

SCIENTIFIC REPORTS

OPEN

Usefulness of CHA₂DS₂-VASc Scoring Systems for Predicting Risk of Perioperative Embolism in Patients of Cardiac Myxomas Underwent Surgical Treatment

Liang Yin*, Jing Wang*, Wei Li*, Xinyu Ling, Qian Xue, Yufeng Zhang & Zhinong Wang

Received: 06 July 2016
Accepted: 22 November 2016
Published: 16 December 2016

Cardiac myxomas are rare but manifested with risk of embolism and often cause unexpected symptoms or sudden death. We retrospectively collected the medical records of patients diagnosed of cardiac myxomas at the cardiac center of our university. Overall 465 patients were included in this study, patients in the embolism group had significantly higher CHA₂DS₂-VASc scores ($P = 0.005$). In embolic group, stroke was recorded in 110 (77.14%) patients, while embolic events in the limbs were observed in 10 (2.15%) and 9 (1.93%) developed splenic infarction. Patients in embolism group had older age ($P = 0.021$) and higher BMI ($P < 0.001$) than those in non-embolism group. There was no significant difference between two groups in terms of time of mechanical ventilation ($P = 0.065$), ICU stay ($P = 0.053$), hospital stay ($P = 0.071$) and volume of drainage ($P = 0.083$), blood transfusions ($P = 0.060$) except that patients with embolic events had significantly higher incidence of postoperative atrial fibrillation ($P = 0.032$) and lower survival rate ($P < 0.001$). Furthermore, the CHA₂DS₂-VASc score was a significant predictor of embolism in patients with cardiac myxomas ($P = 0.015$; $P = 0.003$) and the Kaplan-Meier analysis obtained a higher rate of embolism in patients with higher stratification of CHA₂DS₂-VASc scores ($P = 0.002$). In conclusion, CHA₂DS₂-VASc scoring scheme was strongly predictive of stroke and embolic events in patients with cardiac myxomas.

Cardiac myxomas are rare compared with other cardiac diseases and tumors from other organs, with the incidence of approximately 0.3% in patients underwent cardiac surgery^{1–4}. Cardiac myxomas are the mostly encountered benign cardiac tumors in surgery, with its incidence ranged from 70–80% in cardiac tumors^{5,6}. Because of their various presentations, symptoms of cardiac myxomas vary greatly and they usually present themselves insidiously. Symptoms generated from cardiac tumors include arrhythmias, blood flow obstruction, embolization and other individual findings^{7–9}. Prompt removal of these tumors has been established as the only mode of treatment for these patients¹⁰.

Type, size, and mobility of cardiac myxomas determine their clinical symptoms, which also greatly affect the incidence of embolization in patients. Embolism, intracardiac obstruction, and constitutional symptoms are mostly presented in patients, and the incidence of embolization was reported to be 20–40%^{2,10,11}. Patients who occurred embolic events in the perioperative period had significantly higher morbidity and mortality, which may result in longer hospital stay and increased hospital costs and life quality was severely influenced following surgery^{2,11,12}. Non-invasive procedure, such as echocardiography, computed tomography (CT), and magnetic resonance imaging (MRI) of the heart, are commonly used to diagnose cardiac myxomas and evaluate the risk of stroke in patients at risk¹³, allowing preoperative diagnosis with fair degree of accuracy. But only several scattered indicators and lack of systematic scoring system for predicting risk of stroke deter the assessing process preoperatively, and increased perioperative morbidity and long-term mortality may occur in concerned patients.

Department of Cardiothoracic Surgery, Changzheng Hospital, the Second Military Medical University, Shanghai, China. *These authors contributed equally to this work. Correspondence and requests for materials should be addressed to Y.Z. (email: zhangyufeng1988@163.com) or Z.W. (email: wangzn007@163.com)

Originally, the CHA₂DS₂-VASc [congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled), vascular disease, age 65–74, and sex category (female)] recommended by European Society of Cardiology (ESC) is an easy-to-remember means of assessing stroke risk of patients with AF, which is based on a point system in which 2 points are assigned for a history of stroke or TIA, or age ≥ 75 ; and 1 point each is assigned for age 65–74 years, a history of hypertension, diabetes, recent heart failure, vascular disease (myocardial infarction, complex aortic plaque, and peripheral arterial disease (PAD), including prior revascularization, amputation due to PAD, or angiographic evidence of PAD, etc.), and female sex^{14–16}.

The CHA₂DS₂-VASc score can provide easy and effective assessment of patients with AF in which circumstances they can occur stroke or other thrombus-embolism events¹⁷. There was limited study having investigated the association between CHA₂DS₂-VASc score and prediction of risk of stroke or thrombus-embolism events in patients with cardiac myxomas who is also at high risk of embolism occurrence. In this study, we sought to explore the potential association between CHA₂DS₂-VASc score scheme and its utility of assessment for predicting embolic events in patients with cardiac myxomas underwent surgical treatment.

