Meta-analysis of In-stent Restenosis Factors after Coronary Intervention

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Abstract: This aim is to explore the relevant factors affecting in-stent restenosis after coronary intervention procedures. Relevant research literature was searched through domestic and international databases and Meta-analysis was performed. Smoking, alcohol consumption, hypertension, hyperlipidemia, diabetes mellitus, low-density lipoprotein cholesterol, total cholesterol, triglycerides, uric acid level, number of implanted stents, and stent length were significantly associated with in-stent restenosis (P<0.05). Factors such as gender, age, body mass index, high-density lipoprotein cholesterol, and left ventricular ejection fraction were not significantly correlated with in-stent restenosis (P>0.05).
***Keywords*:** coronary heart disease; in-stent; restenosis

1. Information and methods

1.1 Object of study

Case-control and cross-sectional studies on factors of stent restenosis after coronary intervention [1].

1.2 Literature inclusion and exclusion criteria

Inclusion criteria: (1) The type of study was a cross-sectional or case-control study; (2) The study subjects were patients who suffered from coronary atherosclerotic heart disease and underwent stenting interventions; (3) The ISR of in-stent restenosis was clearly defined as a stenosis of ≥ 50% in stent-implanted segments as shown by late follow-up coronary angiography[1]; (4) Factors related to the stent restenosis under study were clearly defined; (5) The inclusion and exclusion criteria of the study subjects were comparable. (6) Literature whose language was Chinese and English [2].

Exclusion criteria:(1) Repeatedly published literature; (2) Literature with incomplete data or data that could not be extracted for analysis; (3) Literature type belonging to case reports, reviews, theoretical studies, etc.; (4) Literature for which the full text could not be obtained.

1.3 Searching strategy

The Chinese databases searched were China Knowledge Network (CNN), Wipu Information Chinese Journal Service Platform (WISP), China Biomedical Literature Service System (CBLS), Wanfang Medical Network (WFMN), etc., and the English databases were Pub Med, Embase, and Webof Siencec, etc. [3], which were supplemented with manual searches, to collect the relevant literature about case-control and cross-sectional studies on the factors of stent restenosis after coronary heart disease interventional therapy [4], and the search period was from January 1, 2010 to November 30, 2023. The search strategy used a combination of subject terms and free terms, and the Chinese search terms included coronary heart disease, intervention, stent, restenosis, related factors, influencing factors, risk factors, etc. The English search terms included coronary heart disease (CHD), percutaneous coronary intervention (PCI), in-stent restenosis (ISR), in-stent restenosis (ISR), in-stent restenosis (ISR), and in-stent restenosis (ISR). in-stent restenosis(ISR),drug-eluting stents(DES),risk factor ,related fact or ,correlation factor and so on[5].

1.4 Literature Screening and Data Extraction

The screening of literature was conducted independently by two researchers, and when there was a dispute, a third person was asked to assist and make a final judgment on its inclusion [6]. The extracted literature included: (1) general information: title of the literature, first author, year of publication, type of literature, and platform of publication, etc.; (2) the study population: the exposure of the case and control groups and the number of samples in each group; and (3) the definition of each study factor, the unit of data, the sample size of the samples in each group, as well as the mean and standard deviation of the continuous variables, etc. [9].

1.5 Statistical methods

Meta-analysis was performed using Stata 14.0 software. The dominance ratio OR and its 95% CI were used to express

effect sizes. The χ2 test and I2 test were used to analyze the statistical heterogeneity among the included literatures.

2. Result

2.1 Literature Screening Process

The computerized search collected a total of 2,654 pieces of relevant literature, and 1,866 pieces were de-emphasized. Thirty-eight literatures were found to meet the inclusion criteria after reading the title, abstract and full text.

2.2 Basic characteristics and quality of the included literature

A total of 38 papers were included in this study, including 33 papers in Chinese and 5 papers in English; 19 relevant factors were included; the publication years were 2010-2023; and the Newcastle-Ottawa scale scores of the included papers ranged from 6 to 9. See Figure 1.

