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ORIGINAL ARTICLE

Occurrence and predictive factors of restenosis in coronary heart disease patients underwent sirolimus-eluting stent implantation

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Abstract

Background This study aimed to investigate the occurrence and predictive factors of restenosis in coronary heart disease (CHD) patients underwent percutaneous coronary intervention (PCI) with sirolimus-eluting stent (SES).

Methods Demographic data, clinical features, and laboratory tests of 398 CHD patients underwent PCI with SES were retrospectively reviewed. Coronary angiography was performed to evaluate coronary stenosis before PCI and in-stent restenosis at 1-year follow-up.

Results There were 37 (9.3%) patients suffered restenosis, but 361 (90.7%) patients did not develop restenosis at 1-year follow-up. Demographic characteristic (age), cardiovascular risk factors (hypertension and hyperuricemia), biochemical indexes (fasting blood-glucose, total cholesterol, low density lipoprotein cholesterol (LDL-C) and high-sensitivity C-reactive protein (HsCRP)), cardiac function index (cardiac troponin I), lesion features (multivessel artery lesions, target lesion at left circumflex artery (LCX), two target lesions and length of target lesion), and operation procedure (length of stent) were correlated with higher restenosis risk. Moreover, age, hypertension, diabetes mellitus, LDL-C, HsCRP, and target lesion at LCX were independent predictive factors for raised restenosis risk. Based on these independent predictive factors, we established a restenosis risk prediction model, and receiver-operating characteristic curves displayed that this model exhibited an excellent predictive value for higher restenosis risk (areas under the curve 0.953 (95% CI 0.926–0.981)).

Conclusion Our findings provide a new insight into the prediction for restenosis in CHD patients underwent PCI with SES.

Keywords Coronary heart disease · Percutaneous coronary intervention · Predictive factor · Restenosis · Sirolimus-eluting stent

Introduction

Coronary heart disease (CHD), as the most common type of ischemic cardiovascular disorders, is related to serious syndromes such as stable angina and asymptomatic or silent ischemia [1, 2]. According to the 2016 World Health Organization global disease assessment report, CHD has become the leading cause of death in the past 10 years, and it is estimated that the CHD related death will reach 25 million worldwide by 2020 [3–5]. From pathological perspective, it is characterized by coronary atherosclerosis and results from the accumulation of fatty deposits on the arterial vessel walls, which eventually gives rise to stenosis of the arteries [6]. Regarding the treatments to remove stenosis, vascular stent represents the gold standard treatment in CHD during percutaneous coronary intervention (PCI) for most lesions, and drug-eluting stent (DES) is currently the primary choice among the vascular stents [7–9]. As to the drugs applied in DES, sirolimus-eluting stent (SES), which belongs to the first-generation DES, is more frequently applied in clinical practices compared with other DESs (such as paclitaxel-eluting stent, everolimus-eluting stent, and zotarolimus-eluting stent) since it is the first commercially available DES in China; moreover, it has shown superiority in terms of reducing the need for target vessel revascularization compared with the traditional bare-metal stents [10, 11]. Although SES is known as an efficacy and well-

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tolerated PCI strategy, in-stent restenosis still occurs in around 5–15% cases, which is a major problem in the clinical application of PCI with SES [12, 13]. Hence, it is urgently needed to explore factors that predict restenosis risk in CHD patients underwent PCI with SES implantation, which may help establish individual treatment and further improve prognosis in these patients.

According to a few studies, the occurrence of restenosis may be more frequently in patients with multiple conditions such as chronic disease histories (diabetes mellitus, hypertension and congestive heart failure), complex lesions (bypass grafts, bifurcations and longer lesion length), and abnormal biochemical indexes (low density lipoprotein (LDL), white cell count and serum uric acid), and some of these conditions have been identified to be predictive factors for restenosis risk in CHD patients underwent PCI with DES [14–18]. Whereas, most of the previous studies are conducted with small sample size, which may result in weak statistical power to make the data not convincing enough; moreover, comprehensive analysis of the predictive factors for restenosis risk in CHD patients underwent PCI with SES is limited; thus, further study with large sample size to comprehensively analyze the potentially predictive factors for restenosis risk is necessary. In this study, we enrolled a large population to investigate the occurrence, and predictive factors of restenosis in CHD patients underwent PCI with SES.

