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Predictive value and modeling analysis of MSCT signs in gastrointestinal stromal tumors (GISTs) to pathological risk degree

J.-K. WANG

Department of Medical Equipment, Henan Provincial Hospital (Henan Children's Hospital), Zhengzhou, Henan Province, China

Abstract. – OBJECTIVE: By analyzing MSCT (multi-slice computed tomography) signs with different risks in gastrointestinal stromal tumors, this paper aimed to discuss the predictive value and modeling analysis of MSCT signs in GISTs (gastrointestinal stromal tumor) to pathological risk degree.

PATIENTS AND METHODS: 100 cases of primary GISTs with abdominal and pelvic MSCT scan were involved in this study. All MSCT scan findings and enhanced findings were analyzed and compared among cases with different risk degree of pathology. Then GISTs diagnostic model was established by using support vector machine (SVM) algorithm, and its diagnostic value was evaluated as well.

RESULTS: All lesions were solitary, among which there were 46 low-risk cases, 24 medium-risk cases and 30 high-risk cases. For all high-risk, medium-risk and low-risk GISTs, there were statistical differences in tumor growth pattern, size, shape, fat space, with or without calcification, ulcer, enhancement method and peritumoral and intratumoral vessels ($p<0.05$). However, there were no statistical differences in the location of tumor and CT value at each period (plain scan, arterial phase, venous phase) ($p>0.05$). The apparent difference lied in plain scan, arterial phase and venous phase for each risk degree. The diagnostic accuracy of SVM diagnostic model established with 10 imaging features as indexes was 70.0%, and it was especially reliable when diagnosing GISTs of high or low risk.

CONCLUSIONS: Preoperative analysis of MSCT features is clinically significant for its diagnosis of risk degree and prognosis; GISTs diagnostic model established on the basis of SVM possesses high diagnostic value.

Key Words:
Gastrointestinal stromal tumors, MSCT, Pathological risk degree, Support vector machine model.

Introduction

GISTs (gastrointestinal stromal tumors), which originated in the gastrointestinal leaf tissue, are a type of independent tumors with non-directional differentiation and composed of spindle cells and epithelioid cells. According to the accounting for 1%-3% of digestive tract tumors, GISTs account for relatively rare of GI tumors, but they are one of the most common mesenchymal tumors of gastrointestinal tract. Due to its high onset rate in the gastrointestinal muscular layers, it was once considered as other tumors such like leiomyoma, leiomyosarcoma, etc. Although there are substantial domestic clinical researches, only a few of them have noticed and linked to the imaging features and risk degree of GISTs. Coupled with an accurate preoperative assessment of the risk of GISTs is of great clinical significance for guiding clinical selection for reasonable treatment and evaluation of prognosis. Hence, the pathological risk degree of GISTs has become the most concerned problem[1-3]. In 2002, Fletcher et al[3] put forward a classification standard to divide patients into four groups as high-risk group, medium-risk group, low-risk group and extremely low-risk group in accordance with the parameters such as location, size and nuclear division number. Then it was adopted by NIH as formal staging of risk degree and was widely applied to clinical practice. In 2007, National Comprehensive Cancer Network (NCCN) guidelines[4] raised the basis of diagnosing risk degree of GISTs, which included tumor size, mitotic figure, tumor location, tumor necrosis or cystic degeneration, cell density, invasion in adjacent structures, infiltration of serosa, hypervascular tumor and etc. In the NCCN guidelines

Corresponding Author: Jiankun Wang, MD; e-mail: jkwang4@sina.com

(2015), the evaluation of risk degree for benign, extremely low risk, low risk, medium risk, and high risk was removed in respect of the biological behavior prediction of GISTs, while the judgment of recurrence was refined to assure more precise prediction of recurrence risk of patients with GISTs after surgery. Moreover, with a simpler form of statistics, it provides evidence for further study. Fletcher et al[3] standard was adopted in this study. Because of the few cases, the extremely low-risk group was merged into the low-risk group, which is convenient for not only statistical analysis, but also distinction of different risk degrees.

