RESEARCH ARTICLE

Navigating Choices: A Questionnaire-based Study on Usage of Antiplatelet Therapies in Management of Acute Coronary Syndrome in India

PRAFULLA KERKAR*, JAYESH PRAJAPATI†, PK SAHOO‡, PANKAJ RASTOGI#, SUNIP BANERJEE¥, SAUMITRA RAY§, BHUPEN DESAI^, SUNIL SATHE£, JOHANN CHRISTOPHER¶, NARAYANA MURTHY|, CHETAN SHAHΨ, MAYUR MAYABHATEΔ, JESSICA DALIΔ

ABSTRACT

Background: Percutaneous coronary intervention (PCI) is a common invasive cardiac procedure used to treat acute coronary syndrome (ACS). The main objective of anticoagulant therapy in PCI is to minimize the risk of plaque rupture and decrease the formation of blood clots. Understanding clinicians' prescription patterns is crucial for optimizing treatment strategies for patients with ACS who have undergone PCI. **Methods:** It was a cross-sectional, questionnaire-based, noninterventional study which included questionnaire responses from 136 cardiologists, regarding usage of antiplatelets in ACS management. **Results:** Ticagrelor and aspirin dual antiplatelet therapy (DAPT) is favored by 54% cardiologists in managing ACS patients who have undergone PCI, regardless of the presence or absence of type 2 diabetes mellitus (T2DM). Further, 78% of the participants preferred long-term DAPT over short-term and medium-term alternatives. Forty percent respondents preferred a 1-month triple antithrombotic therapy (TAT) for PCI patients with atrial fibrillation. Additionally, the study emphasized the importance of considering factors like age, bleeding history, hemoglobin, and creatinine clearance in determining the optimal antithrombotic strategy. **Conclusion:** This study contributes valuable insights into the real-world practices of health care practitioners, paving the way for more informed and personalized ACS management strategies in Indian patients.

Keywords: Percutaneous coronary intervention, acute coronary syndrome, dual antiplatelet therapy, ticagrelor

Acute coronary syndrome (ACS) is a complication arising from coronary artery disease (CAD) and is one of the primary causes of mortality worldwide. The combined impact of CAD and ACS results in approximately 7 million annual deaths globally. Percutaneous coronary intervention (PCI) is a nonsurgical, invasive method that aims to relieve coronary artery blockage while improving blood flow to ischemic tissues[1]. India faces significant public health and clinical issues due to ACS, which is the most prevalent cause of mortality and morbidity in the country. India has one of the highest ischemic heart diseases (IHD) burdens globally, resulting in 1.54 million deaths and 36.99 million disability-adjusted life years in 2017[2]. In more recent development, the Global Burden of Diseases Collaboration has reported an increase in age-standardized mortality rates for cardiovascular diseases in South Asia, including India, ranging from 248.6 to 350.9 per 1,00,000 persons in 2021[3].

The use of dual antiplatelet therapy (DAPT) in patients experiencing ACS and undergoing PCI, involving

*Consultant Interventional Cardiologist, Asian Heart Institute, Mumbai, Maharashtra, India
†Interventional Cardiologist, Apollo Hospital International Limited, Ahmedabad, Gujarat, India
‡Senior Consultant Cardiologist and Director of Interventional Cardiology, Apollo Hospitals, Bhubaneswar, Odisha, India
#Consultant Cardiologist, Divya Heart Clinic, Lucknow, Uttar Pradesh, India
¥Interventional Cardiologist, Kolkata Heart Lung Centre, Kolkata, West Bengal, India
§Senior Interventional Cardiologist and Director of Invasive Cardiology, AMRI Hospitals, Kolkata, West Bengal, India
^Consultant Interventional Cardiologist, Desai Heart Care Clinic, Mumbai, Maharashtra, India
£Senior Interventional Cardiologist, Cardiac Care and Counseling Center, Pune, Maharashtra, India
¶Consultant - Interventional Cardiology and Cardiac Imaging, CARE Hospitals, Hyderabad, Telangana, India
|Consultant Interventional Cardiologist, Sagar Hospitals, Bengaluru, Karnataka, India
ΨInterventional Cardiologist, Zynova Heart Hospital, Mumbai, Maharashtra, India
ΔMedical Affairs, Alkem Laboratories Ltd., Mumbai, Maharashtra, India
Address for correspondence
Dr Mayur Mayabhate
Medical Affairs, Alkem Laboratories Ltd., Mumbai, Maharashtra, India
E-mail: mayur.mayabhate@alkem.com

