Original Article

Predicting the survival in patients with malignant pleural effusion undergoing indwelling pleural catheter insertion

Muhammad Junaid Akram, Usman Khalid, Mohammad Bilal Ashraf[1], Muhammad Abu Bakar[2], Faheem Mahmood Butt, Faheem Khan[3]

Departments of Internal Medicine and [2]Cancer Registry and Clinical Data Management, Shaukat Khanum Memorial Cancer Hospital and Research Center, [1]Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan, [3]Royal Blackburn Teaching Hospital, East Lancashire Hospitals, NHS Trust, England, UK

Address for correspondence:
Dr. Muhammad Junaid Akram, Shaukat Khanum Memorial Cancer Hospital and Research Center, 7a Block R-3 M A Johar Town, Lahore, Pakistan.
E-mail: drmjunaid001@gmail.com

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Abstract:

CONTEXT: Malignant pleural effusion (MPE) is a common comorbid condition in advanced malignancies with variable survival.

AIMS: The aim of this study was to predict the survival in patients with MPE undergoing indwelling pleural catheter (IPC) insertion.

SETTINGS AND DESIGN: This was a cross-sectional study conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.

METHODS: One hundred and ten patients with MPE who underwent IPC insertion from January 2011 to December 2019 were reviewed. Kaplan–Meier method was used to determine the overall survival (OS) of the patient's cohort with respect to LENT score.

STATISTICAL ANALYSIS USED: The IBM SPSS version 20 was used for statistical analysis.

RESULTS: We retrospectively reviewed 110 patients who underwent IPC insertion for MPE, with a mean age of 49 ± 15 years. 76 (69.1%) patients were females, of which majority 59 (53.6%) had a primary diagnosis of breast cancer. The LENT score was used for risk stratification, and Kaplan–Meier survival curves were used to predict the OS. The proportion of patients with low-risk LENT score had 91%, 58%, and 29% survival, the moderate-risk group had 76%, 52%, and 14% survival, and in the high-risk group, 61%, 15%, and 0% patients survived at 1, 3, and 6 months, respectively. In addition, there was a statistically significant survival difference ($P = 0.05$) in patients who received chemotherapy pre- and post-IPC insertion.

CONCLUSIONS: LENT score seems to be an easy and attainable tool, capable of predicting the survival of the patients with MPE quite accurately. It can be helpful in palliating the symptoms of patients with advanced malignancies by modifying the treatment strategies.

Keywords:

Chemotherapy, indwelling pleural catheter, LENT score, malignant pleural effusion

Malignant pleural effusion (MPE) is one of the most common presenting features of advanced metastatic malignancies.[1,2] Majority of the patients develop symptoms such as cough, chest pain, and breathlessness leading to poor quality of life.[3,4] The prime focus of our treatment in such patients is to palliate the symptoms and improve the overall well-being of the patients.[5] Many treatment modalities are available, each with its own benefits and limitations. Repeated therapeutic thoracentesis is the one in which patients' symptoms can be improved quickly without hospitalization, but its benefit is temporary, as the MPE tends to rebuild quickly.[6] The modalities that provide long-term benefits in such patients include chemical pleurodesis, insertion of indwelling pleural catheter (IPC), or surgical

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intervention along with the management of primary disease with chemotherapy and/or radiotherapy.[1,5,7]

The prognosis in patients with MPE is usually poor, with median survival time ranging between 3 and 12 months.[1,5] The standard treatment of symptomatic MPE with expandable lung and life expectancy of at least 3 months is chemical pleurodesis using talc slurry.[5,8] The success rate of talc pleurodesis, however, is low in patients with longer survival time.[9] Talc can be re-administered after failed pleurodesis, but IPC is an innovative treatment alternative in patients with failed pleurodesis and trap lung.[5,10] It benefits the patient with less hospitalization, low re-intervention rate, and long-term good control of symptoms.[2,3,11]

There are many factors that contribute to predicting the survival in patients with MPE, including comorbidities, extent, and characteristics of malignancies and pleural effusion composition.[12,13] Many scoring systems have been suggested to predict the survival and prognostication in patients with MPE. However, only LENT score has been externally validated.[5] It is a useful tool to predict the survival rate in such patients that facilitates the prognostic information. The tool is comprised of four parameters, namely the pleural fluid lactate dehydrogenase (LDH), the Eastern Cooperative Oncology Group performance status (ECOG-PS), the serum neutrophil-to-lymphocyte ratio (NLR), and the type of primary tumor.[14]

This study is aimed to assess different prognostic factors including performance of LENT score in predicting the survival of the patients with MPE having undergone IPC insertion in Pakistan. The secondary goal is to analyze the impact of other treatment modalities for the primary disease, including chemotherapy and radiotherapy, on the overall prognosis of the patients with MPE who underwent IPC insertion. It will widen the scope of risk stratification, thus helping physicians individualize the treatment strategies for patients of MPE and improve patient care.