文献来源	发表年份	总样本量	ISR样本量	ISR发生率	文献质量评分	结局指标编号
段书云 等[1]	2015	204	67	32.84%	7	1, 2, 4, 6, 8, 10, 14, 15, 17
姚远 等[2]	2015	183	46	25.14%	7	1, 2, 4, 5, 6, 8, 11, 13, 15, 16, 17, 18
满意 等[3]	2017	118	35	29.66%	7	1, 2, 3, 4, 6, 8, 9, 10, 12, 15, 17, 18
张从良 等[4]	2019	160	32	20.00%	7	1, 2, 3, 4, 6, 8, 9, 10, 12, 13, 14, 15
李海滨 等[5]	2016	168	52	30.95%	6	1, 2, 3, 4, 5, 6, 7, 8, 12, 15
罗玉琨 等[6]	2018	376	42	11.17%	6	1, 2, 4, 5, 6, 8, 9, 10, 12, 13, 14, 15
冯明瑞 等[7]	2018	102	38	37.25%	9	1, 2, 4, 5, 6, 8, 9, 10, 12, 13, 14, 15, 16, 17, 18
张代民 等[8]	2020	120	17	14.17%	7	1, 2, 3, 6, 7, 8, 9, 10, 11, 12, 15
杨蕾 等[9]	2012	200	100	50.00%	6	1, 2, 3, 4, 6, 8, 9, 10, 11, 12, 13
尹永厚 等[10]	2014	120	32	26.67%	8	1, 2, 4, 6, 8, 12, 13
刘树英 等[11]	2014	212	102	48.11%	6	1, 2, 3, 4, 6, 8, 9, 10, 11, 12, 13, 14
刘宁 等[12]	2015	208	40	19.23%	9	1, 2, 4, 5, 6, 7, 8, 9, , 10, 11, 12, 13, 14, 16, 17, 18
潘春仰 等[13]	2015	520	258	49.62%	7	1, 2, 4, 6, 7, 8, 9, 10, 11, 12, 16, 17, 18
李丽 等[14]	2016	200	36	18.00%	7	1, 2, 4, 6, 8, 9, 10, 12, 13, 16, 17, 18
金鹏 等[15]	2017	140	55	39.29%	6	1, 2, 4, 5, 6, 7, 8, 12, 13, 14, 17
WangPengfei 等[16]	2019	209	64	30.62%	6	1, 2, 4, 5, 6, 8, 9, 10, 12, 13
欧弘基 等[17]	2019	690	153	22.17%	6	1, 2, 4, 6, 7, 8, 9, 10, 12, 13, 14, 16, 17, 18
Jiayu Zhao 等[18]	2020	398	37	9.30%	6	1, 2, 3, 4, 6, 8, 9, 10, 12
马天翊 等[19]	2016	286	149	52.10%	7	1, 2, 4, 6, 8, 9, 10, 11, 12, 14
侯宏伟 等[20]	2019	317	152	47.95%	6	1, 2, 4, 6, 8, 9, 10, 12
罗江宾 等[21]	2019	200	38	19.00%	6	1, 2, 4, 5, 6, 8, 9, 10, 12, 13, 14
廖家有 等[22]	2021	150	40	26.67%	8	1, 2, 4, 6, 7, 8, 11, 12, 14
Mingrui Li 等[23]	2022	341	62	18.18%	7	1, 2, 4, 5, 6, 7, 8, 11, 12, 13, 16, 17, 18
Juan Zhang 等[24]	2022	350	138	39.43%	7	1, 2, 3, 4, 5, 8, 9, 10, 12, 13
王东 等[25]	2015	180	16	8.89%	7	1, 2, 4, 5, 8, 16, 17, 18
吴小朋 等[26]	2015	168	51	30.36%	9	1, 2, 3, 4, 6, 7, 8, 11, 14, 16, 17, 18
熊青 等[27]	2018	684	45	6.58%	7	1, 2, 9, 10, 16, 17, 18
李立鹏 等[28]	2013	98	71	72.45%	7	1, 2, 3, 4, 5, 6, 8, 9, 10, 13
罗琳璇 等[29]	2023	396	29	7.32%	6	1, 4, 5, 6, 8
卢晓操 等[30]	2020	105	19	18.10%	6	1, 2, 3, 4, 5, 6, 8
黄宗燕 等[31]	2010	208	69	33.17%	8	1, 2, 3, 4, 6, 7, 8
张改 等[32]	2015	230	68	29.57%	6	1, 6, 8
王芳 等[33]	2016	207	100	48.31%	7	1, 2, 3, 4, 6, 7, 8, 14
Morteza Gholami 等[34]	2021	91	40	43.96%	7	1, 2, 3, 6, 8
刘伟涛 等[35]	2021	397	114	28.72%	7	1, 2, 4, 6, 8, 14
简政威 等[36]	2022	300	29	9.67%	7	1, 4, 6, 8, 10, 13
李倩 等[37]	2023	411	76	18.49%	7	1, 2, 4, 6, 8
邓婵翠 等[38]	2016	1342	89	6.63%	6	2, 4, 6, 8, 10, 11

