Clinical-pathological Characteristics and Prognostic Factors for Malignant Peritoneal Mesothelioma in the Elderly

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Research Article

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Abstract

Background: Malignant peritoneal mesothelioma (MPM) is a rare disease characterized by atypical symptoms, difficult diagnosis, variable course and poor prognosis, and it develops mainly in the elderly. The authors aimed to identify the clinical-pathological characteristics, prognosis, and prognostic factors in the elderly MPM patients.

Methods: From the National Cancer Institute Surveillance Epidemiology End Results (SEER) database, 1492 patients with MPM from 1975 to 2016 were selected and divided into the elderly group (≥65) and the adult group (<65). We compared the clinical-pathological characteristics and treatment methods of elderly group (N=665) and adult group (N=827). At the same time, we analyzed specific selected clinical-pathological parameters and prognostic factors for the elderly MPM patients.

Results: Compared with the adult group, the elderly group had a higher percentage of male patients (P = 0.017), white patients (P = 0.043), a lower proportion of insured patients (P < 0.001), married patients (P < 0.001), patients with peritoneal tumors (P = 0.006), patients who underwent surgery (P < 0.001), and chemotherapy (P < 0.001). There was a significant difference in the differentiation grade between the two groups (P = 0.003). The elderly patients had a shorter median survival time compared with the adult patients (6 months vs 19 months). Uninsured (hazard ratio (HR): 5.187, P = 0.005), sarcomatoid type (HR: 3.913, P <0.001), poorly differentiated (HR: 3.900, P < 0.001), distant metastasis (HR: 1.735, P = 0.001), no cancer-directed surgery (HR: 1.733, P < 0.001), and no chemotherapy (HR: 1.532, P < 0.001) were independently associated with poorer prognosis of elderly MPM patients.

Conclusion: Compared with the adult patients, elderly MPM patients had higher male ratio, poor differentiation and relatively conservative treatment. The cancer-specific survival (CSS) rate of elderly MPM patients was significantly lower than that of adult patients. Insurance status, histology type, differentiation grade, stage, surgery status, and chemotherapy status were all independent prognostic factors for elderly MPM patients.

Introduction

Malignant Mesotheliomas (MM) are aggressive tumors arising from serous surfaces: pleura (65%-70%), peritoneum (30%), tunica vaginalis testis, and pericardium (1%-2%)[1]. Occupational or environmental exposures to asbestos were considered to be the pathogenic factors [2], the annual number of MM deaths is increasing, particularly among persons aged above 85 years old, most likely representing exposure many years ago [3]. As a subgroup of MM, Malignant peritoneal mesothelioma (MPM) is a rare cancer originating from the mesothelial and epithelioid tissues inside the patient's abdominal cavity and was first identified by Miller and Wynn in 1908[4]. SV 40 virus, radiation could also be implicated as factors favoring the development of peritoneal mesothelioma [5–7]. About 1–2 in a million people are diagnosed with MPM each year, with an annual incidence in the United States of 200–300 new cases[1]. The patients are mainly elderly, with median diagnosis age of 64 years[8], and the incidence rate in the elderly

has been on the rise in recent years[9]. Previous reports have found that approximately 40–60% of patients have metastases at the time of diagnosis, and the median survival time for untreated patients is less than 1 year[1, 8, 10]. It was demonstrated that age is an important prognostic factor of MPM, and adult patients generally had a better prognosis than elderly patients, with a significantly longer median survival time[10, 11]. Moreover, gender[12–14], histology type[8, 13, 15–18], tumor stage[10, 19, 20], differentiation grade[20], and surgery status[8, 14, 21, 22] were also regarded as independent prognostic factors for MPM, but the results varied from study to study.

However, there were not many studies on the clinical-pathological characteristics and prognostic factors of the elderly patients. Therefore, in this study, we selected patients from the Surveillance, Epidemiology and End Results (SEER) database[23]. With these patients, we studied a number of selected clinical-pathological and treatment characteristics of the adult and elderly patients as well as the 1-, 3- and 5-year cancer-specific survival (CSS). Then, we identified the prognostic factors that were associated with CSS in the elderly MPM patients.

Materials And Methods

Data source and study subjects

A retrospective case series analysis was performed using the SEER database. The database records patients' basic information, diagnosis basis, stage and grade, treatment plan, follow-up time and cause of death, covering about 28% of cancer patients in the United States, providing valuable oncology data for medical researchers worldwide.

Patients with pathologically confirmed MPM were enrolled from 1975 to 2016 using ICD-O-3 histology codes 9050-9053 (mesothelioma, malignant) combined with site codes 48.0, retroperitoneum; 48.1, specified parts of the peritoneum; 48.2, peritoneum not otherwise specified; 48.8, overlapping lesion of retroperitoneum & peritoneum). Patients that had other malignancies or didn’t have active follow-up since the time of MPM diagnosis were excluded from our study cohort. Based on the criterions, our study cohort consisted of a total of 1,492 MPM patients.

Demographic variables of interest to our study included gender, race, age, marital status, and insurance status; clinical data of interest included the status of surgery, radiotherapy, chemotherapy, and survival time (since MPM diagnosis until cause-specific death (CSD), as of December 31, 2016, in months); pathological characteristics of interest included histology type, differentiation grade, and tumor stage.