Methods

In this retrospective cross-sectional observational study, the electronic medical records of the patients who underwent IPC insertion for MPE from January 2011 to December 2019 were reviewed after obtaining approval from the Institutional Review Board of Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH and RC), Lahore, Pakistan. MPE is being managed with different treatment modalities including interval thoracentesis, chemical pleurodesis with talc slurry, and IPC at SKMCH and RC Lahore, Pakistan. IPC insertion has been performed either for trap lung or secondary to failed pleurodesis or as a primary intervention.

All the relevant demographic, clinical, pathological, radiological, and therapeutic information was collected. To include in a predictive model, "the LENT score" that is developed as a risk stratification tool to predict the survival of patients with MPE on the basis of clinical applicability and the result of multivariable analysis, the parameters studied in details were pleural fluid LDH levels, ECOG-PS, NLR in complete blood count, type of malignancy of the patient with MPE, the insertion and removal of IPC, its indications, status of chemotherapy and radiotherapy, incidence of IPC-related infection and other complications, and overall survival (OS) rate as well.

The IBM SPSS version 20 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Mean ± standard deviation was reported to summarize quantitative data, whereas frequencies and percentages were used to organize qualitative data. The association of explanatory variables in relation to patient status (alive or death) was determined using the Chi-square test. Kaplan–Meier survival curves were used to assess OS of the patient's cohort. A log-rank test was applied to compare the OS among the reviewed group of patients. The statistical significance is defined as a two-tailed $P \leq 0.05$.

Results

We retrospectively reviewed 110 patients who underwent IPC insertion for MPE at our center, with a mean age of 49 ± 15 years. The majority of the patients were females (76, 69.1%), of which around 59 (53.6%) had primary diagnosis of breast cancer. In addition, most of the patients had trap lung (46, 41.8%). Moreover, more than half of the patients had uniloculated pleural effusion (67, 60.9%). Fifty-one (46.3%) patients were receiving pre- and post-IPC insertion chemotherapy. Furthermore, 66 (60%) patients were provided with documented domiciliary IPC care education, as shown in Table 1.

On the basis of their respective LENT score, the patients with MPE are categorized into low-risk (score 0–1), $n = 44$ (40%), moderate-risk (score 2–4), $n = 29$ (26.4%), and high-risk (score 5–7), $n = 37$ (33.6%), prognostic groups, for the ease of interpretation, as shown in Table 2.

The Kaplan–Meier survival curves are shown in Figures 1 and 2. The patients with moderate- and high-risk LENT scores had high hazard ratio (95% confidence interval [CI], P value) for mortality of 2.45 (CI = 0.60–10.26, $P = 0.22$) and 5.51 (CI = 1.23–24.74, $P = 0.03$), respectively, compared with those with a low-risk LENT score. The overall median survival

Table 1: Baseline characteristics of patients with postindwelling pleural catheter insertion in patients with malignant pleural effusion

Variables categories	Total, *n* (%)
Age, mean±SD*	49±15
Sex	
Male	34 (30.9)
Female	76 (69.1)
Body mass index, mean±SD*	24±5
Primary disease	
Breast cancer	59 (53.6)
Lymphoma	11 (10.0)
GI tumor	9 (8.2)
Ovarian cancer	8 (7.3)
Renal cancer	2 (1.8)
Lung cancer	8 (7.3)
Miscellaneous	6 (5.5)
Head-and-neck tumors	3 (2.7)
Orthopedic tumor	2 (1.8)
Ewing sarcoma	1 (0.9)
Tonsil cancer	1 (0.9)
Indications	
Trap lung	46 (41.8)
Patient preference/primary intervention	36 (32.7)
Failed pleurodesis	28 (25.5)
Mode of insertion	
Inpatient	81 (73.6)
Outpatient	29 (26.4)
Sonomarking	
Yes	86 (78.2)
No	24 (21.8)
Pleural effusion	
Uniloculated	67 (60.9)
Multiloculated	43 (39.1)
Pre- and postprocedure chemotherapy	
Not administered	59 (53.6)
Administered	51 (46.4)
Domiciliary IPC care education	
Yes	66 (60.0)
No	44 (40.0)
Patient's status	
Death	89 (80.9)
Alive	21 (19.1)

