Published online: 2024 March 18.

**Research Article** 



## Level of Adherence to Dual Anti-platelet Therapy at 6 and 12 Months after Coronary Stenting; The Impact on Post-angioplasty Cardiovascular Events

Azin Alizadehasl 🝺 1, Habibollah Saadat 2, Alia Bahramnejad 🝺 1, Amir Dousti 🝺 2,\*

<sup>1</sup> Cardio-oncology Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran <sup>2</sup> Cardiovascular Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author: Cardiovascular Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: amir.doustiran@gmail.com

Received 2023 October 14; Accepted 2023 October 15.

## Abstract

**Background:** Dual antiplatelet therapy (DAPT) following coronary stenting is used to prevent thromboembolic events. Dual antiplatelet therapy discontinuation and poor compliance to the antiplatelet drugs are common and results in various complication, most importantly cardiovascular events.

**Objectives:** Here, we designated a cross-sectional study to evaluate the association of DAPT adherence and post-angioplasty cardiovascular events.

**Methods:** A total of 150 adult patients from Modarres Hospital undergoing successful stent implantation were included and adherence to DAPT following angioplasty were determined via telephone at 6 and 12 months by Persian version of the 8-item Morisky Medication Adherence Scale (MMAS-8). We also recorded the occurrence of ST segment elevation myocardial infarction (STEMI), acute coronary syndrome (ACS), coronary artery bypass grafting (CABG) and re-angioplasty 6- and 12-months following discharge.

**Results:** During the trial, 50 patients were lost to follow-up due to failure to complete the MMAS-8 check list. We analyzed the association of STEMI, ACS, CABG and re-angioplasty with the level of DAPT adherence 6 and 12-month post-angioplasty. Our data suggested an important association of low and high DAPT adherence with lower cardiovascular events at 12 months post-Percutaneous Coronary intervention (PCI). However, at 6 months post-PCI, there was a minor cardiovascular event in patients with moderate DAPT adherence.

**Conclusions:** Here, we observed a significant association of drug adherence along with patient's risk factors in a course of antiplatelet therapy following coronary stenting.

Keywords: DAPT, PCI, Treatment Adherence

## 1. Background

Percutaneous coronary intervention (PCI) is extensively used as an effective treatment in patients with acute coronary syndromes (ACSs) and other clinically indicated conditions. The goal of dual antiplatelet therapy (DAPT), both Acetyl Salicylic Acid (ASA) and additional inhibitors of the platelet receptor P2Y12 in the months following stent placement is to prevent local thrombotic and systemic thromboembolic events (1). Evidence from randomized controlled trials suggest a minimum of 3 to 6 months DAPT duration, however, extension of DAPT beyond 12 months has contradictory results (2).

Dual antiplatelet therapy discontinuation following PCI is common, in which the physician-directed withdrawal is the most frequent mode within 2 years of stent implantation (3). The second major reason of DAPT discontinuation is drug disruption due to bleeding or non-compliance, and the third reason is the interruption due to surgical indication (3). Various comorbidities such as chronic obstructive pulmonary disease and previous myocardial infarction (MI) has been observed to be associated with DAPT non-

Copyright @ 2024, Multidisciplinary Cardiovascular Annals. This open-access article is available under the Creative Commons Attribution-NonCommercial 4.0 (CC BY-NC 4.0) International License (https://creativecommons.org/licenses/by-nc/4.0/), which allows for the copying and redistribution of the material only for noncommercial purposes, provided that the original work is properly cited.

adherence (4, 5). On the other hand, socioeconomically deprived individuals, i.e. ones with lower education, are also prone to DAPT non-adherence (6).

In the searching for cardinal complications of post-PCI DAPT non-adherence, major adverse cardiovascular events (MACE) have been extensively studied. MACE include MI, indicated re-angioplasty, cardiac death and stent thrombosis (3). Interestingly, the majority of adverse events occurred in individuals who were entirely adherent to the DAPT; yet, disruption owing to poor compliance or significant bleeding enhanced the MACE risk in non-adherent patients (3).

