Oncology and Radiotherapy ©
Vol.17 Iss.10: 001-006 • RESEARCH ARTICLE

Evaluation of the clinical conditions of patients with therapeutic cardiac angiography and In-stent restenosis risk factors for in cancer patients

Wallaa Luay Alfalluji[1], Ali Kadhim Radhi[2], Abbas AbdulWahhab Jumaah Al-Salihi[3]

[1] Assistant professor, Ministry of Higher Education and Scientific Research, Medical College of Hammurabi \ University of Babylon, Babylon, Iraq

[2] Interventional Cardiologist, Iraqi Ministry of Health, Babylon Health Directorate, Imam Alsadiq Teaching Hospital, Babylon, Iraq

[3] Department of Applied Embryology, High Institute for Infertility Diagnosis and Assisted Reproductive Technologies, Nahrain University, Kadhimiya, Baghdad, Iraq

Abstract

Background: In-Stent Restenosis (ISR) is a long-term complication of coronary artery intervention, which represents>50% re-narrowing of the artery within a period from 2 to 6 months from initial intervention. Aim: This study aims to evaluation of the clinical conditions of patients with therapeutic cardiac angiography and In-stent restenosis risk factors for in cancer patients. Material and Methods: This study was implemented. From January 2021 to October 2022, 92 patients with ISR were studied retrospectively, and their clinical and angiographic findings were analyzed. Fifty patients were taken as a controlled group. Factors and variables affecting ISR were demonstrated. Results and discussion: Seventy-three percent of the patients underwent elective Percutaneous Coronary Intervention (PCI), while Adhoc PCI was done to 27.17% of the patients. 93% of the patients underwent Predilutions prior to stent deployment. Residual stenosis was found to be 18.44 ± 6.76, and dissection as complications were occurred in 63.04% of the patients. Clinical presentation of the patients with ISR, in the form of chest pain, which was the most common presenting features, HF and positive Exercise Tolerance Test (ETT) represent 34 and 33%, respectively. Fifty-two percent of the ISRs were focal, 30.43% were diffuse, 10 percent were proliferative, and total occlusion represent 0.65%. Many factors like diabetes, ACS, and others related to the lesion characteristics and procedural aspects significantly predictive of restenosis were identified. Conclusion: Factors predictive of ISR are many and deserved to be addressed and modified.

Key Words: PCI, ISR, platelet glycoprotein and interleukin, apolipoprotein

Address for correspondence:
Dr. Wallaa Luay Alfalluji
Assistant professor, Ministry of Higher Education and Scientific Research, Medical College of Hammurabi \ University of Babylon, Babylon, Iraq. E-mail: Walla.alfalluji@uobabylon.edu.iq

Word count: 3821 **Tables:** 08 **Figures:** 03 **References:** 20

Received: 12 October, 2023, Manuscript No. OAR-23-116402
Editor assigned: 13 October, 2023, Pre-QC No. OAR-23-116402 (PQ)
Reviewed: 23 October, 2023, QC No. OAR-23-116402 (Q)
Revised: 28 October, 2023, Manuscript No. OAR-23-116402 (R)
Published: 05 November, 2023, Invoice No. J-116402

INTRODUCTION

Restenosis is most presented in that it is re-narrowing with diameter stenosis>50%, through inside the stent or within 5 mm proximal or through distal within the stent margin. The restenosis' frequency after bare metal stent implantation is>20% overall, rising to>40% of certain groups of patients [1].

Mechanisms of restenosis are almost exclusively attributable to:

- Elastic recoil
- Coronary arterial spasm
- Accelerated atherosclerosis
- Fibromyointimal hyperplasia

