SYSTEMATIC REVIEW   **Open Access**

A systematic review and bioinformatic study on clinical, paraclinical, and genetic factors predisposing to stent restenosis following percutaneous coronary intervention

Farzad Shahsanaei[1], Abdullah Gharibzadeh[1], Soudabeh Behrooj[1], Shahin Abbaszadeh[1*] and Mahboobeh Nourmohammadi[1*]

Abstract

Background Stent restenosis is a relatively common phenomenon among patients with coronary heart disease undergoing percutaneous coronary intervention (PCI). It seems that a set of clinical, laboratory, and even genetic factors make people susceptible to such a phenomenon and in fact, this is multi-factorial. We aimed to first determine the underlying clinical and laboratory risk factors for the occurrence of stent re-stenosis after PCI based on a systematic review study, and after that, through a bioinformatics study, to evaluate the related genes and microRNAs with the occurrence of stent re-stenosis.

Main text In the first step, the manuscript databases including Medline, Web of Knowledge, Google Scholar, Scopus, and Cochrane were deeply searched by the two blinded investigators for all eligible studies based on the considered keywords to introduce clinical and laboratory determinants of stent re-stenosis. In the bioinformatic phase, and following a review of the literature to identify genes and microRNAs involved in restenosis, the interaction of each gene with other genes associated with stent re-stenosis was determined by GeneMANIA network analysis and Cytoscape software. Overall, 67 articles (including 40,789 patients) on clinical and biochemical predictors for stent restenosis and 25 articles on genetic determinants of this event were eligible for the final analysis. The predictors for this event were categorized into four subgroups patient-based parameters including traditional cardiovascular risk profiles, stent-based parameters including type and diametric characteristics of the stents used, coronary lesion-based parameters including several two target lesions and coronary involvement severity and laboratory-based parameters particularly related to activation of inflammatory processes. In the bioinformatic phase, we uncovered 42 genes that have been described to be involved in such a phenomenon considering a special position for genes encoding inflammatory cytokines. Also, 12 microRNAs have been pointed to be involved in targeting genes involved in stent re-stenosis.

*Correspondence:
Shahin Abbaszadeh
sh.abbaszadeh@hums.ac.ir
Mahboobeh Nourmohammadi
m.nourmohammadi.pz@gmail.com

Full list of author information is available at the end of the article

Conclusions The incidence of stent re-stenosis will be the result of a complex interaction of clinical risk factors, laboratory factors mostly related to the activation of inflammatory processes, and a complex network of gene-to-gene interactions.

Keywords Stent restenosis, ACS, PCI, Bioinformatic, Genes, MicroRNA

Background

Ischemic coronary heart disease is the result of an imbalance between blood distribution and tissue demand in the myocardial muscle. Coronary artery lumen narrowing due to atherosclerosis is responsible for about 98% of ischemic heart disease cases [1]. It should be noted that coronary heart disease mainly affects the age group of 35 to 65 years, and in an important part of society, conflict may occur at the level of young people. In addition, coronary heart disease accounts for 64% of all cardiovascular deaths. According to the published statistics, during the last decade, we have seen an increase in the morbidity caused by ischemic cardiovascular diseases [2]. Of course, it should be kept in mind that with the development of medicinal methods as well as therapeutic interventions such as angioplasty and coronary stenting, the frequency of morbidity and mortality cases caused by these diseases has decreased significantly [3]. The first case of stent implantation was performed in 1986 and after that percutaneous coronary intervention or PCI was listed as one of the standard treatment strategies for these disorders [4]. Today, these methods as endovascular treatments aimed at restoring coronary blood flow have led to the lives of millions of people. However, observations have shown that within 6 months to one year after successful coronary stenting, there is a possibility of angina recurrence due to restenosis of the stent [5]. This issue has even been reported for drug-eluting stents [6]. After initial coronary stenting, the prevalence of restenosis is between 20 and 30% [7]. This stent restenosis occurs for various clinical and even genetic reasons and it seems that a set of pathophysiological processes such as inflammatory processes, proliferation, genomic and epigenetic factors play a role in it [8]. But interestingly, the role of each of these factors can be very different in different societies. In particular, the impact of genetic factors is completely dependent on the demographic characteristics of that society. Today, all kinds of genes, genetic polymorphisms, and microRNAs have been identified and introduced in the incidence of stent re-stenosis, which, along with clinical risk factors, double the risk of this complication. We aimed to first determine the underlying clinical and laboratory risk factors for the occurrence of stent re-stenosis after PCI based on a systematic review study, and after that, through a bioinformatics study, to evaluate the related genes and microRNAs with the occurrence of stent re-stenosis.

Materials and methods

Systematic review phase

The present systematic review and meta-analysis followed the guidelines for the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). Firstly, two questions were suggested based on the author's purposes "What are the main clinical determinants for stent re-stenosis?" and "What are the related and predictive genetic factors for re-stenosis?". In the next step, the manuscript databases including Medline, Web of Knowledge, Google Scholar, Scopus, and Cochrane were deeply searched by the two blinded investigators for all eligible studies based on the considered keywords including "stent", "stenosis", "re-stenosis", "predictor", "risk factor", "gene", "genetics", and "microRNA". The inclusion criteria were considered to retrieve the studies: (1) the studies finally assessed clinical and/or genetic-based risk profiles related to stent re-stenosis, (2) due to the potential effects of other cardiac revascularization procedures such as coronary artery bypass grafting, those studies entering the patients who undergo such revascularization procedures or previous history of cardiac procedures were all excluded from analysis, (3) The studies were restricted to the English language, (4) the studies with unclear or irreproducible results were all excluded, (5) lack of access to the manuscripts full texts were also considered as the inclusion criteria unless the abstracts had enough data for our analysis, (6) case reports, case series, and review papers were all excluded. As shown in the flow diagram of the study selection (Fig. 1), 1536 articles were initially collected by database searching. After removing 13 articles due to evidence of duplication, 1523 records were primarily under-screened. Based on the titles and abstracts, 1426 records were excluded and the remaining 97 citations were assessed for further eligibility. Of those, 5 were also excluded due to the incompleteness of the data and contents. In the final, 67 articles on clinical and biochemical predictors for stent restenosis [10–76] (Table 1) and also 25 articles on genetic determinants of this event were eligible for the final analysis [77–101] (Table 2).

Data abstraction was independently performed by two un-blinded reviewers on structure collection forms without divergences in data collection. We resolved disagreements by consensus or by involving a third person. The study quality was evaluated based on the following criteria: (1) the systematic review and meta-analysis based on the questions primarily described and formulated; (2)
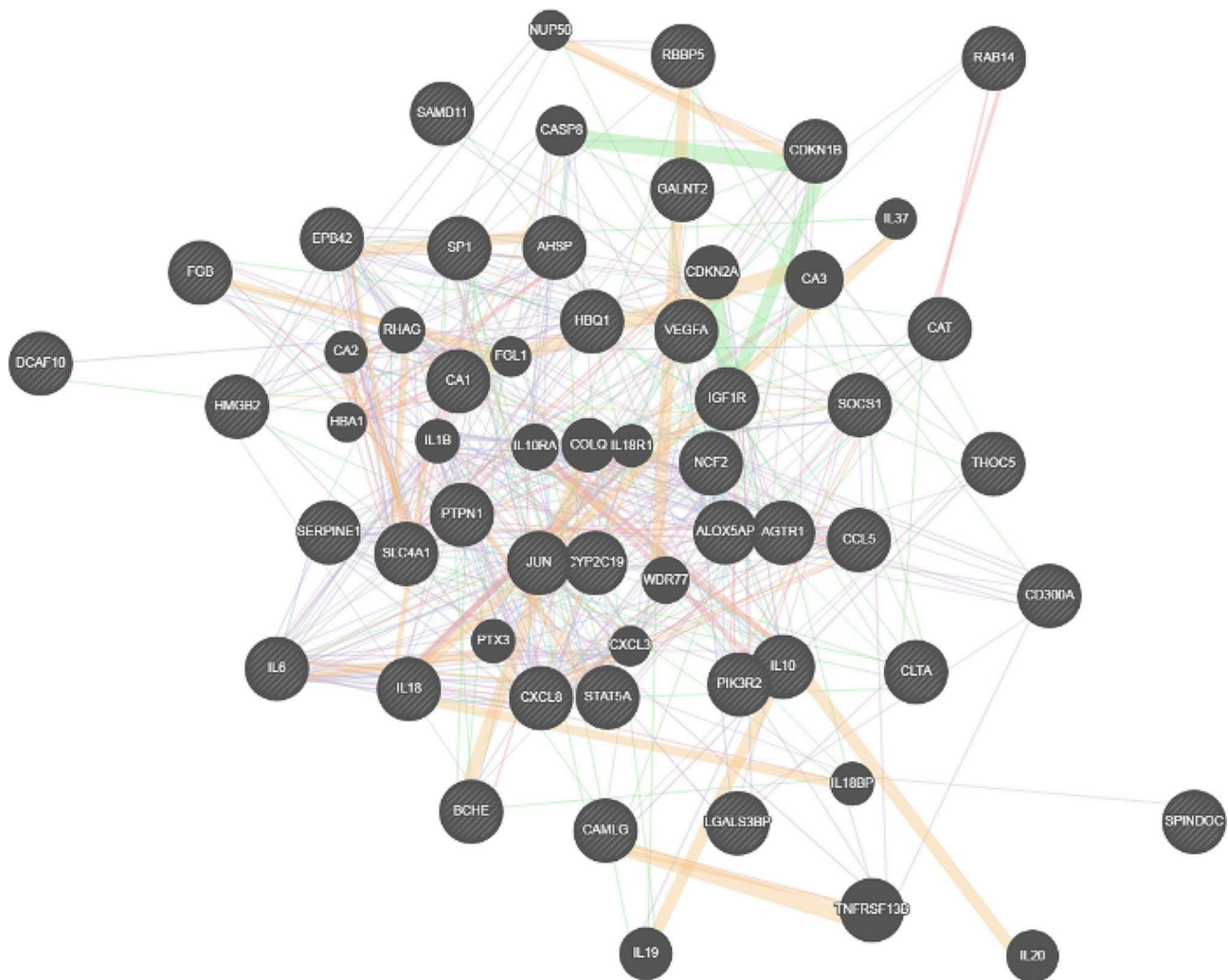
Fig. 1 gene to gene interaction involving stent restenosis