the combination of aspirin with another antiplatelet agent, has emerged as a fundamental aspect of PCI treatment[4]. Patients with ACS undergoing PCI face a heightened risk of thrombotic events attributable to disrupted atherosclerotic plaques and the presence of implanted stents. DAPT is a strategic measure to resolve the risks related to stent thrombosis and major adverse cardiovascular events[5,6]. The DAPT consists of aspirin and a P2Y12 receptor inhibitor, such as clopidogrel, prasugrel, or ticagrelor. Aspirin inhibits platelet activation and aggregation, while the P2Y12 inhibitors contribute to more potent and specific antiplatelet effects[7]. The critical decision of selecting the appropriate P2Y12 inhibitor is contingent upon the patient's clinical characteristics and bleeding risk.

Little is known about usage of DAPT in real-world settings in managing ACS in India. We aimed to comprehensively assess the usage of DAPT in ACS management across the country. Based on the findings of the study, we aim to provide in-clinic recommendations for the use of DAPT in patients with medically managed ACS or ACS patients who have undergone PCI.

METHODOLOGY

The study was pan-India, cross-sectional, questionnaire-based, noninterventional, observational study involving health care professionals (HCPs) managing ACS patients. The survey tool was developed after thorough research and comprised of 8 multiple-choice response questions to be rated as per options provided. It aimed to collect data on the choice of DAPT in patients who have undergone PCI, with or without diabetes, duration of DAPT, factors affecting duration of DAPT, utilization of low-dose ticagrelor, etc. The data was collected digitally from the clinicians through case report form (CRF) via an individual login. The data collected was checked for quality, supervised independently by an investigator, and reviewed by 2 investigators.

Descriptive statistics were used, and the analysis was performed using SPSS 23.0 and Microsoft Excel. For all the variables, estimates were calculated using the total number of responses per question as the denominator. A simple percentage was calculated for all the variables.

Based on the study findings, recommendations were formulated and validated as good practice points by the experts participating in the development of the manuscript.

RESULTS

One hundred thirty-six survey participation invitations were issued to HCPs to participate in the survey digitally. Scoring a 100% response rate, all 136 HCPs returned the response.

Which DAPT is Your Preferred Choice in Patients of ACS Undergone PCI? (With/Without T2DM)

Response: The study respondents mentioned the use of ticagrelor and aspirin combination as their preferred choice (54.1%) in ACS patients who have undergone PCI (with or without T2DM) as depicted in Figure 1.

Which DAPT is Your Preferred Choice in Medically Managed Patients of ACS? (With/Without T2DM)

Response: Clopidogrel and aspirin combination was the most preferred choice, opted by 43.4% as extremely likely and 26.5% as likely option in medically managed

