

Considerations for the Use of Serum IgG4, Total Bilirubin (TBIL) and the IgG4/TBIL Ratio in Differential Diagnosis Between IgG4-related Sclerosing Cholangitis and Cholangiocarcinoma

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Research

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Abstract

Background: Obstructive jaundice is the most frequent even the only manifestation of both IgG4-related sclerosing cholangitis (IgG4-SC) and Cholangiocarcinoma (CCA). It was difficult to distinguish these two diseases, though the treatment strategies were quite different. Serum IgG4 elevation was most frequently seen in IgG4-SC patients, yet the significantly elevated serum IgG4 in several CCA patients should not be neglected. Likewise, the serum level of IgG4 could be interfered by the serum level of TBIL. None of the previous research effort examined the differentiation potential of serum IgG4, CA19-9, TBIL and the IgG4/TBIL ratio for IgG4-SC and CCA.

Methods: A total of 202 cases (131 cases of CCA and 71 cases of IgG4-SC) with pathology results were retrospectively registered. The data of serum IgG4, TBIL and the IgG4/TBIL ratio was captured. ROC-curve analysis was then applied to calculate the optimal cutoff values.

Results: A significantly higher number of IgG4-SC patients experienced abdominal pain than CCA patients ($P = 0.006$). Elevation of the serum IgG4 observed in IgG4-SC and CCA cases showed significant differences ($P < 0.0001$). The optimal value of the IgG4 and the ratio was 1780 (95.3% sensitivity and 94.9% specificity) and 36.10 (96.9% sensitivity and 94.9% specificity) for differential diagnosis of IgG4-SC, respectively. For patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L in 30.1% of all patients and 28.1% IAC patients, the serum levels of IgG4 and the ratio showed stronger differential diagnostic power (AUC=0.873 and AUC=0.968, respectively). The optimal value of the IgG4 and the ratio was 1685 (with 88.9% sensitivity and 84.2% specificity) and 56.02 (94.4% sensitivity, 94.7% specificity). The combination of serum IgG4 and the IgG4/TBIL presented higher specificity (98.5%) and accuracy (99.2%).

Conclusion: The differences were significant in the serum level of IgG4, CA19-9 and the ratio. The IgG4/TBIL ratio has stronger discrimination efficiency than the serum level of IgG4 or TBIL alone for patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L. The combination of the IgG4 and the IgG4/TBIL ratio could further enhance the specificity and accuracy for differentiating IgG4-SC from CCA, especially in patients with serum IgG4 from 650 to 3000 mg/L.

Introduction

IgG4-related sclerosing cholangitis (IgG4-SC) is an IgG4-related disease characterized by elevation of IgG4 serum levels (sIgG4) and infiltration of IgG4-positive plasma cells in the affected tissue.[1] This multi-organ inflammatory disorder shows a high response to steroid therapy. Obstructive jaundice is usually the most frequent even the only manifestation of IgG4-SC and malignant tumors. In most cases, the imaging manifestations are very similar in IgG4-SC and CCA[2]. Additionally, in some cases of CCA, preoperative pathology for definite diagnosis cannot be achieved because of the high serum level of IgG4. Consequently, the diagnosis of IgG4-SC cannot be excluded, even hormone diagnostic therapy is performed, the operation time delays. Meanwhile, almost 30 percent of IgG4-SC patients are diagnosed

after surgical resection of preoperatively diagnosed perihilar carcinoma[3]. Therefore, more accurate indexes for differential diagnosis between the two diseases are necessary.