Serial angiographic studies in human demonstrate that the greatest proliferation occurs between 1 and 6 months, with only a small fraction of stent exhibiting further narrowing between 6 and 12 months. Thereafter, the proliferating smooth muscle cells were changed through inactive fibrosis, often with a slight increase in the minimal luminal diameter. Restenosis may also occur at the edges of the stent, at the site of balloon injury, typically owing to negative vessel remodeling rather than to neointimal growth. Restenosis presents most commonly as stable angina but may progress to unstable angina or rarely to acute myocardial infarction [1-3, 8]. More than half of the patients with angiographic

restenosis, usually those with diameter stenosis of<70%, are asymptomatic. In the absence of spontaneous or exercise-induced ischemia, the prognosis of an asymptomatic patient with silent in-stent restenosis managed medically may be excellent [2, 3]. Revascularization is indicated, however, when symptoms recur or ischemia is demonstrated. Interventional management of the bare metal stent restenosis typically consists of balloon angioplasty, which has a high (>98%) procedural rate and risk of complications [4]. Since the metallic struts are not typically exposed to blood elements, thienopyridine administration is not necessary. The rates of restenosis after balloon angioplasty for ISR have ranged from <10% to >80%, depending on the length of the lesion [5]. described an angiographic classification for the pattern of bare metal stent restenosis, which has proven useful for predicting the response to treatment: a) Focal restenosis equal to 10 mm long. b) Diffuse restenosis>10 mm long confined within the stent. c) Proliferative restenosis>10 mm long, extending beyond the stent margin. d) Total occlusion ISR. To assess the clinical and angiographic characteristics, in addition to characteristics of initial intervention in patients with ISR [6]. According to previous study -stent restenosis is a growing clinical problem, but the incidence of in-stent restenosis in cancer patients is not specifically addressed which discuss various treatment options for in-stent restenosis, including radiation therapy and stent-based drug delivery where ray teen 2000 refer to that no randomized-controlled trials have been published comparing different treatments for in-stent restenosis [7].

The integrated use of the capabilities of modern treatment methods opens up prospects for carrying out full symptomatic treatment of incurable patients with advanced stenosing cancer of the esophagus and cardia. Various palliative care options are used for treatment, in which two main goals are pursued: reducing dysphagia and improving quality of life. The installation of self-expanding metal stents is currently an alternative to traumatic surgical palliative intervention and, undoubtedly, an alternative to gastrostomy. Stenting the cardia zone has some additional features compared to stenting for tumor stenosis of the proximal esophagus and has a higher risk of complications. A distinctive feature of stenting the esophagogastric junction is the higher risk of complications such as stent migration and the appearance of symptoms of gastroesophageal reflux [8].

MATERIAL AND METHOD

It is a retrospective study involved all patients who underwent Coronary Angiography (CA) and proved to have In-Stent Restenosis (ISR) at the Iraqi Center for Heart Disease (ICHD) from January 2021 to October 2022. Fifty patients from those who underwent PCI and didn't develop ISR were taken as a control group.

Detailed study of the case sheets of patients with restenosis had been done, including case sheets of initial admission (for diagnostic CA, PCI, and last admission for which ISR has been diagnosed).

The films of all CA, PCI, and CA that diagnosed ISR have been reviewed by two expert interventional cardiologists, and assessment of the lesions by QCA (Quantitative Coronary Angiography). Review of the procedural log of the PCI of those patients had been done [9].

A pack of cigarettes was used as the unit of measurement for smoking, which is equal to 20 cigarettes smoked each day in a year.
Premature IHD is usually understood to relate to those in whom a first-degree relative has experienced ischemic heart disease under the age of 50. It was formerly described as a positive family history.

The term "stable angina" refers to ischemic heart discomfort brought on by physical activity or mental stress and alleviated through nitroglycerin and/or rest.

Acute chest pain without persistent elevation of the ST-segment (a rather persistent or transient ST-segment depression, as well as T-wave inversion, flat T-wave, pseudo-normalization of T-waves, or no Electrocardiogram (ECG), changes at presentation) was defined as an acute coronary syndrome. This condition is characterized by typical acute ischemic chest discomfort along with persistent (>20 minutes) ST-segment elevation [10, 11].

Critical coronary artery stenosis was defined as 70 % or more stenosis of the diameter in any epicardial coronary vessel except LMS, where is stenosis of 50% or more considered to be critical stenosis. Normal LV function was defined as EF of 50% or more (by Echo or LV angiography), and when EF is below 45%, the LV function is considered to be impaired.
A lesion in the LAD is considered to be ostial when it lies within 2-3 mm from the ostium, proximal when it lies before 1st sub-branch (S1 or D1), mid when it lies between the 1st branch (S1 or D1) and D3 (3rd diagonal branch) and distal when it lies after D3 branch.