For marital status, “Separated”, “Divorced”, “Single”, and “Widowed” were clustered as the “Unmarried” group; for insurance status, patients with “Any Medicaid”, “Insured”, or “Insured/No specifics” were regarded as the “Insured” group. Tumor staging were classified into 4 groups: “Localized”, “Regional”, “Distant”, and “Unknown”.

Statistical Methods

Statistical analyses were performed using the SPSS software (version 26.0). The study subjects were stratified by age into two groups, the adult group (<65) and the elderly group (≥65). Using Student's t test and Chi-square (c2) test, selected clinical-pathological and treatment characteristics were compared between the adult and elderly groups as well as between the males and females in the elderly group. CSS rate was determined by the Kaplan-Meier method, the differences in CSS rates was determined by the 2-sided log-rank test. Cox proportional hazards analysis was performed to assess the independent risk factors of CSD in elderly group. All P values were two-sided, and $P < 0.05$ was considered to be statistically significant.

Results

Patient clinical-pathological and treatment characteristics

From 1975 to 2016, a total of 1,492 MPM patients were identified from the SEER registry, there were 665 individuals in elderly group (≥65). Baseline characteristics of the selected patients are summarized in Table 1. Compared with the adult group, the elderly had a higher percentage of males (58.80% > 52.60%, $P = 0.017$) and the white race (92.63% > 89.12%, $P = 0.043$); a lower proportion of insured patients (35.94% < 38.21%, $P < 0.001$), married patients (59.85% < 60.78%, $P < 0.001$), and patents with peritoneum tumor (94.74% < 97.58%, $P = 0.006$). The differentiation grade in elderly patients was relatively worse than that in adult patients ($P = 0.003$), the ratio of well differentiated patients (4.96% < 10.16%) and moderately differentiated patients (1.65% < 2.06%) was lower than that in adult patients, and the ratio of poorly differentiated patients was higher than that in adult patients (7.22% > 5.68%). Surgery (33.38% < 47.88%, $P < 0.001$) and chemotherapy (44.21% < 59.7%, $P < 0.001$) incidence was less common in elderly than in adult patients.

The clinical-pathological characteristics of the elderly patients

There were 391 (58.80%) males and 274 (41.20%) females in the elderly group. For the elderly MPM patients, the comparison of selected clinical-pathological characteristics between males and females was shown in Table 2. Compared with female patients, most of the male patients were diagnosed with MPM at younger age (73.68 vs 75.28, $P = 0.002$). There were a higher percentage of males than females who underwent surgery (44.53% vs 25.58%, $P < 0.001$).

Survival differences

As of December 31, 2016, a total of 549 patients in the elderly group (N=665) died. The median survival time was six months, the 1-,3- and 5-year CSS rate in the adult and elderly patients are shown in Table 3.The elderly patients had a significantly poorer survival than the adult ($P < 0.001$, Figure 1).

The median survival time and the 1-, 3- and 5-year CSS rate in the different groups of elderly MPM patients were shown in Table 4. The 1-, 3- and 5-year CSS of male patients were 31.46%, 15.73%, and 10.88%, respectively, which were lower than those of female patients. The patients with distant

metastasis had the lowest CSS rate compared with other groups in the same category ($P < 0.001$). The patients who had done surgery for MPM had a higher 5-CSS rate than those who did not (19.14% vs. 8.76%).

Univariate and multivariate analysis of risk factors for CSS rates of the elderly MPM patients

Factors that were associated with CSS of elderly patients included gender ($P = 0.006$, Figure 2a), insurance status ($P = 0.001$, Figure 2b), marital status ($P = 0.046$, Figure 2c), histology type ($P < 0.001$, Figure 2d), differentiation grade ($P < 0.001$, Figure 2e), tumor stage ($P < 0.001$, Figure 2f), surgery status ($P < 0.001$, Figure 2g) and chemotherapy status ($P < 0.001$, Figure 2h). The race (Figure 2i), lesion site (Figure 2j), and radiotherapy status (Figure 2k) were not associated with the CSS of elderly patients according to our study.

Then, these associating variables were included in multivariate analysis, cox proportional hazards analysis showed that insurance status ($P = 0.001$, Figure 3a), histology type ($P < 0.001$, Figure 3b), differentiation grade ($P < 0.001$, Figure 3c), tumor stage ($P < 0.001$, Figure 3d), surgery status ($P < 0.001$, Figure 3e), and chemotherapy status ($P < 0.001$, Figure 3f) were all independent prognostic factors for elderly MPM patients. As the Table 5 shown, compared with the insured patients, the uninsured group had a higher risk of developing CSD (hazard ratio (HR): 5.187, $P = 0.005$). Notably, the elderly MPM patients with biphasic and sarcomatoid types had a higher risk of CSD compared to those with epithelioid type (biphasic type, HR: 2.279, $P = 0.002$; sarcomatoid type, HR: 3.913, $P < 0.001$). The poorly differentiated and undifferentiated patient had a lower CSS rate (poorly differentiated, HR: 3.900, $P < 0.001$; undifferentiated, HR: 2.430, $P = 0.041$) than well differentiated patients. Distant metastasis was a risk factor to poor prognosis (HR: 1.735, $P = 0.001$). No surgery group had 1.733 times the CSD risk of surgery group. Moreover, patients in no chemotherapy or unknown group had 53.2% higher risk than those underwent chemotherapy.