inclusion and exclusion criteria predefined in the studies as eligibility criteria; (3) searching the literature performed on a systematic and comprehensive approach; (4) to minimize the bias, the full texts of the article were dually reviewed; (5) the quality of included studies were rated independently by the reviewers for appraising internal validity; (6) studies' characteristics and findings were comprehensively listed; (7) the publication and risk of bias were listed; and (8) heterogeneity was also assessed. The risk of bias for each study was assessed using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions and also according to the QUADAS-2 tool. Any disagreement was resolved by discussion with the whole study team.

Bioinformatic phase

The details of bioinformatic processing to assess the genes and gene-gene interactions are described by Sheikhvatan et al. previously [102]. Briefly, the interaction of each gene with other genes associated with stent re-stenosis was determined by GeneMANIA software (https://genemania.org/) indexing 2277 association networks containing more than 500 million interactions mapped to 163.599 genes in humans. The interactions were calculated based on FDR (False Discovery Rate) and coverage was classified under four categories (a) Shared protein domains, (b) Co-expression, (c) Co-localization, and (d) Genetic interactions. In this regard, a FDR≤5% was considered to be significant. To design an integrated model of a gene interaction network, the Cytoscape software (version 3.6.1.0) was applied.

Results

Findings of a systematic review

To assess the main correlates of stent re-stenosis based on applied keywords, in total 67 studies finally assessed that published from different countries between 2004 and 2022 (Table 1). According to our risk of bias assessment,

Table 1 Reviewing the studies on the predictors of stent restenosis

Author, year	No. population	Type of stent	Time after PCI (months)	Risk profile
Lin, 2022 [10]	797	DES	6	Higher HbA1c
Feng, 2022 [11]	235	DES	12	Diabetes mellitus, hypercholesteremia, SUA, HsCRP levels, two target lesions
Wang, 2022 [12]	472	BMS	12	Age, hypercholesteremia, raised ApoB, MCV & MCH values, Gensini score, diabetes mellitus
Csató, 2022 [13]	653	BMS, DES		neutrophil to lymphocyte ratio, type of stent, lower stent diameter, longer stents
Wang, 2022 [14]	604	DES	12	apoA-I, HbA1c
Wang, 2022 [15]	564	BMS, DES	12	CRP, HbA1c, lower QKI and COX-2
Zhou, 2022 [16]	215	BMS, DES	36	High RDW, lower stent diameter,
Guo, 2022 [17]	155	DES	24	High Homocysteine
Yi, 2022 [18]	1741	DES	12	Lower GFR, higher FBS, multivessel coronary disease, coronary artery diffuse disease, PCI operation time, emergency PCI, HbA1c
Liu, 2022 [19]	416	DES	12	Higher IgE and CML levels
Chen, 2022 [20]	452		12	Increased lipoprotein-associated phospholipase A2 (Lp-PLA2) and IL-6
Qiu, 2022 [21]	4392	DES	12	monocyte count
Luo, 2022 [22]	477	DES		remnant cholesterol, GS score, medical history of COPD, monocyte
Luo, 2022 [23]	429	DES	12	creatine, history of diabetes, smoking, multi-vessel lesions, peripheral vascular lesions, and blood uric acid
Zhang, 2022 [24]	284	DES	12	Lower AGR
Chen, 2022 [25]	257	DES	12	smoking history, higher fibrinogen
Zheng, 2022 [26]	194	DES		coronary artery calcium score
Li, 2022 [27]	341	DES	34	Lower LVEF, stent number
Hu, 2021 [28]	538		12	Anemia, diabetes mellitus, chronic kidney disease, multiple stenting, bifurcation lesion, calcification
Yoshimura, 2021 [29]	86	BMS	6	Hypertriglyceridemia, lower diastolic blood pressure, lower high-density lipoprotein
Gai, 2021 [30]	968	BMS, DES	12	platelet distribution width (PDW), total cholesterol, systolic blood pressure, low-density lipoprotein cholesterol, lesion vessels
Zhang, 2021 [31]	114	DES	9	stent length ≥ 35 mm
He, 2021 [32]	463	DES	12	prior PCI, hyperglycemia, stents in left anterior descending artery (LAD), stent type, absence of clopidogrel
Alexandrescu, 2021 [33]	235	DES	12	smoking, hypertension, diabetes mellitus, high CRP levels, CKD, TIMI score, stent type, low pressure for stent implantation, multi-stenting
Lee, 2021 [34]	1376	DES	12	severe chronic kidney disease
Sheng, 2021 [35]	847	DES	36	Higher Lp-PLA2
Gupta, 2021 [36]	550	DES		diabetes mellitus, deployment of stent in the left anterior descending (LAD) artery, periprocedural complication during percutaneous coronary intervention
Wang, 2020 [37]	209	DES	12	Hypertension, diabetes, number of coronary artery lesions ≥ 2, LDL-C ≥ 1.9 mmol/L, unstable angina, left anterior descending artery, diameter of stent ≥ 3 mm, length of stent > 20 mm
Wang, 2020 [38]	230	BMS, DES	12	Type D personality, low fruit intake, low vegetable intake
Liang, 2020 [39]	2443	DES	12	S100A12 level
Zhang, 2020 [40]	230	DES	12	Morisky score, anger, low physical activity, low folate intake, low Vitamin C ingestion
Tang, 2019 [41]	2338	BMS, DES	12	the number of stents
Sun, 2019 [42]	226	DES	34	Higher MCV, higher ALT, number of PCI vessels
Zhao, 2019 [43]	358	DES	12	stent diameter, Higher HbA1c
Cheng, 2019 [44]	1132	BMS, DES	12	hs-CRP levels, postoperative homocysteine levels, history of diabetes, coronary bifurcation lesions stent length
Baktashian, 2019 [45]	104	DES	12	Diabetes mellitus, stent type, serum hs-CRP, FBG, serum TG
Wang, 2018 [46]	368	DES	12	VLDL-C, UA, SYNTAX score, history of PCI

Table 1 (continued)

Author, year	No. population	Type of stent	Time after PCI (months)	Risk profile
Hu, 2018 [47]	5232	BMS, DES	36	higher PDW
Wu, 2018 [48]	62	DES	12	post-procedural visfatin level, type 2 diabetes, reference vessel diameter, stent length, stent diameter
Wang, 2018 [49]	173	DES	24	Type D personality
Qin, 2017 [50]	1206	DES	24	Higher VLDL-C
Kurtul, 2018 [51]	358	DES	12	CHA2DS2-VASc score, total stent length, stent diameter, hs-CRP
Zheng, 2017 [52]	96	DES	12	BMP-2 level, diabetes, stent length, and stent diameter
Watanabe, 2017 [53]	131	DES	18	early generation DES, smaller stent, worse left ventricular contractility
Koiwaya, 2017 [54]	157	DES	12	smaller acute gain after initial ballooning, geographic mismatch between PCB position and initial ballooning, use of percutaneous transluminal coronary rotational atherectomy (PTCRA)
Yilmaz, 2017 [55]	1350	BMS	12	diabetes, hyperlipidemia, smoking, stent length, CHA2DS2-VASc score
Zhou, 2016 [56]	364	BMS, DES	12	epicardial adipose tissue volume
Tesche, 2016 [57]	74	DES	84	Calcified plaque volumes, plaque burden, remodeling index, lesion length
Murat, 2017 [58]	273	BMS	12	Lymphocyte-to-Monocyte Ratio, high-sensitivity C-reactive protein, stent diameter, stent length
Wihanda, 2015 [59]	289	BMS, DES	12	stent-type, stent length, bifurcation lesions, smoking, vascular diameter, hypertension, diabetes mellitus
Celik, 2016 [60]	341	BMS	12	Lower serum albumin, stent diameter, reason for stent implantation, body mass index
Bolca, 2015 [61]	404	DES	14	male sex, stent length, admission NLRs, white blood cells, and neutrophil counts
Park, 2015 [62]	595	DES	36	the reference vessel diameter, low-density lipoprotein cholesterol, total lesion length, Lp(a) ≥ 50 mg/dL
Yılmaz, 2015 [63]	675	BMS	12	platelet-to-lymphocyte ratio, serum C-reactive protein, smoking, diabetes mellitus, high-density lipoprotein, stent length
Zhao, 2015 [64]	529	DES	17	insulin resistance
Demyanets, 2014 [65]	387	BMS, DES	12	Serum IL-33 serum level
Shi, 2014 [66]	210	DES	12	Non-alcoholic fatty liver disease
Yildiz, 2014 [67]	131	DES	12	diabetes mellitus, stent length, preprocedural RDW, current smoking
Zhao, 2013 [68]	145	DES	11	serum total bilirubin, hs-CRP, Cystatin C
Aoyama, 2012 [69]	74	DES	12	chronic kidney disease
Lupi, 2012 [70]	267	BMS, DES	6	Higher fibrinogen levels
Munk, 2011 [71]	100	DES	18	flow-mediated vasodilation
Kuwano, 2011 [72]	1076	BMS, DES	12	Higher serum total bilirubin
Li, 2011 [73]	210	BMS, DES	12	Higher serum sLOX-1 levels
Zurakowski, 2009 [74]	73	BMS	12	serum CRP, IL-6, fasting glucose, lower IL-10
Kitta, 2008 [75]	148	BMS	12	low adiponectin levels
Takamori, 2004 [76]	166	DES	6	High plasma heparin cofactor II activity