The left circumflex artery is subdivided into the proximal part, which lies before the OM1 branch (1st obtuse marginal branch), the middle part, which lies between OM1 and OM2, and the distal part, which lies between OM2 and OM3. Similarly, the right coronary artery is subdivided into the proximal part, which started just beyond the ostium, till the first acute marginal branch, the mid part, which lies between 2 acute marginal branches, and the distal part, which lies after AM2 and the second shoulder. Coronary artery lesion was considered to be type A when it fulfills the criteria: Discrete (<10 mm), concentric, readily accessible, non-angulated segment (<45 degrees), smooth contour, little or no calcium, less than totally occlusive, not ostial in locations, no major side branch involvement and absence of thrombus. Type B when it fulfills the following criteria: Tubular (10 mm to 20 mm), eccentric, moderate tortuosity of the proximal segment, moderately angulated segment (>45 degrees and<90 degrees), irregular contour, moderate to heavy calcification, total occlusions<3-month-old, ostial in location, bifurcation lesion requiring double guide wire and some thrombus present. And type C when it fulfills the following criteria: Diffuse (>2 cm length), excessive tortuosity of the proximal segment, extremely angulated segment>90 degrees, total occlusion>3 months, inability to protect the major side branch and degenerated vein grafts with friable lesions. Adhoc PCI was defined as an interventional procedure to revascularized coronary artery lesions at the same time of diagnostic CA.

Coronary lesion was considered to be bifurcated when a medium or large branch (greater than 1.5 mm) originated within the stenosis, and if the side branch is surrounded completely by stenosis, portions of the lesion to be dilated. Residual stenosis was defined as complete normalization of the vessel lumen, which would be the ideal end result of coronary intervention, but the typical result of even a successful intervention is a<10 % residual diameter stenosis. Side branch occlusion was defined as TIMI 0,1 or 2 flow in a side branch>1.5 mm in diameter that previously had TIMI 3 flow. Statistical analysis: all data were presented as mean ± one standard deviation. Multiple regression analysis was used to assess independent risk factors for ISR and presented as P-value, and P-value <0.05 is considered to be significant (Table 1-8) (Figure 1-3).

RESULTS

Tab. 1. Baseline characteristics of studied patients with ISR

Variable	Value	Control	P-value
Total number	92	50	<0.05
Age (year) (Mean ± SD)	53.59 ± 10.38	53.30 ± 8.83	
Male No. (%)	65 (70.65)	35 (70)	
Positive FH of premature IHD No. (%)	46 (50)	18 (36)	<0.05
Diabetes mellitus No.(%)	40 (43.47)	13 (26)	
Duration of D.M (year) (Mean ± SD)	14.05 ± 5.4	10.32 ± 2.83	-
Hypertension No. (%)	42 (45.65)	24 (48)	
Duration of HT (year) (Mean ± SD)	10.09 ± 4.03	10.01 ± 2.04	
Hyperlipidemia No. (%)	58 (63.04)	23 (46)	
Smoking No.(%)	46 (50)	16 (32)	< 0.001
Pack/year (Mean ± SD)	48.06 ± 16.84	25.02 ± 9.66	

Tab. 2. Lesion characteristics of culprit's vessel prior to intervention in patients who are eventually ended with ISR

Variable	Value	Control	P-value
Lesion length (mm) (Mean ± SD)	18.15 ± 5.3	18.42 ± 5.61	<0.09

Lesion type A No. (%)	26 (28.26)	28 (56)	-
Lesion type B No. (%)	42 (46.62)	12 (24)	-
Lesion type C No. (%)	30 (32.60)	10 (20)	-
Reference vessel diameter (mm) (Mean ± SD)	3.22 ± 0.43	4.20 ± 5.02	<0.05
Lesion stenosis diameter (%) (Mean ± SD)	86.88 ± 10.07	82.53 ± 9.87	<0.01
Bifurcated lesion No. (%)	25 (27.17)	8 (16)	-