## 2. Objectives

Here we attempted to study the association of cardiovascular events (MI, acute coronary syndrome (ACS), indicated re-angioplasty, coronary artery bypass grafting (CABG)) with the level of ASA and Clopidogrel adherence, 6 and 12 months following coronary artery stenting. We used the Persian version of the 8-item Morisky Medication Adherence Scale (MMAS-8) to evaluate the level of DAPT adherence.

## 3. Methods

#### 3.1. Patients and Methods

This work was designed as a cross-sectional study. A total of 150 adult patients from Modarres Hospital undergoing successful stent implantation in at least one or more native coronary artery and discharged on DAPT were included and patients' baseline demographic data and phone number were recorded. Adherence to DAPT following angioplasty were determined via telephone at 6 and 12 months by Persian version of the MMAS-8 [validated by Moharamzad et al. (7)]. Demographic information and other variables about past medical history and CAD risk factors were also gathered during the study by means of specific check lists. We recorded the occurrence of STEMI, ACS, CABG and re-angioplasty 12 months after discharge given that one year is the recommended duration for effects of DAPT.

The 8-item Morisky Medication Adherence Scale has eight questions, as shown in Appendix 1, with the eighth being a Likert-type question. Total score is from 0 to 8 that is categorized as follows: Less than 6 (low adherence), 6 or 7 (moderate adherence), and 8 (high adherence).

#### 3.2. Sample Size

According to the data from "PARIS Registry: Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients" (8) and using the formula  $N = 1.96 \times P(1-P)$ , we calculate 150 as our sample size.

#### 3.3. Data Analysis

Descriptive indexes, including mean and standard deviation were used to express quantitative data. Qualitative data were expressed by frequency and percentage. Continuous variables were analyzed by *t*-test and nominal variables were analyzed by chi square test. All analyses were done by the SPSS software for Windows (ver. 20.0.0) and significance level was set at 0.05.

## 4. Results

#### 4.1. Patient Demographics

During the trial, 150 patients were scheduled for follow-up, however 50 were missed due to failure to complete the MMAS-8 check list record at 6- and 12months post-angioplasty. Demographic data of 100 enrolled patients are displayed in Table 1. Table 2 provides the data from recorded DAPT adherence scores of patients, divided by ASA and Clopidogrel, each one in 6 and 12-months post-angioplasty.

# *4.2. Cardiovascular Events in Post-PCI Patients and Adherence to the DAPT*

Major adverse cardiovascular events have been used extensively to indicate the association of post-PCI DAPT adherence and adverse complications. Major adverse cardiovascular events were defined as the composite of cardiac death, definite or probable stent thrombosis, spontaneous myocardial infarction, or clinically indicated target lesion revascularization. Here, we attempted to use STEMI, ACS, CABG and re-angioplasty as cardiovascular events and analyzed their relation to the level of DAPT adherence 6 and 12-months postangioplasty. Table 3 indicated frequency of post-PCI cardiovascular events among the patients.

