

A scoring system based on clinical features for the prediction of sporadic renal angiomyolipoma rupture and hemorrhage

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Abstract

The purpose of this study is to analyze the risk factors of sporadic renal hamartoma and establish a risk scoring system, and to intervene in patients with high-risk sporadic renal hamartoma who are prone to rupture and bleeding as soon as possible.

Retrospective univariate and multivariate logistic analyses were conducted for clinical data of 332 sporadic renal hamartoma patients to screen out independent risk factors of tumor rupture. Score of each independent risk factor was calculated. (Calculation formula: the risk coefficient of each factor = the beta regression coefficient of each factor/the minimum value of the beta regression coefficient of all factors, the value of the smallest beta regression coefficient corresponding to all the factors was assigned 1 point. The score of each factor was equal to the risk coefficient of each variable was taken as an integer value by rounding.) The total score was equal to the sum of all factors. Then the area under the receiver operating characteristics (AUC) curve was compared between high risk factors and scoring system. Finally, the scoring system was evaluated by the area under the curve (AUC) and the Hosmer–Lemeshow method in an independent cohort of 130 patients. Factors such as symptoms at presentation, tumor size, tumor blood supply, and tumor growth pattern were significant predictors of sporadic renal angiomyolipoma rupture in both the univariate and multivariate analyses; these predictors were included in the scoring system to predict sporadic renal angiomyolipoma rupture. There were no significant differences in AUCs between high risk factors and scoring system ($z = 0.6434$, $P = .583$, $AUC = 0.913$, and 0.903 for high risk factors and scoring system, respectively). The sporadic renal angiomyolipoma patients who scored >6 points were prone to rupture. AUROC of the scoring system in the validation set was 0.854 (95%CI: 0.779 , 0.928). Using the Hosmer–Lemeshow method, the value of X^2 was 2.916 , $P = .893$, suggesting the scoring system fitted well.

A scoring system based on clinical features is simple and effective in predicting sporadic angioliopoma rupture and hemorrhage. When the score is higher than 6 points, the probability of hamartoma rupture and hemorrhage is significantly increased and early intervention is needed.

Abbreviations: AML = angiomyolipoma, AUC = area under the curve, CI = confidence interval, RAML = renal angiomyolipoma, ROC = receiver operating characteristic, TSC = tuberous sclerosis complex.

Keywords: clinical feature, renal angiomyolipoma, rupture, scoring system, sporadic

1. Introduction

Renal angiomyolipoma (RAML) originates from renal mesenchymal cells and is the most common benign tumor of the kidney. It consists of smooth muscle, fat, and vascular elements and

accounts for approximately 3% of all solid renal masses.^[1] The prevalence of RAML for the general population is estimated to be 0.13%.^[2] There are 2 types of RAMLs: sporadic angiomyolipomas and tuberous sclerosis complex (TSC)-associated

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angiomyolipomas. TSC-associated angiomyolipomas account for approximately 20%,^[3] and TSC-associated angiomyolipoma is an autosomal dominant disease. The tumors grow rapidly and occur more often in young or female individuals.^[4–6] Multiple systems are sometimes involved.^[6] Sporadic renal hamartoma is even more common, accounting for approximately 80% of renal hamartomas. However, most sporadic RAML patients were usually asymptomatic and diagnosed incidentally when they were examined by ultrasound. Therefore, most patients did not consider management of sporadic RAML unless they were bothered by intractable pain, concerned about the large size of the tumor or the suspicion of malignancy, or alarmed by the risk of life-threatening hemorrhaging.^[4,7] However, spontaneous rupture may result in nephrectomy, hemorrhagic shock, or even death. Additionally, few studies have comprehensively reviewed the risk factors correlated with rupture and the prognosis of sporadic RAML.^[8] Therefore, we conducted this study to establish a basic scoring system for predicting rupture of sporadic RAMLs. As far as we know, this is the first report on the development of a risk scoring system to predict sporadic RAML.

