

## Research Paper

# Survival Analysis in Patients with Malignant Pleural Effusion



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Cancer,  
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## ABSTRACT

**Aims** The present study aimed to assess the survival of patients with malignant pleural effusion (MPE) and identify factors that impact prognosis. It is crucial to identify these factors and provide appropriate treatment for patients with lower survival rates in MPE.

**Materials & Methods** This study analyzed the survival of patients with MPE in oncologic clinics in Yazd from 2011-2021. It was a descriptive cross-sectional study that utilized Kaplan-Meier analysis for survival analysis. The survival time was measured from pathological diagnosis to death. The data were analyzed in SPSS software (version 21).

**Findings** The study involved 135 patients (mean age: 54.24; range: 22-65). Most patients were in their 6th and 7th decades, and only 6.7% of cases were under 40 years old. Regarding gender, 63 cases were male, and 72 subjects were female. The main causes of metastasis in MPE patients were lung cancer, breast cancer, and adenocarcinoma of unknown origin. Chemotherapy, followed by combination therapy, was the common treatment approach. Out of 135 patients, 109 cases passed away during the study. The average survival time was 21.67 months, with a 30% chance of 2-year survival and a 10% chance of 5-year survival. The study found no significant relationship between survival rate and gender or cause of the disease (mesothelioma or metastasis); nonetheless, age, treatment type, and malignancy type exhibited a significant relationship.

**Conclusion** Timely diagnosis and appropriate treatment are crucial for improving patient survival, especially in the first two years. It is essential to prioritize screening, diagnosis, and treatment of low survival rate cancers, such as lung cancer, adenocarcinoma of unknown origin, and renal cell carcinoma.

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## مقاله پژوهشی

# تجزیه و تحلیل بقا در بیماران مبتلا به پلورال افیوژن بدخیم

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## چکیده

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**هدف** این مطالعه با هدف ارزیابی بقای بیماران مبتلا به پلورال افیوژن بدخیم (MPE) و شناسایی عوامل موثر بر پیش آگهی انجام شد. شناسایی این عوامل و ارائه درمان مناسب برای بیمارانی که میزان بقای کمتری در MPE دارند بسیار مهم است.

**مواد و روش ها** این مطالعه به بررسی بقای بیماران مبتلا به پلورال افیوژن بدخیم در کلینیک‌های انکولوژی یزد در سال‌های ۱۳۹۱ تا ۱۴۰۱ می‌پردازد. این مطالعه توصیفی مقطعی بود که از آنالیز کاپلان مایر برای آنالیز بقا استفاده شد. زمان بقا نیز از تشخیص پاتولوژیک تا مرگ اندازه گیری شد. تجزیه و تحلیل‌های آماری نیز با استفاده از نرم‌افزار SPSS نسخه ۲۱ انجام شد.

**یافته‌ها** این مطالعه شامل ۱۳۵ بیمار (میانگین سنی: ۵۴/۲۴ سال، دامنه: ۲۲-۶۵ سال) بود. اکثر بیماران در دهه ششم و هفتم خود بودند که تنها ۶/۷ درصد آنها زیر ۴۰ سال داشتند. از بین بیماران ۶۳ نفر مرد و ۷۲ نفر زن بودند. علل اصلی مناساز در بیماران MPE سرطان ریه، سرطان سینه و آدنوکارسینوم با منشا ناشناخته بود. همچنین، شیمی درمانی به دنبال درمان ترکیبی رویکرد درمانی رایج بود. متأسفانه ۱۰۹ نفر از ۱۳۵ بیمار در طول مطالعه فوت کردند. میانگین مدت بقا ۲۱/۶۷ ماه بود، با ۳۰ درصد احتمال بقای ۲ ساله و ۱۰ درصد احتمال بقای ۵ ساله. این مطالعه رابطه معناداری بین میزان بقا و جنس یا علت بیماری (مزوتلیوم یا مناساز) پیدا نکرد، اما سن، نوع درمان و نوع بدخیمی رابطه معناداری را نشان داد.

**نتیجه‌گیری** تشخیص به موقع و درمان مناسب برای بهبود بقای بیماران، به‌ویژه در ۲ سال اول بسیار مهم است. اولویت‌بندی غربالگری، تشخیص و درمان سرطان‌هایی با میزان بقای پایین مانند سرطان ریه، آدنوکارسینوم با منشا ناشناخته و RCC ضروری است.