Methods

Patient Selection. Informed consent was obtained by each patient included in our study, and the consent procedure of our study was approved by Ethics Committee of Shanghai Changzheng Hospital, all methods performed in this study were carried out in accordance with relevant guidelines and regulations and all experimental protocols were approved by Ethics Committee of Shanghai Changzheng Hospital. This study included a series of patients who were underwent cardiac surgical treatment at the cardiothoracic center of the Second Military Medical University of PLA from January 2003 to December 2013. All patients with the diagnosis of cardiac myxomas treated with open heart surgery have been included in this retrospective study. Included patients were carried out surgery of tumor resection to treat cardiac myxomas with or without valve surgeries and other concomitant cardiac surgeries. Patients with history of recent myocardial infarction (MI) (less than one month), deep venous thrombus (DVT), preoperative renal or hepatic failure, infective endocarditis were excluded^{3,18}.

Patient Management. Complete medical records and follow-up data of each patient, including the medical history, neurologic examination, operative reports, pathology reports, CT or MRI of the brain, were collected using the patient database of our center, and follow-up of patients were conducted by contacting patients using telephone or by outpatient clinics. Pathological diagnosis of cardiac myxomas was obtained from the clinical pathological institute of our center. All patients presented with chest pain or older than 45 were carried out coronary angiography to rule out coronary heart disease (CHD)¹⁹. Preoperative management, anesthetic, and surgical techniques for all patients were standardized. Patients were transferred to the intensive care unit of our department postoperatively and managed accordingly.

CHA₂DS₂-VASc score. The CHA₂DS₂-VASc score was calculated for all the patients by assigning 2 points for age ≥ 75 and for history of stroke, TIA, or thromboembolism and 1 point is assigned for congestive heart failure, hypertension, diabetes mellitus, age 65–75 years, vascular disease (myocardial infarction, complex aortic plaque, and PAD, including prior revascularization, amputation due to PAD, or angiographic evidence of PAD, etc.), and female sex category^{20,21}.

Endpoints and definitions. The main outcome endpoint of interest was new-onset ischemic stroke or any embolic event occurring during the perioperative period (before surgery during hospital, 30-day postoperative period or before discharge). Stroke was defined as new structural changes detected by CT or MRI imaging²², in patients with neurologic deficit lasting > 24 hours without new structural changes in the brain by imaging, and the diagnosis of stroke was confirmed by a neurologist to minimize the error that may contribute to the bias generated in our study^{2,3,23,24}. Embolic event occurring in other parts of the body except the brain was also detected in our study, which was included by presenting symptoms of embolism, analysis of the variables related to embolic potential and stroke lesion patterns, and finally confirmed by ultrasound or digital subtraction angiography (DSA)^{10,25}.

Statistical analysis. Statistical analysis was carried out using SPSS 18.0 software. Quantitative data are expressed as mean \pm SD and were compared with 2-sample *t* tests for independent samples, whereas dichotomous variables were reported as absolute values and proportions. Differences in proportion were compared with a χ^2 test or Fisher exact test as appropriate. Survival rates were estimated using the Kaplan–Meier Method. Variables significantly associated with occurrence of embolic event after univariate analysis ($P < 0.05$) were entered in a multivariable logistic regression model to identify the independent predictors of embolic event²⁶. Additionally, we calculated the area under receiver operating characteristic (ROC) curve to assess the predictive value of CHA₂DS₂-VASc scores for risk of stroke in patients with myxomas^{5,27}.

Results

Clinical Characteristics of patients. We collected data of patient's age, gender, medical history and perioperative data. A total of 465 patients diagnosed of cardiac myxomas were included in this study, of these 152 were male patients and 313 were females, with a mean age of 53.39 ± 16.37 , 58.19 ± 6.37 respectively. A total of 143(30.75%) patients developed stroke or embolic events, and patients were divided into two groups according to whether stroke or embolic event occurred. The result of analysis showed that patients in the embolism group had older age ($P = 0.021$) and higher BMI ($P < 0.001$) than those in non-embolism group, and history of hypertension ($P = 0.035$) and coronary artery disease ($P = 0.004$) were significantly more recorded in embolism group. Furthermore, patients in the non-embolism group had a higher frequency medication history of