Demographic CharacteristicsPercentageGenderKallFenaleFenaleStandAge35.4536.5536.6536.6536.75Under diplomaDiplomaDiplomaBs.SBs.SBiselsEquencingHousevireIndex diplomaObjoreBysinessBusinessBusinessBusinessBusinessBusinessBusinessBusinesi <td< th=""><th>Table 1. Demographic Data</th><th></th></td<>	Table 1. Demographic Data	
GenderGender64Fernale64Fernale64Seta5Seta11Seta65Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta38Seta36Seta36Seta38 <th>Demographic Characteristics</th> <th>Percentage</th>	Demographic Characteristics	Percentage
Make64Image64 <th>Gender</th> <th></th>	Gender	
FanaleSinceAppendixSince4 - 5 - 5Since5 - 6 - 5Since5 - 6 - 5Since5 - 6 - 5Since6 - 5 - 5Since7 - 10 - 10 - 10 - 10 - 10 - 10 - 10 - 1	Male	64
Age4 5-5105 6-50386 6-7538But and all of the second of th	Female	36
35:45       11         46:55       30         46:56       30         66:75       21         televite         2000000000000000000000000000000000000	Age	
46-553056-5331Builder diploma10471032103210321032103210321032103210321032103210321032113212401332143215321632173218321932 <tr< td=""><td>35-45</td><td>11</td></tr<>	35-45	11
§6.6538Eturtor28Eturtor47Diploma28A.D.4Bishertan B.S.72Portor29Busines50Busines62Businesic29Retried29Businesic20<	46-55	30
66-7521Eduction7Inder diploma6Inder diploma6Inder diploma6Inder diploma7Inder diploma7Inder diploma7Inder diploma B.S.7Inder diplom	56 - 65	38
FileI draftpina47I ploma28I ploma28I standard47I glarthan B.47I glarthan B.47I ploma47I ploma </td <td>66 - 75</td> <td>21</td>	66 - 75	21
Inder diploma97Iploma98Iploma98Iploma97Islams As97Iplope97Iplope97Instruction <td>Education</td> <td></td>	Education	
İpİoma28Ab.4Ab.10S.17İplertan B.S.6Journame A.S.6Journame A.S.10Journame A.S.	Under diploma	47
AD.4AD.77Bysee that B.S.77Job70Job70Auswife70Auswife70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Aution70Autoonary Syndrome70Autoonary Syndrome70 <t< td=""><td>Diploma</td><td>28</td></t<>	Diploma	28
I I<	A.D.	4
Igher than B.S.4JebJebJeb Self Self Self Self Self Self Self Self	B.S.	17
j         kinking         A           kinking         A         A	Higher than B.S.	4
Business36Employee77Housewife29Retried38Retried38Sobisty2Obesity2Pargadiction4Family history of early atheroscherosis37Implemention40	Job	
ImployeeImploymeHousewife29Retried18Stetret18Stetret2Imployee2Stetret32Imployee33Imployee34Imployee34Imployee34Imployee34Imployee34Imployee34Imployee34Imployee34Imployee34Imployee34Imployee34Imployee34 <t< td=""><td>Business</td><td>36</td></t<>	Business	36
Housewife29Retried18Bestiv2Øbesity2Prug addiction3Family history of arly atherosclerosis37Hypertension31Øbesity40Øbesity40Øbesity40Øbesity40Øbesity40Øbesity41Øbesity41Øbesity42Øbesity41Øbesity42Øbesity43Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity44Øbesity </td <td>Employee</td> <td>17</td>	Employee	17
Retried18Retried18Restify2I besity2I prug addiction4I prug addiction37I hypertension31I babets40I hypertipidemia44I hypertipidemia41I hypertipidemia41I hypertipidemia41I hypertipidemia41I hypertipidemia41I hypertipidemia41I hypertipidemia32I hypertipidemia34I hypert	Housewife	29
Risk Factors       2         Obesity       2         Drug addiction       4         Family history of early atherosclerosis       37         Hypertension       31         Diabets       40         Diabets       40         Smoking       41         Perturbical history       41         Myocardial infarction       32         Acute coronary syndrome       38         CABG       2         Picturbical filting       38         Picturbical infarction       38         OLAGG       38         Picturbical infarction       38         OLAGG       36         Picturbical infarction       38         OLAGG       38         Picturbical infarction       38         OLAGG       38         Pilace of living       36         Oliging infarction       36         Oliging infarction       38	Retried	18
Obesity2Ing addiction4Family history of early atherosclerosis37Hypertension51Diabetes40Minging and and and and and and and and and and	Risk factors	
Image: Progradiction       4         Image: Progradiction of early atherosclerosis       37         Image: Progradiction of early atherosclerosis       51         Image: Progradiction of early atherosclerosis       51         Image: Progradiction of early atherosclerosis       61         Image: Progradiction of early atherosclerosis       62         Image: Progradiction of early atherosclerosis       62         Image: Progradiction of early atherosclerosis       62         Image: Progradiction of early atherosclerosis       63         Image: Progradiction of early atherosclerosis       64	Obesity	2
Family history of early atherosclerosis       37         Hypertension       51         Diabetes       40         Payerlipidemia       44         Smoking       41         Past weical history       41         Mijoplasty       32         Angioplasty       37         Acute coronary syndrome       38         CABG       2         Pity       51         Village       46	Drug addiction	4
Hypertension51Diabetes40Hyperlipidemia44Smoking41HetterlahtstoryAngioplasty32Myocardial infarction32Acute coronary syndrome38CABG2Plect of living36City96Village4	Family history of early atherosclerosis	37
Diabetes     40       Hyperlipidemia     44       Smoking     41       Past-wetical history     32       Angioplasty     32       Myocardial infarction     37       Acute coronary syndrome     38       CABG     2       Plact-of living     36       City     96       Village     4	Hypertension	51
Hyperlipidemia44Smoking41Past metical history32Angioplasty32Myocardial infarction37Acute coronary syndrome38CABG2Place of living36City96Village4	Diabetes	40
Smoking     41       Past medical history     32       Angioplasty     32       Myocardial infarction     37       Acute coronary syndrome     38       CABG     2       Place of living     26       City     96       Village     4	Hyperlipidemia	44
Past medical history         32           Angioplasty         32           Myocardial infarction         37           Acute coronary syndrome         38           CABG         2           Place of living         36           City         96           Village         4	Smoking	41
Angioplasty     32       Myocardial infarction     37       Acute coronary syndrome     38       CABG     2       Place of living       City     96       Village     4	Past medical history	
Myocardial infarction     37       Acute coronary syndrome     38       CABG     2       Place of living     96       Village     4	Angioplasty	32
Acute coronary syndrome         38           CABG         2           Place of living         96           Village         4	Myocardial infarction	37
CABG     2       Place of living     96       City     96       Village     4	Acute coronary syndrome	38
Place of living       City     96       Village     4	CABG	2
City96Village4	Place of living	
Village 4	City	96
	Village	4