all 67 studies yielded good quality and none of the citations was determined to have a high risk of bias therefore the pooled results should be persuasive. In total, 40,789 patients were assessed and scheduled for primary stenting for coronary artery disease and followed up for 6 to 36 months after the procedure for assessing the occurrence of stent restenosis and its main determinants. The predictors for this event might be categorized as the four subgroups including (1) patient-based parameters including history of diabetes mellitus, hypertension, hyperlipidemia, smoking, history of tenting, chronic renal failure, history of non-alcoholic fatty liver disease, higher age, medical history of COPD, history of PCI, higher body mass index, low physical activity, Type D personality,

Table 2 The genes, polymorphisms, and miRNAs related to stent restenosis

Author, year	Type of Study	miRNA	Targeted genes	Gene polymorphism
Song, 2022 [77]	Integrated microarray	hsa-miR-139-5p hsa-miR-324-5p hsa-miR-513a-5p hsa-miR-513a-5p hsa-miR-525-5p hsa-miR-548b-5p hsa-miR-1253	JUN SP1 RAB14 RBBP5 IGF1R PTPN1 DCAF10	
Chen, 2022 [78]	Integrated microarray		CLTA CAT STAT5A CD300A CA1 NCF2 HBQ1 AHSP SLC4A1 EPB42	
Abdelaziz, 2022 [79]	RT-PCR		ADRβ2 CDKN1B	rs1042713 rs36228499
Yang, 2022 [80]	RT-PCR		M2BP	
Liu, 2021 [81]	RT-PCR		CAMLG GALNT2 C11orf84 THOC5 SAMD11	rs12657663 rs2273970 rs643634 rs737976 rs9988179
Qiu, 2021 [82]	Bioinformatics analysis	hsa-miR-126-3p	PIK3R2	
Carretero, 2021 [83]	Integrated microarray	hsa-miR-30b-5p	62 genes related to vascular remodeling and fibrosis	
Maheronnaghsh, 2021 [84]	Integrated microarray	hsa-miR-152-3p		
Guan, 2018 [85]	Integrated microarray	hsa-miR − 1 hsa-miR − 21		
Zhou, 2017 [86]	RT-PCR		SOCS1 (gene promoter methylation)	
Bagyura, 2017 [87]	RT-PCR		VEGF	rs2010963 rs6999447
Zhu, 2017 [88]	DNA sequencing		A1166C	
He, 2017 [89]	RT-PCR		HMGB2	
Pleva, 2015 [90]	RT-PCR		BCHE	rs1803274
Li, 2015 [91]	RFLP assay		A1166C	
Nozari, 2015 [92]	RT-PCR		CYP2C19	CYP2C19*2
Liu, 2013 [93]	RT-PCR		IL-18	-137G/C
Gao, 2013 [94]	RFLP assay		IL-6	-572 C/G
Gao, 2011 [95]	RFLP assay		IL-10	-592 C/A
Vogiatzi, 2011 [96]	RFLP assay		IL-8	-251 A/T 781 C/T
Vogiatzi, 2009 [97]	RFLP assay		RANTES	-403G/A
Shah, 2008 [98]	RFLP assay		ALOX5AP	RS17222814 RS17216473 RS10507391
Katsaros, 2008 [99]	IHC		SERPINE1	
Wijpkema, 2006 [100]	RT-PCR		AGTR1	1166 A/C
Monraats, 2005 [101]	RT-PCR		FGB	-455G/A

anger, and some nutritional habits including lower folate intake, low fruit intake, low vegetable intake, and low vitamin C ingestion; (2) stent-based parameters including type of stent (BMS versus DES), lower stent diameter, longer stent, (3) coronary lesion-based parameters including two target lesions, Gensini score, TIMI score, coronary artery calcium score, coronary artery diffuse disease, peripheral vascular lesions, bifurcation lesion, CHA2DS2-VASc score, calcified plaque volumes, plaque burden, remodeling index, multiple stenting, stents in left

anterior descending artery (LAD), and SYNTAX score; and (4) laboratory-based parameters including Higher HbA1c level, higher HsCRP level, raised ApoB, MCV and MCH values, higher neutrophil to lymphocyte ratio, higher apoA-I, higher Homocysteine, higher IgE level, increased lipoprotein-associated phospholipase A2 (Lp-PLA2) and IL-6 levels, higher monocyte count, raised creatinine, raised blood uric acid, lower high-density lipoprotein, higher S100A12 level, higher postoperative homocysteine level, higher VLDL-C, higher PDW, higher BMP-2 level, higher lymphocyte-to-Monocyte Ratio, lower serum albumin, higher white blood cell and neutrophil counts, higher lipoprotein A, higher serum IL-33 serum level, higher serum total bilirubin, higher serum Cystatin C, higher fibrinogen levels, higher serum sLOX-1 level, higher serum IL-6, lower serum IL-10, lower adiponectin levels, higher plasma heparin cofactor II activity, and insulin resistance (Table 1).

Findings of bioinformatic study
By reviewing 25 articles on genes involved we uncovered 42 genes that have been described to be involved in such a phenomenon. A complex network of genes, gene-related polymorphisms, and microRNAs were shown to be involved in increasing the likelihood of stent restenosis (Table 2). According to the literature, the up-regulation of some genes including JUN, SP1, RAB14, RBBP5, IGF1R, PTPN1, DCAF10, CLTA, CAT, STAT5A, CD300A, CA1, NCF2, HBQ1, AHSP, SLC4A1, EPB42, ADRβ2, CDKN1B, M2BP, CAMLG, GALNT2, C11orf84, THOC5, SAMD11, PIK3R2 SOCS1, VEGF, A1166C, HMGB2, BCHE, A1166C, CYP2C19, RANTES, ALOX5AP, SERPINE1, AGTR1, and FGB have been indicated by using different gene assessment techniques. Also, the predictive roles of the expression of some genes related to interleukin production (IL-18, IL-6, IL-10, and IL-8) have been highlighted. To determine the central role of the powerful genes related to stent restenosis, functional interactions and functional relationships between spike genes were evaluated by applying the Genemania network and Cytoscapre analytical software. As shown in Fig. 1, multiple pathways and gene-gene interactions seem to play a role in stent restenosis. In this context, many genes could interact with multi-pathway genes, but prominent gene interaction included co-expression (58.03%) followed by genetic interactions (13.28%). In this context, the main pathways activated in the background of this cluster based on FDR values were receptor signaling pathways via STAT with FDR value of 6.77e-8 (relevant genes of VEGFA, SOCS1, CCL5, IL10RA, IL18, STAT5A, and CD300A), cellular response to molecule of bacterial origin with FDR value of 6.77e-8 (relevant genes of HMGB2, IL1B, SERPINE1, CCL5, IL6, IL18, CXCL3, CXCL8) and response to lipopolysaccharide with FDR

value of 6.77e-8 (relevant genes of HMGB2, IL1B, SERPINE1, CCL5, IL6, IL18, CXCL3, CXCL8). Along with gene polymorphisms and changing gene expression, some microRNAs were also assessed influencing genes and mRNA expressions that the studied microRNAs were shown in Table 1. In this regard, the special place of miR-139-5p, miR-324-5p, miR-513a-5p, miR-513a-5p, miR-525-5p, miR-548b-5p and miR-1253 (targeting the genes of JUN, SP1, RAB14, RBBP5, IGF1R, PTPN1 and DCAF10 respectively), miR-126-3p (targeting PIK3R2), and miR-30b-5p (targeting 62 genes related to vascular remodeling and fibrosis) has been shown.

