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Patterns of Care and Survival Among Patients with Malignant Mesothelioma in the United States

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Abstract

Background—Mesothelioma is a rare malignancy that is associated with poor survival. This study aimed to describe the patterns of care and subsequent survival among malignant mesothelioma patients in the United States, while adjusting for patient demographics and comorbidities.

Methods—A random sample of patients diagnosed with histologically confirmed mesothelioma in 2011, as reported to the National Cancer Institute's Surveillance Epidemiology and End Results program, were included. Logistic regression and Cox proportional hazard regression were utilized to identify factors associated with receipt of therapy and all-cause mortality, respectively, among patients with pleural mesothelioma.

Results—This study included 389 patients with pleural mesothelioma and 53 patients with non-pleural mesothelioma. Almost a third (29.3%) of the pleural patients and 21.5% of the non-pleural patients received no therapy. Additionally, approximately 60% of both patient groups received systemic therapy. Among pleural mesothelioma patients, receipt of therapy was less likely among older patients. Median survival was 9 months among the pleural patients and 18 months among the non-pleural patients. Receipt of either surgery or systemic therapy and particularly the combination of these two modalities was associated with better all-cause survival. Additionally, among pleural mesothelioma patients, younger age and lower socioeconomic status were found to be associated with better all-cause survival. Comorbidity score was not found to be associated with receipt of treatment nor was it independently associated with survival among pleural mesothelioma patients.

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Conclusion—These findings indicate the need for efforts to ensure equitable application of currently available therapies to all patients.

Keywords

Mesothelioma; pleural; treatment; survival; SEER

Introduction

Malignant mesothelioma arises from the mesothelial lining of several organs: most commonly the pleura (87%), less commonly the peritoneum (11%) and rarely the pericardium (<1%) and tunica vaginalis of testes (<1%).[1] Approximately 3,200 individuals are diagnosed with malignant mesothelioma annually in the United States.[2] Occupational asbestos exposure is the predominant risk factor and as a result malignant mesothelioma is more common among older, white males.

Malignant mesothelioma is difficult to diagnose and patients often present with advanced disease, resulting in a dismal 5-year survival rate of less than 10%.[3] Biopsy (e.g., via thoracoscopy or peritoneoscopy) remains the “gold standard” for diagnosing malignant mesothelioma. Although serum biomarkers, including mesothelin and osteopontin, have been investigated, none have been validated for clinical diagnostic purposes. Malignant mesothelioma is also difficult to stage; historically, there was no consensus on staging system. Although reliability concerns remain, particularly among patients that do not undergo surgery, malignant pleural mesothelioma is now often classified based on the American Joint Committee on Cancer (AJCC) TNM (tumor, nodes, metastasis) staging system.[4] In comparison to stage, histologic subtype (epithelial; sarcomatoid; and biphasic) continues to be a better predictor of survival. The epithelial subtype is the most common and has the most favorable outcomes.[5] Poorer prognosis has also been associated with demographic and clinical characteristics, including being male, older, and having a lower performance status.

Patients with unresectable mesothelioma- due to extensive local involvement, tumor involvement of lymph nodes, metastatic disease or medical comorbidities that preclude surgery- are treated with systemic chemotherapy with a palliative intent. In contrast, patients with limited stage mesothelioma are considered for multimodality therapy that incorporates radical surgery with or without chemotherapy and/or radiation.[5] Questions remain, however, as to how effective these therapies are. A previous population-based analysis indicated that surgery but not radiation conveyed a survival benefit among patients with pleural mesothelioma.[6] However, comorbidity, surgery type and systemic therapy were not assessed, even though these factors have also been associated with survival. A separate population-based analysis among patients 66 years or older at diagnosis indicated that systemic therapy was also associated with better survival, especially among those who received surgery, after adjusting for comorbidity.[4]

The primary aims of this study were to describe the patterns of care and subsequent survival of malignant mesothelioma in the United States. To address knowledge gaps, information on comorbidity, surgery type and systemic therapy was obtained. Eligibility was not limited to

elderly patients or to those with pleural mesothelioma. To carry out this research we analyzed data collected by the National Cancer Institute (NCI), which included patients diagnosed in 2011 with histologically confirmed malignant mesothelioma who were ascertained through the Surveillance, Epidemiology and End Results (SEER) program.