Abbreviations: AD, after diploma; BS, bachelor of science; CABG, coronary arteries bypass grafting.

Variables	Mean Scores	Low-Adherence (MMAS-8 Score < 6)	Moderate-Adherence (MMAS-8 Score = 6 or 7)	High-Adherence (MMAS-8 Score = 8)
ASA (6 months)	$6\pm1.78$	36	46	18
ASA (12 months)	$5.55 \pm 1.77$	55	33	12
Clopidogrel (6 months)	$6.01 \pm 1.86$	38	38	24
Clopidogrel (12 months)	$5.04 \pm 2.13$	63	20	17

Abbreviation: ASA, acetyl salicylic acid.

Table 4 shows the scores of MMAS-8 of DAPT adherence in 6 and 12-month post-PCI, which were divided to low, moderate and high adherence to

antiplatelet agents, in respect to clinically indicated reangioplasty during 6 and 12-months post-PCI.

Data analysis demonstrated that low adherence to DAPT in 12-months following angioplasty were

Table 3. Frequency of Post-PCI Cardiovascular Events	
Post-PCI events	Numbers Recorded
Re-angioplasty	24
Stent Thrombosis	3
STEMI	21
Bleeding	2
Acute Coronary Syndrome	27
CABG	4

Abbreviations: STEMI, ST segment elevation myocardial infarction; CABG, coronary artery bypass grafting.

Fable 4. Re-angioplasty by Level of Adherence				
Re-Angioplasty	Low-Adherence (MMAS-8 Score < 6)	Moderate-Adherence (MMAS-8 score = 6 or 7)	High-Adherence (MMAS-8 score = 8)	P-Value
ASA (6 month, Fq)				0.503
Yes	11	9	4	
No	25	37	14	
ASA (12 month, Fq)				0.01 <sup>a</sup>
Yes	8	14	2	
No	47	19	10	
Clopidogrel (6 month, Fq)				0.007 <sup>a</sup>
Yes	11	3	10	
No	27	35	14	
Clopidogrel (12 month, Fq)				0.04 <sup>a</sup>
Yes	11	5	8	
No	52	15	9	

Abbreviation: ASA, acetyl salicylic acid.

