The role of prognostic nutritional index in the management of pulmonary sarcomatoid carcinoma

wang yan[1], Junfeng Liu[2], and Yu Cao[2]

[1]Hebei Medical University Fourth Affiliated Hospital and Hebei Provincial Tumor Hospital
[2]Affiliation not available

October 13, 2020

Abstract

Introduction: Pulmonary sarcomatoid carcinoma is characterized by poor survival rates compared with other non-small cell lung cancer. Prognostic nutritional index has significant prognostic value in many malignant tumors. We conducted this retrospective study to investigate the role of prognostic nutritional index in patients with pulmonary sarcomatoid carcinoma and to determine prognostic factors. Methods: Of 8176 patients with resected lung cancer in a single high-volume institution between 2008 and 2015, 91 patients with pathologically diagnosed sarcomatoid carcinoma were included in our study and evaluated. Kaplan-Meier analysis and Cox regression analysis were conducted to analyze clinicopathologic data. Subgroup analysis of overall survival and recurrence-free survival among pulmonary sarcomatoid carcinoma patients were also conducted. Results: Univariate and multivariate analysis showed that, for OS, the pathological stage (HR: 2.464; 95%CI: 1.388-4.376; P=0.002) nodal metastasis (HR: 0.432; 95%CI: 0.201-0.927; P=0.031) and PNI (HR: 0.102; 95%CI: 0.050-0.207; P<0.001) were independent prognostic factors. And for RFS, We found PNI as an independent prognostic factor (HR: 0.078; 95% CI, 0.036–0.169; P<0.001), along with nodal metastasis (HR: 0.418; 95%CI, 0.193-0.906; P=0.027) and the pathological stage (HR: 2.448; 95%CI, 1.364-4.393; P=0.003). In the subgroup of patients with PNI[?]49.4, univariate analysis showed treatment modality was a significant factor of overall survival (P=0.001); multivariate analysis showed patients received postoperative chemotherapy (HR: 0.288; 95%CI, 0.095-0.874; P=0.028) or postoperative chemotherapy with targeted therapy (HR: 0.148; 95%CI, 0.030-0.726; P=0.019) has better overall survival rates. Conclusion: The PNI and the pathological TNM stage are independent prognostic factors for pulmonary sarcomatoid carcinoma. PNI is an important indicator for the selection of postoperative adjuvant therapy. Patients with PNI [?] 49.4 may benefit from postoperative chemotherapy and targeted therapy. We still need further prospective studies to confirm these results

The role of prognostic nutritional index in the management of pulmonary sarcomatoid carcinoma

Abstract

Introduction:

Pulmonary sarcomatoid carcinoma is characterized by poor survival rates compared with other non-small cell lung cancer. Prognostic nutritional index has significant prognostic value in many malignant tumors. We conducted this retrospective study to investigate the role of prognostic nutritional index in patients with pulmonary sarcomatoid carcinoma and to determine prognostic factors.

Methods:

Of 8176 patients with resected lung cancer in a single high-volume institution between 2008 and 2015, 91 patients with pathologically diagnosed sarcomatoid carcinoma were included in our study and evaluated.

Kaplan-Meier analysis and Cox regression analysis were conducted to analyze clinicopathologic data. Subgroup analysis of overall survival and recurrence-free survival among pulmonary sarcomatoid carcinoma patients were also conducted.

Results:

Univariate analysis showed that tumor size(P=0.014 in OS, and P=0.018 in RFS), tumor stage(P<0.001 in OS, and P<0.001 in RFS), nodal metastasis(P<0.001 in OS, and P<0.001 in RFS), pathological stage (P<0.001 in OS, and P<0.001 in RFS), treatment modality (P=0.025 in OS, and P=0.049 in RFS) and PNI (P<0.001 in OS, and P<0.001 in RFS), were significant factors of both OS and RFS. In multivariate analysis, for OS, the pathological stage (HR: 2.464; 95%CI: 1.388-4.376; P=0.002) nodal metastasis (HR: 0.432; 95%CI: 0.201-0.927; P=0.031) and PNI (HR: 0.102; 95%CI: 0.050-0.207; P<0.001) were independent prognostic factors. And for RFS, We found PNI as an independent prognostic factor (HR: 0.078; 95% CI, 0.036–0.169; P<0.001), along with nodal metastasis (HR: 0.418; 95%CI, 0.193-0.906; P=0.027) and the pathological stage (HR: 2.448; 95%CI, 1.364-4.393; P=0.003). In the subgroup of patients with PNI[?]49.4, univariate analysis showed treatment modality was a significant factor of overall survival (P=0.001); multivariate analysis showed patients received postoperative chemotherapy (HR: 0.288; 95%CI, 0.095-0.874; P=0.028) or postoperative chemotherapy with targeted therapy (HR: 0.148; 95%CI, 0.030-0.726; P=0.019) has better overall survival rates.

Conclusion:

The PNI and the pathological TNM stage are independent prognostic factors for pulmonary sarcomatoid carcinoma. PNI is an important indicator for the selection of postoperative adjuvant therapy. Patients with PNI [?] 49.4 may benefit from postoperative chemotherapy and targeted therapy. We still need further prospective studies to confirm these results.

Keywords:

Pulmonary sarcomatoid carcinoma, Prognostic nutritional index, Prognosis

Introduction

Pulmonary sarcomatoid carcinoma (PSC) is considered as a rare subtype of non-small cell lung cancers with very aggressive behavior[1]. The proportion of patients with pulmonary sarcomatoid carcinoma developed recurrence, even after R0 surgery is appreciable[2]. Studies reported poor survival outcome in patients with early-stage PSCs [3]. Several case report showed that PSC is resistant to chemotherapy[4-7]. Therefore, predicting the prognosis of PSC patients accurately is important to improve PSC patients' survival and to provide important information to the management of PSC patients.

The postoperative complications, and the long-term outcomes of patients with malignances have been considered to be associated significantly with preoperative nutritional condition and immunological status [8-10]. The prognostic nutritional index (PNI), calculated based on combining the serum albumin concentration with total peripheral lymphocyte count, was initially used to assess the immune-nutritional status before or after surgery and postoperational complications in patients underwent gastrointestinal surgery[9]. Recent study show that the PNI is a prognostic factor for various carcinomas[10-12]. PNI has not yet been investigated in PSC patients to our knowledge. Therefore, we studied the correlation between the PNI and clinical characteristics and the PNI's impact on the overall survival (OS) and recurrence-free survival (RFS) in PSC patients.

Methods

Patients

Medical records between January 2008 and December 2015 were reviewed for 8176 consecutive patients with resected lung cancer and lymph node dissection at the 4th hospital of Hebei Medical University. Patients diagnosed as pulmonary sarcomatoid carcinoma with R0 resection and complete clinic-pathological data were

included for analysis. Owing to the retrospective design, patient consent was waived. The study protocol was approved by the Ethics Committee of the 4th hospital of Hebei Medical University. The follow-up was conducted at clinic and by telephone call from designated personale in follow-up center in our hospital until October 31, 2019, or patient's death.

Statistical analysis

The categorical variables between groups were compared using the X^2 test. Continuous variables with normal distribution were compared using the t test. The median value of the follow-up was 51 months. The OS was considered as the time from the operation until death. The survival curves were generated by the Kaplan–Meier method. Differences among the curves were demonstrated by log-rank P values. The mean of PNI was used as the cutoff value since PNI value conform to the normal distribution in the population. According to the cutoff value of the PNI, all patients were divided into a PNI-high group or a PNI-low group. Variables found significant in the univariate analysis were entered into a multivariate analysis. All P values of ¡0.05 were considered to be significant, and confidence intervals (CI) were calculated at the 95 % level. The statistical analyses were performed using SPSS software (version 24.0 ; SPSS, Chicago, IL).