SD=Standard deviation, GI=Gastrointestinal, IPC=Indwelling pleural catheter

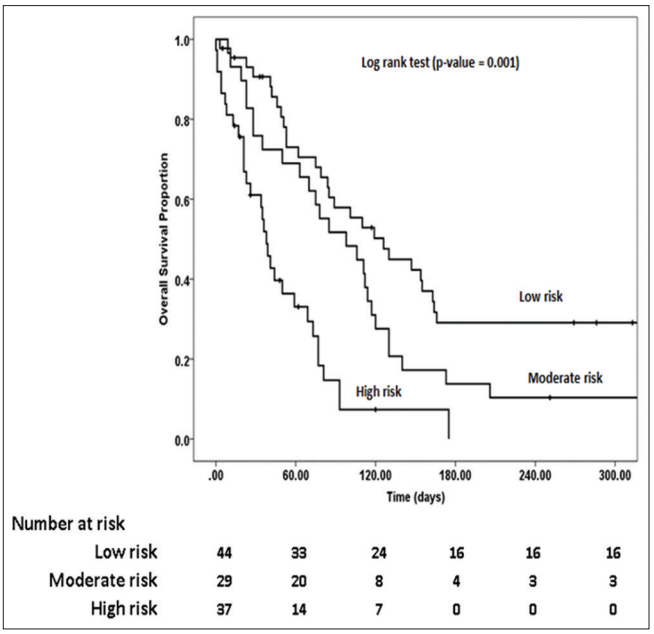

Figure 1: Kaplan–Meier curve and the survival proportion of the patients with malignant pleural effusion at different time intervals according to low-, moderate-, and high-risk "LENT scores"

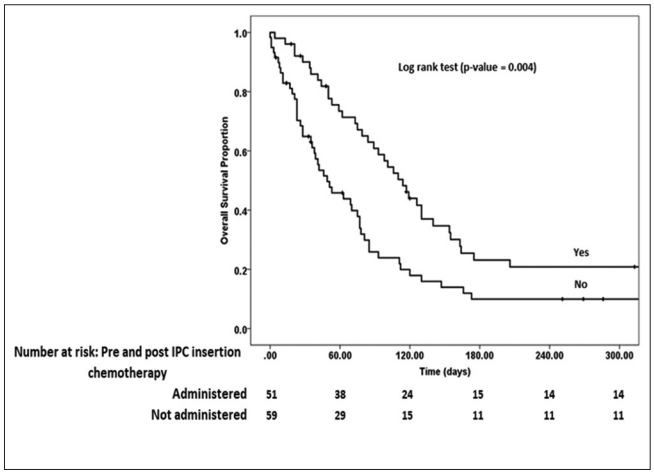

Figure 2: Kaplan–Meier curve and the survival proportion of the patients with malignant pleural effusion who have received pre- and postindwelling pleural catheter insertion chemotherapy at different time intervals (Yes: Received pre- and postindwelling pleural catheter insertion chemotherapy, No: Not received both pre- and post-procedure chemotherapy)

of the entire study population with LENT score was 69 days (range, 1–1373; $n = 110$). In addition, the patients with a low-risk LENT score had a median survival of 105 days (range, 3–1373; $n = 44$), and 91%, 58%, and 29% survived to 1, 3, and 6 months, respectively. Those with a moderate-risk LENT score had a median survival of 98 days (range, 1–502; $n = 29$), and 76% survived to 1 month, 52% to 3 months, and 14% to 6 months. This compares with those with a high-risk LENT score who had a median survival of only 35 days (range, 1–175, $n = 37$), and their chances of surviving 1, 3, and 6 months were 61%, 15%, and 0%, respectively, as shown in Table 3 and Figure 1.

