Novel clinical biomarkers in blood and pleural effusion for diagnosing patients with tuberculosis distinguishing from malignant tumor

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Abstract

Background

Pleural effusion (PE) is a common manifestation of tuberculosis and malignant tumors, but it is difficult to distinguish tuberculous pleural effusion (TPE) and malignant pleural effusion (MPE), especially by non-invasive detection indicators. We aimed to find effective detection indexes in blood and PE for differentiating patients with tuberculosis from a malignant tumor.

Methods

815 patients were collected who diagnosed with tuberculosis or cancer at Taihe hospital from 2014 to 2017. 717 patients were found to have PE by thoracoscopy. The clinical characteristics, patients' blood parameters, and PE indicators information were summarized for analysis.

Results

The patients with MPE had higher percentages to be bloody and negative of Rivalta test in PE than patients with TPE. Then for clinical indicators, comparing specific parameters in blood, we observed 18 indicators were higher in the TPE group than in the MPE group. On contrast, 12 indicators were higher in the MPE group than in the TPE group ($p < 0.01$). In addition, in PE tests, we found there were 3 parameters higher in TPE and other 4 parameters higher in MPE patients group ($p < 0.01$). Then for clinical diagnosing practice, ROC and PCA analysis were applied. Top six relevant indicators with AUC value over 0.70 were screened out: pADA (0.90), pHsCRP (0.79), sMONp (0.75), sHsCRP (0.73), sESR (0.71), and sD-dimer (0.70). Moreover, with the Logistic regression model, a specific combination of 3 biomarkers pADA, sMONp, and sHsCRP could enhance distinguishing tuberculosis from malignant tumor patients with PE (AUC=0.944, 95% CI=0.925-0.964). For the top single marker pADA, we further analyzed its diagnostic function in patients with different group and observed it kept the high specificity and sensitivity.

Conclusions

The six indicators of pADA, pHsCRP, sMONp, sHsCRP, sESR and sD-dimer showed significant diagnostic value for clinicians. Further, the combination of pADA, sMONp, and sHsCRP has high accuracy for differential diagnosis for the first time. Mostly interestingly, pADA single marker maintained high specificity and sensitivity in patients with different status, which has great value for the rapid and accurate diagnosis of suspected cases.

Background

Pleural effusion (PE) is mainly seen in various types of inflammation, tuberculosis, and malignant tumors [1–3]. The onset of tuberculous PE is more insidious [4], with a slow course and lack specificity [5]. Malignant PE is also common, with about 20% being the first symptom and 30–40% occurring in the course of the disease, indicating poor prognosis and short survival[6]. Patients with MPE had a worse prognosis compared to patients without MPE (median survival of 7.49 vs 12.65 months, $p < 0.001$) [6]. Early diagnosis and treatment can lead to a better prognosis.

In the current clinical practice, isolation of mycobacterium tuberculosis in the pleural fluid is difficult and can be negative in the acute setting[7]. However, the main obstacle in diagnosing malignant effusions is the presence of false-negative cytological results in about 40% of cases[8]. More invasive procedures (eg, a pleural biopsy) to identify caseating granuloma from the parietal pleura may be required. Thoracoscopic surgery is decisive for TPE and MPE[9], but it is not widely used because of its invasive property. Consequently, the development of noninvasive methods is important to differentially diagnose these two diseases.

Currently, there has been reported some non-invasive studies to identify patients with PE of tuberculosis from malignant tumor [10–12], such as serum-total protein, albumin, globulin could be significantly higher in tuberculosis(TB) group than lung cancer group, at the same time, serum lactate dehydrogenase(sLDH) higher in lung cancer group than in TB group (p <0.01)[13]. Some researchers found that the serum D-dimer level of TPE patients was higher than MPE patients[14]. It also has been proved that lymphocytes and macrophages were the predominant nucleated cell in MPE, TPE was characterized by a large percentage of leukocytes and lymphocytes ($p < 0.01$) [15]. However, these results all meet the problems of low sensitivity and low specificity. In this study, we investigated clinical data of 717 patients with TPE or MPE, analyzing their clinical characteristics, hydrothorax parameters, and blood parameters. This study has a large sample size. At the same time, significant indicators in the differential diagnosis are preliminarily expounded, which is beneficial to distinguish PE early and improve the accuracy of diagnosis.

Methods

1.1 Data collection

A total of 815 patients diagnosed with tuberculosis or cancer from Taihe hospital, between 2014 and 2017, and were recruited in this study. All patients agreed to participate in the study and signed informed consent forms. All patients underwent thoracoscopic examination, 717 patients had PE. In the tuberculosis group, there were 641 cases, including 453 males and 188 females, aged 15-90 years. Aged<25 years 149 cases, aged 25-45 years 245 cases, aged 45-65 years 191 cases, aged>65 years 56 cases. There were 570 patients with PE. In the cancer group, there were 174 cases, including 92 males and 82 females, aged 15-90 years. Aged<25 years 1 case, aged 25-45 years 15 cases, aged 45-65 years 102 cases, aged>65 years 56 cases. There were 147 patients with PE.

Inclusion criteria for tuberculous PE [16]: Pathological examination revealed tuberculosis foci; Positive for acid-fast staining or positive for the culture of mycobacterium tuberculosis, or significant absorption of PE in anti-tuberculosis treatment; At least one of the above criteria should be met. Inclusion criteria for cancerous PE [17]: imaging examination showed thoracic mass shadow; PE was exudative; negative for acid-fast staining or negative for tuberculosis bacillus culture; The histological or cytological examination confirmed malignant tumor; All the above criteria must be met.

1.2 Pe And Blood Statistical Analysis

All data below were collected from Taihe hospital.