According to the 2012 clinical diagnostic criteria of IgG4-SC put forward by Japanese researchers, the serum level of IgG4 concentrations (> 1350 mg/L) was essential for identification.[4] IgG4, which accounts for only 5% of IgG, is produced by clonal B-cell populations, which plays an important role in the immune system.[5] The serum IgG4 frequently elevated in a limited number of diseases such as IgG4-related sclerosing cholangitis, in which the IgG4 serum levels may be influenced by obstructive jaundice and its subsequent immune response[1, 5]. The serum IgG4 is produced by clonal B-cell populations, which may respond to the mechanical obstruction in the bile duct and the stimulation by inflammations, they all contribute to the elevation of serum IgG4. In IgG4-SC patients, an uncontrolled secretion of IgG4 by clonal B-cells could make the serum IgG4 above 1350 mg/L, while in CCA patients, the serum IgG4 in CCA is mostly lower than 1350 mg/L. However, the serum IgG4 level in several CCA patients can reach above 1350 mg/L, or even in excess of 2700 mg/L. Therefore, merely the serum IgG4 elevation is insufficient for reliable diagnosis and differentiation between IgG4-SC and CCA. [6, 7]

The trigger of elevated IgG4 in the CCA may be the mechanical obstruction in the bile duct. Theoretically, the ratio of the serum IgG4 to the TBIL, which could decrease mechanical obstruction-related disturbance, may become a potentially powerful marker for the differential diagnosis between IgG4-SC and CCA. To date, however, there are no previous studies that had investigated this assumption.

202 participants enrolled in our research were obstructive jaundice patients, covering 71 cases of IgG4-SC and 131 cases of CCA. Systematic analysis revealed the differential roles of the IgG4, TBIL, CA19-9 and the ratio of the IgG4 to TBIL. The evidence indicated that when compared to the elevation of sIgG4 or TBIL alone, the IgG4/TBIL ratio had higher discrimination power for IgG4-SC and CCA diagnosis in patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L.

Methods

Among a total of 202 patients who came to Peking Union Medical College Hospital (PUMCH) from 2013 to 2018 for diagnosis, 131 (82 males and 49 females) people were diagnosed with CCA(all received surgical treatment, with clear postoperative pathological diagnosis), the other 71(52 males and 19 females) patients were diagnosed with IgG4-SC. All patients were retrospectively reviewed and information was collected including their sex, age, symptoms, weight loss (decreased $> 5\%$ within 6 months), and serological tests, including biochemical tests, tumor markers, and the sIgG4 level. Imaging characteristics including endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP), computed tomography (CT), B-ultrasound, and endoscopic ultrasonography (EUS) were likewise collected. Our study protocol was approved by the medical ethics committee of the Peking Union Medical College.

Statistical Analysis

Statistical analysis and graphics production were performed using SPSS software (version 24). The independent samples t test, Mann-Whitney U test and Fisher's exact test were performed to evaluate the patient characteristics. The indexes of the IgG4-SC were used as the baseline and compared with the data of CCA by ANOVA test for repeated measures.

The spearman correlation coefficient was used to assess the degree of correlation between IgG4 and TBIL. Comparison among the indexes, such as the serum level of IgG4, CA19-9, TBIL and the IgG4/TBIL ratio, were evaluated by the receiver operating characteristic (ROC) curve for differentiation efficiency between CCA and IgG4-SC. Youden's Index(sensitivity + specificity-1) was used to determine the optimal cutoff value of the 4 indexes for differential diagnosis. P value Descriptive data was generated for all variables. In all tests, significance levels were set at the 5% level (P values < 0.05).

Results

1. Patients demographics data and disease characteristics

202 patients with immunoglobulin G4-associated cholangitis and biliary adenocarcinoma, including 134(66.3%) male and 68(33.7%) female, were involved in this study. The age ranges between IgG4-SC and CCA patients were similar: between 25–88 years (median age of 62 years) and 28–92 years (median age of 64), respectively, which has no significant differences. The sex distribution of the two diseases also exhibited relatively homogenous that more than two-third of carriers were males (62.6% in CCA and 73.2% in IgG4-SC).

A significantly higher number of IgG4-SC patients experienced abdominal pain than CCA patients (25.2% in CCA vs. 45.1% in IgG4-SC, P = 0.006 Chi-square test). No difference was observed in the incidence of jaundice, fever, weight loss and abdominal mass, as summarized in Table 1.

Table 1
Demographic data and clinical characteristics of the IGG4-SC and CCA Patients enrolled.