There was a statistically significant relationship among patients receiving pre- and postprocedure chemotherapy and their survival time ($P = 0.04$). Those who had not received pre- and post-IPC insertion chemotherapy ($n = 59$) had a median survival of 41 days (range, 1–894), and 65%, 27%, and 10% survived to 1, 3, and 6 months, respectively. Whereas, those who had received pre- and postprocedure chemotherapy ($n = 57$) had a median survival of 106 days (range, 04–1373), and 91% survived to 1 month, 61% to 3 months, and 23% to 6 months, as shown in Figure 2. Overall IPC-related

infections were diagnosed in 28 patients (25.4%), of which mostly are hospital acquired. A statistically significant (P = 0.03) reduction in infection rate was found among patients who received domiciliary IPC care education. Out of 66 (60%) patients who received domiciliary IPC care education, only 12 (18.2%) patients had developed infection. The association of demographic and clinical variables with patients' LENT score (Low, moderate and high) is described in Table 4.

Table 2: The LENT score calculation and risk stratification groups of our study population

	Variables	Total, *n* (%)
L	LDH level in pleural fluid (IU/L)	
	<1500	0
	>1500	1
E	ECOG performance status	
	0	0
	1	1
	2	2
	3-4	3
N	NLR	
	<9	0
	>9	1
T	Tumor type	
	Low-risk tumor types	
	Mesothelioma	0
	Hematological malignancy	
	Moderate-risk tumor types	
	Breast cancer	1
	Gynecological cancer	
	Renal cell carcinoma	
	High-risk tumor types	
	Lung cancer	2
	Other tumor types	
Risk categories	**Total score**	***n* (%)**
Low risk	0-1	44 (40.0)
Moderate risk	2-4	29 (26.4)
High risk	5-7	37 (33.6)

LDH=Lactate dehydrogenase, ECOG=Eastern Cooperative Oncology Group, NLR=Neutrophil-to-lymphocyte ratio

Discussion

Recurrent pleural effusion is one of the most frequent presentations, marking it the common comorbid condition in many patients with advanced malignancies. It ultimately increases the disease burden and causes a major impact of morbidity and mortality.[8,15] The use of IPC is the emerging trend among the physicians in palliating the symptoms of the patients with MPE.[11,16] Initially, guidelines declare chemical pleurodesis as the first-line management of MPE, reserving IPC as a second-line treatment option or for those patients with trap lung.[8] However, recent data have shown an equal efficacy of chemical pleurodesis and IPC insertion as a primary intervention for MPE.[11] However, the clinical outcomes including prevalence of infections and its relation to the oncological treatments such as chemotherapy remain the primary concern;[4,7,17,18] therefore, more randomized controlled trials are required.

Due to heterogeneity in the groups of patients with MPE, the prediction of survival and prognosis is a big challenge. Along with the proper management of MPE with minimally invasive technique and oncological modalities, including chemotherapy and/or radiotherapy, there is a dire need of prognostication to customize the most appropriate treatment.[19]

This study is the first report to predict the survival in patients with MPE undergoing IPC insertion in Pakistan. Our initial results suggest that LENT prognostic score is a useful tool in predicting the survival. It is a helpful prognostic tool for the clinicians in stratifying further management strategies for patients with MPE. The primary malignant cell types causing MPE vary across the globe. The most common cancer type in our study cohorts was breast, followed by lymphoma that is comparable to the previously published literature. MPE occurs in about 8%–38% of patients with breast cancer.[8,19]

Table 3: Comparison of median survival and survival proportion at 3 and 6 months based on LENT score in the current study, with the published literature by Clive *et al*.[20] and Abisheganaden *et al*.,[14]

Variables categories	LENT score		
	Clive *et al*.[20] (*n*=203)	Abisheganaden *et al*.[14] (*n*=70)	Current study (*n*=70)
Survival, days			
High risk (LENT 5-7)	44 (22-77)	190.5 (4-1216)	35 (1-128)
Moderate risk (LENT 2-4)	130 (47-467)	346 (18-1193)	98 (1-502)
Low risk (LENT 0-1)	319 (228-549)	-	105 (3-1373)
Survival rate at 3 months (%)			
High risk (LENT 5-7)	13	-	15
Moderate risk (LENT 2-4)	59	-	52
Low risk (0-1)	98	-	58
Survival rate at 6 months (%)			
High risk (LENT 5-7)	3	53	0
Moderate risk (LENT 2-4)	47	70	14
Low risk (0-1)	86	-	29

