RESEARCH ARTICLE

Frequency of high bleeding risk in patients undergoing percutaneous coronary intervention

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Abstract

Objective: To assess the prevalence of risk factors for bleeding and high bleeding risk in patients undergoing percutaneous coronary intervention.

Method: The single-centre retrospective observational study was conducted at Ittefaq Hospital Lahore and comprised data of patients who underwent percutaneous coronary intervention from February 2018 to December 2019. Minor and major bleeding risk factors were identified on the basis of the consensus definition of the Academic Research Consortium. Patients with high bleeding risk were identified according to the consensus-based criteria of at least one major criterion or two minor criteria. Data was analysed using SPSS 20.

Results: Of the 385 patients, 280(72.7%) were males. The overall mean age was 57.9±11.9 years. The indication of procedure was acute coronary syndrome in 367(95%) patients. Of all the patients, 171(45%) had bleeding risk, with 94(24%) patients having a high bleeding risk. Of these, 60(15.6%) patients had high risk based on the presence of at least one major criterion and 34(8.8%) patients because of the presence of two or more minor criteria. Patients with high bleeding risk were more likely to be older and female with more co-morbidities ($p<0.05$).

Conclusion: Almost half of the patients undergoing percutaneous coronary intervention were found to have at least one bleeding risk factor, and one in four patients had high bleeding risk.

Keywords: Haemorrhage, Dual antiplatelet therapy, Percutaneous coronary intervention. (JPMA 71: 2186; 2021)

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Introduction

Patients undergoing percutaneous coronary intervention (PCI) routinely receive dual antiplatelet therapy (DAPT) to reduce the risk of future ischaemic events.[1] However, DAPT increases the risk of bleeding.[2] Post-discharge bleeding is strongly associated with increased cardiac and all-cause mortality.[3,4] The intensity and duration of DAPT needs to balance the reduction in ischaemic events against increased bleeding.[2,5] Identification of patients at high bleeding risk (HBR) is, therefore, important.

An individual's risk of bleeding is influenced by the presence or absence of certain risk factors, in particular anaemia, advanced age, female gender, history of previous bleeding, concomitant use of oral anticoagulants (OACs) and chronic kidney disease (CKD).[2,6,7] The role of certain other risk factors for bleeding, particularly frailty and ethnicity, is less clear.[6,7] The risk models developed to predict the risk of bleeding in western patients underestimate the risk in east Asian patients. Prolonged DAPT significantly increases risk of bleeding in east Asians without reducing adverse cardiac events(ACEs).[8]

The 2017 European Society of Cardiology focussed update on DAPT awarded a class IIb (level A) recommendation to the use of predictive risk scores to identify a patient's unique bleeding risk.[9,10] However, until recently lack of a consensus definition of HBR has resulted in various estimates, ranging 15-64% of HBR patients undergoing PCI.[6,11] In May 2019, the Academic Research Consortium for High Bleeding Risk (ARC-HBR) developed a consensus definition of PCI patients with HBR.[6]

A subsequent study validated the ARC-HBR consensus criteria and reported that each major and even in isolation each minor computable criterion was associated with HBR.[12] The ARC-HBR consensus criterion has higher sensitivity, but lower specificity when compared with Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy (PRECISE-DAPT) and Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients (PARIS) bleeding risk scores in identifying patients at bleeding risk following PCI.[13]

Only a limited number of studies have looked into the prevalence of HBR in real-world PCI patients using the new consensus criteria. A European PCI registry analysis found that almost 40% meet the ARC definition for HBR.[13] Similarly, a Japanese registry analysis showed that 43%

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patients had HBR.[14] A pooled analysis of 4 post-approval studies in the United States, Japan, China and India, using drug-eluting stents (DES), found that 23% patients had HBR.[15,16]

The burden of atherosclerotic risk factors as well as the clinical characteristics of PCI patients differ in south Asian patients compared to the western population.[17] While recent studies from Pakistan indicate frequent usage of antiplatelet therapy (APT) in patients with ACS, there is paucity of data regarding the prevalence of bleeding risk factors and HBR in south Asian and Pakistani patients undergoing PCI.[17,18] The current study was planned to assess the frequency of HBR and the bleeding risk factors in patients undergoing PCI.