At present, the methods for the diagnosis of GISTs mostly depend on the iconography[5], which mainly including traditional X-ray radiography, MR and MSCT. Owning to the advantages such as fast scanning speed, high space and density resolution, especially dual-phase enhanced scan, MSCT can precisely show tumor's growth pattern, size and shape. Also, it can show if tumors are with or without calcification and ulceration, enhancement pattern and degree, relationship with surrounding tissue, with or without tumor blood supply vessels, which make the MSCT a widely used and one of the best methods of examination[6-8]. The mere usage of imaging method, however, is susceptible to interference of human factor and thereby leading to inaccurate diagnosis. Support vector machine (SVM), proposed by Cortes and Vapnik et al[9] in 1995, is a kind of computer aided diagnosis system and a machine learning method based on VC dimension theory and structural risk minimization principle. SVM shows the specific advantages in solving problems such as small sample, nonlinear and high-dimensional pattern recognition, and it overcomes the problem of "Curse of dimensionality" and "over learning"[9]. Moreover, it can be easily extended to digital signal processing, image processing, intelligent control and other fields. Owing to the firm theoretical foundation and concise mathematical model, SVM has attracted much attention and has been applied to the diagnosis of various diseases.

In this study, through the analysis of different risks of MSCT signs in gastrointestinal stromal tumors, we aimed to discuss the predictive value of MSCT features in gastrointestinal stromal tumor to pathological risk. Based on support vector machine (SVM) algorithm, a mathematical model, which is significant for the diagnosis of GISTs, was established to provide references for clinical practice. This study was approved by the Ethical Committee of Henan Provincial Hospital.

Patients and Methods

Patients

100 cases with abdominal and pelvic 64-slice spiral CT scan from January 2008 to October 2015 in our hospital (Henan Provincial Hospital, Zhengzhou, Henan, China) were collected in this study. All of them were confirmed by operation as primary GISTs and all patients were in a condition of solitary lesion. There were 48 males and 52 females ranging from 16 to 85 years old, average age of which was 60.90±13.35 years old. Among the 100 patients, 45 cases claimed abdominal pain; 21 cases showed abdominal discomfort; 24 cases manifested abdominal mess, dysphagia and difficult defecation and 10 cases were found on physical examination or by chance of other diseases. All patients involved in this study have voluntarily signed the informed consent.

CT Inspection Methods

64-slice spiral CT machine (Siemens China, Beijing, China) was adopted to perform the scanning. Before the CT examination, patients should be fasting for 12 h and drink 800 ml water just before the scanning. Then, the routine supine position was performed. The scanning conditions were stated as followed: the widths of collimator were respectively 0.75 mm and 0.6 mm, with pitch of 1.0 mm; the thickness of reconstructed slice was 5 mm and the gap was 5 mm. In the enhanced scanning, 100 ml iohexol (350-370 mgI/ml) (Saidaotong Biotech Co. Ltd., Shanghai, China) was injected at the dose of 1-2 ml/kg and flow rate of 3.0 ml/s from ulnar vein. Arterial phase scanning was performed at 20-25 s after injection, and venous phase scanning was performed at the 60-70 s. When the scanning was finished, the reconstruction was ready for observing the correlations between the lesions and ambient tissues by using MIP (maximum intensity projection) and MRP (multi-planar reconstruction).

Image Analysis

Through the blinding method, images were interpreted independently to analyze the imaging features of lesion parts by 3 radiologists with CT diagnosis experience of more than 5 years. The imaging features included the lesion location, size, shape, fat space, calcification, intensity, growth pattern, enforcement method, peritumoral and intratumoral vessels, CT value in plain scan, arterial phase and lag phase. In-

Table I. Data extraction of imaging features.