Methods

Study population

The SEER program consists of population-based registries that collect demographic, tumor, diagnostic and treatment characteristics, as well as vital status on all cases of cancer occurring within their defined geographic regions. The SEER registries collectively cover approximately 28% of the United State population.[7] Hospitals serve as the primary source of SEER data, which often results in underreporting of treatment. As a result, the NCI conducts annual Patterns of Care studies to collect additional information among randomly sampled patients with specific cancer diagnoses who were reported to SEER program. Briefly, after obtaining IRB approval, as required by the registries, each year a central training is conducted to ensure consistent abstracting and coding of the data. Data are then re-abstracted from hospital medical records and the patients' treating physicians are contacted to verify all treatment given. Each physician is also asked for the names and addresses of others who might have treated the patient and these individuals are then contacted.

Patients diagnosed in 2011 with histologically confirmed mesothelioma [International Classification of Diseases for Oncology 3rd edition (ICD-O-3) histology codes: 9050–9053, 9055] were eligible for inclusion in the Patterns of Care study. Given the rarity of mesothelioma, all mesothelioma patients were included, except for those reported to the Greater California cancer registry where fifty of the 143 reported cases were randomly sampled due to budgetary constraints. Briefly, patients reported to the Greater California cancer registry were stratified by race/ethnicity and sex. Patients from each strata were then selected at random to ensure an unbiased sample. Sample weights were assign to each included patient, as described below. Patients were ineligible if they were less than 20 years old at diagnosis or had a prior history of cancer.

Variables of Interest

Information on height, weight, comorbidities, smoking and asbestos exposures, insurance status, diagnostic procedures and treatment, including specific systemic agents, and participation in a clinical trial, were available from the Patterns of Care study. Hospital characteristics, including bed size and presence of an approved residency training program were also available. The type of mesothelioma was classified as pleural (ICD-O-3 site codes: C384, C342, C349) and non-pleural. Body mass index (BMI) was calculated based on height and weight ("usual weight" or if that was unavailable "weight at diagnosis") and then categorized as underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9), obese (>30) and unknown. All comorbidities recorded in the hospital record were abstracted and centrally coded before being analyzed using the Charlson comorbidity index, excluding mesothelioma.[8] Insurance was categorized as any private or military insurance, any Medicaid, Medicare only, and other/no/unknown insurance. Age, sex, race/ethnicity, marital

status, tumor characteristics and vital status through December 31, 2013, were available in the SEER data. Race/ethnicity was categorized as non-Hispanic white (NHW), non-Hispanic black (NHB), Hispanic, and other. Stage was categorized based on the American Joint Committee on Cancer, 7th edition (AJCC-7). Patient- level socioeconomic variables were not available, but a composite Yost index that took into account area-level characteristics (e.g. percentage unemployed, poverty level, median income, education level and housing costs) of each patient's residential census tract at the time of diagnosis was calculated using data from the 2009–2013 American Community Survey.[9,10] Census tracts are relatively small geographic entities that represent between 2,500–8,000 residences and are designed to identify homogenous populations with respect to population characteristics, economic status, and living conditions.[11] The Yost index was then categorized into registry-specific quintiles for analyses.

Statistical Analyses

Weighted percentages of patient characteristics, utilization of diagnostic procedures and specific treatments were calculated using stratum-specific sample weights to account for the complex survey design. The percentages reported are weighted to reflect the population from which the sample was drawn. Sample weights were calculated as the inverse of the sampling proportion for each sampling stratum.

Factors associated with the receipt of surgery and systemic therapy among patients with pleural mesothelioma were assessed using bivariate chi-square tests and multivariate logistic regression. Cox proportional hazards models were then constructed to examine factors associated with all-cause mortality among patients with pleural mesothelioma. Factors identified as being associated ($p \leq 0.05$) with the outcomes of interest during bivariate analyses were included in the multivariate models. Strong collinearity in all final regression models was not indicated; when each variable in the model was linearly regressed against the other remaining variables, no variable had a variance inflation factor >2 .[12] Small sample size (n=53) precluded the ability to assess factors associated with receipt of treatment and survival among patients with non-pleural mesothelioma. Analyses were conducted using SAS version 9.3 (SAS Institute, Cary, North Carolina) and SUDAAN version 11.0.1 (Research Triangle Institute, Raleigh, NC). All tests were two sided and statistical significance was assessed using an alpha of 0.05.

Results

The majority of patients (n=389; 89.5%) had pleural mesothelioma; there were 53 cases that were classified as non-pleural mesothelioma. In comparison to the non-pleural mesothelioma patients, pleural mesothelioma patients tended to be older, male, and have more comorbidities, a history of smoking and asbestos exposure, sarcomatoid or biphasic histology, and known stage (Table 1). Notably, patients younger than 50 constituted 23.3% of those with non-pleural mesothelioma compared with only 3.1% of those with pleural mesothelioma. Additionally, over half (54.5%) of all the patients with non-pleural mesothelioma were female compared to 21.1% of pleural patients.