Patients and Methods

This single-centre retrospective observational study was conducted at Ittefaq Hospital Lahore and comprised data of patients who underwent PCI between February 2018 and December 2019. After approval from the institutional ethics review board, the sample size was calculated with a conservative assessment of 50% cases undergoing PCI might have HBR while keeping confidence level at 95% and margin of error at 5%. Data was collected on all patients having undergone PCI at the study site and only data of patients with insufficient information to ascertain ARC-HBR criteria was excluded.

Minor and major bleeding risk factors were identified from the review of clinical and laboratory data using the consensus criteria to identify HBR patients by the presence of either one major risk factor or at least two minor risk factors.[6] Patients with no bleeding risk factor or only a minor risk factor in isolation were classed as non-HBR. HBR was defined by consensus as $\geq$4% risk of Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding[19] or $\geq$1% risk of intracranial haemorrhage (ICH) at 1 year.

The major criteria were anticipated use of long-term OACs, baseline haemoglobin (Hb) $\leq$11g (major anaemia), severe or end-stage CKD (estimated glomerular filtration rate [eGFR] <30mL/min), recurrent bleeding or spontaneous bleeding within the preceding 6 months, moderate or severe thrombocytopenia (platelet count <100 x10^9/L), chronic bleeding diathesis, liver cirrhosis with portal hypertension, active malignancy, previous brain haemorrhage or recent ischaemic stroke, non-deferrable major surgery and recent major surgery or trauma.[6] The minor criteria were age $\geq$75 years, moderate CKD (eGFR 30-59 mL/min), minor anaemia (Hb 11-12.9g/dL for men, 11-11.9g/dL for women), spontaneous bleeding in the preceding 6-12 months, long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) or steroids and any ischaemic stroke not meeting the major criteria. Further definitions of the individual criterion were according to the original consensus document.[6]

Data was analysed using SPSS 20. Demographic and clinical characteristics were compared between the two groups on the basis of HBR status. Descriptive data were presented as Mean $\pm$ standard deviation (SD) for quantitative measures and frequencies and percentages for qualitative variables. Independent sample t-test was used to compare quantitative measures and chi-square test was applied to compare qualitative features. P$\leq$0.05 was considered significant.

Results

Of the 385 patients, 280(72.7%) were males. The overall mean age was 57.9$\pm$11.9 years. Hypertension (HTN) 261(67.8%), dyslipidaemia 203(52.7%), diabetes mellitus (DM) 202(52.5%) and smoking history 128(33.2%) were the most common atherosclerotic risk factors. Besides, 67(17.4%) patients had history of myocardial infarction

Table-1: Demographic and clinical characteristics (n 385).

	N	%
Mean Age (years)	57.9 $\pm$ 11.5	
Male	280	72.7
Female	105	27.3
NSTEMI	145	37.7
Stable CAD	18	4.7
STEMI	175	45.5
Unstable angina	47	12.2
Diabetes mellitus	202	52.5
Hypertension	261	67.8
Dyslipidaemia	203	52.7
Smoker	128	33.2
Atrial fibrillation	5	1.3
CVA at any time	7	1.8
Malignancy	3	0.8
Cirrhosis	1	0.3
Bleeding Diathesis	1	0.3
Spontaneous Bleeding	6	1.6
Anticipated use of Anticoagulation	5	1.3
Recent major surgery or trauma	1	0.3
NSAIDs/Steroids	9	2.3
CKD stage		
Stage I	162	42.1
Stage II	141	36.6
Stage III A	51	13.3
Stage III B	20	5.2
Stage IV	9	2.3
Stage V	2	0.5

SD: Standard deviation; CAD: Coronary artery disease; CKD: Chronic kidney disease; CVA: Cereberovascular accident; NSTEMI: Non-ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction.

Table-2: Frequency of ARC-HBR major and minor criteria in patients undergoing PCI (n 385).