	N(%)		
	CCA(n = 131)	IGG4-SC(n = 71)	P value
Age	61.8 ± 12.7	59.1 ± 10.7	0.231
Male	82(62.6)	52(73.2)	0.170
Female	49(37.4)	19(26.8)	0.170
Jaundice	82(62.6)	46(64.8)	0.876
Abdominal pain	33(25.2)	32(45.1)	0.006
Fever	16(12.2)	6(8.5)	0.559
Weight loss	34(26.0)	23(32.4)	0.419
Abdominal mass	2(1.5)	1(1.4)	0.581

Table Legend: CCA indicates cholangiocarcinoma; IGG4-SC, immunoglobulin G4-associated cholangitis. Significant differences (p < 0.05) are highlighted in grey.

2. The differences and diagnostic efficiency of IgG4, TBIL, CA19-9 and the IgG4/TBIL ratio in CCA and IgG4-SC

- 2.1 The serum level of IgG4 in CCA and IgG4-SC
- 11.9% (7/59) patients were found to have an elevated serum IgG4 level with an average of 644.5 mg/L, ranging from 46 to 2960 mg/L. 97.2% of IgG4-SC patients showed elevated sIgG4 ranging between 659 and 64200 mg/L, with an average of 12325.3 mg/L. The positive rates of elevated serum IgG4 level were significantly different between IgG4-SC and CCA (P < 0.001, chi-square test, Table 2). Of the 59 patients who diagnosed with CCA, the serum level of IgG4 were between 650 mg/L and 3000 mg/L in 33.9% CCA patients. However, among the 71 cases of the IgG4-SC, the serum elevated TBIL was between 650 mg/L and 3000 mg/L in 18 cases (28.1%). As Fig. 1 shows, there were significant differences in the serum IgG4 between IGG4-SC and CCA patients. (P < 0.001, Student t test). On the basis of the Youden index calculation, the best cutoff value for sIgG4 in this cohort was 1790 mg/L with 96.9% sensitivity and 94.9% specificity. Likelihood ratio (LR) syntheses gave an overall positive LR of 3.51 and negative LR of 0.154. The accuracy, the positive predictive value (PPV) and the negative predictive value (NPV) was calculated 95.1%, 93.9% and 96.5%, respectively.

Table 2
Tumor Marker Detection in the IGG4-SC and the CCA Groups

	CCA(n = 131)	IGG4-SC(n = 71)	P value
TBIL			
Cases [n (%)]	98(74.8)	46(64.8)	0.180
Range (umol/L)	107.0 ± 96.5	113.9 ± 127.3	0.625
IgG4			
Cases [n (%)]	7(11.9)	69(97.2)	< 0.001
Range (mg/L)	644.5 ± 594.1	12040.3 ± 12325.3	< 0.001
CA199			
Cases [n (%)]	109(83.2)	33(46.5)	< 0.001
Range (U/mL)	701.7 ± 2176.2	93.1 ± 183.4	< 0.001

There were significant differences in the serum IgG4 between IgG4-SC and CCA patients. ($P < 0.001$, Student t test). (Fig. 1). On the basis of the Youden index calculation, the best cutoff value for sIgG4 in this cohort was 1780 mg/L with 95.3% sensitivity and 94.9% specificity. The positive likelihood ratio LR (+) was 18.68, the negative likelihood ratio LR(-) was 0.049, the accuracy was 95.1%, the positive predictive value (PPV) was 95.3% and the negative predictive value (NPV) was 94.9%.

2.2 The serum level of TBIL in CCA and IgG4-SC

Positive rates of TBIL in CCA patients compared with IgG4-SC patients were 74.8% versus 64.8%, which demonstrated no significant differences (Table 2). In addition, there were no significant differences in the serum TBIL between IgG4-SC and CCA patients from the data in Fig. 1. ($P = 0.625$, Student t test).