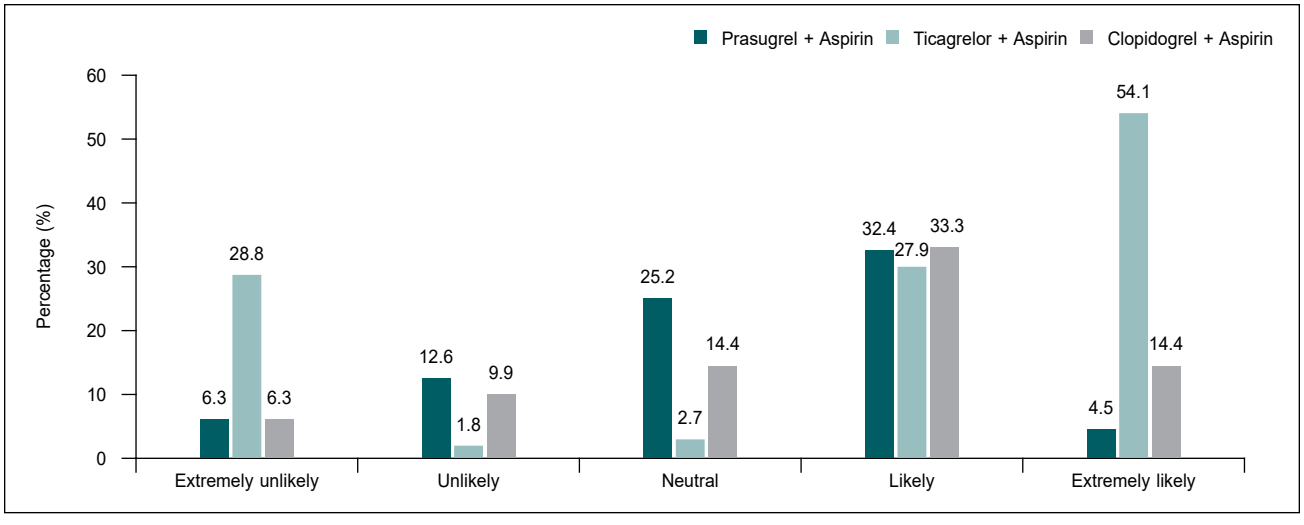

Figure 1. Preferred therapy for ACS patients who have undergone PCI (with/without T2DM).

patients of ACS (with/without T2DM), followed by 30.9% of the participating cardiologists selecting ticagrelor and aspirin combination as the extremely likely choice (Fig. 2).

What is Your Most Preferred DAPT Duration Strategy (up to 1-year Post-PCI)?

Response: It was observed that the standard DAPT regimen of 1 year was the preferred choice among more than 78% of the participating cardiologists compared to short-term and medium-term regimens (Fig. 3).

What is the Most Common APT Strategy >1-year Post-PCI?

Response: 44.4% participating cardiologists preferred clopidogrel + aspirin as the most common APT strategy >1-year post-PCI, followed by 27.3% choosing combination of ticagrelor 60 mg BD + aspirin as the extremely likely option as shown in Figure 4. It was interesting to note that despite the guidelines suggesting ticagrelor 60 mg BD post 1 year of PCI, 42.4% of the participants chose the option to be an extremely unlikely one.

Will You Prefer Ticagrelor 60 mg in Patients having Low Bleeding Risk and Multiple Ischemic Risk Factors?

Response: More than 50% of the participating cardiologists were not sure and around 59% participating cardiologists disagreed that they would prefer ticagrelor 60 mg in patients having low bleeding risk and multiple ischemic risk factors as depicted in Figure 5.

What is the Usual Duration of TAT in PCI Patients with Atrial Fibrillation?

Response: Among the participating cardiologists, most of the doctors (45.3%) preferred the triple antithrombotic therapy (TAT) in PCI patients with atrial fibrillation for 1 month (Fig. 6).

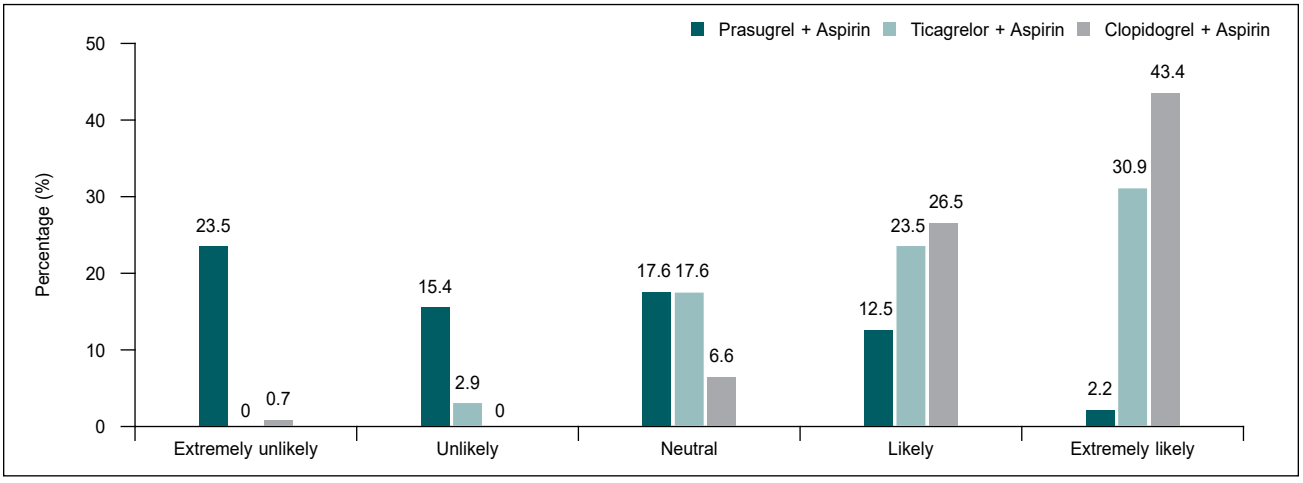

Figure 2. Preferred therapy for medically managed ACS patients (with or without T2DM).