PE analysis indicators include: pADA(hydrothorax adenosine dehydrogenase), pAMS(hydrothorax amylase), pCell(hydrothorax cells), pGLU(hydrothorax glucose), pHsCRP(hydrothorax high sensitivity C reactive protein), pMON(hydrothorax monocytes), pNC(hydrothorax nucleated cells), pTC(hydrothorax total cholesterol), pTP(hydrothorax total protein);

Serum analysis indicators include: sAlb(blood albumin), sALP(blood alkaline phosphatase), sALT(alanine aminotransferase), sAPTT(activated partial prothrombin time), sAST(aspartate aminotransferase), sA/G(blood A/G), sBASp(percentage of blood basophil cells), sCa(serum calcium), sCK(blood creatine kinase), sCKI(blood creatine kinase isoenzyme), sCL(blood chlorine), sCRE(serum creatinine), sD-dimer(blood D-dimer), sEOSp(percentage of eosinophil), sESR(erythrocyte sedimentation rate), sFbg(blood fibrin), sFDP(fibrinogen degradation products), sGLO(globin), sGRANp(percentage of blood granulocytes), $sHCO3^{-}$(blood bicarbonate), sHGB(hemoglobin), sHsCRP(blood high sensitivity C reactive protein), sINR(blood internationalization standardized ratio), sK(Serum kalium), sLDH(serum lactate dehydrogenase), sLYMp(lymphocyte percentage) sMg(serum magnesium), sMONp(percentage of blood monocyte), sNA(blood natrium), sP(serum phosphate), sPA(blood prealbumin), sPLT(platelet), sPT(prothrombin time), sPTA(prothrombin activity), sRBC(red blood cell), sPTR(prothrombin time ratio), sTB(total bilirubin), sTBA(total bile acid), sTP(blood total protein), sTT(blood thrombin time), sUREA(blood urea), sWBC(white blood cell), sαHDH(blood α hydroxybutyrate dehydrogenase), sγ-GT(blood γ glutamyl transpeptidase).

Test results using the numerical analysis, data obey the normal distribution, using SPSS18.0 software for statistical analysis of count data by chi-square test, measurement data using independent t-test, comparison with the analysis of variance between groups, ROC curve to determine the best threshold (cut off) and the AUC, after the series-parallel experiment, $p < 0.05$ difference is statistically significant.

Results

1.1 Demographic and clinical characteristics of the study population

A total of 717 patients with TPE or MPE were recruited in this study. These patients were divided into two groups: 147 MPE patients (20.4%) and 570 TPE patients (79.6%)。 To distinguish TPE and MPE, as shown in Table 1, we analyzed multiple clinical status of patients and physical characteristics of the patient's pleural effusion. Among patients with hydrothorax, tuberculosis patients had a higher possibility to get a fever. Besides, malignant tumor patients (40.0%) were more likely to get bloody PE compared to tuberculosis patients. Moreover, the PE of cancer patients (67.3%) had a higher percentage to be turbid. What's more, among patients with hydrothorax, tuberculosis patients (91.6%) in the Rivalta test had a higher percentage to be positive (detailed data listed in Table 1).

Table 1
Demographic and clinical characteristics of the study population

Features	**Clinical diagnosis**			**F/X^2**
	Tuberculosis	**Cancer**	**Total**	**p-value**
Hydrothorax	641	174	815	
Yes	570(88.9%)	147(84.5%)	717	2.551
No	71(11.1%)	27(15.5%)	98	0.110
Fever	570	147	717	
Yes	346(60.7%)	18(12.2%)	364	109.79
No	224(39.3%)	129(87.8%)	353	0.0001
Total Color of pleural effusion	560	145	705 (12 missed)	
Yellow	471(84.1%)	79(54.5%)	550	73.21
Pink	30(5.4%)	8(5.5%)	38	0.0001
Red	59(10.5%)	58(40.0%)	117	
Total transparency of pleural effusion	569	147	716	
Turbid	270(47.5%)	99(67.3%)	550	18.52
Light turbid	182(32.0%)	29(19.7%)	38	0.0001
Transparent	117(20.6%)	19(12.9%)	117	
Rivalta test	570	146	716(1 missed)	
Negative	48(8.4%)	25(17.1%)	73	9.61
Positive	522(91.6%)	121(82.9%)	643	0.002

1.2 Discriminative indicators in clinical practice to identify TPE and MPE

To observe the clinical features of TPE and MPE, indicators in the blood and PE samples were examined. Firstly, tuberculosis and tumor patients were separated by using unsupervised hierarchical clustering with heatmap shown in Figure 1. We observed serum and PE indicators of tumor patients compared to tuberculosis patients are quite different (Figure 1).

To further find effective identification indicators, we compared and analyzed blood parameters and PE indicators through Mann-Whitney U test (as shown in Table 2 and Figure 2, 37 indicators among 55 indicators between each group was statistically significant, p <0.05). In the serum, the sESR, sMONp, sHsCRP and other 16 indicators were higher in the TPE group than in the MPE group (sESR: 46.27±1.16 vs 29.78±2.32, sMONp:10.35±0.17 vs 7.18±0.20, sHsCRP: 50.30±2.67 vs 19.25±3.20; p <0.01). Moreover, the sWBC, sA/G and other 10 indicators were higher in the MPE group than in the TPE group (sWBC: 7.70±0.24 vs 6.48±0.11, sA/G: 1.49±0.08 vs 1.19±0.02; p <0.01). Among the indicators of pleural effusion, the pADA, pHsCRP and pMON were higher in the TPE group than in the MPE group (pADA: 44.269±0.997 vs 11.902±0.969, pHsCRP: 24.63±1.16 vs 8.07±0.87, pMON: 79.66±0.94 vs 75.33±1.74; p <0.01), the pAMS and 3 other markers was higher in the MPE group than in the TPE group(345.851±79.170 vs 40.725±1.023, p <0.01) (Figure 2, Table 2).

Table 2 Summary of indicators from comparative analysis of serum and pleural effusion