Discussion

MPM is a rare aggressive tumor, regarded as a universally fatal disease. Despite the regulatory actions and the reduction in using of asbestos, the annual number of MPM deaths remained substantial[9, 10, 24]. The elderly made up the majority of the patients, it has been shown that elderly patients have a poorer prognosis than adult patients[10, 11, 15]. Our study combined with SEER database to conduct an in-depth analysis of elderly MPM patients.

Among our study population, the number of male patients was higher than females, similar to the results of the previous studies, to explain such a gender difference, it has been proposed that compared with women, men have more occupational exposure to asbestos, thereby leading to a higher incidence in males[25, 26]. Different from previous studies, in our study, the elderly patients had a larger proportion of male than the adults group (58.80% vs 52.60%), while a multinational multi-center study published in 2011 suggested a prominent higher proportion of men aged 55 and below than patients over 55 (59% vs 41%)[27].The reason may be that all cases in this study were taken from the SEER database, which is

only a collection of data from 18 regions in the U.S. mainland, there are some regional limitations to the results.

Due to the low incidence and the shortage of studies based on large sample cases in various regions, there are not many data on survival analysis of MPM patients, moreover, the results of different regional studies are inconsistent, but the general survival time without treatment is less than 1 year. Salo Sas et al[28]. reported a median survival of only 4 months for 90 MPM patients in Finland between 2000 and 2012. John T. Miura et al. suggested a median overall survival of 9 months[29], and V. de Pangher Manzini et al. showed an even longer survival of 13 months[16]. As for the survival comparison between elderly and adult patients, the elderly was found to be associated with a worse survival[12, 15]. However, Cao C, et al. had shown that there was no statistical difference of the survival time between male MPM patients older than 55 and younger than 55[27]. In this study, elderly patients showed shorter median survival time than adults (6 months vs 19 months), and the survival rate was significant lower than adults. Considering the reasons, maybe it's because that the elderly generally has, compared with the adults, weaker health, more age-dependent physiological changes, as well as more complications, and tend to palliative treatment.

It was found that females with MPM generally had better outcomes than males, without considering age, time to diagnosis, and histology type[13, 27]. A 2018 case study showed that female patients had a higher 5-year survival rate than male (33% > 12%)[15]. Similarly, in this study, the median survival time of female MPM patients in the elderly group was 9 months, longer than male (5 months). Further analysis revealed that only 25.58% of elderly male patients underwent surgery, while 44.53% of female patients did, suggesting that females can receive more aggressive and effective treatment than males.

Several tumor-related studies suggested that married patients' prognosis was better than singles because of earlier disease detection, better financial support and more health care resources[29–31]. Contrary to our expectation, in this study, the married patients had a shorter median survival time and slightly lower CSS than unmarried group. After further analysis, we found the majority of married patients were male (72.11%), and women accounted for most of the unmarried patients (61.34%) in our study. With this in consideration, we may explain why married patients' prognosis was worse in our study.

Consistent with previous study, histology type[10, 21, 32] and differentiation grade[14] were found as independent prognostic factors for the elderly MPM patients. Patients with epithelioid type had the most favorable outcome, while those with biphasic and sarcomatoid type had the worse one (HR: 2.279; 3.913). The risk of CSD in moderately differentiated, poorly differentiated and undifferentiated patients was 0.978, 2.900 and 1.430 times higher than that in well differentiated patients, respectively.

At present, there is no matured TNM staging system for MPM. Yan et al. proposed a set of TNM staging system for diffuse malignant peritoneal mesothelioma in 2010 [33]. SEER database divide the patients into localized staging group, regional staging group and distant metastasis group. It was shown that 40–60% of MPM patients had distant metastasis at the time of detection[8, 10], consistent with our finding (50%). Our results showed that the 5-year CSS rates of the elderly MPM patients in localized, regional, and

distant stage were 22.75%, 18.47% and 8.38%, respectively. Distant metastasis is independently associated with poor survival.

For treatment, the effect of radiotherapy for MPM patients is not clear. Silja A.S. Salo et al. showed that for patients who were treated with radiotherapy alone[22], the median survival time was 2 months and a 1-year CSS rate was 20%. Our study shows that patients who had radiotherapy or not (including unknown group) had the same median survival time for 6 months, the results showed that radiation therapy has no obvious effect on the prognosis of elderly MPM patients.

In this study, only 33.38% of all elderly MPM patients underwent surgery, consistent with Anish Thomas' report in 2015 (32%) [12]. Surgery interventions have been proved to associate with better outcome[14]. We observed that the 5-year survival rate of the patients who underwent surgery were higher than that of those who didn't (19.14% vs 8.76%). No surgery group had 1.733 times the CSD risk of surgery group, surgery was the treatment option to improve prognosis. But, elderly patients mostly have multiple and complex underlying diseases and tend to palliative treatment.