Tab. 3. Mode of presentation for initial intervention in patients who are eventually ended with ISR

SA No. (%)	38 (41.30)
UA/NSTEMI No. (%)	42 (45.65)
STEMI No. (%)	12 (13.04)
Total NO.	92

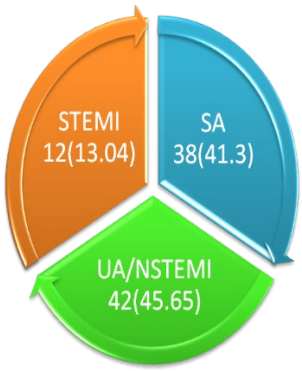

Fig. 1. Distribution of values in comparison of STEMI, SA, and NSTEMI

Tab. 4. ECG finding of patients who are eventually ended with ISR

Variable	Value
Normal No. (%)	12 (13.04)
STT changes No. (%)	62 (67.39)
Q wave No. (%)	15 (16.30)
LBBB No. (%)	3 (3.26)
Total	92

Tab. 5. Anatomical distribution of the coronary lesions for which PCI was done and ended with ISR

Variable	Value
LAD lesion No. (%)	57 (61.95)
Ostial	12 (13.04)
Proximal	31 (33.69)
Mid	13 (14.13)
Distal	1 (1.08)
RCA lesion No. (%)	26 (28.26)
Ostial	1 (1.08)
Proximal	11 (11.95)
Mid	13 (14.13)
Distal	1 (1.08)
LCx lesion No. (%)	11 (11.95)
Ostial	5 (5.43)
Proximal	6 (6.52)
Mid	0
Distal	0
Ramus NO. (%)	1 (1.08)

Tab. 6. Procedure characteristics for lesions which ended with ISR

Variable	Value	Control	P-value
Elective No. (%)	67 (72.82)	-	-
Adhoc No. (%)	25 (27.17)	-	-
Predilatations No. (%)	86 (93.47)	-	-
Primary stenting No. (%)	6 (6.52)	-	-
Stent length (mm) (Mean ± SD)	28 ± 1.5	17.76 ± 3.97	<0.001
Stent No. per lesion (Mean ± SD)	2 ± 0.5	2 ± 0.2	0.0637
Stent diameter (mm) (Mean ± SD)	3.03 ± 0.38	3.07 ± 0.33	<0.07
inflation Pressure used (Bar) (Mean ± SD)	14.88 ± 3.91	13.27 ± 1.94	<0.09
Residual stenosis (%) (Mean ± SD)	18.44 ± 6.76	12.52 ± 6.47	0.001
Dissection No. (%)	59 (63.04)	-	-
LD No. (%)	35 (38.04)	-	-
SD No. (%)	24 (26.08)	-	-

Fig. 2. Lesion burden in patients who underwent coronary angiography that eventually ended with ISR

Tab. 7. Clinical presentation of patients with ISR

Variable	Value
Total No.	92
Duration after initial intervention (months) (Mean ± SD)	6.17 ± 0.85
Chest pain No. (%)	63 (68.46)
HF No. (%)	32 (34.78)
Positive ETT No. (%)	31 (33.69)

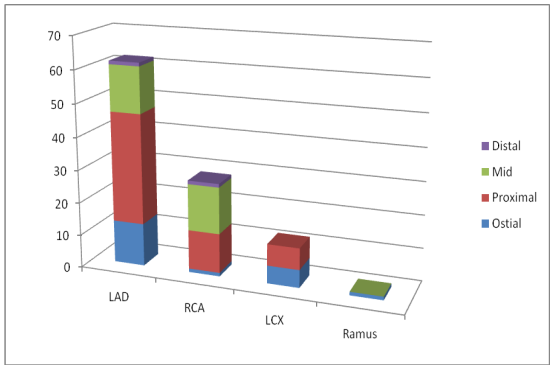

Fig. 3. Anatomical distribution of the coronary artery lesions culminated in the development of ISR.