Indicators	Diagnosis	N	Mean	SEM	Mann-Whitney U Test(Sig.)
pCell	TB	567	19858.46	3463.52	<0.001
	CA	144	59114.03	11069.29	
pMON	TB	563	79.66	0.94	<0.001
	CA	147	75.33	1.74	
pTP	TB	547	47.99	0.79	<0.001
	CA	142	50.44	6.93	
pGLU	TB	548	5.05	0.16	0.001
	CA	142	5.59	0.26	
pAMS	TB	546	40.73	1.02	<0.001
	CA	142	345.85	79.17	
pHsCRP	TB	548	24.63	1.16	<0.001
	CA	142	8.07	0.87	
pADA	TB	547	44.27	1.00	<0.001
	CA	141	11.90	0.97	
sPTA	TB	450	102.62	4.66	<0.001
	CA	121	114.07	8.63	
sPT	TB	537	13.19	1.31	<0.001
	CA	151	11.78	0.66	
sPTR	TB	523	1.46	0.38	<0.001
	CA	146	0.99	0.01	
sINR	TB	537	1.72	0.36	<0.001
	CA	151	1.26	0.24	
sAPTT	TB	537	31.81	0.25	0.013
	CA	152	30.95	0.53	
sFbg	TB	537	5.44	0.08	<0.001
	CA	152	4.77	0.14	
sD-dimer	TB	490	2.69	1.19	<0.001
	CA	141	0.67	0.07	

sFDP	TB	490	9.45	0.42	<0.001
	CA	141	7.17	0.94	
sESR	TB	530	46.25	1.16	<0.001
	CA	136	29.78	2.32	
sWBC	TB	545	6.48	0.11	<0.001
	CA	155	7.70	0.24	
sLYMp	TB	545	19.14	0.45	0.037
	CA	155	20.16	0.64	
sEOSp	TB	545	2.24	0.22	0.003
	CA	155	3.37	0.94	
sMONp	TB	545	10.35	0.17	<0.001
	CA	155	7.18	0.20	
sHGB	TB	545	120.09	0.84	0.037
	CA	155	123.27	1.55	
sPLT	TB	545	292.18	4.25	<0.001
	CA	155	255.16	6.38	
sNA	TB	492	139.38	0.32	<0.001
	CA	127	140.74	0.37	
sCL	TB	491	104.42	1.85	0.001
	CA	127	103.39	0.40	
sALT	TB	512	23.65	1.28	0.029
	CA	123	15.82	1.14	
sγ-GT	TB	512	42.48	2.30	0.001
	CA	123	29.89	2.68	
sTP	TB	425	69.07	1.72	<0.001
	CA	102	64.01	0.67	
sGLO	TB	423	32.46	0.87	<0.001
	CA	102	27.26	0.73	
sA/G	TB	423	1.19	0.02	<0.001

	CA	102	1.49	0.08	
sTB	TB	426	10.37	0.28	<0.001
	CA	104	12.38	0.62	
sTBA	TB	454	4.00	0.27	0.001
	CA	106	2.74	0.24	
sPA	TB	437	148.70	3.70	<0.001
	CA	102	193.11	7.51	
sUREA	TB	495	4.69	0.70	<0.001
	CA	127	6.75	1.89	
sCRE	TB	494	85.45	0.75	0.028
	CA	127	83.70	1.56	
sCKI	TB	58	6.33	0.35	0.038
	CA	24	14.13	5.26	
sLDH	TB	61	170.62	6.02	0.024
	CA	24	221.54	31.01	
sHsCRP	TB	301	50.30	2.67	<0.001
	CA	70	19.25	3.20	

1.3 Effective markers to distinguish tuberculosis and malignant tumor with pleural effusion

To further screen effective diagnostic indicators, these 37 indicators were applied to construct ROC Curves. Based on the AUC (area under the ROC curve value, sensitivity and specificity), top 6 indicators with higher diagnostic value were screened out (AUC ≥ 0.700) (pADA, pHsCRP, sMONp, sHsCRP, sESR and sD-dimer) (Figure 3, Table 3). In addition, PCA (principal component analysis) with these 6 serum or PE indicators revealed a clear separation between tuberculosis and malignant tumor (Figure 4). In the comparison between tuberculosis and tumor, pADA in PE showed the best AUC value of 0.90 (95% CI: 0.87-0.93).

Table 3
ROC analysis of serum and pleural effusion indicators

Features	AUC	Std. Error	95% Confidence Interval	Asymptotic Sig.
pADA	0.90	0.015	0.87-0.93	< 0.001
pHsCRP	0.79	0.021	0.75-0.83	< 0.001
sMONp	0.75	0.02	0.71-0.79	< 0.001
sHsCRP	0.73	0.031	0.67-0.79	< 0.001
sESR	0.71	0.027	0.66-0.76	< 0.001
sD-dimer	0.70	0.027	0.64-0.75	< 0.001

In addition, the potential combination schemes of metabolic biomarkers based on logistic regression analysis were applied to enhance the sensitivity and accuracy of diagnostic of tuberculosis patients from malignant tumor patients with PE. As shown in Figure 5, the combination of 3 markers (pADA, sMONp and sHsCRP), remarkable enhanced the AUC to 0.944 (95% CI: 0.925-0.964). These results indicated that 3 indicators could act as a promising combination for detection of tuberculosis from tumor with PE.

1.4 Diagnostic indicator of pADA for evaluation in different clinical patients' characteristics

According to the above, we observed the best indicator namely pADA was close to the value of combination of three markers (the only one≥0.9). Thus, we were interested in the alteration of indicators in different characters of patients. In the stratified analysis, the AUC of pADA of males was 0.897, females were 0.910, females was higher than males. The AUC of patients with fever was 0.932, and the AUC of patients without fever was 0.894, suggesting that the diagnosis accuracy of fever patients was higher. The AUC of Age <25 was 0.932, 25≤Age <45 was 0.939, 45≤Age <65 was 0.889, and Age≥65 was 0.868. Although with the increase of age, the AUC showed a downward trend, and the diagnostic accuracy decreased (Figure 6). The indicator pADA still showed the continuous distinguishing function as a diagnostic marker for tuberculosis and tumor patients with PE.

Discussion

In clinical practice, it is very common and critical to distinguish TPE from MPE as the pathogenesis, treatment, and recovery of the two diseases are different[18]. Thus early diagnosis is particularly important. In this study, comparing TPE with MPE, the patients of TPE were more likely to have a fever and the MPE was more bloody (p <0.01). It is commonly accepted by clinician that fever is a common symptom in patients with TPE[19]. Other researchers proved that compared PE caused by malignant lymphoma, patients with TPE have a higher probability of fever (Fever >37.5 °C, MPE=12%, TPE=48%, p <0.01) [20]. Moreover, consistent with our results, other clinicians also observed that MPE is mostly

bloody[21], which may be related to tumor invasion and destruction of capillaries leading to blood leakage[22].