Chemotherapy is often combined with surgery to treat MPM, which can be delivered in the form of heated intraperitoneal chemotherapy (HIPEC). Nagata Y et al. found that cisplatin plus pemetrexed showed consistent efficacy with MPM[34], which can be recommended as first-line treatment for unresectable MPM. Yan et al. reported the median survival of 56 months for 372 patients who received HIPEC and 23 months for those who did not (P = 0. 049) [21]. However, some studies had shown that systemic chemotherapy had no positive effect on the prognosis of MPM patients[35]. In this study, patients receiving chemotherapy showed longer median survival time than those did not or unsure (13 months vs 10 months). About 44.21% elderly patients underwent chemotherapy, far more than surgery or radiotherapy. Multivariate analysis demonstrated that chemotherapy was independently associated with improved survival outcomes.

At present, cytoreductive surgery (CRS) combined with HIPEC as the first-line treatment of MPM has been proved to improve the prognosis of MPM patients[36–40]. A systematic review and meta-analysis showed patients receiving CRS and HIPEC had a median survival time of 29.5–100 months, much longer than that of untreated patients[41]. CRS surgery is suitable for patients below 75 years age without distant metastasis, and no contraindication signs of operation[42]. However, the elderly patients who can meet the above conditions are not many. In addition, Deepa Magge et al. found that there may be no benefit gained from CRS-HIPEC in the sarcomatoid type and biphasic groups, compared to those with epthelioid type[19]. Thus, more clinical studies on elderly MPM patients are necessary.

The Limitations In This Study

However, several limitations in our study should be considered. First, the SEER database does not clearly distinguish patients who didn't receive chemotherapy or radiotherapy and those who don't know whether or not they received these, we can't determine the effect of chemotherapy or radiotherapy on elderly MPM patients more precisely. Second, there are no specific chemotherapy regimens in SEER, so the influence of

different chemotherapy regimens on prognosis cannot be studied. Third, for the variables of histology type and differentiation grade, the majority of patients are in the unknown group, which affected the accuracy of our results.

Conclusion

In conclusion, for MPM patients, insured, epthelioid type, well differentiated are the favorable prognostic factors; distant metastasis, no surgery or chemotherapy are independently associated with poorer prognosis. As such, in order to provide effective treatment, and extend the lifespan of the elderly MPM patients, all the risk factors and the specific condition of patients must be carefully assessed in the determination of treatment strategies.

Abbreviations

MPM, malignant peritoneal mesothelioma; MM, malignant mesothelioma; CSS, cancer-specific survival; CSD, cause-specific death; HR, hazard ratio; CRS, cytoreductive surgery; HIPEC, heated intraperitoneal chemotherapy.

Declarations

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Availability of data and materials

The datasets analysed during the current study are available in the Surveillance, Epidemiology and End Results (SEER) database(https://seer.cancer.gov/data/).

Ethical approval statement:

All analysis were based on the Surveillance Epidemiology End Results (SEER), a public database, thus no ethical approval is required.

Consent for publication

The patients have consented to the submission of the report to the journal.

Conflict of Interest:

All authors declare that they have no conflict of interest.

Authors' Contributions:

DP, LS, BC, contributed to the conception and design of the study, DP, MW, WL, Y L contributed to the data collection, statistical analysis, manuscript drafting. All authors contributed to the manuscript revision and approved to the submitted version.

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Tables

Table 1 Baseline characteristics of the adult and elderly MPM patients

Variable	<65 years old[1] N=827 (55.43%)	≥65 years old[1] N=665 (44.57%)	*P* value
Gender			**0.017**
Male	274 (41.20%)	391 (58.80%)	
Female	274 (41.20%)	274 (41.20%)	
Race			**0.043**
White	737 (89.12%)	616 (92.63%)	
Black	47 (5.68%)	24 (3.61%)	
Asian or Pacific Islander	31 (3.75%)	23 (3.46%)	
American Indian/Alaska Native	7 (0.85%)	2 (0.30%)	
Unknown	5 (0.60%)	0	
Insurance status			**<0.001**
Insured	316 (38.21%)	239 (35.94%)	
Uninsured	27 (3.26%)	3 (0.45%)	
Unknown	484 (58.52%)	423 (63.61%)	
Marital status			**<0.001**
Married	527 (60.78%)	398 (59.85%)	
Unmarried	256 (38.50%)	271 (31.26%)	
Unknown	69 (7.96%)	11 (1.65%)	
Site			**0.006**
Peritoneum	807 (97.58%)	630 (94.74%)	
Retroperitoneum	16 (1.93%)	32 (4.81%)	
Ovarlapping lesion of retroperitoneum &peritoneum	4 (0.48%)	3 (0.45%)	
Histology			0.403
Epithelioid	270 (32.65%)	195 (29.32%)	
Biphasic	30 (3.63%)	19 (2.86%)	
Sarcomatoid	21 (2.54%)	19 (2.86%)	
Unknown	506 (61.19%)	432 (64.96%)	
Grade			**0.003**

Well differentiated	84 (10.16%)	33 (4.96%)	
Moderately differentiated	17 (2.06%)	11 (1.65%)	
Poorly differentiated	47 (5.68%)	48 (7.22%)	
Undifferentiated	18 (2.18%)	11 (1.65%)	
Unknown	661 (79.93%)	562 (84.51%)	
Stage			0.751
Localized	86 (10.40%)	68 (10.23%)	
Regional	128 (15.48)	95 (14.29%)	
Distant	493 (59.61%)	414 (62.26%)	
Unknown	120 (14.51%)	88 (13.23%)	
Surgery			**<0.001**
Cancer-directed surgery	396 (47.88%)	220 (33.38%)	
No cancer-directed surgery	407 (49.21%)	430 (64.66%)	
Unknown	24 (2.90%)	13 (1.95%)	
Radiotherapy			0.100
Yes	31 (3.75%)	15 (2.26%)	
No or unknown	796 (96.25%)	650 (97.74%)	
Chemotherapy			**<0.001**
Yes	494 (59.7%)	294 (44.21%)	
No or unknown	333 (40.3%)	371 (55.79%)	

Notes: [1] refers to the age recorded at the time of MPM diagnosis

Abbreviations: MPM, malignant peritoneal mesothelioma.