	Embolism (n = 143)	no-Embolism (n = 322)	p value
Age (y)	59.4 ± 10.9	52.3 ± 12.4	0.021
Age 65–75 y	47 (32.90%)	88 (27.3%)	0.045
Age ≥ 75 y	5 (3.50%)	6 (1.86%)	0.077
Female, n (%)	99 (69.23%)	214 (66.46%)	0.407
Smoke, n (%)	50 (35.2%)	135 (41.92%)	0.438
BMI (kg/m ²)	26.1 ± 2.8	23.3 ± 2.6	0.001
Medical history, n (%)			
Heart failure	67 (46.85%)	154 (47.82%)	0.239
Hypertension	54 (37.76%)	78 (24.22%)	0.035
Diabetes mellitus	32 (22.37%)	49 (15.22%)	0.061
Prior stroke or TIA	5 (3.50%)	11 (3.41%)	0.965
Coronary artery disease	79 (55.24%)	32 (9.93%)	0.004
Carotid artery disease	45 (31.46%)	33 (23.07%)	0.127
Peripheral arterial disease	38 (26.57%)	26 (8.07%)	0.056
Atrial fibrillation	34 (23.77%)	79 (24.53%)	0.876
Atrial flutter	11 (7.69%)	35 (10.86%)	0.551
Concomitant surgery, n (%)			
MVP	13 (9.09%)	34 (10.55%)	0.411
MVR	19 (13.28%)	41 (12.73%)	0.901
AVR	11 (7.69%)	36 (11.18%)	0.658
TVP	8 (5.59%)	19 (5.90%)	0.284
TVR	0 (0%)	3 (0.93%)	0.077
CABG	2 (1.39%)	1 (0.31%)	0.056
Preoperative medication, n (%)			
Warfarin	4 (2.79%)	15 (4.65%)	0.023
Statins	7 (4.89%)	27 (8.38%)	0.047
Aspirin	6 (4.19%)	51 (15.83%)	<0.001
Clopidogrel	1 (0.69%)	9 (2.79%)	0.054
Myxomas			
Size (cm)	6.01 ± 9.2	4.21 ± 3.9	0.021
Atypical type*, n (%)	67 (46.85%)	78 (24.22%)	<0.0001
Distribution of cardiac myxomas			
LA	112 (78.32%)	250 (77.63%)	0.87
RA	10 (6.99%)	18 (5.59%)	0.55
Biatrial	11 (7.69%)	14 (4.35%)	0.14
LV	4 (2.79%)	9 (2.80%)	0.99
Echocardiographic			
LVEF (%)	57.7 ± 5.3	56.5 ± 4.2	0.656
LAD (cm)	6.1 ± 3.4	5.3 ± 1.2	0.011
E/e' ratio	16.5 ± 3.2	11.2 ± 2.5	<0.0001
CHA2DS2-VASc score	3.4 ± 1.7	1.5 ± 1.3	0.005

Table 1. Baseline characteristics of patients. Data are presented as n (%) or mean ± SD. BMI, body mass index; TIA, transient ischemic attack; MVP, mitral valvuloplasty. MVR, mitral valve replacement; AVR, aortic valve replacement; TVP, tricuspid valvuloplasty; TVR, tricuspid valve replacement. CABG, coronary artery bypass grafting; LA, left atrium; RA, right atrium; LV, left ventricle; LVEF, left ventricular ejection fraction. *With an irregular or villous surface and a soft consistency.

warfarin ($P = 0.023$) and aspirin ($P < 0.001$) than patients in the embolism group. The detailed baseline characteristics of patients were depicted in Table 1.

Distribution of cardiac myxomas. According to the result of analysis, 91% ($n = 423$) of all the cardiac myxomas were found in the atrium, with 78% ($n = 362$) in the left atrium (LA) and 6% ($n = 28$) in the right atrium (RA). Whereas, biatrial cardiac myxomas occurred in 25 (5.45%) patients, and there was 13 (2.42%) cases of myxomas with the tumor invading left ventricle (LV). Additionally, the results also showed that patients who developed embolic events had significantly bigger cardiac myxomas in size (6.01 ± 9.2 cm vs 4.21 ± 3.9 cm, $P = 0.021$), and atypical type of myxomas according to previous report (myxomas with soft consistency and very fine villous extensions, an irregular or villous surface) was also more often encountered in embolism group ($P < 0.001$).

Variable	Odds ratio	95%CI	p value
Age (y)	0.965	0.907–1.026	0.254
Gender	0.901	0.807–1.001	0.321
Smoke	1.783	0.691–2.909	0.625
Diabetes	2.476	1.732–13.817	0.111
Hypertension	0.937	0.181–10.009	0.687
BMI (kg/m ²)	6.623	1.117–9.204	<0.0001
Prior stroke or TIA	0.965	0.875–2.334	0.197
Size of myxomas	1.123	1.007–3.084	0.002
Atypical type	9.133	1.117–32.204	0.001
History of anticoagulation	1.003	0.945–2.204	0.065
LAD (cm)	1.694	1.084–2.807	0.022
E/e' ratio	8.006	0.300–12.098	0.045
Arrhythmia	2.341	1.800–3.098	0.068
CHA ₂ DS ₂ -VASc score	1.009	0.897–2.007	0.015

Table 2. Univariate regression analysis for risk factors of embolism. CI, Confidence interval; BMI, body mass index; LAD, left atrial diameter.

Variable	Odds ratio	95%CI	p value
Age (y)	0.765	0.507–1.626	0.021
BMI (kg/m ²)	0.237	0.112–0.894	0.001
E/e' ratio	1.022	0.976–1.724	0.061
Size of myxomas	0.411	0.124–1.081	0.014
Atypical type	1.453	1.004–5.984	0.001
LAD (cm)	1.014	0.651–1.147	0.031
CHA ₂ DS ₂ -VASc score	0.243	0.103–0.844	0.003

Table 3. Multivariate regression analysis for risk factors of embolism. CI, Confidence interval; BMI, body mass index; LAD, left atrial diameter.