 $^{a}$  P < 0.05 was considered statistically significant.

Table 5. Comparison of All Patients Whether They Had Acute Coronary Syndrome Event or Not at 6- and 12-Months Post-PCI with Their Respective Level of Aspirin/Plavix Adherence

Acute Coronary Syndrome	Low-Adherence (MMAS-8 Score < 6)	Moderate-Adherence (MMAS-8 Score = 6 or 7)	High-Adherence (MMAS-8 Score = 8)	P-Value
ASA (6 month, Fq)				0.45
Yes	14	7	6	
No	22	39	12	
ASA (12 month, Fq)				0.049
Yes	11	14	2	
No	44	19	10	
Clopidogrel (6 month, Fq)				0.015
Yes	14	4	9	
No	24	34	15	
Clopidogrel (12 month, Fq)				0.004
Yes	11	11	5	
No	52	9	12	
Abbreviation: ASA acetyl salicyli	c acid			

associated with significantly lower rate of re-angioplasty in comparison to the moderate adherence to these agents at one-year follow-up (15% and 17% of patients on ASA and Clopidogrel respectively in low adherence group, compared to 42% and 2% of patients on ASA and Clopidogrel in moderate adherence group, respectively.

CABG	Low-Adherence (MMAS-8 Score < 6)	Moderate-Adherence (MMAS-8 Score = 6 or 7)	High-Adherence (MMAS-8 Score = 8)	P-Value
ASA (6 month, Fq)			0 ( )	0.143
Yes	0	2	2	
No	36	44	16	
ASA (12 month, Fq)				0.015
Yes	0	4	0	
No	55	29	12	
Clopidogrel (6 month, Fq)				0.233
Yes	0	2	2	
No	38	36	22	
Clopidogrel (12 month, Fq)				0.001
Yes	0	4	0	
No	63	16	17	

P-value < 0.05, Table 4). This pattern is also observed in 12-months followed up post-PCI patients with ACS and CABG events (0 - 16% of patients on DAPT in low adherence group, compared to 12 - 55% of patients on DAPT in moderate adherence group. P-value < 0.05, Tables 5 and 6). Interestingly, no patient required CABG in either low or high adherence to DAPT in the 12-month post-PCI period (Table 6).

On the other hand, high adherence to the DAPT in 12 months post-PCI was accompanied with significantly lower rate of ACS and CABG in comparison to moderate adherence group (16 % and 29 % of patients on ASA and Clopidogrel in low adherence group, compared to 42 % and 55 % of patients on ASA and Clopidogrel in moderate adherence group, respectively. P-value < 0.05, Tables 5 and 6). This pattern was also observed in patients who underwent re-angioplasty, as well as high adherence to aspirin at 12 months post-PCI (Table 4).

In all cardiovascular event groups, there were no significant difference between ASA adherence level in association with the rate of cardiovascular events at 6-month post-PCI (Tables 4 - 6). However, 6-month post-PCI analysis revealed that moderate adherence to Clopidogrel had a significantly lower association with the rate of cardiovascular events, except CABG, in relation to low and high-adherence groups (7 - 10% of patients on Clopidogrel in moderate adherence group, compared to 28 - 42% of patients on Clopidogrel in low/high adherence group. P-value < 0.05, Tables 4 - 6).

## 5. Discussion

Long-term DAPT following coronary stenting has highlighted the importance of drug adherence (9). Also, significant association of DAPT adherence with postangioplasty cardiovascular events has been reported and emphasized the evaluation of rate and cause of poor adherence to antiplatelet agents (3). Multiple factors were shown to be associated with drug nonadherence including communication barriers. socioeconomic factors and motivational circumstances (10). Here we observed an important association of low and high DAPT adherence with lower cardiovascular events at 12 months post-PCI. However, at 6 months post-PCI, there was a minor cardiovascular event in patients with moderate DAPT adherence.