Results

Data

We obtained the clinical characteristics of patients retrospectively from medical records and evaluated these characteristics as prognostic factors. These factors included the patient's age, sex, smoking and drinking habits, tumor size, tumor stage, tumor location, lymph node metastasis, therapeutic methods, and pathological stage. None of these patients received preoperative chemotherapy. Postoperative adjuvant chemotherapy with an platinum-based regimen (pemetrexed + cisplatin) was accepted in a total of 30 patients. And 30 patients received postoperative adjuvant chemotherapy with targeted therapy. We used the 8th edition of the American Joint Committee on Cancer TNM classification system to classified the stage of PSC [13].

Preoperative data were obtained from the patients' medical records, including serum albumin and total lymphocyte count from peripheral blood tests. Then, the following formula was used to calculated the PNI: 10* serum albumin (g/ dl) + 0.005 * total lymphocyte count (cells per mm^3)[9].

PNI and characteristics of patients

At time of final follow-up, We totally monitored 91 patients with completely resected PSC for a median of 51 months (range, 2-89). An expert pathologist performed the pathologic revision of the samples in a centralized blind way. During the revision, spindle cell carcinoma, giant cell carcinoma, pleomorphic carcinoma, carcinosarcoma, and pulmonary blastoma as 5 different subtypes of PSC were identified and distinguished. Spindle and giant cell carcinoma represented (95.6%), pleomorphic carcinoma (2.2%), carcinosarcoma (1.1%) and pulmonary blastoma (1.1%) of our whole cohort.

Mean preoperative PNI was 49.4±5.6. PNI correlated significantly with tumor stage, lymph node metastasis, TNM stage and treatment modality (Table 1). We found patients with T3-4 has significantly lower PNI than patients with T1-2 (48.30 vs. 51.53, P = 0.008). Patients with N0 have higher PNI than patients with N1-3 (50.35 vs. 48.01, P = 0.048). Patients with stage Ia-IIa have significantly higher PNI compared with patients with more advanced TNM stage (51.96 vs. 47.88, P = 0.001). Patients simply underwent surgery have significantly lower PNI than patients with postoperative adjuvant therapy (48.39 vs. 51.47, P = 0.012). Correlation between PNI and sex, age, smoking history, alcohol abuse history, tumor size, tumor location, or histologic subtype was not observed (P¿0.05). A PNI mean of 49.4 was applied to divide patients in this study. We subsequently stratified all patients into two groups, high PNI group (PNI[?]49.4; n = 39) and low PNI group (PNI <49.4; n =52). We didn't find the distributions of TNM categories differ significantly between these two groups.

PNI and survival

We compared OS and RFS in patients categorized by gender (males versus females), age (younger versus older than 60 years), smoking status (former or current smokers versus never-smokers), alcohol status (alcohol abuser versus none alcohol abuser), tumor size (tumor maximum diameter equal or less than 5cm versus larger than 5cm), tumor stage (T1-2 versus T3-4), tumor location (peripheral vs. central vs. both), nodal metastasis (N0 vs. N1-3), pathological stage (Ia-IIa vs. IIb-IIIc), treatment modality (patients received adjuvant therapy vs. patients did not received adjuvant therapy), and PNI ([?]49.4 vs. ¡49.4 (Table 2 and 4). Univariate analysis showed that tumor size (P=0.014 in OS, and P=0.018 in RFS), tumor stage (P<0.001 in OS, and P<0.001 in RFS), nodal metastasis (P<0.001 in OS, and P<0.001 in RFS), pathological stage (P<0.001 in OS, and P<0.001 in RFS), treatment modality (P=0.025 in OS, and P=0.049 in RFS) and PNI (P<0.001 in OS, and P<0.001 in RFS), were significant factors of both OS and RFS. In multivariate analysis, for OS, we found the pathological stage (HR: 2.464; 95%CI: 1.388-4.376; P=0.002), nodal metastasis (HR: 0.432; 95%CI: 0.201-0.927; P=0.031) and PNI (HR: 0.102; 95%CI: 0.050-0.207; P<0.001) were independent prognostic factors (Table 3). And for RFS, we found PNI was an independent prognostic factor (HR: 0.078; 95% CI, 0.036–0.169; P<0.001) (Table 4), the pathological stage (HR: 2.448; 95%CI, 1.364-4.393; P=0.003) and nodal metastasis (HR: 0.418; 95%CI, 0.193-0.906; P=0.027) were also independent prognostic factors (Table 5). In the high-PNI group, The adjusted HR was significantly lower than that in the low-PNI group, which suggested that patients with lower PNI had reduced survival as a group.

PNI and Long-Term Outcome

In Kaplan-Meier analysis, five-year OS rates were 4.1% and 56.4% in the low- and high- PNI groups, respectively (Fig 1) (P < 0.001). Five-year RFS rates were 4.1% and 46.2% in the low- and high- PNI groups, respectively (Fig 2) (P < 0.001). Figure 3A-D showed five-year OS and RFS curves which were stratified according to PNI among patients with stage pIa-IIa and pIIb-IIIc disease. In the group of patients with stage pIa-IIa disease, HR for OS was 0.167 (95% CI, 0.060–0.463) and HR for RFS was 0.145 (95% CI, 0.052–0.410). and in the group of patients with stage pIIb-IIIc disease, HR for OS was 0.052 (95% CI, 0.017–0.156) and HR for RFS was 0.017 (95% CI, 0.002–0.129). In the group of patients with higher PNI (PNI[?]49.4),

PNI and Causes of Death

During follow-up, 23 patients (59.0%) and 49 patients (94.2%) in the high- and low-PNI group died, respectively. In the high-PNI group, causes of death included tumor recurrence (n =10 [43.5%]), other malignancies (n =8 [34.8%]), and other causes (n =5 [21.7%]), respectively. And in the low-PNI group, tumor recurrence (n =41 [83.7%]), other malignancies (n =5 [10.2%]), and other causes (n = 3 [6.1%]),respectively. Significant difference was found between the low-PNI group (78.8%) and the high-PNI group (25.6%; p =0.005) for tumor recurrence–related death.

PNI and Treatment therapy

The difference in OS rates was significant between the group of patients with surgery and the group of patients with postoperative chemotherapy (P=0.004) but not with postoperative chemotherapy and targeted therapy (P=0.185), neither between the group of patients with postoperative chemotherapy and the group of patients with postoperative chemotherapy and targeted therapy (P=0.331). (Fig 4) The difference in RFS rates was significant between the group of patients with surgery and the group of patients with postoperative chemotherapy (P=0.009) but not with postoperative chemotherapy and targeted therapy (P=0.229), neither between the group of patients with postoperative chemotherapy and the group of patients with postoperative chemotherapy and targeted therapy (P=0.295). (Fig 5) In the subgroup of patients with PNI[?]49.4, univariate analysis showed treatment modality was a significant factor of overall survival (P=0.001) and recurrence-free survival (P=0.005); multivariate analysis showed patients received postoperative chemotherapy (HR: 0.288; 95%CI, 0.095-0.874; P=0.028) or postoperative chemotherapy with targeted therapy (HR: 0.148; 95%CI, 0.030-0.726; P=0.019) has better overall survival rates; In the subgroup of patients with PNI¡49.4, we didn't find the same results. In the subgroup of patients with PNI[?]49.4, patients received postoperative chemotherapy with targeted therapy has better OS rates than those received postoperative

chemotherapy (P=0.048, X^2=3.924); In the subgroup of patients with PNI¡49.4, we didn't find the same results (P=0.143, X^2=2.145)(Table 6, 7)(Fig 6 A-D).