Utilization of diagnostic mesothelioma biomarkers was uncommon (Table 2); 4.5% of the pleural mesothelioma patients had a serum mesothelin test and none had a serum osteopontin test. Almost half of all pleural mesothelioma patients (46.7%) had a positron emission tomography (PET) scan; the percentage increased to 56.9% when restricted to patients diagnosed with stage I-III tumors. Only 29.7% of all non-pleural mesothelioma patients had a PET scan.

Roughly half (56.9%) of the pleural mesothelioma patients had a therapeutic thoracentesis and 33.7% had a pleurodesis. Understandably, among non-pleural mesothelioma patients' therapeutic thoracentesis and pleurodesis were uncommon. Almost a third (29.3%) of the pleural mesothelioma patients received no treatment, 27.1% received surgery, 18.4% received radiation and 62% received systemic therapy. Among the non-pleural mesothelioma patients, 21.5% received no treatment; 51.8% received surgery, 4.9% received radiation and 61.6% received systemic therapy. Among the pleural mesothelioma patients who received surgery, 66.8% had a pleurectomy/decortication and 17% had an extrapleural pneumonectomy; 25.1% of pleural mesothelioma patients who had surgery had documented clear margins. Margins were less likely (13.2%) to be clear among the non-pleural mesothelioma patients who had surgery. Among the pleural mesothelioma patients who had systemic therapy, cisplatin plus pemetrexed was the most common (43.0%) first-line regimen and 29.1% received two or more lines of therapy. Among the non-pleural mesothelioma patients who had systemic therapy, first line platinum-based regimens with pemetrexed were less common and more patients (40.1%) received two or more lines of therapy. Only 4.6% of the pleural mesothelioma patients and 1.6% of the non-pleural mesothelioma patients participated in a clinical trial.

Bivariate analyses indicated that receipt of surgery among pleural mesothelioma patients was significantly associated with age, stage, hospital bed size and treatment at a hospital with an approved residency program (Table 3). When these factors were included in a multivariate model, significant associations remained between receipt of surgery and older age [70+y vs. <50y: odds ratio (OR): 0.15] and later stage (stage III vs. I: OR: 3.72).

Bivariate analyses indicated that receipt of systemic therapy among pleural mesothelioma patients was significantly associated with age, BMI, asbestos exposure, stage, hospital bed size and treatment at a hospital with an approved residency program. When these factors were included in a multivariate model, significant associations remained between receipt of systemic therapy and older age [70+y vs. <50y: OR range: 0.17–0.19], BMI (vs. normal weight; overweight: OR: 2.58; obese: OR: 3.18; unknown: OR: 2.64) and later stage (stage III vs. I: OR: 4.24).

More than 86% of the pleural mesothelioma patients, compared to 55% of the non-pleural mesothelioma patients, were deceased by the end of 2013; median survival among non-pleural mesothelioma patients was 18 months compared to 9 months among the pleural mesothelioma patients (data not shown). Among both patient groups receipt of surgery and/or systemic therapy was associated better unadjusted all-cause survival (Figure 1). Bivariate analyses also indicated that all-cause survival among pleural mesothelioma patients was associated with age, socioeconomic status, histology, stage, hospital bed size,

treatment at a hospital with an approved residency program, and receipt of and radiation (Table 4). When all of the factors that were significant during bivariate analyses were included in a multivariate model, significant associations remained between poorer all-cause survival and older age [70+y vs. <50y: hazard ratio (HR) range: 2.43–2.45]; higher socioeconomic status (quintile 5 vs. 1: HR: 1.78; 95% confidence interval: 1.13–2.79); histology (vs. epithelioid mesothelioma; sarcomatoid HR: 2.58 95% CI: 1.79–3.72; not otherwise specified HR: 1.53 95% CI: 1.12–2.10, respectively); and stage IV (vs. stage I: HR: 1.85; 95% CI: 1.13–3.04). Better all-cause survival was associated with receiving systemic therapy, regardless of regimen (HR range: 0.58–0.65) and surgery (HR range: 0.58–0.71), although the association with having an extrapleural pneumonectomy was not significant.