Occurrence of stroke and embolic events. Stroke or embolism related events occurred in 143 patients during the perioperative period, with the incidence rate of 30.75%. In patients who developed stroke or embolic events, female (124 (87%)) contributed to the most contribution and with the remaining male genders, the average age of patients occurred embolism related events was 59.40 ± 10.9 . In terms of type of embolic events, stroke was recorded in 110 (77.14%) patients with most of the patients presented the signs of neurological symptoms related to acute ischemic stroke, while embolic events in the limbs were observed in 10 (2.15%) patients. We also detected 9 (1.93%) patients who developed splenic infarction because of falling of the fragment of the myxomas, which was verified by abdominal CT scan. In addition, pulmonary embolism and retinal artery occlusion was detected in 7 (1.50%) patients respectively.

CHA₂DS₂-VASc score. According to the algorithm of the score scheme, every point was assigned to each component of CHA₂DS₂-VASc score system for every patient included. Data of CHA₂DS₂-VASc scores of each patient included in our study were presented in Table 1. The exact percentage of patients in each point was as follows: 0-(n = 3, 8.57%), 1-(n = 6, 8.82%), 2-(n = 11, 19.64%), 3-(n = 15, 20.55%), 4-(n = 16, 26.23%), 5-(n = 25, 41.67%), 6-(n = 28, 44.44%), 7-(n = 17, 62.96%), 8-(n = 13, 100%), 9-(n = 9, 100%). Patients who developed stroke or embolism related event in the perioperative period had significant higher CHA₂DS₂-VASc score than those without embolism ($P = 0.005$), and the univariate and multivariate regression analysis showed that the CHA₂DS₂-VASc score were significant predictors of incidence of stroke or embolic events in patients of myxoma ($P = 0.015$; $P = 0.003$) (Tables 2 and 3).

As shown in Fig. 1, the incidence rate of stroke or embolic event was strongly associated with CHA₂DS₂-VASc score. The incidence of embolic events incrementally increased with CHA₂DS₂-VASc score raised, and higher score was predictive of higher stroke and embolism incidence rate.

In the Kaplan-Meier analysis, we stratified CHA₂DS₂-VASc scores. We categorized score 0–1 as A, score 2–3 as B, score 4–5 as C and score greater than 6 as D. As demonstrated in Fig. 2, the cumulative event rates of stroke and embolic events in Kaplan-Meier survival curves showed that patients with higher stratification of CHA₂DS₂-VASc score had a significant higher incidence rate of perioperative stroke or embolic events ($P = 0.002$).

The predictive value of CHA₂DS₂-VASc score for incidence of stroke and embolic event in patients diagnosed with cardiac myxomas was depicted in Fig. 3, the area under ROC was 0.83 (95%CI, 0.789–0.873, $p < 0.001$).

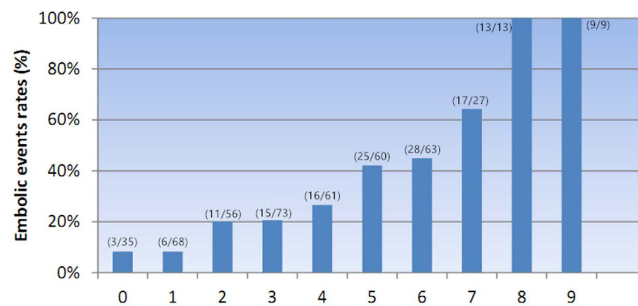


Figure 1. Embolic events rates and CHA₂DS₂-VASc scores. The embolic events rates incrementally increased as the CHA₂DS₂-VASc score increased.

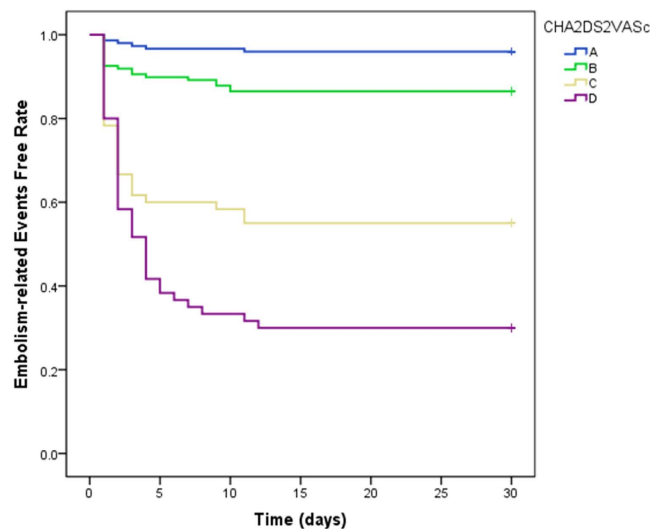


Figure 2. Embolism-related events free rate curves for patients with CHA₂DS₂-VASc score. The Kaplan-Meier survival analysis showed that patients with higher stratification of CHA₂DS₂-VASc score had a higher event rate than those who had lower stratification of CHA₂DS₂-VASc score. ($P = 0.002$). A-(0-1 point), B-(2-3 points), C-(4-5 points), D-(≥ 6 points).