Tab. 8. Lesion characteristics of ISR

Variable	Value
Percent of the stenosis (Mean ± SD)	73.99 ± 15.89
Length of the stenosis (mm) (Mean ± SD)	15.02 ± 6.12
Involvement of the area outside the stent No. (%)	33 (35.86)
Type of ISR No. (%)	
Focal	48 (52.17)
Diffuse	28 (30.43)
Proliferative	10 (10.86)
Total	6 (0.65)

DISCUSSION

This study represents the experience of a single cardiac center. Most of the patients were middle-aged, and 70% of them were male, which is a significant difference regarding gender, and this may reflect the population that underwent PCI initially as ISR pooled from that population while another study showed similar results regarding male gender was predominant sex for ISR although most of the patients were elderly [12]. Diabetes is a significant risk factor for ISR P<0.05; hypertension and hyperlipidemia aren't significant risks for ISR. Smoking is a common and significant factor among patients with ISR P<0.05 [13]. Van Belle et al. study showed that restenosis in diabetics is highly significant; similar findings were obtained in Kip et al. and Elezi et al., in which restenosis was high among diabetics in comparison with non-diabetics; also, in both studies, smoking was an important risk factor for restenosis. The coronary lesions that eventually ended with ISR in this study were relatively long (18.15 mm ± 5.3 mm), most commonly of type B complexity. However, the reference lumen diameters were large (3.22 mm ± 0.43 mm), while in other studies, the reference vessel diameter was small, which is considered a significant risk factor for ISR [14]. The lesion which is submitted for intervention was more complicated than the type B lesion, and it was too long. Fifty-eight percent of the patients who underwent their first CA had ACS. However, ad hoc PCI wasn't done for all of them (27.17%) versus elective PCI (72.28%), as a good percentage of them were stabilized on medical treatment, and scheduled PCI was done for them later. Similarly, in other study which showed that, most of the patients were presented with ACS [15]. In this study, LAD was the most common vessel in which ISR had been developed. This result is comparable to the Fischman et al. study, which showed that LAD was the most predictor vessel for ISR. In this study, most of the PCI that eventually resulted in ISR is characterized by balloon predilatations (93.47%) versus (6.52%) for primary stenting with relatively long stent (28 mm ± 1.5 mm). As inflation with a balloon makes more injuries to the arterial wall, and in some occasions, there is a discrepancy between the length of the balloon, which is used in predilatations, and the stent length, which is used to cover the lesion. The diameter of the stents used was (3.03 mm ± 0.38 mm). Foley et al. and other studies showed the significance of the stent length, diameter, and the expanding pressure in the development of restenosis [16]. The mean number of stents per lesion was 2.0 ± 0.5 which was a non-significant risk factor for the development of ISR, while in another studies, the increased number of the stents per lesion is considered as a risk factor for restenosis in comparison with a single stent for a single lesion. High inflation pressure of the stents was used in most patients in this study (14.88 Bar ± 3.91 Bar) since the high

pressure makes a good stent deployment and more stent's strut alignment to the wall of the artery thus decreasing the residual stenosis, which is one of the precipitants for ISR .this result is comparable to another study which also found that low inflation pressure is considered to be one of the important predictors for the development of ISR [17]. Dissection was a very common procedural complication in this study (63.04%) [18]. The site of the injury and the aggressive inflammatory response may be responsible for the increased ISR rate. Similarly, other studies showed that local complications during balloon dilatation or stent implantation may end in restenosis. Most of the patients with ISR in this study presented with chest pain (68.47%). However, positive ETT was present in 33.69% of the patients and HF in 34.78% of patients, while in other studies, the patients presented with chest pain, or they discovered during ETT, and on rare occasions, they may develop myocardial infarction [19]. In this study, the mean of ISR was 73.99% ± 15.89% with an average length of 15.02 mm ± 6.12 mm, and the focal type of ISR represents the most common type (52.17%). However, in 35.86% of ISR, there is the involvement of the area outside the stent, whether proximally or distally. Similarly, in Mehran et al., most of the ISRs classified as focal type, and there is 16% of the new lesions involved areas outside the stent [20].

CONCLUSION

ISR is an important problem and major challenge that faced interventionists.

There are many risk factors and precipitants for restenosis; these are either related to the clinical aspect of the patients who are undergoing the intervention or related to the procedure and technique used to deployed the stent.