2. Materials and methods

2.1. Patients

Four hundred sixty two of patients diagnosed with sporadic RAML were enrolled in this retrospective study at the Urinary Surgical Department of the First Affiliated Hospital of Chongqing Medical University, China, from January 2012 to April 2019. All of the 462 patients are from Southwest China. 323 patients are female (69.91%), and 139 patients are male (30.09%). Their age ranged within 8 to 83 years old. Among them, 72 patients had no obvious cause of spontaneous rupture and hemorrhage. RAML was diagnosed by observing lipomatous components in the kidney tumors by enhanced computed tomography (CT). A perirenal or subcapsular hematoma indicated tumor rupture. Therefore, patients without complete medical records were excluded from the study. This study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (NO.2019–262). In addition, all patients and their families agreed and provided a signed informed consent.

2.2. Methods

Clinical data of patients was collected as follows: age(years), sex (female, male), hypertension (yes, no), diabetes (yes, no), other organs containing AMLs (yes, no), renal cyst (yes, no), multiplicity (single, multiple/bilateral), tumor location (left, right, bilateral), symptoms at presentation (asymptomatic, symptomatic(including flank pain, abdominal tenderness, hematuria, shock), tumor size (cm), Body Mass Index (BMI) polar position (upper, middle, lower, other), tumor blood supply (rich/poor), and tumor growth pattern (completely endophytic, <50% exophytic growth, and ≥50% exophytic growth). Among these factors, the symptoms at presentation in all the patients occurred before RAML rupture and hemorrhage. The maximum diameter of the tumor represented the size of tumor according to CT scans. If there were multiple tumors on the same side, the diameter of the largest 1 was calculated. In addition, the tumor size was converted into 2 classification variables: ≥4 cm and <4 cm (because the tumors ≥4 cm have been used as one of the pointers for hamartoma intervention) BMI also was converted into 2

classification variables: ≥24 kg/m² and <24 kg/m² (Chinese BMI ≥24 kg/m² means overweight or obese, etc. <24 kg/m² means normal or lean). Whether the blood supply of the tumor was rich was determined by CT or color Doppler ultrasound. The criteria for a rich blood supply was as follows: the tumors were significantly enhanced on the CT arterial phase; There was evidence of the angiogenesis in 2 small arteries or 1 feeding branch artery in the tumor; 3 or more punctate blood flow signals were observed on the color ultrasound image.^[9] Otherwise, the tumors were classified as having a poor blood supply.

2.3. Statistical analysis

Four hundred sixty two patients in the study were divided into 2 sets: the training set and the validation set. Three hundred thirty two patients enrolled from January 2012 to April 2017 entered into the training set for developing a scoring system for the risk of rupture of sporadic RAML. One hundred thirty patients enrolled from May 2017 to April 2019 entered into the validation set for evaluating the performance of the scoring system. The patients in the training set were split into 2 subsets: a ruptured group (patients with ruptured renal angiomyolipomas) and an unruptured group (patients with unruptured renal angiomyolipomas).

The statistical analysis was performed using SPSS version 25.0 for Windows (SPSS Inc., Chicago, IL, USA). Univariate analysis was used to compare the clinical data between the rupture group and nonrupture group and to find associated variables in the training set. The univariate analysis included chi-square tests for categorical variables and t-tests for continuous variables. These significant variables in univariate analysis and covariates considered clinically influential were then analyzed by multivariate stepwise logistic regression (backward stepwise logistic regression) to identify significant variables affecting RAML rupture. $P < .05$ was considered statistically significant.

Then, we could calculate the risk coefficient of each variable according to beta regression coefficient of each variable in the multivariate logistic regression. Calculation formula: the risk coefficient of each variable = the beta regression coefficient of each variable/the minimum value of the beta regression coefficient of all variables, the value of the smallest beta regression coefficient corresponding to all the variables was assigned 1 point. The score of each variable was equal to the risk coefficient of each variable was taken as an integer value by rounding. A scoring system was developed based on score of each variable. Additionally, calculating the total score of each patient, analyzing the ROC curve of the total score, determining the cutoff value in accordance with the Youden index, the study divided the patients into low-risk groups and high-risk groups. To compare the diagnostic values of the scoring system with high risk factors prediction model, areas under the receiver operating characteristic (ROC) curves (AUC) were used as the performance indices. The AUCs were calculated by the trapezoid rule. The Z test was used for the comparison of the AUCs and no difference between high risk factors and scoring system.