Table 2 Baseline characteristics of the female and male elderly MPM patients

Variable	Male	Female	*P* value
	N=391 (58.80%)	N=274 (41.20%)	
Age at diagnosis	73.68±6.21	75.28±7.06	**0.002**
Race			0.083
White	369 (94.37%)	247 (90.15%)	
Black	10 (2.56%)	14 (5.11%)	
Asian or Pacific Islander	12 (3.07%)	11 (4.01%)	
American Indian/Alaska Native	0	2 (0.73%)	
Insurance status			0.838
Insured	137 (35.04%)	102 (37.23%)	
Uninsured	2 (0.51%)	1 (0.36%)	
Unknown	252 (64.45%)	171 (62.41%)	
Marital status			**<0.001**
Married	287 (73.40%)	111 (40.51%)	
Unmarried	99 (25.32%)	157 (57.30)	
Unknown	5 (1.28%)	6 (2.19%)	
Site			0.878
Peritoneum	369 (94.37%)	261 (95.26%)	
Retroperitoneum	20 (5.12%)	12 (4.38%)	
Ovarlapping lesion of retroperitoneum &peritoneum	2 (0.51%)	1 (0.36%)	
Histology			0.531
Epithelioid	116 (29.67%)	79 (28.83%)	
Biphasic	11 (2.81%)	8 (2.92%)	
Sarcomatoid	8 (2.05%)	11 (4.01%)	
Unknown	256 (65.47%)	176 (64.23%)	
Grade			0.274
Well differentiated	14 (3.58%)	19 (6.93%)	
Moderately differentiated	7 (1.79%)	4 (1.46%)	
Poorly differentiated	27 (6.91%)	21 (7.66%)	

Undifferentiated	5 (1.28%)	6 (2.19%)	
Unknown	338 (86.44%)	224 (81.76%)	
Stage			0.190
Localized	32 (8.18%)	36 (13.14%)	
Regional	58 (14.83%)	37 (13.50%)	
Distant	251 (64.19%)	163 (59.49%)	
Unknown	50 (12.79)	38 (19.87%)	
Surgery			**<0.001**
Cancer-directed surgery done	100 (25.58%)	122 (44.53%)	
No cancer-directed surgery	284 (72.63%)	146 (53.28%)	
Radiotherapy			0.605
Yes	10 (2.56%)	5 (1.82%)	
No/Unknown	381 (97.44%)	269 (98.18%)	
Chemotherapy			0.342
Yes	178 (45.78%)	115 (42.97%)	
No/Unknown	212 (54.22%)	159 (58.03%)	

Abbreviations: MPM, malignant peritoneal mesothelioma.

Table 3 Comparison of the 1-, 3- and 5-year CSS rate between adult and elderly MPM patients

	Number	Death toll	Median survival time(months)	1-year CSS rate (%)	3-year CSS rate (%)	5-year CSS rate (%)
<65[1]	827	569	19	58.41	36.96	29.30
≥65[1]	665	549	6	36.18	18.68	12.53
P value[2]				**<0.001**	**<0.001**	**<0.001**

Note: [1] refers to the age recorded at the time of MPM diagnosis; [2] refers to the comparison of cause specific survival rate.

Abbreviations: MPM, malignant peritoneal mesothelioma; CSS, cancer-specific survival.

Table 4 The influence of specific prognostic factors on the CSS of elderly MPM patients, based on the log-rank test

Variable	Number	Death toll	Median survival time (months)	1-year CSS rate (%)	3-year CSS rate (%)	5-year CSS rate (%)	*P* value (CSS)[1]
Gender							**0.006**
Male	391	335	5	31.46	15.73	10.88	
Female	274	214	9	43.1	22.97	14.79	
Race							0.507
White	616	511	6	36.27	18.07	1175	
black	24	16	8	-	-	-	
Asian or Pacific Islander	23	21	2	-	-	-	
American Indian/Alaska Native	2	1	7	-	-	-	
Insurance status							**<0.001**
Insured	239	167	10	45.77	27.82	20.86	
Uninsured	3	3	1	-	-	-	
Unknown	423	379	5	31.20	14.23	8.75	
Marital status							**0.046**
Married	398	337	6	33.8	16.08	10.55	
Unmarried	256	205	7	38.77	21.47	13.99	
Unknown	11	7	15	-	-	-	
Site							0.936
Peritoneum	630	522	6	36.41	18.54	12.52	
Retroperitoneum	32	25	3	-	-	-	
Ovarlapping lesion of Retroperitoneum &peritoneum	3	2	1	-	-	-	
Histology							**<0.001**
Epithelioid	195	147	13	50.77	26.41	19.69	
Biphasic	19	17	4	-	-	-	
Sarcomatoid	19	18	1	-	-	-	
Unknown	432	341	5	32.06	16.87	10.44	