Methods

Patients

We retrospectively reviewed 398 CHD patients who underwent PCI with SES between January 2014 and June 2018. The screening criteria included the following: (i) diagnosed as CHD; (ii) age ≥ 18 years; (iii) underwent PCI with sirolimus-eluting stents; (iv) 1-year restenosis information were complete and available; (v) medical records and follow-up records were complete (at least included baseline characteristics, operation procedures and post-procedure managements); (vi) no history of PCI, coronary artery bypass grafting or other cardiovascular major surgery; (vii) no history of malignancies. This study was approved by the Institutional Review Board of The Second Hospital of Hebei Medical University, and the written informed consents were provided by patients or their guardians.

Data collection

The clinical data of patients were collected from medical records, which included (1) demographic characteristics (such as age, gender, and body mass index (BMI)); (2) cardiovascular risk factors (such as current smoke status, hypertension, diabetes mellitus, hypercholesteremia, hyperuricemia, and family history of coronary artery disease (CAD)); (3) blood pressure index (mean arterial pressure (MAP)); (4) biochemical index (such as fasting blood-glucose (FBG), glycated hemoglobin, triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), high-sensitivity C-reactive protein (Hs-CRP), erythrocyte sedimentation rate (ESR), white blood cell (WBC), neutrophil, serum creatinine (Scr), and serum uric acid (SUA)); (6) cardiac function index (such as left ventricular ejection fraction (LVEF), cardiac troponin I (cTnl), and N-terminal probrain natriuretic peptide (NT-proBNP)); (6) angiographic information (such as multivessel artery lesions, location of target lesion, two target lesions, stenosis degree of target lesion, and length of target lesion); (7) operation procedures (such as length of stent, diameter of stent, time of stent dilation, and balloon dilation pre-stent); (8) medication used after surgery (such as aspirin, nitrates, statins, β receptor blockers, angiotensin converting enzymes inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and calcium channel blockers).

In-stent restenosis assessment

For all patients, the PCI procedure and the implantation of sirolimus-eluting stent (Lepu (Beijing) Medical Devices Co., Ltd. Beijing, China) were performed according to PCI guideline [19]. The information of coronary angiography follow-up was collected from the follow-up records. Before PCI, all patients received coronary angiography to assess the clinical status. Immediately post-PCI, coronary angiography was conducted for the patients to evaluate the degree of stenosis after PCI. After discharge, if the patients with clinical indication, coronary angiography was performed when clinical visit. And for the patients without clinical indication, coronary angiography was carried out at 1-year follow-up. Based on the coronary angiograms, in-stent restenosis was assessed by the quantitative coronary angiography (QCA) analysis as previous studies described [20, 21], and the percentage diameter stenosis (PDS) was automatically calculated by computer-based system cardiovascular angiographic analysis system (CAAS) II (Pie Medical Imaging, Maastricht, the Netherlands). The in-stent restenosis was defined as the PDS of stent-implanted segment at 1-year follow-up exceeded 50% compared with lumen assessed immediately after PCI [16]. According to the 1-year restenosis, patients were further classified as restenosis group and non-restenosis group.

Statistical analysis

The normality of continuous variables was analyzed by Kolmogorov-Smirnov test. The normally distributed continuous variables were displayed as mean ± standard

deviation (SD), and the non-normal distributed continuous variables were presented as median and interquartile range (IQR). The categorical variables were expressed as count (percentage). Comparison of continuous variables between two groups was determined by Student's t test or Wilcoxon rank sum test, and comparison of categorical variables between two groups was determined by chi-square test, Yates' corrected chi-square test, or Fisher's exact test. Factors predicting restenosis were analyzed by univariate logistic regression, and the variables with P value < 0.1 were further screened by forward stepwise multivariate logistic regression. Based on the independent predicting factors screened from multivariate logistic regression, the restenosis risk prediction model was generated as follows: $P = [\exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]/[1 + \exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]$, $-2\ln$ (likelihood ratio) = 107.321. The predicting performance of restenosis risk prediction model and independent predicting factors were analyzed using receiver operating characteristic (ROC) curves and the areas under the curve (AUC) with 95% confidence intervals (CI). SPSS 22.0 statistical software (SPSS Inc., Chicago, USA) was used for all statistical analyses, and GraphPad Prism 7.00 software (GraphPad Software Inc., San Diego, USA) was used to plot figures. P value < 0.05 was considered significant.

Results

Clinical characteristics of CHD patients

A total of 398 CHD patients underwent PCI with SES (including 71 (17.8%) females and 327 (82.2%) males) were enrolled in this study, with mean age of 64.0 ± 9.3 years and mean BMI value of 24.5 ± 3.7 kg/m^2 (Table 1). Other information of clinical characteristics including cardiovascular risk factors, blood pressure indexes, biochemical indexes, cardiac function indexes, angiographic data, operation procedures, and medications used after surgery was exhibited in Table 1.