2.3 The ratio of serum level of IgG4 to TBIL in CCA and IgG4-SC

Of the 59 patients with CCA, the ratio of serum IgG4 to TBIL all less than 100 in 59 cases. Among the 64 cases of IgG4-SC, the ratio less than 100 in 28 cases (43.8%), 100–1000 in 31 cases (48.44%), more than 1000 in 5 cases (7.8%). As shown in Fig. 1, the ratio of sIgG4 to TBIL in IgG4-SC was significantly higher than that in CCA ($P = 0.0053$, Student t test). At a cutoff value of 56.02 (with sensitivity of 85.9% and specificity of 91.5%), the PPV was 94.4%, NPV as 94.7%, the diagnostic accuracy as 94.6%, LR for positive test as 17.81, and LR for negative test as 0.059.

2.4 The correlation between the serum value of sIgG4 and the value of TBIL in IgG4-SC and CCA

A positive correlation was found between sIgG4 and TBIL in IgG4-SC ($y = 33.55e0.00002x$, $R^2 = 0.06002$, Spearman's rank correlation coefficient, $P < 0.0001$). There was a significant positive correlation between sIgG4 and TBIL in CCA as well ($y = 59.61e0.0003x$, $R^2 = 0.02217$, Spearman's rank correlation coefficient, $P < 0.0001$). Taken together, these results suggested that the serum level of CA19-9 could be influenced by the the serum level of TBIL in both IgG4-SC and CCA (Fig. 2).

3. The diagnostic efficiency of the serum level of IgG4, CA19-9, TBIL and the IgG4/TBIL ratio for CCA and IgG4-SC differentiation

It can be seen from the ROC curve in Fig. 3A that the AUC of the IgG4, TBIL and their ratios were 0.984, 0.351 and 0.977 for the differential diagnosis of IgG4-SC and CCA, respectively. For the whole range of cut-offs the Youden index was calculated by the formula (Youden index = sensitivity + specificity - 1) and the cut-off with maximal Youden index was retained. The optimal value of the sIgG4 and the ratio was 1780 (with 95.3% sensitivity and 94.9% specificity) and 36.10 (sensitivity 96.9%, specificity 94.9%) in the IgG4-SC differential diagnosis, respectively. When a cutoff value of 1780 the sIgG4 was considered, the PPV was 95.3% whereas the NPV was 94.9%. Meanwhile, the positive likelihood ratio (LR+) was 18.68, the negative likelihood ratio (LR-) was 0.049, and the accuracy was 95.1% in picking this cutoff value. The most suitable cutoff value of the ratio was calculated as 32.84 (sensitivity 85.9%, specificity 91.5%), according to which the positive LR, negative LR, accuracy, positive predictive value and negative predictive value were calculated as 10.10, 0.154, 88.6%, 97.1% and 85.7%, respectively. When the cutoff value of the ratio was determined to be 36.10, the LR (+) was 19, the LR (-) was 0.033, the accuracy was 93.5%, the PPV was 93.8% and the NPV was 93.1%.

For patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L, receiver operating curve (ROC) analysis revealed that the area under curve (AUC) of IgG4, TBIL, CA199 and the ratio were 0.873, 0.120 and 0.968, respectively, as can be seen from the Fig. 3B. Based on the ROC analysis, the optimal cutoff values of the sIgG4 and the ratio were determined for differentiation between IgG4-SC and CCA. The optimal cutoff value of the sIgG4 was indicated at 1685, with a sensitivity of 88.9% and a specificity of 84.2%, the positive LR was 5.63, the negative LR was 0.131, the accuracy was 83.8%, the positive predictive value (PPV) was 84.2% and the negative predictive value (NPV) was 83.3%. We also demonstrated the cutoff values of the ratio for the IgG4-SC differential diagnosis and identified that the optimal value was 56.02. At the optimal cutoff value of 56.02, the sensitivity and the specificity were calculated as 94.4% and 94.7% (LR+ = 17.81, LR- = 0.059, accuracy = 94.6%, PPV = 94.4%, NPV = 94.7%). This cutoff value has higher accuracy.