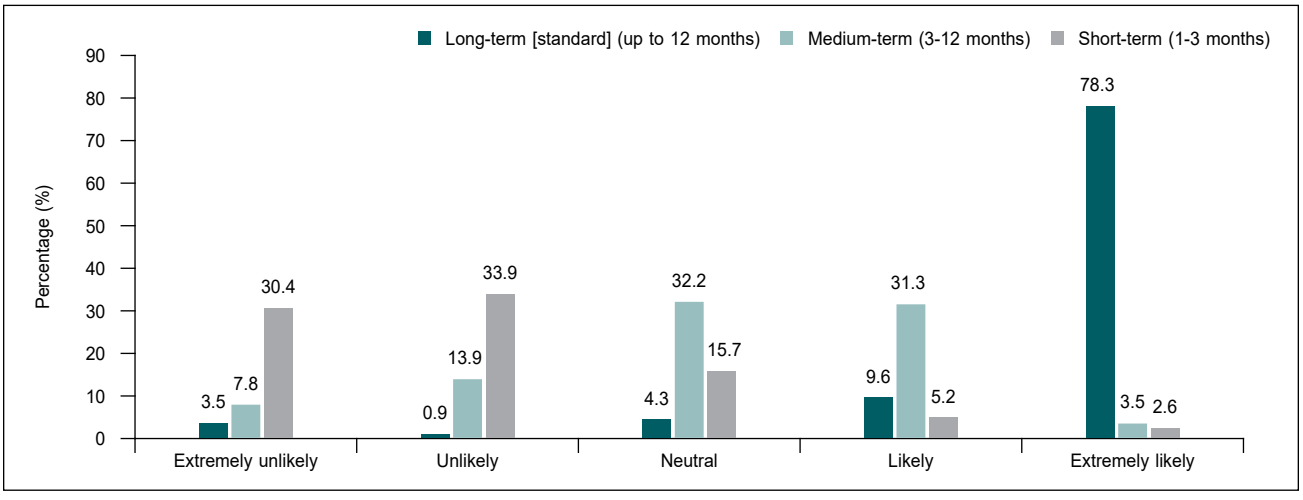

Figure 3. Preference of physicians for the duration of DAPT therapy in patients with ACS who have undergone PCI.