The percentage of Rivalta test positive of TPE was higher than MPE in our results (p <0.01). It has reported that the positive rate of the Rivalta test is parallel to the amount of total protein in body cavity effusion [23]. Some researchers showed that the protein level in TPE is higher than MPE (p <0.05) [24]. Consistently, out results showed that the total protein (sTP) in TPE is higher than MPE (69.09±1.72 vs 64.01±0.67, p = 0.15) which could explain that the percentage of Rivalta test positive of TPE was higher than MPE.

In the study, the serum D-dimer were higher in the TPE group than the MPE group (2.69±1.19 vs 0.67±0.07, p = 0.37). It is proved by other researchers that the serum D-dimer level of TPE patients was higher than MPE patients[14]. However, they found the difference of D-dimer in PE was more obvious[14]. These show that D-dimer is a highly sensitive index in serum and PE, which helps to identify TPE and MPE.

We also observed the sLDH were higher in the MPE group than in the TPE group (221.54±31.01 vs 170.62±6.02, p = 0.12). It has been reported that sLDH level was positively correlated with lymphoma-associated malignant PE (L-MPE) (OR: 1.005, 95% confidence interval: 1.003-1.007, p <0.001). sLDH > 460U/L distinguishes L-MPE from TPE with a sensitivity of 76% and a specificity of 81%[20]. Consistent with our results, other researchers observed that the sLDH in MPE is higher than in TPE(p = 0.08) [25]. In multivariate logistic regression analysis, the ratio of sLDH: pleural fluid lymphocyte count (PELC) was positively correlated with MPE. The sensitivity and specificity of the ratio of sLDH: PELC were 0.63 (95% CI 0.51–0.73) and 0.85 (95% CI 0.68–0.94)[25]. So sLDH is an important indicator for distinguishing TPE from MPE.

High sensitivity C reactive protein (HsCRP) is widely used as a sensitive but non-specific marker of systemic inflammation [26, 27]. Increased sHsCRP levels have been reported in many lung diseases, including tumors and tuberculosis [28, 29]. In our study, the median levels of both pHsCRP and sHsCRP were both higher in the TPE group than in the MPE group (24.63±1.16 vs 8.07±0.87 and 50.30±2.67 vs 19.25±3.20, p <0.01). The AUC of pHsCRP and sHsCRP were 0.79 and 0.73. Consequently, HsCRP is an important reference indicator to differentiate TPE from MPE. A meta-analysis showed that the optimal critical value of pHsCPR was 21.9 mg/dL, which values above the critical value were classified as TPE and below the critical value were classified as MPE, the sensitivity was 0.91 (0.73 to 0.98), and specificity was 0.82 (0.7 to 0.9)[30].

Although HsCRP is a valuable diagnostic indicator, the diagnosis efficiency is low, so the choice of multi-index joint analysis is conducive to improving the diagnosis efficiency and accuracy. Through logical analysis, we had selected six relevant indicators (pADA, pHsCRP, sD-dimer, sESR, sHsCRP, and sMONp), with the Logistic regression model, 3 variables of pADA, sMONp, and sHsCRP could better help distinguish patients with PE by tuberculosis from malignant tumor. The combined AUC of the three factors can reach 0.94 (95% CI: 0.91 ~ 0.97), higher than any single index, which has great significance

for the clinical differentiation between TPE and MPE. Agreed with our data, there is a study analyzed 118 patients, including 84 patients with MPE (71.2%) and 34 patients with TPE (28.8%). They also found the pADA of TPE is higher than MPE (p <0.05) [25]. Moreover, others have proved that the elevated levels of sHsCRP and pADA in PE were useful in distinguishing TPE from MPE[31]. However, there is one study with a different result. After analyzing 17 patients with L-MPE and 216 patients with TPE. They found there was no statistically significant difference in sHsCRP and pADA levels between the two groups[20] which could be related to number of MPE patients included in the study.

At present, to achieve better treatment efficacy in clinical practice, many researchers were interested in exploring the differentiation between TPE and MPE [32–34]. Some of them were focused on the inflammatory factors. It has been reported that the biomarkers of PE in 22 patients with MPE and 5 patients with TPE were compared. IL-1, IP-10, IL-13 and IFN-γ were significantly higher in TPE (p <0.05). The level of basic fibroblast growth factor in MPE was higher than that in TPE (p <0.05) [33]. The highest AUC is IP-10 (AUC =0.95, 95% confidence interval, p <0.01), followed by IL-13 (AUC =0.86, 95% confidence interval, p <0.05) [33]. However, though one of the indicators in this study has a high value of AUC, the detection is not a common clinical indicator, and the detection is complicated. And the sample size is small, the reliability is weak, and it is difficult to perform stratified analysis. Another study found that Fibronectin (FN) and cathepsin G (CTSG) in patients with MPE were significantly higher than in patients with TPE, while the leukotriene-a4 hydrolase (LTA4H) was lower than in patients with TPE[34]. The AUC value was determined to be 0.285 for FN (95% CI: 0.174–0.396), 0.64 for LTA4H (95% CI: 0.518–0.762), 0.337 for CTSG (95% CI: 0.218–0.456), and 0.793 for a combination of these candidate markers (95% CI, 0.697–0.888). The AUC value is significantly lower than in our study.

In this study, our results has more significant advantages of high diagnostic accuracy (high AUC value, high sensitivity, and specificity) and large sample size which mean high data reliability. More favorably, pADA, sHsCRP and sMONp are all clinically common and easy-to-collect specimens, which are convenient and cheap to test, and will not increase the additional burden on patients. Because of the large sample size, hierarchical analysis can be performed and it is found that the diagnostic efficiency of pADA is different in various age groups, and as the age increases, the diagnostic efficiency of pADA gradually decreases. This phenomenon could be related to the percentage of tuberculosis decreased while the cancer diagnosis increased with the age growth. It suggests that the patients under 45 years old could choose the single indicator of pADA for diagnostic detection.

Of course, the gold standard for differentiating TPE and MPE in clinical practice still relies on pathological tissue biopsy[32], all cases in this study were examined by thoracoscopy, and pathological biopsy was completed in most cases, which ensured the accuracy of the diagnosis of the patients, but for some patients who refuse to accept the invasive examination, or whose constitution is difficult to bear invasive examination, the effective detection index of non-invasive provides a strong basis for timely diagnosis and accurate treatment. It is worth doing further research and exploration.