Figure 1. Basic characteristics and quality of the included literature

2.3 Restenosis rate after coronary intervention

A total of 38 papers were included in this study, including 33 papers in Chinese and 5 papers in English; 19 relevant factors were included; the publication years were 2010-2023; and the Newcastle-Ottawa scale scores of the included papers ranged from 6 to 9. See Figure 1.

2.4 Meta-analysis result

The effect values of factors associated with ISR restenosis in the literature reporting >7 were combined and analyzed by Meta-analysis, which showed that: hypertension, hyperlipidemia, smoking, alcohol consumption, diabetes mellitus, high low-density lipoprotein cholesterol level, high cholesterol, high triglyceride, high uric acid, number of multiple stents, and stent length bias were all risk factors for the occurrence of ISR ($P < 0.05$); high bilirubin was a ISR protective factor for the occurrence of ISR; variables such as gender, age, BMI, high-density lipoprotein cholesterol, left ventricular ejection fraction, and number of stents were not statistically significant ($P>0.05$) for the incidence of ISR, as shown in Figure 2.

结局指标编号	结局指标	纳入研究数(个)	总样本量	ISR样本量	ISR发生率	异质性检验结果		效应模型	meta分析结果	
						P值	I^2		OR(95%CI)	P值
1	性别(男/女)	40	9597	2552	26.59%	0.000	53.3%	随机效应模型	0.968[0.82, 1.143]	0.703
2	年龄(n year)	40	10013	2515	25.12%	0.003	44.2%	随机效应模型	0.013[-0.035, 0.062]	0.59
3	BMI	17	2603	863	33.15%	0.000	95.9%	随机效应模型	-0.42[-0.874, 0.033]	0.069
4	吸烟(是/否)	38	9814	2471	25.18%	0.000	74.2%	随机效应模型	1.71[1.382, 2.117]	0.000
5	饮酒(是/否)	16	3056	710	23.23%	0.802	0.0%	固定效应模型	1.416[1.163, 1.723]	0.001
6	高血压(是/否)	42	9725	2442	25.11%	0.000	69.0%	随机效应模型	1.388[1.138, 1.693]	0.001
7	高脂血症(是/否)	13	3070	937	30.52%	0.085	38.4%	固定效应模型	1.298[1.061, 1.589]	0.011
8	糖尿病(是/否)	42	10255	2596	25.31%	0.000	69.3%	随机效应模型	1.968[1.627, 2.380]	0.000
9	HDL-C(mmol/L)	18	5448	1547	28.40%	0.000	86.9%	随机效应模型	-0.06[-0.243, 0.123]	0.522
10	LDL-C(mmol/L)	25	7294	1732	23.75%	0.000	85.8%	随机效应模型	0.297[0.134, 0.46]	0.000
11	LVEF(%)	17	3880	994	25.62%	0.000	82.0%	随机效应模型	-0.153[-0.347, 0.042]	0.124
12	总胆固醇 TC (mmol/L)	26	5735	1712	29.85%	0.000	73.9%	随机效应模型	0.15[0.028, 0.271]	0.016
13	甘油三酯 TG (mmol/L)	18	4089	1078	26.36%	0.557	0.0%	固定效应模型	0.116[0.043, 0.19]	0.002
14	尿酸UA(μmol/L)	17	3650	1061	29.07%	0.000	94.50%	随机效应模型	0.608[0.277, 0.94]	0.000
15	总胆红素(μmol/L)	8	1271	297	23.37%	0.000	96.40%	随机效应模型	-1.082[-1.852, -0.312]	0.006
16	支架数量(n)	13	3276	745	22.74%	0.000	84.20%	随机效应模型	0.262[0.175, 0.349]	0.000
17	支架长度(mm)	18	3738	902	24.13%	0.000	84.70%	随机效应模型	0.263[0.05, 0.476]	0.015
18	支架直径(mm)	18	3394	780	22.98%	0.000	91.50%	随机效应模型	-0.121[-328, 0.085]	0.25