Discussion
Stent re-stenosis after primary stenting in patients with acute coronary syndrome is an uncommon but multifactorial phenomenon. This phenomenon is created and expanded as a result of the interaction of a set of clinical and laboratory factors as well as genetic predisposing factors. Obviously, due to the multifactorial nature of this incident, it will not be possible to accurately determine its prevalence. On the other hand, for the same reasons, it will not be possible to accurately estimate the occurrence of such an event. In this regard and based on a review of the literature, a wide set of background factors are involved in the occurrence of stent restenosis. Among the clinical factors, the presence of classic underlying risk factors of cardiovascular diseases has been completely predictable, in such a way that the risk of stent re-stenosis is higher in elderly patients, obese patients, hypertensive and diabetic patients, patients with hyperlipidemia, as well as patients with The history of chronic renal failure as well as the history of ischemic heart disease have been completely predictable. Also, among the laboratory risk factors, a special place can be given to inflammatory markers, because the occurrence of atherosclerosis is also the result of the interaction between underlying risk factors and inflammatory factors, and such a process can also be predicted in the case of stent re-stenosis. The basis of the occurrence of such a complication has a strong link with the activation of the inflammatory cascade. Additionally, the genomic polymorphisms have also provided the basis for the emergence and spread of stent restenosis. In this direction and during the last two decades, efforts have been made to identify the genetic factors related to the occurrence of this event using various genetic techniques, to identify types of gene polymorphisms, changes in the expression of various genes, and also to identify microRNAs related to it, which play an important role in the changes of the targeted genes involved. There is growing evidence of genetic contribution to vascular remodeling and ultimately coronary calcification and atherosclerosis through extracellular matrix changes and also MicroRNAs involvement in

endothelial cell and vascular smooth muscle dysfunction in diabetic patients which makes it an interesting topic to evaluate in the context of in-stent restenosis.

Conclusions

Therefore, it seems that the incidence of stent re-stenosis will be the result of a complex interaction of clinical risk factors, laboratory factors mostly related to the activation of inflammatory processes, and a complex network of gene-to-gene interactions, and therefore, it will not be possible to indicate on only one or a limited number of predisposing factors. However, special attention to some background factors can be considered. For example, identifying and tracking increased expression or discovering polymorphisms related to genes encoding various types of inflammatory interleukins can provide a way for early diagnosis and prevention of this complication. It is also obvious that controlling the traditional risk factors of cardiovascular diseases will be successful in preventing the occurrence of such a complication.

Abbreviations

PCI	Percutaneous coronary intervention
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis
BMS	Bare-metal stent
DES	Drug-eluting stent

Author contributions
F.S and S.B analyzed and interpreted the data. SH.A and A.GH was a major contributor in writing the manuscript. M.N revised the manuscript and supervised All the above from beginning to end. Authors read and approved the final manuscript.

Data availability
All data generated or analyzed during this study are included in this published article, and further detailed ones are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
¹Cardiovascular Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

References
1. World Health Organization. Cardiovascular diseases. http://www.who.int/mediacentre/factsheets/fs317/en/. Accessed 9 February 2016.
2. Tardif J-C. Coronary artery disease in 2010. Eur Heart J. 2010;12(suppl C):C2–10. https://doi.org/10.1093/eurheartj/suq014. [CrossRef] [Google Scholar].
3. Medical statistics [In Russian]. http://www.medinfo.kz/medstat.jsp. Accessed 9 February 2016.
4. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. N Engl J Med. 1987;316(12):701–6. [PubMed] [CrossRef] [Google Scholar].
5. Fischman D, Leon M, Baim D, Schatz R, Savage M, Penn I, Detre K, Veltri L, Ricci D, Nobuyoshi M, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. Stent Restenosis Study investigators. N Engl J Med. 1994;331(8):496–501. [PubMed] [CrossRef] [Google Scholar].
6. Spertus J, Nerella R, Kettlekamp R, House J, Marso S, Borkon A, Rumsfeld J. Risk of restenosis and health status outcomes for patients undergoing percutaneous coronary intervention versus coronary artery bypass graft surgery. Circulation. 2005;111(6):768–73. [PubMed] [CrossRef] [Google Scholar].
7. Otsuki S, Sabate M. Drug-eluting stents and acute myocardial infarction: a lethal combination or friends? World J Cardiol. 2014;6(9):929–38. https://doi.org/10.4330/wjc.v6.i9.929. [PMC free article] [PubMed] [CrossRef] [Google Scholar].
8. Jukema J, Verschuren J, Ahmed T, Quax P. Restenosis after PCI. Part 1: pathophysiology and risk factors. Nat Rev Cardiol. 2011;9(1):53–62. https://doi.org/10.1038/nrcardio.2011.132. [PubMed] [CrossRef] [Google Scholar].
9. Sheikhvatan M, Chaichian S, Moazzami B. A systematic review and Bioinformatics Study on genes and micro-RNAs involving the Transformation of endometriosis into Ovarian Cancer. Microrna. 2020;9(2):101–11. https://doi.org/10.2174/2211536608666190917152104.
10. Xiao Long Lin 1, Qiu Yu Li 1, Dong Hui Zhao 1, Jing Hua Liu 1, Qian Fan 1. Serum glycated albumin is associated with in-stent restenosis in patients with acute coronary syndrome after percutaneous coronary intervention with drug-eluting stents: An observational study. Front Cardiovasc Med. 2022;9:943185. https://doi.org/10.3389/fcvm.2022.943185. eCollection 2022.
11. Qiang Feng 1, Zhao Y 2, Wang H 1, Zhao J 2, Wang X. 2, Jianping Shi 1. A predictive model involving serum uric acid, C-reactive protein, diabetes, hypercholesteremia, and multiple lesions for restenosis risk in everolimus-eluting stent-treated coronary heart disease patients. Front Cardiovasc Med. 2022;9:857922. https://doi.org/10.3389/fcvm.2022.857922. eCollection 2022.
12. Wang J. 1, Yuchun Yang 1, Lei Zhang 1, Pengyi He 1, Huyati Mu 1. Predictors of Stent Restenosis in Han and Uygur Patients with Coronary Heart Disease after PCI in the Xinjiang Region. Cardiol Res Pract. 2022;2022:7845108. https://doi.org/10.1155/2022/7845108. eCollection 2022.
13. Gábor Csató 1, Nóra Erdei 1, Beatrix Ványai 2, Tímea Balla 1, Dániel Czuriga 1, Zoltán Csanádi 1, Zsolt Koszegi 1, István Édes 1, Gábor Tamás Szabó 1. Predictors of restenosis following percutaneous coronary stent implantation: The role of trimetazidine therapy. Front Cardiovasc Med. 2022;9:873899. https://doi.org/10.3389/fcvm.2022.873899. eCollection 2022.
14. Xin W. # 1, Min Zhang # 2, Jie Cheng 3, Hua Zhou 4. Association of serum apoA-I with in-stent restenosis in coronary heart disease. BMC Cardiovasc Disord. 2022;22(1):355. https://doi.org/10.1186/s12872-022-02762-y.
15. Ping Wang YK 2, Liu Y 2, Zhang Y 3, Gao H, 2, Qilin Ma 4. Levels of plasma Quaking and cyclooxygenase-2 predict in-stent restenosis in patients with coronary artery disease after percutaneous coronary intervention. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2022;47(6):739–747. https://doi.org/10.11817/j.issn.1672-7347.2022.210716.
16. Jing Z. 1, Dayang Chai 1, Yuxiang Dai 2, Aichao Wang 1, Ting Yan 3, Shu Lu 1. Predictive Value Analysis of in-Stent Restenosis Within Three Years in Older Acute Coronary Syndrome Patients: A Two-Center Retrospective Study. Clin Appl Thromb Hemost. 2022 Jan-Dec;28:10760296221107888. https://doi.org/10.1177/10760296221107888.
17. Jiqiang, Guo. 1 2 3, Ying Gao 1 2 3, Mohammad Ahmed 4, Pengfei Dong 4, Yuping Gao 2 3, Zhihua Gong 2 3, Jinwen Liu 2 3, Yajie Mao 2 3, Zhijie Yue 2 3, Qingli Zheng 1, Jiansheng Li 2 3, Jianrong Rong 2 3, Yongnian Zhou 2 3, Meiwen An 1, Linxia Gu 4, Jin Zhang 2. Serum homocysteine level predictive capability for severity of Restenosis Post Percutaneous Coronary intervention. Front Pharmacol. 2022;13:816059. https://doi.org/10.3389/fphar.2022.816059. eCollection 2022.
18. Ming Yi 1 2 3, Xu W-HT. 2, Xiao Ke 1 2, Qiang Liu 2 4. Investigation Into the Risk Factors Related to In-stent Restenosis in Elderly Patients With Coronary Heart Disease and Type 2 Diabetes Within 2 Years After the First Drug-Eluting

Stent Implantation. Front Cardiovasc Med. 2022;9:837330. https://doi.org/10.3389/fcvm.2022.837330. eCollection 2022.

19. Jingmeng Liu 1, Qiujing Chen 1 2. Association of Circulating IgE and CML Levels with In-Stent Restenosis in Type 2 Diabetic Patients with Stable Coronary Artery Disease. J Cardiovasc Dev Dis. 2022;9(5):157. https://doi.org/10.3390/jcdd9050157. Lin Lu 1 2, Qi Jin 1, Yangyang Bao 1, Tianyou Ling 1, Changjian Lin 1, Fenghua Ding 1, Xiaoqun Wang 1, Weifeng Shen 1 2, Ying Shen 1, Yang Dai 1 2, Liqun Wu 1.

20. Chen D 1, Lu XX. 2, Shengli Chen 1, Sunmei Lin 1. Predictive Value of Perioperative Cytokine Levels on the Risk for In-Stent Restenosis in Acute Myocardial Infarction Patients. Contrast Media Mol Imaging. 2022;2022:7832564. https://doi.org/10.1155/2022/7832564. eCollection 2022.

21. Li S. 1, Hong Qiu 2, Zhaorong Lin 1, Lin Fan 1, Yongzhe Guo 1, Yujie Zhang 1, Lianglong Chen 1. The Early Predictive Value of Circulating Monocytes and Eosinophils in Coronary DES Restenosis. Front Cardiovasc Med. 2022;9:764622. https://doi.org/10.3389/fcvm.2022.764622. eCollection 2022.