Incidence of 1-year restenosis

Among total patients, there were 37 (9.3%) patients suffered restenosis, and 361 (90.7%) patients did not develop restenosis at 1-year follow-up (Fig. 1), and patients were further classified as restenosis group as well as non-restenosis group respectively.

Table 1 Clinical characteristics

Items	CHD patients (N = 398)
Demographic characteristics	
Age (years)	64.0 ± 9.3
Gender	
Female	71 (17.8)
Male	327 (82.2)
BMI (kg/m^2)	24.5 ± 3.7
Cardiovascular risk factors	
Current smoke	112 (28.1)
Hypertension	281 (70.6)
Diabetes mellitus	103 (25.9)
Hypercholesteremia	231 (58.0)
Hyperuricemia	150 (37.7)
Family history of CAD	81 (20.4)
Blood pressure index	
MAP (mmHg)	104.7 ± 17.8
Biochemical index	
FBG (mmol/L)	5.9 (5.2–6.6)
Glycated hemoglobin (%)	6.0 (5.0–7.3)
TG (mmol/L)	1.8 (1.0–2.5)
TC (mmol/L)	4.6 ± 1.0
LDL-C (mmol/L)	2.8 ± 0.6
HDL-C (mmol/L)	1.0 ± 0.3
HsCRP (mg/L)	4.6 (2.0–8.9)
ESR (mm/L)	12.1 (6.6–20.6)
WBC (× 10^9/L)	6.1 (4.9–7.1)
Neutrophil (× 10^9/L)	3.5 ± 0.9
Scr (μmol/L)	81.2 (70.1–91.8)
SUA (μmol/L)	333.2 (283.9–395.4)
Cardiac function index	
LVEF (%)	65.0 (60.0–70.0)
cTnI (pg/mL)	29.2 (17.4–46.4)
NT-proBNP (pg/mL)	76.1 (42.1–124.5)
Angiographic information (lesion features)	
Multivessel artery lesions	277 (69.6)
Target lesion at LAD	222 (55.8)
Target lesion at LCX	145 (36.4)
Target lesion at RCA	155 (38.9)
Patients with two target lesions	124 (31.2)
Stenosis degree of target lesion (%)	85.0 (82.0–89.0)
Length of target lesion (mm)	35.0 (27.0–40.0)
Operation procedures	
Length of stent (mm)	38.0 (31.0–44.0)
Diameter of stent (mm)	3.3 (3.0–3.4)
Time of stent dilation (s)	15.0 (13.0–18.0)
Balloon dilation pre stent	125 (31.4)
Medication used after surgery	
Aspirin	398 (100.0)
Nitrates	398 (100.0)
Statins	394 (99.0)

Table 1 (continued)

Items	CHD patients ($N = 398$)
β receptor blockers	362 (91.0)
ACEIs/ARBs	269 (67.6)
Calcium channel blockers	122 (30.7)

Kolmogorov-Smirnov test was used to determine the normality of continuous variables. The normally distributed continuous variables were displayed as mean ± standard deviation (SD), and the non-normal distributed continuous variables were presented as median and interquartile range (IQR). The categorical variables were expressed as count (percentage)

CHD, coronary heart disease; *SD*, standard deviation; *BMI*, body mass index; *CAD*, coronary artery disease; *MAP*, mean arterial pressure; *FBG*, fasting blood-glucose; *IQR*, interquartile range; *TG*, triglyceride; *TC*, total cholesterol; *LDL-C*, low density lipoprotein cholesterol; *HDL-C*, high density lipoprotein cholesterol; *HsCRP*, high-sensitivity C-reactive protein; *ESR*, erythrocyte sedimentation rate; *WBC*, white blood cell; *Scr*, serum creatinine; *SUA*, serum uric acid; *LVEF*, left ventricular ejection fraction; *cTnI*, cardiac troponin I; *NT-proBNP*, N-terminal-proB-type natriuretic peptide; *LAD*, left anterior descending branch; *LCX*, left circumflex artery; *RCA*, right coronary artery; *ACEIs*, angiotensin converting enzymes inhibitors; *ARBs*, angiotensin receptor blockers

Comparison of clinical characteristics between restenosis group and non-restenosis group