Ferreira-González and colleagues evaluated 1 622 patients who underwent PCI with drug-eluting stents and discovered that discontinuing anti-platelet therapy after the first month of coronary stenting was transitory and did not significantly increase the incidence of MACE (11). Furthermore, recent medical history has been linked to a higher risk of DAPT cessation in patients who had undergone PCI 12. Individuals who had no prior MI or CABG and had less cardiovascular risk factors, such as diabetes, were more likely to terminate their DAPT (12).

Our data suggest that low adherence to the antiplatelet therapy at one year following PCI was associated with lower rate of cardiovascular events, which was later than first month of stenting and may be among patients with low risk past medical history. Although we noted patient's medical record, they were not adjusted by post-PCI cardiovascular events in our study. Since we had a large number of patients lost to follow up (50 persons), this should be noted that poor follow up by the patients itself in the low adherence group could be resulted in fewer cardiovascular events in relation to moderate adherence group.

High adherence to antiplatelet therapy was almost always associated with lower MACE (11). Still, important hemorrhage consequences are the major adverse results of long-term DAPT. Our data indicated a significant lower rate of cardiovascular events among the patients with high adherence to DAPT. This effect was observed at 12 months post-PCI, however, there was no significant difference between adherence groups and STEMI occurrence. Majority of previous studies have not specifically considered STEMI, independent of other cardiovascular events following PCI (3, 13, 14).

Interestingly, we noted a significant interrelation between moderate Clopidogrel adherence and lower number of cardiovascular events at 6-month post PCI, compared to low/high drug adherence. Comparing moderate and high DAPT adherence, the impact of cardiovascular risk factors and past medical history could be notable as we mentioned above (12). Sun et al. (15) reported a direct association of high adherence to P2Y12 antagonists with lower risk of MACE. This is not consistent with our results, nevertheless, patients with high adherence to DAPT composed a small portion of our studied patients. Another point of view is that moderate adherence patients scored 6 or 7 on the MMAS-8 scale, which is higher than our mean Plavix adherence scores at 6 months post-PCI and might be deemed moderate-to-high adherence.

Overall, here we introduced an important impact of drug adherence along with patient's risk factors in a course of antiplatelet therapy following coronary stenting. Still our data were limited and require further studies to evaluate the impact of patient's demographics on the risk of post-PCI cardiovascular events and also carefully adjust the confounding factors. Other important limitation of this study was the large number of patients lost to follow up that may be due to telephone-only data gathering way and resulted in inaccessibility to mortality data.

## Footnotes

Authors' Contribution: Study concept and design: Habibollah Saadat; Acquisition of data: Amir Dousti; Analysis and interpretation of data: Alia Bahramnejad; Drafting of the manuscript: Amir Dousti; Critical revision of the manuscript for important intellectual content: Azin Alizadehasl; Statistical analysis: Alia Bahramnejad; Administrative, technical, and material support: Habibollah Saadat; Study supervision: Azin Alizadehasl.