Conclusion

In summary, our results show that we have found some non-invasive and valuable markers for differentiating TPE from MPE. Although the gold standard for differentiating TPE and MPE still relies on pathological tissue biopsy, but for some patients who refuse to accept the invasive examination, or whose constitution is difficult to bear invasive examination, the effective detection index of non-invasive provides a strong basis for timely diagnosis and accurate treatment.

Abbreviations

AUC, area under curve; CA, cancer; CTSG, cathepsin G; FN, Fibronectin; HsCRP, high sensitivity C reactive protein; LDH, lactate dehydrogenase; LTA4H, leukotriene-a4 hydrolase; L-MPE, lymphoma-associated malignant pleural effusions; MPE, malignant pleural effusion; PE, pleural effusion; PELC, pleural fluid lymphocyte count; pADA, hydrothorax adenosine dehydrogenase; pAMS, hydrothorax amylase; pCell, hydrothorax cells; pGLU, hydrothorax glucose; pHsCRP, hydrothorax high sensitivity C reactive protein; pMON, hydrothorax monocytes; pNC, hydrothorax nucleated cells; pTC, hydrothorax total cholesterol; pTP, hydrothorax total protein; sAlb, blood albumin; sALP, blood alkaline phosphatase; sALT, alanine aminotransferase; sAPTT, activated partial prothrombin time; sAST, aspartate aminotransferase; sA/G, blood A/G; sBASp, percentage of blood basophil cells; sCa, serum calcium; sCK, blood creatine kinase; sCKI, blood creatine kinase isoenzyme; sCL, blood chlorine; sCRE, serum creatinine; sD-dimer, blood D-dimer; sEOSp, percentage of eosinophil; sESR, erythrocyte sedimentation rate; sFbg, blood fibrin; sFDP, fibrinogen degradation products; sGLO, globin; sGRANp, percentage of blood granulocytes; $sHCO3^-$, blood bicarbonate; sHGB, hemoglobin; sHsCRP, blood high sensitivity C reactive protein; sINR, blood internationalization standardized ratio; sK, Serum kalium; sLDH, serum lactate dehydrogenase; sLYMp, lymphocyte percentage; sMg, serum magnesium; sMONp, percentage of blood monocyte; sNA, blood natrium; sP, serum phosphate; sPA, blood prealbumin; sPLT, platelet; sPT, prothrombin time; sPTA, prothrombin activity; sRBC, red blood cell; sPTR, prothrombin time ratio; sTB, total bilirubin; sTBA, total bile acid; sTP, blood total protein; sTT, blood thrombin time; sUREA, blood urea; sWBC, white blood cell; sαHDH, blood α hydroxybutyrate dehydrogenase; sγ-GT, blood γ glutamyl transpeptidase; TB, tuberculosis; TPE, tuberculous pleural effusion.

Declarations

Ethics approval and consent to participate

The study received approval from ethics committee of Shiyan Taihe Hospital. All patients agreed to participate in the study and signed informed consent forms.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing financial interests.

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Authors' contributions

(I) Conception and design: ELHL, RZL, MFW, XJY; (II) Administrative support: LL, YJT; (III) Provision of study materials or patients: MFW, TR, ZXF, XXF, HDP; (IV) Collection and assembly of data: MFW; (V) Data analysis and interpretation: RZL, WYM, JW, IK; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Figures

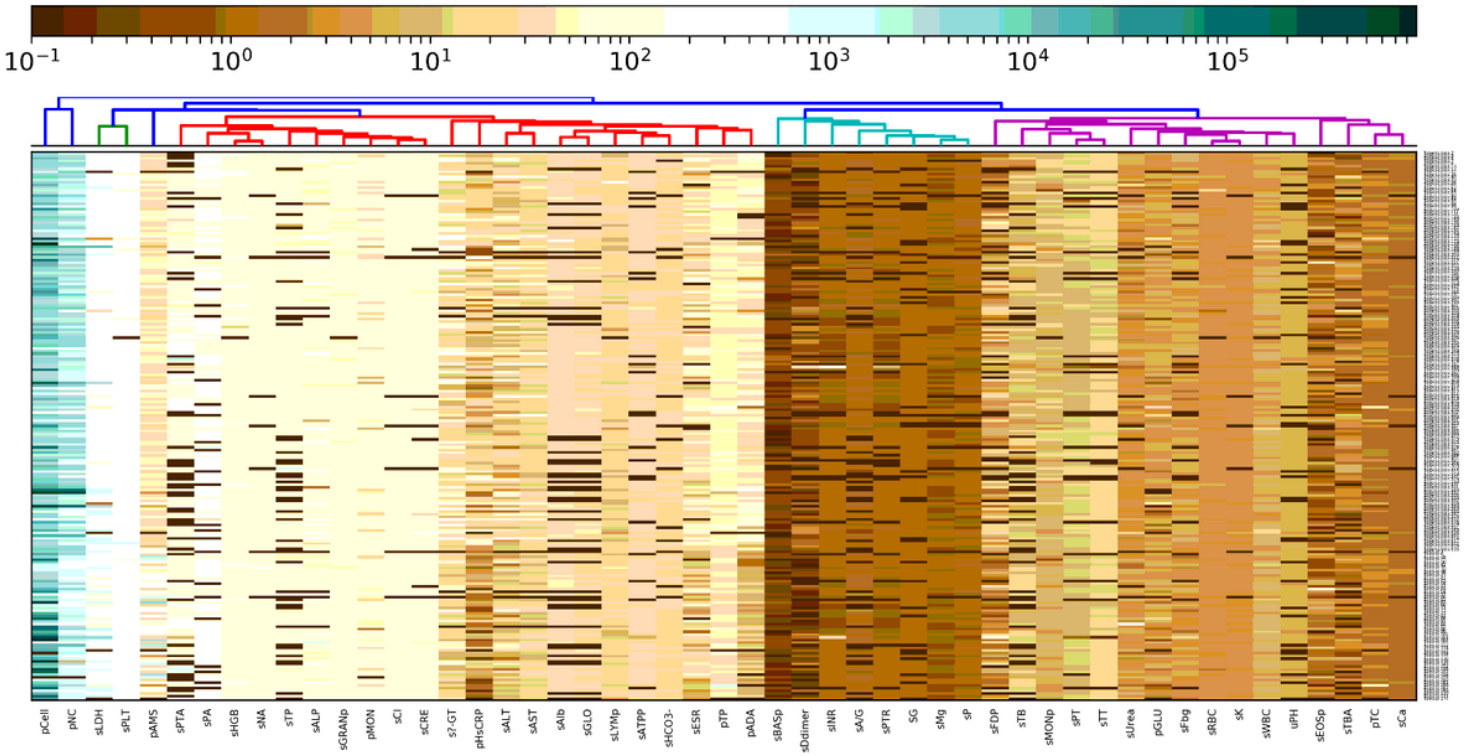

Figure 1

Tuberculosis and tumor patients were grouped by unsupervised hierarchical clustering of serum and pleural effusion clinical indicators