## کلیدواژه‌ها:

آنالیز بقا  
پلورال افیوژن بدخیم  
پیش آگهی  
سرطان

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## Introduction

**M**alignant pleural effusion (MPE) is the most common complication of advanced tumor in patients, with up to 25% and 50% of patients with lung and breast cancer, respectively, suffering from increased pleural fluids and symptomatic pleural effusion [1, 2]. In general, breast and lung cancer are the most common causes of MPE. In fact, malignancies involving the pleura are the third leading cause of pleural effusion [2]. About 50% of patients with metastatic cancers develop MPE. The presence of MPE in these patients indicates that these tumors are incurable by surgery, reducing the survival rate of patients. Moreover, the quality of life of these patients is significantly reduced due to such symptoms as shortness of breath and cough. There are several treatment options for MPE, and appropriate treatment is selected based on the patient's symptoms and function, primary cancer and its response to systemic treatment, and reopening of the lung following drainage of pleural fluid [2, 3]. Meanwhile, conventional therapies do not improve all patients and impose high costs on patients. Surgical procedures are often not welcomed by patients due to their invasive nature [4, 5].

The MPE indicates an advanced underlying disease with an average survival of 3-12 months [6]. In a study by DeBiasi et al., the mortality rate of patients with MPE was 37% and 77% 30 days and 12 months after diagnosis [7]. Due to the heterogeneity in the group of patients with MPE, predicting the prognosis and survival of these patients is a challenge. The improvement of treatment methods for MPE and various oncological treatments highlights a need to evaluate the prognosis of the disease and choose the type of treatment to improve patient survival. Various factors, such as tumor type and function and systemic inflammatory markers, affect patient survival [8].

Therefore, identifying the factors affecting the survival of patients with MPE is of great importance in promoting and improving lifestyle, life expectancy, and quality of life, as well as increasing the success rate of treatment in these patients. In light of the aforementioned issues, the present study aimed to evaluate survival in patients with MPE.

## Materials and Methods

This descriptive cross-sectional study was performed to evaluate the survival analysis in patients with MPE in oncologic clinics in Yazd, Iran, from 2011-2019. A total of 135 patients with MPE until 2019 were included in the study, and patients who had incomplete medical records or could not access them to complete the data and had other malignancies were excluded from the study. The Ethics Committee of the Islamic Azad University of Medical Sciences approved this study in accordance with

the Helsinki Declaration guidelines.

After making the necessary coordination with the management of oncology clinics and medical records, the list of all patients with MPE up to 2019 was extracted. Thereafter, eligible patients were recruited in the study after reviewing the medical records, inclusion and exclusion criteria, as well as additional information extracted from their medical records. Following that, demographic characteristics, including age, gender, history of smoking, and history of underlying diseases, such as diabetes, hypertension, and cardiovascular disease, were extracted from patients' medical records. Moreover, other studied variables, such as the type of treatment and the underlying cancer, were extracted and recorded. Patients or their families were contacted for the patient's survival status. It is worth noting that throughout the study, patients' personal information was only available to the project manager, and every effort was made to protect the information.

Statistical analyses were performed using the SPSS software (version 21). The relationship between prognostic factors and outcome was modeled statistically by univariate Kaplan-Meier survival analysis. For each potential predictor, stepwise modeling was performed to screen variables for inclusion in the model. The multivariate Cox regression or proportional hazards regression method was used to investigate the effect of several independent variables (prognostic factors) on survival time. The Cox model provides an estimate of the hazard ratio and its 95% confidence intervals (CIs). The resultant risk variables in the Cox regression analysis were visualized by Kaplan-Meier curves. Statistical comparisons were performed using the Kaplan-Meier method with the log-rank test. A type I error probability of 0.05 (a two-tailed p-value) was used as the threshold for statistical significance. A 95% CI was calculated to assess the clinical importance of the results.

## Results

This descriptive-analytical cross-sectional study was performed with the aim of survival analysis in patients with MPE in oncology clinics in Yazd, Iran, from 2011-2021. This study was conducted on 135 patients with a mean age of  $54.24 \pm 9.43$  years (range of 22-65). Most patients were in the 6th and 7th decades of their lives. Regarding gender, 63 (46.7%) subjects were male, and 72 (53.3%) cases were female. Moreover, 10 (7.4%) cases of MPE were caused by mesothelioma, and 125 (92.6%) cases were due to metastasis. The most common causes of metastasis in patients with MPE were lung cancer (31.1%), breast cancer (19.2%), and adenocarcinoma with unknown origin (17%), respectively. In this study, the most common treatment for patients with MPE was chemotherapy (57.8%), followed by combination therapy

(chemotherapy with thoracentesis) (37.8%). Table 1 displays the characteristics of 135 patients in the study and the causes of MPE.