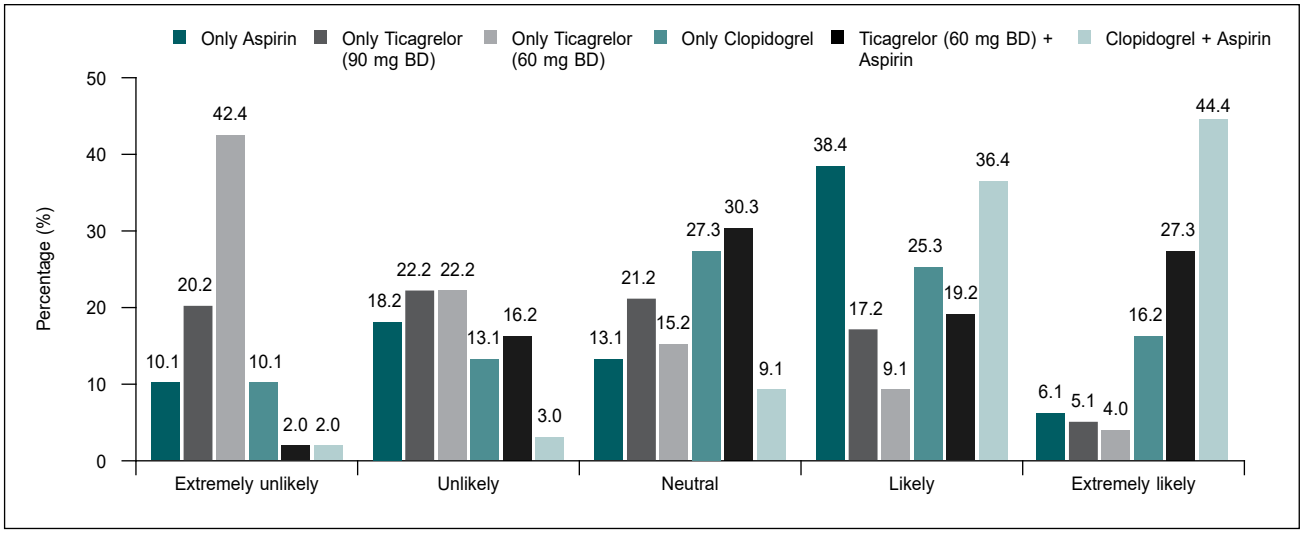

Figure 4. Most common APT strategy >1-year post-PCI.

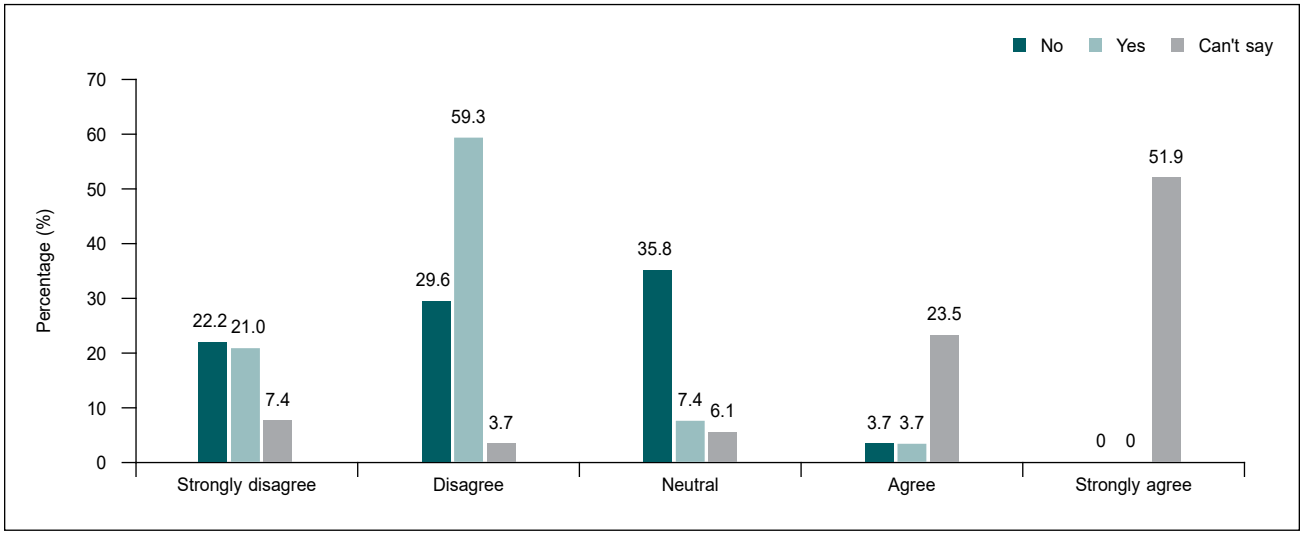

Figure 5. Preference rate for opting ticagrelor 60 mg BD in patients having low bleeding risk and multiple ischemic risk factors.