Finally, the predictive accuracy of the scoring system was evaluated by constructing receiver operating characteristic (ROC) curves, measuring the areas under the curves (AUCs) and further validation in the validation set. The fitness of each model was evaluated using the Hosmer–Lemeshow goodness-fit test. The 2-sided test for significance level was set as $\alpha = .05$, and $P < .05$ was still considered statistically significant.

3. Results

A total of 462 patients were divided into a training set (332 patients, 72%) or a validation set (130 patients, 28%). The sample size of the validation set was approximately two-fifths that of the training set. There were no statistical differences between the training and validation sets in clinical features (age, tumor size, sex, hypertension, diabetes, renal cyst, multiplicity, tumor location, symptoms at presentation, tumor growth pattern, BMI, polar position, other organs containing AMLs, tumor blood supply) (Table 1).

3.1. Single factor regression analysis

In the training set, 322 cases of patients diagnosed with sporadic RAML, 49 patients had RAML rupture. Out of the 14 variables studied, the univariate analysis identified 6 parameters associated with tumor rupture. The univariate analysis (Table 2) showed that the factors significantly associated with tumor rupture were age ($P=.022$), other organs containing AMLs ($P=.025$), symptoms at presentation ($P<.001$), tumor size ($P<.001$), tumor blood supply ($P<.001$), and tumor growth pattern ($P<.001$). No significant differences were found for sex,

Table 1
Comparison of clinical features between the training and the validation set.

	All patients (n=462) (n%)	Validation set (n=130) (n%)	Training set (n=332) (n%)	χ^2/T	P
Age (years)*	48.43 ± 12.79	46.96 ± 12.67	49.01 ± 12.80	1.548	.122
Tumor size (cm)	4.80 ± 3.51	4.89 ± 3.11	4.76 ± 3.66	0.368	.713
Sex					
Female	323 (69.1%)	97 (74.6%)	226 (68.1%)	1.901	.618
Male	139 (30.9%)	33 (25.4%)	106 (31.9%)		
Hypertension					
Yes	71 (15.4%)	16 (12.3%)	55 (16.6%)	1.303	.254
No	391 (84.6%)	114 (87.7%)	277 (83.4%)		
Diabetes					
Yes	27 (5.8%)	5 (3.8%)	22 (6.6%)	1.312	.252
No	435 (94.2%)	125 (96.2%)	310 (93.4%)		
Other organs containing AMLs†					
Yes	65 (14.1%)	23 (17.7%)	42 (12.7%)	1.964	.161
No	397 (85.9%)	107 (82.3%)	290 (87.3%)		
Renal cyst					
Yes	119 (25.8%)	28 (21.5%)	91 (27.4%)	1.684	.194
No	343 (74.2%)	102 (78.5%)	241 (72.6%)		
Multiplicity					
Single	385 (83.3%)	110 (84.6%)	275 (82.8%)	0.214	.644
Multiple / Bilateral	77 (16.7%)	20 (15.4%)	57 (17.2%)		
Tumor location					
Left	196 (42.4%)	51 (39.2%)	145 (43.7%)	2.508	.357
Right	207 (44.8%)	58 (44.6%)	149 (44.8%)		
Bilateral	53 (11.8%)	21 (16.2%)	38 (11.4%)		
Symptoms at presentation					
Asymptomatic	345 (74.7%)	95 (73.1%)	250 (75.3%)	2.733	.435
Symptomatic‡	117 (25.3%)	35 (26.9%)	82 (24.7%)		
Growth pattern					
≥50% exophytic growth	198 (43.0%)	58 (44.6%)	140 (42.2%)	0.598	.741
<50% exophytic growth	107 (23.1%)	27 (20.8%)	80 (24.1%)		
Completely endophytic	157 (33.9%)	45 (34.6%)	112 (33.7%)		
Tumor size					
<4 cm	240 (51.9%)	60 (46.2%)	180 (54.8%)	2.433	.119
≥4 cm	222 (48.1%)	70 (53.8%)	152 (45.8%)		
BMI					
<24 kg/m ²	236 (51.1%)	72 (55.4%)	164 (49.4%)	1.34	.247
≥24 kg/m ²	226 (48.9%)	58 (44.6%)	168 (50.6%)		
Polar position					
Upper	149 (32.3%)	39 (30%)	110 (33.1%)	6.195	.103
Middle	141 (30.5%)	45 (34.6%)	96 (28.9%)		
Lower	150 (32.5%)	37 (28.4%)	113 (34.0%)		
Others§	22 (4.7%)	9 (6.9%)	13 (3.9%)		
Tumor blood supply					
Poor	270 (58.4%)	70 (53.8%)	200 (60.2%)	1.573	.21
Rich	192 (41.6%)	60 (46.2%)	132 (39.8%)		