The age in restenosis group (68.7 ± 10.3 years) was higher compared with non-restenosis group (63.5 ± 9.0 years) ($P = 0.001$) (Table 2). The proportions of patients with hypertension ($P = 0.009$) and hyperuricemia ($P = 0.031$) were both increased in restenosis group compared with non-restenosis group. For biochemical indexes, elevated levels of FBG ($P = 0.023$), TC ($P = 0.016$), LDL-C ($P < 0.001$), and HsCRP ($P < 0.001$) were observed in restenosis group compared with non-restenosis group. As to cardiac function indexes, restenosis group showed higher cTnI level compared with non-restenosis group ($P = 0.039$). For angiographic information (lesion features), multivessel artery lesions ($P = 0.019$), target lesion at LCX ($P = 0.048$), two target lesions ($P = 0.016$), and length of target lesion ($P = 0.005$) were increased in restenosis group compared with non-restenosis group. Regarding operation procedures, restenosis group had longer length of stent compared with non-restenosis group ($P = 0.007$). Besides, no difference of other characteristics was found between restenosis group and non-restenosis group (Table 2).

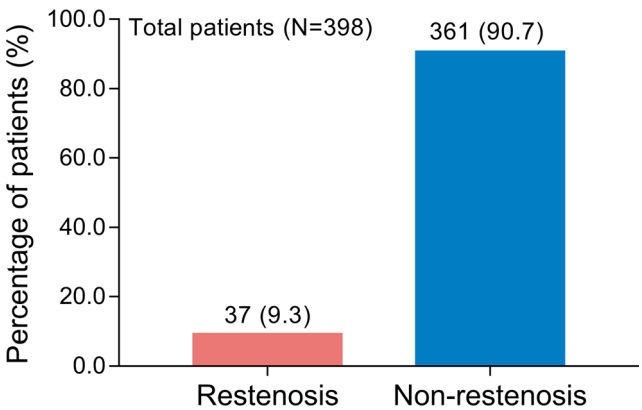

Fig. 1 Restenosis occurrence at 1-year follow-up. Percentages of patients with restenosis and non-restenosis were 9.3% and 90.7% respectively

Analysis of factors affecting restenosis risk

Univariate logistic regression analysis showed that higher age ($P = 0.001$, OR = 1.068), hypertension ($P = 0.014$, OR = 3.759), hyperuricemia ($P = 0.034$, OR = 2.090), higher TC ($P = 0.018$, OR = 1.523), higher LDL-C ($P < 0.001$, OR = 2.737), higher HsCRP ($P < 0.001$, OR = 1.268), higher SUA ($P = 0.035$, OR = 1.005), multivessel artery lesions ($P = 0.025$, OR = 3.030), patients with two target lesions ($P = 0.018$, OR = 2.279), larger length of target lesion ($P = 0.005$, OR = 1.059), and larger length of stent ($P = 0.007$, OR = 1.055) were associated with elevated restenosis risk (Table 3). Moreover, multivariate logistic regression analysis displayed that higher age ($P = 0.033$, OR = 1.064), hypertension ($P = 0.001$, OR = 22.397), diabetes mellitus ($P < 0.001$, OR = 25.534), higher LDL-C ($P < 0.001$, OR = 20.911), higher HsCRP ($P < 0.001$, OR = 1.604), and target lesion at LCX ($P = 0.027$, OR = 3.348) independently predicted raised restenosis risk (Table 4).

Predictive values of candidate factors for restenosis risk

Since several factors were identified as independent predictive factors for restenosis risk by multivariate logistic regression, we performed ROC curve analysis to further evaluate the predictive values of these independent predictive factors. ROC curves showed that age (AUC 0.654 (95% CI 0.548–0.761)), hypertension (AUC 0.602 (95% CI 0.517–0.688)), LDL-C (AUC 0.676 (95% CI 0.591–0.761)), and HsCRP (AUC 0.876 (95% CI 0.830–0.921)) could predict elevated restenosis risk, while diabetes mellitus (AUC 0.566 (95% CI 0.465–0.667)) and target lesion at LCX (AUC 0.582 (95% CI 0.484–0.681)) presented with poor values in predicting restenosis risk (Fig. 2). Based on these independent predictive factors, we established a restenosis risk prediction model ($P = [\exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]/\ [1 + \exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]$, −2ln (likelihood ratio) = 107.321). Compared with the predictive value of separately independent factor for restenosis risk, the restenosis

Table 2 Comparison of clinical characteristics between restenosis and non-restenosis patients