These results suggest that the IgG4 (≥ 1780) and the ratio (≥ 56.02), in combination, further increased the specificity (95.3–98.5%) and accuracy of IgG4-SC (93.5–99.2%) for patients with elevation of serum IgG4 between 650 and 3000 mg/L. When the sIgG4 reached above 1780 and the ratio of sIgG4 to TBIL exceeded 56.02, the possibility of CCA could be eliminated. For patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L, the diagnostic power of the ratio to

differentiate IgG4-SC from CCA was higher than the serum value of IgG4 or TBIL alone. Taken together, these results suggest that the ratio of sIgG4 to TBIL had better potential to discriminate IgG4-SC from CCA(Fig. 3).

Discussion

IgG4-SC was recently recognized as an independent disease from other IgG4-related diseases, and there are no epidemiology data for IgG4-SC based on a large population. Currently, it is a challenge to distinguish between IgG4-SC and CCA, as both may cause similar signs and symptoms. These patients presented with obstructive jaundice, pruritus, abdominal discomfort, and weight loss, vomiting, pancreatitis either as a single symptom or in combination.[8]

In this study, we examined the clinical data collected from patients who were diagnosed with either IgG4-SC or CCA. We also observed similar incidences of IgG4-SC in both males and females, which agrees with other studies reported earlier. No significant demographic differences were observed between IgG4-SC and CCA patients. However, weight loss in IgG4-SC patients was one of the symptoms that was significantly different from that of CCA patients. This result was in line with the formal research, and may provide a clue for differentiated the two diseases.[9]

Other diagnostic methods such as ultrasound, CT, and MRI could be applied for detecting the organ involvement. Multiple organ involvement such as the kidney, and the salivary and lacrimal glands is specific in IgG4-SC patients, while the biliary tract was always the only involved organ in CCA. [7] Approximately 90% IAC patients have symptoms of AIP, which can be obviously observed in imageological examinations. These typical manifestation helps differentiate IAC patients from CCA. However, organ involvement may be occult in several IAC patients. Therefore, IAC and CCA patients may exhibit similar imaging characteristics, such as dilatation, thickening wall, or occupying lesion, which makes it difficult to distinguish one from the other. [10, 11]

Histopathologic examination has been the gold standard and definitive method for IgG4-SC and CCA diagnosis. However, obtaining pathologic samples by puncture or ERCP brush before surgery is invasive and may not be suitable for all patients, such as elderly patients, patients with coagulopathy, or those with high bilirubin. In addition, the low positive rate of brush check may cause more problems. [12, 13] Therefore, clinical examination and experimental treatment are of great importance a differential diagnosis. We observed complete response of IgG4-SC patients to the steroid treatment, although in some cases the stent placement also played a part in the symptom alleviation.

Therefore, classification of benign-malignant biliary strictures has traditionally been regarded as a serious challenge. In many suspected IgG4-SC patients, the accuracy of the existing diagnostic methods is still deemed to be unsatisfactory, which may lead to misdiagnosis of CCA. These reporting of results should be interpreted carefully since cholangiocarcinoma is a high malignant cancer.

IgG4-SC patients may be positive for tumor markers, whereas CCA patient can also exhibit elevated sIgG4. The serum CA19-9 is an essential tumor marker which is extensively used to differentiate the IgG4-SC and CCA cases[14]. Previous studies have revealed that 70%-90% pancreatic or biliary adenocarcinoma demonstrated with elevation of serum CA19-9. In our study, the serum CA199 level was found to be increased in most of the CCA patients(81.1%). In IgG4-SC patients, the serum CA199 level also increased, but at a significantly lower incidence and a significantly lower level. These findings were consistent with the studies published earlier.[15] However, the differentiation proficiency of CA19-9 may be interfered by obstructive jaundice and the subsequent inflammatory responses. Many strategies have been investigated to raise the discrimination proficiency of CA19-9 for IgG4-SC and CCA diagnosis, such as choosing a higher cutoff value and combining it with other inflammatory markers. [16]

The sIgG4 level is a major characteristic of IgG4-related diseases. In the IgG4-SC diagnosis criteria proposed by Japanese scholars, the minimum level of IgG4 was set as 1350 mg/L. However, the specificity at this cutoff is not sufficient to distinguish IgG4-SC and CCA. In our study, 11.1% of the CCA patients had an elevated sIgG4 level (range 46 to 2960 mg/L), which could mislead to an IgG4-SC diagnosis, although the level was significantly lower than that of the IgG4-SC group.