* Arithmetic mean ± standard deviation.

† AML originates from mesenchymal cells and consists of smooth muscle, fat, and vascular elements, which is involved multiple organ systems, mainly in the lungs, kidneys, liver, and hypothalamus.

‡ Including flank pain, abdominal tenderness, hematuria, shock.

§ It is not possible to simply describe the position of the hamartoma with the upper, middle and lower poles of the kidney, such as the hamartoma occupying most or all of the kidneys and multiple mismatched tumors located at different locations in the kidney.

Table 2
Univariate analysis of clinical factors in the training set.

	Training set (332)	Unruptured group (283)	Ruptured group (49)	χ^2/T	<i>P</i>
Age (years)*	49.01 ± 12.80	49.16 ± 12.33	48.1 ± 15.39	5.316	.022
Sex					
Female	226	198	28	3.159	.075
Male	106	85	21		
Hypertension					
Yes	55	44	11	1.439	.23
No	277	239	38		
Diabetes					
Yes	22	17	5	1.189	.276
No	310	266	44		
Other organs containing AMLs					
Yes	42	31	11	4.994	.025
No	290	252	38		
Renal cyst					
Yes	91	76	15	0.296	.586
No	241	207	34		
Multiplicity					
Single	275	237	38	1.127	.288
Multiple / Bilateral	57	46	11		
Tumor location					
Left	145	119	26	3.479	.176
Right	149	133	16		
Bilateral	38	31	7		
Symptoms at presentation					
Asymptomatic	250	240	10	93.133	.001
Symptomatic	82	43	39		
Tumor size					
<4cm	180	173	7	36.926	.001
≥4cm	152	110	42		
Growth pattern					
≥50% exophytic growth	140	101	39	33.585	.001
<50% exophytic growth	80	74	6		
Completely endophytic	112	108	4		
BMI					
<24 kg/m ²	164	140	24	0.004	.949
≥24 kg/m ²	168	143	25		
Polar position					
Upper	110	94	16	5.862	.119
Middle	96	88	8		
Lower	113	91	22		
Others	13	10	3		
Tumor blood supply					
Poor	200	189	11	34.278	.001
Rich	132	94	38		

* Arithmetic mean ± standard deviation.

hypertension, diabetes, renal cyst, multiplicity, tumor location, BMI, or polar position (*P* > .05).

3.2. Multi-single factor regression analysis

Four variables (symptoms at presentation, tumor size, tumor blood supply, and tumor growth pattern) were significantly correlated with RAML rupture in the multivariate regression analysis (Table 3), while age, and other organs containing AMLs, sex, hypertension, diabetes, and multiplicity were not independently associated with sporadic RAML rupture (*P* > .05).

3.3. Establishment of risk scoring system

In addition to playing an essential role in sporadic RAML rupture, these 4 high-factors (symptoms at presentation, tumor

size, tumor blood supply, and tumor growth pattern) are easy to identify clinically. Thus, they were applied in the predictive scoring system for sporadic RAML rupture. According to the calculation formula, the risk coefficient of each variable was obtained (in Table 3). The risk coefficient of each variable was rounded to an integer to get the score of each variable (Table 4). The occurrence of clinical symptoms, <50% exophytic growth, a tumor size ≥4cm and a tumor with a rich blood supply were assigned values of 3, 1, 2, and 2, respectively. The total score was calculated by summing the individual scores of all the significant variables. With an increasing total score, the probability of RAML rupture increased gradually.