Discussion

The findings from this study indicate the patterns of care and survival among patients diagnosed in 2011 with malignant mesothelioma in the United States. A sizable proportion (20–30%) of patients with malignant mesothelioma received no cancer-directed therapy. Additionally, only 60% of patients with malignant mesothelioma received systemic therapy. Among pleural mesothelioma patients, receipt of therapy was consistently less likely among older patients. Receipt of either surgery or systemic therapy and particularly the combination of these two modalities appeared to be associated with better all-cause survival. Additionally, among pleural mesothelioma patients, younger age and lower socioeconomic status were found to be associated with better all-cause survival. Comorbidity score was not found to be associated with receipt of treatment nor was it independently associated with survival among pleural mesothelioma patients.

Patients with malignant mesothelioma tend to be older individuals who frequently have functional impairment and may not be able to tolerate aggressive therapy. Among patients older than 66 years, only 54% in the current study received systemic therapy (data not shown), which is higher than a previous estimate (45%) among cases diagnosed in 2005–2009.[4] Despite the fact that a large proportion of patients with malignant mesothelioma are elderly, information remains scant on how best to treat these patients. However, it is clear that therapeutic decisions in the elderly with cancer should not be based just on chronological age but should also take into account the life expectancy and patient preferences, functional age, presence of comorbidities and estimated benefits and risks.[13] In fact, available data suggest that elderly patients with good functional status might obtain comparable benefits in terms of disease control rate and survival compared to their younger counterparts.[14] Whereas therapeutic nihilism might be the most obvious explanation for the apparent under treatment of the elderly, additional studies are warranted to fully understand the factors underlying the limited utilization of systemic therapy in the elderly mesothelioma population.

Although generally considered to be an incurable disease, a subset of mesothelioma patients come to medical attention with potentially resectable disease. These patients might benefit from a multimodality approach consisting of surgery, systemic therapy and radiation. Unfortunately, our data indicates that such patients constitute only 10% of pleural

mesothelioma patients in the real world. In this study, the median survival among non-pleural mesothelioma and pleural mesothelioma patients were 18 months and 9 months, respectively. Consistent with previous reports, epithelioid histology, receipt of systemic therapy, and surgery were all associated with improved outcomes in pleural mesothelioma patients.[15] It remains an open question whether extrapleural pneumonectomy- a more aggressive surgery which involves removal of the lung- might offer any benefit over pleurectomy and decortication of the visceral and pleural parietal pleura alone.[16] Although we found that having any surgery was associated with improved survival (adjusted HR=0.66; data not shown), the study did not have adequate sample size to identify differences between the individual surgical procedures.

Combination of pemetrexed and cisplatin was approved for treatment of patients with malignant mesothelioma by the United States Food and Drug Administration (FDA) in 2004. In clinical practice, carboplatin is often substituted for cisplatin in patients who cannot tolerate or have contraindications to cisplatin. In this study, 76.7% of patients with pleural mesothelioma and 54.9% of patients with non-pleural mesothelioma received a platinum-pemetrexed combination therapy. Only about 30% of patients with pleural mesothelioma received second line or additional systemic therapies.

Well conducted clinical trials offer the best hope of finding more effective treatments for mesothelioma. In our study, less than 5% of patients with pleural mesothelioma and less than 2% of patients with non-pleural mesothelioma participated in a clinical trial. To our knowledge, this is one of the first population based studies to establish the rates of participation of mesothelioma patients in clinical trials. Perhaps not surprisingly, the lower accrual rates of mesothelioma patients in clinical trials are comparable to accrual rates for cancer patients in general. It has been estimated that as few as 3–5% of newly diagnosed cancer patients participate in clinical trials.[17] Expanding our understanding of the particular challenges to participation in clinical trials in mesothelioma is essential to making an impact on this disease.

This study had strengths, namely that it was population-based, oversampled minority groups, and had physician verified treatment. This study also had limitations. First, this was an observational study; therefore, the findings should be interpreted with caution, particularly the observation that treatment was associated with better survival. This observation may due to the treatment itself but may also be because patients receiving treatment were healthier at diagnosis. Charlson score was also calculated based on retrospective chart review; therefore, it is possible that comorbidity status may have been misclassified. Additionally, although Charlson score was included as a covariate, information on performance status and severity of comorbidities, which may influence treatment and/or survival, was unavailable. Small sample size among the non-pleural mesothelioma group also precluded more in-depth analyses to identify factors associated with treatment and survival among these patients. Finally, the patients included in this study were diagnosed in 2011 prior to the publication of promising clinical trials;[18] thus, the current findings may not accurately represent current treatment patterns.

Taken together, our findings indicate that only a subset of mesothelioma patients realize the benefit of established treatment options. This data is critical as there is considerable interest and spending related to finding newer, more effective agents for patients with mesothelioma. Our findings indicate the need for efforts to ensure equitable application of currently available therapies among patients.