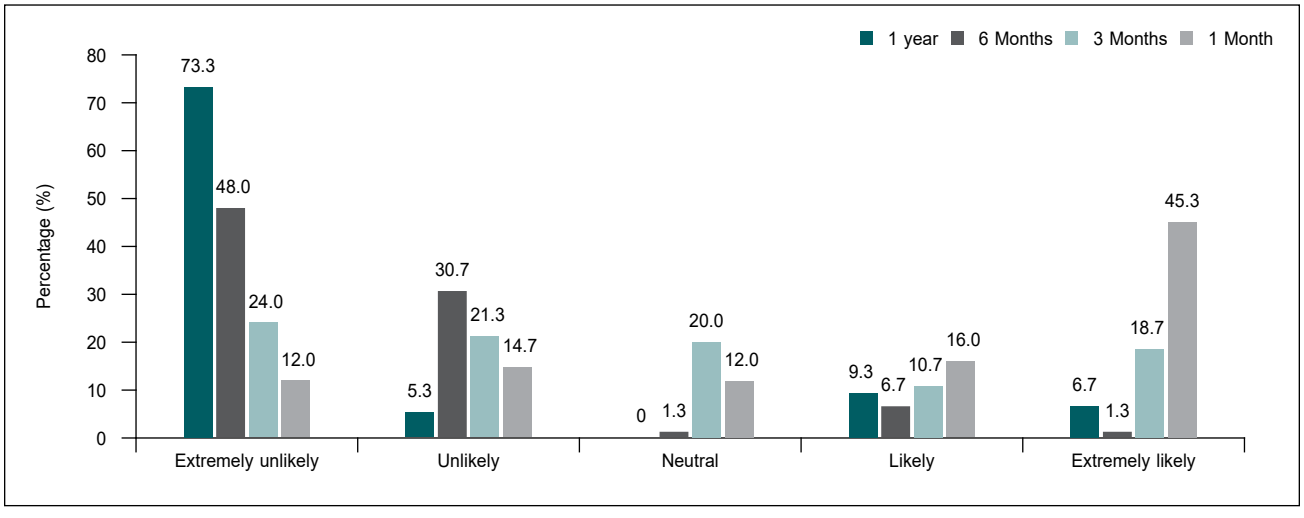

Figure 6. Preferred duration of TAT.

Additionally, the study also observed that over 50% of cardiologists believed that age is a crucial factor in deciding the duration of a DAPT regimen. It also emphasized that history of prior bleeding, hemoglobin, creatinine clearance and liver function test were more important in determining the optimal antithrombotic strategy when compared with left ventricular ejection fraction and WBC.

DISCUSSION

The findings of our study reported ticagrelor to be the preferred option in the treatment of patients with ACS treated with PCI, while still clopidogrel and aspirin combination seem to be preferred by majority of the doctors in the medically managed cases and treatment of patients post 1 year of PCI. The results led to a class I recommendation for their use in individuals with ACS, with or without ST-segment elevation[8,9]. Large-scale clinical trials (NCT00097591, NCT00391872) have unequivocally shown that ticagrelor and prasugrel outperform clopidogrel in inhibiting platelet aggregation, leading to a significant reduction in the occurrence of ischemic events[10-12]. A study by Sawhney et al (2019), demonstrated the use of ticagrelor in various real-world settings for different types of ACS management strategies in India. It reported that majority of patients diagnosed with ST-segment elevation myocardial infarction (STEMI) who underwent PCI were prescribed ticagrelor[1]. A similar picture is observed in the current study.

A meta-analysis by Tan et al (2017) indicated that ticagrelor may reduce the occurrence of the composite end point involving cardiovascular death, myocardial infarction, and stroke, along with reducing platelet reactivity in patients with T2DM experiencing ACS. Given the divergent platelet reactivity observed between T2DM patients and the general ACS population, it is advisable to exercise caution when incorporating ticagrelor into clinical applications[13]. Ticagrelor also exhibited lower all-cause mortality in patients with ACS, myocardial infarction, or stroke, compared to clopidogrel, and its overall tolerance was favorable, without increasing major bleeding rates[9].

The results of the TWILIGHT trial have revealed that ticagrelor monotherapy following a brief DAPT regimen proves to be an effective and safe strategy to prevent bleeding in high-risk patients undergoing PCI with drug-eluting stents[14,15]. It is important to mention that while the recommendation for ticagrelor use extends to high-risk cases undergoing PCI as well as those with stable angina, its benefits persist irrespective of the chosen therapeutic approach, whether medical, invasive, or surgical[16].