Discussion

This study offers the first evidence of the prognostic value of PNI in patients with completely resected Pulmonary sarcomatoid carcinoma. Pulmonary sarcomatoid carcinoma (PSC) comprises less than 1% of lung cancers, and they respond poorly to systemic therapy [14]. Immuno-nutritional status plays an important role in postoperative outcomes. Therefore, we attempted to explore the PNI which was designed to represent immune-nutritional status as a new prognostic factor [10–13]. In our study, multivariate analysis showed that PNI and TNM classification are strong predicting factors in patients with resectable PSC.

In 2017, Lococo et al. in a multicenter study found that among their cohort, spindle cell carcinoma represented (29%), giant cell carcinoma (8%), pleomorphic carcinoma (62%), carcinosarcoma (1%), pulmonary blastoma (0%) [15]. In 2017, M. Rahouma et al. went through the the SEER database between 1973 and 2013, and revealed predominance of less aggressive histological subtypes in the 1993-2013 time period. They found spindle and giant cell carcinoma represented (72.9%), pleomorphic carcinoma (13.4%), carcinosarcoma (11.5%) and pulmonary blastoma (2.2%)[16]. Our findings in histologic subtype of PSCs seem to be inconsistent with these results of previous studies. In the present study, our results indicated that giant and spindle cell carcinoma represented the majority of the entire cohort. It might be reasonable that this rate was higher than those reported previously considering the race and region differences.

In our study, low PNI significantly correlated with advanced TNM stage, backing up the hypothesis that patients with a low PNI have a worse tumor progression. The advanced pathological stage may cause impaired immune-nutritional status. In this study, we didn't find low PNI was associated with smoking which indicated that in the low PNI group, smoking-related inflammation's contribution was limited. Similar results can be found in previous studies regarding resectable NSCLC [17]. We also found that low PNI significantly correlated with treatment modality. It might be reasonable that the patients with better nutrition status and less systemic inflammation may be recommended to receive adjuvant therapy at the pre-gene therapy time.

The most commonly used modified PNI, was first reported in prediction of postoperative complications in gastrointestinal operation. [8]. Many studies have reported that the PNI has prognostic value for various malignancies [9-12]. Qiu et al. reported that the PNI was an independent prognostic factor for patients who were received radical surgery with NSCLC [18]. Hong et al. proved that PNI could assist to identify small cell lung cancer patients with poor prognosis[19]. F. Shoji et al. indicated the PNI's value in predicting postoperative recurrence in patients with stage I NSCLC[20]. Similarly in this study, OS and RFS rates were found significantly different between the low- and high-PNI group, the PNI was an independent predicting factor in patients with resectable PSC. We also revealed that the incidences of recurrence and recurrence-related death were significantly higher in the low-PNI group. These results indicated that a low PNI may be strongly associated with disease-specific death, and lead to a worse outcome in patients with PSC.

Vieira T et al. in 2016, Velcheti V et al. in 2013, Fallet V et al. in 2015 and Schrock et al. in 2017 presented the evidence of the spectrum of genomic abnormalities that PSCs harbor might be therapeutically actionable [21-24]. In 2017, Schrock et al. reported clinical outcomes for 10 PSC patients received targeted or immunotherapy, three had partial responses and three had stable disease [24]. These reports suggest that targeted therapies and immunotherapy might have encouraging outcomes for patients with PSCs. However, in this study, we found that the overall survival of patients who received adjuvant chemotherapy combined with targeted therapy was not significantly better than that of patients who simply received adjuvant chemotherapy. In this study, the adjuvant chemotherapy regimen was pemetrexed plus cisplatin for 4 cycles. After the emergence of targeted therapy, we prescribed gefitinib or icotinib orally for 2 years or until disease progression in patients with 19Del or L858R mutations along with adjuvant chemotherapy. According to the results of this study, patients with pulmonary sarcomatoid carcinoma who received adjuvant chemotherapy combined with targeted therapy do not have an improved prognosis compared with those who simply re-

ceived adjuvant chemotherapy. Further stratified analysis revealed that the subgroup of patients with higher PNI(PNI[?]49.4) has better overall survival in the targeted therapy combined with adjuvant chemotherapy group than in the adjuvant chemotherapy group. The same advantage was not found in the subgroup of patients with PNI < 49.4. Therefore, we infer that the level of PNI in patients with pulmonary sarcomatoid carcinoma may determine whether they can benefit from targeted therapy after surgery. This study's result suggested that targeted therapy combined with adjuvant chemotherapy should be selected for patients with lung sarcomatoid carcinoma with higher PNI after surgery. For patients with pulmonary sarcomatoid carcinoma with PNI < 49.4, postoperative adjuvant chemotherapy is the best choice.

Limitation of our study was a retrospective study in a single high-volume institution, a prospective study with multicenter-participated to evaluate the optimal cutoff value of PNI and treatment strategies for patients with high or low PNI is warranted to validate our results.

Conclusions

This study indicated that the PNI and the pathological stage system are strong predictors of OS and RFS for patients with PSC. Patients with low PNI have even worse prognosis in this population.

Glossary of Abbreviations:

PSC: Pulmonary sarcomatoid carcinoma, PNI: prognostic nutritional index, OS: overall survival, RFS: recurrence-free survival, HR: hazard ratio, CI: confidence interval.

References

Yendamuri S, Caty L, Pine M, Adem S, Bogner P, Miller A. Outcomes of sarcomatoid carcinoma of the lung: a surveillance, epidemiology, and end results database analysis. Surgery 2012; 152:397–402.

Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JH, Beasley MB, et al. The 2015 World Health Organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. J Thorac Oncol 2015; 10:1243–60.

Pelosi G, Gasparini P, Cavazza A, Rossi G, Graziano P, Barbareschi M, et al. Multiparametric molecular characterization of pulmonary sarcomatoid carcinoma reveals a nonrandom amplification of anaplastic lymphoma kinase (ALK) gene. Lung Cancer 2012; 77:507–14.

Ouziane I, Boutayeb S, Mrabti H, Lalya I, Rimani M, Errihani H. Sarcomatoid carcinoma of the lung: a model of resistance of chemotherapy. N Am J Med Sci 2014; 6:342–5.

Steuer CE, Behera M, Liu Y, Fu C, Gillespie TW, Saba NF, et al. Pulmonary sarcomatoid carcinoma: an analysis of the National Cancer Data Base. Clin Lung Cancer 2017; 18:286–92.

Yendamuri S, Caty L, Pine M, et al. Outcomes of sarcomatoid carcinoma of the lung: A Surveillance, Epidemiology, and End Results database analysis. Surgery 2012; 152: 397-402.

Pelosi G, Gasparini P, Cavazza A, et al. Multiparametric molecular characterization of pulmonary sarcomatoid carcinoma reveals a nonrandom amplification of anaplastic lymphoma kinase (ALK) gene. Lung Cancer 2012; 77: 507-514.

Buzby GP, Mullen JL, Matthews DC, et al. Prognostic nutritional index in gastrointestinal surgery. Am J Surg 1980; 139: 160-167.

Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai Zasshi 1984; 85:1001-1005.

Yang Y, Gao P, Song Y, et al. The prognostic nutritional index is a predictive indicator of prognosis and postoperative complications in gastric cancer: A meta-analysis. Eur J Surg Oncol 2016;42: 1176-1182.

Kanda M, Fujii T, Kodera Y, Nagai S, Takeda S, Nakao A. Nutritional predictors of postoperative outcome in pancreatic cancer. Br J Surg 2011; 98:268–74.

Broggi MS, Patil D, Baum Y, et al. Onodera's prognostic nutritional index as an independent prognostic factor in clear cell renal cell carcinoma. Urology 2016; 96:99–105.

Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer, J Thorac Oncol. 2016; 11: 39-51.

Vieira T, Girard N, Ung M, et al. Efficacy of first-line chemotherapy in patients with advanced lung sarcomatoid carcinoma. J Thorac Oncol. 2013; 8:1574–1577.