Table 4: Descriptive statistics of independent variables with patients' LENT score (low, moderate, and high) postindwelling pleural catheter insertion in patients with malignant pleural effusion

Variables categories	Low risk (*n*=44; 40.0%), *n* (%)	Moderate risk (*n*=29; 26.4%), *n* (%)	High risk (*n*=37; 33.6%), *n* (%)	*P*
Age, mean±SD*	50±17	46±13	49±15	0.78
Sex				
Male	6 (13.6)	12 (41.4)	16 (43.2)	0.01
Female	38 (86.4)	17 (58.6)	21 (56.8)	
Body mass index, mean±SD*	24±6	25±5	24±5	0.45
Primary disease				
Breast cancer	36 (81.8)	12 (41.4)	11 (29.7)	0.001
Lymphoma	6 (13.6)	3 (10.3)	2 (5.4)	
GI tumor	1 (2.3)	4 (13.8)	4 (10.8)	
Ovarian cancer	1 (2.3)	4 (13.8)	3 (8.1)	
Renal cancer	0	1 (3.4)	1 (2.7)	
Lung cancer	0	0	8 (21.6)	
Miscellaneous	0	3 (10.3)	3 (8.1)	
Head-and-neck tumors	0	0	3 (8.1)	
Orthopedic tumor	0	2 (6.9)	0	
Ewing sarcoma	0	0	1 (2.7)	
Tonsil cancer	0	0	1 (2.7)	
Indications				
Trap lung	20 (45.5)	11 (37.9)	15 (40.5)	0.17
Patient preference/primary intervention	15 (34.1)	13 (44.8)	8 (21.6)	
Failed pleurodesis	9 (20.5)	5 (17.2)	14 (37.8)	
Mode of insertion				
Inpatient	32 (72.7)	21 (72.4)	28 (75.7)	0.94
Outpatient	12 (27.3)	8 (27.6)	9 (24.3)	
Sonomarking				
Yes	34 (77.3)	25 (86.2)	27 (73)	0.50
No	10 (22.7)	4 (13.8)	10 (27.0)	
Pleural effusion				
Uniloculated	27 (61.4)	20 (69.0)	20 (54.1)	0.47
Multiloculated	17 (38.6)	9 (31.0)	17 (45.9)	
Infection status				
Yes	12 (27.3)	6 (20.7)	10 (27.0)	0.79
No	32 (72.7)	23 (79.3)	27 (73.0)	
Bacteremia status				
MSSA *Escherichia coli Enterobacter*	3 (6.8)	0 (0.0)	2 (5.4)	
Acinetobacter MRSA proteus serratia	8 (18.2)	6 (20.7)	3 (8.1)	
MSSA *Morganella morganii*	0 (0.0)	0 (0.0)	1 (2.7)	
Streptococcus intermedius	1 (2.3)	0 (0.0)	0 (0.0)	
No bacteria	32 (72.7)	23 (79.3)	31 (83.8)	
Pre- and postprocedure chemotherapy				
Not administered	19 (43.2)	19 (65.5)	21 (56.8)	0.15
Administered	25 (56.8)	10 (34.5)	16 (43.2)	
Domiciliary IPC care education				
Yes	26 (59.1)	20 (69.0)	20 (54.1)	
No	18 (40.9)	9 (31.0)	17 (45.9)	
Death status				
Alive	12 (27.3)	3 (10.3)	6 (16.2)	0.17
Death	32 (72.7)	26 (89.7)	31 (83.8)	

SD=Standard deviation, GI=Gastrointestinal, IPC=Indwelling pleural catheter, MRSA=Methicillin-resistant *Staphylococcus aureus*, MSSA=Methicillin-sensitive *Staphylococcus aureus*

LENT score is an easy and cheap predicting tool that is developed as a risk stratification system for patients with MPE, based on the analysis of simple parameters including pleural fluid LDH, ECOG-PS, serum NLR, and the primary tumor type.[20] A combination of high pleural fluid LDH, poor ECOG-PS, raised NLR, and

cancer type other than mesothelioma, hematological malignancies, breast cancer, gynecological cancer and renal cell carcinoma, score highest according to the LENT scoring system.[20]