Items	Non-restenosis patients ($n = 361$)	Restenosis patients ($n = 37$)	P value
Demographic characteristics			
Age (years)	63.5 ± 9.0	68.7 ± 10.3	*0.001*
Gender, No. (%)			0.787
Female	65 (18.0)	6 (16.2)	
Male	296 (80.2)	31 (83.8)	
BMI (kg/m^2)	24.5 ± 3.7	24.9 ± 3.3	0.513
Cardiovascular risk factors			
Current smoke	98 (27.1)	14 (37.8)	0.168
Hypertension	248 (68.7)	33 (89.2)	*0.009*
Diabetes mellitus	89 (24.7)	14 (37.8)	0.081
Hypercholesteremia	212 (58.7)	19 (51.4)	0.387
Hyperuricemia	130 (36.0)	20 (54.1)	*0.031*
Family history of CAD	72 (19.9)	9 (24.3)	0.529
Blood pressure index			
MAP (mmHg)	104.8 ± 17.9	103.9 ± 17.9	0.763
Biochemical index			
FBG (mmol/L)	5.8 (5.1–6.6)	6.1 (5.8–6.6)	*0.023*
Glycated hemoglobin (%)	6.0 (4.9–7.2)	6.4 (5.0–7.6)	0.512
TG (mmol/L)	1.8 (1.0–2.5)	1.9 (1.0–2.6)	0.756
TC (mmol/L)	4.6 ± 1.0	5.0 ± 0.9	*0.016*
LDL-C (mmol/L)	2.7 ± 0.6	3.1 ± 0.6	*< 0.001*
HDL-C (mmol/L)	1.0 ± 0.2	1.0 ± 0.3	0.476
HsCRP (mg/L)	4.2 (1.9–7.9)	10.8 (8.4–15.3)	*< 0.001*
ESR (mm/L)	12.1 (6.4–20.6)	13.3 (7.9–22.7)	0.256
WBC (× 10^9/L)	6.1 (4.9–7.1)	6.2 (5.1–7.3)	0.398
Neutrophil (× 10^9/L)	3.5 (2.8–4.1)	3.6 (2.9–4.1)	0.245
Scr (μmol/L)	80.8 (70.0–91.3)	81.9 (73.6–93.8)	0.409
SUA (μmol/L)	332.9 (280.5–392.1)	350.2 (292.0–446.6)	0.084
Cardiac function index			
LVEF (%)	65.0 (60.0–70.0)	65.0 (58.0–70.0)	0.309
cTnI (pg/mL)	29.1 (16.9–45.8)	35.8 (22.8–52.1)	*0.039*
NT-proBNP (pg/mL)	75.0 (41.8–123.7)	81.1 (43.1–146.6)	0.267
Angiographic information (lesion features)			
Multivessel artery lesions	245 (67.9)	32 (86.5)	*0.019*
Target lesion at LAD	199 (55.1)	23 (62.2)	0.412
Target lesion at LCX	126 (34.9)	19 (51.4)	*0.048*
Target lesion at RCA	142 (39.3)	13 (35.1)	0.618
Patients with two target lesions	106 (29.4)	18 (48.6)	*0.016*
Stenosis degree of target lesion (%)	85.0 (82.0–89.0)	87.0 (83.0–89.5)	0.255
Length of target lesion (mm)	34.0 (27.0–40.0)	38.0 (30.5–46.0)	*0.005*
Operation procedures			
Length of stent (mm)	38.0 (31.0–43.0)	41.0 (34.5–49.0)	*0.007*
Diameter of stent (mm)	3.3 (3.0–3.4)	3.1 (3.0–3.3)	0.526
Time of stent dilation (s)	15.0 (13.0–18.0)	14.0 (12.0–18.0)	0.112
Balloon dilation pre-stent	113 (31.3)	12 (32.4)	0.888
Medication used after surgery			
Aspirin	361 (100.0)	37 (100.0)	–
Nitrates	361 (100.0)	37 (100.0)	–
Statins	358 (99.2)	36 (97.3)	0.324
β receptor blockers	328 (90.9)	34 (91.9)	1.000
ACEIs/ARBs	245 (67.9)	24 (64.9)	0.710
Calcium channel blockers	111 (30.7)	11 (29.7)	0.898

Kolmogorov-Smirnov test was used to determine the normality of continuous variables. The normally distributed continuous variables were displayed as mean ± standard deviation (SD), and the non-normal distributed continuous variables were presented as median and interquartile range (IQR). The categorical variables were expressed as count (percentage). Data set in italics were considered significant (P value < 0.05). Comparison was determined by Student's t test, chi-square test, Yates' corrected chi-square test, Fisher's exact test, or Wilcoxon rank sum test