Features	Assignment
Location	Stomach: 0, small intestine: 5, others: 10
Growth pattern	intra-luminal type: 0, extra-luminal type: 5, mixed type: 10
Size	≥5 cm: 10, <5cm: 0
Shape	Irregular: 10, regular: 0
Fat space	Vague: 10, clear: 0
Calcification	Without: 10, with:0
Plain scanning density	Nonuniform: 10, uniform: 0
Ulcer	Without: 10, with: 0
Enhancement method	Nonuniform: 10, uniform:0
Peritumoral and intratumoral vessel	Without: 10, with: 0

consistent opinions were discussed to reach a final consensus. In CT assessment, there were certain classifications: the sizes were ≥ 5 cm or < 5 cm; the shapes were regular (circular or Quasi-circular) or irregular (lobulated); the fat spaces were clear or vague; the growth patterns were intra-luminal type, extra-luminal type or mixed type; the calcifications were with or without; the intensities were uniform, non-uniform or liquefaction necrosis; the enhancements were uniform or non-uniform and the peritumoral and intratumoral vessels were with or without. When CT values were measured in plain scan, arterial phase and venous scan, the obviously enhanced solid region (except blood vessels) within the lesion was selected as region of interest.

GISTs Diagnostic Model Based on SVM

Diagnostic model based on SVM divided all cases into three classes, low risk, medium risk, and high risk, which were assigned value of 1, 2, and 3, respectively. Then, each class was divided into two groups as training set and test set. Three classifiers, SVM 0, SVM 1, and SVM 2 were constructed by using LIBSVM 3.17 proposed by Lin et al[10], in which 10 imaging features (Table I) were taken as input vectors, and a currently popular algorithm, sequential minimal optimization was employed.

Statistical Analysis

SPSS16.0 software package (SPSS Inc., Chicago, IL, USA) was adopted to statistically analyze all statistics; X^2-test was used to analyze the relation of CT features and risk degree; one-way analysis of variance was used to analyze the relation of CT value in each phase and risk degree. Paired samples test were adopted to analyze the relation of CT value of each group in arterial phase and venous phase.

Results

Clinical Manifestations

Among a total of 100 cases, low-risk group contained 46 cases, in which there were 23 males and 23 females with an average age of 58.3±13.05 years old; medium-risk group contained 24 cases, in which there were 11 males and 13 females with an average age of 63.75±15.71 years old; high-risk group contained 30 cases, in which there were 30 cases, in which there were 14 males and 16 females with an average age of 62.61±11.32 years old. The distribution of gender and age was not statistically significant. Clinical manifestations were as follows, 45% of patients showed abdominal pain; 21% of patients showed abdominal discomfort; 24% of patients showed abdominal mass, dysphagia and difficult defecation; 10% of patients were just found the disease by chance in physical examination or because of other diseases.

The Relation Between MSCT Features of GISTs and Risk Degree of Tumor

All of the 100 cases were solitary lesions, among which there were 63 cases in stomach, 28 cases in small intestinal and 9 cases in other cases. The pathological risk degrees of these cases of GISTs were as follows: 46 low-risk cases, 24 medium-risk cases and 30 high-risk cases. There was no statistical significance in contrast between the locations of GISTs of different pathological risk degrees, but the rest of factors were statistically significant (p<0.05). The results are shown in Table II.

The Relation of risk Degree to CT Value in Different Phase and Enhancement Degree of GISTs

CT values of GISTs in different phases (plain scan, arterial phase, venous phase) in different

Table II. The relation between MSCT features of GISTs and risk degree of tumor.

Features		Classification Pathological risk degree				
		Low risk (n=46)	Medium risk (n=24)	High risk (n=30)	X^2	p
Location					8.732	0.068
	Stomach	35	14	14		
	Small intestinal	10	7	11		
	others	1	3	5		
Growth pattern					15.904	0.003
	Intra-luminal type	27	5	7		
	Extra-luminal type	10	11	9		
	Mixed type	9	8	14		
Size					38.076	0.000
	< 5 cm	36	4	5		
	≥ 5 cm	10	20	25		
Shape					7.263	0.026
	Regular	23	6	7		
	Irregular	23	18	23		
Fat space					26.600	0.000
	Clear	44	14	13		
	Vague	2	10	17		
Calcification					6.032	0.049
	With	3	5	8		
	Without	43	19	22		
Plain scanning density					12.873	0.002
	Uniform	27	7	6		
	Nonuniform	19	17	24		
Ulcer					7.311	0.026
	With	10	6	15		
	Without	36	18	15		
Enhancement method					18.635	0.000
	Uniform	22	5	1		
	Nonuniform	24	19	29		
Peritumoral and intratumoral vessel					20.758	0.000
	With	14	14	25		
	Without	32	10	5		

Note: $p<0.05$ indicates that difference is statistically significant.