Lococo F, Rapicetta C, Cardillo G, et al. Pathologic Findings and Long-Term Results After Surgical Treatment for Pulmonary Sarcomatoid Tumors: A Multicenter Analysis. Ann of Thorac Surg. 2017; 103:1142-1150.

Rahouma M, Kamel M, Narula N, et al. Pulmonary sarcomatoid carcinoma: an analysis of a rare cancer from the Surveillance, Epidemiology, and End Results database. Euro J of Cardio-Thorac Surg. 2018; 53:828-834.

Ding J, Yao K, Wang P, et al. Clinical significance of prognostic nutritional index in patients with glioblastomas. Medicine. 2018; 97: e13218.

Qiu C, Qu X, Shen H, et al. Evaluation of prognostic nutritional index in patients undergoing radical surgery with non-small cell lung cancer. Nutr Cancer 2015;67: 741–747.

Hong S, Zhou T, Fang W, et al. The prognostic nutritional index(PNI) predicts overall survival of small-cell lung cancer patients. Tumour Biol.36 (2015) 3389–3397.

Shoji F, Morodomi Y, Akamine T, et al. Predictive impact for postoperative recurrence using the preoperative prognostic nutritional index in pathological stage I non-small cell lung cancer. Lung Cancer 2016; 98:15–21.

Vieira T, Antoine M, Hamard C, et al. Sarcomatoid lung carcinomas show high levels of programmed death ligand-1 (PD-L1) and strong immune-cell infiltration by TCD3 cells and macrophages. Lung Cancer. 2016;98:51–58.

Velcheti V, Rimm DL, Schalper KA. Sarcomatoid lung carcinomas show high levels of programmed death ligand-1 (PD-L1). J Thorac Oncol. 2013; 8:803–805.

Fallet V, Saffroy R, Girard N, et al. High-throughput somatic mutation profiling in pulmonary sarcomatoid carcinomas using the Lung CartaTM Panel: exploring therapeutic targets. Ann Oncol. 2015; 26:1748–1753.

Schrock AB, Li SD, Frampton GM, et al. Pulmonary sarcomatoid carcinomas commonly harbor either potentially targetable genomic alterations or high tumor mutational burden as observed by comprehensive genomic profiling. J Thorac Oncol. 2017; 12:932–942.

Figure Legends:

Fig 1. Kaplan-Meier survival curves evaluate the overall survival(OS) in patients with completely resected PSC(n=91) stratified according to prognostic nutritional index (PNI). OS rate was significantly worse for patients with PNI less than 49.4 than for patients with PNI equals or higher than 49.4 (P¡0.001)

Fig 2. Kaplan-Meier survival curves evaluate the recurrence-free survival(RFS) in patients with completely resected PSC(n=91) stratified according to prognostic nutritional index (PNI). RFS rate was significantly worse for patients with PNI less than 49.4 than for patients with PNI equals or higher than 49.4 (P¡0.001)

Fig 3. Kaplan-Meier survival curves evaluate the overall survival(OS) and recurrence-free survival(RFS) in patients with completely resected PSC(n=91) stratified according to prognostic nutritional index (PNI) among patients with stage pIa-IIa (A, OS; B, RFS) or pIIb-IIIc(C,OS; D, RFS) disease. Hazard ratios (HR) of PNI for OS and RFS are lower in stage pIIb-IIIc than in stage pIa-IIa. (A, HR : 0.167, 95% CI

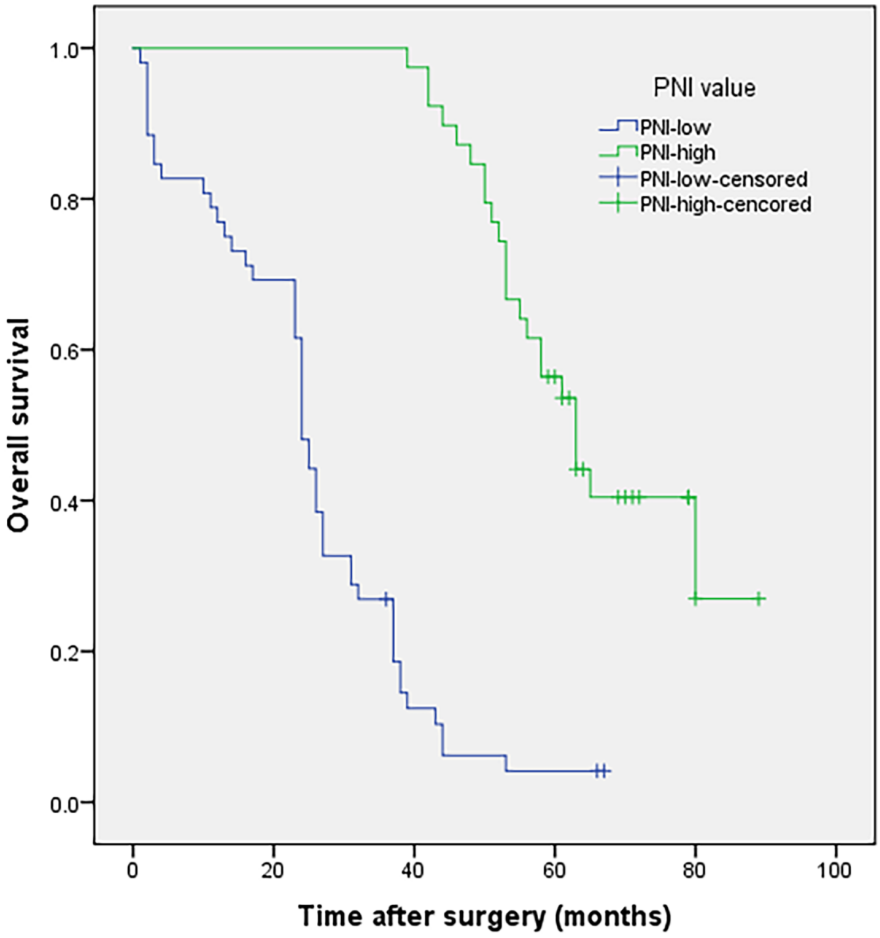
: 0.060-0.463; B, HR:0.145, 95%CI: 0.052-0.410; C, HR :0.052, 95%CI :0.017-0.156; D, HR: 0.017, 95%CI : 0.002-0.129. CI, confidence interval).