Grade							**<0.001**
Well differentiated	33	17	51	-	-	-	
Moderately differentiated	11	7	7	-	-	-	
Poorly differentiated	48	46	3	-	-	-	
Undifferentiated	11	9	4	-	-	-	
Unknown	562	470	6	36.08	18.27	12.31	
Stage							**<0.001**
Localized	68	43	16	57.98	31.37	22.75	
Regional	95	78	11	46.13	27.58	18.47	
Distant	414	356	5	29.72	12.85	8.38	
Unknown	88	72	6	39.46	26.03	17.36	
Surgery							**<0.001**
Cancer-directed surgery done	222	170	13	53.47	28.65	19.14	
No cancer-directed surgery	430	370	4	26.65	12.96	8.76	
Unknown	13	9	16	-	-	-	
Radiotherapy							0.173
Yes	15	15	6	-	-	-	
No/Unknown	650	534	6	36.8	19.19	12.88	
Chemotherapy							**0.001**
Yes	294	240	10	43.11	21.99	14.25	
No/Unknown	371	309	3	30.72	16.08	11.25	

Note: [1] refers to the comparison of overall CSS until the end of follow up; "-" refers that the number of people in the corresponding group was less than 50 and survival rates were not counted.

Abbreviations: MPM, malignant peritoneal mesothelioma; CSS, cancer-specific survival.

Table 5 Univariate and Multivariate analysis of the elderly MPM patients

Variable	Univariate analysis		Multivariate analysis	
	Log-rank c^2 test	*P*-value	HR (95% CI)	*P* value
Insurance status	26.663	<0.001		
Insured			Reference	
Uninsured			5.187 (1.628-16.524)	**0.005**
Unknown			1.326 (1.100-1.600)	**0.003**
Histology	58.350	<0.001		
Epithelioid			Reference	
Biphasic			2.279 (1.339-3.877)	**0.002**
sarcomatoid			3.913 (2.347-6.523)	**<0.001**
Unknown			2.301 (1.400-3.782)	**0.012**
Grade	39.596	<0.001		
Well differentiated			Reference	
Moderately differentiated			1.978 (0.811-4.824)	0.134
Poorly differentiated			3.900 (2.194-6.933)	**<0.001**
Undifferentiated			2.430 (1.038-5.689)	**0.041**
Unknown			2.301 (1.400-3.782)	**0.001**
Stage	23.936	<0.001		
Localized			Reference	
Regional			1.244 (0.855-1.811)	0.254
Distant			1.735 (1.255-2.401)	**0.001**
Unknown			1.165 (0.792-1.713)	0.438
Surgery	43.605	<0.001		
Cancer-directed surgery			Reference	
No cancer-directed surgery			1.733 (1.433-2.095)	**<0.001**
Unknown			0.857 (0.435-1.689)	0.656
Chemotherapy	18.157	<0.001		
Yes			Reference	
No or unknown			1.532 (1.282-1.831)	**<0.001**

Abbreviation: MPM, malignant peritoneal mesothelioma; HR, hazard ratio; CI, confidential interval.