Multivariable logistic analysis. The relationship of myxomas-related stroke or embolism with risk factors was assessed using the multivariate logistic regression analysis. After adjustment for history of anticoagulants use and history of atrial fibrillation, independently and significantly high risk factors contributing to stroke and embolism in patients with cardiac myxomas in our study were age (OR: 0.765; $p = 0.021$), type of myxomas (OR: 1.453; $p = 0.001$), size of myxomas (OR: 0.411; $p = 0.014$), E/e' ratio (OR: 1.022 = 0.061), LAD (OR: 1.014; $p = 0.031$) and CHA₂DS₂-VASc score (OR: 0.243; $p = 0.003$) (Table 3). The result of analysis revealed that CHA₂DS₂-VASc score was significantly higher in the embolism group, and higher CHA₂DS₂-VASc score was significant predictors of embolic events. Additionally, larger diameter of myxomas and LAD were also relatively predictors in patients with cardiac myxomas.

In-hospital mortality and long-term follow up. Among 465 patients diagnosed with cardiac myxomas included in our study underwent surgical treatment at our institution, 5 (1.07%) in-hospital deaths (3 in embolism group and 2 no-embolism group) occurred (death occurring within 30 days of operation or before discharge) because of bleeding and serious heart failure. Complications related to surgery postoperatively were recorded in 63 (13.54%) patients, and there were 26 (5.59%) patients had episodes of arrhythmias and 27 (5.80%) had major bleeding, renal dysfunction and wound infection were both observed in 5 (1.07%), 8 (1.72%) case respectively.

Information on postoperative complications related to surgery was depicted in Table 4. There was no significant difference between two groups in terms of time of mechanical ventilation ($P = 0.065$), ICU stay ($P = 0.053$), hospital stay ($P = 0.071$) and volume of drainage ($P = 0.081$), blood transfusions ($P = 0.060$), as well as other perioperative variables except that patients with embolic events had significantly higher incidence of postoperative atrial fibrillation ($P = 0.0325$).

Discussion

In this study, we present a series of cardiac myxomas involving reviewed comprehensive clinical data of these consecutively diagnosed patients in our center. Comparing with most of previous reports, we uniquely utilize the

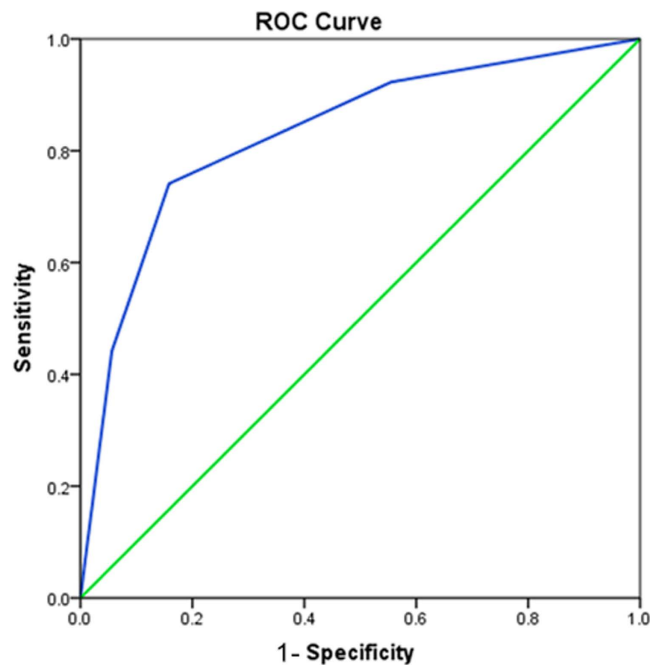


Figure 3. Predictive value of CHA₂DS₂-VASc score for incidence of stroke and embolic events under ROC, area under ROC was 0.83 (95%CI, 0.789–0.873, $p < 0.001$).

	Embolism (n = 143)	no-Embolism (n = 322)	p
Operation time (min)	131.55 ± 38.95	135.00 ± 21.64	0.198
Drainage (ml)	450.43 ± 346.40	567.66 ± 556.00	0.083
Mechanical ventilation time (d)	2.34 ± 3.68	2.12 ± 0.62	0.065
Transfusion (ml)	321.22 ± 657.29	292.66 ± 567.18	0.060
ICU stay (d)	1.63 ± 0.88	1.48 ± 1.00	0.053
Total hospital stay (d)	12.39 ± 4.67	11.65 ± 3.69	0.071
Wound infection, n (%)	3 (2.09)	5 (1.55)	0.625
Renal failure, n (%)	1 (0.21)	4 (1.24)	0.067
POAF	18 (12.58)	8 (2.48)	0.032
Major bleeding	10 (6.99)	17 (5.27)	0.052
In-hospital deaths, n (%)	3 (2.09)	2 (0.62)	0.059

Table 4. Perioperative data of patients. ICU, Intensive Care Unit, POAF, postoperative atrial fibrillation.