The overall median survival also varies in different study cohorts. The median survival time in our study population is comparable with the survival time reported by Clive *et al*.[20] However, another study reported the median survival time of 241 days[14] which is better than the survival reported in our study and Clive *et al*.[20] cohorts. In the current study, according to the LENT risk stratification groups, the median survival time for patients in the low-, moderate-, and high-risk groups at 3 months is comparable with the previously published literature; however, the proportion of median survival in low-, medium-, and high-risk categories at 6 months is lower as compared to the previously available literature. The likely explanation of this experience may be the demographics, variability in the clinical outcome of the primary disease and tolerability and response to different treatment modalities, and presence of other comorbidities in patients with advanced malignancies.[21-24]

The decision regarding continuation of the oncological treatment is also a very important contributing factor in predicting the survival of the patients with MPE. The results of our study are consistent with the published literature[4,25,26] that the patients who received pre- and post-IPC insertion chemotherapy have better survival proportion as compared to those who did not receive any oncological treatment before and after the intervention.

Infection is one of the most common complications of IPC. The infection rate in our study cohorts is comparable with the previously published data.[18] However, as reflected in our study, one can achieve a significant reduction in IPC-related infection by providing domiciliary IPC care education.[27] By preventing IPC-related infections, clinicians can get the maximum benefit from IPC in palliating the symptoms of the terminally ill patients that ultimately can be an important contributing factor in improving the survival of the patients. Therefore, all patients who have undergone IPC insertion should be provided with detailed IPC home care education including proper drainage using sterile technique. The appropriate follow-up appointments should be scheduled for IPC insertion site inspection, suture removal, and drainage record and to address any queries of the patient or caregiver.

Conclusions

We conclude that the LENT score is a meritorious tool in predicting the survival of the patients with MPE undergoing IPC insertion. It can easily be calculated and influential in modifying the MPE management pathway in advance malignancies. The continuation of oncological treatment including chemotherapy is also an important contributing factor in such patients. Those who were categorized as low or moderate risk can be offered either chemical pleurodesis or an IPC according to the availability of resources and expertise as their OS is good, whereas those with high risk can be further stratified according to their symptoms and access to the health care. Some patients with expected survival of more than 1 month may get benefit from chemical pleurodesis, however, try to minimize the pain and discomfort for those with lesser survival and extremely poor prognosis.

Limitation

Retrospective study design and lower number of lung cancer patients are the limitations of our study. It is likely due to poor prognosis of patients with lung cancer at their presentation to the hospital, or most of them are undiagnosed as sick enough to be suitable for any invasive investigation to find the likelihood cause of their malignancy. There is a significant lack of awareness among the general population as there is no dedicated national cancer screening pathway. Due to the limitation of resources, hospitals have stringent criteria to accept and treat patients with the advance disease and poor PS.

In addition, the current study group includes only those patients who have underwent IPC insertion for the management of MPE, not representing the whole group of patients with MPE. However, in comparison with previously published data, this study is self-representative and has its own genuine effect. The current study can provide the platform for more robust studies on the use of LENT score and other contributing factors such as chemotherapy in predicting the survival in patients with MPE.

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Conflicts of interest

There are no conflicts of interest.

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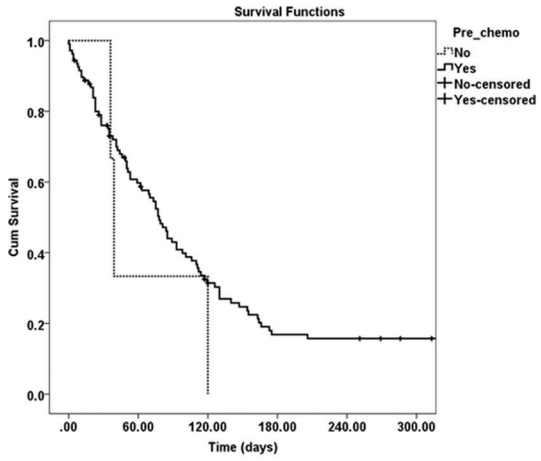
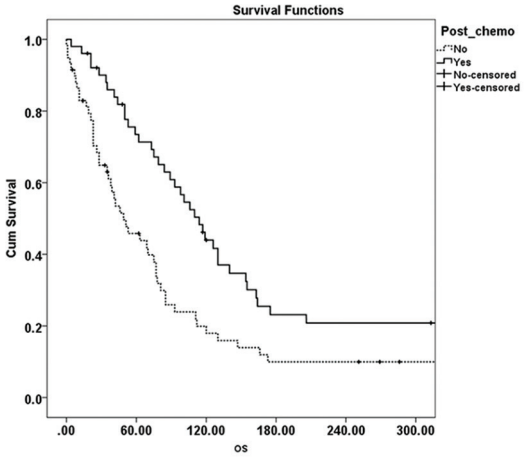
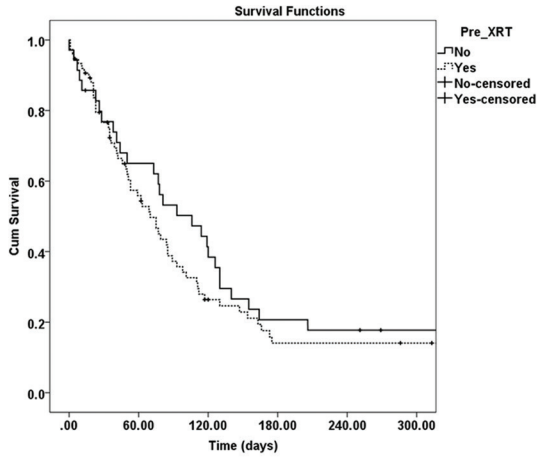
Supplementary material