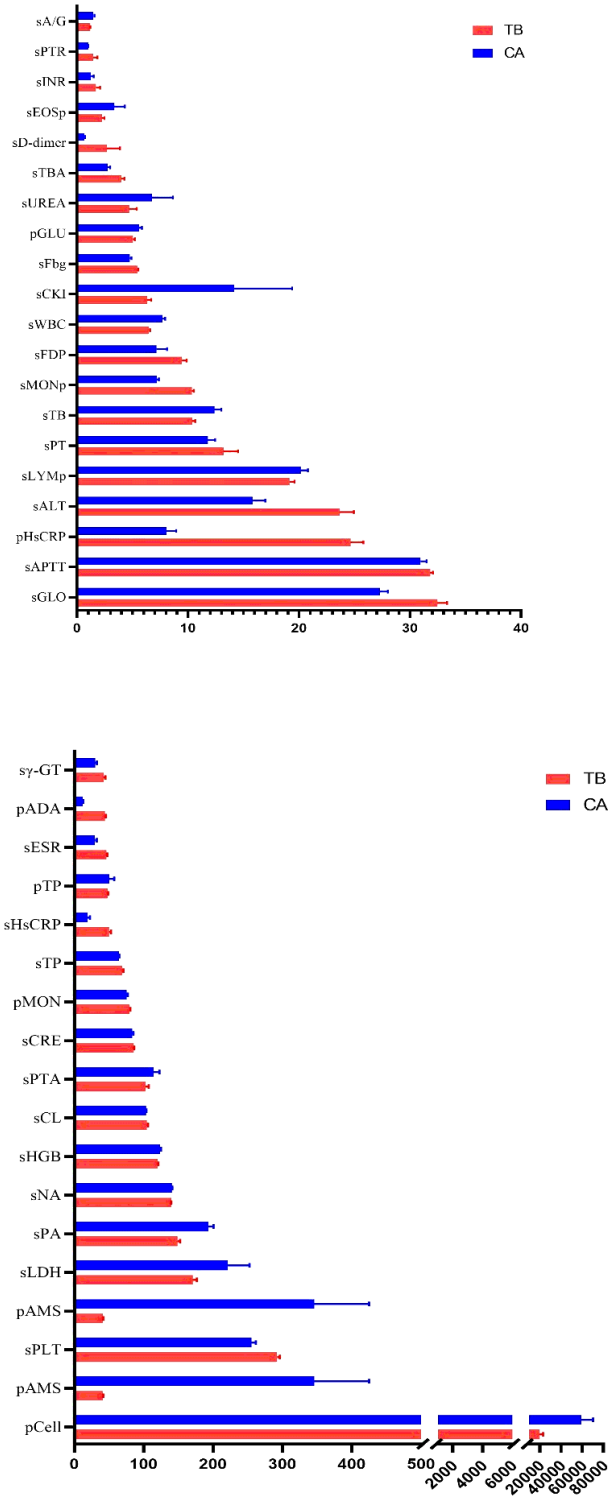

Figure 2

Serum and pleural effusion clinical indicators (N=37) with statistical significance of tuberculosis and tumor (mean value with SD)