CHA₂DS₂-VASc score system, which used to assess the stroke risk of patients with AF, for predicting embolism related events in patients diagnosed of cardiac myxomas who were also at high risk of occurring such perioperative events.

In our data analysis, the patients included with cardiac myxomas contributed to 3.21% of all the continuous patients underwent cardiac surgeries in our center, which was similar to previous studies^{4,19,28}. And a percentage of 30.75% of stroke or embolic events contributed to the overall included patients, a little slightly higher than the incidence reported in other studies which ranged from 20–25%²⁹. We uniquely utilize the CHA₂DS₂-VASc score scheme, which used to be an easy-to-remember tool to identify patients with AF who are at risk of occurring stroke, to assess the risk of stroke and embolic event in patients diagnosed of cardiac myxomas. The result from our study showed that CHA₂DS₂-VASc score scheme was also a useful predictive system for predicting stroke and embolic events in patients with cardiac myxomas, and patients with CHA₂DS₂-VASc score at higher stratification had a significant higher occurrence of embolization related events than those who had lower stratification. We also calculated the individual occurrence of embolism event in each patient based on different points from naught to the highest whose result are shown in Fig. 1. Furthermore, in our multivariable regression analysis, the CHA₂DS₂-VASc score was valuable predictors for embolism in patients with cardiac myxomas.

With the incidence rate of 0.5 per million each year, cardiac myxomas can occur at any age stage of patients, while usually females with the age 40~60 are commonly encountered, and mostly located in the LA and RA, which are rarely seen in left and right ventricle^{1,3,28,30}. Intracardiac obstruction and peripheral embolism are the two main constitutional symptoms in most patients diagnosed with cardiac myxomas. In early reports, a

frequency of 30~40% of embolization have been reported^{5,6,11,28,31,32}. Recent reports of the sign of stroke and embolism associated with cardiac myxomas showed a downward trend with the frequency of 20~25%⁶, and in this retrospective study we reported the incidence of 30.75%.

The CHA₂DS₂-VASC score scheme is accurate and is both easily and widely used in prediction of severity and outcome of strokes, providing decision-making management in patients with AF^{17,18}. As demonstrated in previous studies, an incremental deterioration of left ventricle (LV) systolic and diastolic dysfunction may cause left atrium (LA) enlargement, which is strongly associated with the occurrence of postoperative atrial fibrillation (POAF) which is associated with stroke or embolism^{16,21}, and whose underlying mechanism were similar to patients with myxomas. Congestive heart failure, one of the most important components in CHA₂DS₂-VASC score system, is morbid condition that shares common risk factors and frequently coexisted with cardiac myxomas, which ranged 46~47% in this study. Furthermore, the unstable hemodynamic status of patients with myxomas also contribute to deteriorated embolism events occurrence, which increased morbidity and mortality significantly²⁰. Hypertension, diabetes, and vascular disease, another several components of CHA₂DS₂-VASC score system, also can promote the incidence of stroke and embolic event in patients with myxomas.

Although originally CHA₂DS₂-VASC score was not designed to identify patients with cardiac myxomas who were also at risk of occurring stroke and embolism, which was similar to patients of AF, and the underlying mechanism and potential under which embolic event occurred were either different between two groups of patients. The results from our study showed that CHA₂DS₂-VASC score scheme was also an effective predictive tool for identifying myxomas patients at risk of embolism. Additionally, patients with CHA₂DS₂-VASC score at higher stratification had a significant higher occurrence of embolization related events than those who had lower stratification. This relationship may be helpful to discriminate patients who were predisposed to high stroke and embolism occurrence, and which may also provide us decision-making strategies of preoperative prophylactic medication. We recommended that high risk patients diagnosed of cardiac myxomas with a CHA₂DS₂-VASC score greater than 4 may be strongly associated with the embolic event in the perioperative period, and preoperative prophylactic management may be needed in these patients to minimize the risk of embolism. In patients with higher CHA₂DS₂-VASC score, we recommended use of anticoagulants including low molecular weight heparin (LMWH), warfarin or new oral anticoagulant (NOAC) to minimize the risk of thrombosis. Additionally, owing to different mechanism from embolism caused by cardiovascular disease, unstable and atypical type of myxomas were also independent risk factors for embolism, so early accurate diagnose and typing of myxomas and surgical removal were critical in preventing embolism events occurred. In surgical techniques of removing myxomas, embolic excision of the tumor without residue including pedicles was essential, repeated syringe with saline inside the atrial and ventricular chambers on arrested heart was also critical.