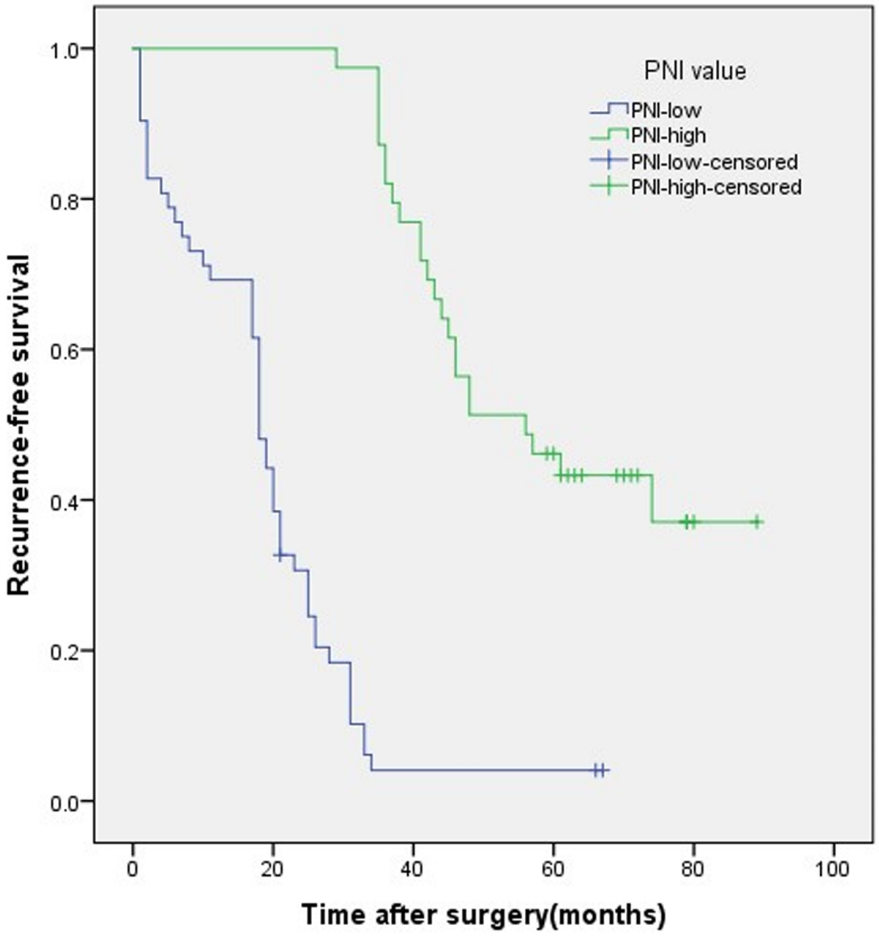
Fig 4. Kaplan-Meier survival curves evaluate the overall survival(OS) in patients with completely resected PSC(n=91) stratified according to treatment modality. The difference in OS rates was significant between the group of patients with surgery and the group of patients with postoperative chemotherapy (P=0.004) but not with postoperative chemotherapy and targeted therapy (P=0.185), neither between the group of patients with postoperative chemotherapy and the group of patients with postoperative chemotherapy and targeted therapy (P=0.331).

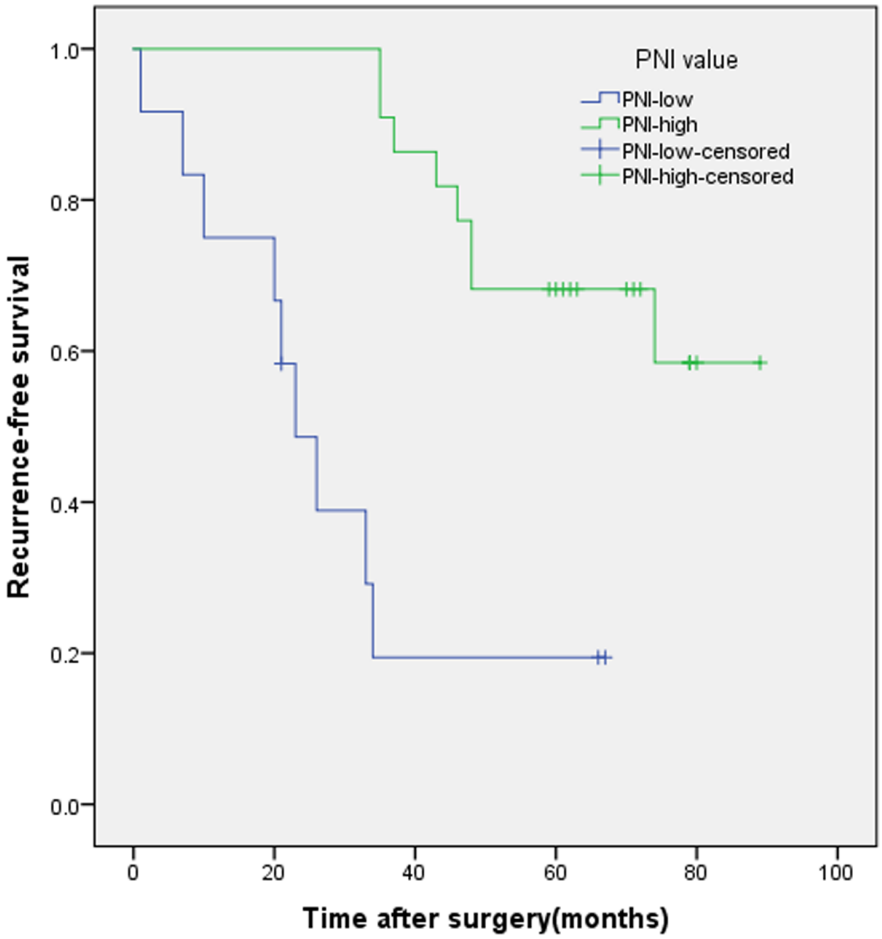
Fig 5. Kaplan-Meier survival curves evaluate the recurrence-free survival(RFS) in patients with completely resected PSC(n=91) stratified according to treatment modality. The difference in RFS rates was significant between the group of patients with surgery and the group of patients with postoperative chemotherapy (P=0.009) but not with postoperative chemotherapy and targeted therapy (P=0.229), neither between the group of patients with postoperative chemotherapy and the group of patients with postoperative chemotherapy and targeted therapy (P=0.295).

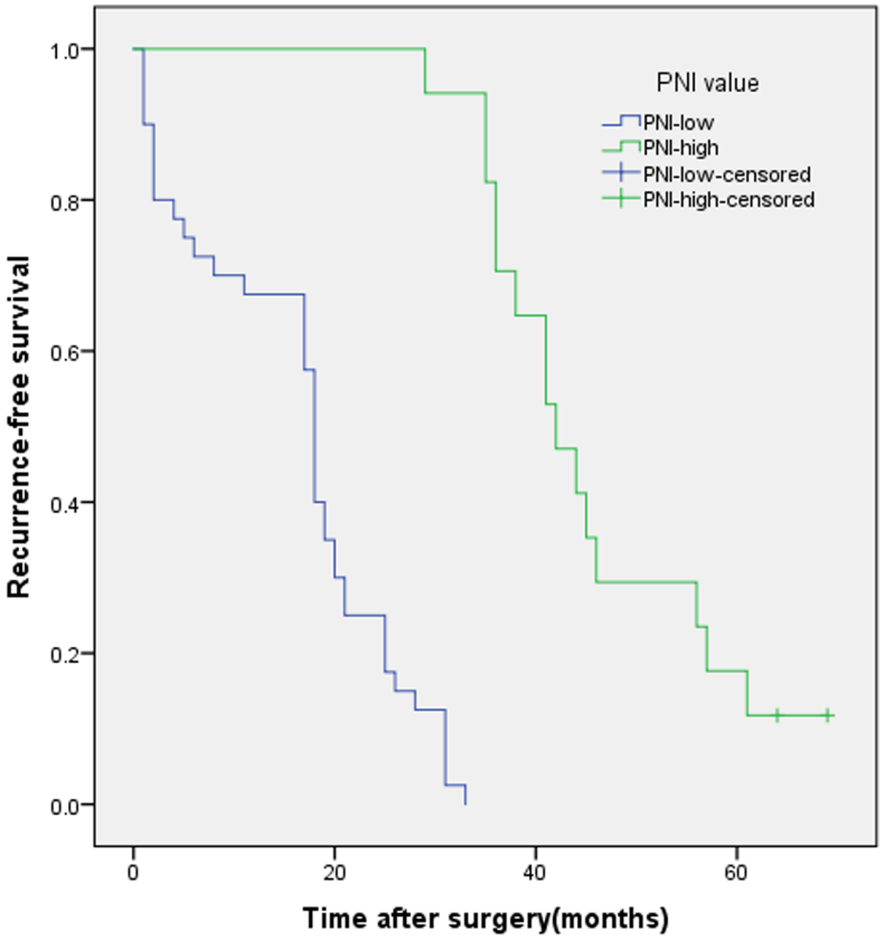
Fig 6. Kaplan-Meier survival curves evaluate the overall survival(OS) and recurrence-free survival(RFS) in patients with completely resected PSC(n=91) stratified according to treatment modality among patients with higher PNI (PNI[?]49.4) (A, OS, P=0.002; B, RFS, P=0.020) or lower PNI (PNI¡49.4)(C,OS, P=0.369; D, RFS, P=0.466).