Major	Number of cases	Minor	Number of cases
		Age ≥75 years	32 (8.3)
Anticipated use of OAC*	5(1.3)		
eGFR <30 mL/min	11 (2.8)	eGFRr 30–59 mL/min	71 (18.4)
Haemoglobin <11 g/dL	39 (10.1)	Hb 11–12.9 g/dL (men) & 11–11.9 g/dL (women)	Male = 56(20.0) Female = 28(26.7) Total = 84 (26.5)
Spontaneous major bleeding (in the past 6 month) or at any time, if recurrent	0	Spontaneous bleeding not meeting the major criterion	6(1.6)
Baseline thrombocytopenia† (platelet count <100×109/L)	0		
Chronic bleeding diathesis	1 (0.3)		
Liver cirrhosis	1 (0.3)		
		Use of NSAIDs/ steroids	9 (2.3)
Active malignancy‡	3 (0.8)		
Previous ICH or bAVM or recent ischaemic stroke	0	Stroke not meeting the major criterion	7 (1.8)
Non-deferrable major surgery on DAPT	0		
Recent major surgery or major trauma	1 (0.3)		

bAVM: Brain arteriovenous malformation; CKD: Chronic kidney disease; DAPT: Dual antiplatelet therapy; eGFR: Estimated glomerular filtration rate; ARC-HBR: Academic Research Consortium high bleeding risk; ICH: Intracranial haemorrhage; NSAID: Nonsteroidal anti-inflammatory drug; OAC: Oral anticoagulation; PCI: Percutaneous coronary intervention. *This excludes vascular protection doses.42
†Baseline thrombocytopenia is defined as thrombocytopenia before PCI.
‡Active malignancy is defined as diagnosis within 12 months and/or ongoing requirement for treatment (including surgery, chemotherapy, or radiotherapy). §National Institutes of Health Stroke Scale score ≥5.

Table-3: Comparison of clinical characteristics between HBR and non-HBR patients undergoing PCI (n 385).

	HBR (N=94)		Non-HBR (N=291)		
	n	%	n	%	p-value
Mean Age (years)	65.1 ± 11.4		55.6 ± 10.5		<0.001
Male	58	61.7	222	76.3	0.009
Female	36	38.3	69	23.7	
Diabetes mellitus	57	60.6	145	49.8	0.088
Hypertension	63	67.0	198	68.0	0.955
Dyslipidaemia	43	45.7	160	55.0	0.150
Smoker	24	25.5	104	35.7	0.089
Atrial fibrillation	5	5.3	0	0.0	0.001
History of MI	18	19.1	49	16.8	0.721
History of PCI	10	10.6	30	10.3	1.000
History of CABG	1	1.1	6	2.1	0.505
CVA at any time	6	6.4	1	0.3	0.001
Malignancy	3	3.2	0	0.0	0.014
Cirrhosis	1	1.1	0	0.0	0.244
Bleeding Diathesis	1	1.1	0	0.0	0.244
Spontaneous Bleeding	5	5.3	1	0.3	0.004
Use of Anticoagulation	5	5.3	0	0.0	0.001
Major surgery or trauma	1	1.1	0	0.0	0.244
NSAIDs/Steroids	5	5.3	4	1.4	0.043
Mean Haemoglobin (G/dl)	11.5 ± 1.8		14.1 ± 1.5		<0.001
Mean Platelets (109 /L)	284 ± 89		279 ± 81		0.633
Mean WCC (4.0-11(109 /L)	10.4 ± 3.5		10.8 ± 3.5		0.342
Mean Creatinine (mg/dl)	1.4 ± 0.7		1.0 ± 0.3		<0.001
Mean eGFR (ml/minute)	57.0 ± 21.0		81.0 ± 13.3		<0.001

SD: Standard deviation; HBR: High bleeding risk; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; CVA: Cereberovascular accident; NSAID: Nonsteroidal anti-inflammatory drug: eGFR: Estimated glomerular filtration rate; WCC: White Cell Count.