Table III. Comparison of MSCT dual-phase enhancement and risk degree of GISTs in different risk degree.

Risk degree	Plain scan	Arterial phase	Venous phase	p^a
Low risk	31.50±5.64	63.37±20.16	77.65±24.90	0.003
Medium risk	31.79±5.52	65.59±22.14	77.69±18.78	0.047
High risk	33.10±4.93	67.00±21.53	78.63±20.52	0.036

Note: [a]Between arterial phase and venous phase; $p<0.05$ indicates statistical significance.

risk degree, are shown in Table III. There was obvious difference among the three phases of each risk degree, and the p-values of arterial phase and venous phase can be seen in Table III. On the other hand, the difference of each phase among the three risk degrees was not obvious.

Modeling of GISTs Diagnostic Model Based on SVM

SVM parameters were chosen by using parallel grid search algorithm. In grid search algorithm, M values of penalty parameter C and N values of nuclear parameter were taken and combined into

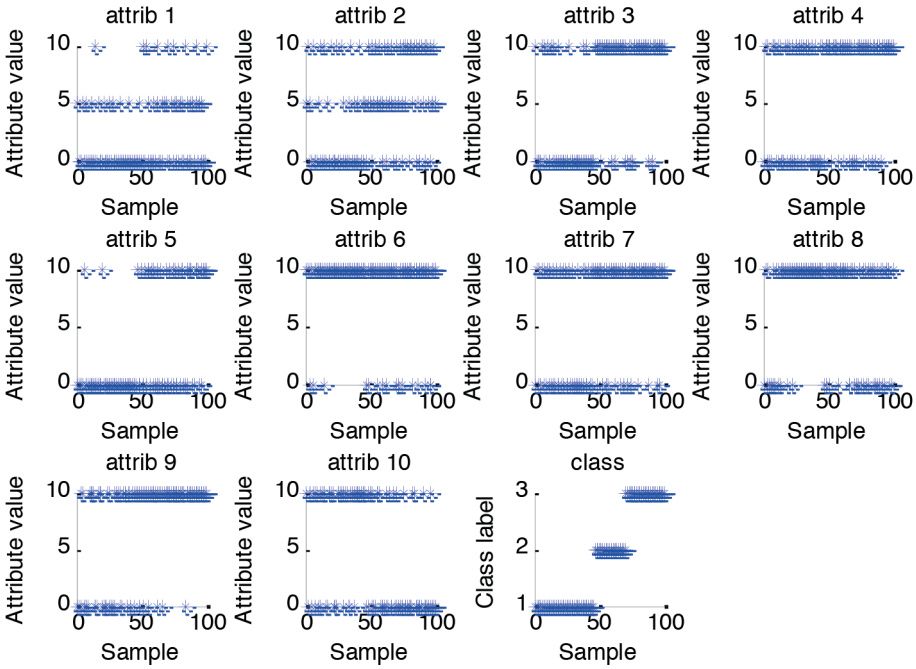

Figure 1. Training results of SVM models.

M×N groups of (C, γ); then different SVMs were obtained and their predictive accuracies were estimated, from which the group with the highest predictive accuracy was gained as the optimal parameter. Through validation[11,12], was confirmed as an optimal parameter. 10 imaging features were included in the training of SVM models, and their property values are shown in Figure 1. 1-37 in the first class, 47-65 in the second class, 71-94 in the third class were included in training set, and 38-46 in the first class, 66-70 in the second class, and 95-100 in the third class were included in test set. As seen in Table II, the test results showed that the predictive accuracy of samples in test set was 70.0% (14/20).

Discussion

GIST, originated from mesenchymal tissues of the digestive tract, is a primitive mesenchymal stem cell tumor with multiple differentiation potentials. The main clinical symptoms include nausea, vomiting, upper abdominal discomfort, abdominal pain, black stool, abdominal mass, obstruction, marasmus, and anemia. Due to latent early onset and non-specific clinical performance, lump is often large when it is diagnosed positively, and the early clinical diagnose rate is relatively low.