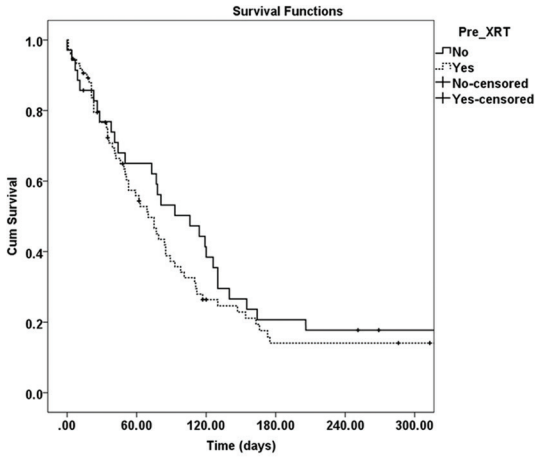
Kaplan-Maier curve: survival of patients with MPE who received chemotherapy alone (pre IPC insertion)



Kaplan-Maier curve: survival of patients with MPE who received chemotherapy alone (post IPC insertion)



Kaplan-Maier curve: survival of patients with MPE who received radiotherapy alone (pre IPC insertion)



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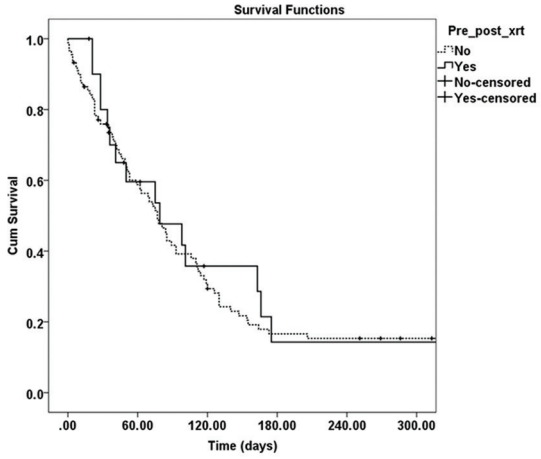
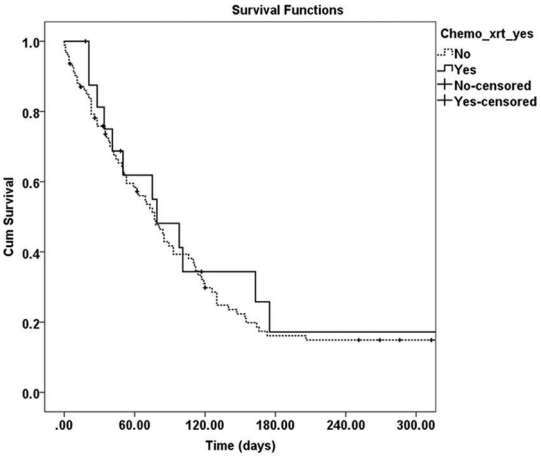


Kaplan-Maier curve: survival of patients with MPE who received radiotherapy alone (pre and post IPC insertion)



Kaplan-Maier curve: survival of patients with MPE who received combination of chemotherapy and radiotherapy (pre and post IPC insertion)