SD, standard deviation; *BMI*, body mass index; *CAD*, coronary artery disease; *MAP*, mean arterial pressure; *FBG*, fasting blood-glucose; *IQR*, interquartile range; *TG*, triglyceride; *TC*, total cholesterol; *LDL-C*, low density lipoprotein cholesterol; *HDL-C*, high density lipoprotein cholesterol; *HsCRP*, high-sensitivity C-reactive protein; *ESR*, erythrocyte sedimentation rate; *WBC*, white blood cell; *Scr*, serum creatinine; *SUA*, serum uric acid; *LVEF*, left ventricular ejection fraction; *cTnI*, cardiac troponin I; *NT-proBNP*, N-terminal-proB-type natriuretic peptide; *LAD*, left anterior descending branch; *LCX*, left circumflex artery; *RCA*, right coronary artery; *ACEIs*, angiotensin converting enzymes inhibitors; *ARBs*, angiotensin receptor blockers

Table 3 Analysis of factors predicting restenosis risk

Items	*P* value	OR	95% CI	
			Lower	Higher
Higher age	*0.001*	1.068	1.026	1.112
Male	0.787	1.135	0.455	2.831
Higher BMI	0.512	1.031	0.942	1.128
Current smoke	0.172	1.634	0.808	3.302
Hypertension	*0.014*	3.759	1.301	10.864
Diabetes mellitus	0.085	1.860	0.918	3.769
Hypercholesteremia	0.388	0.742	0.377	1.461
Hyperuricemia	*0.034*	2.090	1.058	4.132
Family history of CAD	0.529	1.290	0.583	2.855
Higher MAP	0.762	0.997	0.978	1.016
Higher FBG	0.057	1.307	0.992	1.722
Higher glycated hemoglobin	0.373	1.089	0.903	1.314
Higher TG	0.869	1.031	0.717	1.483
Higher TC	*0.018*	1.523	1.076	2.157
Higher LDL-C	*< 0.001*	2.737	1.556	4.815
Higher HDL-C	0.476	1.624	0.429	6.157
Higher HsCRP	*< 0.001*	1.268	1.175	1.369
Higher ESR	0.430	1.014	0.980	1.048
Higher WBC	0.441	1.095	0.869	1.379
Higher Neutrophil	0.146	1.310	0.911	1.885
Higher Scr	0.084	1.018	0.998	1.039
Higher SUA	*0.035*	1.005	1.000	1.010
Higher LVEF	0.173	0.964	0.915	1.016
Higher cTnI	0.108	1.012	0.997	1.027
Higher NT-proBNP	0.295	1.003	0.998	1.007
Multivessel artery lesions	*0.025*	3.030	1.151	7.978
Target lesion at LAD	0.413	1.337	0.667	2.682
Target lesion at LCX	0.051	1.969	0.997	3.886
Target lesion at RCA	0.618	0.835	0.412	1.694
Patients with two target lesions	*0.018*	2.279	1.151	4.513
Higher stenosis degree of target lesion	0.223	1.044	0.974	1.118
Larger length of target lesion	*0.005*	1.059	1.017	1.102
Larger length of stent	*0.007*	1.055	1.015	1.097
Larger diameter of stent	0.882	0.927	0.339	2.531
Longer time of stent dilation	0.117	0.937	0.863	1.017
Balloon dilation pre stent	0.888	1.053	0.511	2.172
Statins	0.305	0.302	0.031	2.976
β receptor blockers	0.835	1.140	0.332	3.915
ACEIs/ARBs	0.710	0.874	0.430	1.778
Calcium channel blockers	0.898	0.953	0.455	1.996

Data set in italics were considered significant (*P* value < 0.05). Factors predicting restenosis risk was analyzed by univariate logistic regression

OR, odds ratio; *CI*, confidence interval; *BMI*, body mass index; *CAD*, coronary artery disease; *MAP*, mean arterial pressure; *FBG*, fasting blood-glucose; *IQR*, interquartile range; *TG*, triglyceride; *TC*, total cholesterol; *LDL-C*, low density lipoprotein cholesterol; *HDL-C*, high density lipoprotein cholesterol; *HsCRP*, high-sensitivity C-reactive protein; *ESR*, erythrocyte sedimentation rate; *WBC*, white blood cell; *Scr*, serum creatinine; *SUA*, serum uric acid; *LVEF*, left ventricular ejection fraction; *cTnI*, cardiac troponin I; *NT-proBNP*, N-terminal-proB-type natriuretic peptide; *LAD*, left anterior descending branch; *LCX*, left circumflex artery; *RCA*, right coronary artery; *ACEIs*, angiotensin converting enzymes inhibitors; *ARBs*, angiotensin receptor blockers

risk prediction model exhibited a much higher predictive value for increased restenosis risk, with the AUC of 0.953 (95% CI 0.926–0.981).