22. Yinhua Luo # 1, Ni Tan # 2, Jingbo Zhao 3, Yuanhong Li 3. A Nomogram for Predicting In-Stent Restenosis Risk in Patients Undergoing Percutaneous Coronary Intervention: A Population-Based Analysis. Int J Gen Med. 2022;15:2451–2461. https://doi.org/10.2147/IJGM.S357250. eCollection 2022.

23. Yinhua L. # 1, Shengyu Cui # 2, Changjiang Zhang 2, Rui Huang 2, Jinbo Zhao 3, Ke Su 3, Dan Luo 3, Yuanhong Li 3. Prognostic Role of Fasting Remnant Cholesterol with In-Stent Restenosis After Drug-Eluting Stent Implantation. Int J Gen Med. 2022;15:1733–1742. https://doi.org/10.2147/IJGM.S348148. eCollection 2022.

24. Zhang R 1, Tao Z. 1, Jing Gong 1, Zhenjun Ji 1, Mingming Yang 1, Genshan Ma 1, Yongjun Li 1. Albumin to globulin ratio was associated with in-stent restenosis and revascularization events after percutaneous coronary intervention. Clin Transl Sci. 2022;15(5):1187–1195. https://doi.org/10.1111/cts.13236. Epub 2022 Feb 27.

25. Bo-Wen Chen 1, Jia-Jing Liu 1, Jun-Hui Xing 1, Heng-Dao Liu 1, Yu-Zhen Wei 1, Xiao-Fei Xue 1, He-Ping Gu 1, Hai-Long Tao 1. Analysis of the Correlation Between the Ratio of Monocytes to High-Density Lipoprotein Cholesterol and in-Stent Restenosis in Patients with Premature Coronary Heart Disease. Clin Appl Thromb Hemost. 2022 Jan-Dec;28:10760296221079334. https://doi.org/10.1177/10760296221079334.

26. Xiaowen Z 1, Xu K, Yang X, Yang W, Zhang W, Jiang Y, Zhang Y, Qiu X, Shi H, Jiang L, Shen L, Ben He. Association between coronary artery calcium score and in-stent restenosis after drug-eluting stent implantation. Coron Artery Dis. 2022;33(4):284–94. https://doi.org/10.1097/MCA.0000000000001124. Epub 2022 Jan 25.

27. Mingrui Li. # 1 2, Jingyuan Hou # 3 4, Xiaodong Gu 3 4, Ruiqiang Weng 3 4, Zhixiong Zhong 5, Sudong Liu 6 7. Incidence and risk factors of in-stent restenosis after percutaneous coronary intervention in patients from southern China. Eur J Med Res. 2022;27(1):12. https://doi.org/10.1186/s40001-022-00640-z.

28. Huilin H. 1, Shijun Wang 1, Guanmin Tang 1, Changlin Zhai 1, Liang Shen 2. Impact of anemia on in-stent restenosis after percutaneous coronary intervention. BMC Cardiovasc Disord. 2021;21(1):548. https://doi.org/10.1186/s12872-021-02355-1.

29. Masayuki Yoshimura 1 2. Seiji Umemoto 3 4, Reo Kawano 3, Mitsuyuki Hiromoto 5, Michio Yamada 6, Tatsuhiro Fujimura 1, Masakazu Tanaka 7, Tomoko Nao 8, Toshiro Miura 9, Masafumi Yano 1. Non-fasting Hypertriglyceridemia as an independent risk factor for coronary In-Stent restenosis after primary Bare Metal Stent Implantation in patients with coronary artery disease. Int Heart J. 2021;62(5):970–9. https://doi.org/10.1536/ihj.21-015.

30. Min-Tao G. # 1, Bing Zhu # 2, Xiao-Cui Chen 1, Fen Liu 1, Xiang Xie 2, Xiao-Ming Gao 2, Xiang Ma 2, Zhen-Yan Fu 2, Yi-Tong Ma 3 4, Bang-Dang Chen 5 6. A prediction model based on platelet parameters, lipid levels, and angiographic characteristics to predict in-stent restenosis in coronary artery disease patients implanted with drug-eluting stents. Lipids Health Dis. 2021;20(1):118. https://doi.org/10.1186/s12944-021-01553-2.

31. Ling Zhang YW # 1, Zhang Z 2. Hongyuan Liang 1, Liang Wu 1, Liang Ni 1, Guiju Gao 1, Di Yang 1, Hongxin Zhao 3, Jiang Xiao 4. Risk factors of in-stent restenosis among coronary artery disease patients with syphilis undergoing percutaneous coronary intervention: a retrospective study. BMC Cardiovasc Disord. 2021;21(1):438. https://doi.org/10.1186/s12872-021-02245-6.

32. Wenbo H. # 1 2 3, Changwu Xu # 1 2 3, Xiaoying Wang 4, Jiyong Lei 1 2 3, Qinfang Qiu 1 2 3, Yingying Hu 1 2 3, Da Luo 5 6 7. Development and validation of a risk prediction nomogram for in-stent restenosis in patients undergoing percutaneous coronary intervention. BMC Cardiovasc Disord. 2021;21(1):435. https://doi.org/10.1186/s12872-021-02255-4.

33. Dan-Mihai. Alexandrescu 1 2, Ovidiu Mitu 1, Irina Iuliana Costache 1, Liviu Macovei 1, Ivona Mitu 3, Anca Alexandrescu 2, Catalina Arsenescu Georgescu 1. Risk factors associated with intra-stent restenosis after percutaneous coronary intervention. Exp Ther Med. 2021;22(4):1141. https://doi.org/10.3892/etm.2021.10575. Epub 2021 Aug 9.

34. Hsin-Fu Lee 1, Yu-Wen Cheng 2, Jian-Rong Peng 3, Chiu-Yi Hsu 4, Chia-Hung Yang 3, Yi-Hsin Chan 5, Pao-Hsien Chu 6. Impact of chronic kidney disease on long-term outcomes for coronary in-stent restenosis after drug-coated balloon angioplasty. J Cardiol. 2021;78(6):564–570. doi: 10.1016/j.jjcc.2021.08.010. Epub 2021 Aug 26.

35. Guohua Sheng 1, Juan Zhou 2, Chi Zhang 3, Caijuan Wu 4, Kairong Huang 5, Xiaotong Qin 6, Jie Wu 4. Relationship between Lp-PLA2 and in-stent restenosis after coronary stenting: a 3-year follow-up study. Scott Med J. 2021;66(4):178–185. doi: 10.1177/00369330211034809. Epub 2021 Jul 28.

36. Praveen KG, 1, Jayaram Balachander 2. Predictor of in-stent restenosis in patients with drug-eluting stent (PRIDE)- a retrospective cohort study. Clin Investig Arterioscler. 2021 Jul-Aug;33(4):184–194. doi: 10.1016/j.arteri.2020.11.003. Epub 2021 Feb 20.

37. Pengfei Wang H, Qiao. 2, RuiJuan Wang 3, Ruitian Hou 3, Jingtao Guo 2. The characteristics and risk factors of in-stent restenosis in patients with percutaneous coronary intervention: what can we do. BMC Cardiovasc Disord. 2020;20(1):510. https://doi.org/10.1186/s12872-020-01798-2.

38. Yini Wang SZ 2, Zhang G. 3, Bo Yu 4, Xueqin Gao 4, Zhenguo Dai 4, Xiuxian Yang 2, Xiaohui Qiu 2, Zhengxue Qiao 2, Jiawei Zhou 2, Ping Lin 5, Deyu Fang 6, Yanjie Yang 7. Association between type D personality and in-stent restenosis in patients treated with percutaneous coronary intervention: A mediation analysis of dietary patterns. J Psychosom Res. 2020;138:110244. https://doi.org/10.1016/j.jpsychores.2020.110244. Epub 2020 Sep 10.

39. Hengyi Liang 1. Yuqi Cui 1 2, Haoran Bu 1, Hang Liu 3, Pengcheng Yan 1, Lianqun Cui 1, Liming Chen 1. Value of S100A12 in predicting in-stent restenosis in patients with coronary drug-eluting stent implantation. Exp Ther Med. 2020;20(1):211–8. https://doi.org/10.3892/etm.2020.8721. Epub 2020 May 6.

40. Zhang G 1, Li S, Lin P, Chen Y. An analysis of factors related to the development of in-stent restenosis after percutaneous coronary intervention. Med (Baltim). 2020;99(5):e18915. https://doi.org/10.1097/MD.0000000000018915.

41. Cui LT 1. The number of stents was an independent risk of stent restenosis in patients undergoing percutaneous coronary intervention. Med (Baltim). 2019;2(50):e18312. https://doi.org/10.1097/MD.0000000000018312. Dan-Ping Liu 1, Ying-Ying Fu 1.

42. Lin S. 1, Chunyan Zhang 1, Yinghui Ju 1, Bin Tang 2, Meixiu Gu 1, Baishen Pan 1, Wei Guo 1, Beili Wang 1. Mean Corpuscular Volume Predicts In-Stent Restenosis Risk for Stable Coronary Artery Disease Patients Receiving Elective Percutaneous Coronary Intervention. Med Sci Monit. 2019;25:3976–3982. https://doi.org/10.12659/MSM.914654.