In clinical work, it was usually found that several patients with a high level of CA19-9 or sIgG4 gradually return to normal when their TBIL fall back into the normal range after PTBD, ERBD or ENBD used to decrease obstructive jaundice. Even if IAC patients have not received hormone therapy, their sIgG4 may immediately decrease in after relief of obstructive jaundice, so we considered that the serum level of Tbil may affect the serum level of IgG4.[17] According to our results of linear regression, the elevation of IgG4 was positively correlated with the elevation of TBIL in the exponential model, which supported our hypothesis. In a study investigating the ratio of the increase-folds of CA19-9 to increase-folds of TBIL, Liu W and his colleague found the CA19-9/ TBIL ratio has higher differentiating power for IgG4-SC and CCA than CA19-9 or TBIL alone. [6] However, there are almost no historical studies in the area of the efficiency of the serum IgG4/TBIL ratio for differentiation between IgG4-SC and CCA.

On the basis of this study, we concluded that the best cutoff value for sIgG4 level was 1780 mg/L, with 95.3% sensitivity and 94.9% specificity. Unfortunately, IgG4 seems to be sufficiently effective for differential diagnosis in overall patients, and the ratio of IgG4 to TBIL can not further improve the diagnostic effectiveness. Therefore, a stratified analysis is necessary. As we observed, for those patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L, who are difficult to be diagnosed before resection, the discrimination capacity of the IgG4/TBIL ratio was higher than the serum value of IgG4 or TBIL, which suggested that the ratio IgG4/TBIL had higher differentiation potentials for IgG4-SC and CCA, respectively. The combination of the serum IgG4 and the IgG4/TBIL ratio was confirmed to have increased the specificity and accuracy for differentiating IgG4-SC from CCA.

The production of IgG4 is related to the expression of several immune genetic factors, such as MHCII, nuclear factor-kB, and Fc-receptor-like molecules. For instance, reduced naive Tregs can activate a Th1 immune response with secretion of proinflammatory cytokines to antigens such as self-antigen or

microorganisms. Th2 immunoreaction may be involved in the subsequent progression of the disease, resulting in the release of IgG4.[18] But there is no literature about the Th2-type immune responses caused by bilirubin stimulation, which needs further research. Likewise, bilirubin may have an effect on laboratory serum detection of IgG4, though there is no related study.

The generalisability of these results is subject to certain limitations. For instance, the retrospective nature of this study made it difficult to obtain data of a single variable from all patients. The case number of the IGG4-SC and CCA was low, which may affect the significance of the study. In addition, there is no exact literature on the relationship between serum IgG4 and bilirubin levels, which needs more experimental investigations.

Conclusion

Our study suggested that serum sIgG4 levels above 1790 mg/L, tumor markers (CA199), and TBIL could be invoked as reference criteria for the differential diagnosis of IgG4-SC and CCA. For patients with serum level IgG4 between 650 and 3000 mg/L, the sIgG4/TBIL ratio demonstrated higher potential power for IgG4-SC and CCA differentiation than the serum value of IgG4 or TBIL alone.

Abbreviations

IgG4-SC

IgG4-related Sclerosing Cholangitis; CA19-9:carbohydrate antigen 19 – 9; TBIL:total bilirubin;

CCA:Cholangiocarcinoma; ROC curve:receiver operating characteristic curve; AUC:area under curve;

LR+:positive likelihood ratio; LR-:negative likelihood ratio; PPV:positive predictive value; NPV:negative predictive value.

Declarations

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Availability of data and material

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

Ethics approval and consent to participate

Our study was approved by the medical ethics committee of the Peking Union Medical College. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication

Based on the Declaration of Helsinki, written informed consent was obtained from the patient included in the trial.

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Not applicable.