In summary, cardiac myxomas comprise a small percentage of cardiac diseases which also had high risk of stroke and embolism. Using CHA₂DS₂-VASC score to identifying patients at risk of stroke and embolism was an effective management in the perioperative period. Once identified as patients at high risk with high CHA₂DS₂-VASC score, elaborative prophylactic management was necessary to decrease perioperative morbidity and mortality.

The main limitation of our study is its retrospective design. Also, we evaluated the risk factors consisting of CHA₂DS₂-VASC score alone without analysis with other risk factors which may contribute to bias in our study. And the follow-up period of patients were not investigated in this study. Although the meaningful findings in our study, CHA₂DS₂-VASC score is useful to predict embolic events in most populations including patients with AF, and this finding may not entail highly specific and sensitive predictions in patients with cardiac myxomas. Nevertheless, our study provided useful information related to the risk factors of stroke and embolism in patients with cardiac myxomas. A larger clinical trial is necessary to assess the underlying usefulness of CHA₂DS₂-VASC scores in predicting risk of stroke to assure whose clinical utility.

References

1. Agarwal, V., Agarwal, S. K., Srivastava, A. K. & Kapoor, S. Primary cardiac tumors: surgical experience and follow-up. *Indian heart journal* **55**, 632–636 (2003).
2. Barnes, H., Conaglen, P., Russell, P. & Newcomb, A. Clinicopathological and surgical experience with primary cardiac tumors. *Asian cardiovascular & thoracic annals*, doi: 10.1177/0218492314528922 (2014).
3. Barreiro, M. *et al.* Primary cardiac tumors: 32 years of experience from a Spanish tertiary surgical center. *Cardiovascular pathology: the official journal of the Society for Cardiovascular Pathology* **22**, 424–427, doi: 10.1016/j.carpath.2013.04.006 (2013).
4. Blondeau, P. Primary cardiac tumors—French studies of 533 cases. *The Thoracic and cardiovascular surgeon* **38** Suppl 2, 192–195, doi: 10.1055/s-2007-1014065 (1990).
5. Dell'amore, A., Albertini, A. & Lamarra, M. Twenty years experience in oncologic surgery for primary cardiac tumors. *Il Giornale di chirurgia* **34**, 106–111 (2013).
6. Padalino, M. A. *et al.* Surgery for primary cardiac tumors in children: early and late results in a multicenter European Congenital Heart Surgeons Association study. *Circulation* **126**, 22–30, doi: 10.1161/CIRCULATIONAHA.111.037226 (2012).
7. Hou, C. H. *et al.* [Management of refractory ventricular tachycardia in patients with non-myxomas primary cardiac tumors]. *Zhonghua xin xue guan bing za zhi* **40**, 502–504 (2012).
8. Sirin, G., Ozker, E., Fotbolcu, H., Ozden, K. & Demirsoy, E. Myxoma developing after open heart surgery: is radiofrequency ablation responsible for the formation of the tumor? *Acta chirurgica Belgica* **112**, 154–156 (2012).
9. Sveinsson, O., Herrman, L. & Ivert, T. Cardiac myxomas may debut as TIA or stroke. Echocardiography provides tumor diagnosis. *Lakartidningen* **110**, 1285–1287 (2013).
10. Cresti, A. *et al.* Incidence rate of primary cardiac tumors: a 14-year population study. *Journal of cardiovascular medicine*, doi: 10.2459/JCM.0000000000000059 (2014).
11. Strecker, T., Rosch, J., Weyand, M. & Agaimy, A. Primary and metastatic cardiac tumors: imaging characteristics, surgical treatment, and histopathological spectrum: a 10-year-experience at a German heart center. *Cardiovascular pathology: the official journal of the Society for Cardiovascular Pathology* **21**, 436–443, doi: 10.1016/j.carpath.2011.12.004 (2012).