43. Sheng Gang Zhao 1 2, Xu JJ. 2, Zhen Hao Tao 3, Lei Jin 4, Qin Liu 3, Wen Yue Zheng 5, Li Qin Jiang 2, Ning Fu Wang 1. CHA2DS2-Vasc score and CHA2DS2-Vasc-HS score are poor predictors of in-stent restenosis among patients with coronary drug-eluting stents. J Int Med Res. 2019;47(6):2533–2544. https://doi.org/10.1177/0300060519841836. Epub 2019 Apr 30.

44. Gong Cheng 1 2, Feng-Jun. Factors Influencing Stent Restenosis After Percutaneous Coronary Intervention in Patients with Coronary Heart Disease: A Clinical Trial Based on 1-Year Follow-Up. Med Sci Monit. 2019;25:240–7. https://doi.org/10.12659/MSM.908692. Chang 1, Yi Wang 1, Peng-Hua You 1, Hai-Chao Chen 1, Wen-Qi Han 1, Jun-Wei Wang 1, Ni-Er Zhong 1, Zhi-Qian Min 3.

45. Mojtaba Baktashian 1, Sara Saffar Soflaei 2, Negin Kosari 3, Mansoor Salehi 4, Alireza Khosravi 5, Maliheh Ahmadinejad 6, Mohsen Moohebati 7, Mahmood Ebrahimi 8, Farzad Rahmani 9, Ramin Khameneh-Bagheri 10, Mostafa Ahmadi 11, Fatemeh Sadabadi 12, Maryam Tayefi 13, Suzan Bazhdanzadeh 14, Gordon A Ferns 15, Seyed Mohammad Hashemi 16, Alireza Pasdar 17, Majid Ghayour-Mobarhan 18. Association of high level of hs-CRP with in-stent restenosis: A case-control study. Cardiovasc Revasc Med. 2019;20(7):583–587. https://doi.org/10.1016/j.carrev.2018.08.015. Epub 2018 Aug 18.

46. Wang J-L. 1, Zheng Qin 1, Zhi-Jian Wang 1, Dong-Mei Shi 1, Yu-Yang Liu 1, Ying-Xin Zhao 1, Li-Xia Yang 1, Wan-Jun Cheng 1, Yu-Jie Zhou 1. New predictors of in-stent restenosis in patients with diabetes mellitus undergoing percutaneous coronary intervention with drug-eluting stent. J Geriatr Cardiol. 2018;15(2):137–145. https://doi.org/10.11909/j.issn.1671-5411.2018.02.011.

47. Cheng-Ping H. 1, Yu Du 1, Yong Zhu 1, Chao Shi 1, Zheng Qin 1, Ying-Xin Zhao 1. Platelet Distribution Width on Admission Predicts In-Stent Restenosis in Patients with Coronary Artery Disease and Type 2 Diabetes Mellitus

Treated with Percutaneous Coronary Intervention. Chin Med J (Engl). 2018;131(7):757–763. https://doi.org/10.4103/0366-6999.228247.

48. Xie X-AW. 1, Xiu-Qi Li 1, Hui-Ting Wu 1, Xiang Wang 2. The value of serum visfatin in predicting in-stent restenosis of drug-eluting stents. Clin Chim Acta. 2018;479:20–24. https://doi.org/10.1016/j.cca.2018.01.004. Epub 2018 Jan 3.

49. Yini Wang G 1, Liu X, Gao Z, Zhao L, Li W, Chen H, Tao B, Yu, Ping Lin. Prognostic value of type D personality for In-stent restenosis in coronary artery disease patients treated with drug-eluting stent. Psychosom Med. 2018;80(1):95–102. https://doi.org/10.1097/PSY.0000000000000532.

50. Zheng Qin 1, Fang-Wu Zheng 2, Chuang Zeng 3, Kuo Zhou 1, Yu Geng 1, Jian-Long Wang 1, Yue-Ping Li 1, Qing-Wei Ji 1, Yu-Jie Zhou 4. Elevated Levels of Very Low-density Lipoprotein Cholesterol Independently Associated with In-stent Restenosis in Diabetic Patients after Drug-eluting Stent Implantation. Chin Med J (Engl). 2017;130(19):2326–2332. https://doi.org/10.4103/0366-6999.213575.

51. Alparslan Kurtul 1. Usefulness of the CHA2DS2-VASc score in Predicting In-Stent restenosis among patients undergoing revascularization with Bare-Metal stents. Clin Appl Thromb Hemost. 2018;24(4):589–95. Epub 2017 Jul 4.

52. Yang W-PZ. 2, Li-Xiao Su 3, Yu Ning 4, Wan-Wan Wen 4, Man-Kun Xin 4, Xin Zhao 4, Ming Zhang 5. Association between plasma BMP-2 and in-stent restenosis in patients with coronary artery disease. Clin Chim Acta. 2017;471:150–153. https://doi.org/10.1016/j.cca.2017.05.033. Epub 2017 May 27.

53. Yusuke Watanabe 1, Kensuke Takagi 1. Independent predictors of in-stent restenosis after drug-eluting stent implantation for ostial right coronary artery lesions. Int J Cardiol. 2017;240:108–13. https://doi.org/10.1016/j.ijcard.2017.04.083. Epub 2017 Apr 26. Toru Naganuma 1, Hiroyoshi Kawamoto 1, Yusuke Fujino 1, Hisaaki Ishiguro 1, Satoko Tahara 1, Naoyuki Kurita 1, Koji Hosawa 1, Shotaro Nakamura 1, Sunao Nakamura 2.

54. Hiroshi Koiwaya 1. Predictors of Recurrent In-Stent Restenosis After Paclitaxel-Coated Balloon Angioplasty. Circ J. 2017;81(9):1286–92. https://doi.org/10.1253/circj.CJ-17-0095. Epub 2017 Apr 28. Nozomi Watanabe 1, Nehiro Kuriyama 1, Shun Nishino 1, Kenji Ogata 1, Toshiyuki Kimura 1, Tatsuya Nakama 1, Hirohide Matsuura 1, Makoto Furugen 1, Yoshisato Shibata 1.

55. Samet Yilmaz 1. Mehmet Kadri Akboga 2, Dursun Aras 2, Serkan Topaloglu 2. Evaluation of the predictive value of CHA2DS2-VASc score for In-Stent restenosis. Angiology. 2018;69(1):38–42. Epub 2017 Mar 27.

56. Ying Zhou 1, Zhang H-W 2, Chen FT. 3, Tian-Wen Han 2, Ya-Hang Tan 4, Jia Zhou 5, Tao Zhang 2, Jing Jing 2, Yun-Dai Chen 2. Influence of increased epicardial adipose tissue volume on 1-year in-stent restenosis in patients who received coronary stent implantation. J Geriatr Cardiol. 2016;13(9):768–775. https://doi.org/10.11909/j.issn.1671-5411.2016.09.012.

57. Christian Tesche 1, Carlo N, De Cecco R, Vliegenthart M, Duguay 4 AC. Stubenrauch 4, Russell D Rosenberg 5, Akos Varga-Szemes 4, Richard R Bayer 2nd 5, Junjie Yang 6, Ullrich Ebersberger 1, Moritz Baquet 7, David Jochheim 7, Ellen Hoffmann 8, Daniel H Steinberg 9, Salvatore A Chiaramida 9, U Joseph Schoepf 10. Coronary CT angiography-derived quantitative markers for predicting in-stent restenosis. J Cardiovasc Comput Tomogr. 2016 Sep-Oct;10(5):377 – 83. https://doi.org/10.1016/j.jcct.2016.07.005. Epub 2016 Jul 6.

58. Sani Namik Murat 1. The Relationship Between Lymphocyte-to-Monocyte Ratio and Bare-Metal Stent In-Stent Restenosis in Patients With Stable Coronary Artery Disease. Clin Appl Thromb Hemost. 2017;23(3):235–40. doi: 10.1177/1076029615627340. Epub 2016 Jul 9. Mikail Yarlioglues 1, Ibrahim Etem Celik 1, Alparslan Kurtul 1, Mustafa Duran 1, Alparslan Kilic 1, Fatih Oksuz 1.

59. Dedi Wihanda 1, Alwi I, Yamin M, Shatri H, Mudjaddid E. Factors Associated with In-stent restenosis in patients following percutaneous coronary intervention. Acta Med Indones. 2015;47(3):209–15.

60. Ibrahim Etem Celik 1, Mikail Yarlioglues 2, Alparslan Kurtul 2, Mustafa Duran 2, Cemal Koseoglu 2, Fatih Oksuz 2, Ozlem Aksoy 2, Sani Namik Murat 2. Preprocedural Albumin Levels and Risk of In-Stent Restenosis After Coronary Stenting With Bare-Metal Stent. Angiology. 2016;67(5):478 – 83. https://doi.org/10.1177/0003319715598084. Epub 2015 Aug 3.

61. Osman Bolca 1, Güngör Bariş, Özcan KS, Fatma Ö, Karadeniz A, Sungur B, Köroğlu N, Bakhshyaliyev NS, Yelgeç. Baran Karataş, Göktürk İpek, Hale Yilmaz, Recep Öztürk. The neutrophil-to-lymphocyte ratio is associated with bare-metal stent restenosis in STEMI patients treated with primary PCI. Coron Artery Dis. 2015;26(5):402–8. https://doi.org/10.1097/MCA.0000000000000254.