GISTs occur in both males and females and mainly among the middle and old aged people, namely, they rarely occur in people under 35 years old. However, the younger the patient is, the higher the probability of malignant lesion is.

In this study, the results showed that the locations of GISTs and CT values in different phases (plain scan, arterial phase, venous phase) were not statistically significant in different risk degrees. The difference of growth pattern, size, shape, fat space, calcification, plain scanning density, ulcer, enhancement method, peritumoral and intratumoral vessel in each risk degree was statistically significant ($p<0.05$). The difference in CT value of plain scan, arterial phase, venous phase in each risk degree was obvious ($p<0.05$). As for the relation between growth pattern and risk degree, there were different research results. Kim et al[2] and Horton et al[11] held the belief that extra-luminal growth was not a potential malignancy indication, while Tateishi et al[12] believed it was. The results of this study showed that there was a relation between growth pattern and risk degree, but the specific relationship still needs further study. Consistent with part of results in this study, it was reported in literature[13-16] that the conditions of tumor including larger than 5 cm, inhomogeneous dual-phase enhancement, peritumoral and intratumoral vessel were CT signs of high risk of GI-

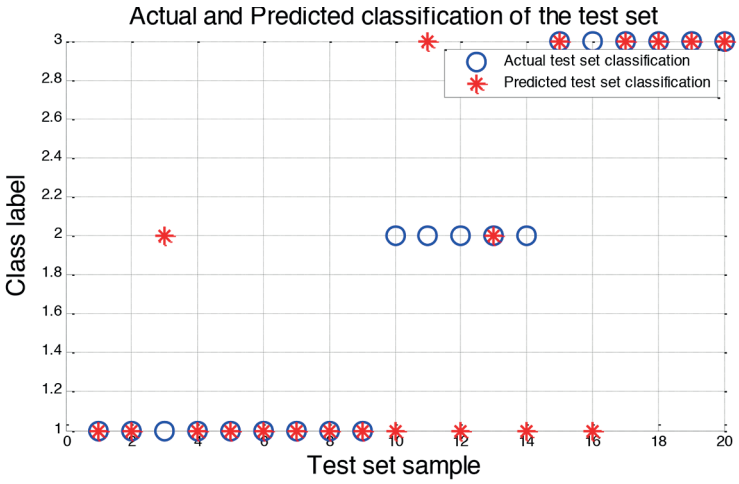

Figure 2. Test results of SVM models. Note: ◦refers to actual test set classification; *refers to predicted test set classification.

STs. CT value in venous phase of GISTs lesion in each risk degree was obviously higher than that in arterial phase, which can be used to identify other tumors in gastrointestinal. This study showed that features including extra-luminal growth, bigger lump, irregular shape, vague fringe, obvious inhomogeneous enhancement in enhanced MSCT scan, more obvious enhancement in arterial phase than in venous phase, peritumoral and intratumoral vessels, indicated higher risk of gastrointestinal stromal tumors, which was in accordance with the studies of Burkill et al[16], Sandrasegaran et al[17] and others authors[18-21]. Based on GISTs imaging features and their assignments, SVM model was constructed by Matlab to judge pathological risk degree. The diagnostic accuracy of SVM model was 70%, which has high reference value for distinguishing high and low-risk degree. It can be taken as supplement for various international rating standards and provide references for GISTs diagnosis and treatment. Currently, researches on SVM predictive modeling for CT imaging information mining have been developed in some diseases; for example Wang et al[21] achieved great results in detecting pulmonary lesion on CT imaging by using 3D SVM model. Based on CT imaging features such as serology, spiculation and lobulation, Zhao et al[22] established SVM model to predict nature of solitary pulmonary nodules, whose accuracy was 80.0%. However, related research on pathological risk degree of GISTs is still blank now. In a follow-up study, the sample size is to be expanded to improve the model, aiming to increase the diagnostic accuracy and provide foundation for GISTs diagnosis and treatment.

Conclusions

Consequently, preoperative analysis of MSCT features is clinically significant for the diagnosis of risk degree and evaluation of prognosis, and GISTs diagnostic model based on SVM is of great diagnostic value.

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Conflict of interest

The authors declare no conflicts of interest.

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