(MI), while 40(10.4%) had previously undergone PCI and 7(1.8%) had coronary artery bypass graft (CABG) surgery. CKD stage III-V was present in 82(21%) patients with overall eGFR mean of 75.2±18.6mL/min, and 123(32%) patients had anaemia with overall Hb mean of 13.4±1.9 g/dl). Patients who underwent PCI had acute coronary syndrome (ACS) in 367(95.3%) cases; ST-elevation MI (STEMI) 175(45.5%), Non-ST elevation MI (NSTEMI) 145(37.7%) and unstable angina 47(12.2%) of the cases (Table-1).

Overall, 171(44%) patients had at least a minor or major risk factor for bleeding. Among them, 77(20%) patients had only a minor risk factor, while 94(24.4%) had HBR. Among those with HBR, 60(15.6%) patients had at least a major criterion and 34(8.8%) patients had two or more minor criteria (Table-2).

Patients with high bleeding risk were more likely to be older and female with more co-morbidities (Table-3).

Discussion

The current study has important findings. Almost half of the patients undergoing PCI had one or more risk factors for bleeding; one in four patients had HBR; and advanced age, anaemia and CKD accounted for almost 90% of the risk with most other risk factors for bleeding present only in a minority of patients.

A limited number of studies, in particular the analyses of BernPCI registry[13] and Coronary Revasculazrization Demonstrating Outcome Study in Kyoto (CREDO-Kyoto) registry cohort-2,[14] have looked into the prevalence of HBR in PCI patients using the ARC-HBR consensus criteria. Overall prevalence of HBR in the current patient population was considerably lower compared to BernPCI registry (24.4% vs 39.4%) and CREDO-Kyoto registry cohort-2 (43%).

Analysis of patients with HBR reveals that difference in frequency of HBR patients among BernPCI,[13] CREDO-Kyoto registry cohort-2[14] and the current data is likely to be secondary to different baseline patient characteristics. Frequency of patients aged ≥75 years was 8% in the current cohort compared to 32% in BernPCI and 31% in CREDO-Kyoto registry cohort-2. Moderate or worse CKD was present in 25.5%, 37.6% and 21%; need for anticoagulation in 10.5%, 8% and 1.3%; active malignancy in 1.9%, 9% and 0.8%; and previous ICH or stroke in 8%, 11% and 1.8% in BernPCI, CREDO-Kyoto registry cohort-2 and our patients respectively. Anaemia was more frequent (32%) in the current patient population compared to BernPCI registry (26%), but it was similar in CREDO-Kyoto registry cohort-2 (31%). However, similar to BernPCI registry[13] analysis and CREDO-Kyoto registry cohort-2,[14] HBR patients in the current study were more frequently older, and more frequently female with higher co-morbidities, like primarily anaemia and CKD. Smokers were less likely to be in HBR cohorts in all the three analyses.

Recently a pooled analysis[15] of 4 post-approval Xience V stent registries in US, Japan, India[16] and China reported sex related differences in HBR. Overall, 23% patients were HBR (30% women vs 20% men). A significant proportion of patients in this analysis had HBR because of OAC (17.4% in women and 27.9% in men).[15] In our study, 34% of the female patients were HBR, compared to 21% of the male patients. An analysis of ShorT and OPtimal Duration of AntiPlatelet Therapy-2 (STOPDAPT-2) randomised controlled trial (RCT) (n=3009) conducted in Japan recently reported that 1054 (35%) patients were HBR according to the ARC-HBR criteria.[20]

The role of individual risk factors of bleeding is important. The ARC-HBR regards age ≥75 years a minor risk factor. Of the 32 (8%) patients ≥75 years of age in the current study, 25 (78%) were classed as HBR because of the presence of an additional risk factor. The most frequent additional minor risk factors of HBR in the elderly patients were the presence of moderate CKD and mild anaemia. This is in keeping with the observation that elderly patients have more co-morbidities and additional risk factors of bleeding.[11]

In the present cohort, 82(21%) patients undergoing PCI had CKD stage III or higher (eGFR <60 mL/min), which is lower than the US National Cardiovascular Data Registry (NCDR) Cath-PCI registry data.[21] Only a minority of patients 11(2.8%) had severe or end-stage CKD (eGFR <30 mL/min). Anaemia is considered a significant risk factor of bleeding with Hb<11g/dL being a major ARC-HBR criterion. In BernPCI and CREDO-Kyoto registry cohort-2, major anaemia was present in 9% and 12% patients, and minor anaemia in 17.3% and 19% respectively. In the current study, 123(32%) patients had anaemia, with 39(10.1%) having major anaemia and 84(21%) with minor anaemia. Of the patients with anaemia, 36% were female.