**Table 1.** Baseline characteristics of the study population (n = 135)

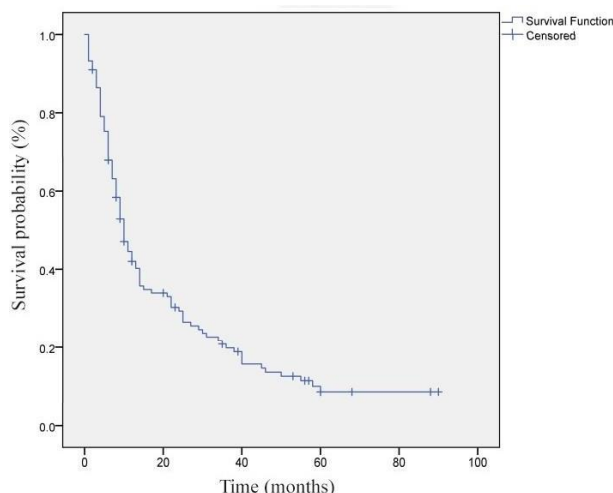
Characteristics	Value
Male, n (%)	63 (46.7)
Females, n (%)	72 (53.3)
Age Average, years	54.24 (22-65)
Age SD	9.43
Lung Cancer, n (%)	42 (31.1)
Breast Cancer	24 (19.2)
adenocarcinoma with Unknown Origin	23 (17)
Gastrointestinal Cancer	15 (12)
Gynecologic Cancer	10 (8)
Renal Cell Carcinoma	3 (2.4)
Other	8 (6.4)
Thoracentesis	6 (4.4)
Chemotherapy	78 (57.8)
Combination Therapy	51 (37.8)

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Out of 135 patients, 109 (80.7%) cases died during the study. The mean survival of patients in this study was 21.67±2.38 months (95% CI 17.01-26.34). In this study, the rates of 2-year and 5-year survival were obtained at 30% and 10%, respectively. The results of this study pointed out that the survival rate of patients was not significantly related to gender and the cause of the disease

(mesothelioma or metastasis); nonetheless, a significant relationship was observed with age, type of treatment, and type of metastasis.

Figure 1 showing Kaplan-Meier curve of the survival of all 135 patients. Also Table 2 shows Univariate analysis of the association between potential prognostic factors and survival for all 135 patients with malignant pleural effusions.



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**Figure 1.** Kaplan-Meier curve showing the survival of all 135 patients

**Table 2.** Univariate analysis of the association between potential prognostic factors and survival for all 135 patients with malignant pleural effusions

Factor	Categories	Patients (n)	Mean Survival Time (Months)	P-value
Gender	Male	63	20.72	0.34
	Females	72	21.71	
Age	<40	9	30	0.01
	40-49	35	37.1	
	50-59	38	14.61	
	>60	53	15.58	
Group	Mesothelioma	10	10.5	0.24
	Metastasis	125	22.8	
Type of Cancer	Lung Cancer	42	17.97	0.006
	Breast Cancer	24	40.26	
	Adenocarcinoma with Unknown Origin	23	9.32	
	Gastrointestinal Cancer	15	20.3	
	Gynecologic Cancer	10	21.5	
	Renal Cell Carcinoma	3	10.66	
	Other	8	25.5	

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## Discussion

Due to the dearth of studies on the survival of patients with MPE in Iran, the present research aimed to analyze the survival of patients with MPE in oncology clinics (Yazd, Iran) from 2010-2021. The results of the present study demonstrated most patients were in the 6th and 7th decades of their lives. Regarding gender, more than 50% of patients were female. Male-to-female and the mean

age of 60 years are similar to the demographic characteristics described in several studies [9, 10]. Notably, 92.6% of MPEs were metastases from underlying cancers. In line with several studies mentioned by Light [11-13], lung cancer (31.1%), breast cancer (19.2%), and adenocarcinoma with unknown origin (17%) were the most frequent primary diagnoses in our studies. Consistent with the present research, Zamboni et al. (2015), in a study on 165 patients with

MPE, pinpointed that 53% of patients were female and the mean age of patients was years [13].

MPE is slightly more common in women since one of the most prevalent causes of MPE is breast cancer. Similar to the present study, the most common causes of MPE were lung cancer (36%), breast cancer (26%), and lymphoma (13%). In a study by Hassan, 60 patients with MPE and a mean age of 74.1 years were evaluated [14]. Similar to the present study, the most common underlying factors for MPE were lung cancer and breast cancer. In the current study, the 2-year and 5-year survival rates of patients were 30% and 10%, respectively. Kaplan-Meier univariate analysis illustrated that survival was significantly associated with age, treatment type, and underlying cancer. Nonetheless, the survival rate of patients has no significant relationship with gender and the cause of the disease (mesothelioma or metastasis).