**Conflict of Interests:** The authors have no conflicts of interest.

**Data Availability:** The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Funding/Support: There was no funding.

## References

- Mehta SR, Yusuf S, Peters RJ, Bertrand ME, Lewis BS, Natarajan MK, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet.* 2001;**358**(9281):527-33. [PubMed ID: 11520521]. https://doi.org/10.1016/s0140-6736(01)05701-4.
- Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2016;68(10):1082-115. [PubMed ID: 27036918]. https://doi.org/10.1016/j.jacc.2016.03.513.
- Mehran R, Baber U, Steg PG, Ariti C, Weisz G, Witzenbichler B, et al. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. *Lancet.* 2013;**382**(9906):1714-22. [PubMed ID: 24004642]. https://doi.org/10.1016/S0140-6736(13)61720-1.
- Zhu B, Zhao Z, McCollam P, Anderson J, Bae JP, Fu H, et al. Factors associated with clopidogrel use, adherence, and persistence in patients with acute coronary syndromes undergoing percutaneous coronary intervention. *Curr Med Res Opin*. 2011;27(3):633-41. [PubMed ID: 21241206]. https://doi.org/10.1185/03007995.2010.551657.
- Ferreira-Gonzalez I, Marsal JR, Ribera A, Permanyer-Miralda G, Garcia-Del Blanco B, Marti G, et al. Background, incidence, and predictors of antiplatelet therapy discontinuation during the first year after drugeluting stent implantation. *Circulation*. 2010;**122**(10):1017-25. [PubMed ID: 20733100]. https://doi.org/10.1161/CIRCULATIONAHA.110.938290.
- Jura-Szoltys E, Chudek J. Epistaxis as the reason for premature discontinuation of clopidogrel after percutaneous coronary angioplasty with stent implantation. *Kardiol Pol.* 2011;69(8):817-23. [PubMed ID: 21850627].
- 7. Moharamzad Y, Saadat H, Nakhjavan Shahraki B, Rai A, Saadat Z, Aerab-Sheibani H, et al. Validation of the Persian Version of the 8-Item Morisky Medication Adherence Scale (MMAS-8) in Iranian

 Hypertensive Patients. Glob J Health Sci. 2015;7(4):173-83. [PubMed ID:

 25946926].
 [PubMed Central ID: PMC4802120].

 https://doi.org/10.5539/gjhs.v7n4p173.

- 8. Moliterno D. The PARIS Registry: Patterns of Non-Adherence to Antiplatelet Regimens In Stented Patients - An Observational Single Arm Study.In: Mehran R, editor. *23rd Annual Transcatheter Cardiovascular Therapeutics Conference*. Washington, USA. 2011.
- Iakovou I, Schmidt T, Bonizzoni E, Ge L, Sangiorgi GM, Stankovic G, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA*. 2005;293(17):2126-30. [PubMed ID: 15870416]. https://doi.org/10.1001/jama.293.17.2126.
- Baroletti S, Dell'Orfano H. Medication adherence in cardiovascular disease. *Circulation*. 2010;**121**(12):1455-8. [PubMed ID: 20351303]. https://doi.org/10.1161/CIRCULATIONAHA.109.904003.
- Ferreira-Gonzalez I, Marsal JR, Ribera A, Permanyer-Miralda G, Garcia-Del Blanco B, Marti G, et al. Double antiplatelet therapy after drugeluting stent implantation: risk associated with discontinuation within the first year. *J Am Coll Cardiol.* 2012;60(15):1333-9. [PubMed ID: 22999716]. https://doi.org/10.1016/j.jacc.2012.04.057.

- Czarny MJ, Nathan AS, Yeh RW, Mauri L. Adherence to dual antiplatelet therapy after coronary stenting: a systematic review. *Clin Cardiol.* 2014;**37**(8):505-13. [PubMed ID: 24797884]. [PubMed Central ID: PMC4140973]. https://doi.org/10.1002/clc.22289.
- Rossini R, Capodanno D, Lettieri C, Musumeci G, Nijaradze T, Romano M, et al. Prevalence, predictors, and long-term prognosis of premature discontinuation of oral antiplatelet therapy after drug eluting stent implantation. *Am J Cardiol.* 2011;**107**(2):186-94. [PubMed ID: 21211596]. https://doi.org/10.1016/j.amjcard.2010.08.067.
- Daemen J, Wenaweser P, Tsuchida K, Abrecht L, Vaina S, Morger C, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. *Lancet.* 2007;**369**(9562):667-78. [PubMed ID: 17321312]. https://doi.org/10.1016/S0140-6736(07)60314-6.
- Sun Y, Li C, Zhang L, Hu D, Zhang X, Yu T, et al. Poor adherence to P2Y12 antagonists increased cardiovascular risks in Chinese PCI-treated patients. *Front Med.* 2017;11(1):53-61. [PubMed ID: 28213881]. https://doi.org/10.1007/s11684-017-0502-2.