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Highlights

- 29.3% of the pleural patients and 21.5% of the non-pleural patients do not receive cancertherapy.
- Older pleural patients (>70 vs. <50) were less likely to receive therapy.
- Median survival was 8 months among patients pleural patients and 18 months among non-pleural patients.
- Among pleural patients receipt of surgery and systemic therapy was associated with the best survival.

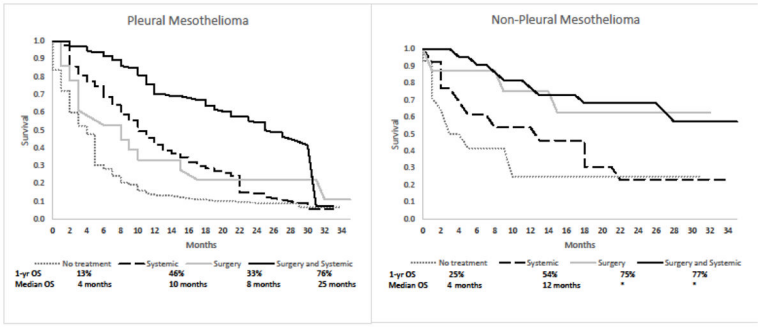

Figure 1.

Kaplan-Meier curves among patients diagnosed in 2011 with pleural or non-pleural mesothelioma by treatment received, Patterns of Care.

OS: Overall survival. *Not able to calculate due to insufficient follow-up.

Table 1

Multilevel characteristics pertaining to patients diagnosed in 2011 with mesothelioma by site, Patterns of Care (n=442).

	Pleural (N[1]=389)	Non-Pleural (N[1]=53)	
Characteristics	**%[2]**	**%[2]**	**p[3]**
Age at diagnosis			
<50	3.1	23.3	<0.01
50–59	8.7	20.6	
60–69	28.3	21.3	
70–79	27.7	21.1	
80+	32.3	13.7	
Sex			
Male	78.9	45.5	<0.01
Female	21.1	54.5	
Race/Ethnicity			
Non-Hispanic white	79.6	74.2	0.11
Non-Hispanic black	3.8	8.2	
Hispanic	11.8	14.4	
Other	4.8	3.3	
Marital status			
Married, living as married	61.4	49.2	0.12
Not married	38.6	50.8	
BMI, kg/m^2			
Underweight <18.5	2.0	1.8	0.31
Normal 18.5–24.9	26.0	29.2	
Overweight 25.0–29.9	36.5	22.2	
Obese 30+	17.9	28.6	
Unknown	17.5	18.2	
Charlson comorbidity index			
0	48.2	75.5	<0.01
1+	51.8	24.5	
Ever Smoker			
No	30.8	42.1	<0.01
Yes	64.4	40.5	
Unknown	4.8	17.4	
Asbestos Exposure			
No	25.9	39.4	<0.01
Yes	54.9	14.2	
Unknown	19.2	46.5	

	Pleural (N[1]=389)	Non-Pleural (N[1]=53)	
Characteristics	**%[2]**	**%[2]**	**p[3]**
Insurance status			
Private/Military/VA	75.4	76.5	0.20
Any Medicaid	14.4	5.5	
Medicare only	8.5	6.9	
Other/None/Unknown	1.7	11.1	
Socioeconomic status, Yost index[4]			
Quintile 1 (Low)	14.8	21.8	0.17*
Quintile 2	16.5	27.8	
Quintile 3	26.7	20.4	
Quintile 4	22.6	12.7	
Quintile 5 (High)	17.8	17.3	
Unknown	1.6	0.0	
Histology (ICD-O-3)			
Epithelioid mesothelioma 9052	35.0	45.1	0.04**
Sarcomatoid mesothelioma 9051	12.4	7.3	
Mesothelioma, biphasic 9053	9.8	0.0	
Mesothelioma, not otherwise specified 9050	42.8	47.6	
Stage, AJCC-7			
I	12.7	3.3	<0.01
II	9.5	1.6	
III	21.1	8.2	
IV	44.5	49.6	
Unknown	12.2	42.2	
Hospital bed size			
< 200 beds, out patient only, unknown	20.0	19.3	0.59
200–299 beds	15.9	14.5	
300–399 beds	21.9	19.5	
400–499 beds	12.1	20.7	
500+ beds	30.1	26.0	
Approved residency training program			
No/Unknown	40.5	42.1	0.84
Yes	59.5	57.9	

AJCC-7: American Joint Committee on Cancer, 7th edition; BMI: body mass index; ICD-O-3: International Classification of Diseases for Oncology 3rd edition; VA: Veterans Administration

[1]Unweighted sample size.