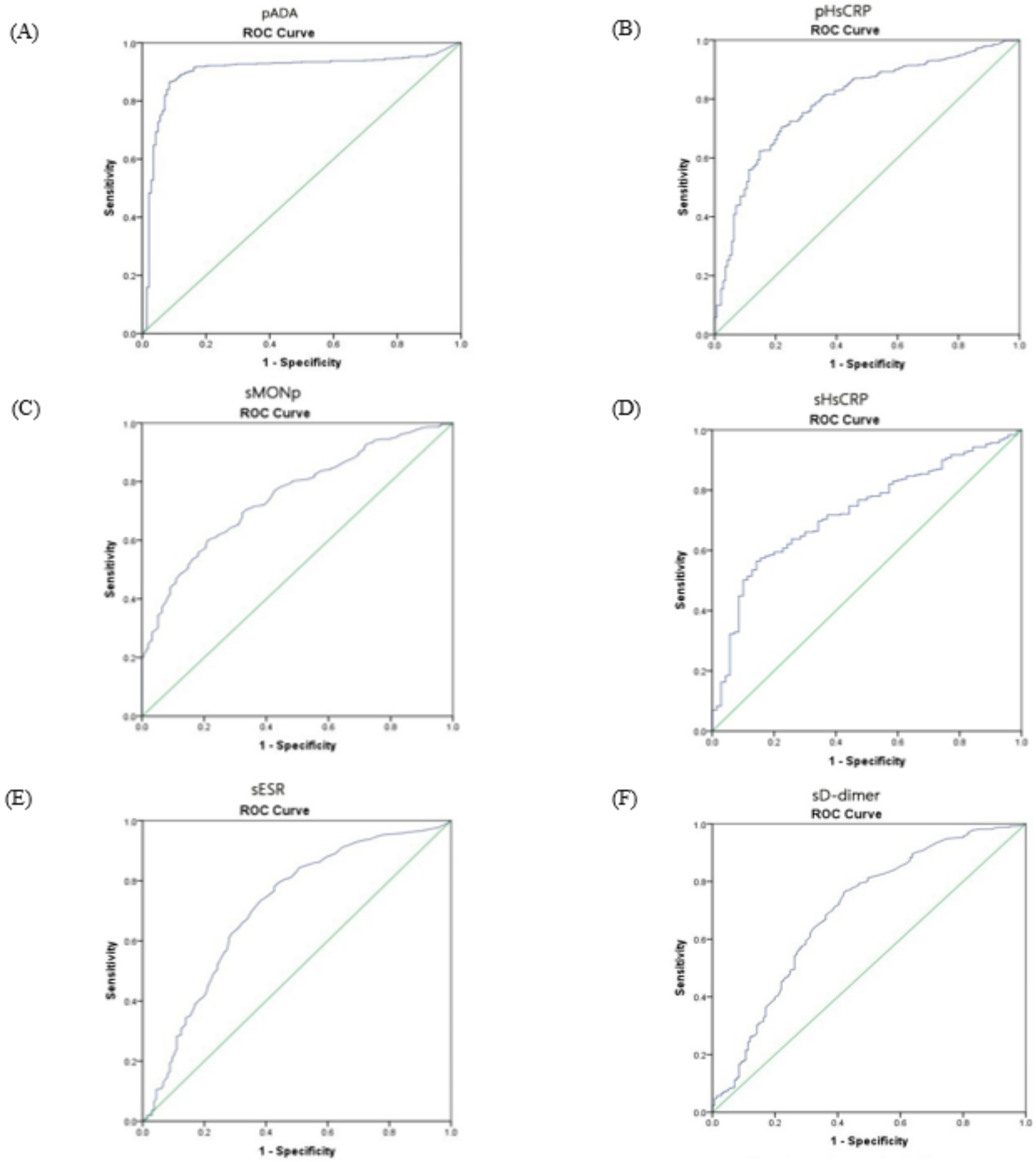

Figure 3

ROC analysis of serum and pleural effusion clinical indicators distinguishing tuberculosis from tumor patients (AUC > 0.7)

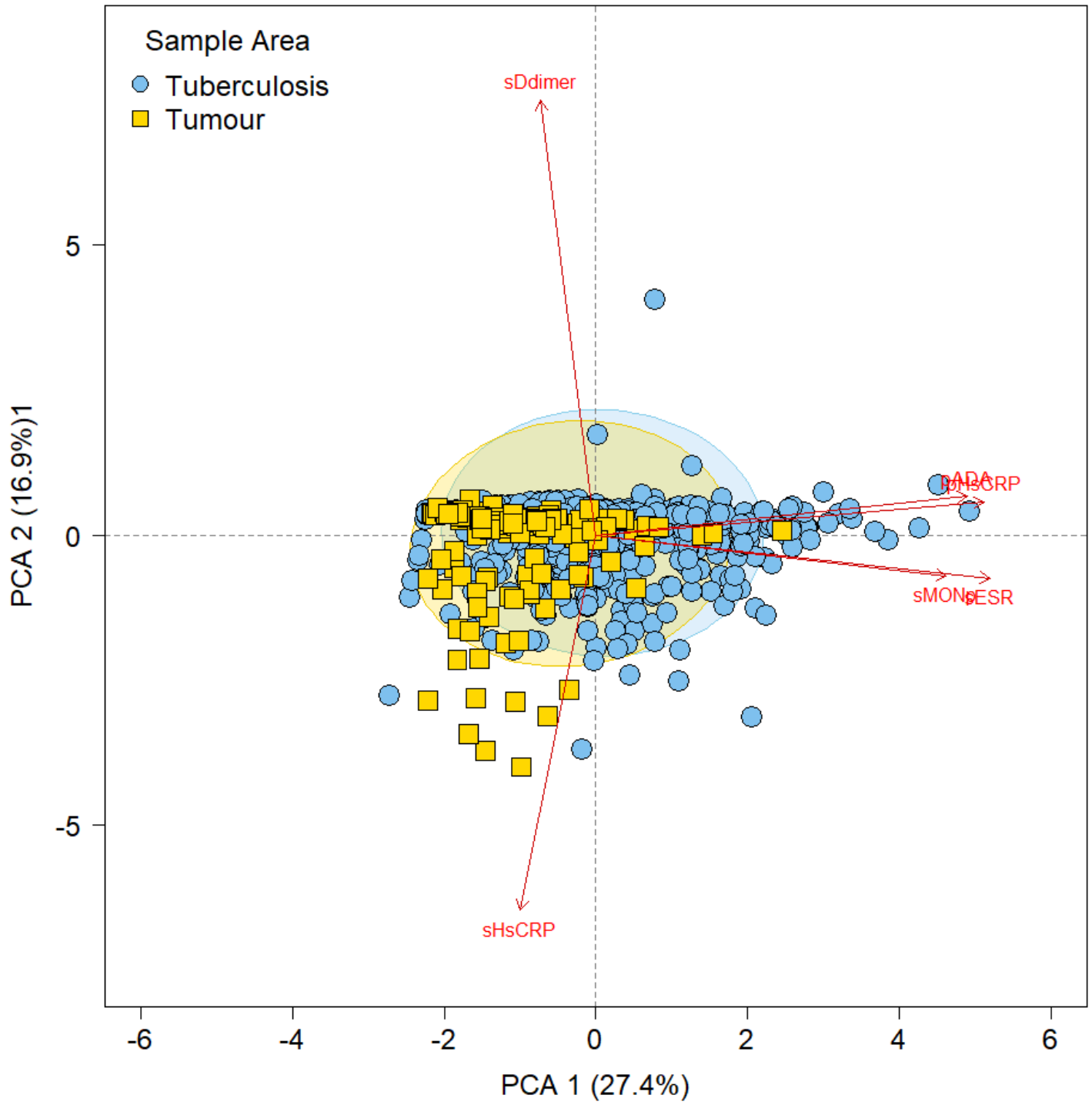

Figure 4

PCA analysis of 6 comparable serum and pleural effusion indicators of tuberculosis and tumor patients