Figure 2. Results of Meta-analysis of ISR-related factors

2.5 Sensitivity analysis

The results of the sensitivity analysis showed that the Meta-analysis results for each of the other influencing factors were unchanged after removing the sample of any single paper and remained within the 95% confidence intervals, and that each of the significant variables was insensitive to the change in the results after the deletion of any single paper[10] .

2.6 Publication bias

The results of the sensitivity analysis showed that the Meta-analysis results for each of the other influencing factors were unchanged after removing the sample of any single paper and remained within the 95% confidence intervals, and that each of the significant variables was insensitive to the change in the results after the deletion of any single paper[9] . See Figure 3.

结局指标	效应模型	meta分析结果		Egger's检验结果	
		OR(95%CI)	P值	t值	P值
吸烟(是/否)	随机效应模型	1.71[1.382, 2.117]	0.000	0.28	0.781
饮酒(是/否)	固定效应模型	1.416[1.163, 1.723]	0.001	1.92	0.079
高血压(是/否)	随机效应模型	1.388[1.138, 1.693]	0.001	-0.04	0.965
高脂血症(是/否)	固定效应模型	1.298[1.061, 1.589]	0.011	0.13	0.902
糖尿病(是/否)	随机效应模型	1.968[1.627, 2.380]	0.000	0.51	0.616
LDL-C(mmol/L)	随机效应模型	0.297[0.134, 0.46]	0.000	0.81	0.429
总胆固醇 TC (mmol/L)	随机效应模型	0.15[0.028, 0.271]	0.016	0.03	0.974
甘油三酯 TG (mmol/L)	固定效应模型	0.116[0.043, 0.19]	0.002	1.11	0.284
尿酸UA(μmol/L)	随机效应模型	0.608[0.277, 0.94]	0.000	-0.06	0.955
总胆红素(μmol/L)	随机效应模型	-1.082[-1.852, -0.312]	0.006	0.82	0.452
支架数量(n)	随机效应模型	0.262[0.175, 0.349]	0.000	0.27	0.792
支架长度(mm)	随机效应模型	0.263[0.05, 0.476]	0.015	2.56	0.026

Figure 3. ISR Significant Factors Egger's Test Results Table

3. Discussion

In this study, the following conclusions were obtained by the method of Meta-analysis of 38 national and international literatures: smoking, alcohol consumption, hypertension, hyperlipidemia, diabetes mellitus, LDL cholesterol level, cholesterol level, triglyceride, uric acid, number of stents, and length of stents showed statistically significant ($P < 0.05$) on in-stent restenosis; gender, age, BMI, HDL The variables of gender, age, BMI, HDL cholesterol, left ventricular ejection fraction, and number of stents were not statistically significant on the incidence of ISR ($P>0.05$), and the results of all the studies showed insensitivity to the exclusion of a single included literature; there was a publication bias in each of the studies on the length of the stent, and there was no publication bias for any of the other variables.

In conclusion, smoking, alcohol consumption, hypertension, hyperlipidemia, diabetes mellitus, high low-density lipoprotein cholesterol level, high cholesterol, high triglycerides, high uric acid, higher number of stents, stent length, and low total bilirubin level are risk factors for in-stent restenosis. Smoking, alcohol consumption, hypertension, hyperlipidemia, diabetes mellitus, high LDL cholesterol levels, high cholesterol, high triglycerides, high uric acid, high number of stents, longer stent lengths, and low total bilirubin levels should be of high concern in the prevention of in-stent restenosis in patients after coronary intervention.

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