The PEGASUS-TIMI 54 trial showed that extended use of DAPT with either doses of 60 mg and 90 mg of ticagrelor significantly reduced ischemic events and major adverse cardiovascular events compared to aspirin alone[17,18]. PLATO trial demonstrated that a 12-month course of ticagrelor was more effective than clopidogrel in reducing the primary composite end point of myocardial infarction, stroke, or cardiovascular death. Ticagrelor also exhibited a lower all-cause mortality compared to clopidogrel and its overall tolerance was favorable, without an increase in the rate of overall major bleeding, but with an increased risk of nonprocedure-related bleeding relative to clopidogrel[9,19]. In our study also, the cardiologists preferred the standard DAPT, extending up to 1 year following a PCI.

The latest guidelines from the American College of Cardiology/American Heart Association regarding the duration of DAPT following PCI using drug-eluting stents strongly recommend maintaining DAPT for a minimum of 12 months after experiencing an ACS and for at least 6 months after revascularization in cases of stable IHD[20]. In the PEGASUS trial, adjunctive ticagrelor therapy significantly reduced ischemic recurrences on top of aspirin, albeit at the expense of increased bleeding complications. Low-dose ticagrelor seems an appealing strategy to optimize ischemic and hemorrhagic risk in elevated-risk patients with stable CAD undergoing PCI[21]. In a study conducted by Sharma et al (2020), the results showed that ticagrelor 60 mg twice daily is recommended for duration of up to 3 years in high-risk patients[17]. In the present study, however, ticagrelor 60 mg BD was shown to be extremely unlikely to be used post 1 year of PCI. The study also reported that cardiologists did not prefer using ticagrelor 60 in patients with low bleeding risk and multiple ischemic risk factors. In a study by Calderone et al (2020), it was observed that among patients with a history of myocardial infarction (1-3 years prior) and cardiovascular risk factors, ticagrelor caused a significant reduction in ischemic events compared to a placebo, however, with an increased risk of bleeding. Notably, the ticagrelor 60 mg twice-daily regimen showed the most favorable safety profile[22].

In an observational study involving 568 unselected patients who underwent PCI, researchers found that a 1-month duration of TAT yielded comparable rates of ischemic events, bleeding events, and overall clinical outcomes compared to longer durations. Consequently,

shortening TAT to 1 month could be a viable option for patients at high risk of bleeding. However, these findings need validation through prospective studies that evaluate TAT regimens of predetermined lengths, customized to the ischemic and bleeding risks of individual patients[23].

In another network meta-analysis, data from 12,329 patients concluded that short-term TAT offers advantages in reducing bleeding events to varying extents. The findings suggest that short-term TAT should be considered as the default approach, unless there exists a notable risk of stent thrombosis that justifies extending the duration of TAT appropriately[24].

In the initial month following PCI, there is a higher risk of thrombotic complications. Hence, it is sensible to employ TAT for 1 month in patients with a high thrombotic risk and a relatively low risk of bleeding. However, extending TAT beyond this 1-month period after PCI is not advisable[5,25].

The responses obtained in the current research are in sync with the earlier research and guideline recommendations.

RECOMMENDATIONS

Recommendations for the management of ACS patients who are medically managed and who may have undergone PCI (with or without T2DM)

- **Recommendation 1:** Ticagrelor and aspirin combination is the preferred therapy of choice in ACS patients who have undergone PCI (with or without T2DM).
- **Recommendation 2**. DAPT is preferred to be used over the long-term (up to 1-year post-PCI).
- **Recommendation 3**: The precise risk of bleeding and ischemic events should be assessed before determining the optimal antithrombotic strategy for individual patients.
- **Recommendation 4**: The duration of TAT in PCI patients with atrial fibrillation should be 1 month.
- **Recommendation 5**: The major factors which decide the duration of DAPT are age, history of prior bleeding, hemoglobin, and creatinine clearance in the Indian settings.

CONCLUSION

This study highlights the usage patterns of DAPT in the management of ACS among HCPs in India. The study reveals a preference for a ticagrelor and aspirin combination in ACS patients who have undergone PCI, mostly for period of 1 year. Multiple trials have demonstrated the greater efficacy of ticagrelor in reducing the ischemic events compared to clopidogrel, and the cardiologists seem to view it as a valuable option besides clopidogrel. The recommendations underscore the importance of assessing factors like age, bleeding history, hemoglobin, and creatinine clearance for determining the optimal antithrombotic strategy. The study contributes valuable insights into the real-world practices of health care practitioners, paving the way for more informed and personalized ACS management strategies in Indian patients.

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