiology, and End Results database. *J. Surg. Res.* **2015**, *196*, 23–32. [CrossRef] [PubMed]