Figure 1 showed the ROC curve of scoring system and high-risk factors respectively. The area under the ROC (AUROC) curve of predicted probability of high risk factors was 0.913 (95%CI:0.876,0.950) *P* < .001; the area under the ROC

Table 3
Multivariate stepwise logistic analysis of clinical factors in the training set and calculating risk coefficient of each variable.

Variable	Risk coefficient	β	SE	Wald	Sig.	Exp (B)	Exp (B)95.0%CI	
							Lower limit	Higher limit
Symptoms at presentation		2.367	0.38	38.37	.001	10.664	5.043	22.551
Asymptomatic	0							
Symptomatic	3.301							
Tumor size		1.195	0.51	5.452	.02	3.303	1.212	9.004
<4 cm	0							
≥4 cm	1.667							
Growth pattern								
Completely endophytic	0			5.691	.058			
<50% exophytic growth	1	0.717	0.8	0.804	.37	2.049	0.427	9.823
≥50% exophytic growth	2.058	1.476	0.68	4.776	.029	4.375	1.164	16.435
Tumor blood supply		1.406	0.44	10.36	.001	4.079	1.732	9.603
Poor	0							
Rich	1.961							
Constant		-6.67	1.03	41.9	.001	0.001		

The risk coefficient of each variable = the beta regression coefficient of each variable/the minimum value of the beta regression coefficient of all variables, the value of the smallest beta regression coefficient corresponding to all the variables was assigned 1 point. CI = confidence interval, SE = standard error.

(AUROC) curve of the scoring system in the training set was 0.903(95%CI:0.861, 0.945) ($P < .001$). The data showed that there was no difference for AUCs between high risk factors and scoring system($Z=0.6437, P=.464$), which proved that scoring system can well simulate the prediction model constructed by high-risk factors. When the cutoff value was between a score of 6 and a score of 7, the Youden index (sensitivity+ specificity-1) reached the maximum value (0.657). The sensitivity and specificity were 73.5% and 92.2%, respectively; Calculations based on the above data showed that a score of 0–6 points was associated with a 7.5% risk of tumor rupture, and the risk increased to as high as 67.5% when the score was 7–9 points (Table 5). Therefore, patients with a total score of 0–6 points were considered the low-risk group, while patients with a total score of 7–9 were considered the high-risk group ($P < .001$ based on the Chi-Squared test).

3.4. Evaluation of the scoring system

In a validation set of 130 patients, 23 patients presented RAML ruptured (17.7%, 23/130). One hundred fifteen patients in the validation set had a total score of 0–6 (low-risk), among which only 12.2% experienced sporadic RAML rupture. A total of 15 patients scored 7–9 points (high-risk), among which 60.0% suffered from sporadic RAML rupture (Table 6). The results of the validation set were similar to those in the training set. Figure 2 shows the AUROC of the scoring system in the validation set was

0.854 (95%CI:0.779, 0.928) ($P < .001$), which indicated the scoring system can distinguish moderately. When the Hosmer–Lemeshow method was used ($P > .05$), the value of X^2 was 2.916, $P = .893$, suggesting that the scoring system fitted well.

4. Discussion

Rupture and hemorrhage are the most severe complications of sporadic RAML. The disease develops rapidly at the time of tumor rupture and hemorrhage, which usually lead to nephrectomy or hemorrhagic shock or even death if not treated in time. Therefore, it is especially important to elucidate the risk factors and early intervention strategies for sporadic RAML rupture and hemorrhage, which is one of the essential clinical problems to be solved in urology. At present, there is a lack of systematic and complete research reports on predicting sporadic RAML rupture and hemorrhage. This study aimed to establish a scoring system for predicting sporadic RAML rupture to initiate early interventions in high-risk RAML patients and guide clinical treatment. The univariate and multivariate analyses revealed that symptoms at presentation (flank pain on the affected side, etc), tumor size, tumor blood supply, and tumor growth pattern were independent factors affecting RAML rupture. A scoring system based on these 4 independent risk factors showed that patients with sporadic RAML who had high scores (score ≥ 7) were prone to RAML rupture, and early intervention was required.