The current data shows that only a small number of patients had other risk factors for bleeding, in particular there were no patients with history of ICH, significant thrombocytopenia, non-deferrable major surgery on DAPT and recurrent bleeding or spontaneous bleeding within the preceding 6 months. This is likely a reflection of approach towards the management of coronary artery disease where patients with such co-morbidities may preferably be treated conservatively. Similarly, only a

minority of patients had atrial fibrillation requiring anticoagulation.

An overwhelming majority of patients in the current study had ACS, with only very few patients undergoing PCI for stable angina. While this may well be because of physician's approach towards selective intervention in stable angina cases, this is probably more reflective of patients' preference to delay intervention unless the unstable coronary syndrome sets in.

Both BernPCI[13] and CREDO-Kyoto registry cohort-2[14] analyses highlight that the presence of even a minor risk factor for bleeding in isolation (and hence non-HBR by ARC-HBR criteria) is associated with a significantly increased risk of bleeding.[12-14] In the current study, 77(20%) patients had only one minor criterion present. These patients, despite not meeting the criteria for ACR-HBR, may not be considered low-risk. This may suggest a need to consider an intermediate risk classification. While the relationship between many risk factors and bleeding is continuous, the ARC-HBR classification is binary. A risk score which reflects the continuum of risk posed by each individual risk factor may eventually prove to be more useful than the binary classification proposed in the current consensus document.[9,10]

Further follow-up research should be carried out to study the current patterns of prescription of DAPT, especially in patients with HBR. Perhaps most importantly the actual bleeding outcomes should be studied to validate the predictive risk scores and ARC-HBR consensus criteria for HBR in Pakistani patients. The current study indicates that compared to European[13] and North American[6] patients, a much smaller portion of Pakistani patients undergoing PCI are >75 years of age. The risk scores and criteria based on studies primarily performed in Caucasians should be validated in the local population to take into account the relative young age of Pakistani patients undergoing PCI.

The current study has some limitations. First, the single-centre observational design of the study may limit generalisability of the findings. It is, therefore, essential that further multi-centre studies be performed in Pakistani population to better define the extent of HBR. Second, as the study is retrospective, there was no information regarding some aspects of patients' characteristics, in particular frailty and body mass index (BMI). These factors, however, are not part of the ARC-HBR consensus and do not have an impact on the validity of the current analysis.

Conclusion

Almost half of the patients undergoing PCI had at least one bleeding risk factor, and one in four patients had HBR. Anaemia, CKD and advanced age were the frequent risk factors, accounting for almost 90% patients having HBR.