Figures

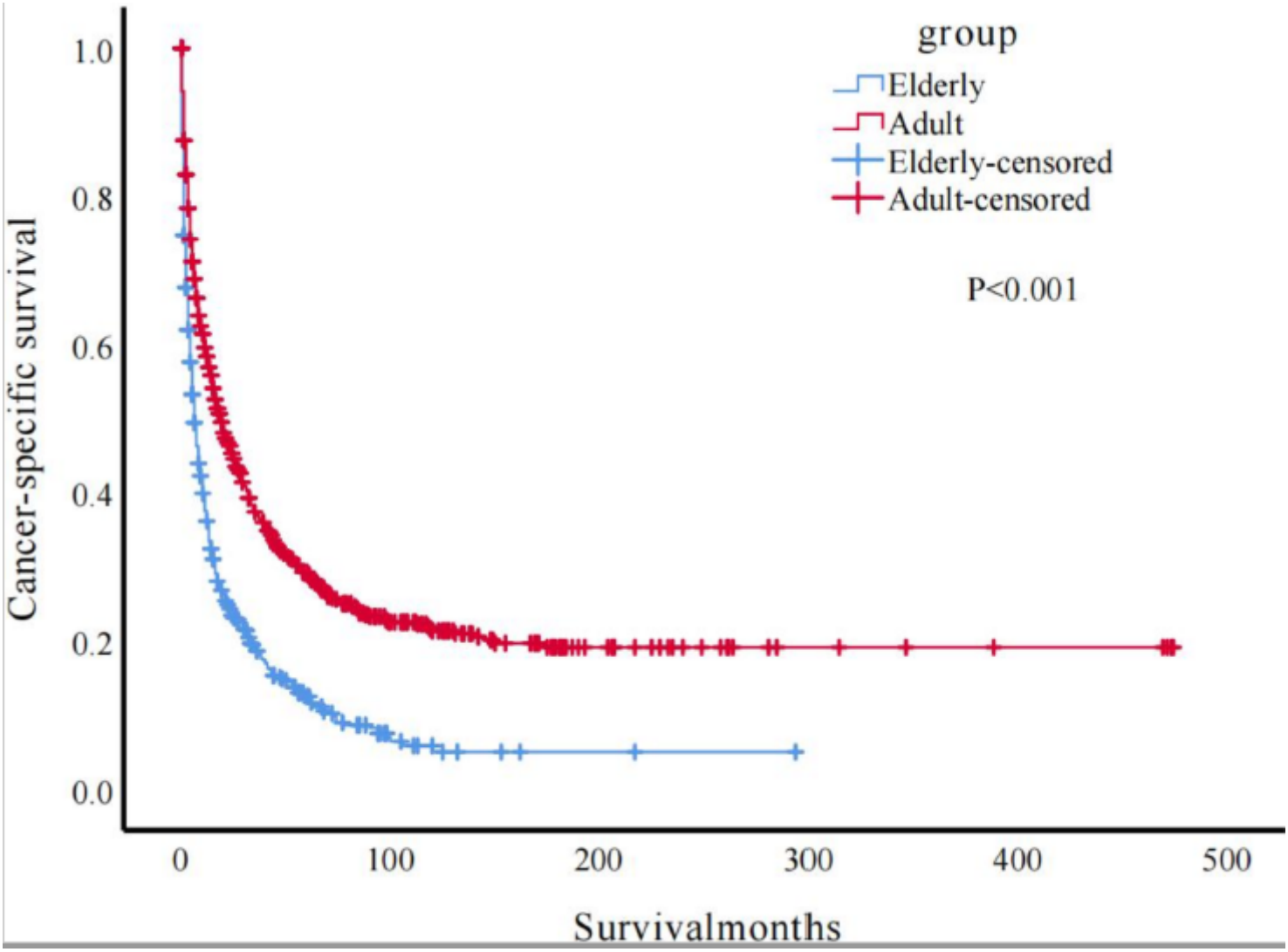

Figure 1

Kaplan-Meier survival analysis between the elderly and adult MPM patients.