Attention should turn towards the prevention of ISR through addressing and modification of the precipitant factors which may have a role for restenosis.

REFERENCES

1. Grossman W. Grossman's cardiac catheterization, angiography, and intervention. Lippincott Williams Wilkins; 2006.
2. Popma Jeffery J, Baim Donald S, Resnic Frederic S. Percutaneous Coronary and Valvular Intervention; Braunwald' s Heart Disease.
3. Lanzer P, Topoleski LT. Coronary arteries. Phila: Lippincott Williams Wilkins; 2006.
4. Popma JJ. Coronary arteriography and intravascular imaging. Braunwald's heart dis. 2008:465-508.
5. Libby P. Mechanisms of acute coronary syndromes and their implications for therapy. N Engl J Med. 2013;368:2004-2013.
6. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). G ital cardiol (2006), 2012;13:171-228.
7. Force T, Steg PG, James SK, Atar D, Badano LP, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012;33:2569-2619.
8. Singh IM, Filby SJ, El Sakr F, Gorodeski EZ, Lincoff AM, et al. Drug-eluting stents versus bare-metal stents for treatment of bare-metal in-stent restenosis. Catheter Cardiovasc Interv. 2010;76:257-262.
9. Jones GT, van Rij AM, Hill GB, Wilkins GT, Williams MJ. Common carotid intimal-medial thickness is associated with coronary in-stent restenosis. J Vasc Ultrasound 2008;32:129-132.
10. Bhavanadhar P, Reddy YV, Otikunta AN, Srinivas R. Evaluation of relationship between common carotid artery intima-media thickness and coronary in-stent restenosis: A case-control study. Interv Med Appl Sci. 2018;10:38-44.
11. Corrado E, Camarda P, Coppola G, Muratori I, Ciaramitaro G, et al. Prognostic role of endothelial dysfunction and carotid intima-media thickness in patients undergoing coronary stent implantation. Int angiol. 2009;28:12
12. Cortese B, Berti S, Biondi-Zoccai G, Colombo A, Limbruno U, et al. Drug-coated balloon treatment of coronary artery disease: a position paper of the Italian Society of Interventional Cardiology. Catheter Cardiovasc Interv. 2014;83:427-435.
13. Cortese B, Bertoletti A. Paclitaxel coated balloons for coronary artery interventions: a comprehensive review of preclinical and clinical data. Int j cardiol. 2012;161:4-12.
14. Cassese S, Byrne RA, Schulz S, Hoppman P, Kreutzer J, et al. Prognostic role of restenosis in 10,004 patients undergoing routine control angiography after coronary stenting.
15. Zhao LP, Xu WT, Wang L, Li H, Shao CL, et al. 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;26:5-10.
16. Kedhi E, Joesoef KS, McFadden E, Wassing J, Van Mieghem C, et al. Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice (COMPARE): a randomised trial. The Lancet. 2010;375:201-209.
17. Harjai KJ, Kondareddy S, Pinkosky B, Harjai N, Orshaw P, et al. Everolimus-Eluting Stents Versus Sirolimus-or Paclitaxel-Eluting Stents: Two-Year Results from the Guthrie Health Off-Label Stent (GHOST) Registry. J interv cardiol. 2013;26:153-162.
18. Costa JR, Sousa A, Moreira AC, Costa RA, Cano M, et al. Incidence and predictors of very late (≥ 4 years) major cardiac adverse events in the DESIRE (Drug-Eluting Stents in the Real World)-Late registry. JACC: Cardiovasc Interv. 2010;3:12-18.
19. Lee SY, Hur SH, Lee SG, Kim SW, Shin DH, et al. Optical coherence tomographic observation of in-stent neoatherosclerosis in lesions with more than 50% neointimal area stenosis after second-generation drug-eluting stent implantation. Circ: Cardiovasc Interv. 2015;8:001878.

20. Otsuka F, Vorpahl M, Nakano M, Foerst J, Newell JB, et al. Pathology of second-generation everolimus-eluting stents versus first-generation sirolimus-and paclitaxel-eluting stents in humans. Circulation. 2014;129:211-223.