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References

1. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019; 40:87-165.
2. 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; 68:1082-115.
3. Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KAA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation. 2006; 114:774-82.
4. Généreux P, Giustino G, Witzenbichler B, Weisz G, Stuckey TD, Rinaldi MJ, et al. Incidence, Predictors, and Impact of Post-Discharge Bleeding After Percutaneous Coronary Intervention. J Am Coll Cardiol. 2015; 66:1036-45.
5. Costa F, Van Klaveren D, Feres F, James S, Räber L, Pilgrim T, et al. Dual Antiplatelet Therapy Duration Based on Ischemic and Bleeding Risks After Coronary Stenting. J Am Coll Cardiol. 2019; 73:741-54.
6. Urban P, Mehran R, Colleran R, Angiolillo DJ, Byrne RA, Capodanno D, et al. Defining High Bleeding Risk in Patients Undergoing Percutaneous Coronary Intervention. Circulation. 2019; 140:240-61.
7. Pavasini R, Maietti E, Tonet E, Bugani G, Tebaldi M, Biscaglia S, et al. Bleeding Risk Scores and Scales of Frailty for the Prediction of Haemorrhagic Events in Older Adults with Acute Coronary Syndrome: Insights from the FRASER study. Cardiovasc Drugs Ther. 2019; 33:523-32.
8. Kang, J, Park KW, Palmerini T, Stone GW, Lee MS, Colombo A, et al. Racial Differences in Ischaemia/Bleeding Risk Trade-Off during Anti-Platelet Therapy: Individual Patient Level Landmark Meta-Analysis from Seven RCTs. Thromb Haemost. 2019; 119:149-62.
9. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. Eur J Cardio-thoracic Surg. 2018; 53:34-78.
10. Costa F, van Klaveren D, James S, Heg D, Räber L, Feres F, et al. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. Lancet. 2017; 389:1025-34.
11. Urban P, Meredith IT, Abizaid A, Pocock SJ, Carrié D, Naber C, et al. Polymer-free drug-coated coronary stents in patients at high bleeding risk. N Engl J Med. 2015; 373:2038-47.
12. Corpataux N, Spirito A, Gragnano F, Vaisnora L, Galea R, Svab S, et al. Validation of high bleeding risk criteria and definition as proposed by the academic research consortiumfor high bleeding risk. Eur Heart J. 2020; 41:3743-9.
13. Ueki Y, Bär S, Losdat S, Otsuka T, Zanchin C, Zanchin T, et al. Validation of Bleeding Risk Criteria (ARC-HBR) in Patients Undergoing Percutaneous Coronary Intervention and

Comparison with Contemporary Bleeding Risk Scores. EuroIntervention. 2020; 16:371-9.
14. Natsuaki M, Morimoto T, Shiomi H, Yamaji K, Watanabe H, Shizuta S, et al. Application of the Academic Research Consortium High Bleeding Risk Criteria in an All-Comers Registry of Percutaneous Coronary Intervention. Circ Cardiovasc Interv. 2019; 12:1-12.
15. Chandiramani R, Cao D, Claessen BE, Sorrentino S, Guedeney P, Blum M, et al. Sex-Related Differences in Patients at High Bleeding Risk Undergoing Percutaneous Coronary Intervention: A Patient-Level Pooled Analysis From 4 Postapproval Studies. J Am Heart Assoc. 2020; 9:e014611.
16. Seth A, Patel TM, Stuteville M, Kumar R, Mullasari AS, Kaul U, et al. ScienceDirect Three-year data from the XIENCE V Ò INDIA study : Safety and efficacy of XIENCE V Ò in 1000 real world Indian patients. Indian Heart J. 2014; 66:302-8.
17. Akhter Z, Rind IA, Aijaz S, Sattar S, Malik R, Pathan A. Management, hospital outcome and revascularization trends in non-ST elevation myocardial infarction with high GRACE risk score. J Pak Med Assoc. 2019; 69:1486-92.
18. Aijaz S, Rind IA, Malik R, Akhter Z, Sattar S, Pathan A. In-hospital management and intermediate term outcomes in stable patients with ST segment elevation myocardial infarction presenting between 12-48 hours of symptom onset versus 2-7 days after the onset of chest pain; a single center study. J Pak Med Assoc. 2019; 69:1657-62.
19. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials: A consensus report from the bleeding academic research consortium. Circulation. 2011; 123:2736-47.
20. Watanabe H, Domei T, Morimoto T, Natsuaki M, Shiomi H, Toyota T, et al. Details on the effect of very short dual antiplatelet therapy after drug-eluting stent implantation in patients with high bleeding risk: insight from the STOPDAPT-2 trial. Cardiovasc Interv Ther. 2021; 36:91-103.
21. Feldman DA, Shroff AR, Bao H, Curtis JP, Minges KE, Ardati AK. Stent selection among patients with chronic kidney disease: Results from the NCDR CathPCI Registry. Catheter Cardiovasc Interv. 2020; 96:1213-21.