12. Mihali, E., Muresan, M., Rusu, M. L. & Fodor, D. Cardiac metastasis and tumor embolism in a patient with adenocarcinoma of the colon presenting with paraneoplastic polymyositis. *Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie* **54**, 897–900 (2013).
13. Takano, T. & Amano, J. Cardiac tumor, constrictive pericarditis and pulmonary thromboembolism. *Kyobu geka. The Japanese journal of thoracic surgery* **64**, 658–665 (2011).
14. American College of Cardiology, F. *et al.* Management of patients with atrial fibrillation (compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS recommendations): a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *Circulation* **127**, 1916–1926, doi: 10.1161/CIR.0b013e318290826d (2013).
15. Camm, A. J. *et al.* 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. *European heart journal* **33**, 2719–2747, doi: 10.1093/eurheartj/ehs253 (2012).
16. Curtis, A. B. Update on the clinical management of atrial fibrillation: guidelines and beyond. *Postgraduate medicine* **123**, 7–20, doi: 10.3810/pgm.2011.11.2491 (2011).
17. Andrikopoulos, G. Comments on the 2012 update of the ESC guidelines for the management of atrial fibrillation: what is new and what is important for the clinician? *Hellenic J Cardiol* **53**, 407–411 (2012).
18. Sivakumar, K., Singhi, A., Mohanraj, A. & Ezhilan, J. Tumor embolism from a right atrial myxoma leads to acute right heart failure after surgery and atrial septal patch dehiscence. *Journal of the American College of Cardiology* **63**, 2579, doi: 10.1016/j.jacc.2014.02.608 (2014).
19. Nield, L. E. *et al.* Clinical review of obstructive primary cardiac tumors in childhood. *Congenital heart disease* **9**, 244–251, doi: 10.1111/chd.12134 (2014).
20. Hung, C. Y., Lin, C. H., Loh el, W., Ting, C. T. & Wu, T. J. CHADS(2) score, statin therapy, and risks of atrial fibrillation. *Am J Med* **126**, 133–140, doi: 10.1016/j.amjmed.2012.06.027 (2013).
21. Meiltz, A., Zimmermann, M., Urban, P., Bloch, A. & Association of Cardiologists of the Canton of, G. Atrial fibrillation management by practice cardiologists: a prospective survey on the adherence to guidelines in the real world. *Europace* **10**, 674–680, doi: 10.1093/europace/eun086 (2008).
22. Dursun, M. *et al.* Cardiac MRI findings of intramyocardial myxoma in a child. *European Journal of Radiology Extra* **66**, e39–e41, doi: http://dx.doi.org/10.1016/j.ejrex.2008.01.019 (2008).
23. Mariano, A. *et al.* Primary cardiac tumors in children: a 16-year experience. *Revista portuguesa de cardiologia: orgao oficial da Sociedade Portuguesa de Cardiologia=Portuguese journal of cardiology: an official journal of the Portuguese Society of Cardiology* **28**, 279–288 (2009).
24. Fuchs, J., Leszczyszyn, D. & Mathew, D. Cardiac Myxoma Causing Acute Ischemic Stroke in a Pediatric Patient and a Review of Literature. *Pediatric Neurology* **50**, 525–529, doi: http://dx.doi.org/10.1016/j.pediatrneurol.2014.01.011 (2014).
25. Marboeuf, P. *et al.* Echocardiographic, cardiac magnetic resonance imaging, surgical and pathological findings of an unusual right atrial tumor: a giant papillary fibroelastoma. *The Annals of thoracic surgery* **93**, e133, doi: 10.1016/j.athoracsur.2011.12.057 (2012).
26. Lorenzo-Seva, U., Ferrando, P. J. & Chico, E. Two SPSS programs for interpreting multiple regression results. *Behavior research methods* **42**, 29–35, doi: 10.3758/BRM.42.1.29 (2010).
27. Pardo, A., Ruiz, M. A. & San Martin, R. How to fit and interpret multilevel models using SPSS. *Psicothema* **19**, 308–321 (2007).
28. Bordalo, Á. D. B. *et al.* New clinical aspects of cardiac myxomas: A clinical and pathological reappraisal. *Revista Portuguesa de Cardiologia (English Edition)* **31**, 567–575, doi: http://dx.doi.org/10.1016/j.repce.2012.07.003 (2012).
29. Yu, L. *et al.* Primary malignant cardiac tumors. *Journal of cancer research and clinical oncology* **140**, 1047–1055, doi: 10.1007/s00432-014-1651-1 (2014).
30. Amano, J. *et al.* Cardiac myxoma: its origin and tumor characteristics. *Annals of thoracic and cardiovascular surgery: official journal of the Association of Thoracic and Cardiovascular Surgeons of Asia* **9**, 215–221 (2003).
31. Toufan, M., Jodati, A., Safaei, N., Kazemi, B. & Pourafkari, L. Myxomas in all cardiac chambers. *Echocardiography* **29**, E270–272, doi: 10.1111/j.1540-8175.2012.01803.x (2012).
32. Lin, Y. *et al.* Treating cardiac myxomas: a 16-year Chinese single-center study. *Journal of cardiovascular medicine*, doi: 10.2459/JCM.000000000000114 (2014).

Acknowledgements

This work was supported by the National Nature Science Foundation of China (NO. 81300102, NO. 81170232 and NO. 81270419) and Shanghai Shenkang Emerging Advanced Technology Project (SHDC12014107). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Author Contributions

(I) Conception and design: Liang Yin, Zhinong Wang; (II) Administrative support: Jing Wang; (III) Provision of study materials or patients: Wei Li, Jing Wang, Yufeng Zhang; (IV) Collection and assembly of data: Xinyu Ling; (V) Data analysis and interpretation: Wei Li, Qian Xue; (VI) Manuscript writing: All authors.

Additional Information

Competing financial interests: The authors declare no competing financial interests.

How to cite this article: Yin, L. *et al.* Usefulness of CHA₂DS₂-VASc Scoring Systems for Predicting Risk of Perioperative Embolism in Patients of Cardiac Myxomas Underwent Surgical Treatment. *Sci. Rep.* **6**, 39323; doi: 10.1038/srep39323 (2016).

Publisher's note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



This work is licensed under a Creative Commons Attribution 4.0 International License. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>

© The Author(s) 2016