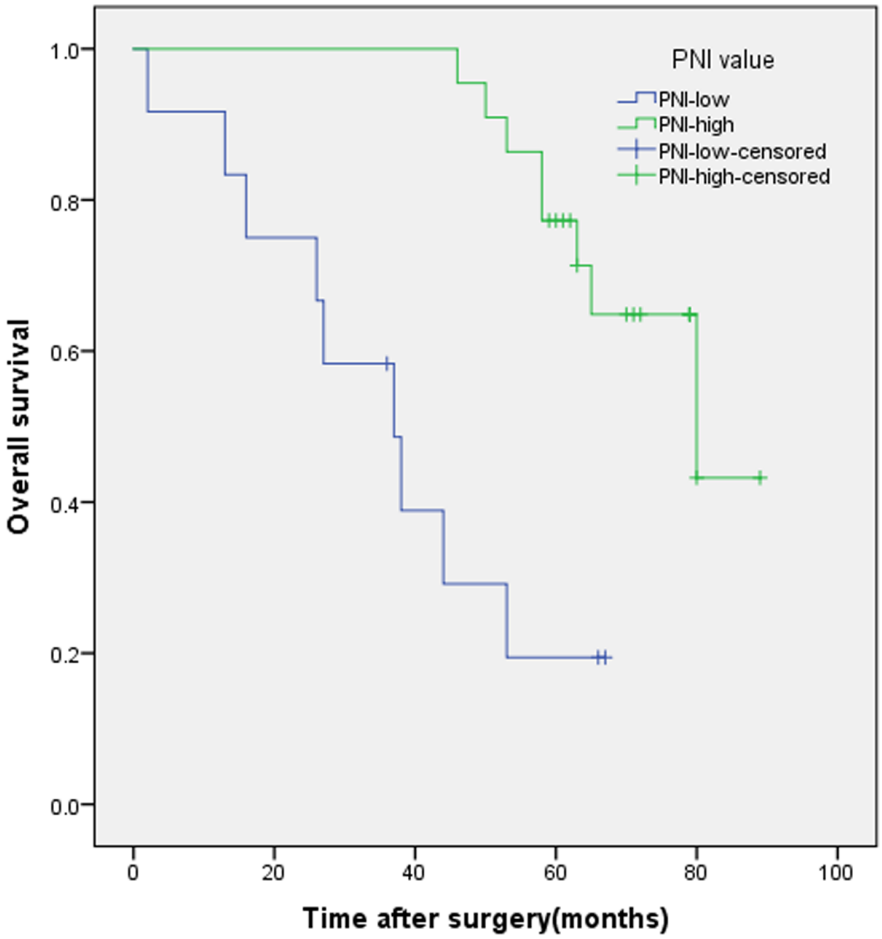
Page numbers : 15

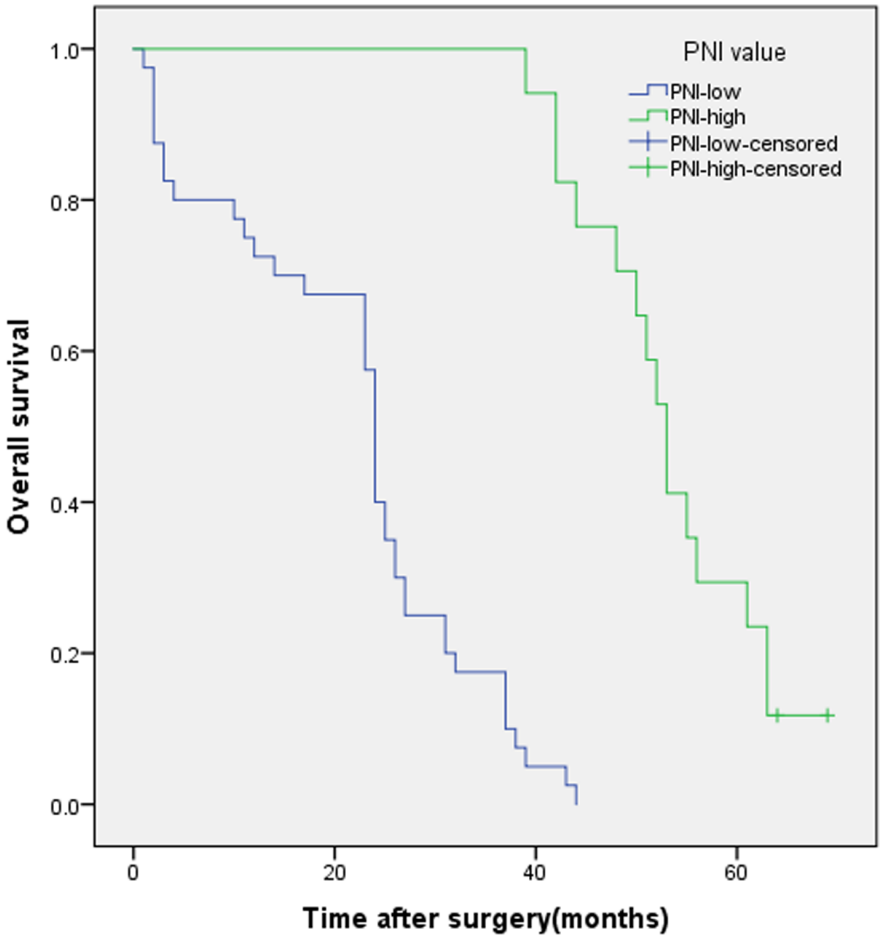


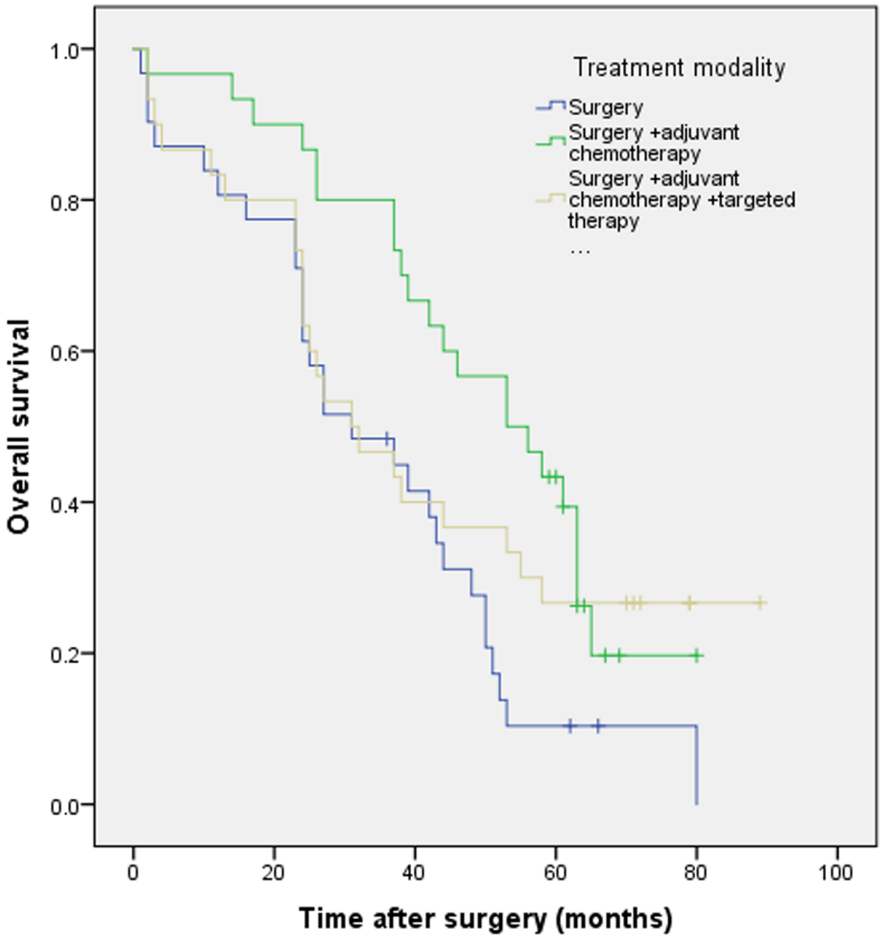


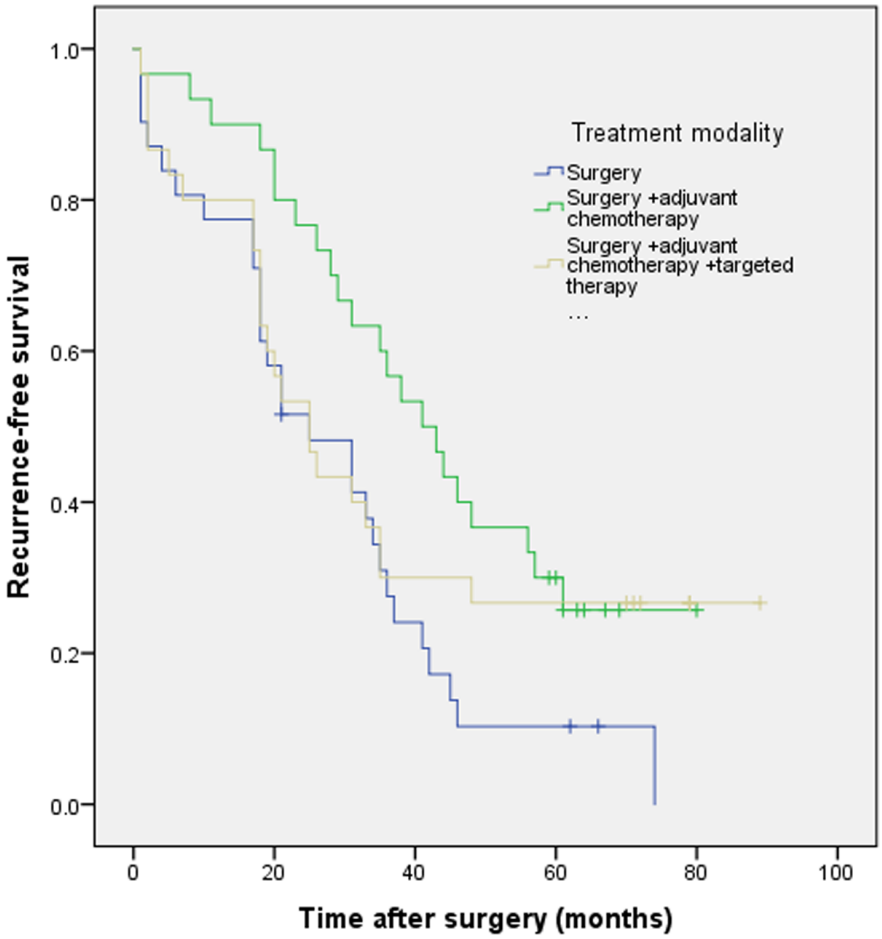


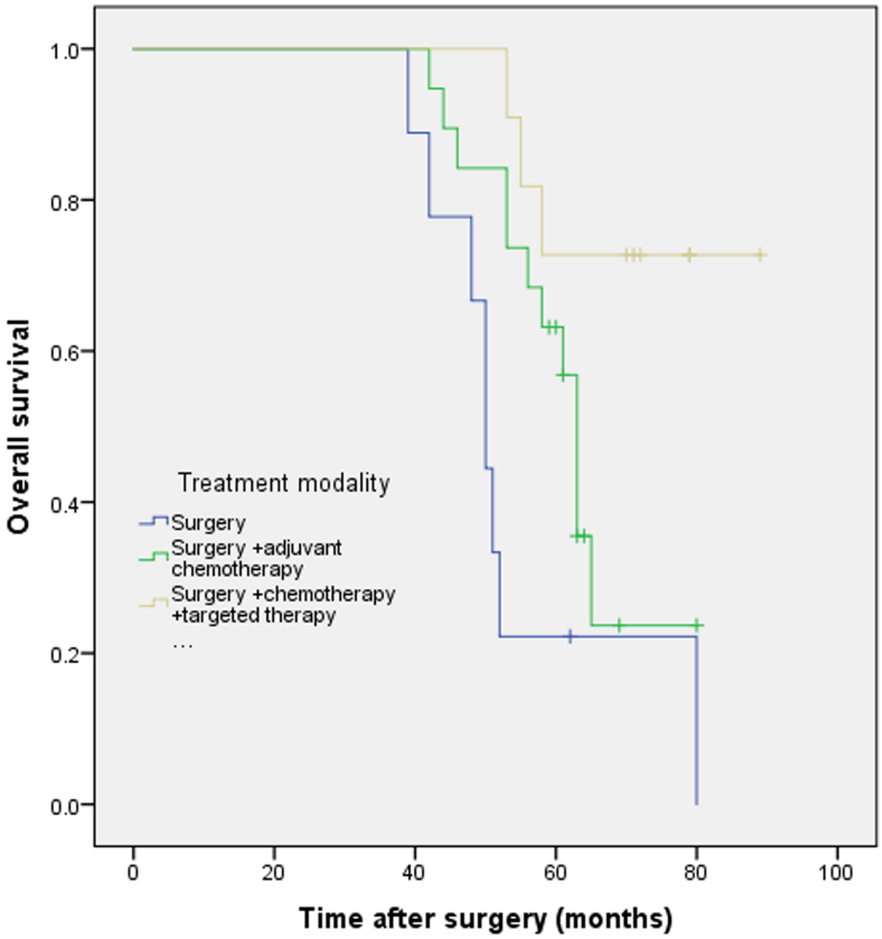


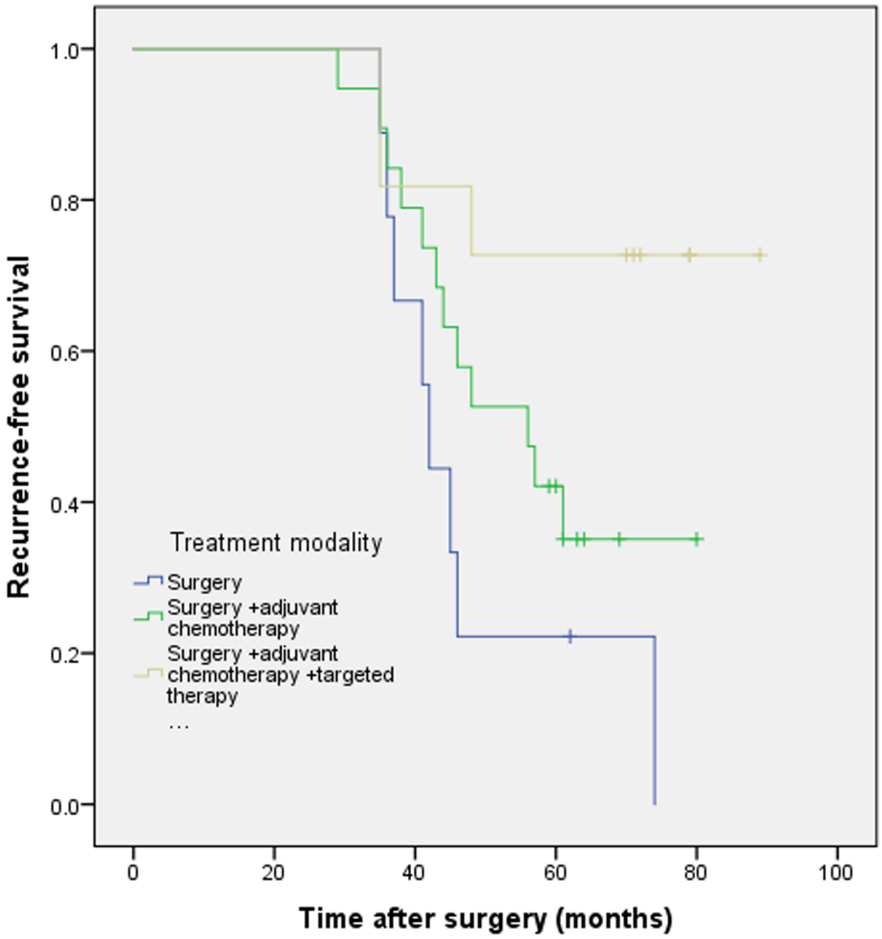


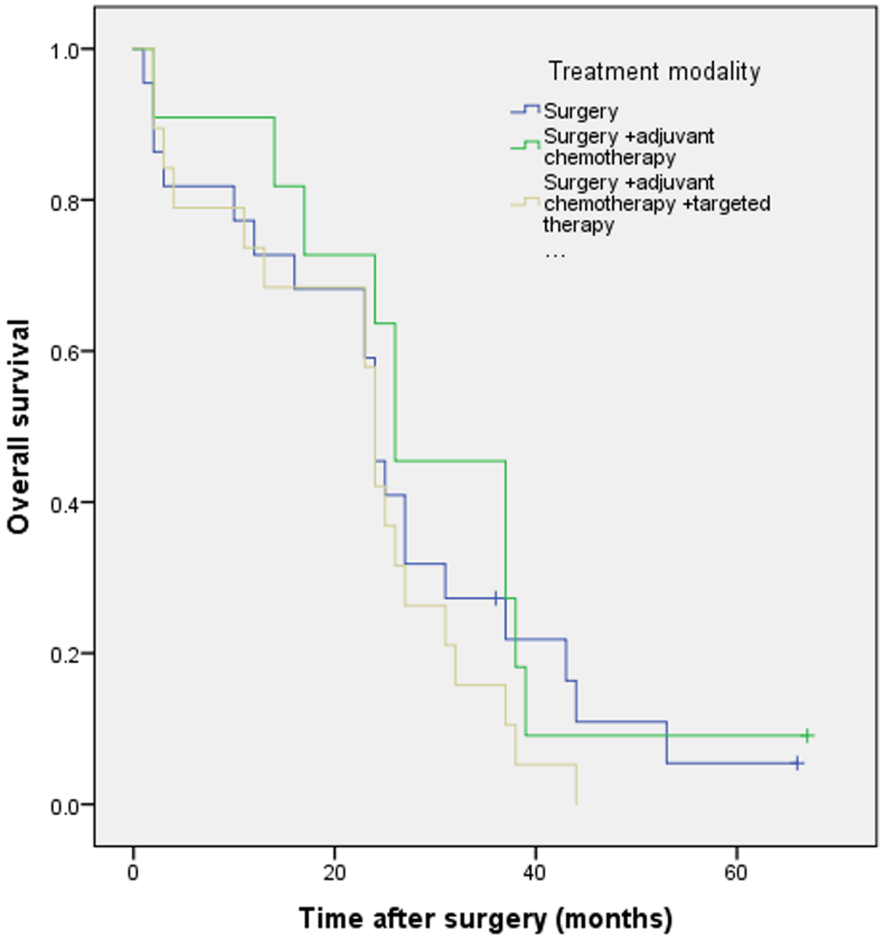


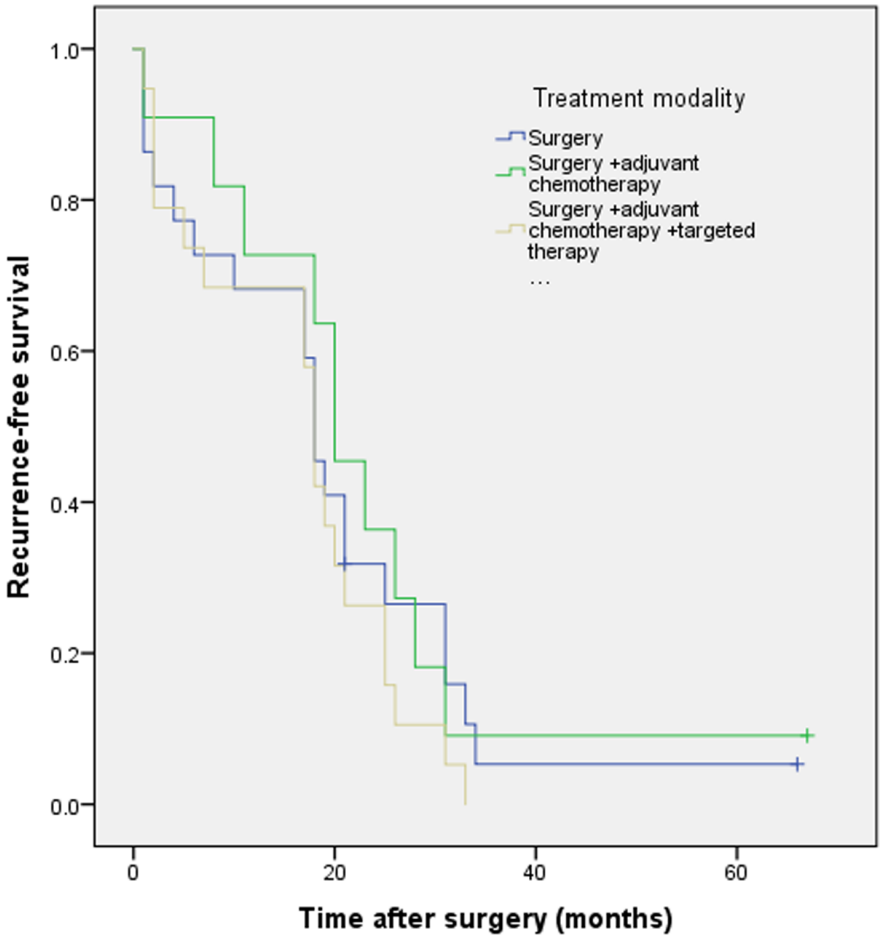












Hosted file

Table 1.pdf available at https://authorea.com/users/366710/articles/486388-the-role-of-prognostic-nutritional-index-in-the-management-of-pulmonary-sarcomatoid-carcinoma

Hosted file

Table 2.pdf available at https://authorea.com/users/366710/articles/486388-the-role-of-prognostic-nutritional-index-in-the-management-of-pulmonary-sarcomatoid-carcinoma

Hosted file

Table 3.pdf available at https://authorea.com/users/366710/articles/486388-the-role-of-prognostic-nutritional-index-in-the-management-of-pulmonary-sarcomatoid-carcinoma

Hosted file

Table 4.pdf available at https://authorea.com/users/366710/articles/486388-the-role-of-prognostic-nutritional-index-in-the-management-of-pulmonary-sarcomatoid-carcinoma

Hosted file

Table 5.pdf available at https://authorea.com/users/366710/articles/486388-the-role-of-prognostic-nutritional-index-in-the-management-of-pulmonary-sarcomatoid-carcinoma

Hosted file

Table 6 PNI high.pdf available at https://authorea.com/users/366710/articles/486388-the-role-of-prognostic-nutritional-index-in-the-management-of-pulmonary-sarcomatoid-carcinoma

Hosted file

Table 7 PNI low.pdf available at https://authorea.com/users/366710/articles/486388-the-role-of-prognostic-nutritional-index-in-the-management-of-pulmonary-sarcomatoid-carcinoma