62. Choi S-HP 2, Park J-Y. 3, Ung Jeon 1, Hong-Seog Seo 2, Eung-Ju Kim 2, Jin-Oh Na 2, Cheol-Ung Choi 2, Jin-Won Kim 2, Hong-Euy Lim 2, Chang-Gyu Park 2, Dong-Joo Oh 2. Impact of high lipoprotein(a) levels on in-stent restenosis

and long-term clinical outcomes of angina pectoris patients undergoing percutaneous coronary intervention with drug-eluting stents in Asian population. Clin Exp Pharmacol Physiol. 2015;42(6):588 – 95. https://doi.org/10.1111/1440-1681.12396.

63. Samet Yılmaz S, Ünal Cağri, Yayla Özcan, Özeke D, Aras S, Topaloglu. Sınan Aydogdu. Usefulness of the platelet-to-lymphocyte ratio in predicting bare-metal stent restenosis. Scand Cardiovasc J. 2015;49(1):39–44. doi: 10.3109/14017431.2014.989537. Epub 2014 Dec 26.

64. Xu L-PZ, Wang L, Li H, Shao C-L, Gu H-B, Chan S-P, Xu H-F. Xiang-Jun Yang. Influence of insulin resistance on in-stent restenosis in patients undergoing coronary drug-eluting stent implantation after long-term angiographic follow-up. Coron Artery Dis. 2015;26(1):5–10. https://doi.org/10.1097/MCA.0000000000000170.

65. Svitlana Demyanets 1, Jarai IT 2, Katharina M, Katsaros 3. Serdar Farhan 2, Anna Wonnerth 4, Thomas W Weiss 2, Johann Wojta 3, Walter S Speidl 4, Kurt Huber 5. An increase of interleukin-33 serum levels after coronary stent implantation is associated with coronary in-stent restenosis. Cytokine. 2014;67(2):65–70. https://doi.org/10.1016/j.cyto.2014.02.014. Epub 2014 Mar 27.

66. Wu F-L, Liu W-Y, Zhao C-C, Chen C-X, Xie Y-Y, Wu S-J, Lin X-F, Chen Y-P. Danny Ka-Ho Wong, Man-Fung Yuen, Ming-Hua Zheng. Non-alcoholic fatty liver disease and risk of in-stent restenosis after bare metal stenting in native coronary arteries. Mol Biol Rep. 2014;1(7):4713–20. https://doi.org/10.1007/s11033-014-3342-z. Epub 2014 Apr 2.

67. Abdulmelik Yildiz 1, Tekiner F, Karakurt A, Sirin G, Duman D. Preprocedural red blood cell distribution width predicts bare metal stent restenosis. Coron Artery Dis. 2014;25(6):469–73. https://doi.org/10.1097/MCA.0000000000000105.

68. Chunyu Zhao L 1, Yang L, Mao L, Zhong X, Li S, Wei. Cystatin C associates with the prediction of in-stent restenosis among patients receiving stent implantation: results of the 1-year follow-up. Coron Artery Dis. 2013;24(5):357–60. https://doi.org/10.1097/MCA.0b013e328361b3a4.

69. Yutaka Aoyama 1, Hirayama H, Ishii H, Kobayashi K, Ishikawa K, Takigawa M, Nanasato M, Yoshida Y. Toru Aoyama, Daiji Yoshikawa, Tatsuaki Matsubara, Toyoaki Murohara. Impact of chronic kidney disease on a re-percutaneous coronary intervention for sirolimus-eluting stent restenosis. Coron Artery Dis. 2012;23(8):528–32. https://doi.org/10.1097/MCA.0b013e3283599463.

70. Alessandro Lupi 1, Secco GG, Rognoni A, Rossi L, Lazzero M, Nardi F, Rolla R, Bellomo G. Angelo Sante Bongo, Carlo Di Mario. Plasma fibrinogen levels and restenosis after primary percutaneous coronary intervention. J Thromb Thrombolysis. 2012;33(4):308–17. https://doi.org/10.1007/s11239-011-0628-z.

71. Peter Scott Munk 1, Butt N. Alf Inge Larsen. Endothelial dysfunction predicts clinical restenosis after percutaneous coronary intervention. Scand Cardiovasc J. 2011;45(3):139–45. https://doi.org/10.3109/14017431.2011.564646. Epub 2011 Mar 29.

72. Takashi Kuwano 1, Miura S-I, Shirai K, Ike A, Mori K, Shimizu T, Zhang B, Iwata A, Nishikawa H, Kawamura A, Keijiro Saku. Serum levels of bilirubin as an independent predictor of coronary in-stent restenosis: a new look at an old molecule. J Atheroscler Thromb. 2011;18(7):574–83. https://doi.org/10.5551/jat.6643. Epub 2011 Mar 18.

73. Li B 1, Zhang Li-hua, Yang Xin-guo, Liu Y. Xiong-Tao Liu, Yin-Gang Ren. Postprocedural serum sLOX-1 levels are associated with coronary in-stent restenosis in patients with stable coronary artery disease. Coron Artery Dis. 2011;22(4):259–63. https://doi.org/10.1097/MCA.0b013e328344ede9.

74. Aleksander Zurakowski 1, Wojakowski W, Dzielski T, Milewski K. Kinga Gościńska-Bis, Michał Tendera, Paweł Buszman. Plasma levels of C-reactive protein and interleukin-10 predict late coronary in-stent restenosis 6 months after elective stenting. Kardiol Pol. 2009;67(6):623–30.

75. Yoshinobu Kitta 1, Takano H, Nakamura T, Kodama Y, Umetani K, Fujioka D, Saito Y, Kawabata K-I, Obata J-E. Akira Mende, Tsuyoshi Kobayashi, Kiyotaka Kugiyama. Low adiponectin levels predict late in-stent restenosis after bare metal stenting in native coronary arteries. Int J Cardiol. 2008;131(1):78–82. https://doi.org/10.1016/j.ijcard.2007.09.004. Epub 2008 Jan 4.

76. Nobuyuki Takamori 1, Azuma H, Kato M, Hashizume S, Aihara Ken-ichi, Akaike M, Tamura K, Matsumoto T. High plasma heparin cofactor II activity is associated with reduced incidence of in-stent restenosis after percutaneous coronary intervention. Circulation. 2004;109(4):481–6. https://doi.org/10.1161/01.CIR.0000109695.39671.37. Epub 2004 Jan 26.

77. Linghong Song 1, Yufei Feng 1, Feng Tian 1 2, Xiaoang Liu 3, Shan Jin 1, Chengyan Wang 1, Wuyue Tang 1, Juncang Duan 4, Na Guo 1, Xihua Shen 1, Jianming Hu 1, Hong Zou 1, Wenyi Gu 5, Kejian Liu 1 6, Lijuan Pang 1 7. Integrated microarray for identifying the hub mRNAs and constructed

miRNA-mRNA network in coronary in-stent restenosis. Physiol Genomics. 2022;54(10):371–379. https://doi.org/10.1152/physiolgenomics.00089.2021. Epub 2022 Aug 15.

78. Chen M 1, Zhang YD 3, Liu S. 3. Identification of differentially expressed genes associated with coronary in-stent restenosis by integrated bioinformatics approaches. Ann Palliat Med. 2022;11(6):1940–1953. https://doi.org/10.21037/apm-21-2681. Epub 2022 Feb 9.

79. Tarek A, Abdelaziz 1, Randa H, Mohamed M. Gad 1, Mohamed G Ghareeb 1, Sara F Saadawy 2. Single-nucleotide polymorphism of ADRβ2 and CDKN1B genes in Egyptian patients with coronary artery in-stent restenosis. Coron Artery Dis. 2022;33(4):277–283. https://doi.org/10.1097/MCA.0000000000001123.

80. Le Yang H, Zhu. 2 3, Yuanyuan Sun 4, Pengcheng Yan 2, Xiaoning Song 2, Fayun Xu 1, Haitao Yuan 1 2, Liming Chen 1. Value of M2BP in predicting in-stent restenosis in patients after coronary drug-eluting stent implantation. Clin Cardiol. 2022;45(3):308–314. https://doi.org/10.1002/clc.23775. Epub 2022 Jan 15.

81. Yen-Wen Liu 1 2, Huang M-S 1, Hsu L-W. 2, Hsien-Yuan Chang 1 2, Cheng-Han Lee 1, Chi-Ying Lee 3, Dao-Peng Chen 3, Yi-Heng Li 1, Ting-Hsin Chao 1, Pei-Fang Su 4, Meng-Ru Shen 5 6, Ping-Yen Liu 1 2. Genetic risk model for in-stent restenosis of second-and third-generation drug-eluting stents. iScience. 2021;24(9):103082. https://doi.org/10.1016/j.isci.2021.103082. eCollection 2021 Sep 24.

82. Xianke Qiu 1, Wang J. 2, Zhongping Shi 2, Xiaojun Ji 2, Yiwei Huang 2, Haiyue Dai 2. Predictive value of miRNA-126 on in-stent restenosis in patients with coronary heart disease: A protocol for meta-analysis and bioinformatics analysis. Medicine (Baltimore). 2021;100(22):e25887. https://doi.org/10.1097/MD.0000000000025887.

83. Encarnación G-C. 1 2 3, Isabel Mayoral-González 1 2, Francisco Jesús Morón 4, Mónica Fernández-Quero 3, Alejandro Domínguez-Rodríguez 1, Antonio Ordóñez 1 2, Tarik Smani 1 5. miR-30b-5p downregulation as a predictive biomarker of coronary In-Stent restenosis. Biomedicines. 2021;9(4):354. https://doi.org/10.3390/biomedicines9040354.