The results pinpointed that the mean survival of patients decreased significantly with age so that in the 6th and 7th decades of life, the mean survival of patients was less than that in the 5th and 4th decades. The probability of survival of patients in the 6th, 7th, and 2nd years was almost the same as in other age groups; however, after two years, a sharp decrease was observed in patient survival, while the survival probability of patients under 40 years and 40-49 years remained almost constant. In this study, the lowest survival was related to adenocarcinoma with unknown origin, renal cell carcinoma, and lung cancer, with mean scores of 9.32, 10.66, and 17.97 months, respectively. The highest survival rate pertained to breast cancer, with an average of 40.26. Moreover, the survival rate of patients undergoing combination therapy was higher than other treatments alone.

In a study by Jeba et al. 2018, 48 patients with a mean age of 53 years with MPE were evaluated. In accordance with the present study, the most common underlying cancers were lung cancer, followed by breast cancer. The mean survival of patients in their study was 14.5 months, which was less than that in the present study. Nonetheless, this difference can be ascribed to treatment, type of underlying disease, and various factors. Furthermore, the follow-up time of patients in a study by Jeba was two years. The stated research pointed out that the mean survival of patients was significantly correlated with bilateral involvement, type of treatment; however, consistent with the present study, gender, clinical signs, and lung metastasis had no effect on patient survival [15]. In their study on patients undergoing thoracentesis, DeBiasi et al. illustrated that mortality was higher in patients with bilateral MPE in the first 30 days [7].

Jeba et al. reported that patients with lung cancer had the lowest survival rates. In the present study, the lowest survival rates were related to adenocarcinoma with unknown origin, RCC, and lung cancer. Among different

cancers, consistent with the present study in which the highest survival rates were related to breast and gynecologic cancers, studies have indicated that the best survival rate is related to lymphoma (26 months), followed by breast and gynecologic cancers [10, 15].

Median overall survival was five months in a study by Zamboni et al., while in the present research, the median survival was 10 months, and the mean was 21.67 months. Consistent with the present research, in their study, patient survival had a significant relationship with the initial site of cancer, metastasis, and positive cytology; nonetheless, no significant relationship was observed with age and gender. However, in the mentioned study, the age division was limited to those who were less than 60 years old and over. In the refereed research, similar to the present study, the best survival rates were related to breast and ovarian cancers [13]. Hassan et al. pinpointed that the survival rate of patients treated with pleurodesis was higher than that of patients who did not receive treatment [14].

A study by John et al. revealed that the most common underlying causes of MPE were breast, mesothelioma, and lung cancers. The median overall survival of patients in their study was 7.1 months, which is lower than the current study (10 months). Similar to the present research, in their study, breast cancer had a higher survival rate than other cancers; nonetheless, no significant relationship was observed between patient survival and cancer type. In addition, factors, such as age, gender, weight loss, hemoglobin, creatinine, and alkaline phosphatase were not associated with patient survival; however, albumin, white blood cell count, alanine aminotransferase, Pao2, and BMI were associated with patient survival, which was not evaluated in the present study [16]. Kasapoglu et al. (2016) showed that in patients with MPE, factors, including gender, metastasis, low albumin levels, low pleural protein, increased LDH, increased CRP and WBC, and the type of treatment, affect patient survival and mortality [17]. Another study by Quek et al. in 2019 found that gender, age, type of treatment, and tumor type were the underlying predictors of mortality in patients with MPE [18]. Therefore, since MPE is an advanced disease associated with a poor prognosis and considering the most common underlying causes, lung and breast cancer, timely diagnosis and treatment are crucial steps to improve patient survival.

Among the limitations of the present study are the lack of evaluation of the underlying risk factors of the disease, laboratory findings, and relapse after treatment. Nonetheless, due to the limited studies in this field, it seems that more extensive studies are necessary to accurately identify the factors affecting the survival rate of patients with MPE. Although MPE reflects the advanced stages of the disease, identifying the factors affecting survival would be effective in managing and

selecting the type of treatment and follow-up of the patient.

## Conclusion

It seems that various factors, such as the type of treatment, age, and type of underlying cancer, play a role in the prognosis of patients with MPE. However, various studies have demonstrated various other factors that are in conflict. Therefore, it provides the basis for more extensive studies to improve the survival and quality of life of these patients by determining the effective factors in the prognosis of patients.

## Ethical Considerations

### Compliance with ethical guidelines

This study received the ethics code

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## Authors' contributions

All the authors have contributed to conducting the research.

## Conflicts of interest

The authors declared no conflict of interest.

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