Table 4 Analysis of independent factors predicting restenosis risk

Items	*P* value	OR	95% CI	
			Lower	Higher
Higher age	0.033	1.064	1.005	1.126
Hypertension	0.001	22.397	3.701	135.524
Diabetes mellitus	< 0.001	25.534	6.721	97.002
Higher LDL-C	< 0.001	20.911	6.661	65.642
Higher HsCRP	< 0.001	1.604	1.386	1.856
Target lesion at LCX	0.027	3.348	1.146	9.780

The independent predicting factors of restenosis risk were screened by forward stepwise multivariate logistic regression from variables with *P* value < 0.1 in univariate logistic regression, and the restenosis risk prediction model was as follows: $P = [\exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]/\ [1 + \exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]$, −2ln (likelihood ratio) = 107.321

OR, odds ratio; *CI*, confidence interval; *LDL-C*, low density lipoprotein cholesterol; *HsCRP*, high-sensitivity C-reactive protein; *LCX*, left circumflex artery

Discussion

In this study, we reviewed the comprehensive characteristics of 398 CHD patients underwent PCI with SES, and explored the 1-year restenosis occurrence as well as the predictors for restenosis risk in these patients. Firstly, we found that the incidence of 1-year restenosis was 9.3%. Secondly, age, hypertension, diabetes mellitus, LDL-C, and HsCRP as well as target lesion at LCX were independent predictive factors for increased restenosis risk. Thirdly, the restenosis risk prediction model involving these independent factors had an excellent value for predicting restenosis.

In clinical practices for treating CAD, PCI with DES is regarded as revolutionized technology in interventional cardiology, which has exhibited great performance in reducing restenosis and decreasing the need for repeated revascularization, especially PCI with SES, which is the first commercially available and most commonly used DES [7, 8]. A study enrolling 115 patients with ischemic heart disease has shown that the patients received SES presents with much lower risk of restenosis compare with patients received bare metal stent [18]. And a study reviewed 19 trials displays that SES results in a great reduction in the risk of target lesion revascularization compared with other PCI strategies including paclitaxel-eluting stent, drug-coated balloons, and bare-metal stents [22]. Thus, these data reveal that SES is advantageous in prevention of restenosis and target lesion revascularization, and the reason for the superiority of SES might due to the advantage of sirolimus in promoting aggressive neointimal suppression [23, 24]. Furthermore, regarding the restenosis rate in patients

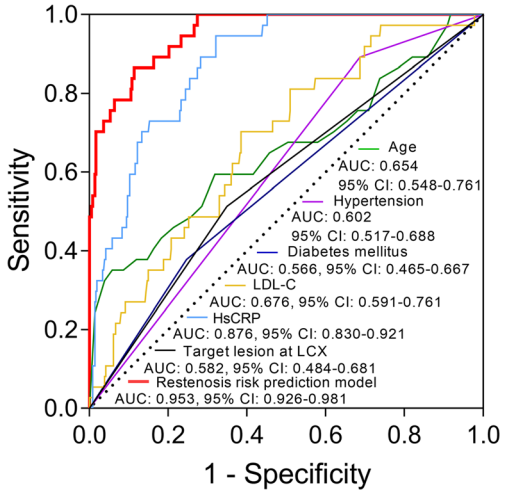

Fig. 2 Predictive values of various factors for restenosis risk by ROC curve analysis. Predictive values of age, hypertension, diabetes mellitus, LDL-C, HsCRP, target lesion at LCX, and restenosis risk prediction model for restenosis risk, which were evaluated by ROC curves. ROC curves, receiver operating characteristic curves; LDL-C, low density lipoprotein cholesterol; HsCRP, high-sensitivity C-reactive protein; LCX, left circumflex artery; AUC, area under the curve; CI, confidence interval

underwent PCI with SES, a study displays a 9-month restenosis rate of 13.7% in 73 chronic total occlusion patients underwent PCI with SES [25]. And another study displays a 6-month restenosis rate of 9.2% in 122 chronic total occlusion patients underwent PCI with SES [26]. In line with these data, our study showed that the 1-year restenosis rate was 9.3% in CHD patients underwent PCI with SES.