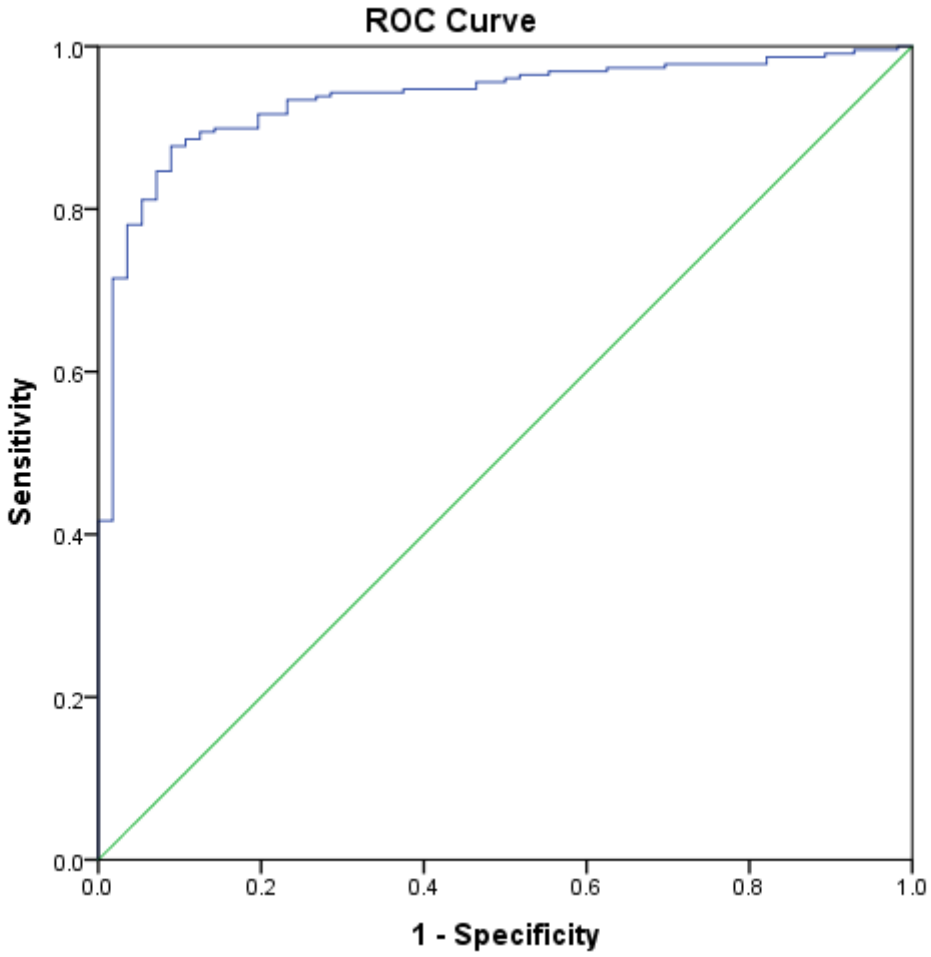

Figure 5

ROC analysis of combined indicators in tuberculosis detection form tumor patients

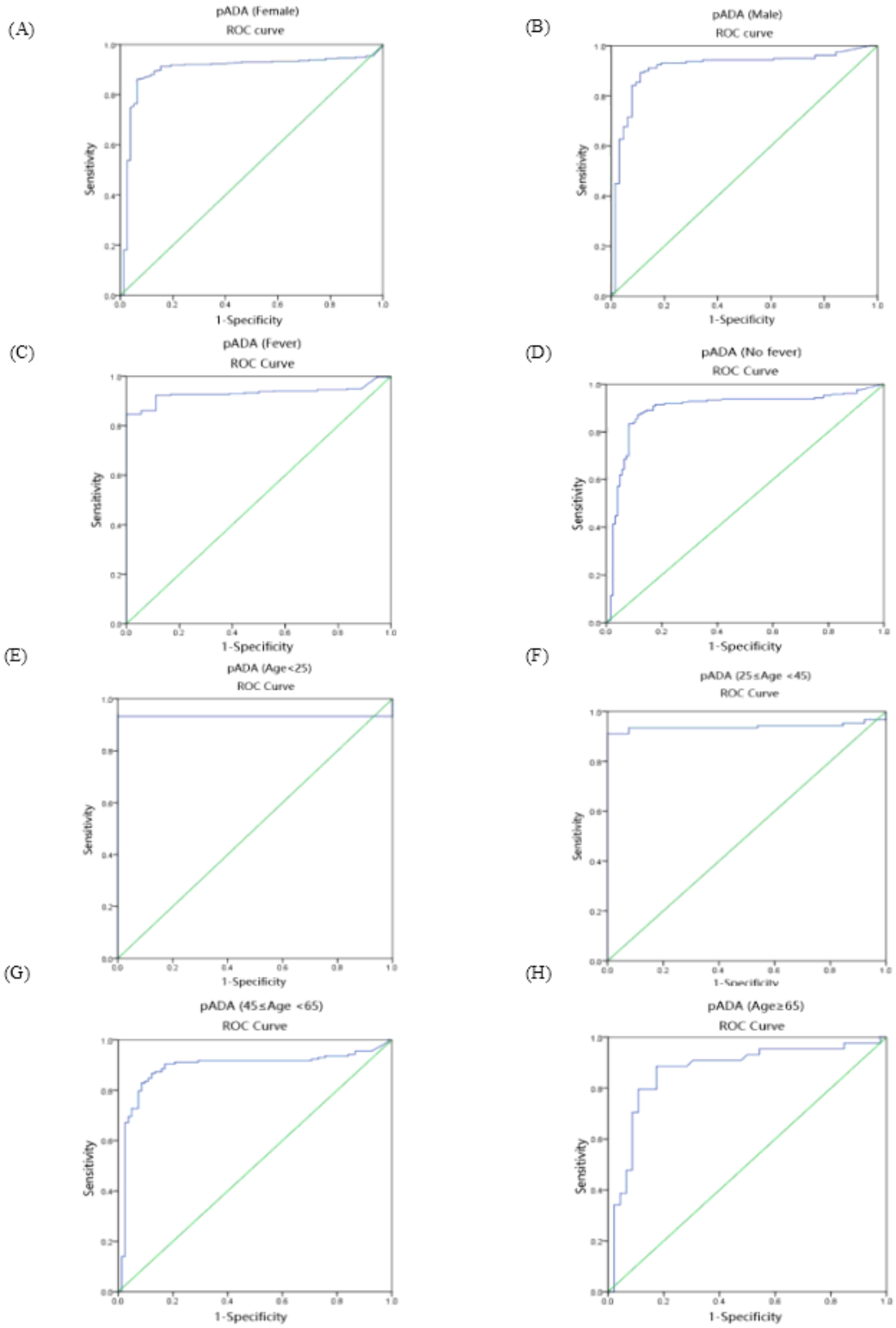

Figure 6

ROC analysis of selected indicator pADA in different status of patients