[2]Weighted column percentage.

[3]Chi-Square comparing the two groups.

[4] Based on a patient's census tract data; quintile cut point were registry specific.

[*] Due to small cell size unknown was combined with quintile 5.

[**] Due to small cell size biphasic was combined with sacomatoid.

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Table 2

Clinical care among patients diagnosed in 2011 with mesothelioma by site, Patterns of Care (total n=442).

	Pleural (N[1]=389)	Non- Pleural (N[1]=53)
Characteristics	%[2]	%[2]
Serum mesothelin test	4.5	0.0
Serum osteopontin test	0.0	0.0
Positron emission tomography (PET) scan		
Among all patients	46.7	29.7
Among stage I-III patients	56.9	0.0
Therapeutic thoracentesis	56.9	3.6
Pleurodesis	33.7	2.0
Treatment, mutually exclusive		
No treatment	29.3	21.5
Surgery only	6.6	13.6
Radiation only	1.1	3.3
Systemic only	36.4	21.8
Surgery and radiation	1.1	0.0
Surgery and systemic	9.4	38.2
Radiation and systemic	6.2	1.6
Surgery, radiation and systemic	10.1	0.0
Type of surgery, among pleural patients who had surgery		
Pleurectomy/decortication	66.8	
Extrapleural pneumonectomy	17.0	
Unknown	16.2	
Pathological margins, among those who had surgery		
Margins of resection pathologically free of tumor	25.1	13.2
Tumor at margins of resection, or residual tumor in area of primary	39.2	39.9
Unknown, not stated	35.8	46.9
1st systemic regimen, among those who had systemic therapy		

	Pleural (N[1]=389)	Non- Pleural (N[1]=53)
Carboplatin, Pemetrexed	33.7	23.4
Cisplatin, Pemetrexed	43.0	31.5
Other	23.3	45.2
Receipt of additional systemic therapy, among those who had any systemic therapy	29.4	40.1
Clinical trial participation	4.6	1.6

[1] Unweighted sample size.

[2] Weighted percentage.

Table 3

Characteristics associated with the receipt of surgery and systemic therapy among patients diagnosed in 2011 with pleural mesothelioma, Patterns of Care (n=389).

	Surgery				Systemic therapy			
Characteristics	**%[1]**	**p[2]**	**OR[3]**	**95% CI**	**%[1]**	**p[2]**	**OR[3]**	**95% CI**
Age at diagnosis								
<50	59.6	<0.01	1.00	ref	93.8	<0.01	1.00	ref
50–59	31.9		0.33	0.08–1.32	72.0		0.39	0.09–1.69
60–69	45.1		0.46	0.13–1.58	79.1		0.54	0.15–2.04
70–79	20.3		0.15	0.04–0.54	71.0		0.17	0.04–0.69
80+	12.7		0.15	0.04–0.56	33.5		0.19	0.05–0.80
Sex								
Male	25.5	0.25			63.1	0.49		
Female	33.2				57.8			
Race/Ethnicity								
Non-Hispanic white	28.6	0.48			61.4	0.73		
Non-Hispanic black	18.3				55.0			
Hispanic	19.0				67.6			
Other	29.0				63.0			
Marital status								
Married, living as married	25.1	0.49			66.4	0.24		
Not married	30.3				55.0			
BMI, kg/m^2								
Underweight <18.5	40.0	0.17			77.6	<0.01	4.82	0.78–29.94
Normal 18.5–24.9	14.7				54.2		1.00	ref
Overwight 25.0–29.9	31.9				69.6		2.58	1.16–5.74
Obese 30+	33.2				77.6		3.18	1.27–7.97
Unknown	27.7				39.8		2.64	1.08–6.45
Charlson comorbidity index								