Regarding the predictive factors for restenosis, a few studies with small sample size disclose some potential factors that may forecast restenosis risk. For instance, a study displays that hypertension independently predicts elevated restenosis risk in 50 patients with ischemic heart diseases underwent PCI with SES [27]. Additionally, a study shows that higher CRP is an important predictor for raised restenosis occurrence in 167 hemodialysis patients with coronary lesions who underwent PCI with SES [28]. Besides, a study discloses that higher age is an independent predictive factor for higher restenosis occurrence in 49 patients with underwent PCI with SES [29]. Partially consistent with these previous studies, our study chose some factors that might potentially affect the restenosis in CHD patients, and investigated the predictive factors for restenosis in 398 CHD patients underwent PCI with SES, which sample size was larger than the previous studies, and we observed that age, hypertension, diabetes mellitus, LDL-C, HsCRP, and target lesion at LCX were independent predictive factors for increased restenosis risk in these patients. The following reasons might explain our results: (1) elder patients had thicker arterial wall and decreased anticoagulant ability, thus they were more liable to develop atherosclerosis, which led to restenosis [16, 17]; (2) hypertension resulted in increased blood flow impact on the vessels and caused injury on the vascular endothelium, which facilitated the formation of atherosclerotic plaque and further contributed to atherosclerosis, thus it predicted raised restenosis risk [30]; (3) the patients with diabetes mellitus might have elevated advanced glycation end products (AGE) level, which increased reactive oxygen species, accelerated vein graft arterialization as well as atherosclerosis, and eventually resulted in restenosis, thus diabetes mellitus predicted higher restenosis risk [17, 31, 32]; (4) excess LCL-C level caused more cholesterol accumulation on the arterial wall, thereby contributed to atherosclerosis and further led to restenosis [33]; (5) elevated HsCRP indicated the enhanced local inflammatory response, which activated platelets and fibrinogen to recruit to the stent-induced direct arterial wall injury and further facilitated atherosclerotic plaque to results in restenosis, thereby increased restenosis risk [17, 34, 35]; (6) stent implantation on the target lesion at LCX was subjected to flexion, torsion, as well as rotational forces, and it might induce shear stress due to the acute angle as well as hinge motion; thus, it promoted the vascular endothelium injury and enhanced the occurrence of restenosis in CHD patients underwent PCI with SES [36].

Based on the independent predictive factors screened from multivariate logistic regression analysis, we generated these factors into the restenosis risk prediction model ($P = [\exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]/[1 + \exp(-23.423 + 0.062\ (\text{age}) + 3.109\ (\text{hypertension}) + 3.240\ (\text{diabetes mellitus}) + 3.040\ (\text{LDL-C}) + 0.473\ (\text{HsCRP}) + 1.208\ (\text{target lesion at LCX}))]$, $-2\ln(\text{likelihood ratio}) = 107.321$) and speculated whether this model was able to predict restenosis risk. We observed that the restenosis risk prediction model presented with a great predictive value for raised restenosis risk (AUC 0.953 (95% CI 0.926–0.981)) in CHD patients underwent PCI with SES, and the predictive value was stronger compared with any other factor alone. These data indicated that our restenosis risk prediction model would contribute to the prevention of restenosis in CHD patients underwent PCI with SES.

Several limitations of our study needed to be highlighted. One was that, the follow-up duration (1 year) was relatively short, and restenosis rate assessment with longer follow-up duration was not investigated. Secondly, this was a retrospective study, and a prospective study was needed to validate our results. Thirdly, as a single-center study, selective bias might exist in our study; Finally, the effect of the common indexes on predicting the restenosis risk in recurrence/restenosis patients who initiate PCI with DES statement was not investigated in this present study. Further multi-

center study enrolling recurrence/restenosis patients is needed to validate our findings.

In conclusion, the restenosis risk prediction model, which involves age, hypertension, diabetes mellitus, LDL-C, HsCRP, and target lesion at LCX, may serve as an excellent predictor for increased restenosis risk in CHD patients underwent PCI with SES implantation. These findings provide a new insight into the prediction for restenosis in CHD patients underwent PCI with SES.

Compliance with ethical standards

This study was approved by the Institutional Review Board of The Second Hospital of Hebei Medical University, and the written informed consents were provided by patients or their guardians.

Conflict of interest The authors declare that they have no conflict of interest.

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