Competing interests

The authors declare that they have no conflicts of interest.

Authors' contributions

He XD conceived the idea of the study; Xiao JC and Zhou WZ collected the information, interpreted the results and wrote the paper.

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Figures

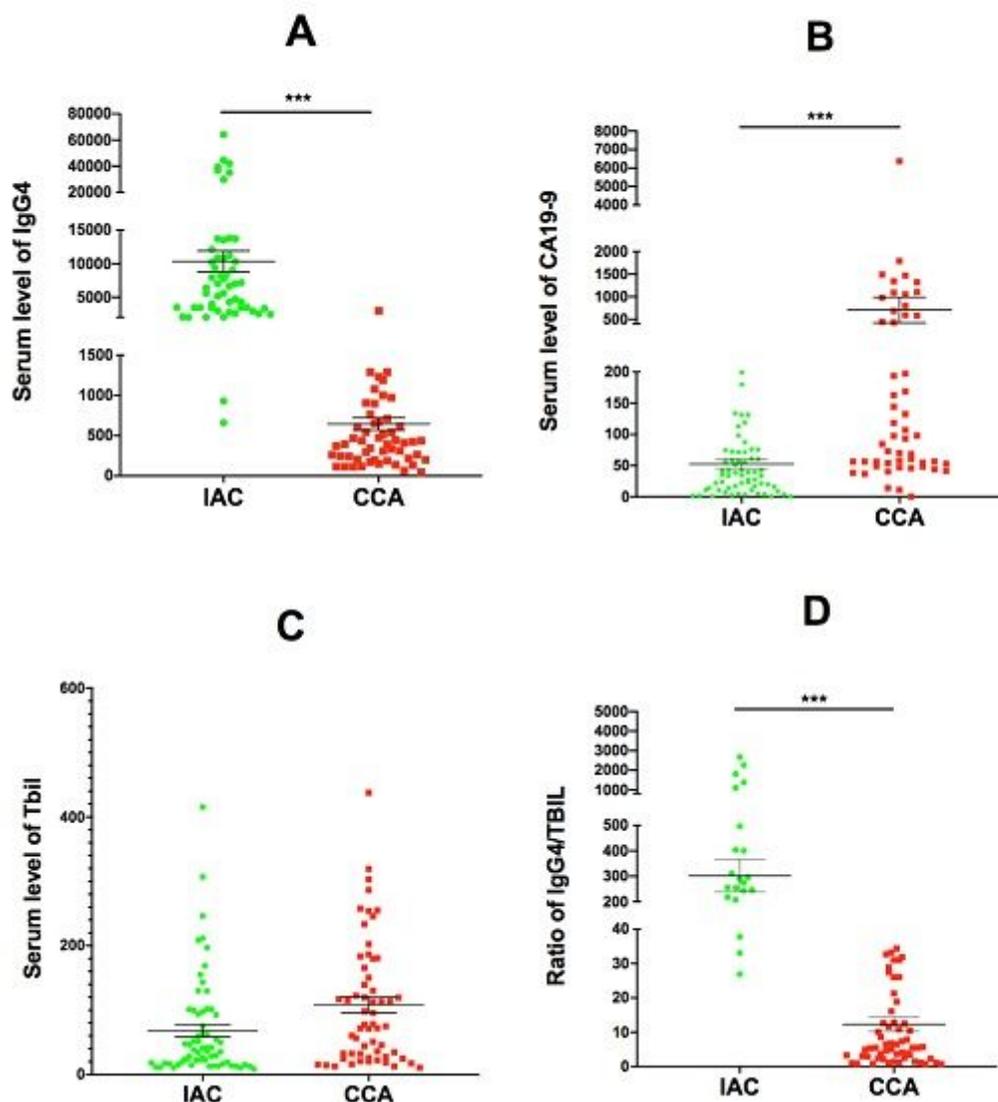


Figure 1

The differences of the serum level of IgG4, TBIL, CA19-9 and the IgG4/TBIL ratio in IGG4-SC and CCA (median value \pm interquartile range): the IgG4 and the IgG4/TNIL ratio in IGG4-SC patients were significantly higher than those in CCA patients, ***, $P < 0.05$