84. Maheronnaghsh 1 M, Niktab 2 I, Enayati 3 S, Amoli 3 MM, Hosseini 4 SK, J Tavakkoly-Bazzaz 5. Differentially expressed miR-152, a potential biomarker for in-stent restenosis (ISR) in peripheral blood mononuclear cells (PBMCs) of coronary artery disease (CAD) patients. Nutr Metab Cardiovasc Dis. 2021;31(4):1137–47. https://doi.org/10.1016/j.numecd.2020.09.030. Epub 2020 Oct 20.

85. Zhang J-JG 2, Liu Y-J. 2. Effects of miRNA-1,miRNA-21 in plasma on in-stent restenosis in patients with coronary heart disease and diabetes mellitus after percutaneous coronary intervention. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2018;34(4):304–308 384. https://doi.org/10.12047/j.cjap.5643.2018.070.

86. Liang Zhou N, Wang. 1, Hong Li 1, Guoxin Tong 1, Jianmin Yang 1, Lei Lai 1, Hao Pan 1, Xianhua Ye 1, Jinyu Huang 1. SOCS1 gene promoter methylation status is associated with in-stent restenosis after percutaneous coronary intervention. Oncotarget. 2017;8(34):56959–56967. https://doi.org/10.18632/oncotarget.18398. eCollection 2017 Aug 22.

87. Zsolt Bagyura 1. Loretta Kiss 1, Kristóf Hirschberg 1 2, Balázs Berta 1, Gábor Széplaki 1, Árpád Lux 1, Zsolt Szelid 1, Pál Soós 1, Béla Merkely 1. Association between VEGF Gene Polymorphisms and In-Stent restenosis after coronary intervention treated with Bare Metal Stent. Dis Markers. 2017;2017:9548612. https://doi.org/10.1155/2017/9548612. Epub 2017 Mar 7.

88. Min Zhu 1 2. Association of seven renin angiotensin system gene polymorphisms with restenosis in patients following coronary stenting. J Renin Angiotensin Aldosterone Syst. 2017;18(1):1470320316688774. https://doi.org/10.1177/1470320316688774. Minjun Yang 1 3, Jiangbo Lin 1 3, Huanhuan Zhu 1 3, Yifei Lu 1 3, Bing Wang 1 3, Yinshen Xue 1 3, Congfeng Fang 1 3, Lijiang Tang 1 3, Baohui Xu 4, Jianjun Jiang 1 3, Xiaofeng Chen 1 2 3.

89. Yu HH 1, Wang XQ 1, Zhang J. 1, Zhu Hui Liu 1, Wen Qi Pan 1, Ying Shen 1, Zheng Bin Zhu 1, Ling Jie Wang 1, Xiao Xiang Yan 1, Ke Yang 1, Rui Yan Zhang 1, Wei Feng Shen 1, Feng Hua Ding 1, Lin Lu 2. Association of Serum HMGB2 Levels With In-Stent Restenosis: HMGB2 Promotes Neointimal Hyperplasia in Mice With Femoral Artery Injury and Proliferation and Migration of VSMCs. Arterioscler Thromb Vasc Biol. 2017;37(4):717–729. https://doi.org/10.1161/ATVBAHA.116.308210. Epub 2017 Feb 9.

90. L Pleva 1 2, Kovarova P 3 4, L Faldynova 5 6, P Plevova 7 8, S, Hilscherova. 9 10, J Zapletalova 11, P Kusnierova 12 13, P Kukla 14. The rs1803274 polymorphism of the BCHE gene is associated with an increased risk of coronary in-stent restenosis. BMC Cardiovasc Disord. 2015;15:135. https://doi.org/10.1186/s12872-015-0128-8.

91. Li Y. 1, Fang Chen 1, Xiaoling Zhang 1, Yuechun Gao 1, Changyan Wu 1, Haiyan Li 1, Yuchen Zhang 1. Angiotensin type 1 receptor A1166C gene polymorphism is associated with endothelial dysfunction and in-stent restenosis after percutaneous coronary intervention. Int J Clin Exp Pathol. 2015;8(6):7350-7. eCollection 2015.

92. Younes Nozari 1, Vosooghi S, Boroumand M, Poorhosseini H, Nematipour E, Salarifar M, Kassaian SE, Amirzadegan A. Mohammad Alidoosti, Ali Mohammad Haji-Zeinali, Sepideh Saroukhani. The impact of cytochrome P450 2C19 polymorphism on the occurrence of one-year in-stent restenosis in patients who underwent percutaneous coronary intervention: a case-match study. Anatol J Cardiol. 2015;15(5):348–53. https://doi.org/10.5152/akd.2014.5418.

93. Wenwei Liu Y 1, Liu H, Jiang X, Ding R, Zhu B, Li Y, Zhao. Plasma levels of interleukin 18, interleukin 10, and matrix metalloproteinase-9 and – 137G/C polymorphism of interleukin 18 are associated with incidence of in-stent restenosis after percutaneous coronary intervention. Inflammation. 2013;36(5):1129–35. https://doi.org/10.1007/s10753-013-9647-6.

94. Jing Gao Y 1, Liu R-Z, Cui Y-M, Mao J, Zhou Q, Chen F-M, Zhao. Gui-Ming Yang. Relationship of interleukin-6-572 C/G promoter polymorphism and serum levels to post-percutaneous coronary intervention restenosis. Chin Med J (Engl). 2013;126(6):1019–25.

95. Jing Gao Rang-zhuang 1, Cui Y, Liu Yong-min, Mao J, Zhou Q, Chen Fu-mei, Zhao Gui-ming, Yang, Ting Liu. Relationship of interleukin-10 gene polymorphism with restenosis after percutaneous coronary intervention in Chinese. Zhonghua Yi Xue Yi Chuan Xue Za Zhi. 2011;28(1):42–6. https://doi.org/10.3760/cma.j.issn.1003-9406.2011.01.010.

96. Konstantina Vogiatzi 1, Apostolakis S, Voudris V, Thomopoulou S, Kochiadakis GE, Demetrios A, Spandidos. Interleukin 8 gene polymorphisms and susceptibility to restenosis after percutaneous coronary intervention. J Thromb Thrombolysis. 2010;29(1):134–40. https://doi.org/10.1007/s11239-009-0338-y.

97. Konstantina Vogiatzi 1, Voudris V, Apostolakis S, Kochiadakis GE, Thomopoulou S, Zaravinos A, Demetrios A, Spandidos. Genetic diversity of RANTES gene promoter and susceptibility to coronary artery disease and restenosis after percutaneous coronary intervention. Thromb Res. 2009;124(1):84–9. https://doi.org/10.1016/j.thromres.2008.12.043. Epub 2009 Feb 7.

98. Svati HS 1, Hauser ER, Crosslin D, Wang L, Haynes C, Connelly J, Nelson S, Johnson J, Gadson S, Nelson CL, Seo D, Gregory S, Kraus WE, Granger CB. Pascal Goldschmidt-Clermont, L Kristin Newby. ALOX5AP variants are associated with in-stent restenosis after percutaneous coronary intervention. Atherosclerosis. 2008;201(1):148 – 54. https://doi.org/10.1016/j.atherosclerosis.2008.01.011. Epub 2008 Feb 12.

99. Katsaros 1 KM, Speidl WS, Kastl SP, Zorn G, Huber K, Maurer G, Glogar D, Wojta J, Christ G. Plasminogen activator inhibitor-1 predicts coronary in-stent restenosis of drug-eluting stents. J Thromb Haemost. 2008;6(3):508–13. https://doi.org/10.1111/j.1538-7836.2007.02884.x. Epub 2007 Dec 25.

100. Jasper S, Wijpkema 1 PL, van Haelst PS, Monraats M, Bruinenberg AH, Zwinderman F, van der Zijlstra RJ, de Winter, Pieter AFM, Doevendans J, Waltenberger JW, Jukema. René A Tio. Restenosis after percutaneous coronary intervention is associated with the angiotensin-II type-1 receptor 1166A/C polymorphism but not with polymorphisms of angiotensin-converting enzyme, angiotensin-II receptor, angiotensinogen or heme oxygenase-1. Pharmacogenet Genomics. 2006;16(5):331-7. https://doi.org/10.1097/01.fpc.0000205001.07054.fa.

101. Pascalle S, Monraats 1 JS, Rana AH, Zwinderman, Moniek PM, de Maat JP, Kastelein, Willem RP, Agema, Pieter AF, Doevendans RJ, de Winter RenéA, Tio J, Waltenberger, Rune R, Frants A, van der Laarse, Ernst E, van der Wall JW, Jukema. -455G/A polymorphism and preprocedural plasma levels of fibrinogen show no association with the risk of clinical restenosis in patients with coronary stent placement. Thromb Haemost. 2005;93(3):564–9. https://doi.org/10.1160/TH04-11-0708.

102. Sheikhvatan M, Chaichian S, Moazzami B. A systematic review and Bioinformatics Study on genes and micro-RNAs involving the Transformation of endometriosis into Ovarian Cancer. Microrna. 2020;9(2):101–11. https://doi.org/10.2174/2211536608666190917152104. PMID: 31530272; PMCID: PMC7366012.

Publisher's Note