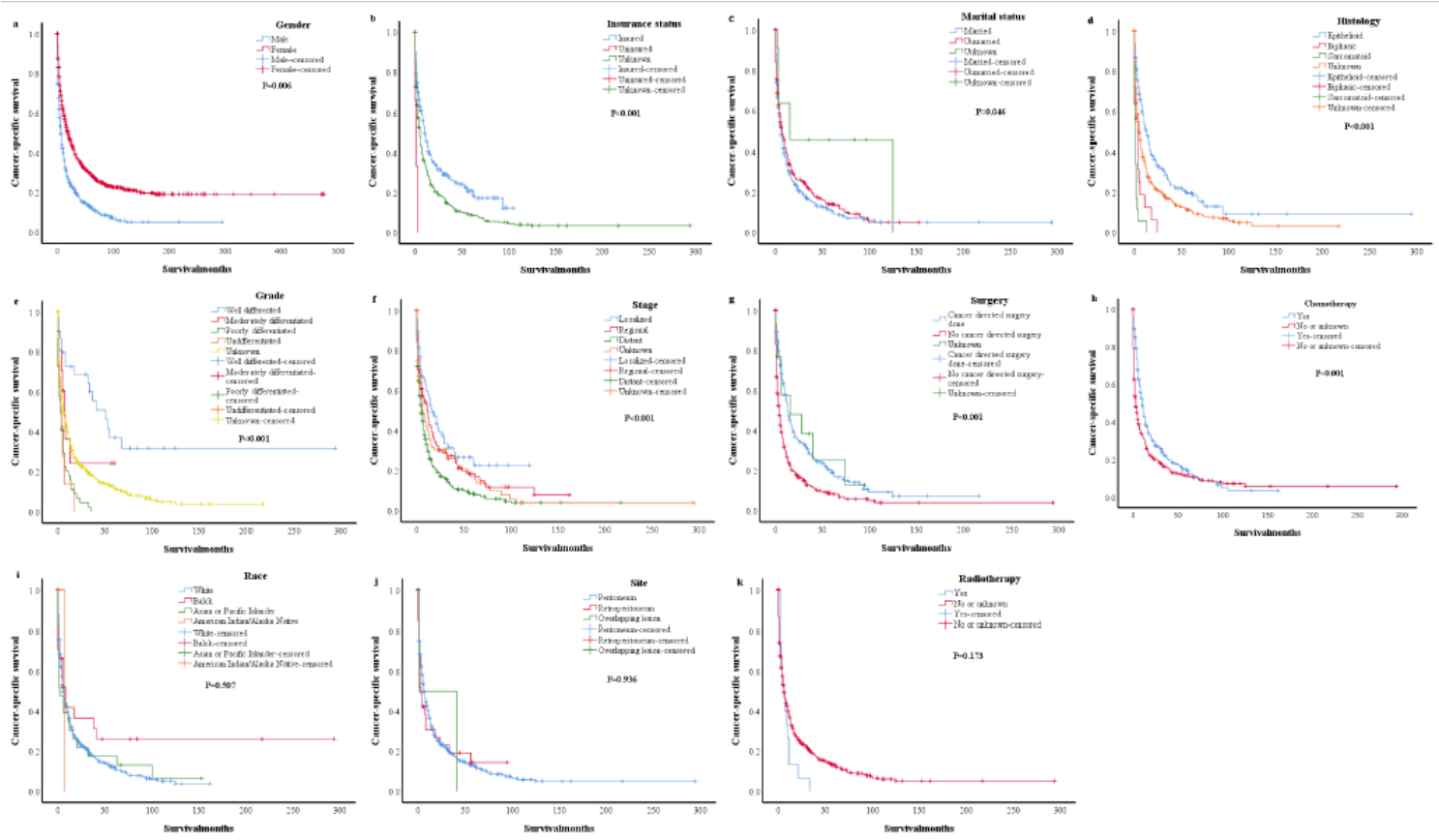

Figure 2

Kaplan-Meier survival analysis of CSS between different groups in the elderly MPM patients: (a) between different gender groups (P=0.006); (b) between different insurance status groups (P = 0.001); (c) between different marital status groups (P = 0.046); (d) between different histology type groups (P < 0.001); (e) between different differentiation grade groups (P < 0.001); (f) between different tumor stage groups (P < 0.001); (g) between different surgery status groups (P < 0.001); (h) between different chemotherapy status groups (P < 0.001); (i) between different race groups (P = 0.507); (j) between different lesion sites groups (P = 0.936); (k) between different radiotherapy status groups (P = 0.173).

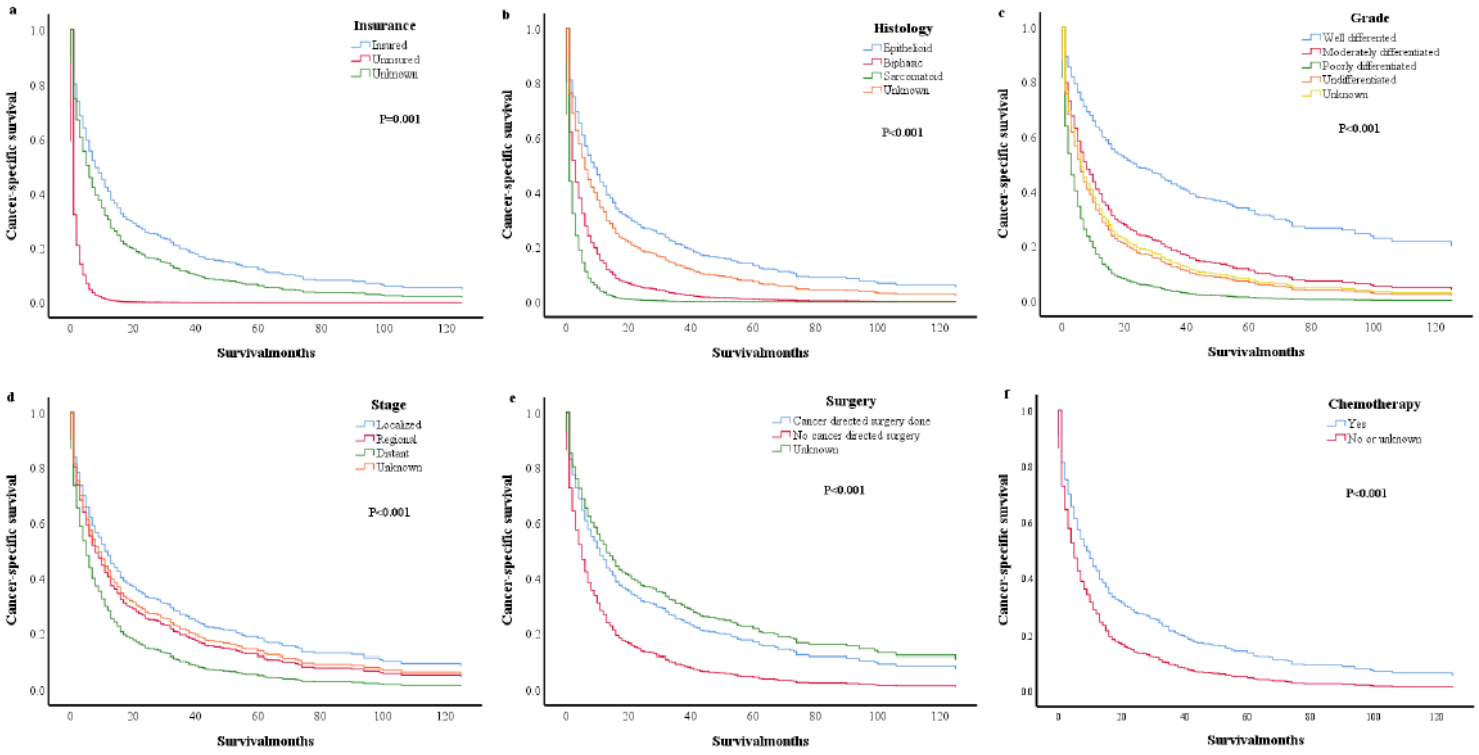

Figure 3

Cox proportional hazards analysis of CSS between different groups in the elderly MPM groups: (a) between different insurance status groups (P = 0.001); (b) between different histology type groups (P < 0.001); (c) between different differentiation grade groups (P < 0.001); (d) between different tumor stage groups (P < 0.001); (e) between different surgery status groups (P < 0.001); (f) between different chemotherapy status groups (P < 0.001).