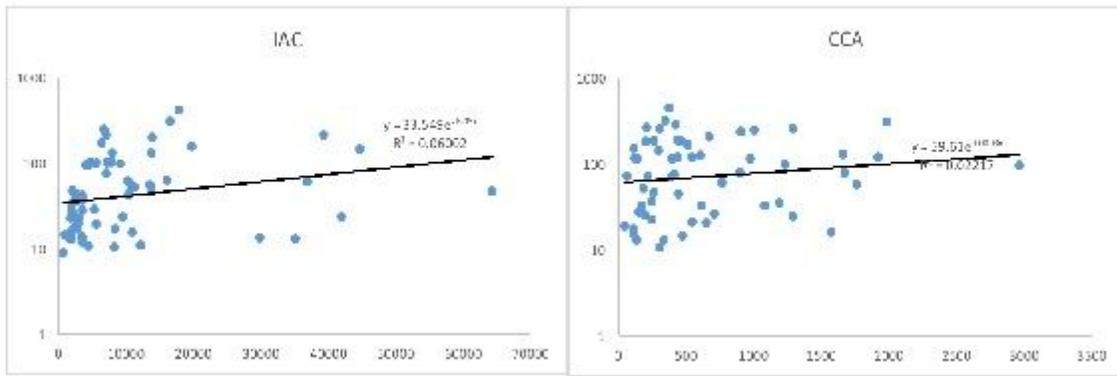
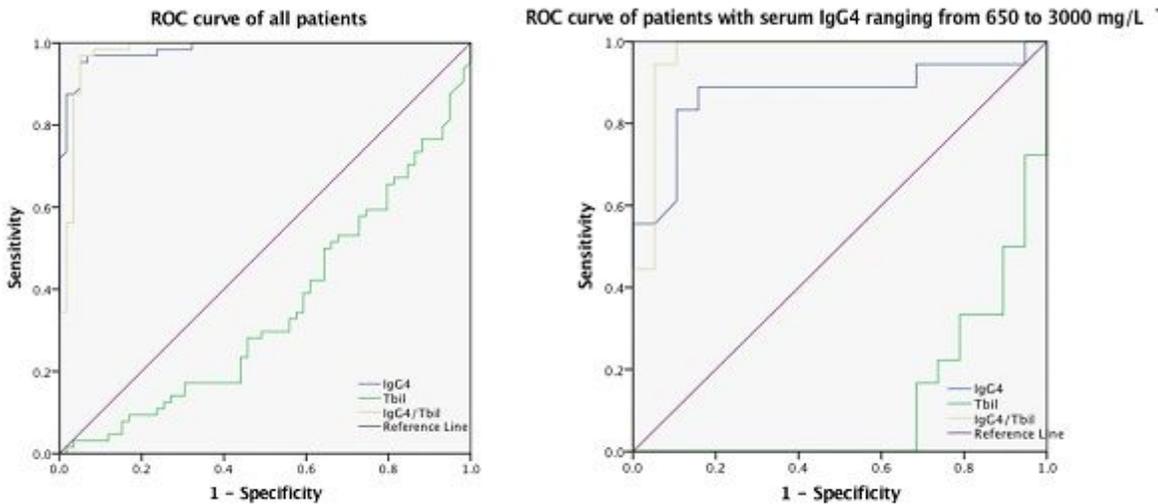


Figure 2

The correlations between serum level of IgG4 and TBIL in IGG4-SC and CCA: Exponential model analysis revealed positive correlations between the serum level of IgG4 and TBIL in both IGG4-SC and CCA.



A. ROC curve of all patients for IgG4-SCB. ROC curve of patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L

Figure 3

The AUC of the ROC of the IGG4-SC: In patients for patients with elevation of serum IgG4 ranging from 650 to 3000 mg/L, the AUC of the IgG4/TBIL ratio was higher than that of the of IgG4, CA19-9 or TBIL alone.