Table 4
The scoring system based on clinical features for the prediction of sporadic renal angiomyolipoma rupture and hemorrhage.

Score	Symptoms at presentation	Tumor size	Growth pattern	Tumor blood supply
0	Asymptomatic	< 4cm	Completely endophytic	Poor
1			<50% exophytic growth	
2	Symptomatic*	≥4cm	≥50% exophytic growth	Rich
3				

* Including flank pain, abdominal tenderness, hematuria, shock.

Calculated score = Symptoms at presentation (Symptomatic/ Asymptomatic) (score 3 or 0) + Tumor size (≥4 cm/<4 cm) (score 2 or 0) + Growth pattern (Completely endophytic/<50% exophytic growth/≥50% exophytic growth) (score 0 or 1 or 2) + Tumor blood supply (Rich /Poor) (score 2 or 0).

Patients with a total score of 0–6 points are considered having a lower probability of tumor rupture and hemorrhage and active surveillance is recommended. While patients with the score is higher than 6 points, the probability of angiomyolipoma rupture and hemorrhage is significantly increased and early intervention is needed.

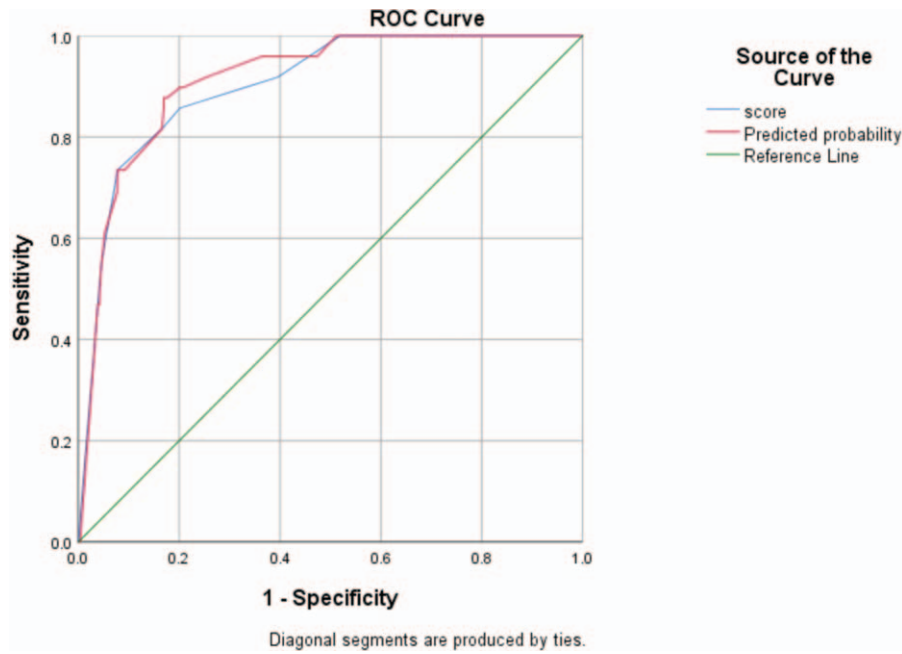


Figure 1. ROC curve of predicted probability of high risk factors and ROC curve of total scores of clinical features to respectively predict sporadic renal angiomyolipoma rupture and hemorrhage in the training set. The area under the ROC (AUROC) curve of predicted probability of high risk factors was 0.913 (95% CI:0.876, 0.950) $P < .001$; The area under the ROC (AUROC) curve of total scores of clinical features was 0.903 (95% CI:0.861, 0.945), $P < .001$. ROC = receiver operating characteristic, AUC = area under the curve, CI = confidence interval.

RAML with flank pain on the affected side was highly associated with tumor rupture and hemorrhage and was the most critical risk factor for RAML rupture. RAMLs grow slowly, are usually asymptomatic in the early stages and are often detected during physical examination.^[10] In patients who have different degrees of flank pain, hematuria, or even shock, this urological emergency is called Wunderlich syndrome.^[11] This syndrome often indicates that the tumor has ruptured and may be related to the stimulation of the dorsal renal nerves when the tumor grows or ruptures. If the tumor invades the renal collecting system, hematuria may develop. Oesterling et al^[12] and Lee, et al^[13] reported that half of the patients with clinical symptoms had ruptured tumors. Similar results were observed in our study; 47.6% of the patients with clinical symptoms had ruptured tumors, and 4% of the patients without clinical symptoms had ruptured tumor. The former was 11.9 times higher than the latter. Therefore, when RAML manifests with clinical symptoms, it is suggested that the risk of rupture and hemorrhage is increased, and early intervention is required.