	Surgery				Systemic therapy			
Characteristics	**%**[1]	**p**[2]	**OR**[3]	**95% CI**	**%**[1]	**p**[2]	**OR**[3]	**95% CI**
0	31.5	0.31			65.6	0.43		
1+	23.0				58.6			
Ever Smoker								
No	34.3	0.24			65.0	0.81		
Yes	23.9				60.7			
Unknown	22.9				59.6			
Asbestos Exposure								
No	22.8	0.27			47.6	<0.01	0.83	0.44–1.64
Yes	31.5				72.7		1.00	ref
Unknown	20.4				50.7		0.77	0.34–1.77
Insurance status								
Private	28.2	0.59			66.0	0.16		
Military/VA/IHS	28.9				54.7			
Any Medicaid	18.1				52.6			
Medicare only	32.8				42.5			
Other/None/Unknown	23.6				74.8			
Socioeconomic status, Yost index[4]								
Quintile 1 Low	40.8	0.27			68.2	0.71		
Quintile 2	25.6				61.7			
Quintile 3	19.3				58.9			
Quintile 4	26.8				55.0			
Quintile 5 High	27.0				68.2			
Histology								
Epithelioid mesothelioma 9052	36.1	0.22			66.4	0.19		
Sarcomatoid mesothelioma 9051	20.5				58.0			
Mesothelioma, biphasic 9053	37.1				79.6			
Mesothelioma 9050	19.3				55.5			
Stage, AJCC								

	Surgery				Systemic therapy			
Characteristics	%[1]	p[2]	OR[3]	95% CI	%[1]	p[2]	OR[3]	95% CI
I	23.2	<0.01	1.00	ref	49.2	0.05	1.00	ref
II	32.3		1.48	0.57–3.83	59.9		1.75	0.65–4.67
III	59.4		3.72	1.59–8.72	76.9		4.24	1.76–10.23
IV	16.4		0.59	0.27–1.27	56.8		0.67	0.29–1.54
Unknown	10.2		0.39	0.11–1.41	69.8		0.39	0.10–1.48
Hospital bed size								
< 200 beds, out patient only, unknown	21.4	0.05	1.00	ref	55.7	<0.01	1.00	ref
200–299 beds	15.8		0.48	0.18–1.26	48.5		0.43	0.15–1.23
300–399 beds	20.9		0.65	0.27–1.56	47.0		0.56	0.21–1.53
400–499 beds	35.0		1.13	0.43–3.00	71.6		1.20	0.41–3.50
500+ beds	38.2		0.94	0.37–2.35	80.4		0.80	0.29–2.16
Approved residency training program								
No/Unknown	15.1	<0.01	1.00		44.7	<0.01	1.00	ref
Yes	35.2		1.70	0.88–3.29	73.7		1.78	0.87–3.64

AJCC-7: American Joint Committee on Cancer, 7th edition; BMI: Body mass index.

[1] Weighted row percentage of patients who had treatment.

[2] Chi-square p-value assessing association between variable and treatment.

[3] Odds ratio from a multivariate model that included all variables that were significant (<0.05) duirng bivariate analyses.

[4] Based on a patient's census tract data; quintile cut points were registry specific.

Table 4

Characteristics associated with all-cause mortality among patients diagnosed in 2011 with pleural mesothelioma with follow-up through 12/31/2013, Patterns of Care (n=389).

			Bivariate			Multivariate	
Characteristics	**N**[1]	**%**[1]	**HR**	**95% CI**	**p**[2]	**HR**[3]	**95% CI**
Age at diagnosis							
<50	8	53.1	1.00	ref	<0.01	1.00	ref
50–59	31	80.6	2.09	1.09–3.99		1.47	0.68–3.18
60–69	90	79.1	1.55	0.79–3.02		1.52	0.75–3.08
70–79	100	90.2	2.90	1.54–5.46		2.43	1.21–4.86
80+	98	94.8	3.55	1.76–7.16		2.45	1.17–5.10
Sex							
Male	246	88.4	1.00	ref	0.22		
Female	81	79.6	0.81	0.58–1.13			
Race/Ethnicity							
Non-Hispanic white	250	87.7	1.00	ref	0.99		
Non-Hispanic black	13	78.3	0.95	0.60–1.50			
Hispanic	46	85.2	0.96	0.67–1.38			
Other	18	78.0	0.97	0.59–1.59			
Marital status							
Married, living as married	206	88.6	1.00	ref	0.61		
Not married	121	83.3	0.89	0.56–1.41			
BMI, kg/m[2]							
Underweight <18.5	9	90.6	0.94	0.51–173	0.06		
Normal 18.5–24.9	96	92.5	1.00	ref			
Overwight 25.0–29.9	120	87.9	0.60	0.42–0.85			
Obese 30+	51	80.0	0.68	0.40–1.16			
Unknown	51	81.0	0.80	0.44–1.46			
Charlson comorbidity index							
0	179	78.7	1.00	ref	0.48		
1+	114	93.7	1.33	0.81–2.21			