Tumor size is directly related to RAML rupture and hemorrhage.^[14,15] Most researchers consider 4cm as the standard for intervention.^[5] In this study, it was found that only 3.9% of RAMLs less than 4cm had ruptured, while 27.6% of RAMLs 4cm or greater had ruptured. Studies have reported

that 82% to 94% of RAMLs approach or exceed 4cm in diameter, and 50% to 60% of them have the possibility of spontaneous rupture.^[16] The rate of spontaneous rupture was only 27.6% in the training set. This may be attributed to differences in the research groups. However, Bhatt JR et al.^[10] suggested that most patients with large AMLs >4cm can undergo current active surveillance. Therefore, we should consider whether RAMLs requires further treatment after considering multiple clinical high-risk factors.

The tumor growth pattern was also a key factor leading to tumor rupture. Our study showed that RAMLs growing on the surface of the kidneys were prone to rupture. Pathological examination showed that the renal hamartomas lacked a complete capsule or pseudocapsule. Hamartomas located on the surface of the kidney often break through the renal capsule due to the lack of protection of the renal capsule and its thin and incomplete vascular walls. Tumors were prone to rupture and hemorrhage under the action of external forces.^[17] Therefore, giant hamartomas located on the surface of the kidney are a high-risk factor for rupture and bleeding and require early intervention.

Renal hamartomas are rich in microvessels. The formation of microaneurysms and incomplete vascular walls are high-risk factors for rupture and bleeding.^[6,18] In this study, tumor blood

Table 5
Incidence of rupture in different populations in training set.

Risk stratification	Unruptured	Ruptured	Total
Low risk (score of 0–6)	270 (92.5%)	22 (7.5%)	292 (88.0%)
High risk (score of 7–9)	13 (32.5%)	27 (67.5%)	40 (12.0%)
Total	283 (85.2%)	49 (14.8%)	332 (100%)

Table 6
Incidence of rupture in different populations in validation set.

Risk stratification	Unruptured	Ruptured	Total
Low risk (score of 0–6)	101 (87.8%)	14 (12.2%)	115 (88.5%)
High risk (score of 7–9)	6 (40.0%)	9 (60.0%)	15 (11.5%)
Total	107 (82.3%)	23 (17.7%)	130 (100%)

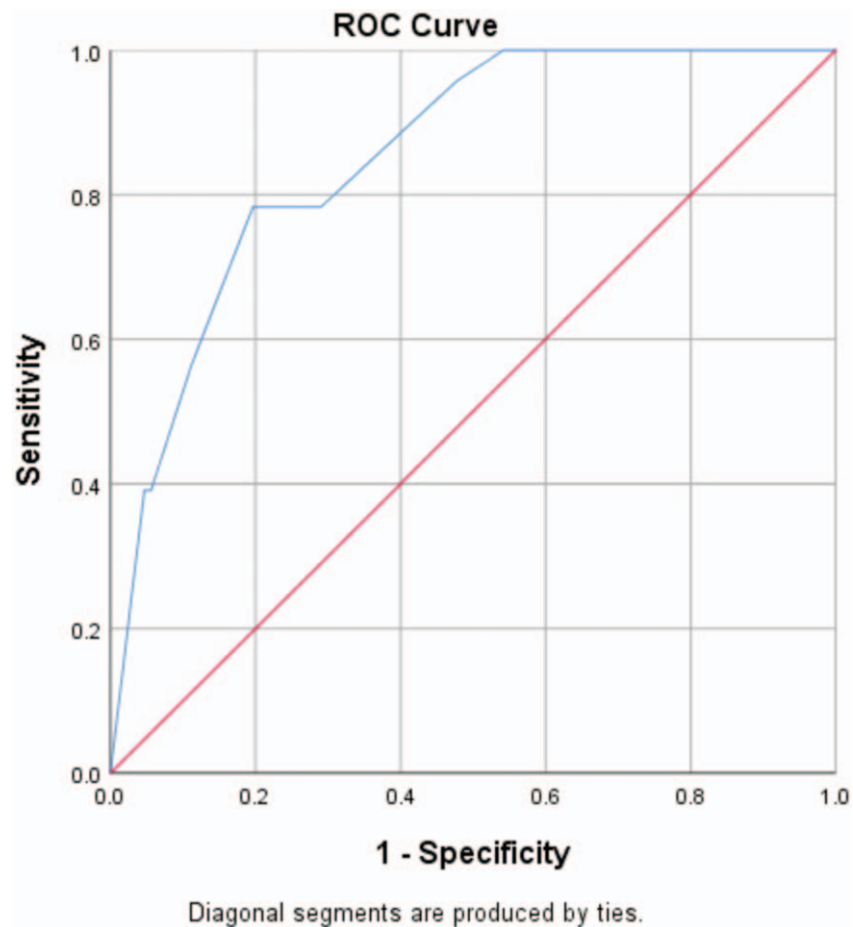


Figure 2. ROC curve of total scores of clinical features to predict sporadic renal angiomyolipoma rupture and hemorrhage in the validation set. The AUC value was 0.854 (95% CI:0.779, 0.928), $P < .001$. ROC = receiver operating characteristic, AUC = area under the curve, CI = confidence interval.

supply was used to describe the situations mentioned above. In the research, it was found that tumors with a rich blood supply were significantly associated with spontaneous RAML rupture. As shown in Table 2, the prevalence of tumors rich in blood supply were 77.6% and 32.1% in the ruptured and unruptured groups respectively. The probability of rupture in patients who had tumors with a rich blood supply was 5.23 times higher than that of patients who had tumors with a poor blood supply. The excessive proliferation of tiny blood vessels in the tumor; a healthy blood supply, especially in the renal cortex^[16]; and substantial intravascular pressure led to tumor rupture and bleeding. In addition, the components of the deformed blood vessels in the tumor also played an important role in the breach of the tumor; the tumor wall was incomplete, lacked an elastic layer, was fibrosis, and showed transparent changes, and the small and medium arteries formed aneurysms. Under the condition of a rich blood supply, the blood vessel wall can rupture and cause tumor hemorrhaging.^[18] Other studies also found that pregnancy, coagulopathy, trauma, and hormone levels were attributed to RAML rupture.^[18–20] However, these factors need further confirmation.

Based on the effects of the above 4 high-risk factors on renal hamartoma rupture, this study established a scoring system to predict the possibility of renal hamartoma rupture. The contribution of each risk factor to the risk of rupture varied, so

the corresponding scores were different; the more risk factors the patient had, the higher the total score was. According to the Youden index obtained from the ROC curve, the scores were divided into 2 subsets: 0–6 points and 7–9 points, according to the corresponding cutoff values. There was a large difference in the probability of tumor rupture between the 2 subsets, which provided good clinical guidance. Patients with scores ≤ 6 points are less likely to experience rupture and bleeding and can be followed closely, while patients with scores ≥ 7 points require timely intervention because the probability of rupture and bleeding is 10.93 times higher than that in patients with scores ≤ 6 points, as shown in Table 5. The scoring system was applied to another independent dataset, and similar results were obtained, suggesting that the scoring system was accurate.

There were some limitations in our study. First, there was study population bias, as our study collected the clinical data of only inpatients. Second, the sample size was limited, and large-scale multicenter sample validation is still needed.

In conclusion, we developed a simple, easy-to-use, and highly accurate scoring system by analyzing the distribution of the weighted values of the 4 independent factors of sporadic renal hamartoma. This scoring system can effectively guide urologists to determine which type of renal hamartoma requires early intervention, which is of great significance to the protection of the kidneys and the life of patients.

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Author contributions

X-fX, X-hH and YZ participated in the study design, Q-mZ, JZ, H-yX collected and analyzed the clinical data. X-fX and X-hH co-wrote the manuscript. Y Z assisted in literature search and provided critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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