			Bivariate			Multivariate	
Characteristics	**N[1]**	**%[1]**	**HR**	**95% CI**	**p[2]**	**HR[3]**	**95% CI**
Ever Smoker							
No	122	83.7	1.00	ref	0.62		
Yes	187	87.9	1.09	0.76–1.54			
Unknown	18	86.6	1.24	0.78–1.97			
Asbestos Exposure							
No	84	82.2	1.00	ref	0.34		
Yes	179	88.0	0.89	0.61–1.28			
Unknown	64	88.2	1.26	0.74–2.17			
Insurance status							
Private	233	86.9	1.00	ref	0.82		
Military/VA/IHS	9	82.1	1.17	0.53–2.58			
Any Medicaid	44	86.1	1.21	0.77–1.90			
Medicare only	36	90.5	1.25	0.84–1.86			
Other/None/Unknown	5	61.2	1.01	0.37–2.71			
Socioeconomic status, Yost index[3]							
Quintile 1 (Low)	44	87.1	1.00	ref	0.03	1.00	ref
Quintile 2	62	79.6	1.18	0.61–2.26		0.94	0.57–1.53
Quintile 3	87	95.0	1.61	0.82–3.19		1.34	0.84–2.13
Quintile 4	72	82.4	1.43	0.75–2.73		1.19	0.71–2.01
Quintile 5 (High)	59	89.5	1.81	0.95–3.45		1.78	1.13–2.79
Unknown	3	39.2	0.38	0.11–1.34		0.38	0.09–1.69
Therapeutic thoracentesis							
No	142	85.9	1.00	ref	0.82		
Yes	185	87.1	1.05	0.69–1.61			
Pleurodesis							
No	208	87.2	1.00	ref	0.78		
Yes	119	85.2	0.95	0.66–1.36			
Histology (ICD-O-3)							
Epithelioid mesothelioma 9052	126	76.9	1.00	ref	<0.01	1.00	ref
Sarcomatoid mesothelioma 9051	53	94.5	2.27	1.68–3.07		2.58	1.79–3.72

		Bivariate				Multivariate	
Characteristics	**N[1]**	**%[1]**	**HR**	**95% CI**	**p[2]**	**HR[3]**	**95% CI**
Mesothelioma, biphasic 9053	27	89.8	1.10	0.81–1.49		1.15	0.79–1.67
Mesothelioma, NOS 9050	121	91.4	1.60	0.96–2.65		1.53	1.12–2.10
Stage, AJCC							
I	47	78.6	1.00	ref	<0.01	1.00	ref
II	34	75.5	0.78	0.48–1.28		1.02	0.54–1.93
III	68	84.9	0.76	0.44–1.30		1.53	0.89–2.63
IV	141	90.7	1.54	1.08–2.20		1.85	1.13–3.04
Unknown	37	91.3	0.99	0.64–1.50		0.98	0.57–1.70
Hospital bed size							
< 200 beds, out patient only, unknown	53	89.2	1.00	ref	0.03		
200–299 beds	63	83.1	0.81	0.53–1.24		0.83	0.53–1.29
300–399 beds	72	85.6	0.97	0.53–1.78		1.26	0.71–2.25
400–499 beds	45	80.7	0.72	0.46–1.12		1.13	0.64–1.97
500+ beds	94	89.7	0.64	0.44–0.94		1.40	0.78–2.50
Approved residency training program							
No/Unknown	127	91.8	1.00	ref	<0.01	1.00	ref
Yes	200	83.0	0.52	0.42–0.65		0.58	0.40–0.84
Surgery							
No/unknown	244	90.1	1.00	ref	<0.01	1.00	ref
Pleurectomy/decortication	52	79.6	0.47	0.30–0.72		0.69	0.48–0.99
Extrapleural pneumonectomy	14	64.4	0.39	0.25–0.62		0.71	0.40–1.29
Had surgery, unknown surgery type	17	80.1	0.55	0.35–0.86		0.58	0.34–0.98
Radiation							
No/Unknown	277	86.6	1.00	ref	<0.01	1.00	ref
Yes	50	86.3	0.56	0.38–0.82		0.72	0.51–1.02
Systemic therapy, based on 1st regimen							
No/unknown	129	89.5	1.00	ref	<0.01	1.00	ref
Carboplatin, Pemetrexed	69	87.3	0.62	0.38–1.00		0.64	0.45–0.93
Cisplatin, Pemetrexed	87	82.5	0.43	0.31–0.61		0.65	0.45–0.93
Other systemic	42	85.4	0.47	0.33–0.66		0.58	0.41–0.83

AJCC-7: American Joint Committee on Cancer 7th edition

[1]Weighted percentage of patients whowere deceased as of December 31, 2013.

[2]Global Wald Chi-Square test.

[3]Hazard ratio from a multivate model.